10:30-10:50 25 Sept 2017 Monday
A-PSDE / WEO Colorectal Cancer Screening Committee (CRCSC) Meeting
Room S228 (2/F)

Endocuff, EndoRings, FUSE and other devices

Prof Rupert Leong,
Director of Endoscopy, Head of IBD Professor of Medicine UNSW, University of Sydney, Concord Hospital Australia
Disclosures

- Advisory board: AbbVie, Aspen, Ferring, Hospira, Janssen, Pfizer, Takeda
- Research: Shire, Endochoice, Janssen
Long-Term Colorectal-Cancer Incidence and Mortality after Lower Endoscopy

Reiko Nishihara, Ph.D., Kana Wu, M.D., Ph.D., Paul Lochhead, M.B., Ch.B., Teppei Morikawa, M.D., Ph.D.,

- n=88,902: 22 year
- 1,815 incident CRC, 474 deaths
  - polypectomy: HR CRC 0.57 (95% CI: 0.45-0.72)
  - HR CRC death 0.32 (0.24-0.45)

Colonoscopy reduces CRC and CRC Mortality
Adenoma Detection Rate and Risk of Colorectal Cancer and Death

n = 136 gastroenterologists ADR: 7.4-52.5%

1% increase in ADR decrease 3% risk CRC HR: 0.77 (0.96-0.98)
improve adenoma detection:
- 1. optimize patient selection
- 2. improve quality
- 3. colonoscopy technique
  - i. optimize bowel preparation
  - ii. withdrawal time >6 minutes
  - iii. “look again”: re-insertion, retroflex, work folds
  - iv. technology: Endocuff, Endoring, panoramic

Increase ADR decreases risk of CRC

Corte, Leong. *J Gastroenterol Hepatol* 2015
New Technologies

- improve adenoma detection
  - flat
  - behind folds
  - blind spots

- fold-flattening
- panoramic endoscopy
Fold flattening devices

- Transparent Cap
- Endocuff
- G-Eye Balloon
- EndoRing

Panoramic endoscopy

Third Eye Retroscope

FUSE

Third Eye Panoramic

Panoramic device

Standard colonoscope

Catheter

Clip

Right side LED

Colonoscope video camera

Additional TED and video camera located on left side

Cap Assisted Colonoscopy

- **cap**:  
  - polyps RR 1.08 (1.0-1.17)  
  - caecal intubation time -0.64min  

Ng *Am J Gastroenterol* 2012
Endocuff

- n=1,063, n=530 Endocuff, n=533 CC
- surveillance, symptoms, screen, FIT
- ADR 52% CC vs 52% Endocuff

<table>
<thead>
<tr>
<th>Polyps</th>
<th>1020</th>
<th>898</th>
<th>0.10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenomas</td>
<td>722</td>
<td>621</td>
<td>0.08</td>
</tr>
<tr>
<td>Per patient (mean, SD)</td>
<td>1.36 (2.10)</td>
<td>1.17 (1.65)</td>
<td>0.08</td>
</tr>
<tr>
<td>Patients with ≥1 adenoma</td>
<td>275 (52%)</td>
<td>278 (52%)</td>
<td>0.92</td>
</tr>
<tr>
<td>Advanced adenomas</td>
<td>150</td>
<td>153</td>
<td>0.91</td>
</tr>
</tbody>
</table>

- flat adenomas 0.27/ individual vs 0.16 (P<0.01); small adenomas 0.91 vs 0.74 (P=.03)
- 22 failed sigmoid intubation

van Doorn Gut 2015
NaviAid G-EYE Balloon

- reusable balloon & inflation system
  - 0.1mm diameter
- straighten folds and flexures
- n=126 tandem colonoscopy
  - balloon colonoscopy missed 7.5% vs 45% colonoscopy ($P=0.0002$)
  - detection 81% additional adenomas

Halpem *Endosc* 2015
Third Eye Retroscope

- retroflexed 2\textsuperscript{nd} camera
- uses up channel
Third Eye Retroscope

- n=29: +4 polyps; 11.8% increased yield
- n=249: +16% adenomas
- n=298: +11% adenomas
- n=349: +23% adenomas

Triadafilopoulos Endosc 2008
DeMarco Gastrointest Endosc 2010
Waye Gastrointest Endosc 2010
Leuflkens Gastrointest Endosc 2011
Third Eye Panoramic cap

- CMOS, LED
- 300 degree viewing
- frees channel
- ICV intubation challenge
- lens wash
- reusable version

Rubin World J Gastro 2015
Third Eye Panoramic cap

- n=33, screening, surveillance, diagnostic
- ADR 44%
- 100% caecal intubation; intubation time 8min

Rubin *World J Gastro* 2015
Full Spectrum Endoscopy (FUSE)
- 168cm length
- 12.8mm diameter
- high res
- full tip mobility
- 3.8mm channel
Conventional Colonoscopy
Full Spectrum Endoscopy
Caecum
Standard forward-viewing colonoscopy versus full-spectrum endoscopy: an international, multicentre, randomised, tandem colonoscopy trial


- tandem colonoscopy study
- 18-70yo; screening, assessment, follow up
- conventional colonoscopy first or FUSE first

<table>
<thead>
<tr>
<th></th>
<th>Conventional Colonoscopy n=88</th>
<th>FUSE n=97</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoma miss rate</td>
<td>20/49 (41%)</td>
<td>5/67 (7%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Gralnek *Lancet Oncol* 2015
## FUSE vs Conventional Colonoscopy

<table>
<thead>
<tr>
<th></th>
<th>Standard colonoscopy (n=88)</th>
<th>FUSE (n=97)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missed adenoma by 1\textsuperscript{st} procedure</td>
<td>20 / 49 (41%)</td>
<td>5 / 67 (7%)</td>
</tr>
<tr>
<td>Morphology: total</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Pedunculated</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Sessile</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td>Size : ≥10mm</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>6-9mm</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>&lt;5mm</td>
<td>14</td>
<td>5</td>
</tr>
<tr>
<td>Subtype</td>
<td>TA (18), TVA (1) and villous (1)</td>
<td>Tubular (5)</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>Left</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Finding required to change in surveillance</td>
<td>9.1% (8/88)</td>
<td>0% (0/97)</td>
</tr>
</tbody>
</table>

Conventional colonoscopy misses small, proximal colonic polyps

Gralnek Lancet Oncol 2015
Full-spectrum (FUSE) versus standard forward-viewing colonoscopy in an organised colorectal cancer screening programme

Cesare Hassan,¹ Carlo Senore,² Franco Radaelli,³ Giovanni De Pretis,⁴

- screening +ve FIT; 7 Italian centres

<table>
<thead>
<tr>
<th></th>
<th>Conventional Colonoscopy n=330</th>
<th>FUSE n=328</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADR n (%)</td>
<td>150/330 (45.5)</td>
<td>143/328 (43.6)</td>
</tr>
<tr>
<td>Advanced ADR n (%)</td>
<td>23.0%</td>
<td>64/328 (19.5)</td>
</tr>
</tbody>
</table>

- high ADR (40%), first gen, learning curve
  - 1 adenoma identified = ADR already met

Cesare Gut 2016
FUSE: Adenoma Miss Rate

- Adenoma Miss Rate RR: 0.35 (95% CI: 0.25-0.48)
## FUSE: Adenoma Detection Rate

- Adenoma Detection Rate: 1.05 (0.94-1.17)

<table>
<thead>
<tr>
<th>Study or Subg M-H, Random, 95% CI Year</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gralnek</td>
<td>1.20 [0.78, 1.84] 2014</td>
</tr>
<tr>
<td>Hassan</td>
<td>0.96 [0.81, 1.14] 2016</td>
</tr>
<tr>
<td>Nuatez</td>
<td>1.07 [0.91, 1.27] 2017</td>
</tr>
<tr>
<td>Papanikolaou</td>
<td>1.19 [0.82, 1.74] 2017</td>
</tr>
<tr>
<td>Leong</td>
<td>3.24 [0.72, 14.59] 2017</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total (95% CI)</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.05 [0.94, 1.17]</td>
</tr>
</tbody>
</table>

### Heterogeneity:
- Test for overall
FUSE: Colonoscopy Time

- Total colonoscopy time

<table>
<thead>
<tr>
<th>Study or Subg</th>
<th>Mean Difference</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gralnek</td>
<td>-2.30 [-3.28, -1.32]</td>
<td>2014</td>
</tr>
<tr>
<td>Neumann</td>
<td>-4.18 [-6.06, -2.30]</td>
<td>2015</td>
</tr>
<tr>
<td>Leong</td>
<td>2.10 [-1.87, 6.07]</td>
<td>2017</td>
</tr>
<tr>
<td>Martinez-Alcala</td>
<td>-4.60 [-7.93, -1.27]</td>
<td>2017</td>
</tr>
</tbody>
</table>

Total (95% CI) -2.60 [-4.60, -0.61]

Heterogeneity:
Test for overall

Facciorusso J Gastro Hepatol 2017
## FUSE vs CC: Meta-analysis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Adenoma Detection RR (95% CI)</th>
<th>Adenoma Miss Rate RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Right-sided</strong></td>
<td>1.10 (0.87-1.39)</td>
<td>0.27 (0.10-0.73)</td>
</tr>
<tr>
<td><strong>Left-sided</strong></td>
<td>0.92 (0.69-1.21)</td>
<td>0.33 (0.14-0.77)</td>
</tr>
<tr>
<td><strong>Size ≤5mm</strong></td>
<td>1.09 (0.99-1.24)</td>
<td>0.26 (0.15-0.48)</td>
</tr>
<tr>
<td><strong>Size &gt;5mm</strong></td>
<td>1.01 (0.94-1.43)</td>
<td>0.38 (0.09-1.60)</td>
</tr>
<tr>
<td><strong>Flat / sessile</strong></td>
<td>1.32 (0.35-4.99)</td>
<td>0.26 (0.13-0.51)</td>
</tr>
<tr>
<td><strong>Pedunculated</strong></td>
<td>1.04 (0.83-1.30)</td>
<td>0.15 (0.01-3.00)</td>
</tr>
</tbody>
</table>

**FUSE: small adenomas; R & L colons ADR same**
Adaptive Matrix Imaging

- Always on capability
- Maintains natural colors
- Smart enhancement
- Designed to reduce distraction

Gastro-esophageal Junction

Flat Sessile Polyp

Pending FDA clearance
Not for sale in the US
Cost-effectiveness of “full spectrum endoscopy” colonoscopy for colorectal cancer screening

Cesare Hassan\textsuperscript{a,*}, Ian M. Gralnek\textsuperscript{b}

- Markov model
  - cost-effectiveness of FUSE
  - +16\% increased cancer prevention: 58\% to 74\%
  - gain of 9 days per person
  - cost of cancer care decreased $90M to $57M
  - savings $145 per person
Extra Wide Angle View Colonoscopy

- 232 degrees

- n=319: ADR 1.1 vs 1% ($P=0.43$)
Tandem Colonoscopy Studies

<table>
<thead>
<tr>
<th>Tandem Studies</th>
<th>Adenoma Miss Rates</th>
<th>Adenomas Detected by 2nd Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rex 1997 <em>Gastro</em> n=183</td>
<td>TFV 24%</td>
<td>2nd Pass 31%</td>
</tr>
<tr>
<td>Rex 2011 <em>GI Endosc</em> n=1,000</td>
<td>2nd Pass +12% on retroflexion</td>
<td></td>
</tr>
<tr>
<td>Siersema 2012 <em>World J Gastro</em> n=349</td>
<td>TFV 31%</td>
<td>Third Eye 46%</td>
</tr>
<tr>
<td>Gralnek 2014 <em>Lancet Oncol</em> n=185</td>
<td>TFV 41%</td>
<td>FUSE 69%</td>
</tr>
<tr>
<td></td>
<td>Technology</td>
<td>Improvement</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Cap</td>
<td>flatten folds</td>
<td>cheap</td>
</tr>
<tr>
<td>Third Eye Retroscope</td>
<td>through working channel</td>
<td>reverse view</td>
</tr>
<tr>
<td>Third Eye Panoramic Cap</td>
<td>clip on, 3 cameras</td>
<td>330 degrees</td>
</tr>
<tr>
<td>Full spectrum endoscopy</td>
<td>3 cameras incorporated, LUMOS</td>
<td>330 degrees</td>
</tr>
<tr>
<td>Endocuff</td>
<td>flatten folds</td>
<td>cheap</td>
</tr>
<tr>
<td>EndoRing</td>
<td>flatten folds</td>
<td>cheap</td>
</tr>
</tbody>
</table>
Limitations

- what is the best measure of quality?
- who will benefit most from technologies?
  - high ADRs? low ADRs?
- incremental gain?
  - slow withdrawal, high quality bowel prep?
- negatives?
  - learning curve, difficult intubation, use channel
- cost benefit?
  - cheap cap vs FUSE
Conclusions

- endoscopic technology
  - decreases adenoma miss rate
    - improve CRC screening efficacy; reduces interval CRC

- FUSE:
  - decreased adenoma miss rates; ADR not increased

- other techniques: less established
Where is the panda?
<table>
<thead>
<tr>
<th></th>
<th>Gralnek</th>
<th>Leong</th>
<th>Cesare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>mixed</td>
<td>IBD surveillance</td>
<td>+ve FIT</td>
</tr>
<tr>
<td>Endpoint</td>
<td>adenoma miss rate</td>
<td>adenoma miss rate</td>
<td>adenoma detection rate</td>
</tr>
<tr>
<td>Adenoma Miss Rate</td>
<td>7% FUSE vs 41% CC</td>
<td>25% FUSE vs 71% CC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P= 0.0001</td>
</tr>
<tr>
<td>Adenoma Detection Rate</td>
<td>73% FUSE vs 27%</td>
<td>43.6% FUSE vs 45.5% CC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P= 0.007</td>
</tr>
</tbody>
</table>