Role of New Technology to Improve Adenoma Detection

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Objectives

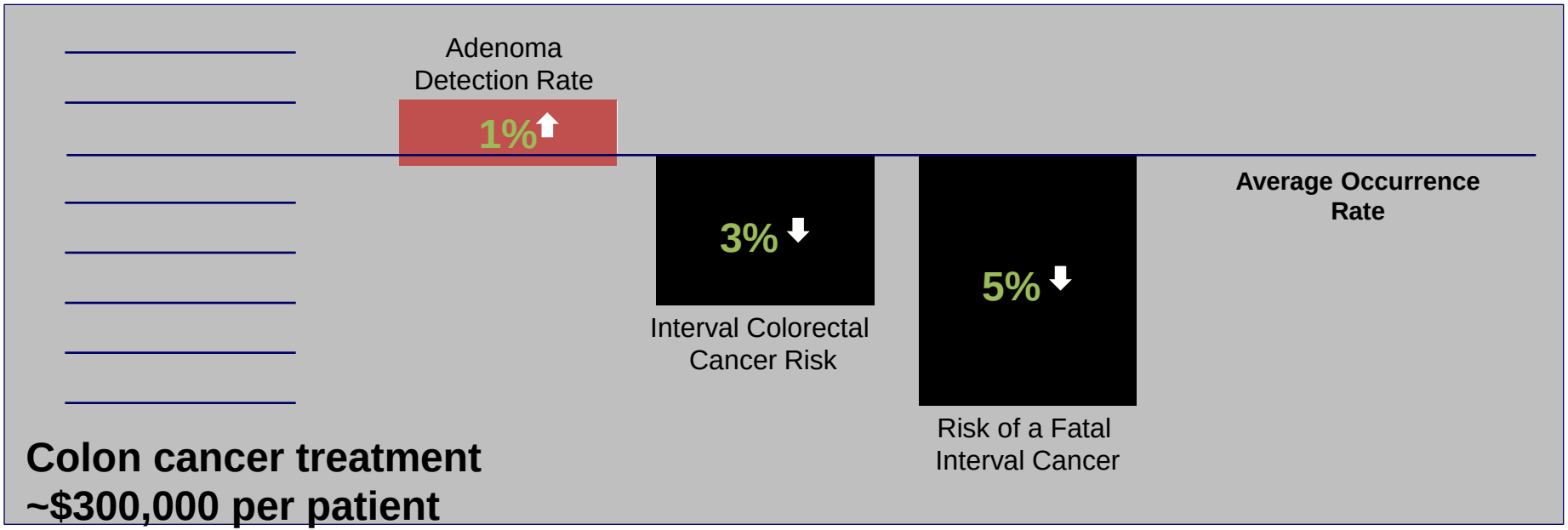
- Review quality metrics in colonoscopy
- Optical and mechanical enhancements for colonoscopy

Colonoscopy Polyp Miss Rate

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

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]



Corley DA, Jensen CD, Marks AR, et al. *N Engl J Med* 2014; 370:1298-306.

nature publishing group

Quality Indicators for Colonoscopy

Douglas K. Rex, MD, Philip S. Schoenfeld, MD, MSEd, MSc (Epi), Jonathan Cohen, MD, Irving M. Pike, MD, Douglas G. Adler, MD, M. Brian Fennerty, MD, John G. Lieb II, MD, Walter G. Park, MD, MS, Maged K. Rizk, MD, Mandeep S. Sawhney, MD, MS, Nicholas J. Shaheen, MD, MPH, Sachin Wani, MD and David S. Weinberg, MD, MSc

Am J Gastroenterol 2015; 110:72–90; doi:10.1038/ajg.2014.385; published online 2 December 2014

Originally Published in 2006, Revised 2015

ACG and ASGE joint collaboration

Landmark colonoscopy quality guidelines

23 common endoscopic quality indicators

15 colonoscopy specific quality indicators

3 Priority Quality Indicators

1. ADR

2. Colonoscopy follow recommendations:

Post-polypectomy and post-cancer resection surveillance intervals

3. Cecal intubation with notation of landmarks and photo-documentation of landmarks

ADR Facts

- Adenoma detection rate (primary measure)
  - ≥ 30% in men
  - ≥ 20% in women
- Withdrawal time (secondary measure)
  - Should average at least 6 minutes in normal colonoscopies without biopsy or polypectomy

Three Important Questions: Effectiveness of Colonoscopy

- Is the colonoscopy quality operator dependent?
- Does withdrawal time make a difference?
- Does the equipment and technology make a difference?

Does Withdrawal Time Matter?

Yes and No

Does Withdrawal Time Matter? Yes

Variable	<6 Minutes (N=3)	> or = 6 Minutes (N=9)
All Adenomas	ADR = 11.8 %	ADR= 28.3%
Advanced Adenomas	ADR= 2.4%	ADR= 6.4%

Barclay RL et al, Colonoscopic withdrawal times and adenoma detection during screening colonoscopy, *N Engl J Med,* 2006 355:2533-2541

Does Withdrawal Time Matter?
No

- N = 42 physicians and 23,910 colonoscopies
- Establishment of mandatory withdrawal time of 7 min or greater
- Increase in compliance from 65% to 100%
- No increase in polyp detection

Sawhney et al., Effect of institution-wide policy of colonoscopy withdrawal time > or = 7 minutes on polyp detection. *Gastroenterology* 2008; 135:1892-1898

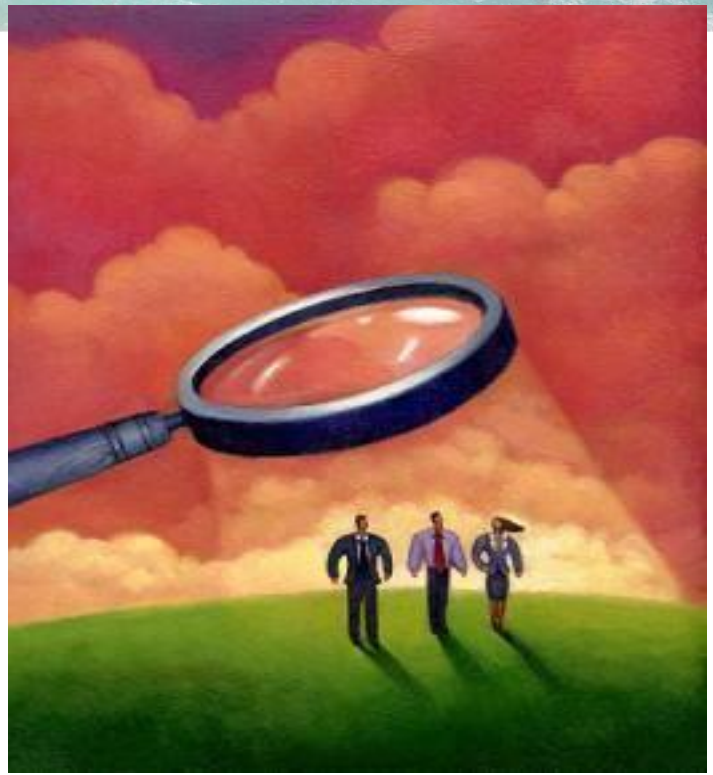
Technique May Matter More

- Study using Video Recording and Technique Grading
- Grading System:
  - Fold examination
  - Distension
  - Cleansing
- Withdrawal Time:
  - No significant difference in withdrawal time between highest ADR endoscopist (6.6 min) and lowest ADR (7.4 min) endoscopist
- Technique:
  - Two-fold difference in technique score between highest ADR endscopist and and lowest ADR endoscopist

Lee RH et al., *Gastrointestinal Endoscopy* 2011; 74: 128-134

Hawthorne Effect

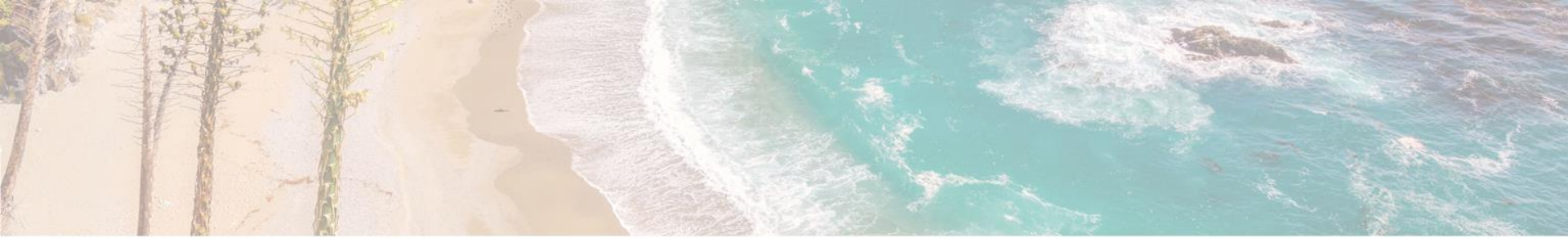
- 1924-1932
- Lighting evaluated to improve productivity in factory workers
- The lighting did improve productivity initially, then it dropped after the study was concluded
- *Overall Conclusion:* variables related to **observation** were responsible for the improved outcome.



Are Report Cards a Factor?

- Report Cards given to endoscopists quarterly:
  - Bowel preparation quality
  - Before-procedure patient assessment
  - Cecal intubation
  - Withdrawal time
  - ADR
- Adenoma detection: 53.9% (from 44.7%)
- Cecal intubation rates: 98.1% (from 95.6%)
- The increment in ADR was due mostly to increased detection of proximal adenomas.

Kaji CJ et al., Impact of a quarterly report card on colonoscopy quality measures. Gastrointest Endosc. 2013



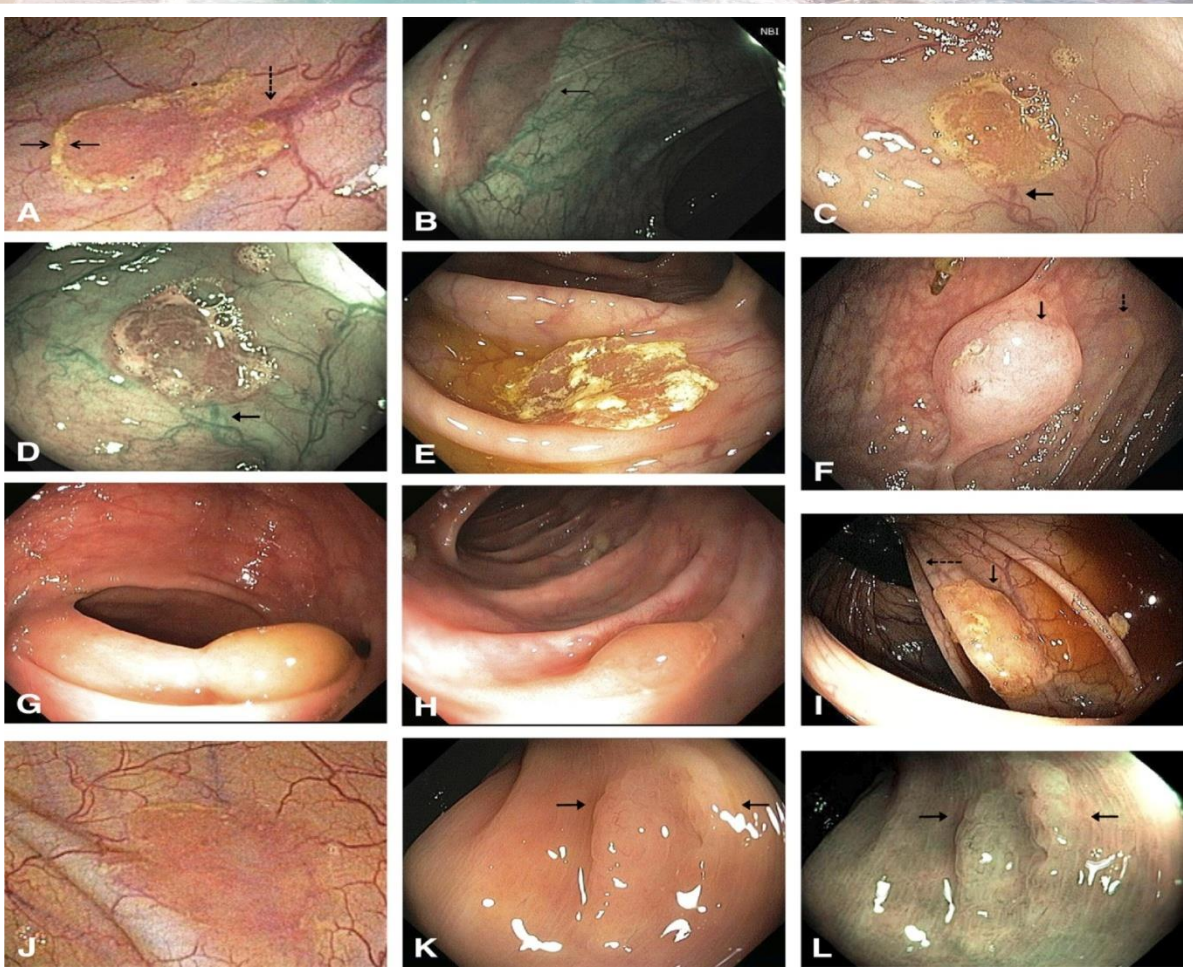
Will new technology help you a do a more effective colonoscopy?

Adenoma Challenge

- Average colon length – 189 cm[1]
- Some colons >2.5 meters[2]
- >100 haustral folds per colon
- Colonic flexures = “blind spots”

(1) Khashab et al. Endoscopy 2009 (2) Hansen & Pickhardt AJR 2007

What do these polyps have in common?



Gastrointestinal Endoscopy 2011; 74:1360-1368

Serrated Polyps

- Common polyp type
- Sessile/flat
- 80% proximal colon (right side)
- Endoscopic detection challenge
  - Similar color to surrounding mucosa
  - Indiscrete edges
  - Always flat or sessile
  - Layer of adherent mucous

Table 1. 2012 Recommendations for Surveillance and Screening Intervals in Individuals With Baseline Average Risk

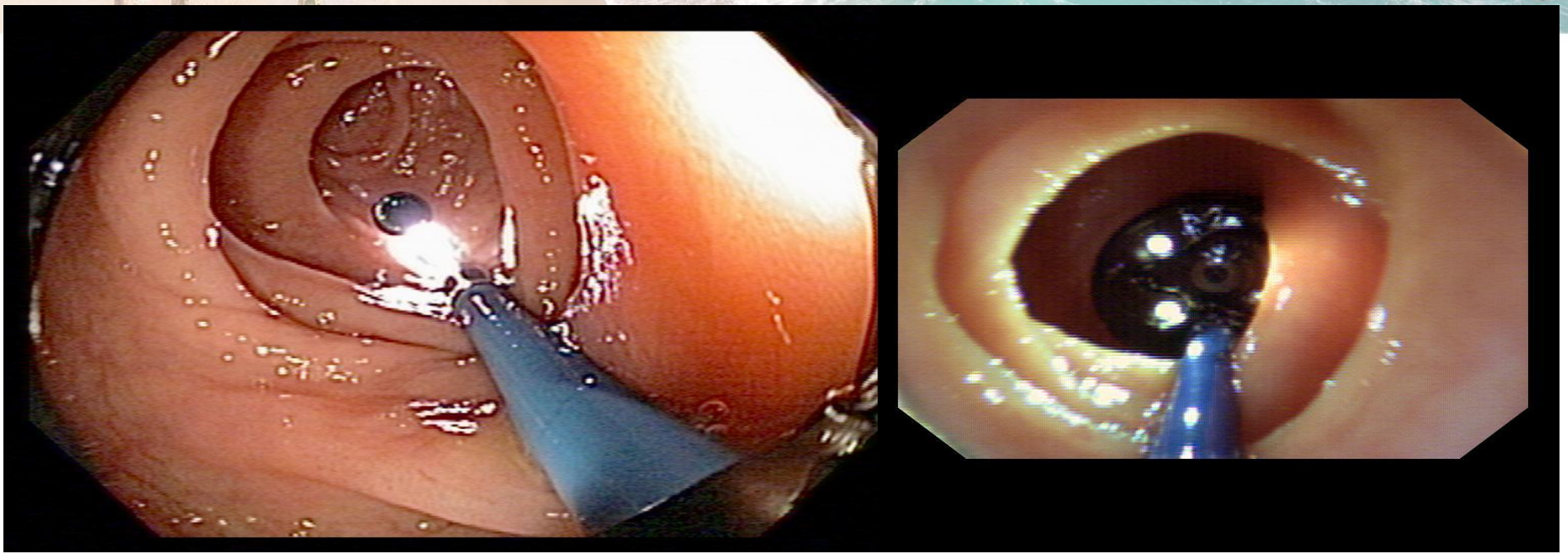
Baseline colonoscopy: most advanced finding(s)	Recommended surveillance interval (*y*)	Quality of evidence supporting the recommendation	New evidence stronger than 2006
No polyps	10	Moderate	Yes
Small (<10 mm) hyperplastic polyps in rectum or sigmoid	10	Moderate	No
1–2 small (<10 mm) tubular adenomas	5–10	Moderate	Yes
3–10 tubular adenomas	3	Moderate	Yes
>10 adenomas	<3	Moderate	No
One or more tubular adenomas ≥10 mm	3	High	Yes
One or more villous adenomas	3	Moderate	Yes
Adenoma with HGD	3	Moderate	No
Serrated lesions			
Sessile serrated polyp(s) <10 mm with no dysplasia	5	Low	NA
Sessile serrated polyp(s) ≥10 mm	3	Low	NA
OR			
Sessile serrated polyp with dysplasia			
OR			
Traditional serrated adenoma			
Serrated polyposis syndrome[a]	1	Moderate	NA

NOTE. The recommendations assume that the baseline colonoscopy was complete and adequate and that all visible polyps were completely removed.

NA, not applicable.

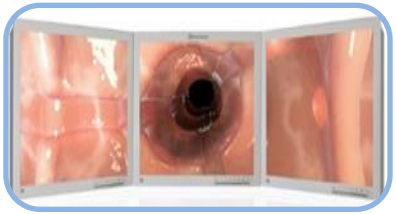
[a]Based on the World Health Organization definition of serrated polyposis syndrome, with one of the following criteria: (1) at least 5 serrated polyps proximal to sigmoid, with 2 or more ≥10 mm; (2) any serrated polyps proximal to sigmoid with family history of serrated polyposis syndrome; and (3) >20 serrated polyps of any size throughout the colon.

3rd Eye Retroscope

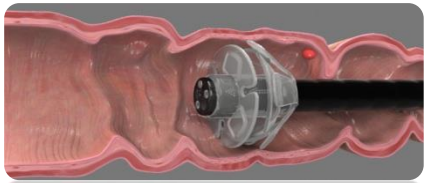


Improving Polyp Detection
"Inspection Behind Folds"

Optical

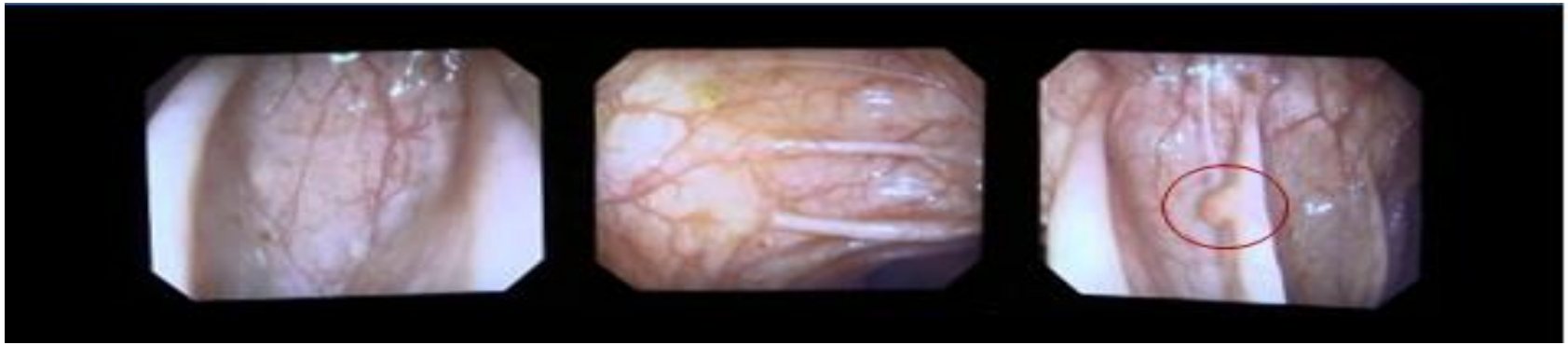


Mechanical Fold Flattening



Optical Enhancements

Like Driving Your Car

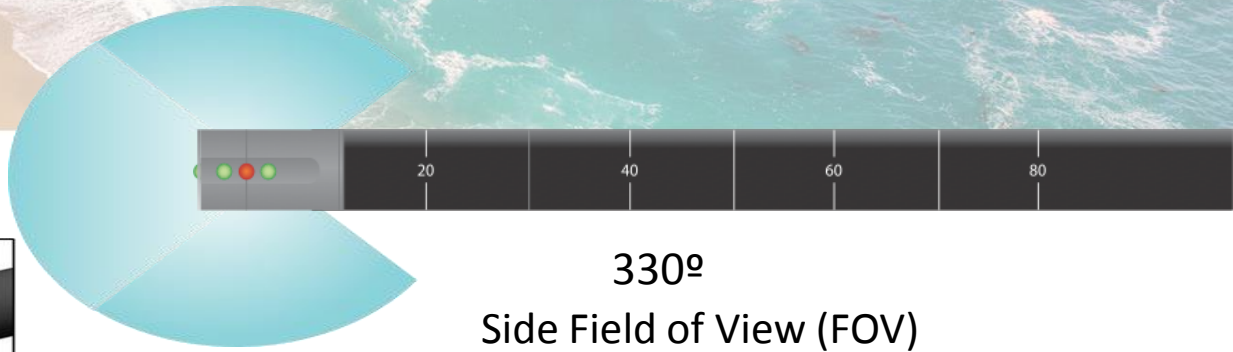


Full Spectrum Endoscopy

170º

Forward Field of View (FOV)

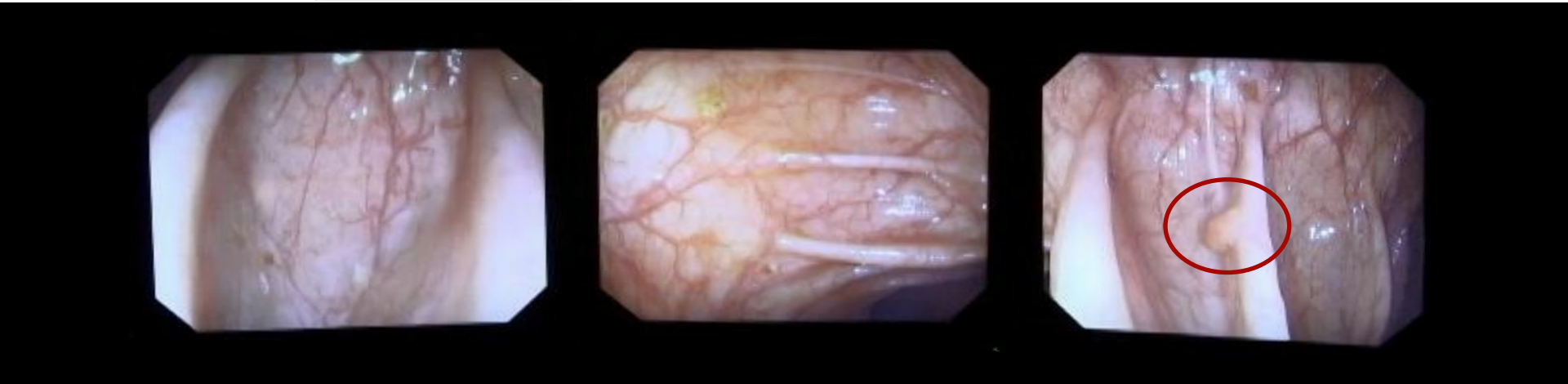
The front lens provides a viewing angle similar to current scope platforms



330º

Side Field of View (FOV)

Full Spectrum Endoscopy™ produces an enhanced peripheral viewing area



Standard forward-viewing colonoscopy versus full-spectrum endoscopy: randomised, tandem colonoscopy trial

Randomized (concealed allocation)

- Tandem colonoscopy design
- Same day, back-to-back, by the same endoscopist
- 170^{o} TFV vs. Fuse 330^{o}

All polyps removed when identified

- Except hyperplastic rectal polyps (1mm-2mm)
- All adenomas and cancers confirmed by pathology

Multicenter

- Israel (3) Netherlands (1) USA (2)

Gralnek et al. Lancer Oncology 2014

	Adenomas detected with standard forward-viewing colonoscopy	Adenomas detected with full-spectrum colonoscopy	Total number of adenomas identified	Adenoma miss rate with standard forward-viewing colonoscopy*	Adenoma miss rate with full-spectrum colonoscopy*
Standard forward-viewing colonoscopy first (n=88)	29	20	49	20/49 (41%);† 27·0–56·0	..
Full-spectrum colonoscopy first (n=97)	5	62‡	67	..	5/67 (7%); 2·5–16·6

Data are n or n/N (%) with 95% CI. *Full-spectrum colonoscopy *vs* standard forward-viewing colonoscopy adenomas missed, p<0·0001. †Includes three advanced adenomas (two adenomas with villous histology and one adenoma ≥10 mm in size). ‡Includes two cancers.

Table 3: **Adenomas detected and missed with standard forward-viewing and full-spectrum colonoscopy**

	Patients with adenomas detected by standard forward-viewing colonoscopy or full-spectrum endoscopy	Patients with adenomas detected by full-spectrum or standard forward-viewing colonoscopy	Unique patients with adenomas detected by full-spectrum or standard forward-viewing colonoscopy	Total patients with adenomas	Patients with false-negative results from standard forward-viewing colonoscopy or full-spectrum colonscopy*	Patient miss rate (adenomas) with standard forward-viewing colonoscopy or full-spectrum colonscopy†
Standard forward-viewing colonoscopy first (n=88)	25 (28%)	15 (17%)	5 (6%)	30 (34%)	5/88 (6%); 1·9–12·8	5/30 (17%); 5·6–34·7
Full-spectrum colonoscopy first (n=97)	33 (34%)	5 (5%)	0	33 (34%)	0/97; 0–3·7	0/33; 0–10·6

Data are n (%), or n/N (%) with 95% CI. A per-patient analysis. *p=0·02 Fisher's exact test †p=0·02 Fisher's exact test.

Table 4: **Adenomas detected and missed per patient**

Gralnek et al. Lancer Oncology 2014

Lower Adenoma Miss Rate with FUSE vs. Conventional Colonoscopy with Proximal Retroflexion: A Randomized Back-to-Back Trial

Aim:

- Compare adenoma miss rates of FSC with those of conventional colonoscopy complemented by right-colon re-examination using scope retroflexion (CC/R).

Results:

- Randomized 220 patients.
- Withdrawal times were similar for FSC and CC/R (7.7 minutes vs. 7.6 minutes).
- Findings: 3 cancers and 153 adenomas (FSC = 92; CC/R = 61);
- 81 were detected in the proximal colon, 3 of which were detected by retroflexed examination. FSC showed a significantly lower adenoma miss rate compared with CC/R
- overall (10.9 % [95 % confidence interval (CI) 3.8 to 18.1] vs. 33.7 % [95 %CI 23.4 to 44.1]) the proximal colon (13.9 % [95 %CI 2.6 to 25.2] vs. 42.2 % [95 %CI 27.8 to 56.7]).
- Advanced adenoma miss rate was lower with FSC overall (4.3 % [95 %CI - 4.0 to 12.7] vs. 25.9 % [95 %CI 9.4 to 42.5]).

Conclusions:

- FSC outperformed for both overall and in the proximal colon.

Papanikolaou IS, et al. Endoscopy. 2017

Full-spectrum (FUSE) versus Standard Forward-Viewing Colonoscopy in an Organized Colorectal Cancer Screening Program

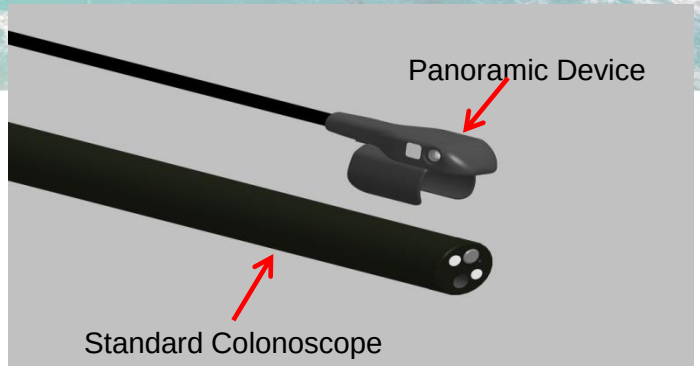
- **Objective:** Compare ADR between standard forward viewing (SFV) and FUSE colonoscopy

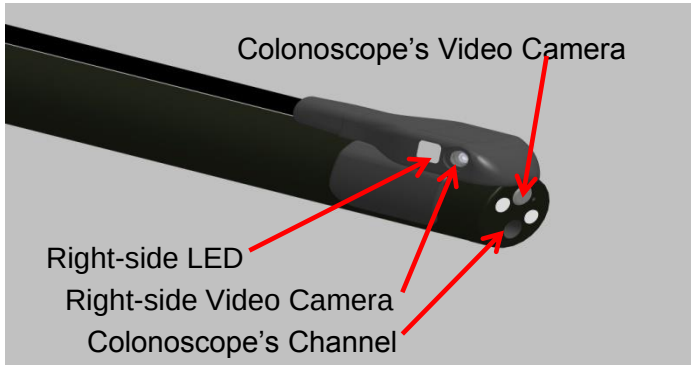
- **Methods:** Consecutive subjects undergoing colonoscopy following a + FIT.
  Randomised between colonoscopy with either FUSE or SFV colonoscopy in seven
- **Results:**
  658 patients enrolled FUSE (n=328) or SFV (n=330)
  FUSE Arm: ADR and A-ADR were **43.6% and 19.5%**
  SFV Arm: ADR and A-ADR were **45.5% and 23.9%**
  No difference in SSPDR or multiplicity was detected between the two arms

- **Conclusions**: No statistically significant difference in ADR and A-ADR between FUSE and SFV colonoscopy

Panoramic Cap

- Clips onto the exterior of any colonoscope
  - Preserves benefits of existing colonoscopes – HD, NBI, scope handling, reliability, etc.
  - Working channel free for suction and instrumentation
- Reusable





This device is currently under 510(k) review by the FDA, not available for sale in United States

Normal Colon

Left-side image Colonoscope image Right-side image

- Feasibility study with 25 patients showed:
  - Cecum was reached in all subjects
  - No interference with
    - Mobility
    - Tip deflection
    - Retroflexion
    - Polypectomy
  - No adverse events

Lesion Hidden from Colonoscope's View

Adenoma was seen only in lateral view

Rubin et al. DDW poster 2014

Mechanical Enhancements

Balloon Integrated Colonoscopy

Endoscope incorporating a permanently integrated balloon at its bending section
Compatible with all brands

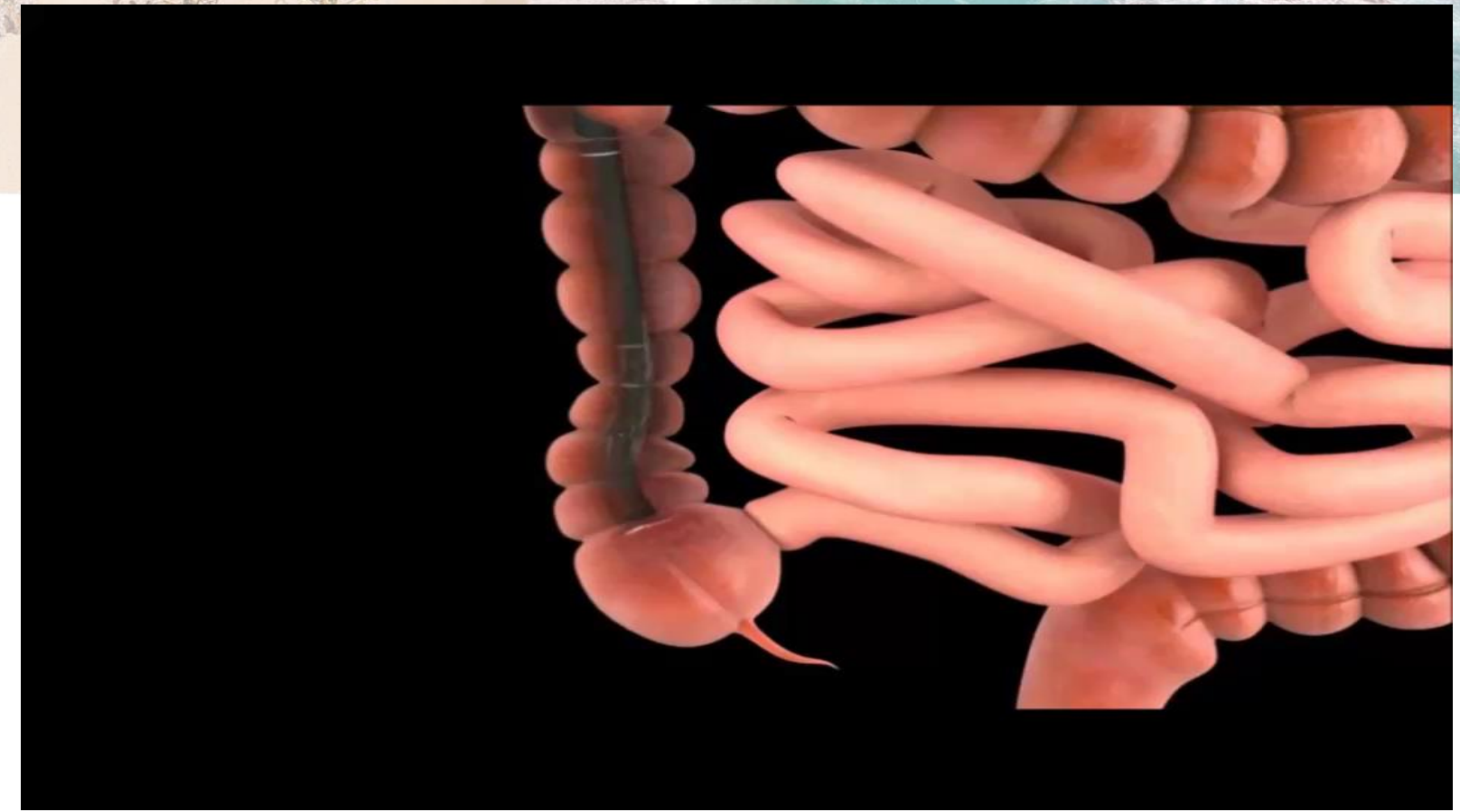
Inflation system enabling the user to select between partial pressure, and anchoring pressure

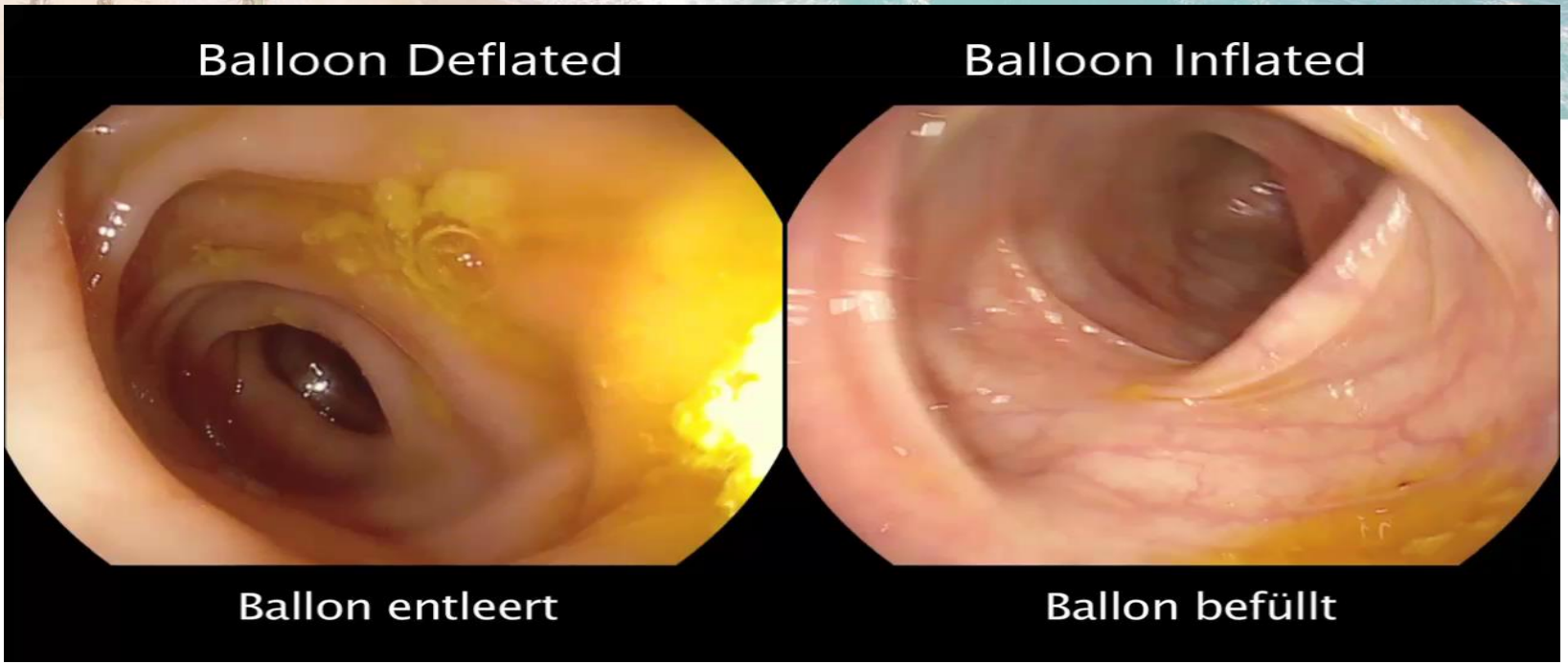
- Partial pressure → ADR enhancement
- Anchoring pressure → Endoscope stabilization during treatment

Regulatory Status

✓ CE Mark, Health Canada license

✓ Cleared for both upper and lower GI endoscopy

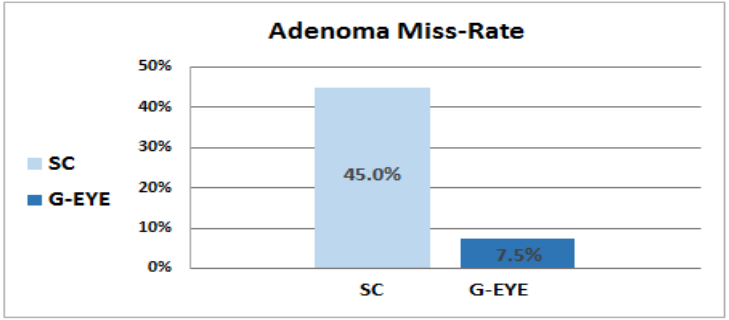


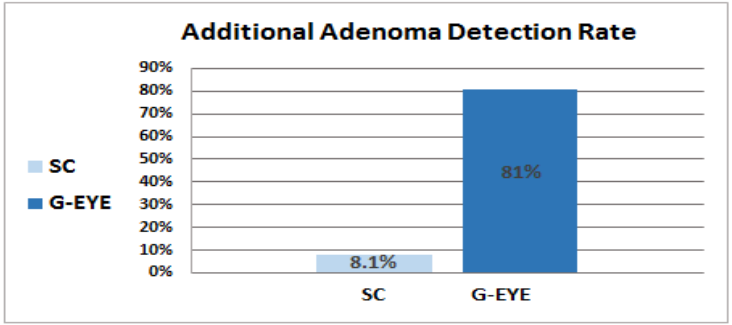

Balloon Deflated
Balloon Inflated
Ballon entleert
Ballon befüllt

Multicenter Tandem Study

Comparison of adenoma detection and miss rates between a novel balloon colonoscopy and standard colonoscopy (Halpern, Endoscopy 2015)

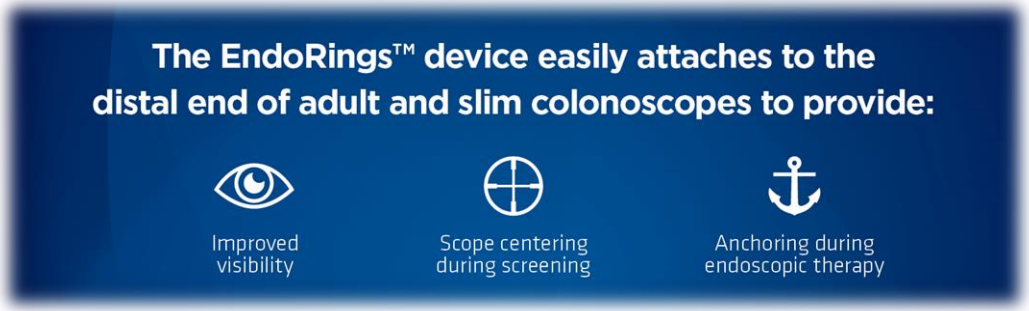
- 126 patients
- Study design similar to FUSE™ tandem study
- Adenoma miss-rate: G-EYE 7.5% ; SC 45.0%
- Adenoma additional detection rate: G-EYE 81% ; SC 8.1%
- ADR: 56% increase with G-EYE over SC





EndoRings: Mode of Operation

- Device has multiple rings which stretches out the folds of the colon, providing better colon tissue view
- Device centers and stabilizes the endoscope
- Protects against endoscope back slippage when not held by the practitioner
- Maintains identical depth and breadth of endoscope's viewing field



Study Design

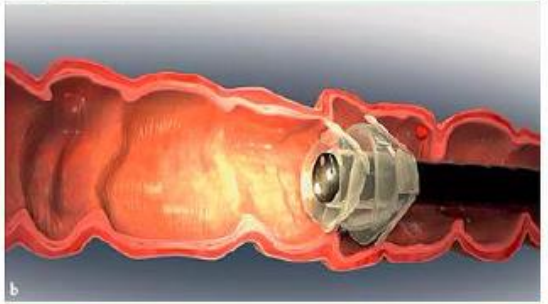
- Multi-center study, procedures were performed at three centers:
  - University Hospital, Utrecht, Netherlands
  - Indiana University Health, Indiana, USA
  - Elisha Medical Center, Haifa, Israel
- Two screenings per patient. Sequence was randomized
- 126 treated patients were enrolled into the study
- Subjects between the ages of 40 and 75
- Patients were undergoing colonoscopy for screening, surveillance in follow-up of previous polypectomy or for diagnostic workup

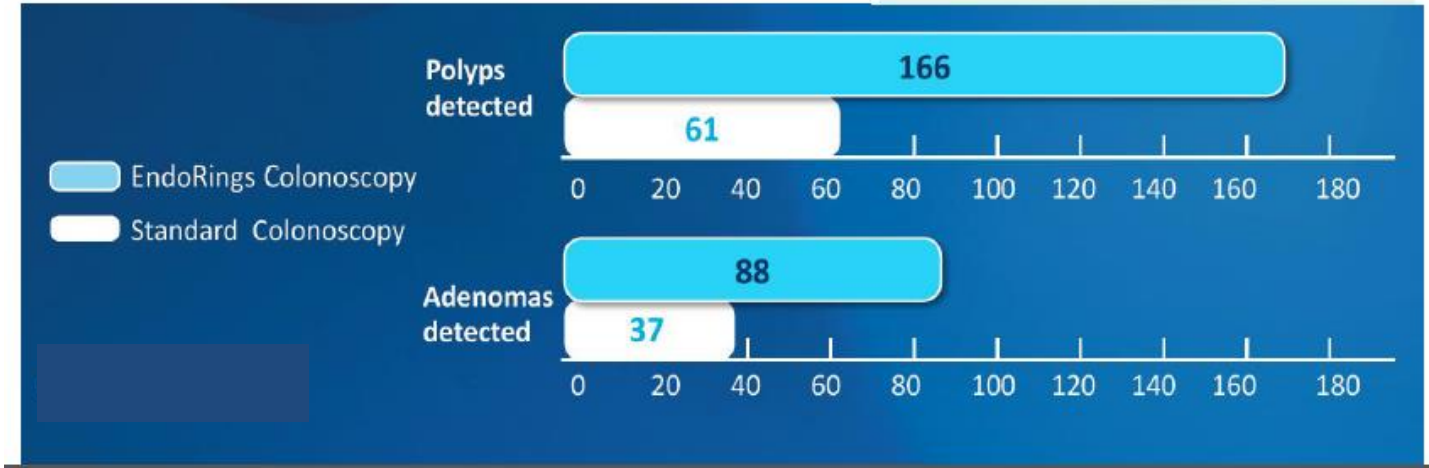
Dik et al. Endoscopy 2015

Results:

ADR with standard colonoscopy- 28.8%

ADR with EndoRings - 50.9%

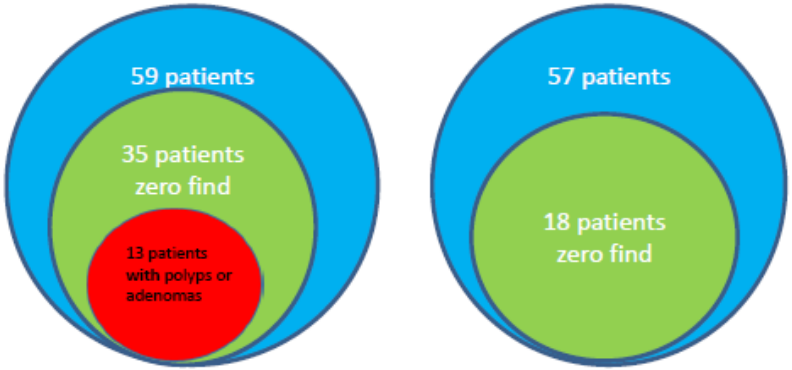




Dik et al. Endoscopy 2015

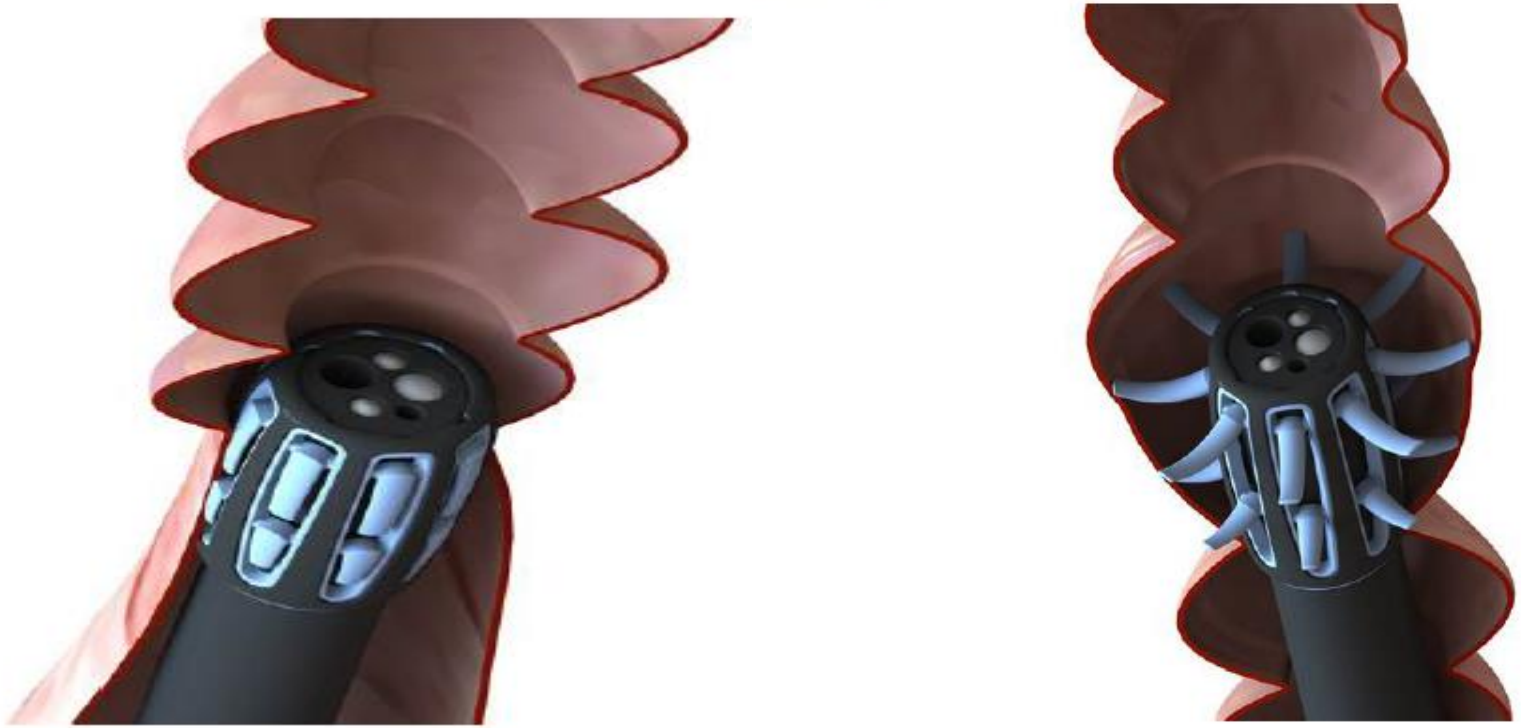
Zero Detection Failure

	Standard Colonoscopy	EndoRings Colonoscopy
Out of:	59 patients	57 patients
First pass Zero findings:	35 patients	18 patients
Second pass with EndoRings:	**13 patients** (from 35) had a hyperplastic polyp/adenoma detected with EndoRings Colonoscopy (37%)	**0 patients** (from 18) had a hyperplastic polyp/ adenoma detected with Standard Colonoscopy

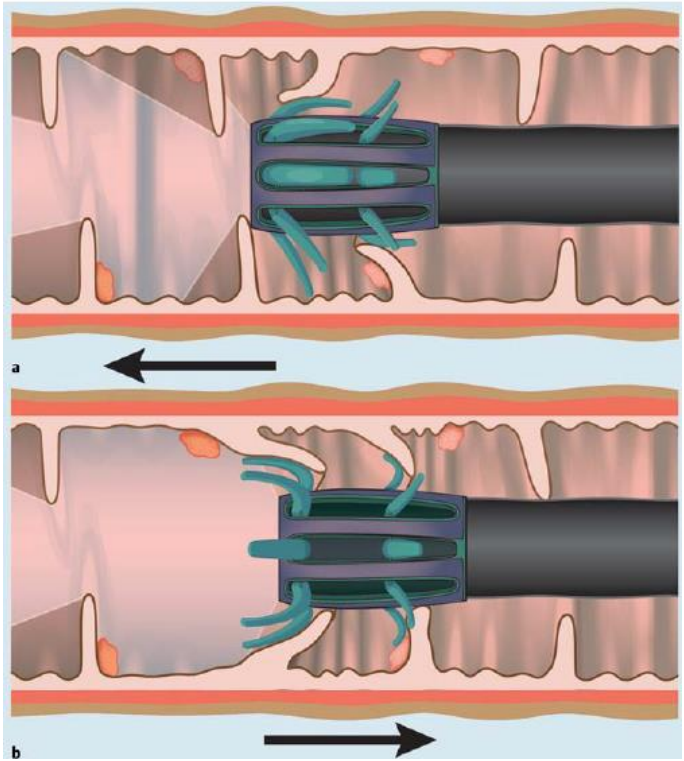


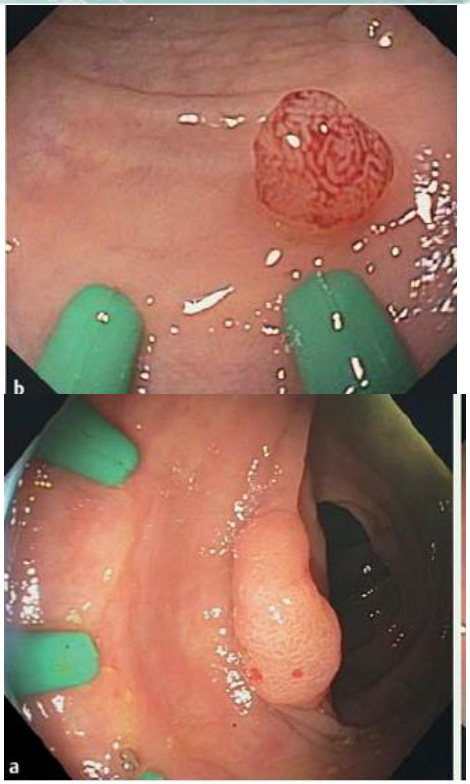
Dik et al. Endoscopy 2015

Cuff Assisted Colonoscopy



Principles of Mechanical Enhancement





Potential Benefits

- Arms grip colon to prevent slippage
- Scope stabilization during inspection and polypectomy
- Improved surface area inspection
- Loop reduction
- Reduced slippage
- Anoscopy

ENDOCUFF Meta-analysis

Table 1 Study details

Ref.	Study design	Location	Practice setting	Study period	Procedure Indication	Number patients	Gender	Age (yr)	Primary outcome	ADR EAC standard	EAC Complications	Cecal intubation rate/time EAC standard
Marsano *et al*[13] 2014	Retrospective chart review	New York	Academic, community	9/13-11/13	Screening, surveillance	318	NR	NR	ADR	47% 30%	NR	NR/NR NR/NR
Biecker *et al*[14] 2015	Randomized prospective 2-center RCT	Germany	Academic	2/13-8/13	Screening, surveillance, diagnostic	498	249 male (50%) 249 female (50%)	67 (56-75), Median (IQR)	Polyps/ procedure	35% 27%	Mucosal injury (9) Loss of cuff (6)	98%/NR 98%/NR
Floer *et al*[15] 2014	Randomized prospective 4-center RCT	Germany	Academic	2/14-7/14	Screening, surveillance, diagnostic	492	231 male (47%) 261 female (53%)	64 (54-73), Median (IQR)	ADR	35% 21%	Mucosal injury (18)	96%/NR 94%/NR
Tsiamoulos *et al*[16] 2015	Prospective observational single center	United Kingdom	Academic	4/13-9/14	Screening	399	NR	NR	ADR	69% 58%	Elective removal (1) Discomfort (1)	NR/7.5 min (mean) NR/9.5 min (mean)
van Doorn *et al*[17] 2015	Randomized prospective 5-center RCT	Netherlands	Academic	8/13-10/14	Surveillance, FIT positive, family history, diagnostic	1063	549 Male (51.6%) 514 Female (48.4%)	65, Median	Adenomas/ patient, ADR	54% 53%	Elective removal (22) Post-polypectomy bleeding (2) Thromboembolic event (1)	98%/7 min (median) 99%/8.3 min (median)
Shah *et al*[18] 2015	Retrospective chart review	California	Veterans Affair's Hospital	1/14-2/15	Screening, diagnostic	449	417 male (92.9%) 32 female (7.1%)	NR	ADR, SSADR	62% 49%	NR	NR/NR NR/NR
Cattau *et al*[19] 2015	Prospective randomized multi center RCT	Tennessee	Community	NR	Screening	658	317 male (48.2%) 341 female (51.8%)	58 ± 8, mean ± SD	ADR	50% 46%	NR	99%/NR 98%/NR
Grewal *et al*[20] 2015	Retrospective chart review	California	Academic	8/14-5/15	Screening, surveillance, diagnostic	1237	595 male (48.1%) 642 female (51.9%)	61 (54-69) Median (IQR)	SSADR	NR	NR	NR/NR NR/NR
Chin *et al*[21] 2015	Retrospective chart review	California	Academic	8/14-5/15	Screening	510	234 male (45.9%) 276 female (54.1%)	57 (52-61), Median (IQR)	ADR	56% 45%	NR	99%/12 min (mean) 97%/11 min (mean)

Chin, Karnes, Jamal, et al. World J Gastroenterol 2016.

Endpoints	#Patients	Studies	SC	EC
ADR	4387	9	43.3%	50.4%
Right Colon ADR	1326	3	24.0%	33.4%
Sessile Serrated Adenomas	1686	2	5.6%	11.6%

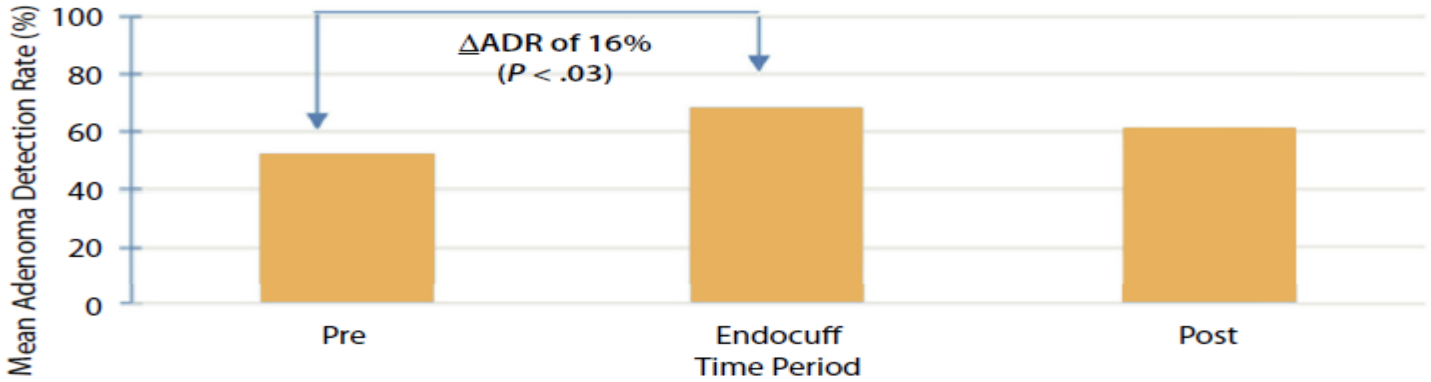
Chin, Karnes, Jamal, et al. World J Gastroenterol 2016.

Impact of a New Distal Attachment on Colonoscopy Performance in an Academic Screening Center

- 410 patients
  - 137 pre cuff group
  - 136 cuff group
  - 137 post cuff group

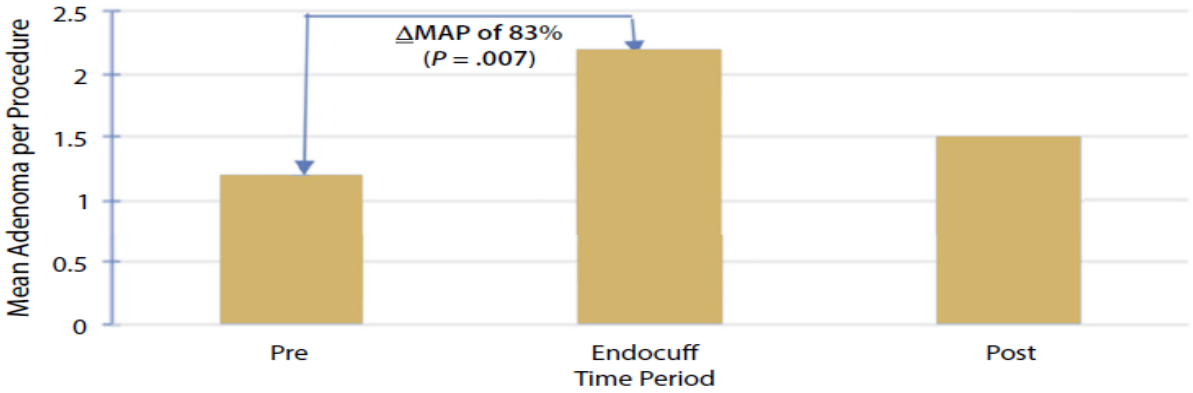
Tsiamoulos et al. GIE 2017.

Impact on ADR



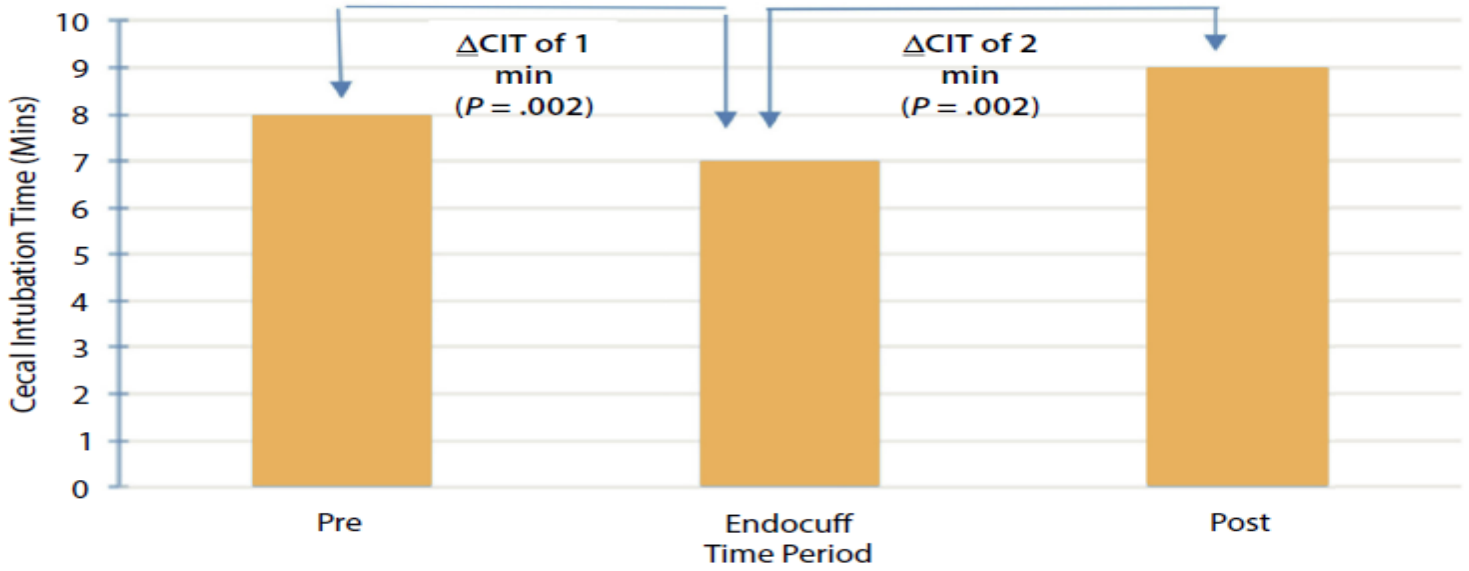
Tsiamoulos et al. GIE 2017.

Impact on MAP



Tsiamoulos et al. GIE 2017.

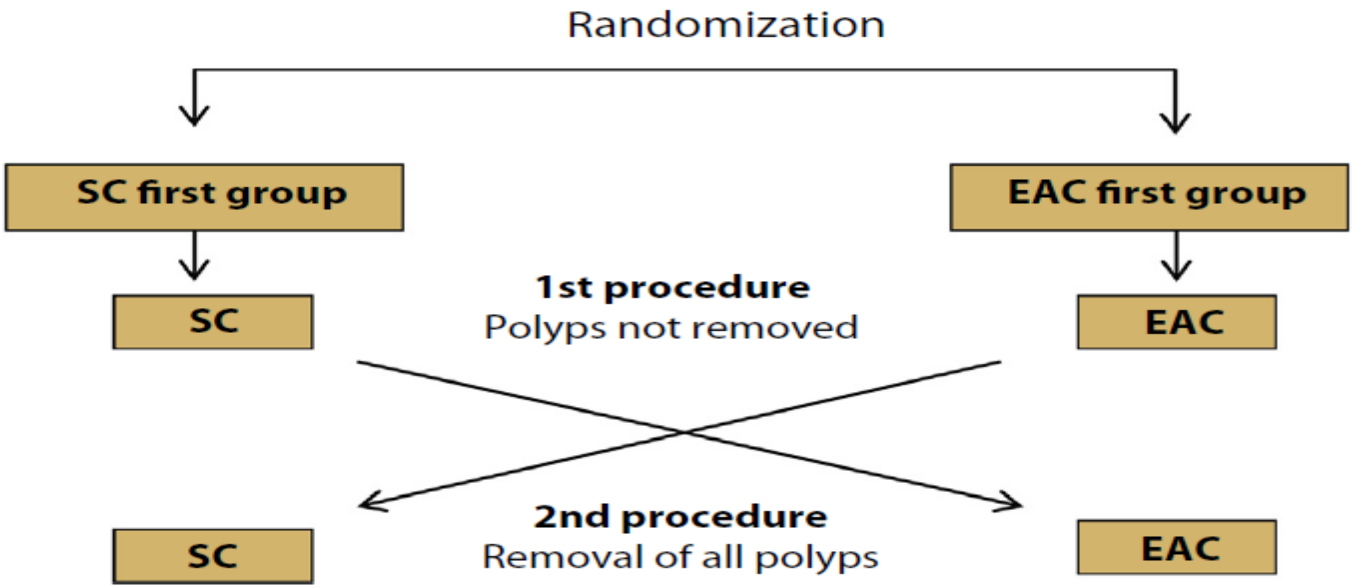
Impact on Cecal Intubation



Zacharias P. Tsiamoulos, MBBS PhD,

Tsiamoulos et al. GIE 2017.

Cap Cuff-assisted Colonoscopy Versus Standard Colonoscopy: Randomized Study



De Palma et al. GIE. 2017

Results

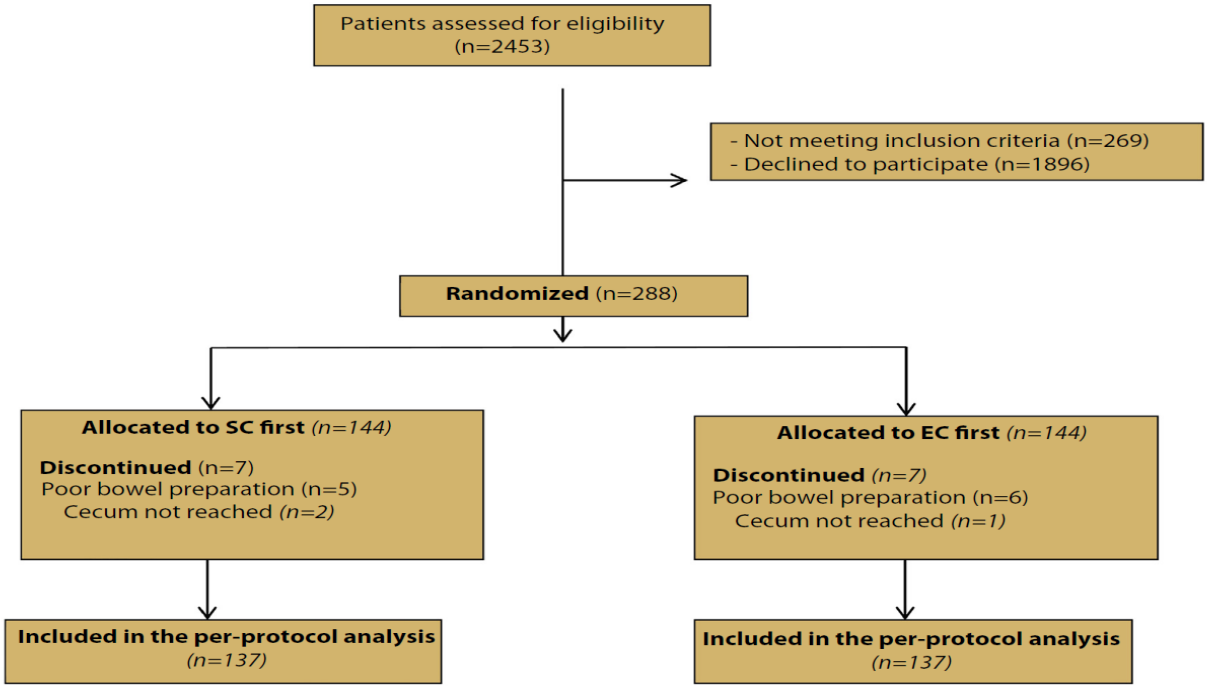


Figure 2. CONSORT diagram. *SC,* standard colonoscopy; *EAC,* EndoCuff-assisted colonoscopy.

De Palma et al. GIE. 2017

Impact on ADR

TABLE 3. Adenoma detected, overall results

	Standard colonoscopy	EndoCuff colonoscopy	*P* value
Patients with at least one adenoma (ADR), no. (%)	72 (26.3%)	81 (29.6%)	.002
Adenoma detected, no.	129	176	< .001
Adenoma detected by dimension, no.			
<5 mm	84	129	< .001
5-10 mm	29	35	.056
>10 mm	16	12	.317
Adenoma detected by location, no.			
Right side of colon	63	83	.002
Transverse colon	20	20	1
Left side of colon	46	73	.009

ADR, Adenoma detection rate.

De Palma et al. GIE. 2017

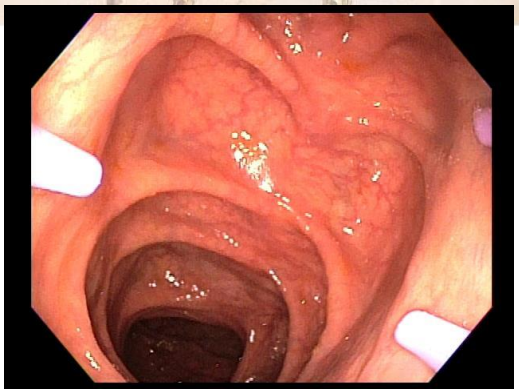
Impact on Surveillance

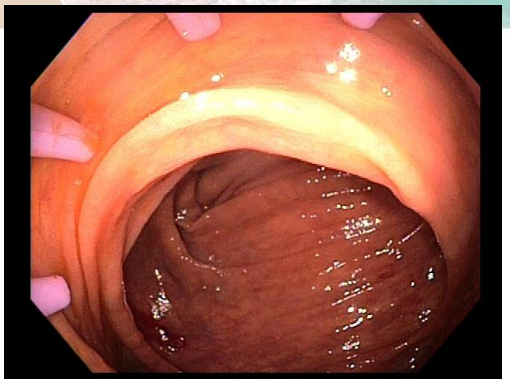
	U.S. guidelines	European Union guidelines
Standard colonoscopy shortened SI compared with EAC	4 pts (1.4%) 4 pts from 5-3 y	4 pts (1.4%) 1 pt from routine to 1 y 3 pts from routine to 3 y
EAC shortened SI compared with standard colonoscopy	20 pts (7.3%) 4 pts from 10-3 y 3 pts from 10-5 y 13 pts from 5-3 y	18 pts (6.6%) 1 pt from routine to 1 y 16 pts from routine to 3 y 1 pt from 3-1 y

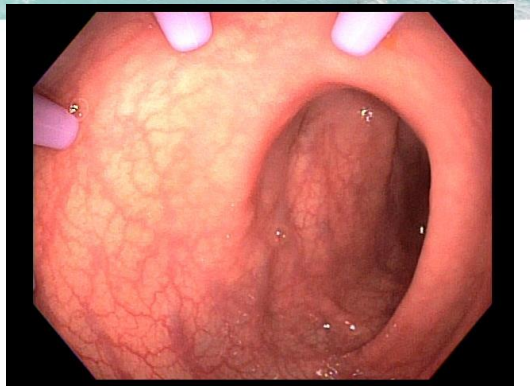
- Identified small adenoma throughout the colon resulting in increased ADR.

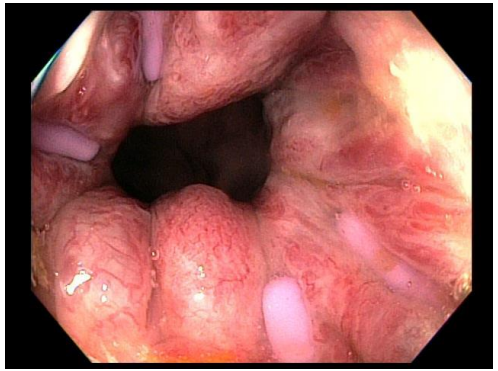
De Palma et al. GIE. 2017

Cuff Assisted Colonoscopy









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Conclusion

- ADR is a core quality metric for colonoscopy
- Colonoscopy is the best test, but polyps can be missed

  Decreased Blind Spots + Controlled withdrawal = Increased Adenomas

- Mechanical enhancements appear to be more beneficial then optical enhancements