



My Financial Disclosures:

Bayer

GI View

Takeda

Bio View

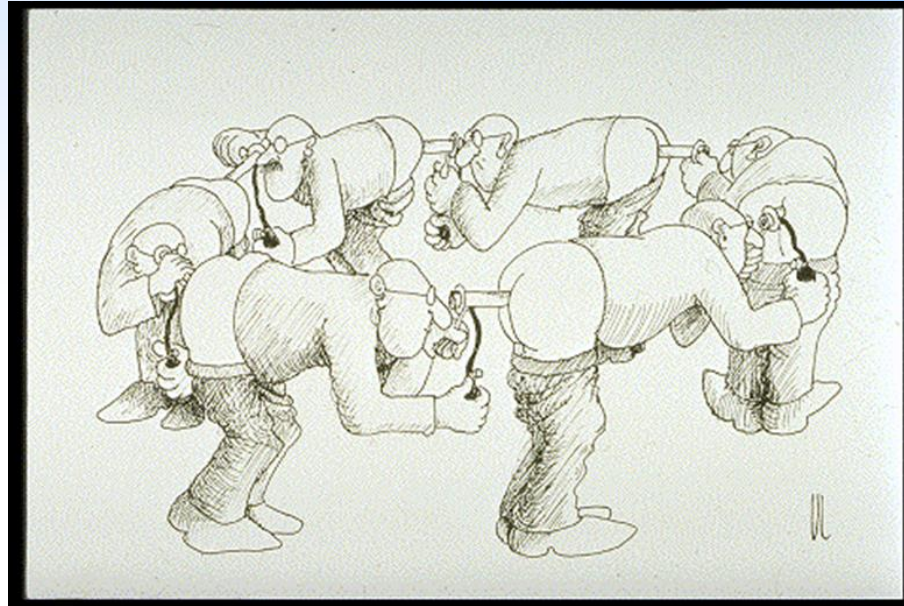
Check-Cap

Bio-Explorer

Nawe-Pharma

Nucleix

Can We Improve Screening Methods of CRC?



Nadir Arber MD, MBA, MSc

Health Promotion Center and

Integrated Cancer Prevention Center

Tel Aviv Medical Center and Tel Aviv University



Yes we can!!!

Ideal CRC Screening Test

- *Organized program*
- *High Uptake*
- *Test accuracy (**NPV**, PPV, Spec, Sens)*
- *Quality (FIT, colonoscopy, polypectomy)*
- *Costs*
- *Adherence to surveillance*
- *Reduced incidence of CR neoplasia*
- *Reduced specific morbidity*
- *Reduced specific mortality*
- *Reduced overall mortality*



Different Screening Modalities

- ▶ **Blood tests** (*Septin9, Medial, CD24*)
- ▶ **Stool Tests** (*FOBT, FIT, Cologuard, M2-PK*)
- ▶ **Sigmoidoscopy**
- ▶ **Colonoscopy**
- ▶ **CT-colonography**
- ▶ **Capsule endoscopy** (*Mea*)



When was the last time you looked down the l



The best screening test is the one that gets done

Each one has different preferences

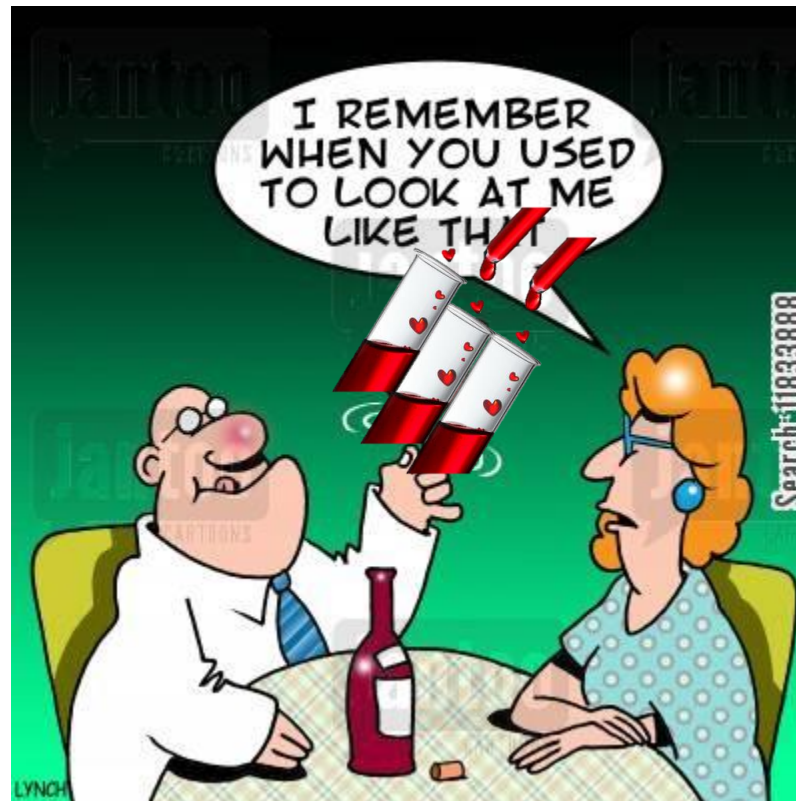


**No one likes
stool testing**



And you thought your job sucked

**Blood test is highly
desire but still does
not exist**



Low Public Compliance with CRC Screening

→
Colon Exam



Adapted from Jack Tippet, Saturday Evening Post



In 2017
Any Screening
Modality is Better
than Nothing

But colonoscopy is
still the best option



The New England Journal of Medicine

(2006; 355,1863)



ORIGINAL ARTICLE

Colonoscopy in Colorectal-Cancer Screening for Detection of Advanced Neoplasia

Jaroslav Regula, M.D., Maciej Rupinski, M.D., Ewa Kraszewska, M.Sc.,
Marcin Polkowski, M.D., Jacek Pachlewski, M.D., Janina Orlowska, M.D.,
Marek P. Nowacki, M.D., and Eugeniusz Butruk, M.D.

ABSTRACT

BACKGROUND

Recommendations for colorectal-cancer screening are based solely on age and family history of cancer, not sex.

METHODS

We performed a cross-sectional analysis of the data from a large colonoscopy-based screening program that included 50 148 participants who were 40 to 66 years of age

From the Department of Gastroenterology, Medical Center for Postgraduate Education, and the Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology (J.R., M.R., M.P., J.P., J.O., E.B.); and the Departments of Biostatistics (E.K.) and Colorectal

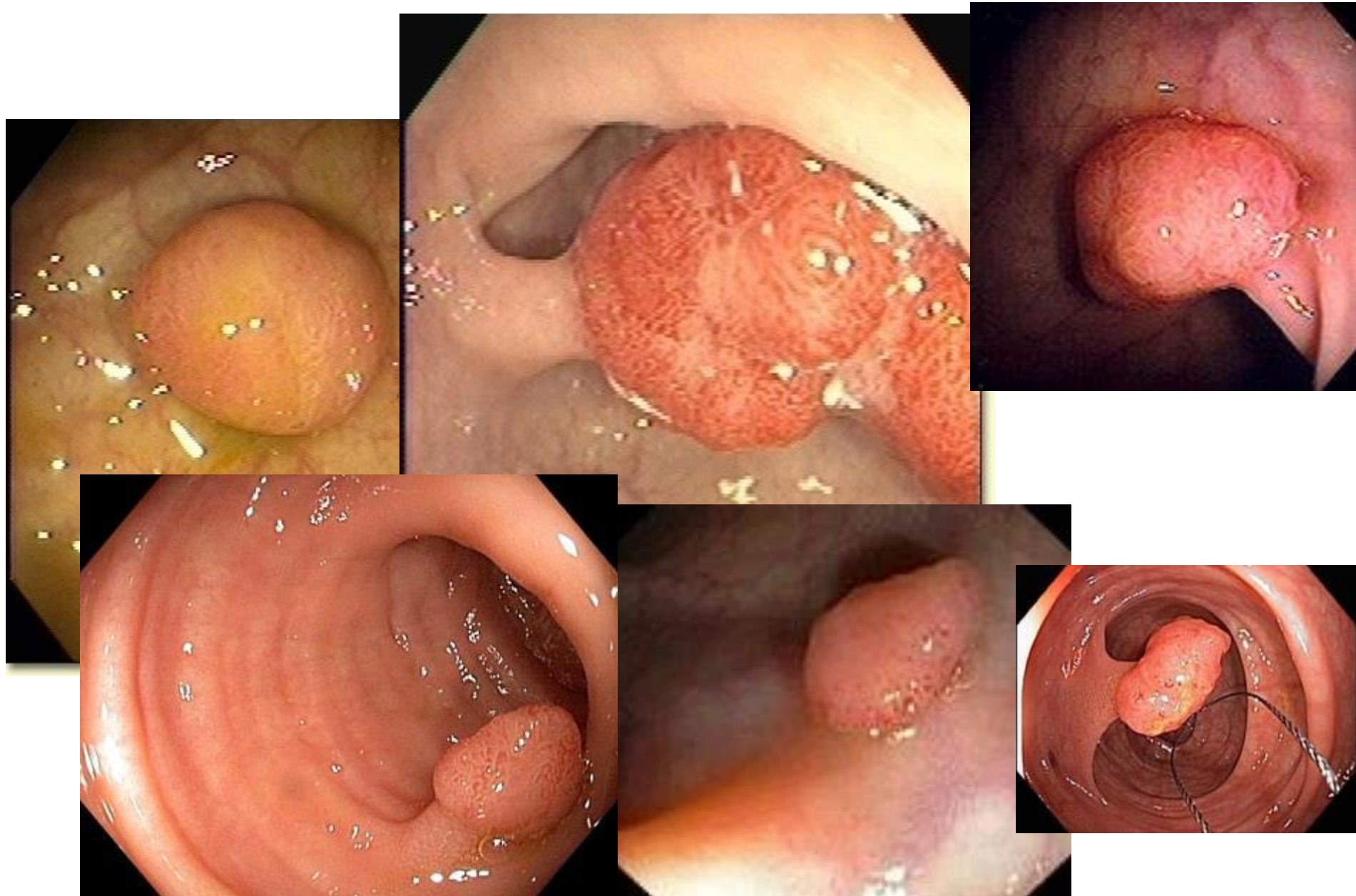
My wife is perfect.....

I think I am

**But colonoscopy
is definitely not
perfect...**



Adenomas are missed...



High ADR Decreases the Risk of Interval Cancer:

Colonoscopy-based CRC screening

186 endoscopists

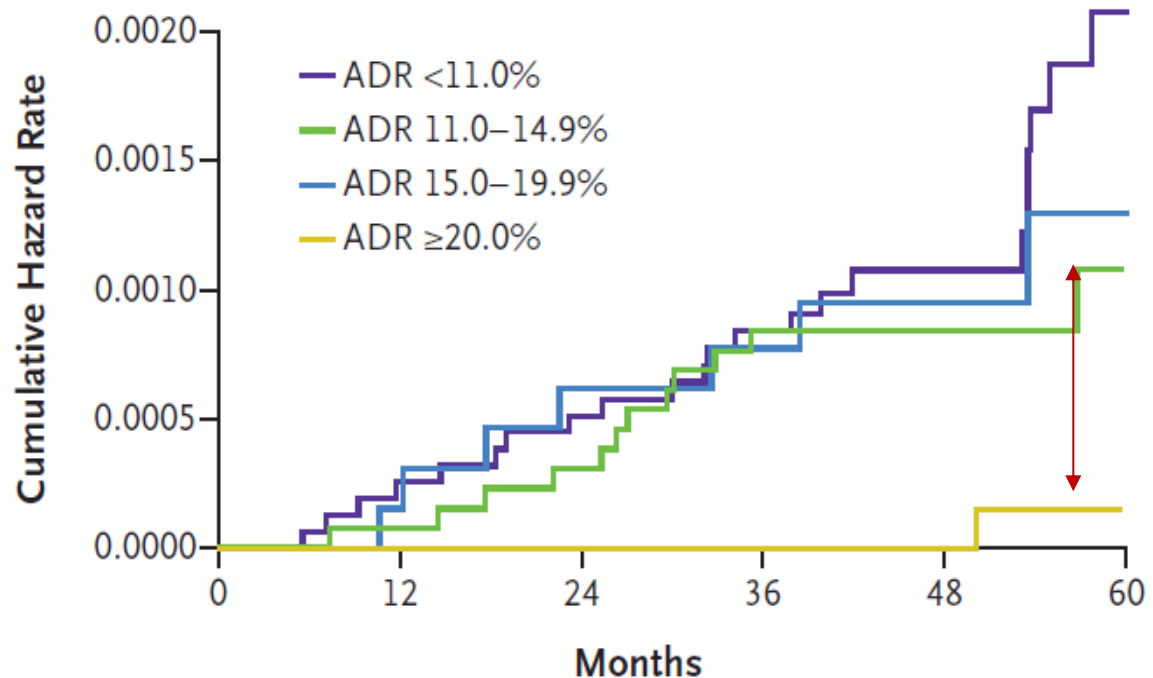
46,032 subjects

188,788 persons-years

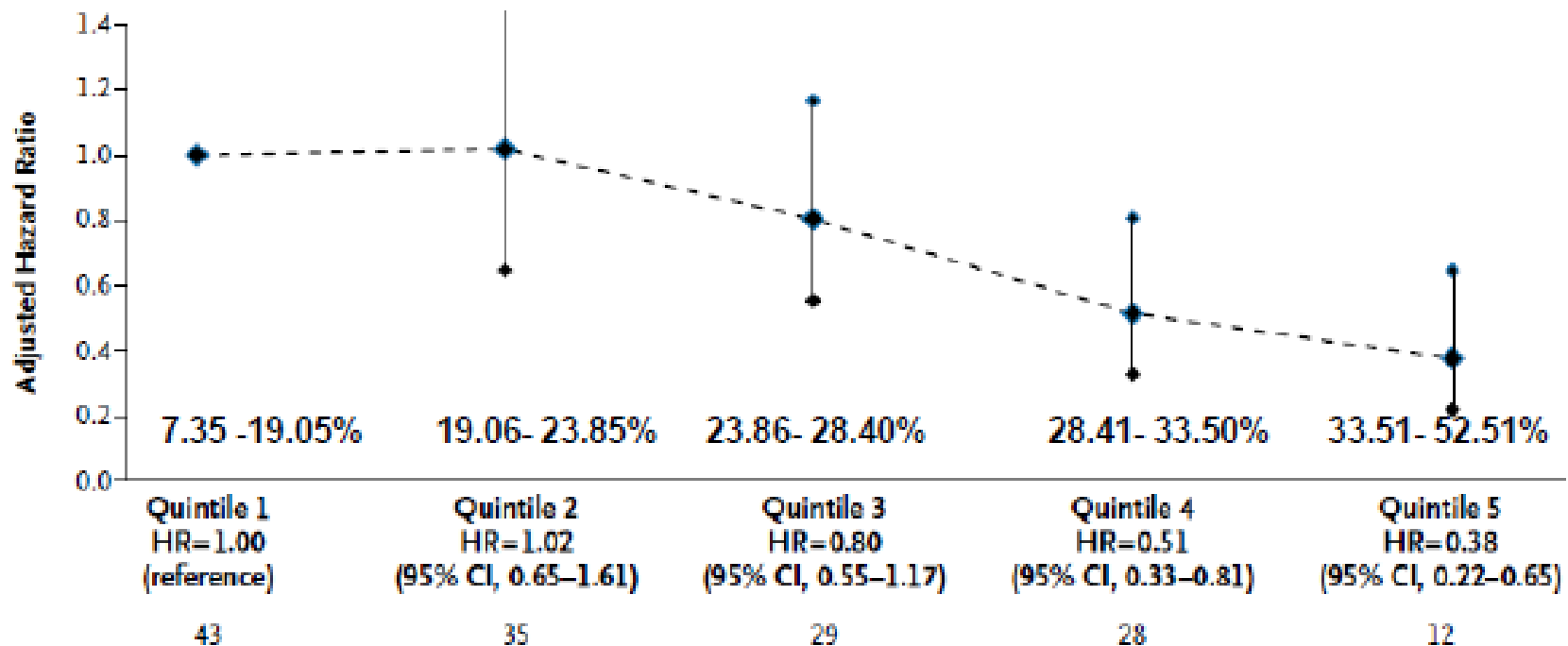
42 interval cancers

Interval cancers according to ADR:

Endoscopist ADR	HR (95% CI)
$\geq 20\%$	1
15-19.9%	12.50 (1.5-103.4)
11-14.9%	10.75 (1.3-85.0)
< 11%	10.94 (1.3-87.0)



High ADR Decreases the Risk of CRC Death:



Each 1% ADR increase = 5% decrease in CRC death

Why Do We Miss Adenomas?

- Inadequate colon prep
 - Flat/depressed lesions
 - Colon anatomy (proximal folds and flexures)
 - Suboptimal technique
 - Short withdrawal time
 - Missing cecal intubation
- } **Low ADR**
- **Current technology limitations**

ORIGINAL ARTICLE

Quality Indicators for Colonoscopy and the Risk of Interval Cancer

Michal F. Kaminski, M.D., Jaroslaw Regula, M.D., Ewa Kraszewska, M.Sc.,
Marcin Polkowski, M.D., Urszula Wojciechowska, M.D., Joanna Didkowska, M.D.,
Maria Zwierko, M.D., Maciej Rupinski, M.D., Marek P. Nowacki, M.D.,
and Eugeniusz Butruk, M.D.



Quality Colonoscopy

- **Bowel Prep given in split doses**
- **Cecum should be intubated and documented by photography**
- **Colonoscopists should measure adenoma detection rate**
 - **20% in women**
 - **30% in men**
- **Withdrawal time in negative screening exams should average at least 6 minutes**



Improving Polyps Detection

- *Extra Wide Angle View Endoscope (Olympus)*
- *Full Spectrum Endoscopy (EndoChoice)*
- *Third Eye Retroscope and Panoramic*
- *Aer-O-scope (GI-View)*
- *G-Eye (Pentax)*
- *EndoCuff (Medivator)*
- *EndoRings (Endoaid)*
- *Colonic Capsule (Medtronic)*
- *Prepless Colonic Capsule (Check-Cap)*



Mechanical Fold Flattening Approach



**Cap assisted
colonoscopy**



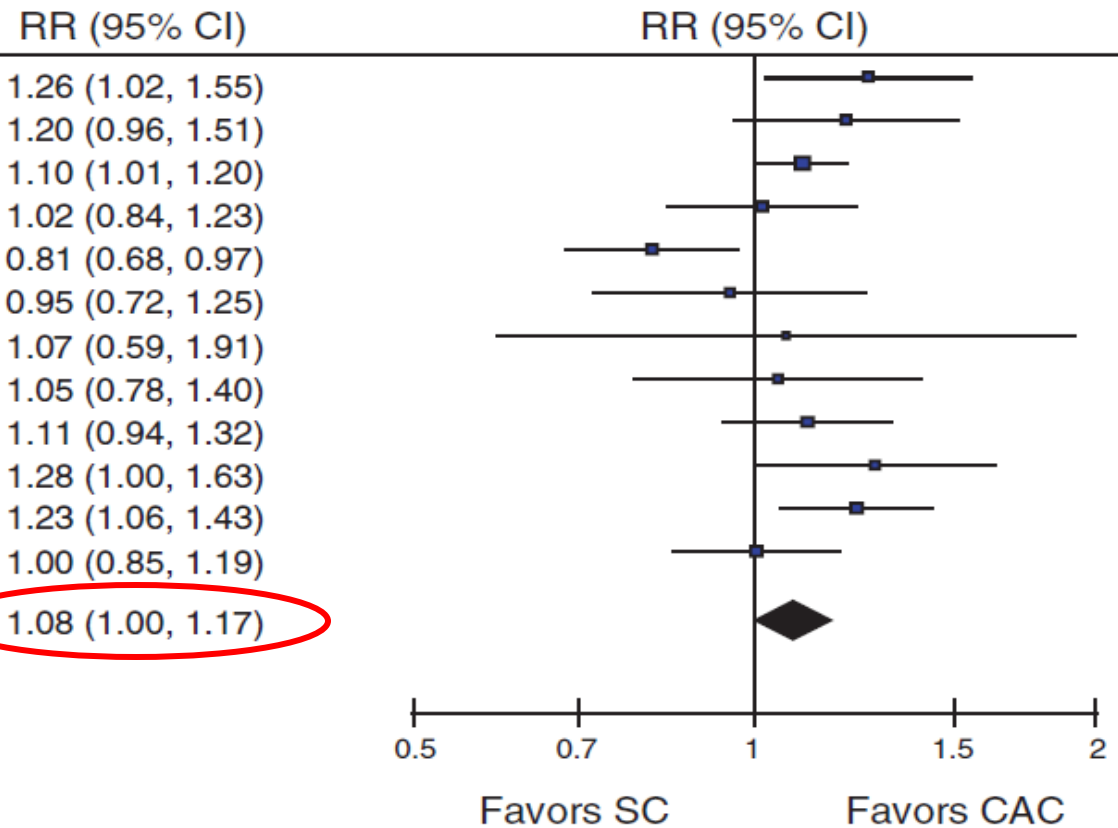
**Endocuff/
Endoings
Endoscopic Over
tube**



**G-EYE™
Colonoscope**

Cap-Assisted Colonoscopy: A Meta-Analysis with Borderline Efficacy

Endpoint = Polyp Detection

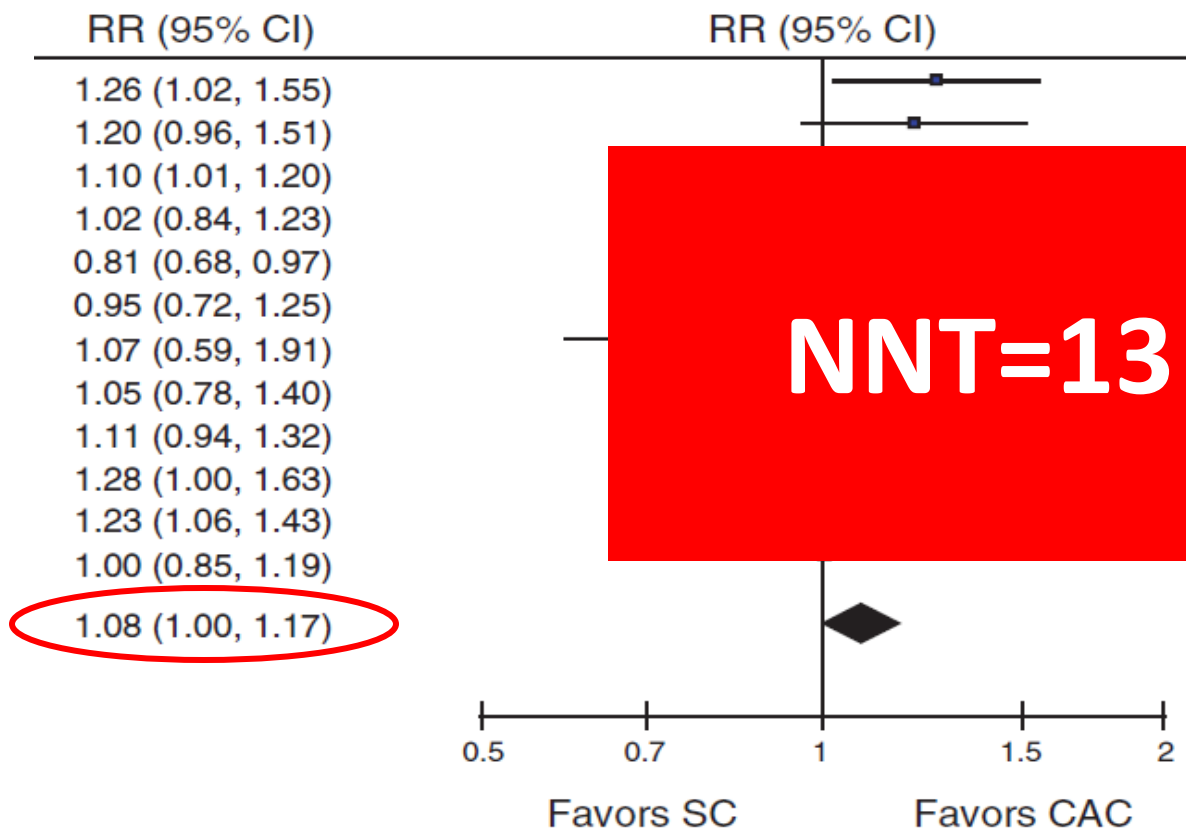


16 RCTs, n= 8,991

Phol et al. Endoscopy 2015, Ng SC et al. Am J Gastroenterol 2012

Cap-Assisted Colonoscopy: A Meta-Analysis with Borderline Efficacy

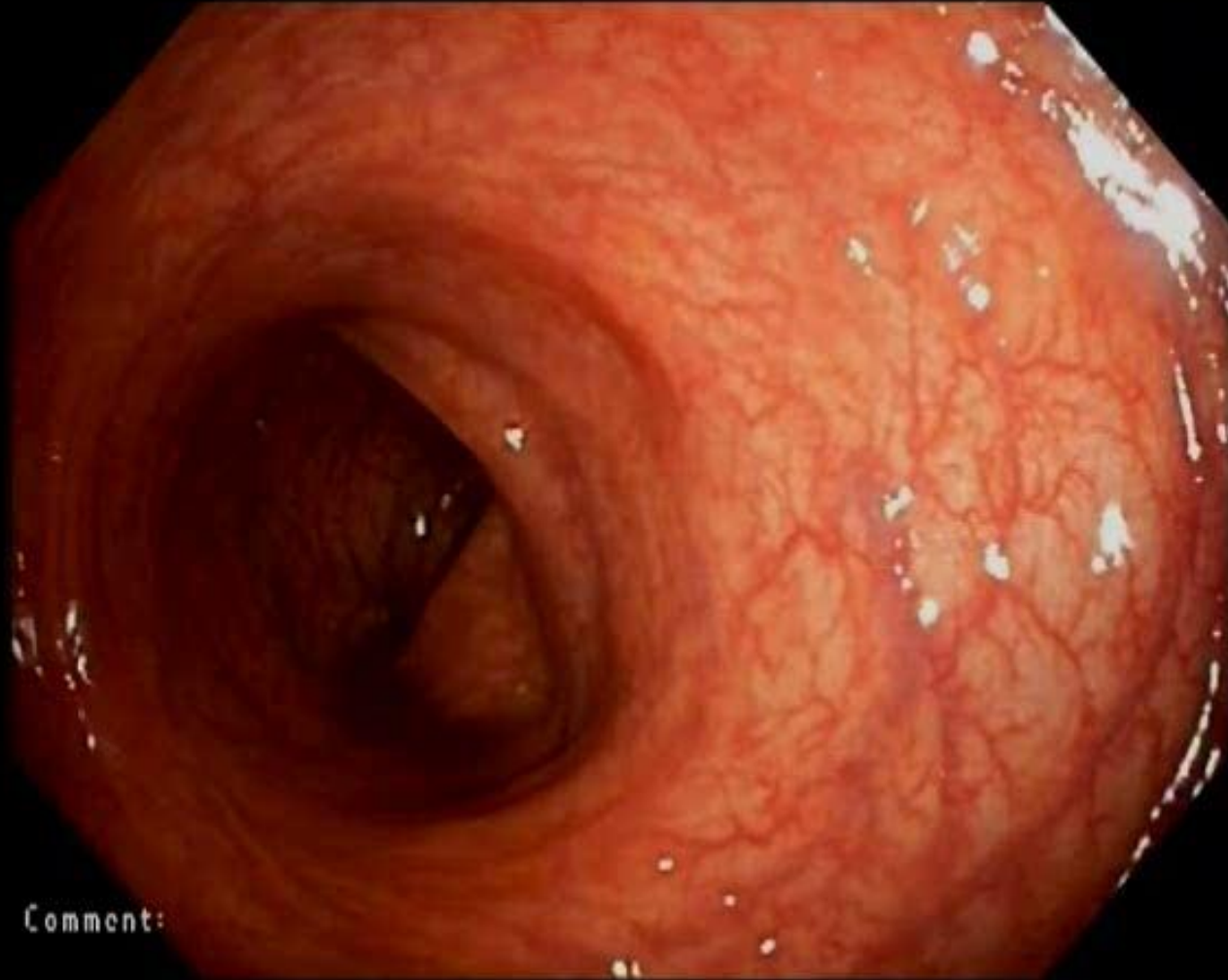
Endpoint = Polyp Detection



16 RCTs, n= 8,991

Phol et al. Endoscopy 2015, Ng SC et al. Am J Gastroenterol 2012

Cap-Assisted Colonoscopy



NaviAid™ G-EYE™ Balloon-Colonoscope

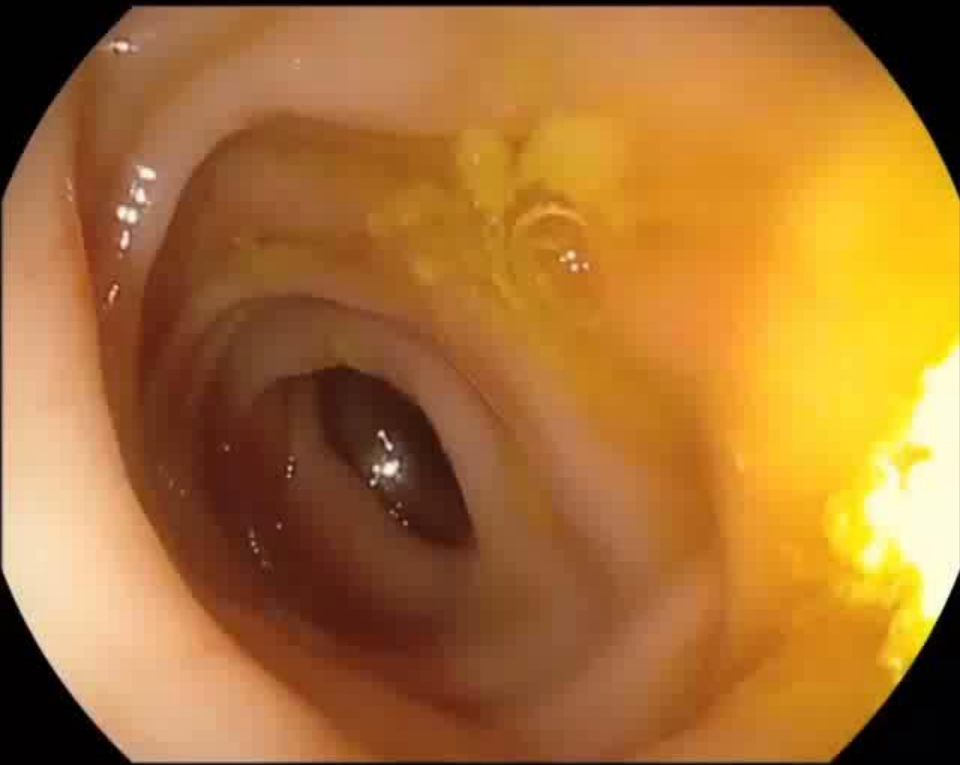
SMART Medical Systems, Ra'anana, Israel

- Pentax colonoscope with permanently integrated, reusable balloon
- Balloon inflated by the endoscopist (foot pedal) through the colonoscope internally, no external mounted accessories
- Cecum with balloon deflated
 - ✓ Balloon inflated to engage the colon walls & withdrawn
 - ✓ Mechanical straightening of folds & flexures

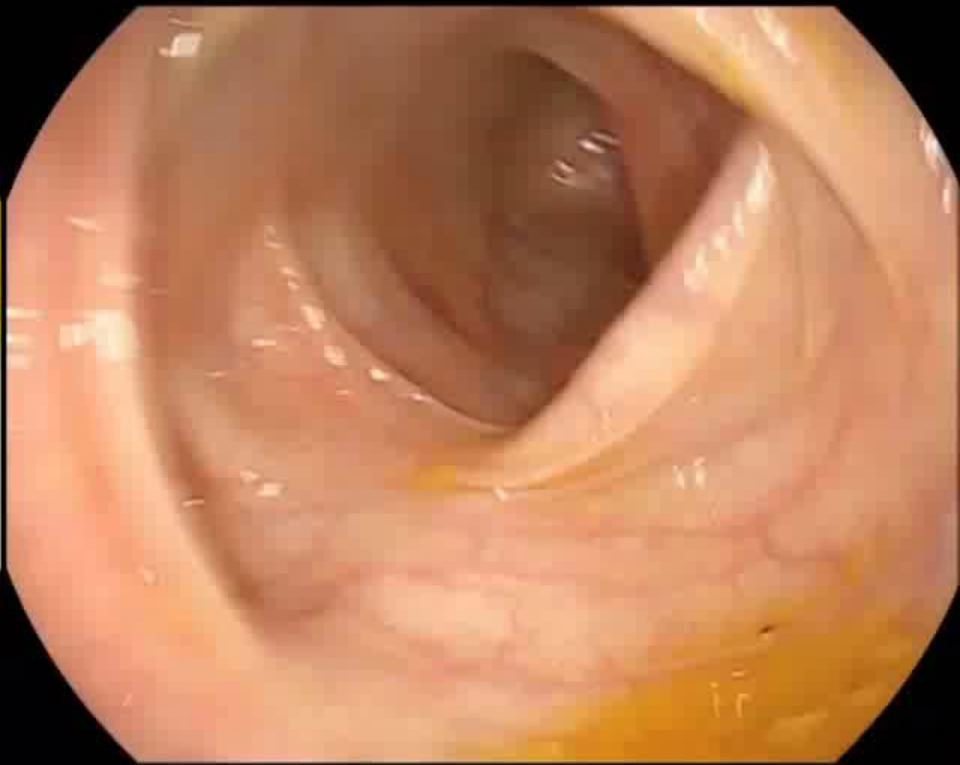


NaviAid™ G-EYE™

Balloon Deflated



Balloon Inflated



EndoCuff™ (Medivators)



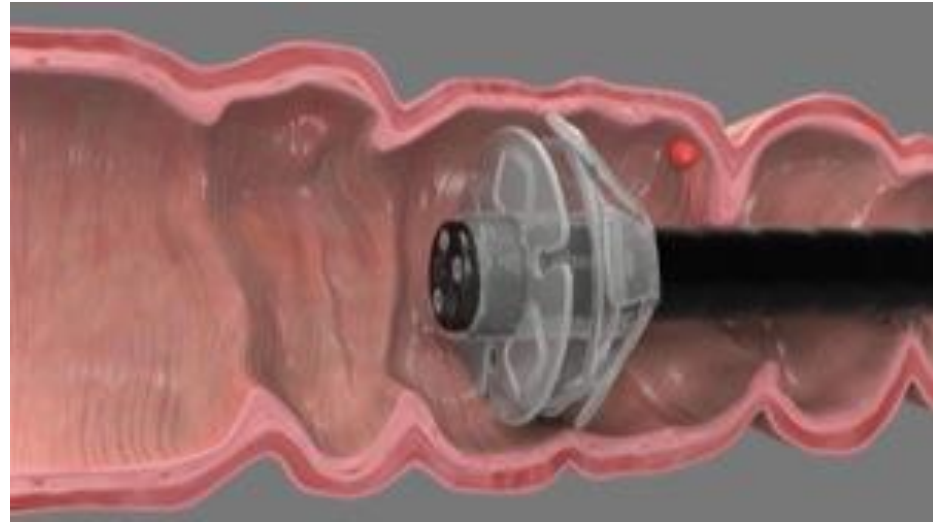
EndoCuff™

- *RCT, 2 centers, n=498*
- *Colonoscopy with and without endocuff,*
- *EC - 63% more polyps detected*
- *PDR = **EC 56%** vs **no EC 42%**, $p=0.001$*
- *EC – significantly more polyps (<1cm) detected in **cecum** ($p=0.001$) and **sigmoid** ($p=0.002$)*
- ***ADR** significantly increased by **86%** ($P=0.002$)*
- *No adverse events*

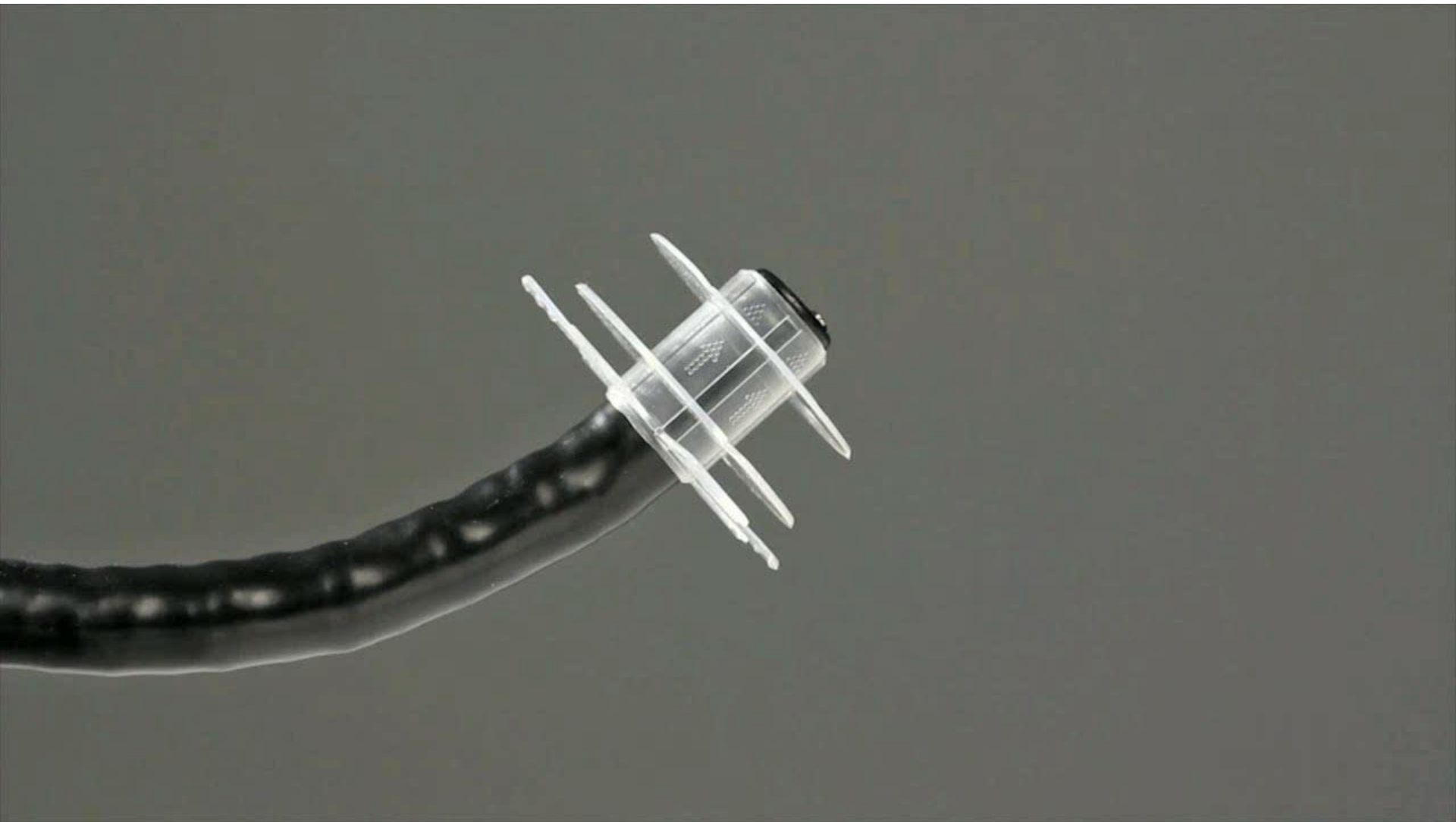


EndoRings™

EndoAid, Israel



The Beauty of Simplicity



EndoRings – CLEVER Study

- **RCT, N=116** *Dik, Siersema, Gralnek et al. (Endoscopy, 2015)*
- **Tandem colonoscopy design,**
- **Study endpoint = adenoma miss rate**
 - **With endorings = 15%**
 - **Without endorings = 48%, $p < 0.01$**
- **Time to cecum (9.6 min vs. 8.1 min, $p=0.17$)**
- **Withdrawal times (7.2 vs. 6.8 min, $p=0.14$)**
- **No adverse events**

Improving Polyps Detection “Inspection Behind Folds”

Optical Approach



The third eye



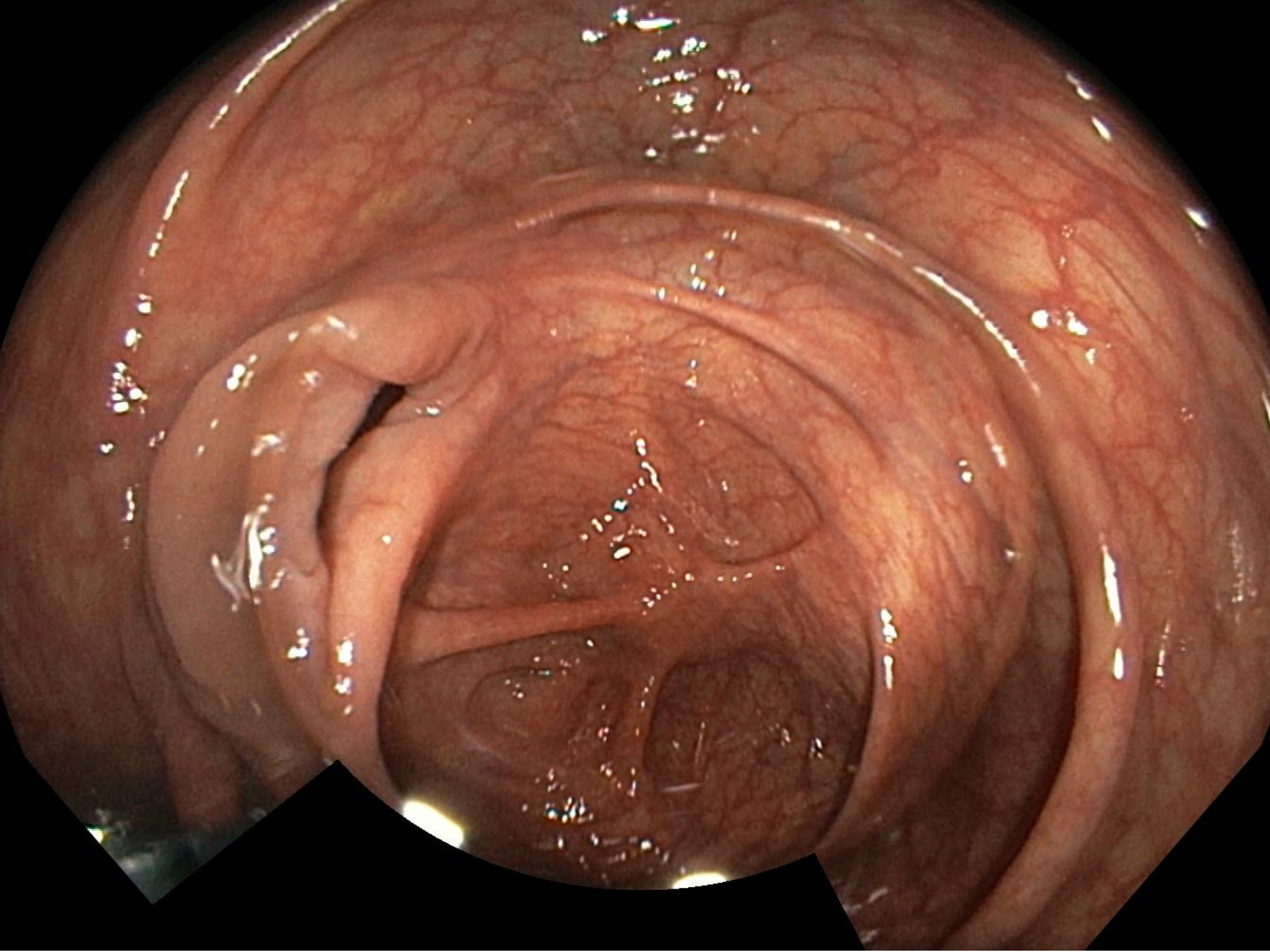
**FUSE full
spectrum
endoscopy**



Omnivision

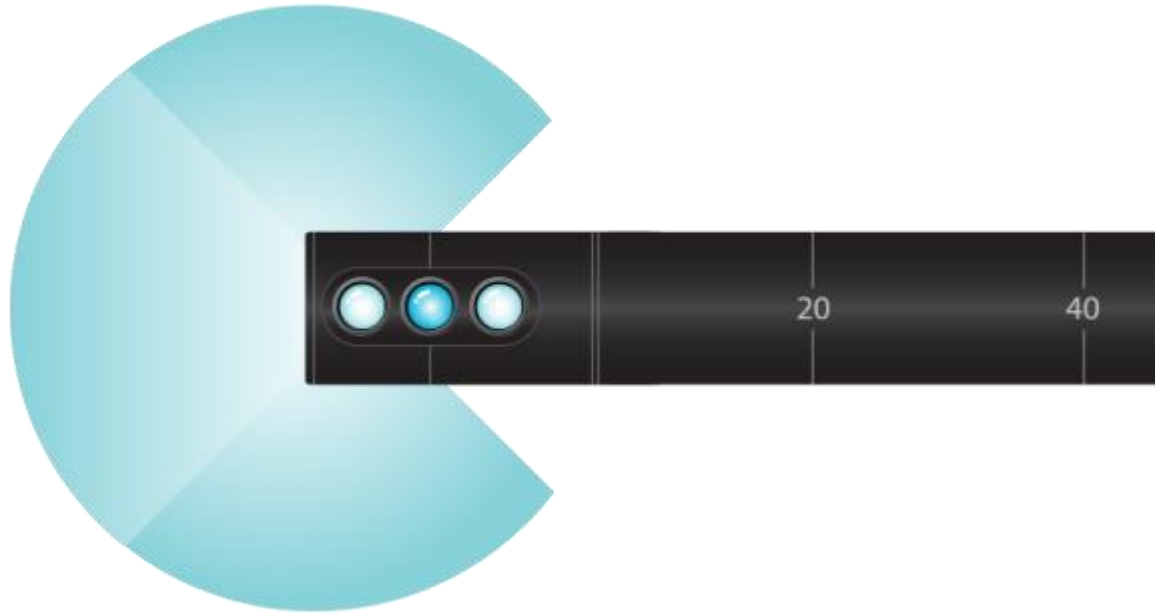
Extra Wide Angle View Endoscope (Ewave)







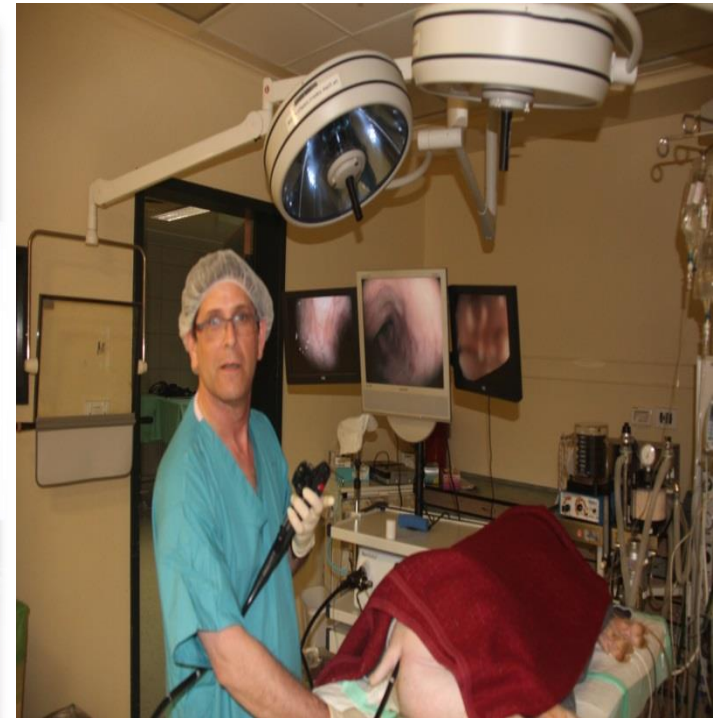
330°
Field of View



The Fuse Story



- ◆ **Kitchen trial: home made colon model**
- ◆ **Animal Lab : 3 screens**





The Fuse Study

Gralnek et al. Lancet Oncol 2014

	SFV followed by Fuse (n=88)	Fuse followed by SFV (n=97)	p-value
Age, years (mean \pm SD)	55.9 \pm 9.5	55.7 \pm 9.7	0.88
Gender, female (%)	46 (52.3%)	55 (56.7%)	0.55
Ottawa Bowel Preparation Score (mean \pm SD)	3.4 \pm 2.6	3.4 \pm 2.8	0.89
Indication for Colonoscopy			
Screening n, (%)	53 (60.2%)	50 (51.5%)	0.24
Surveillance n, (%)	16 (18.2%)	20 (20.6%)	0.68
Diagnostic Evaluation n, (%)	19 (21.6%)	27 (27.9%)	0.33
Additional Adenomas Detected	69%	8%	p<0.0001
Adenoma Miss Rate	20/49 (40.8%)	5/67 (7.5%)	p<0.0001
ADR	30/88 (34.1%)	34/97 (35.1%)	0.89

FUSE Study in Italy – Not that Promising



Arnaldo Amato², Andrea Anderloni³, Franco Armelao⁵, Arrigo Arrigoni¹, Maurizio Cavina⁶, Giovanni DePretis⁵, Gianpiero Manes⁴, Gianni Miori⁵, Alessandra Mondardini¹, Franco Radaelli², Alessandro Repici³, Romano Sassatelli⁶, Nereo Segnan⁸,
Cesare Hassan⁷

Endoscopy Unit, AOU Città della Salute e della Scienza – Ospedale San Giovanni Antica Sede, Turin¹; Endoscopy Unit, Ospedale Valduce, Como²; Endoscopy Unit, Istituto Clinico Humanitas, Rozzano (Milan)³; Endoscopy Unit, Ospedale di Circolo, Rho (Milan)⁴; Endoscopy Unit, Ospedale S Chiara, Trento⁵; Endoscopy Unit, IRCCS S Maria Nuova, Reggio Emilia⁶; Endoscopy Unit, Ospedale Nuovo Regina Margherita, Rome⁷; AOU Città della Salute e della Scienza, CPO Piemonte, Turin⁸.

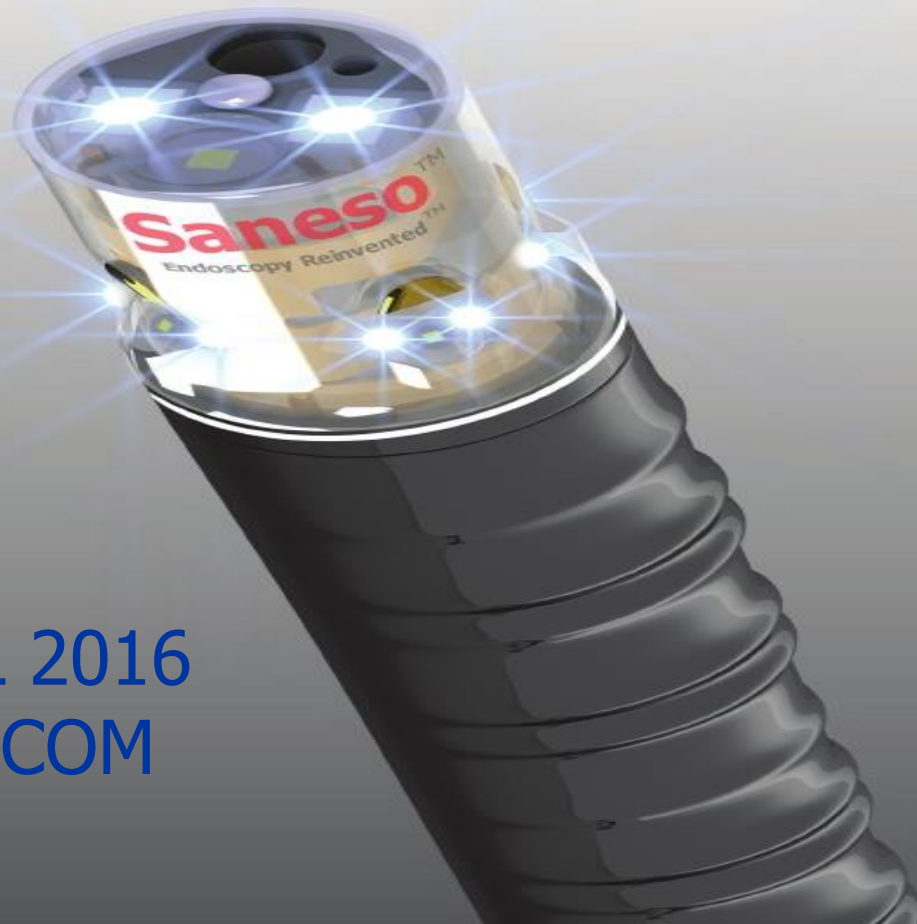
FUSE Study in Italy – Not that Promising



Arnaldo Amato², Andrea Anderloni³, Franco Armelao⁵, Arrigo Arrigoni¹,
Maurizio Cavina⁶, Giovanni DePretis⁵, Gianpiero Manes⁴, Gianni Miori⁵,
Alessandra Monfardini¹, Franco Radaelli², Alessandro Repici³, Romano
Sassatelli⁶, Nereo Segnan⁸,
Cesare Hassan

Endoscopy Unit, AOU Città della Salute e della Scienza – Ospedale San Giovanni
Antica Sede, Turin¹; Endoscopy Unit, Ospedale Valduce, Como²; Endoscopy
Unit, Istituto Clinico Humanitas, Rozzano (Milan)³; Endoscopy Unit, Ospedale di
Circolo, Rho (Milan)⁴; Endoscopy Unit, Ospedale S. Maria, Trento⁵; Endoscopy
Unit, IRCCS S Maria Nuova, Reggio Emilia⁶; Endoscopy Unit, Ospedale Nuovo
Regina Margherita, Rome⁷; AOU Città della Salute e della Scienza CPO
Piemonte, Turin⁸.

SanesoTM
Endoscopy ReinventedTM

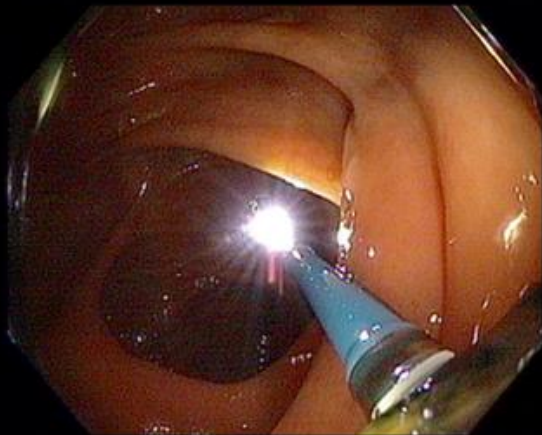


ARRIVING FALL 2016
WWW.SANESO.COM

Third Eye Retroscope



- *Device that passes through scope channel*
 - *Automatically retroflexes 180°*
 - *Provides forward and backward view simultaneously on side-by-side monitor*
- Courtesy of Prof. Jerry Way*



Forward View



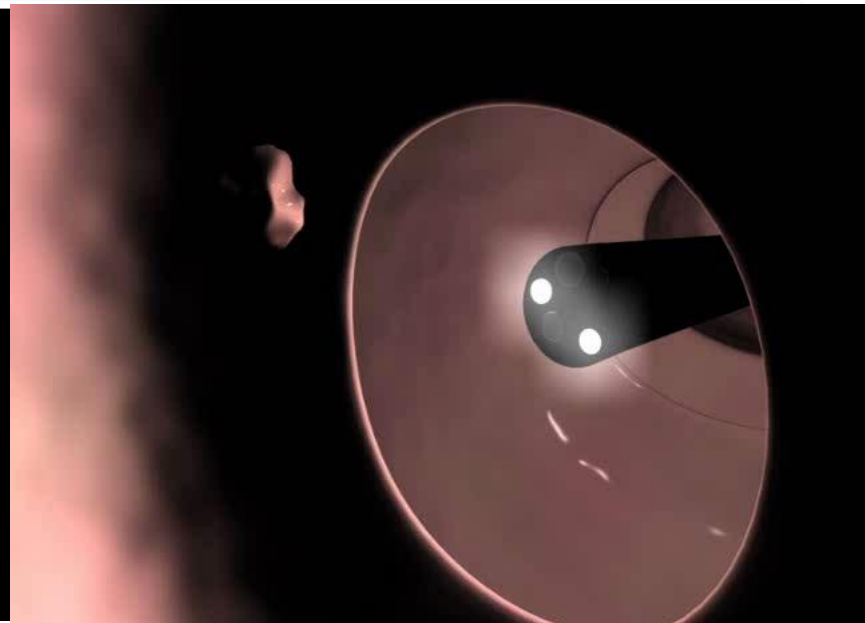
Retrograde View

TER: Leufkens et al. GIE 2011

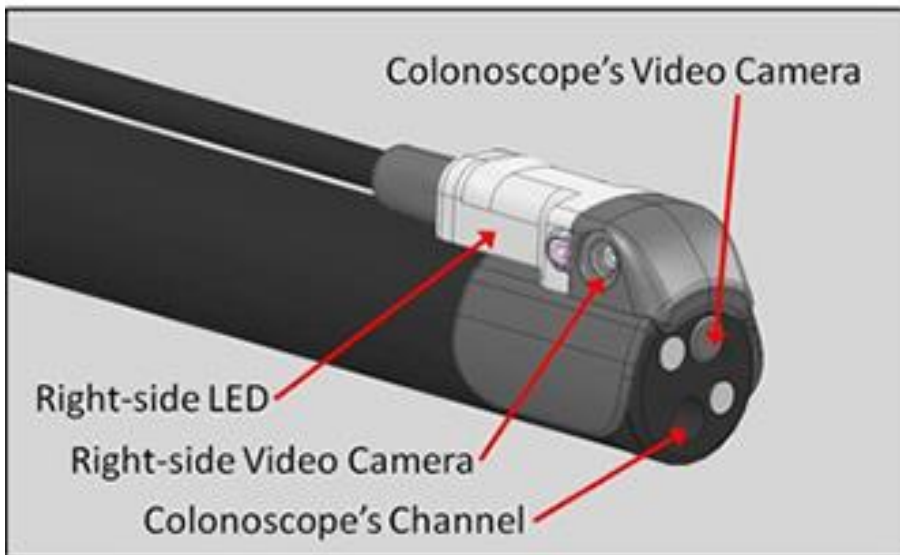
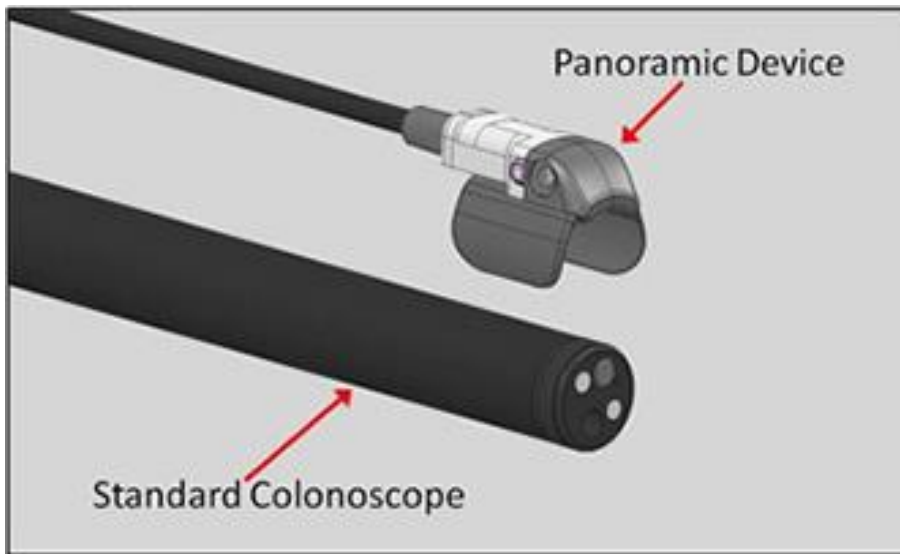
N=349		<u>Adenoma Miss Rates</u>	<u>Additional Adenomas Detected</u>
	VS.	SFV 31.4%	SFV 22.6%
		TER 18.4%	TER 45.8%
SFV colonoscopy			
Third-Eye Retroscope			

Limitations of Third Eye:

- 1. Not user friendly***
- 2. Takes up working channel***
- 3. Increases procedure time***
- 4. Costs***



Third-Eye Panoramic (Avantis)



- Pilot and feasibility
- Single use device
- CMOS chips, LEDs
- N=17
- 100% cecal intubation

Aer-O-Scope™ Key Advantages

- *OMNI-directional 360° vision*
- *Joystick controlled self propelled colonoscope*
- *Scanner induces lower pressure on the colonic wall*
- *Extremely safe system*
- *Disposable*
- *Single operator*
- ***The only available FDA approved self propelled colonoscope***



Aer-O-Scope® (Israel)

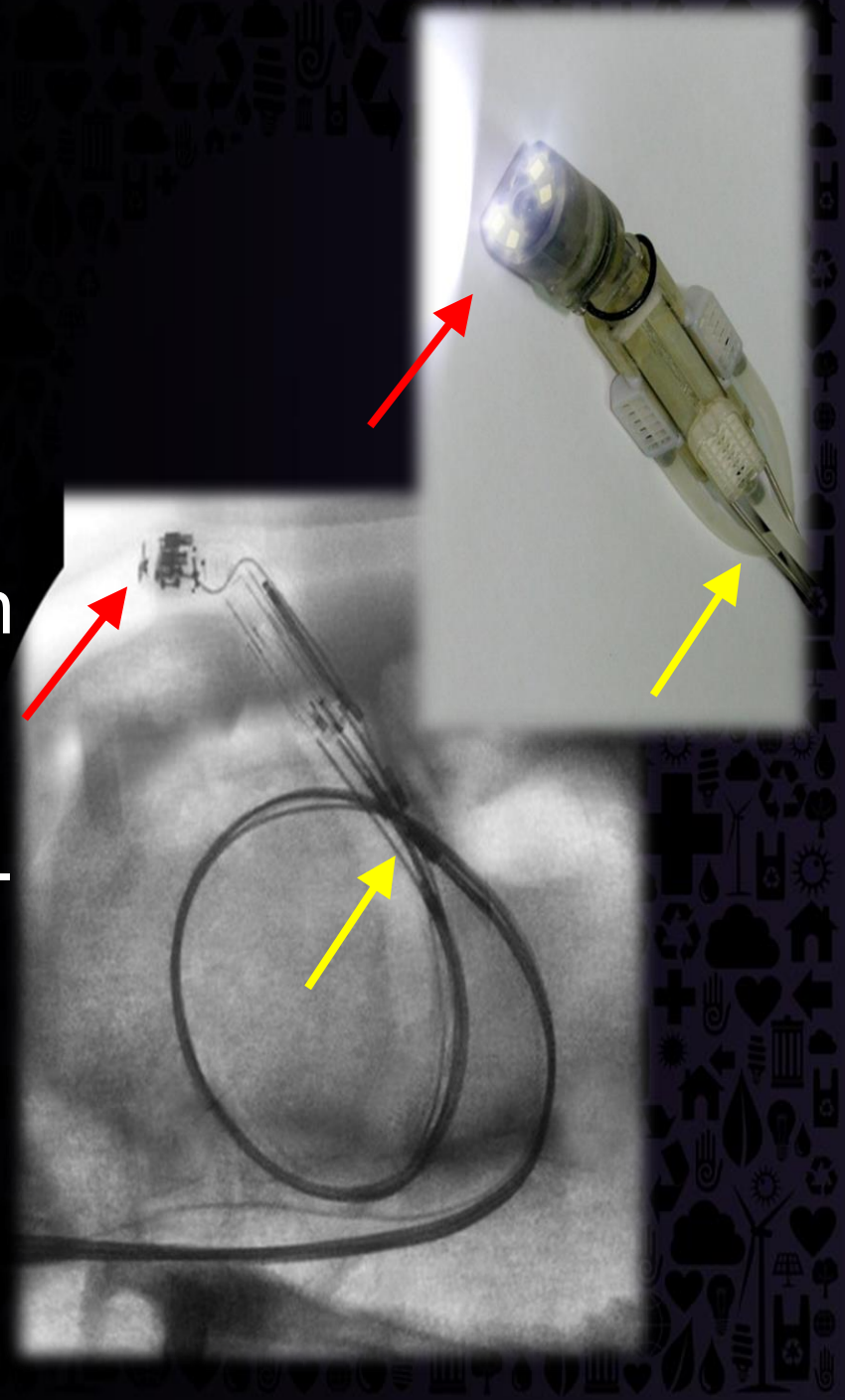


**AER-O-SCOPE™ Colonoscope
System by GI View Ltd.**



Motus GI

- ◆ Started in Boris house in Nazareth as a self-propelled single use colonoscope
- ◆ First funded an Arab - Jewish incubator
- ◆ *Changed direction* to an add-on device that cleans the colon during colonoscopy



PURE-VU (Israel)

Motus – Clinical Trial Real Movie ...

Still not FDA approved



Capsule Endoscopy

Overcome invasiveness



02:40:14

15 Feb 12

VR



PillCam[®] COLON 2

Pillcam Colonoscopy: What did we learn?



■ ESGE 2012

- Average risk patients
- Incomplete colonoscopy
- Unwilling to undergo conventional colonoscopy
- Colonoscopy contraindicated

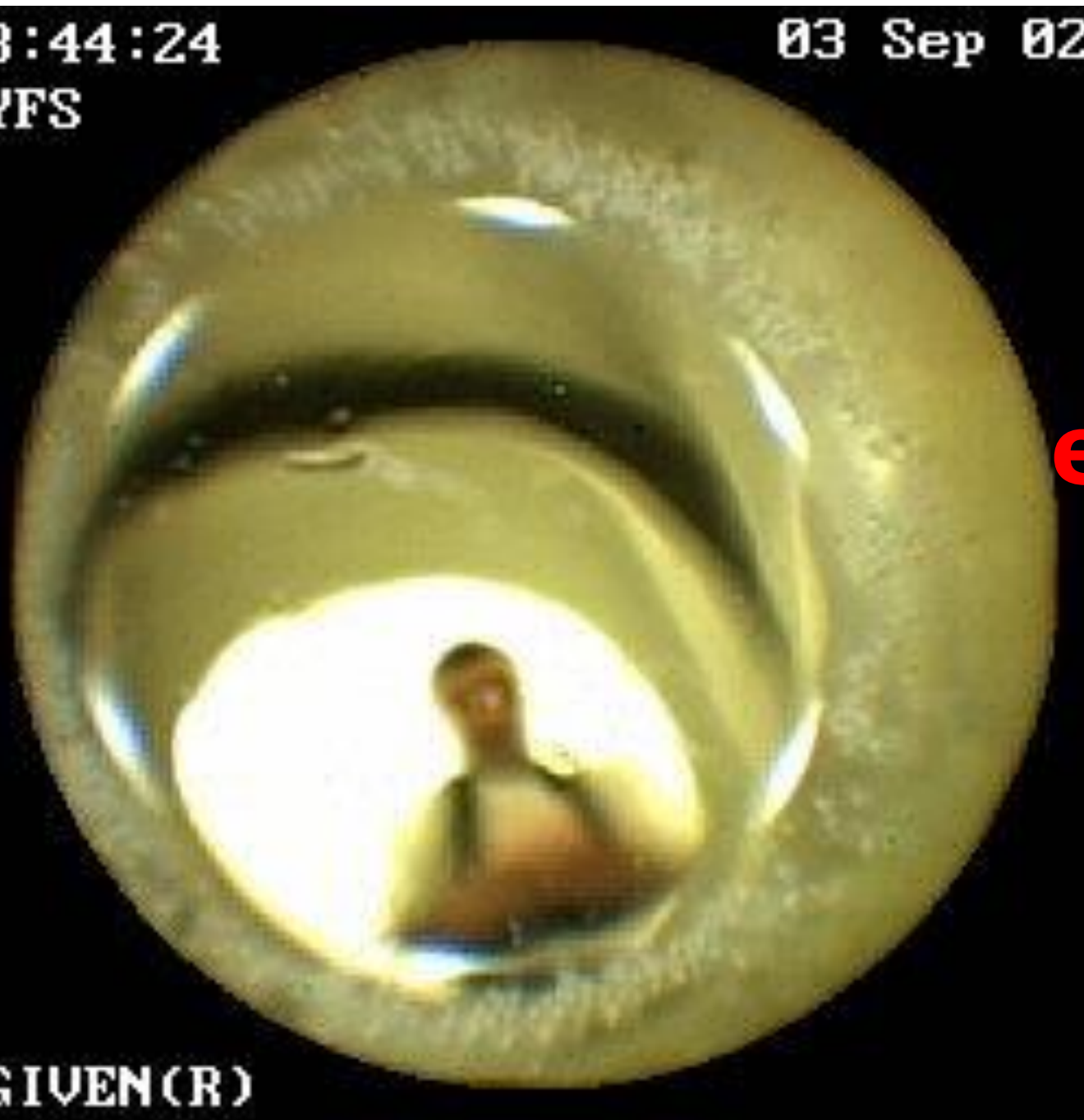
■ FDA 2014

- Incomplete colonoscopy
- Colonoscopy contraindicated

For	Against
Patient preference	Physician preference Novelty Training Remuneration
Increased capacity	Increased work load
Pan-endoscopy	Histology
Non medical reading	Intervention
Increased access	Cost
Safety?	Time Lag

3:44:24
YFS

03 Sep 02



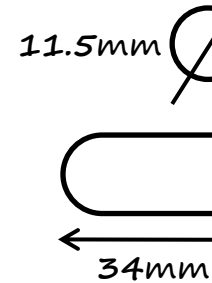
**An
expensive
Selfi!!!!**

**Courtesy:
Rami Eliakim**

GIVEN(R)

Prepress Capsule Colonoscopy: Ultra Low Dose X-ray-Based Imaging Technology (Check-Cap, Israel)

- Ultra-low dose (0.03 mSv)
- Low energy (56 – 70 Kev)

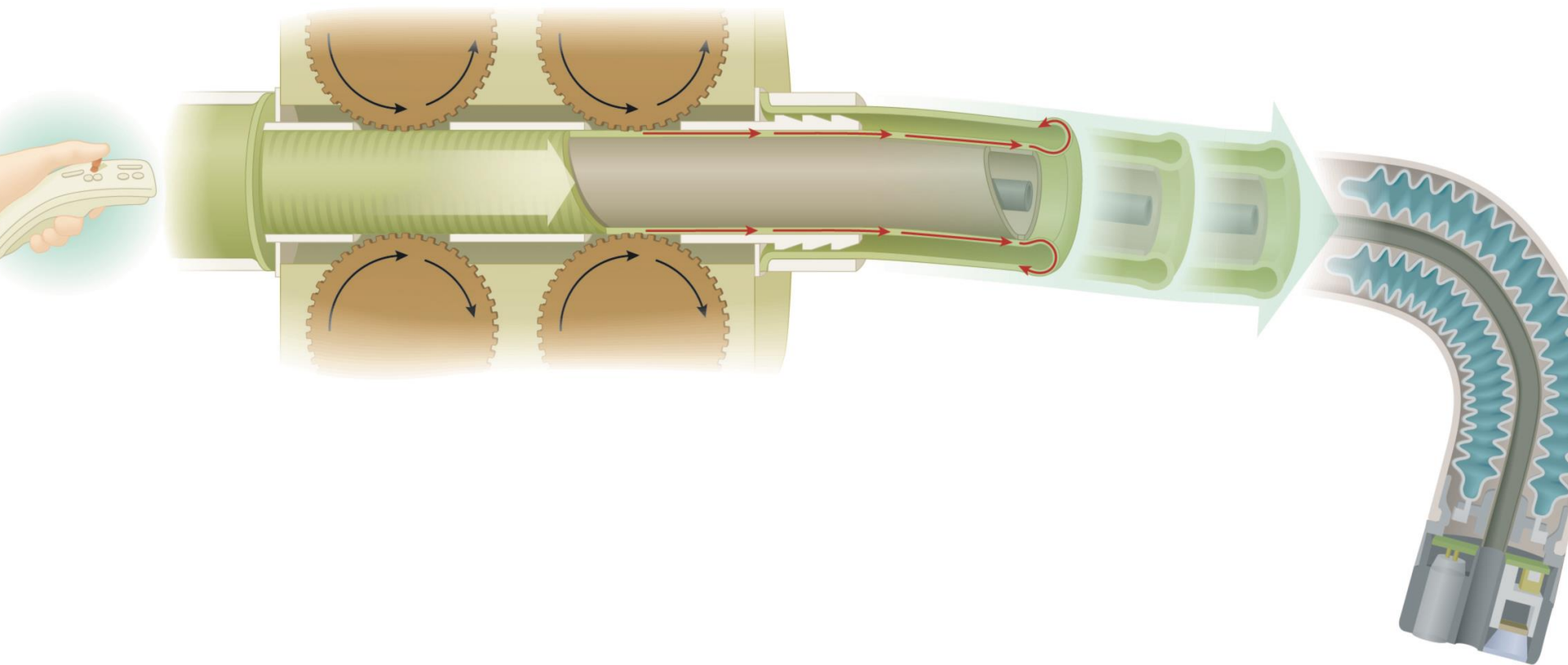


C-Scan[®]
for Colorectal Cancer Prevention



Moshkowitz, Gluk, Arber (Gut 2016)

Invendoscope (Germany)

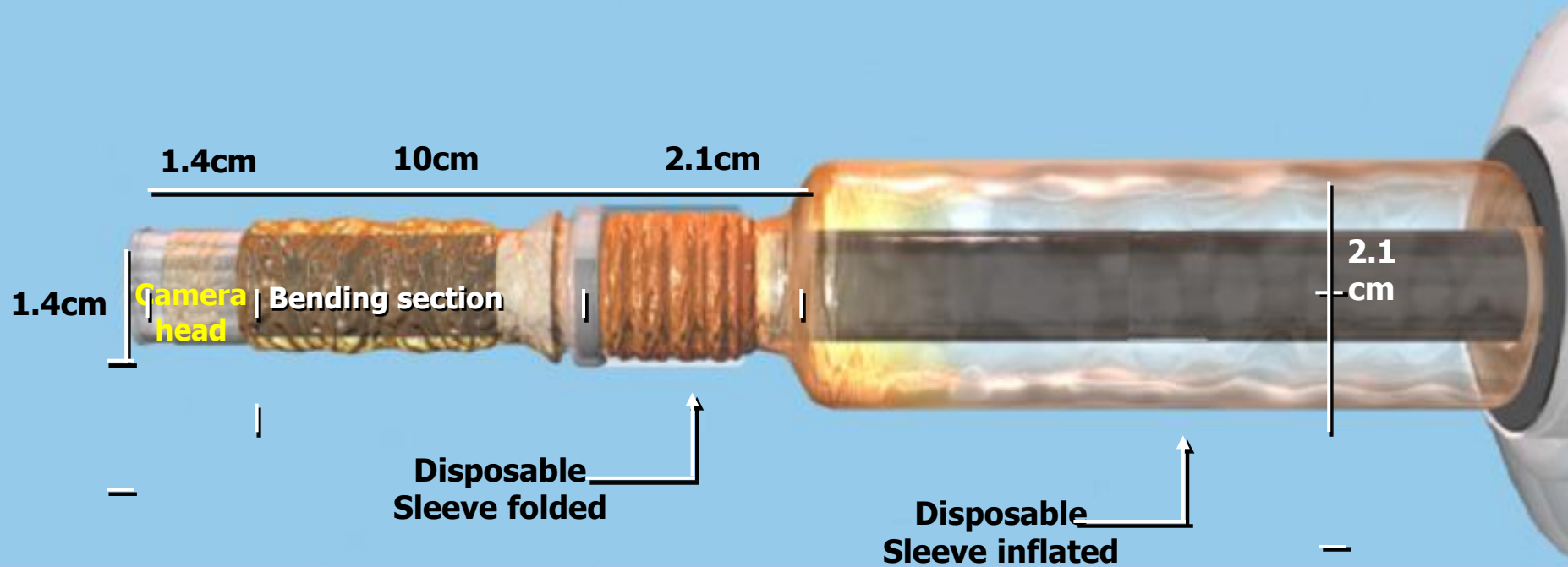


Invendoscope (Germany)

Failed



ProtectiScope Israel



Power-assisted force at the tip to advance the scope

Stryker

ClearPath (Israel)

Efficient Irrigation and Evacuation System

ISO 13485 Certified

FDA approved, 2009

CE Cleared, 2009



ClearPath (Israel)

Efficient Irrigation and Evacuation System

Withdrawn

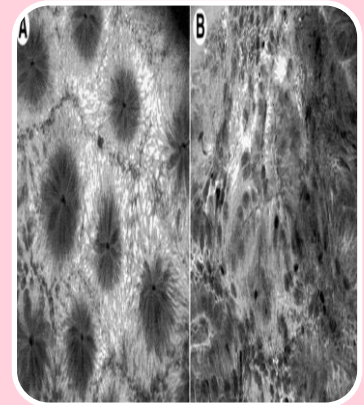
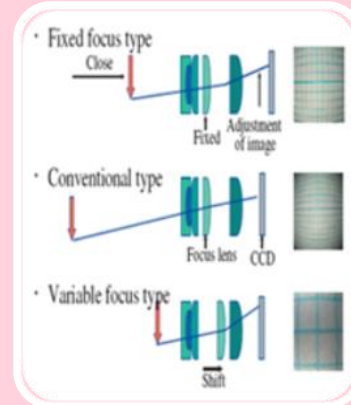
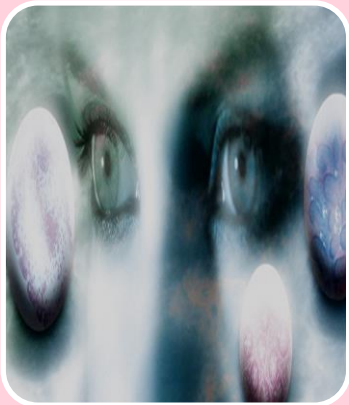


Improve Imaging



© Can Stock Photo - csp8717968

Increase Magnification



**Standard
Endoscopy
(SD)**

**0.4
megapixel**

**High
definition
(HD)**

**1.2
megapixel**

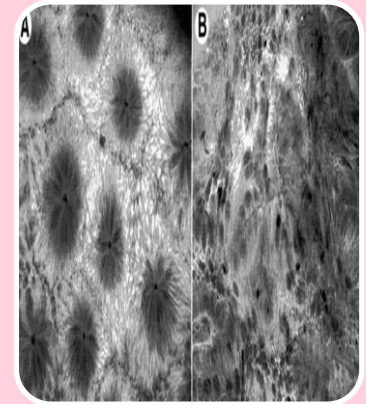
**Magnifying
colonoscopy**

Zoom X300

**Confocal
Laser
endo-
microscopy**

X1000

Increase Magnification



No significant

**Standard
Endoscopy
(SD)**

**0.4
megapixel**

**High
definition
(HD)**

**1.2
megapixel**

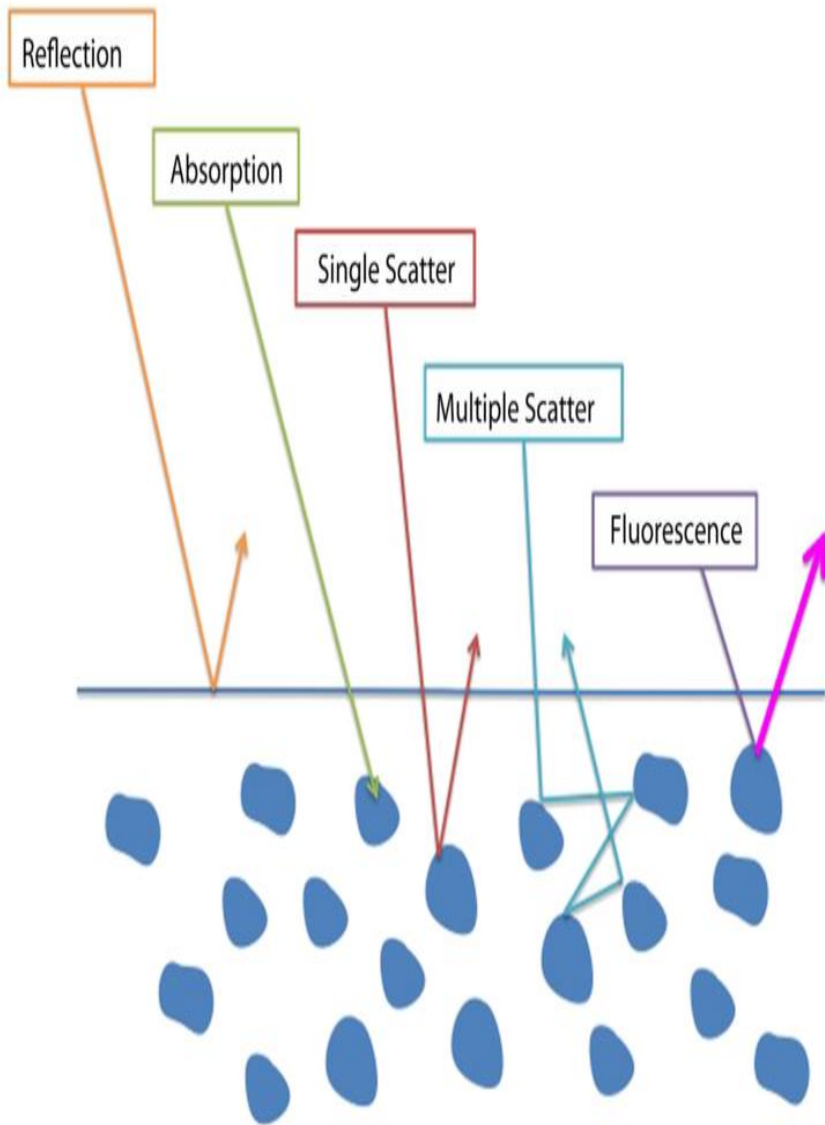
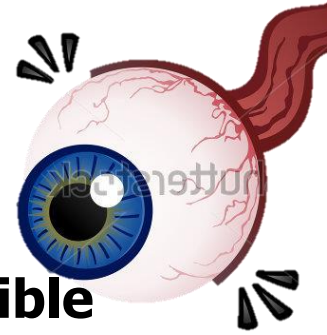
**Magnifying
colonoscopy**

Zoom X300

**Confocal
Laser
endo-
microscopy**

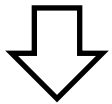
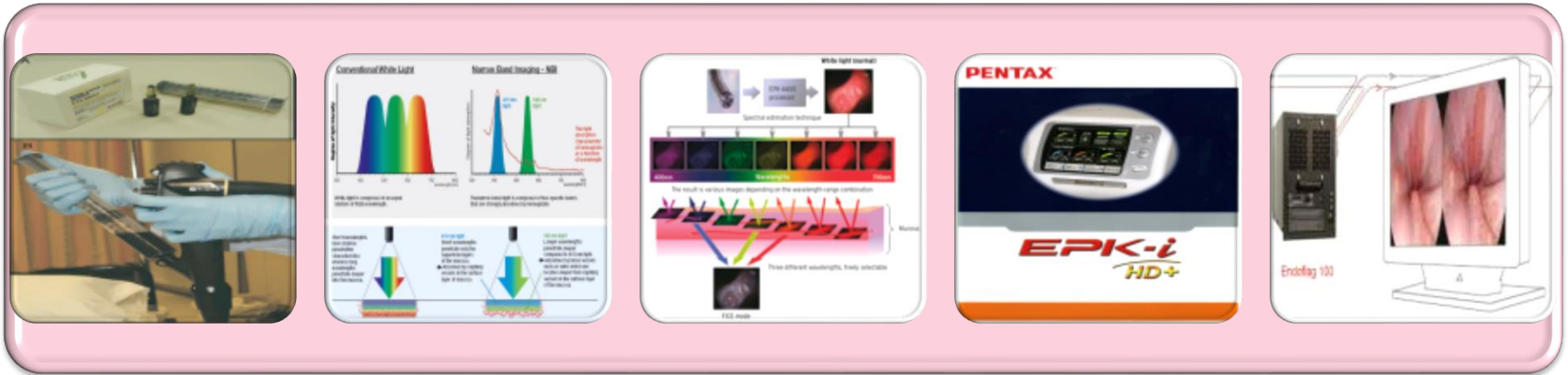
X1000

Optic Imaging

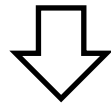


- **The behavior of visible ultraviolet and infrared light omitted from a source [i.e. laser, xenon] to a surface is variable**
- **Light may interact with tissue in various ways that can be measured and analyzed**
- **These interactions provide information about tissue type, Hb content, micro- structure, and molecular characteristic**

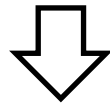
Image Enhanced Endoscopy



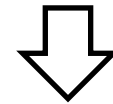
**Chromo-
endoscopy**



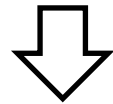
**NBI
filter**



FICE



i SCAN



Endoflag

Olympus

Fujinon

Pentax

Endopix

Courtesy of Prof. Halpern

Chromoendoscopy

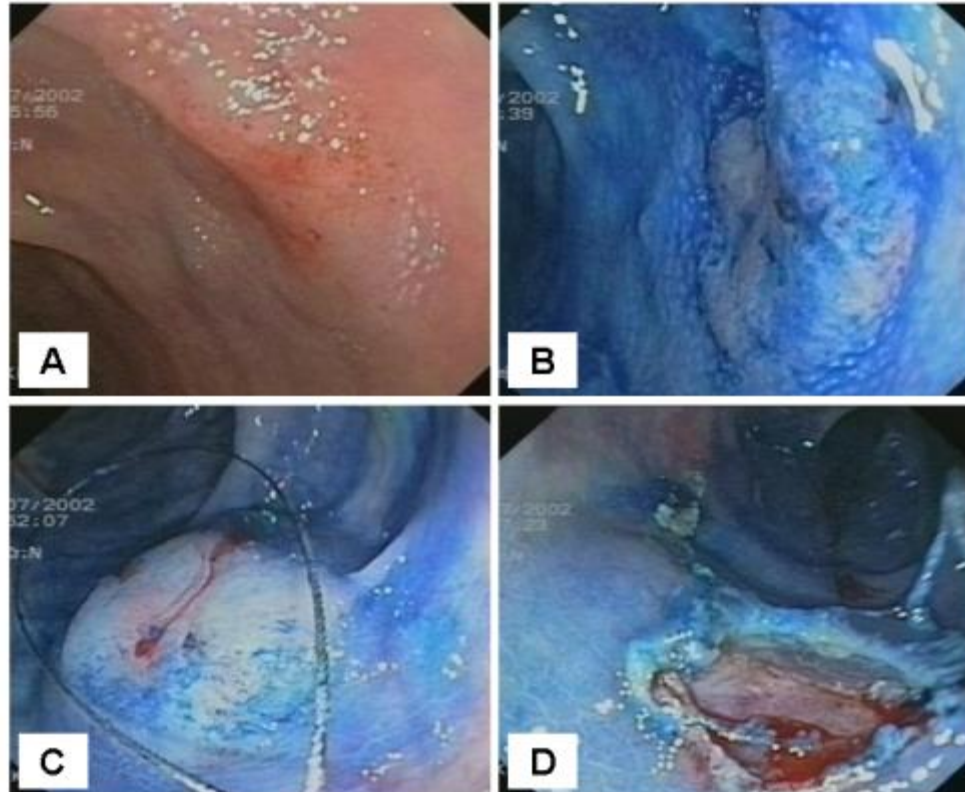


- **Absorptive stains**
 - Lugol's solution
 - Methylene blue
 - Crystal violet
 - Acetic acid
- **Contrast stains**
 - Indigocarmine

Chromoendoscopy is Most Useful in the Evaluation of Nonpolypoid Colorectal Neoplasms

(Kiesslich, Eur J Gastroenterol 2005)

In the real world....it is not

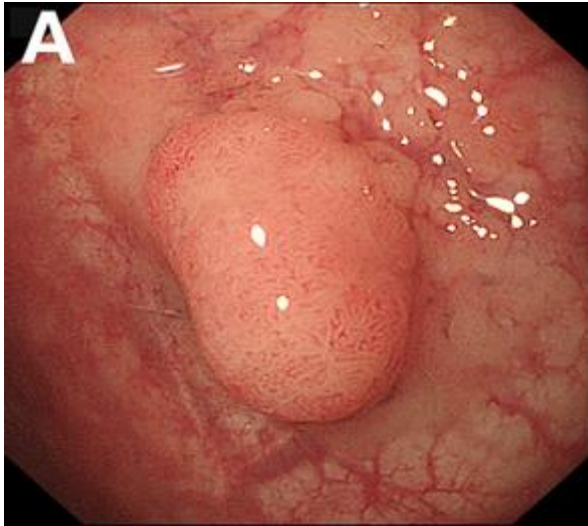


Prevalence of flat adenomas:

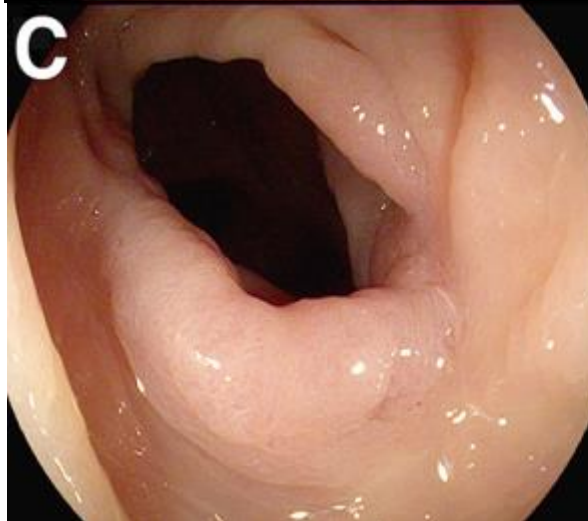
without Chromoendoscopy 1-5%

with Chromoendoscopy 20-35%

Electronic Chromoendoscopy?



NBI



i-Scan

In real life.....probably no added value

Narrow Band Imaging →

CC



Chromoendoscopy →

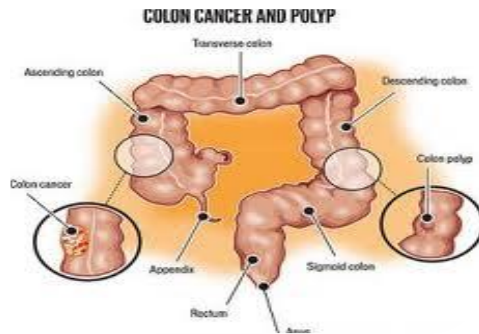


NBI is equal to chromoendoscopy for distinguishing neoplastic from non-neoplastic lesions

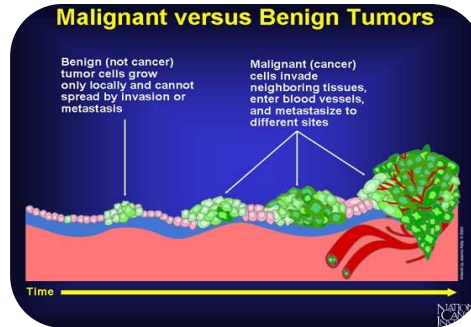
Machida, Endoscopy 2004

Courtesy of Prof. Halpern

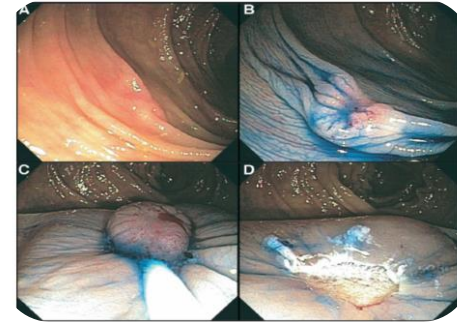
The Future is Molecular Imaging



**Improved
detection of
tumor location**



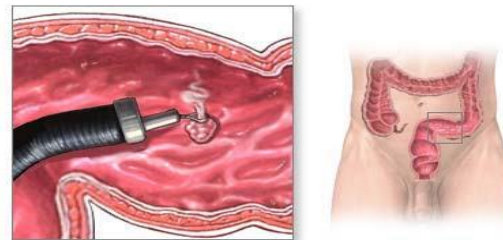
**Malignant Vs
Benign**



Tumor Margins



**Pharmacologic
al therapy
[response]**



Tissue is removed from
the colon for examination

ADA

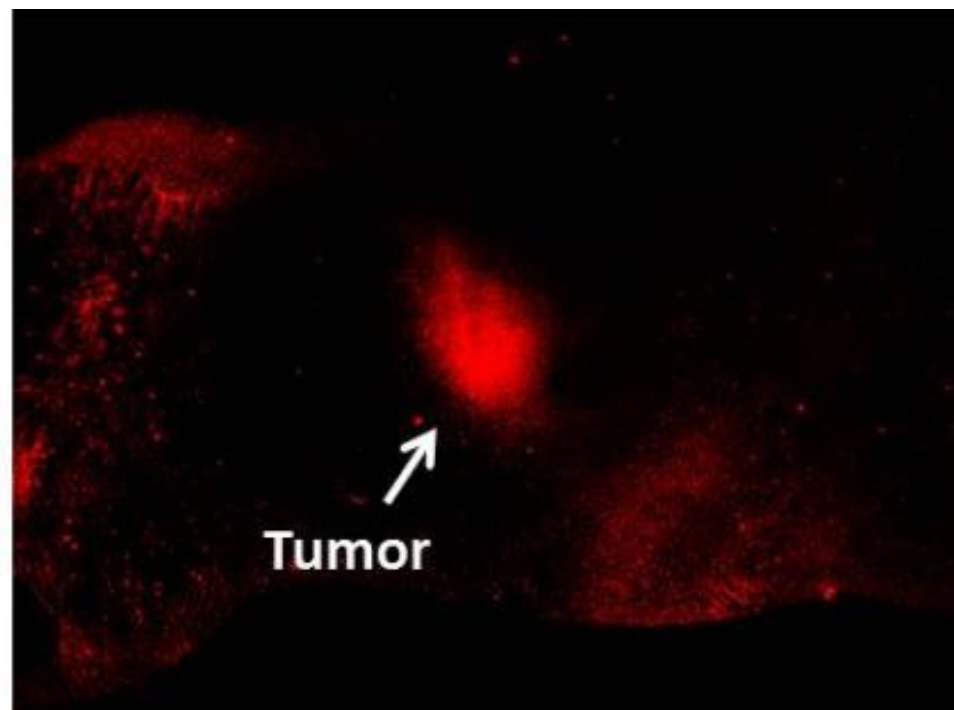
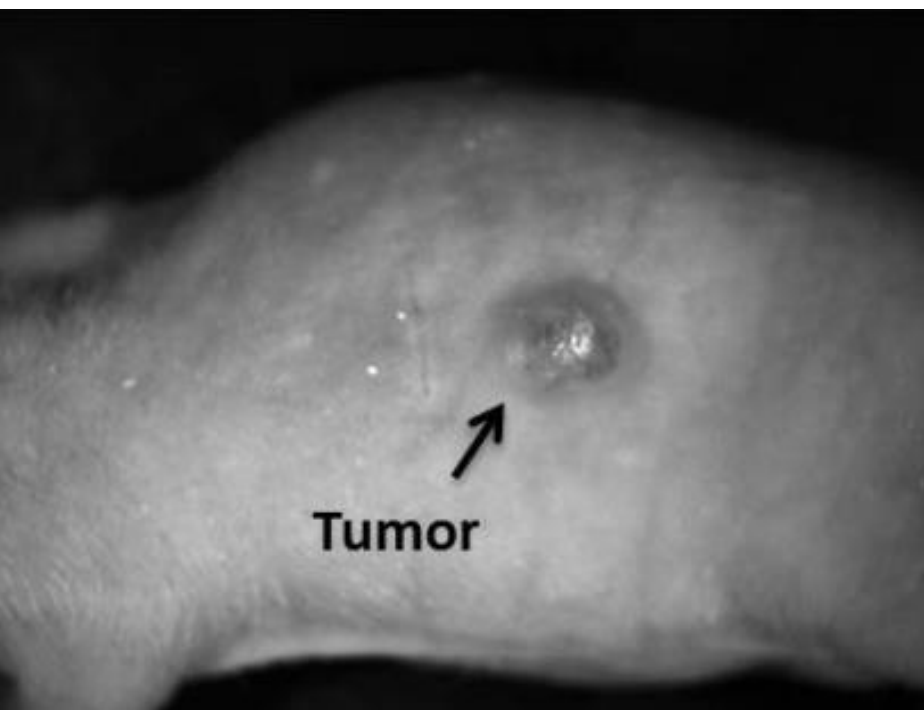
**Minimize
number of
biopsy**



**Dysplasia in
inflamed
mucosa**



mAb to CD24 concentrating in CRC in nude mice (Arber's lab)



...jumping into CONCLUSIONS

“A test is better than none, and the best test is the one that is done”

- *Two stages approach*
- *Non invasive test as the initial step*
 - ❑ *Blood test*
 - ❑ *Stool test/virtual colonoscopy/ capsule/ prepress cap?*



One Stage Colonoscopy



One Stage Colonoscopy

The big brother quality control

ADR/withdrawl time/cecal intubation rate

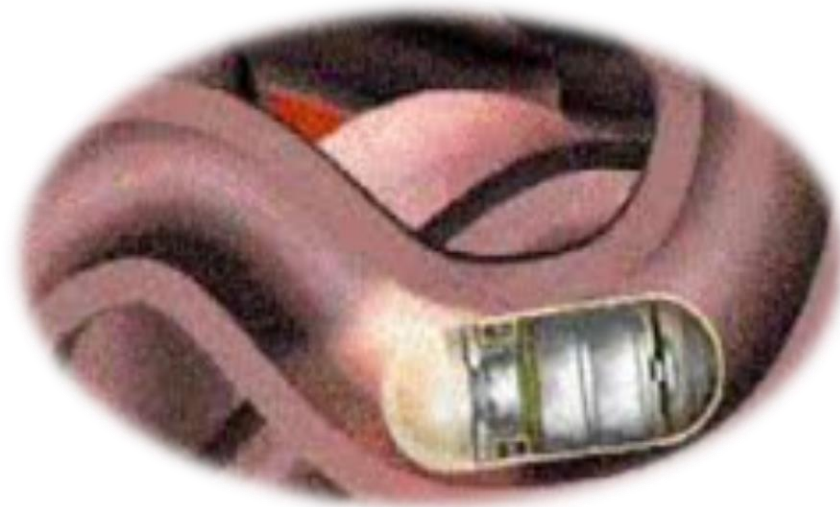
**Advanced technologies are
available, but are time and
money consuming**

- *Public demands*
- *Legal issues*





**No Matter How Advanced
the Technology and
Equipment are.....**





**What Really
Matter...**



**Is the
Gastroenterologist!!!**

THANK YOU FOR YOUR ATTENTION

**PLEASE CLAP AND DO NOT MAKE TOUGH
QUESTIONS**