Devices To Improve Colon Polyp Detection

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Objectives

- Define elements of high quality colonoscopy
- Significance of ADR
- Discuss traditional methods of improving ADR
- Newer devices & endoscopic technology
- Outcomes/evidence
- Summary & take home points
Paradox

Colon cancer is the #2 cause of cancer death

Colon cancer is preventable and curable

Physician Perceptions on Colonoscopy Quality

- Survey of 1500 ACG members, 12% responded
- 38% reported receiving feedback on their colonoscopy quality

Split Prep is Superior to Other Preps

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Favors 4L split dose</th>
<th>Favors comparator</th>
<th>Odds ratio</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>1 L:1 L Excellent – good prep</td>
<td>107</td>
<td>83</td>
<td>103</td>
<td>83</td>
</tr>
<tr>
<td>Aavoo E, et al. 2005</td>
<td>52</td>
<td>68</td>
<td>41</td>
<td>73</td>
</tr>
<tr>
<td>Coper Cancel R, et al. 2010</td>
<td>147</td>
<td>155</td>
<td>136</td>
<td>153</td>
</tr>
<tr>
<td>Zittermann B, et al. 2011</td>
<td>65</td>
<td>103</td>
<td>59</td>
<td>97</td>
</tr>
<tr>
<td>El-Ezzi N, et al. 2011</td>
<td>49</td>
<td>101</td>
<td>54</td>
<td>205</td>
</tr>
<tr>
<td>鎏鑫等, et al. 2011</td>
<td>163</td>
<td>210</td>
<td>95</td>
<td>215</td>
</tr>
<tr>
<td>Sullivan P, et al. 2011</td>
<td>101</td>
<td>20</td>
<td>95</td>
<td>152</td>
</tr>
<tr>
<td>Subtotal (95%) CI</td>
<td>684</td>
<td>735</td>
<td>1482</td>
<td>100%</td>
</tr>
</tbody>
</table>

Compared 4L PEG split prep to all others
9 studies; 7 of 9 favored split prep
Split Prep superior for excellent-good prep; OR 3.46 (95% CI 2.43 – 4.89)

Enestvedt BK et al. 4-Liter Split-Dose Polyethylene Glycol is Superior to Other Bowel Preparations, Based on Systematic Review and Meta-analysis. Clin Gastroenterology and Hepatology, 2012-11-01, 10(11) ; 1225-1231

Split Prep = Higher ADR

Adenoma Detection Rate (ADR)

ADR during screening colonoscopies in average risk men and women over the age of 50, in a given time period (per endoscopist)

- Higher ADR = higher quality exam = fewer missed cancers
- Goal was:
  - ≥ 25% for men ≥ 50 yrs
  - ≥ 15% for women ≥ 50 years

ADR and Interval Cancers

Shaukat et al. Longer withdrawal time is associated with a reduced incidence of interval cancer after screening colonoscopy. Gastroenterology (2015); 149(4):952-957
WT and Interval Cancer

Physician’s average annual withdrawal times were inversely associated with interval cancers (p < 0.0001)

Shankat et al. Longer withdrawal time is associated with a reduced incidence of interval cancer after screening colonoscopy. Gastroenterology (2015); 149(4): 952-957

Factors Associated with Higher ADR

- Patient Level: Age, Gender, Family History
- Procedure Level:
  - Preparation Quality
  - Completion Rate
  - Withdrawal Time
  - Withdrawal Technique
- Physician Level:
  - Training/Skill/Specialty of endoscopist
  - Experience

Stevra I. How to improve the performances in diagnostic colonoscopy? J Gastrointestin Liver Dis 2007; 16: 363-7
Adrians et al. AJG 2011; 106: 1070-1074
### Adenoma Miss Rates for Colonoscopy

<table>
<thead>
<tr>
<th>1st Author</th>
<th>Year</th>
<th>Journal</th>
<th>Results</th>
<th>Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rex</td>
<td>1997</td>
<td>Gastro-enterology</td>
<td>24% of adenomas missed with colonoscopy (6% of large adenomas missed)</td>
<td>183 patients; Tandem study</td>
</tr>
<tr>
<td>Van Rijn</td>
<td>2006</td>
<td>Am Journal of Gastro-enterology</td>
<td>22% of adenomas missed with colonoscopy (2.1% of large adenomas missed)</td>
<td>465 patients total; Meta-analysis of 6 tandem studies</td>
</tr>
<tr>
<td>Heresbach</td>
<td>2008</td>
<td>Endoscopy</td>
<td>21% of adenomas missed with colonoscopy (11% of advanced adenomas missed)</td>
<td>286 patients; Tandem study</td>
</tr>
<tr>
<td>Pickhardt</td>
<td>2004</td>
<td>Annals of Internal Medicine</td>
<td>a) 11.8% of large adenomas (&gt;1 cm) missed during colonoscopy (found with CT) b) 2/3 of missed adenomas were located on back side of folds</td>
<td>1,223 patients; CT colonography vs. colonoscopy</td>
</tr>
<tr>
<td>Rex</td>
<td>2011</td>
<td>Gastro-intestinal Endoscopy</td>
<td>12.0% of large adenomas in ascending colon missed with standard colonoscopy (found with retroflexed colonoscope)</td>
<td>1,000 patients; Retroflexed scope for second look</td>
</tr>
<tr>
<td>Siersema</td>
<td>2012</td>
<td>World Journal of Gastro-enterology</td>
<td>11.8% of large adenomas throughout colon missed with standard colonoscopy (found with Third Eye colonoscopy)</td>
<td>395 patients; Tandem exams with and without Third Eye Retroscope</td>
</tr>
</tbody>
</table>

### Increasing ADR Lowers Mortality & Reduces Healthcare Cost

A 1% increase in ADR results in a 3% decrease in the risk of interval cancer and a 5% decrease in the risk of a fatal interval colorectal cancer.¹

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**Adenoma Detection Rate**

- 1%

**Interval Colorectal Cancer Risk**

- 3%

**Risk of a Fatal Interval Cancer**

- 5%

Colon cancer treatment

~$300,000 per patient

ADR Challenge

- Average colon length – 189 cm
- Some colons >2.5 meters
- >100 haustral folds per colon
- Colonic flexures = “blind spots”


Goals of Device & Imaging Technology

Detection of Neoplasia
- Highlighting flat lesions
  - NBI (Olympus)
  - FICE (Fujinon)
  - I Scan (Pentax)
  - Autofluorescence (Olympus)
  - Chromoendoscopy

Determination of Histology
- Differentiating adenoma from hyperplastic
  - NBI (Olympus)
  - FICE (Fujinon)
  - I Scan (Pentax)
  - Autofluorescence
- Identifying dysplasia grade and presence of cancer
  - Confocal laser (Pentax, Mauna Kea)
  - Endocytoscopy (Olympus)

Exposure of hidden mucosa
- Third-Eye Retroscope
- Panoramic endoscope
- Cap-fitted colonoscopy
- Wide angle colonoscopy
- Full spectrum endoscopy (FUSE)
- Endocuff/Endo-ring
Optical Enhancements

High Definition vs. Standard Video Endoscopies

- 5 studies; n = 4422
- Incremental yield for adenoma detection with HD: 3.5% (95% CI 0.9% - 6.1%)
- No difference in the detection of advanced adenomas, -0.1% (95% CI -1.7% - 1.6%)


<table>
<thead>
<tr>
<th>Study name</th>
<th>Statistics for each study</th>
<th>Polyphotal HD</th>
<th>Polyphotal SVE</th>
<th>Incremental yield (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>East</td>
<td>0.039 -0.139 0.138</td>
<td>67/78</td>
<td>37/72</td>
<td></td>
</tr>
<tr>
<td>Pollitt</td>
<td>0.040 -0.029 0.129</td>
<td>134/110</td>
<td>110/110</td>
<td></td>
</tr>
<tr>
<td>Burke</td>
<td>0.030 -0.035 0.096</td>
<td>170/128</td>
<td>173/128</td>
<td></td>
</tr>
<tr>
<td>Buchner</td>
<td>0.029 -0.010 0.098</td>
<td>108/126</td>
<td>110/126</td>
<td></td>
</tr>
<tr>
<td>Tribosch</td>
<td>0.191 0.012 0.205</td>
<td>123/153</td>
<td>194/157</td>
<td></td>
</tr>
<tr>
<td>Padial</td>
<td>0.030 0.010 0.047</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
HD-NBI vs. HD-white light Colonoscopy for the Detection of Adenomas

- 6 studies, n = 2,284; OR 1.01, CI: 0.74 – 1.37
- No significant difference in the detection of adenomas


HD-NBI vs. HD-white light Colonoscopy for the Detection of Flat Adenomas

- 6 studies, n = 2,284; OR 1.01, CI: 0.74 – 1.37
- No significant difference in the detection of adenomas

Wide-Angle Colonoscope

- Older colonoscopes allowed for 140° field of view
- Current generation colonoscopes: 170° field of view
  - Designed to increase visualization, potentially increasing surface area examined
  - Wide-angle lens incorporates 3 light bundles vs. 2 on standard colonoscopes to illuminate a larger field of view

Current HD Wide-Angle Colonoscope
Mechanical Enhancements

Advances in Endoscope Design

- Extra Wide-Angle Colonoscope
- Colonoscope with multiple lenses: Fuse®
  Full Spectrum Endoscopy®
- Short-turn radius Colonoscope: Retroview
- Balloon-assisted Colonoscopy: NaviAid™
  G-EYE™
Extra-wide-angle-view Colonoscope

- **Features**
  - Front window
  - Lateral lightings
  - Front lightings
  - Lateral window
  - Nozzle
  - Front lightings
  - Channel
  - Lateral-backward view area
  - Forward view area area

Fuse® Full Spectrum Endoscopy®

- 3 camera lens system, allows for 3 separate images that provide a 330° left-to-right field of view
  - Dimensions and specifications are similar to standard colonoscope
  - Lens location:
    - One on the tip of the colonoscope, providing a forward-view
    - One on each side of the shaft (2), allowing for side-view imaging
Fuse® Full Spectrum Endoscopy®

Full Spectrum Endoscopy
**Full Spectrum Endoscopy vs. COL**

- Multi-center RCT, n = 185
- Same day back-to-back tandem COL with FV colonoscope and FUSE

**Results:**
- More adenomas detected with FUSE
- No difference in ADR
- Lower adenoma miss rate (8% vs 41%)
- ? Impact on clinical outcomes

<table>
<thead>
<tr>
<th>Outcomes in Patients Undergoing Tandem Colonoscopy with TFV versus FUSE</th>
<th>TFV</th>
<th>FUSE</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional Adenomas Detected</td>
<td>6.2%</td>
<td>71.4%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adenomas missed (per lesion)</td>
<td>41.7%</td>
<td>7.9%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>False-Negative Colonoscopies (per patient)</td>
<td>5.7%</td>
<td>0%</td>
<td>0.02</td>
</tr>
<tr>
<td>ADR per colonoscope type at first colonoscopy</td>
<td>27.7%</td>
<td>33.3%</td>
<td>0.40</td>
</tr>
</tbody>
</table>

**Retrofitview Colonoscope**

- Has standard 140° field of view with short-turn radius, allowing for:
  - Easy retroflexion in right colon
  - Withdrawal possible in full retroflexion

- Able to visualize proximal aspects of colon folds and flexures
  - 210° tip deflection in the upward position vs. 180° for standard Pentax colonoscope
Retroview Colonoscope

Colonoscope with an integrated balloon on the flexible tip

- Can be reprocessed and re-inflated by the endoscopist without withdrawal of the scope
- Balloon inflation allows for visualization of hidden anatomic areas, potentially increasing polyp detection

G-EYE™ Colonoscope
NaviAid™ G-EYE™ Colonoscope

Colonoscope Accessories To Improve Polyp Detection

- EndoRings
- EndoCuff
- Amplifye
- Third-eye® Panoramic™ Device
- Transparent/clear Cap
EndoRings

- Series of 3 rings, positioned sequentially on a cylindrical cuff
- Slides onto the distal tip of the colonoscope
- Single-use
- Rings engage and mechanically stretch the mucosa and colonic folds during withdrawal
  - Device can also provide traction to maintain position during loop reduction
Comparing standard colonoscopy with EndoRings colonoscopy: a randomized, multicenter tandem colonoscopy study – CLEVER study

- Multicenter tandem colonoscopy study
  - ERC followed by SC
  - SC followed by ERC
- 66 subjects (61% male, mean age 57.6 ± 9.6 years)
- Indication Screening and surveillance
- ADR Miss rate
  - ERC then SC 15% (p<0.01)
  - SC then EC 48%

Dik et al DDW. 2014
Endocuff Mechanical Cap

- 165 patients received Endocuff (EC) and 153 patients underwent standard colonoscopy (SC).

- Average polyps detected per patient in the EC group was 1.31 vs. 0.82 in standard colonoscopy (p=<0.001).

- Average adenoma per patient 0.8 vs 0.38 (p=<0.001).

- The ADR was higher in EC group compared to standard colonoscopy (46.6% vs. 30.0%, p=0.002).

- ADR was also increased with EC in right sided adenomas (32.1% vs 18.3%; p=0.004).

Gross et al DDW 2014
Gross et al. DDW 2014

Endocuff Video

Manipulates Large Folds
Third-eye® Panoramic™ Device

- Attaches to distal tip of the colonoscope
- Compatible with any standard colonoscopy system
- Multi-use (proposed)
- Provides 330° field of view, while allowing colonoscope to maintain working channel
  ◆ Produces an image from left-to-right side view in high-definition (1080p)
Feasibility study with 25 patients showed:
- Cecum was reached in all subjects
- No interference with
  - Mobility
  - Tip deflection
  - Retroflexion
  - Polypectomy
- No adverse events

Normal Colon

![Normal Colon](image)

Lesion Hidden from Colonoscope’s View

![Lesion Hidden from Colonoscope’s View](image)

Transparent Cap

- Transparent, single-use attachment
- Placed on distal end of colonoscope
- Can manipulate and deflect colon folds, allowing visualization of proximal aspects
- Also assists with EMR of polyps
Transparent Cap

Cap-assisted Colonoscopy vs.
Standard Colonoscopy

- 16 RCT’s, n = 8,891; 6 with ADR reported
- Marginal difference in the detection of adenoma
- RR: 1.04; 95% CI: 0.90 – 1.19
- Reduced the cecal intubation time with CAC by ~40 sec; mean difference -0.64 min; 95% CI: -1.19 to -0.10

Retrograde view reveals deep pocket-like depressions that are hidden behind folds and are difficult to see – even if folds are flattened with tip of colonoscope.

### Retrograde Viewing Device

<table>
<thead>
<tr>
<th>Indication</th>
<th>Group A (SC, then TEC)</th>
<th>Group B (TEC, then SC)</th>
<th>Net additional detection with TEC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SC 1st</td>
<td>TEC 2nd</td>
<td>Additional in 2nd exam (%)</td>
</tr>
<tr>
<td>All indications</td>
<td>107</td>
<td>49</td>
<td>45.8</td>
</tr>
<tr>
<td>Screening</td>
<td>54</td>
<td>19</td>
<td>35.2</td>
</tr>
<tr>
<td>Surveillance</td>
<td>37</td>
<td>20</td>
<td>54.1</td>
</tr>
<tr>
<td>Diagnostic</td>
<td>16</td>
<td>10</td>
<td>62.5</td>
</tr>
<tr>
<td>Surveillance + diagnostic</td>
<td>55</td>
<td>30</td>
<td>56.6</td>
</tr>
</tbody>
</table>

- Second look increases ADR
- Benefit of retrograde viewing marginal


**TEC:** Third Eye colonoscopy, **SC:** Standard colonoscopy
Integrated Balloon Colonoscope Platform
The “G-Eye” Colonoscope

Device
- Based on standard colonoscope and video processor
- Permanently integrated, reusable balloon (reprocessable)
- CE Mark granted (Europe), FDA pending (USA)

Features
- Controlled withdrawal with balloon partially inflated
  - Straightening of colon folds
  - Smoothening colon topography
  - Preventing endoscope slippage
  - Centralizing endoscope optics

Advantages
- Detected polyps readily removed (forward view)
- Colonoscope stabilization during intervention

G Eye Scope Video
G-EYE Endoscope

- Case series, n = 47
- Cecal intubation: 100%
- ADR 44.7%
- 2 minor adverse events
- Safe and feasible
- Comparative trials underway


G Eye Tandem Study: Adenoma Detection Rate (ADR)

106 Patients

Group A - 54 pts
S.C \(\rightarrow\) G-EYETM

1st Pass

14/54 pts. [25.9%]
[21 adenoma]

2nd Pass

10/54 pts. [3 additional pts.]
[17 adenoma]

81%
G-EYE additional detection (adenomas)

Group B - 52 pts
G-EYETM \(\rightarrow\) S.C

1st Pass

21/52 pts. [40.4%]
[37 adenoma]

2/52 pts. [0 additional pts.]
[3 adenoma]

7.5%
G-EYE miss rate (adenomas)

Gross DDW 2013,
Endoscopy 2015
**G-Eye vs Standard Colonoscopy**

- A total of 250 patients were included in this study
  - Standard colonoscopy: 131 patients
  - G-EYE colonoscopy: 119 patients
- PDR in the SC group was 42% compared with 58% in the G-EYE group
  - 38% increase in PDR with the G-EYE™ endoscope
- ADR for standard colonoscopy and G-EYE colonoscopy was 24% and 36%, respectively
  - The G-EYE™ endoscope increased ADR by 50%, without significantly impacting withdrawal time
- The G-EYE™ endoscope detected an average of 0.61 adenomas per patient, 65% higher than that of a standard colonoscope

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**Summary: Take Home Points**

- Colon polyp detection is key to prevent cancer
- Polyp miss rates remain unacceptably high
- No substitute for:
  - Careful, meticulous withdrawal
  - Good bowel prep
- Endoscope design and development
- Endoscope accessories development
- More data will clarify role for new technology