Beyond the Colonoscope: Are Colon Capsule, CT Colonography or Stool DNA Ready for Prime Time?

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CAPSULE COLONOSCOPY
Capsule Colonoscopy

- The size of a large vitamin Pill
- Battery (9 Hours)
- Transmitter
- Digital Camera (CMOS)
- 2 Light Sources
- Takes 4-35 frames/sec

PillCam® COLON 2 System:
Components

- PillCam COLON capsule
- PillCam recorder DR3 with real-time viewing
- PillCam COLON sensor belt or sensor array
- RAPID® software v8.0
Prep Used in the US Registration Study

Before ingestion of PillCam COLON:
- 4 (12mg) Senna tablets- 2 days prior to the procedure
- 2 liters PEG the evening prior to the procedure
- 2 liters PEG the morning of the procedure

After ingestion of PillCam COLON:
- Reglan: If necessary during procedure for gastric emptying*
- 2 boosts of SUPREP® - to enhance capsule propulsion and maintain adequate cleansing
  - 6 oz. SUPREP** solution
  - 3 oz. SUPREP** solution*
- Suppository, if needed*
- Light meal, if needed*

*Indicates potential procedure requirements

** SUPREP © Braintree Laboratories Inc., Braintree, MA.
Colon Capsule Studies
Tierney WM, Colonoscopy Versus Capsule: Sharing the Spotlight.
Gastroenterology, 2015; 148:892-894

Table 1: Major Studies of Colon Capsule Endoscopy Versus Colonoscopy

<table>
<thead>
<tr>
<th>Reference</th>
<th>Capsule Generation</th>
<th>N Age Range (y)</th>
<th>Average Risk Screening (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gossum et al.</td>
<td>1st</td>
<td>378 (22-84)</td>
<td>0</td>
<td>Capsule size ≤ 50% vs colonoscopy size</td>
<td>64</td>
</tr>
<tr>
<td>Eliakim et al.</td>
<td>2nd</td>
<td>96 (18-77)</td>
<td>32</td>
<td>Capsule size ≤ 50% vs colonoscopy size</td>
<td>89</td>
</tr>
<tr>
<td>Spada et al.</td>
<td>2nd</td>
<td>109 (18-86)</td>
<td>0</td>
<td>Capsule size ≤ 50% vs colonoscopy size</td>
<td>84</td>
</tr>
<tr>
<td>Rex et al.</td>
<td>2nd</td>
<td>655 (50-75)</td>
<td>130</td>
<td>Capsule size ≤ 50% vs colonoscopy size ≥ 50%</td>
<td>81</td>
</tr>
</tbody>
</table>

*Note the differences in size matching between the current study and prior studies.*

### Capsule Colonoscopy

#### Sensitivity (%)

<table>
<thead>
<tr>
<th>POLYP PATHOLOGY</th>
<th>&gt;6 mm</th>
<th>&gt;10 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoma</td>
<td>88</td>
<td>92</td>
</tr>
<tr>
<td>Sessile Serrated Polyp</td>
<td>29</td>
<td>33</td>
</tr>
<tr>
<td>Hyperplastic Polyp</td>
<td>74</td>
<td>81</td>
</tr>
</tbody>
</table>

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**Poor Detection of Sessile Serrated Polyps**

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Colon Capsule Limitations

- More extensive bowel prep
- Technical failures
  - 9% Rex study
    - Transit time < 40 min
    - Poor Prep
- Poor identification of serrated lesions
- Difficulty performing same-day colonoscopy for positive capsule result

Colon Capsule Benefit

Just take a pill
Colon Capsule After Incomplete Colonoscopy

N=75 patients

33 (44%) Patients with findings
17 (23%) Neoplastic lesions


<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Polyp Yield</th>
<th>Significant Polyp Yield</th>
<th>OC+CCE Completion</th>
<th>Colon Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spada</td>
<td>97</td>
<td>53%</td>
<td>25%</td>
<td>98%</td>
<td>0</td>
</tr>
<tr>
<td>Baltes</td>
<td>74</td>
<td>49%</td>
<td>28%</td>
<td>95%</td>
<td>1</td>
</tr>
<tr>
<td>Nogales</td>
<td>96</td>
<td>45%</td>
<td>NR</td>
<td>93%</td>
<td>2</td>
</tr>
</tbody>
</table>

Spada et al. Gut 2014; Baltes et al. GIE 2014 (S supp); Nogales et al. UEGJ 2013 Vol (1):Supp1; P793
CT COLONOGRAPHY
(Virtual Colonoscopy)

CT Colonography

- 3D rendered CT scan of the Abdomen/Pelvis
- Requires the same bowel prep as colonoscopy
- A small tube is placed in the rectum for air insufflation
- If polyps are detected, a colonoscopy is required to remove them
- Included in the multisociety CRC screening guidelines
- Not included in the USPSTF guidelines
- Minimal Radiation - Cumulative dose could be an issue
- Generally not covered by insurance for screening
- 5mm polyps are not documented
Colonoscopy

CTC

CT Colonography
CT Colonography: ACRIN Data

<table>
<thead>
<tr>
<th>Polyp Size (MM)</th>
<th>&gt;5</th>
<th>&gt;6</th>
<th>&gt;7</th>
<th>&gt;8</th>
<th>&gt;9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>65%</td>
<td>78%</td>
<td>84%</td>
<td>87%</td>
<td>90%</td>
</tr>
</tbody>
</table>

If all patients were referred for Colonoscopy:

- With a lesion measuring 5mm or more: 17%
- With Extracolonic findings: 66%
- With Extracolonic findings requiring evaluation: 16%

Johnson et al, NEJM, 359:12, 2008
What if a CT Colonography shows a polyp and Colonoscopy does not?

- 9336 adults (mean age, 57.1 years) underwent CT colonography, (113 months)
  - 2606 non-diminutive (≥6 mm) polyps
  - 1731 polyps that underwent colonoscopy
  - 181 (10%) were not confirmed with initial endoscopy (ie, discordant)
  - 144 of the 181 (80%) were categorized as potential colonoscopy false-negatives
- 21.5% (31 of 144) of all discordant lesions had real pathology: Colonoscopy False Negatives
  - 1.7% of all polyps sent for colonoscopy
  - 8.5 mm ± 3.3 in diameter
  - More likely to be located in the right
  - 81% (21 of 26) were neoplastic (adenomas or serrated lesions), 43% advanced
  - 89% (8 of 9) of advanced lesions occurred in the right colon
- Conclusion: For CTC positive, but colonoscopy negative, lesions, review with radiologist is essential, and if the lesion is still concerning, repeat colonoscopy or CTC.

Incomplete Colonoscopy:
Colon Capsule Vs. CT Colonography

- 100 Patients with a previous incomplete colonoscopy underwent CCE and CTC followed by colonoscopy
- CTC was performed after colon capsule excretion or 10-12 h post-ingestion
- CCE and CTC were able to achieve complete colonic evaluation in 98% of cases.
- Polyp detection ≥6 mm
  - CCE = 24.5%
  - CTC = 12.2%
- Polyp detection ≥10 mm, these values were
  - CCE = 5.1%
  - CTC = 3.1%

Conclusion:
The overall diagnostic yield of colon capsule was superior to CT Colonography

Cristiano Spada et al. Gut 2015;64:272-281

Missed Polyp on CT Colonography

Colon capsule endoscopy (CCE) ‘new finding’:
≥10 mm polyp detected by the CCE but not detected by CT colonography (CTC).
Colon capsule endoscopy and CT colonography: Same findings detected

Cristiano Spada et al. Gut 2015;64:272-281
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STOOL DNA
Initial Stool DNA
Imperiale et al, NEJM 351:2704-14, 2004

- Sensitivity: 52% (13% Hemoccult II)
- Specificity 93-97%
- Multi-target assay panel
- 21 point mutations in ras, APC, and p53 genes
- Microsatellite instability (MSI) marker (BAT-26)
- DNA Integrity Assay (DIA)
  - Reflects abnormalities in the apoptosis pathway

WHAT ABOUT “THE NEW GUAIAIC” STOOL TEST?
FIT
FIT: Fecal Immunochemical Test

- Evaluates for occult blood
- Detects globin protein of hemoglobin molecule
- Does not require dietary modification
- More accurate than guaiac FOBT
- Must be done annually for CRC screening
- Inexpensive (about $25)

FIT: Meta Analysis for Colon Cancer

- Sensitivity 79%
- Specificity 94%
- Colon Cancer detection test, not a preventative test

FIT: Meta Analysis for Colon Cancer

Sensitivity  Specificity

1. Good test for colon cancer if done annually
2. Inexpensive
3. FIT should replace Guaiac Testing

What about combining FIT and Stool DNA?
New Stool Multi-target DNA/FIT: Cologuard

- Three Components
  - Two Gene Methylation Markers (NDRG4 and BMP3)
  - 7 KRAS Mutation markers
  - Fecal Hb (FIT)
- Cancer Sensitivity: 92% for Colorectal Cancer (73.8% FIT alone)
- Polyp Sensitivity: 42% polyps > 1 cm
- Specificity: 87%

Imperiale et al., Multitarget stool DNA testing for colorectal-Cancer screening, NEJM, 2014; 370(14):1287-97

USPSTF

- Preliminary Recommendations Surprising
- Does NOT recommend CTC or Stool DNA
- Recommends:
  - Colonoscopy every 10 years
  - FIT annually
  - FIT annually with Flex Sig every 10 years
Ready for Prime time?

- **Capsule Colon**
  - Alone, not yet, but becoming more compelling as an alternative.
    - Rigorous prep
    - High number of Technical Failures (Fast capsule exit, poor prep)
    - Significant time commitment, difficult to do same day colonoscopy if positive
    - Poor sensitivity for identifying Serrated lesions
  - Yes for incomplete colonoscopy, better than CTC

- **CT Colonography**
  - Alone, not yet
  - Need to work out recommendations for 6mm-9mm polyps.
  - Does not look like it will be recommended by the USPSTF for screening
  - Needs to have same day colonoscopy available when positive
  - Yes for incomplete colonoscopy
  - Perhaps as alternative to colonoscopy

- **Stool DNA**
  - Not commercially available alone
  - With FIT =Cologuard. Unclear if it will be covered. A cancer detection test.
  - Surprising lack of recommendation by USPSTF
  - Yes as alternative to colonoscopy, particularly in patients where there may be increased risk for screening colonoscopy

- **FIT**:
  - Yes, definitely, but remember that this is a cancer detection test.
  - There is no excuse not to do an FIT in patients who are not willing to do a colonoscopy

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Thank You

Mark.Pochapin@NYUMC.org
What is the Best Prep and How Do I Assess the Adequacy of the Prep

David Greenwald, MD, FACG
Mount Sinai Hospital, New York
ACG Annual Postgraduate Course
October 17, 2015

Time For Your Colonoscopy
(The Prep was Rough)....

C'mon now Jim

It's time for your colonoscopy
Colonoscopy Preparation: Importance

- Incomplete colonoscopy common
  - Some estimates up to 10%
  - Inability to achieve cecal intubation
  - Inability to visualize mucosa effectively
- Inadequate bowel preparation leads to
  - Missed lesions
  - Increased risk of procedure related adverse events
- Bowel prep is a colonoscopy quality indicator


Colonoscopy Preparation: Ideal

- Reliably empty colon of all fecal material
  - Rapidly
  - No changes in gross or histologic appearance of colon
- No shifts in fluids or electrolytes
- No patient discomfort
- Safe
- Convenient
- Well tolerated
- Inexpensive
Predictors of inadequate bowel preparation

- Previous inadequate bowel preparation
- Language barriers
- Financial barriers
- Inpatient status
- Polypharmacy (especially opiates)
- Obesity
- Male
- Comorbidities
  - Stroke, dementia, Parkinson’s
  - Poor adherence to instructions
  - Longer wait times for colonoscopy appointments

Many of these are modifiable

Improving preparation

- Effective education
  - Written instructions—simple, easy to follow, native language
  - Educational booklets
  - Visual aids
  - Smartphone apps
  - Internet resources
    - ACG: Your doctor has ordered a colonoscopy
    - ASGE: Understanding bowel preparation
Colonoscopy Preparation: Timing

Split dose
- Results in higher quality bowel preparation than ingestion night or day before
- Better bowel prep leads to higher adenoma detection rate
- Improves patient tolerability
- Typically split between night before and day of test
- Timing of second dose
  - Must allow for ingestion, desired responses and travel to test
  - Typically 4-6 hours before test

Colonoscopy Preparation: Timing

Morning only

– Appropriate for motivated patients with afternoon procedures
  • Equivalent or superior bowel preparation
    – Better tolerability
    – Less impact on daily activities
    – Better sleep quality


Colonoscopy Preparation: USMSTF 2014

• “Use of split dose bowel cleansing regimen is strongly recommended for elective colonoscopy”
• “Same day regimen acceptable alternative to split doing, especially for patients having afternoon procedures”
• “Second dose should begin 4-6 hours before time of colonoscopy, and completed at least 2 hours before procedure time”

Colonoscopy Preparation: General Considerations

- Combination of dietary restriction and cathartics
- Clear liquid diet commonly recommended up to 2 hours before
  - Avoid red liquids
  - Low residue diet may be as effective as clear liquid diet
    - Increases patient satisfaction
  - Attention to medications such as iron, diabetes medications and anticoagulants/antiplatelet agents

Colonoscopy Preparation: General Considerations

Low residue diet day prior to colonoscopy

<table>
<thead>
<tr>
<th>Table 1. Indinavir diet plan</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Easy to prepare</td>
<td>Healthy</td>
<td>Restaurant</td>
</tr>
<tr>
<td>Breakfast</td>
<td>2 eggs (frittata, omelet, or poached) with/without condiments</td>
<td>1/2 cup yogurt (no seeds, nuts, or fruit)</td>
<td>1 plain bagel with cream cheese, jelly, or butter</td>
</tr>
<tr>
<td></td>
<td>2 white bread slices or 1 plain bagel with butter, jelly, or cream cheese</td>
<td>1 banana</td>
<td>1 egg McMuffin with Canadian bacon taken off</td>
</tr>
</tbody>
</table>
| Lunch                       | 1 plain chicken or turkey sandwich on white bread with condiments only: lettuce or tomato
OR 1 cup macaroni and cheese
OR 1 baked potato w/ skin with butter or sour cream | 1 chicken breast – pan fried or baked | 1 plain chicken sandwich with condiments only: no lettuce or tomato
OR 5 chicken tenders or 10 nuggets with condiments
OR 1 cup macaroni and cheese |
| Snack                       | 1 handful pretzels | 1 banana | 1 handful pretzels |

Please do not eat anything after starting the bowel prep. Eat exactly what is permitted. Do not take liberties.
Key Guidelines

Bowel Preparation Before Colonoscopy

Osmolarity
- Isosmotic
- Hyposmotic
- Hyperosmotic

Fluid Volumes
- “High volume”
  - At least 4 liters cathartic solution
- “Low volume”
  - Lower volumes of cathartics, but often with additional fluids
Regimens for Bowel Preparation: Isosmotic

High volume polyethylene glycol preparations

- Polyethylene glycol (PEG)
  - Inert polymer of ethylene oxide
  - Non-absorbable solution
  - Pass through bowel without absorption or secretion
  - Osmotically balanced with non-fermentable balanced electrolyte solutions
  - 4 liter PEG-ELS is “gold standard”
    - Note not approved to be used in split dose fashion, although ample evidence suggests this as best practice

Regimens for Bowel Preparation: Isosmotic

High volume PEG-ELS preparations (Golytely)

- Generally well tolerated
- 5%-15% do not complete
  - Large volume, abdominal cramping, fullness
  - Sulfate associated taste (only partially masked by flavors)
- No change in patient weight, electrolytes, histology
- Safe for patients with CHF, renal failure, ascites
- Addition of bisacodyl, prokinetics or enemas does not improve outcomes
- May be used via NG tube and in 6-8 liter fashion for rapid purge
Regimens for Bowel Preparation: Isosmotic

High volume PEG-ELS preparations

— Significant adverse events generally rare
  • Nausea
  • Vomiting
  • Aspiration (rare)
  • Mallory-Weiss tear
  • Pancreatitis
  • Lavage induced pill malabsorption
  • Cardiac arrhythmias

Regimens for Bowel Preparation: Isosmotic

Sulfate-free PEG-ELS (*Nulytely, Trilyte, Colyte*)

— PEG based lavage solutions developed to improve taste and smell of PEG-ELS
  • Improved taste
    — Elimination of sodium sulfate
    — Decrease in potassium
    — Increase in chloride

— Sulfate free PEG-ELS compared to PEG-ELS
  • Less salty
  • More palatable
  • Equal for colon cleansing and safety

Regimens for Bowel Preparation: Isosmotic

Low volume PEG preparations
- Designed to provide more tolerable bowel preparation and similar efficacy to original 4 liter PEG-ELS solutions
- One low volume 2 liter PEG-ELS with ascorbic acid is FDA–approved and available in 2015 (*Moviprep*)
  - Requires one additional liter of clear liquid
  - Similar efficacy to 4 liter PEG-ELS
  - Ascorbic acid may provoke hemolysis in patients with G6PD deficiency

Regimens for Bowel Preparation: Hyposmotic

Low volume PEG preparations
PEG-3350-SD (*Miralax-SD*)
- Low volume PEG solution (PEG-3350) with additional of commercially available electrolyte solution (sports drink)
- Hyposmotic
- Not FDA approved for colonoscopy preparation
- Not equivalent to FDA approved 2 liter isotonic PEG-ELS solutions

Ell C, et al. Am J Gastroenterol 2008;103;888-93
Regimens for Bowel Preparation:
Hyposmotic

PEG-3350-SD

- Widely used
- Often administered with bisacodyl
- Mixed results compared to standard 4 liter solutions
  - Generally equivalent
  - Safety issues
    - Bisacodyl addition benefit unclear
    - Theoretical potential for unabsorbed carbohydrates to be metabolized to explosive gases, but no reports
    - Hyponatremia reported
    - Metabolic effects of PEG-3350-SD similar to other PEG-ELS


Regimens for Bowel Preparation:
Hyperosmotic

Oral sodium sulfate (*Suprep*)

- Hyperosmotic, but not seen to have significant fluid shifts due to sulfate being poorly absorbed
- Non inferior to 2 liter PEG-ELS with ascorbic acid
- Better results in one study than 4 liter SF-PEG-ELS
  - Less bloating
  - More frequent excellent prep (71% vs 34%, P=0.01)
- Superior successful prep in one study vs sodium picosulfate/magnesium citrate (95% vs 86%, P=0.06)
- No serious reported adverse events

**Regimens for Bowel Preparation: Hyperosmotic**

**Magnesium citrate**
- Magnesium cations act osmotically
- Stimulates release of CCK
- Not FDA approved as a colonoscopy preparation
- Limited efficacy data, rarely used alone
- Avoid in patients with renal disease

**Sodium phosphate**
- Low volume hyperosmotic aqueous solution
- Associated with phosphate nephropathy
  - Often in patients with poor renal function, HTN on ACE inhibitors or ARBs, but also with normal renal function
- Associated with hyperphosphatemia in up to 40%
- Brand name solution voluntarily removed from market
  - Not recommended as a colonoscopy preparation
  - Available “over the counter” as a laxative
- Tablet form (Osmoprep) available but has black box warning

**Regimens for Bowel Preparation: Combination Agents**

**Sodium picosulfate/magnesium citrate (Prepopik)**

- Sodium picosulfate is a stimulant laxative in the colon
  - Increases frequency and force of peristalsis
- Magnesium citrate is an osmotic laxative
- Superior in one trial and non-inferior in another trial compared with 2 liter PEG-ELS and bisacodyl administered day before procedure (overall adequate cleansing 83%-84%)
- Adverse events
  - Increased cramping, nausea/vomiting
  - Electrolyte disturbances


**Regimens for Bowel Preparation: Combination Agents**

**Oral sodium sulfate/SF-PEG-ELS (Suclear)**

- Compared to 2 liter PEG-ELS and ascorbic acid
  - Similar successful bowel preps (94%)
  - More vomiting
- Compared to PEG-ELS and bisacodyl
  - Successful bowel prep: Non inferior
  - Overall discomfort slightly worse for sodium sulfate/SF-PEG-ELS
- No major adverse events

Regimens for Bowel Preparation

Table 3: Commerciially available bowel preparations

<table>
<thead>
<tr>
<th>Product</th>
<th>PEG-ES</th>
<th>SF-PG41S</th>
<th>Some solution</th>
<th>Lowdine</th>
<th>polyethylene glycol 4000</th>
<th>magnesium</th>
<th>sorbitol</th>
<th>oral saline</th>
<th>magnesium citrate</th>
<th>PEG-ES</th>
<th>SF-PG41S</th>
<th>Some solution</th>
<th>Lowdine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Company (manufacturer)</td>
<td>Becton Dickinson</td>
<td>Becton Dickinson</td>
<td>Becton Dickinson</td>
<td>Pfizer</td>
<td>Pfizer</td>
<td>Pfizer</td>
<td>Pfizer</td>
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<td>Pfizer</td>
<td>Pfizer</td>
<td>Pfizer</td>
<td>Pfizer</td>
<td>Pfizer</td>
</tr>
<tr>
<td>Compounds</td>
<td>Electrolytes</td>
<td>Electrolytes</td>
<td>Electrolytes</td>
<td>Electrolytes</td>
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<td>Electrolytes</td>
<td>Electrolytes</td>
<td>Electrolytes</td>
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</tr>
<tr>
<td>Parenteral administration</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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</tr>
<tr>
<td>Dosage</td>
<td>1000 mL</td>
<td>1000 mL</td>
<td>1000 mL</td>
<td>1000 mL</td>
<td>1000 mL</td>
<td>1000 mL</td>
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<td>1000 mL</td>
</tr>
<tr>
<td>Dosage regimen</td>
<td>1 day before and 1 day of procedure</td>
<td>1 day before and 1 day of procedure</td>
<td>1 day before and 1 day of procedure</td>
<td>1 day before and 1 day of procedure</td>
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</tr>
</tbody>
</table>

**Regimens for Bowel Preparation:**

**Additional Agents**

**Laxatives**

– Bisacodyl or magnesium citrate

– Used to try to reduce volume of lavage solution needed

– Bisacodyl

• Some studies show use allows lower volume of PEG-ELS

• Associated with abdominal cramping and ischemic colitis

• Not FDA approved in any available commercially available prep

– Magnesium citrate

• May improve outcomes when used with 2 liter SF-PEG-ELS as compared to 4 liter PEG-ELS (equal efficacy, better tolerability)

• Avoid in renal failure or renal insufficiency

**Flavoring**

– PEG-ELS available in multiple flavors

– Use of other drinks as flavoring

• Renders solutions no longer isotonic

• Substrates possibly metabolized to explosive gases

• May not actually improve tolerance even if improves flavor

– One study supports use of sugar-free menthol candy drops to improve tolerability

**Regimens for Bowel Preparation: Additional Agents**

- **Metoclopramide**
  - No change in colonic motility
  - May reduce nausea and bloating
  - No impact on colon cleansing
  - Not recommended

- **Simethicone**
  - May reduce number of adherent bubbles present on exam
  - No change in quality of bowel preparation

**Documentation of Bowel Preparation Quality**

**US Multisociety Task Force (USMSTF) on Colorectal Cancer**

- Definition of adequate examination
  - Confident that lesions other than < 5 mm can be seen
- Grading of prep quality should be done
  - After removal of residual effluent
  - After removal of fecal debris

Bowel Preparation Quality: Validated Scoring Systems

Aronchick Scale
– Assesses quality of preparation during initial inspection

<table>
<thead>
<tr>
<th>Points</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Inadequate (repeat prep needed)</td>
</tr>
<tr>
<td>4</td>
<td>Poor (semisolid stool, &lt;90% of mucosa seen)</td>
</tr>
<tr>
<td>3</td>
<td>Fair (semisolid stool, &gt;90% of mucosa seen)</td>
</tr>
<tr>
<td>2</td>
<td>Good (clear liquid covering up to 25%, &gt;90% of mucosa seen)</td>
</tr>
<tr>
<td>1</td>
<td>Excellent (&gt;95% of mucosa seen)</td>
</tr>
</tbody>
</table>

Ottawa Bowel Preparation Scale
– Assesses 3 colon segment scores that are summed and then a rating for amount of fluid in whole colon
– Scale from 0 (excellent) to 14 (very poor)

<table>
<thead>
<tr>
<th>Points</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Inadequate (solid stool not cleared with washing and suctioning)</td>
</tr>
<tr>
<td>3</td>
<td>Poor (necessary to wash and suction to obtain a reasonable view)</td>
</tr>
<tr>
<td>2</td>
<td>Fair (necessary to suction liquid to obtain a reasonable view)</td>
</tr>
<tr>
<td>1</td>
<td>Good (minimal turbid liquid in segment)</td>
</tr>
<tr>
<td>0</td>
<td>Excellent (mucosal detail clearly visible)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Points</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Large amount of fluid</td>
</tr>
<tr>
<td>1</td>
<td>Moderate amount of fluid</td>
</tr>
<tr>
<td>0</td>
<td>Small amount of fluid</td>
</tr>
</tbody>
</table>
Bowel Preparation Quality: Validated Scoring Systems

Boston Bowel Prep Score
- Assesses 3 colon segment scores after all cleansing maneuvers
- Overall total 0 to 9

<table>
<thead>
<tr>
<th>Points</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Unprepared colon segment with stool that cannot be cleared</td>
</tr>
<tr>
<td>1</td>
<td>Portion of mucosa in segment seen after cleaning, but not all areas</td>
</tr>
<tr>
<td>2</td>
<td>Minor residual material after cleaning, but mucosa generally well seen</td>
</tr>
<tr>
<td>3</td>
<td>Entire mucosa well seen</td>
</tr>
</tbody>
</table>

- Score of 5 or higher associated with a 2% rate of recommending shorter surveillance intervals

Bowel Preparation Quality: Validated Scoring Systems

- Quite subjective
- Allows standardization
- Registry reporting (GIQuIC)
  - Excellent and good map to adequate
  - Fair and poor map to inadequate
- USMSTF and European Guidelines endorse evaluation after clearing fluid and residual material
- Learn one scale and use it

What is the Best Prep and How Do I Assess the Adequacy of the Prep

Summary

- The best prep is the one that gets done!!
- Bowel prep is a colonoscopy quality indicator
- Bowel preps must be individualized
  - Efficacy, cost, safety, tolerability
- Verbal counseling along with written instructions that are easy to follow
- Patients with predictors for poor preparation should get more intensive education and possibly more aggressive regimens
What is the Best Prep and How Do I Assess the Adequacy of the Prep

Summary

• Low residue or clear liquid diet in conjunction with an FDA approved bowel preparation
  – Use of a low volume bowel cleansing agent is associated with greater willingness to undergo repeat colonoscopy
    (US Multisociety Task Force on Colorectal Cancer)
• Split dose preps for all
  – Portion of preparation taken within 4-6 hours of test
  – Split dose cleansing is associated with greater willingness to repeat regimen
    (US Multisociety Task Force on Colorectal Cancer)

What is the Best Prep and How Do I Assess the Adequacy of the Prep

Summary

• Avoid sodium phosphate and magnesium citrate preparations in elderly or with renal disease
• Document quality of exam using a standard system that has been validated
  – USMSTF recommends use of scoring system after all efforts to clear residual debris completed
    • Does not recommend Aronchick or Ottawa scales
• Measurement of the rate of adequate colon cleansing should be conducted routinely
That’s All Folks
New Colonoscopy Techniques to Improve ADR: To Roll, Cap or Retroflex

Douglas K Rex MD
Indiana University Health
Indianapolis, Indiana

Adenoma Detection Rate

- 2002: ADR introduced by MSTF on CRC
  - % of persons age ≥ 50 ≥ 1 adenoma
  - Thresholds: ≥ 25% in men; 15% in women
- 2006: modified by ACG/ASGE Task Force
  - % of first time screening colonoscopies in persons age ≥ 50 with ≥ 1 adenoma
  - Thresholds: unchanged from 2002
- 2015: ACG/ASGE Task Force on Quality
  - Thresholds: ≥ 30% in men; 20% in women
New thresholds for ADR

- **Men:** 30%
- **Women:** 20%
  - Rex et al AJG 2015;110:72-90
  - Rex et al GIE 2015;81:31-53

Definition of ADR

- Fraction of patients age ≥ 50 y undergoing first time screening colonoscopy who have ≥ conventional adenoma(s) (adjusted only for gender)
- **Why?**
  - Surveillance examinations run 5-7% higher
  - Sessile serrated adenomas (SSA/P)
    - Are not adenomas
    - Cannot be reliably identified by pathologists
  - No other factors require adjustment
Definition of ADR

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**Why?**
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- Sessile serrated adenomas (SSA/P)
  - Are not adenomas
  - Cannot be reliably identified by pathologists
- No other factors require adjustment
### Reliable Colon Polyp Pathology?

<table>
<thead>
<tr>
<th>Not reliable</th>
<th>Reliable</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Conventional adenomas</td>
<td>▪ Placing lesions into the conventional adenoma class vs serrated class</td>
</tr>
<tr>
<td>▪ Dysplasia grade</td>
<td>▪ Identifying cancer</td>
</tr>
<tr>
<td>▪ Tubular vs tubulovillous</td>
<td></td>
</tr>
<tr>
<td>▪ Serrated class lesions</td>
<td></td>
</tr>
<tr>
<td>▪ SSP vs hyperplastic</td>
<td></td>
</tr>
<tr>
<td>▪ Identifying TSA</td>
<td></td>
</tr>
</tbody>
</table>

### Pathologic differentiation of SSA/P from HP

- **MVHP**
- **SSA/P**
**Definition of ADR**

- Fraction of patients age ≥ 50 y undergoing first time screening colonoscopy who have ≥ conventional adenoma(s) (adjusted only for gender)

- **Why?**
  - Surveillance examinations run 5-7% higher
  - Sessile serrated adenomas (SSA/P)
    - Are not adenomas
    - Cannot be reliably identified by pathologists
  - No other factors require adjustment
    - Jensen et al CGH; 2015; 13:739-46

**ADR: Strengths and Weaknesses**

- **Strengths**
  - Reliable measure of endoscopist performance in examining colons
  - Validated predictor of cancer protection

- **Weaknesses**
  - Potentially subject to gaming
  - Requires manual entry of pathology data
    - Recent solutions: software linkages and natural language processing
### Impact of ADR on Prevention of Cancer

- For each 1% increase in ADR:
  - 3% decline in incidence of interval CRC
  - 5% decline in incidence of fatal CRC
    - Corley et al NEJM;2014;370:1298-306
- Increasing ADR is cost-effective
  - Higher cost of more colonoscopies is outweighed by the reduction in cost of cancer care
    - Meester et al JAMA 2015;313:2349-58

### Withdrawal time

- Should be recorded in every examination (for medical-legal purposes alone)
- Correlates with ADR in numerous retrospective studies
  - Barclay et al NEJM 2006;355:2533-41
- Correlated with cancer prevention in a recent study
  - Shaukat et al Gastroenterology 2015;149:952-7
- Doesn’t work when used prospectively as a corrective measure
  - Sawhney et al Gastroenterology 2008;135:1892-8
Don’t get sucked in by WT

- If you examine the colon carefully with proper technique you will have WTs that meet the standard
- If you use WT as the sole quality indicator and don’t change technique you will not improve detection

Non-device measures to increase ADR
Non-procedural tools to increase ADR

- Training in lesion recognition and withdrawal technique
  - Barclay CGH 2008;6:1091-8
  - Coe AJG 2013; 107:1265
- Reporting to physicians
  - Kahi GIE 2013;77:335
- Reporting to the public
  - Abdul-Baki GIE 2015;82:668
- Split-dosing bowel preparation
  - Gurudu GIE 2013;76:603

Non-device dependent techniques to increase ADR

- Videorecording
  - Rex AJG 2010;105:2312
  - Madhoun GIE; 2012:75:127
- 8 minute timer (with education!)
  - Barclay CGH 2008;6:1091-8
- Retroflexion
- Rolling (position change)
Retroflexion during colonoscopy

- Essential for some polypectomies
  - Rex GIE; 2006; 63: 144
  - Pishvaian AJG 2006; 101: 1479

- Overrated in the rectum
  - Cutler AJG 1999; 94: 1537
  - Saad WJG 2008; 14: 6503

- Not better than second examination in forward view in the right colon

Retroflexion for right colon detection

- Descriptive studies
  - Hewett GIE 2011; 74: 246
  - Chandran GIE; 2015; 81: 608

- Randomized controlled trials
  - Harrison AJG 2004; 99: 519
  - Kushnir AJG 2015; 110: 415
Descriptive studies of right colon retroflexion

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Success rate</th>
<th>Gain in ADR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hewett</td>
<td>1000</td>
<td>94.9%</td>
<td>4.4%</td>
</tr>
<tr>
<td>Chandran</td>
<td>1351</td>
<td>95.9%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Retroflexion for right colon detection

- Descriptive studies
  - Hewett GIE 2011; 74: 246
  - Chandran GIE; 2015; 81:608

- Randomized controlled trials
  - Harrison AJG 2004; 99:519
  - Kushnir AJG 2015;110:415
RCT of second exam in retro vs forward view (Kushnir)

850 patients with right colon clearing

At least one more adenoma

Forward view 10.5%  \( P=0.13 \)

Retro view 7.5%

Retroflexion: Bottom line

- Examine the right colon twice sometimes:
  - First exam shows polyps
  - Older age, male gender
  - Lynch syndrome
- A second exam in the forward view is as good as a second exam in retroflexion
Position change

- Possible mechanisms of action
  - Bowel distention
  - Change in bowel conformation

Mechanism in positive study

- ADR with position change 34% vs 23% with LLD only
- ADR in segments with adequate distention scores 16% vs 7% with suboptimal scores
  - East GIE 2011; 73:456
  - East GIE; 2007;65:263
# RCTs of position change

<table>
<thead>
<tr>
<th>Study</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rex 1997</td>
<td>No effect</td>
</tr>
<tr>
<td>East 2011</td>
<td>Positive (overall 11% gain in ADR)</td>
</tr>
<tr>
<td>Ou 2014</td>
<td>No effect</td>
</tr>
<tr>
<td>Ball 2015</td>
<td>Positive in right colon (8.5% gain in polyp detection; LLD vs supine)</td>
</tr>
<tr>
<td></td>
<td>No effect in left colon</td>
</tr>
</tbody>
</table>

## Position change: bottom line

- Hard to do with propofol; may not be safe
- Should be able to distend the colon without position change
  - Use CO2
  - Prevent gas from escaping the colon
  - If still unable to fill segment use water
Other Tools and Devices for ADR

Early polyp detection tools and devices

Mucosal exposure
- 170-230 angle of view
- Cap-fitted *
- Third-Eye

Highlighting flat lesions
- Chromoendoscopy *
- High definition *
- Narrow band imaging
- FICE
- i-scan
- Autofluorescence

* some benefit
New effective devices

- FUSE*
- Endocuff*
- Endorings*
- G-EYE

Full Spectrum Endoscopy™
FDA cleared & CE Mark

330° Field of View
Full Spectrum Endoscopy (FUSE)

Endocuff
Endocuff

EndoRing
Endorings

G – Eye
## Tandem studies

<table>
<thead>
<tr>
<th>Technology</th>
<th>Author</th>
<th>Number of patients</th>
<th>Technology adenoma miss rate (per lesion)</th>
<th>Standard colonoscopy adenoma miss rate</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>FUSE (3 CCD 330 angle of view scope)</td>
<td>Grainek</td>
<td>185</td>
<td>7%</td>
<td>41%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>G-EYE (balloon – Pentax only)</td>
<td>Gross</td>
<td>112</td>
<td>4%</td>
<td>44%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Endorings (OTS fold straightener)</td>
<td>Dik</td>
<td>71</td>
<td>15%</td>
<td>48%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

## Endocuff RCTs

<table>
<thead>
<tr>
<th>Author</th>
<th>With Endocuff</th>
<th>No Endocuff</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with ≥ 1 adenoma (ADR)</td>
<td>Biecker J Clin Gastro 2014</td>
<td>36%</td>
<td>28%</td>
</tr>
<tr>
<td>Total adenomas per patient (APC)</td>
<td>Biecker J Clin Gastro 2014</td>
<td>2.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Total adenomas per patient (APC)</td>
<td>Floer UEGW 2014</td>
<td>0.90</td>
<td>0.54</td>
</tr>
</tbody>
</table>
Third Eye® Panoramic™ Device

- Two side-viewing video cameras with LED light sources supplement colonoscope’s view
- Creates panoramic image (~ 330°)
- Clips onto exterior of any standard pediatric or adult colonoscope

Panoramic View in Normal Colon

Summary

- ADR is important!!
- Effective methods to improve ADR:
  - Education: lesion recognition and excellent technique (adequate time)
  - Effective bowel preparation
  - Measurement, reporting
  - High definition scopes
  - Chromoendoscopy works (but you probably won’t do it)
  - New devices: FUSE, Endocuff, Endorings
Philip S. Schoenfeld, MD, MSEd, MSc(Epi), FACG

Why do we tell patients to get repeat colonoscopy sooner than recommended by guidelines?

We're all worried that the patient with a normal screening colonoscopy.....

Comes back in < 10 years with an interval or "missed" CRC
How Much Overuse of Colonoscopy for Screening and Surveillance?

- 5% national sample of Medicare enrollees from 2000-08 identified 24,071 average-risk individuals with a normal CRC screening colonoscopy between 2001-03.

- 46.2% underwent a repeat examination in < 7 years.

Among this group, no indication except CRC screening in 42.5%.

In other words, almost 1 in 4 (23.5%) of all study patients had repeat colonoscopy < 7 yrs with no indication to repeat colonoscopy early!

How Often Do We Recommend Appropriate Intervals for Repeat Colonoscopy?

- National sample of 50-64 year old, average-risk Veterans with colonoscopy in FY 2008 at 25 VA hospitals.
- Among 1455 Veterans, recommendation for repeat colonoscopy was consistent with guidelines in 64%
  - No polyps: 19% told to get repeat scope in 5 years
  - Hyperplastic polyp: 32% told to get repeat scope in 5 years
  - 1-2 small adenomas: 34% told to get repeat scope in 3 years

This is a VA study. Endoscopists had no fiduciary incentive to recommend early repeat colonoscopy.


Why Don’t Gastroenterologists Follow Colon Polyp Surveillance Guidelines?....

- Survey of 116 gastroenterologists attending GI Board Review Course for Re-Certification in 2003, which represented 57% of GIs taking 2004 re-certification exam.

  - Completed 24-item questionnaire to assess knowledge of recommended surveillance intervals after colonoscopy.

Why Don’t Gastroenterologists Follow Colon Polyp Surveillance Guidelines?…

- Survey of 116 gastroenterologists attending GI Board Review Course for Re-Certification in 2003, which represented 57% of GIs taking 2004 re-certification exam.

- Completed 24-item questionnaire to assess knowledge of recommended surveillance intervals after colonoscopy.

- As part of questionnaire, respondents stated if they were “certain” that their answer was correct AND if they varied from guideline recommendation routinely in their practice.


Why Don’t Gastroenterologists Follow Colon Polyp Surveillance Guidelines?…

Because they think that recommended intervals are too long

- 27.4% disagreed with 10-yr interval after finding hyperplastic polyps
- 28.8% disagreed with 5-yr interval after finding 1-2 small adenomas

These respondents usually recommended earlier intervals in their own practices.

Why does interval or “missed” CRC occur? Is it due to “rapidly growing” polyps?

- Polyps that do not grow in the traditional adenoma-carcinoma sequence and probably grow more quickly.$^{1-3}$
  - Contain BRAF oncogene, DNA methylation aberration of CpG islands (CIMP phenotype), and microsatellite instability.$^{2-3}$

- Approximately 30% of interval CRC are probably due to these “rapidly growing” polyps with these genetic mutations.

Why does interval or “missed” CRC occur?
Most common reason is missed polyps.

Missed the polyp—approximately 50% of interval CRC:
– Factors associated with missed polyps: location, size, quality of bowel preparation, withdrawal time, ADR

Why does interval or “missed” CRC occur? Another common reason is incomplete resection.

- Missed the polyp—approximately 50% of interval CRC:  
  - Factors associated with missed polyps: location, size, quality of bowel preparation, withdrawal time, ADR

- Incomplete Resection of Polyp—about 20% of interval CRC:
  - More likely with large (> 10 mm) vs small polyps (17% vs 6.8%);
  - More serrated polyps vs conventional adenomas: 31% vs 7.2% 
  - More adenomas removed piecemeal vs en bloc: 20.4% vs 8.4%  

What is our goal by repeating screening or surveillance colonoscopy early?

To find “missed” or incompletely resected polyp before it becomes CRC, but...

Many (majority?) interval CRC are found in ≤ 3 years from index colonoscopy!

Caveat: This is based on limited database research that does not include 10-year follow-up.

What factors are associated with recommendation to do an “early” repeat colonoscopy?

- UM Retrospective Database Study of patients with normal colonoscopy
- Compared to pts with “excellent/good” prep, pts with “fair” prep were more likely to be told to return in < 10 yrs: OR = 18.0 (95% CI: 12.0-28.0)

Fair bowel prep is commonly associated with recommendation to do “early” colonoscopy

- UM Retrospective Database Study of patients with normal colonoscopy
- Compared to pts with “excellent/good” prep, pts with “fair” prep were more likely to be told to return in < 10 yrs: OR = 18.0 (95% CI: 12.0-28.0)


24% of ALL patients told to return in < 10 yrs.
Many (majority?) interval CRC are found in ≤ 3 years from index colonoscopy!


Many (majority?) interval CRC are found in ≤ 3 years from index colonoscopy!

If prep is “fair” and you may have missed adenomas, then repeat colonoscopy ≤ 1 yr!

What is the Harm in Repeating Colonoscopy Sooner than Recommended?

“I suppose it is tempting, if the only tool that you have is a hammer, to treat everything as if it were a nail”

-Abraham Maslow, 1966
What is the Harm in Repeating Colonoscopy Sooner than Recommended?

- Unplanned hospital visit (emergency department visit, observation stay, hospitalization) within 7 days of outpatient colonoscopy: **17.5 per 1000 colonoscopies**

- CMS is piloting a facility-level 7-day Risk-Standardized Hospital Visit Rate after Outpatient Colonoscopy as a quality indicator.


Performing post-polypectomy/screening colonoscopy at appropriate interval is quality indicator in Physician Quality Reporting System (PQRS) & ACG/ASGE Position Statement.
Remember: 100% adherence to each quality indicator is not expected!

What is the Harm in Repeating Colonoscopy Sooner than Recommended?

Performing post-polypectomy/screening colonoscopy at appropriate interval is quality indicator in Physician Quality Reporting System (PQRS) & ACG/ASGE Position Statement.

<table>
<thead>
<tr>
<th>Quality Indicator</th>
<th>Target</th>
<th>Grade of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-Procedure:</strong> Colonoscopy is being performed at recommended post-polypectomy and post-cancer resection surveillance intervals and appropriate intervals after normal screening colonoscopy in average-risk individuals</td>
<td>90%</td>
<td>1A</td>
</tr>
<tr>
<td><strong>Post-Procedure:</strong> Appropriate timing of repeat colonoscopy should be documented after review of histologic findings.</td>
<td>90%</td>
<td>1A</td>
</tr>
</tbody>
</table>

What research is needed?

What surveillance intervals are appropriate for serrated polyps?

When Should You Repeat Colonoscopy After an 8mm Serrated Polyp in the Ascending Colon?

- Some serrated polyps may not grow in the traditional adenoma-carcinoma sequence
- Some may contain BRAF oncogene, DNA methylation aberration of CpG islands (CIMP phenotype), and microsatellite instability

We need more data to offer moderate-high quality recommendations

Slide courtesy of Charles Kahi
### 2012 Multi-Society Task Force
Surveillance Guidelines: Serrated Polyps

<table>
<thead>
<tr>
<th>Baseline Finding</th>
<th>Surveillance Interval (yrs)</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectosigmoid: small (&lt;10 mm) hyperplastic polyps</td>
<td>10</td>
<td>Moderate</td>
</tr>
<tr>
<td>Sessile serrated polyps &lt;10 mm and no dysplasia</td>
<td>5</td>
<td>Low</td>
</tr>
<tr>
<td>Sessile serrated polyp ≥ 10 mm</td>
<td>3</td>
<td>Low</td>
</tr>
<tr>
<td>Sessile serrated polyp with dysplasia</td>
<td>3</td>
<td>Low</td>
</tr>
<tr>
<td>Traditional serrated adenoma (uncommon!)</td>
<td>3 years</td>
<td>Low</td>
</tr>
<tr>
<td>Serrated polyposis syndrome</td>
<td>1 year</td>
<td>High</td>
</tr>
</tbody>
</table>