

# **Classification & Detection of Colorectal Polyps**

## *A Changing Landscape*

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# Disclosures

## Relationship with Exact Sciences

- *Mayo Clinic*
  - Equity investor
  - Licensed technologies
- *Dr. Ahlquist*
  - Scientific Advisor
  - Inventor of licensed technology
  - Research collaborator

# Polyp Detection by Colonoscopy

## *Questions*

**Is there a problem?**

**What are we looking for?**

**How can we improve detection?**

**Which methods benefit most?**

## The Problem

- Despite screening in US, CRC remains the #2 cancer killer
- Shift to the right ( $\geq 50\%$  prox)

1980 → 2000 (rate/100,000)

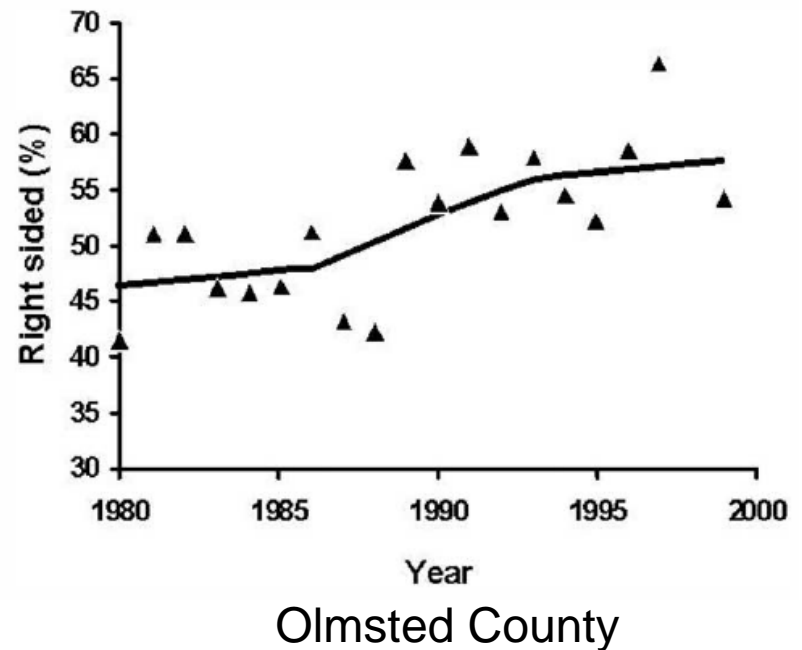
Polypectomies: 86 → 320

CRC incidence: 60 → 46

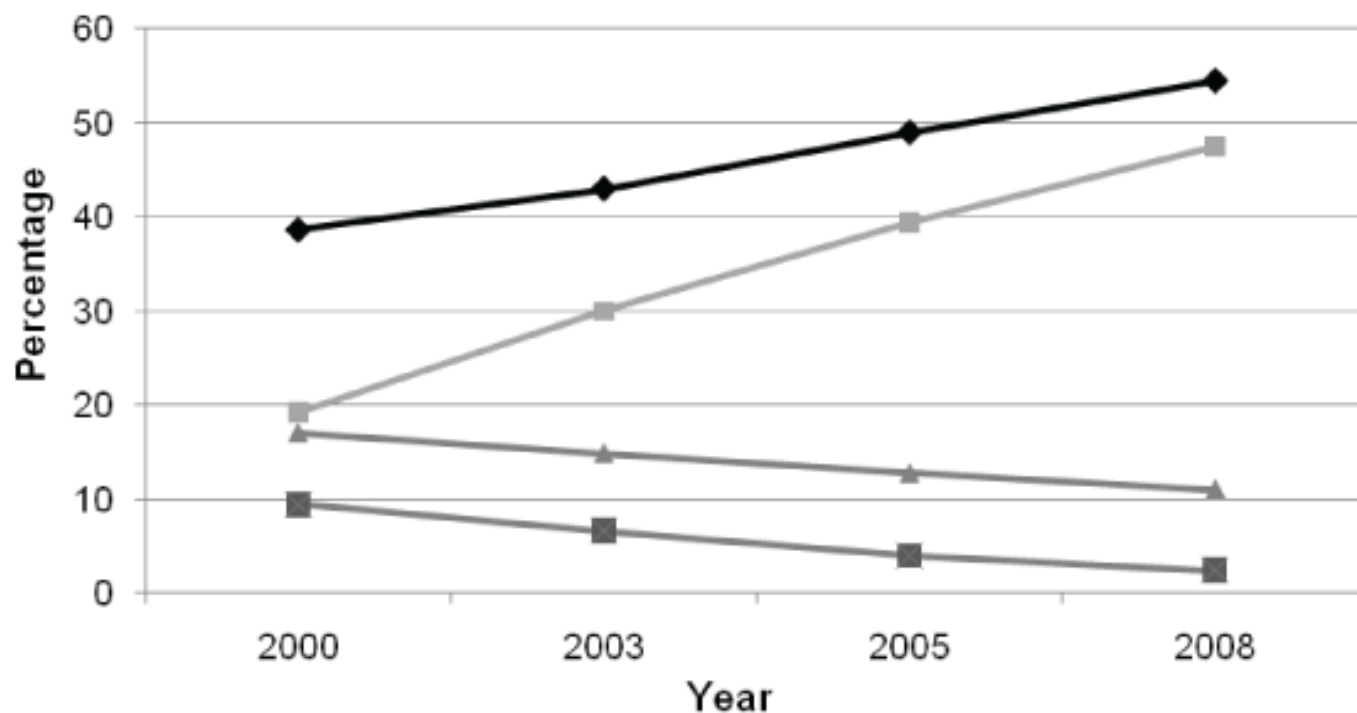
Left 32 → 19

Right 27 → 27

Gupta et al. CGH 2005;3:150



# Colorectal Cancer Screening Modalities in US



No Screening  
~50%

- ◆ Any exam (FOBT in past year, sigmoidoscopy in past 5 years, or colonoscopy in past 10 years)
- Colonoscopy in past 10 years
- ▲ Home FOBT in past year
- Sigmoidoscopy in past 5 years

National Health Interview Survey  
National Ctr for Health Stat

# Effectiveness of Colonoscopy?

## Recent Wake-up Calls

### Large case-control studies

- **CRC mortality** (Baxter et al. Ann Intern Med 2009;150:1)

- L sided ~ 70%
- R sided 0%



- **CRC incidence** (Brenner et al. JNCI 2010;102:89)

- L sided ~ 70%
- R sided 0%



## Screening Outcomes by Specialty

	Colonoscopy by GI doctors	Colonoscopy by non-GI doctors
<b>Rex Indiana 1997</b>	CRC miss rate 3%	CRC miss rate 13%
<b>Rabeneck Ontario 2010</b>	Reference rate 1.0	HR for interval CRC Surgeons 1.39 Others 1.28
<b>Baxter Ontario 2010</b>	Reference rate 1.0	HR for interval CRC Surgeons 1.23 Others 1.87

Adapted from Dr Doug Rex

# Long Term CRC Risk Reduction after Colonoscopy & Polypectomy

*Nishihara et al (DDW 2012)*

- **Prospective cohort study (Harvard System)**

N ~ 100,000

F/U ~ 2.5 million person-yrs

- **Relative CRC risk, HR**

Never screened 1.0 (ref)

Neg colonoscopy 0.45

Left 0.26

Right 0.66

After polypectomy 0.64



# Adenoma Detection Rates

## *Variation among Gastroenterologists*

	<b>Number doctors</b>	<b>Lowest ADR</b>	<b>Highest ADR</b>	<b>Absolute Difference</b>
<b>Barclay Illinois 2006</b>	<b>12</b>	<b>9.4%</b>	<b>32.7%</b>	<b>23%</b>
<b>Chen Indiana 2007</b>	<b>9</b>	<b>15.5%</b>	<b>41.1%</b>	<b>26%</b>
<b>Imperiale Indiana 2009</b>	<b>25</b>	<b>7%</b>	<b>44%</b>	<b>37%</b>
<b>Shaukat Minnesota 2009</b>	<b>51</b>	<b>10%</b>	<b>39%</b>	<b>29%</b>

Adapted from Dr Doug Rex

# Serrated Polyp Detection Rates

## *Variation among Gastroenterologists*

	Number doctors	Lowest proximal detection rate	Highest proximal detection rate	<b>Absolute Difference</b>
<b>Hetzel Boston</b>	<b>13</b>	<b>1.1%</b>	<b>7.6%</b>	<b>6%</b>
<b>Kahi Indiana</b>	<b>15</b>	<b>1%</b>	<b>18%</b>	<b>17%</b>

Adapted from Dr Doug Rex

# Quality Indicators and Risk of Interval CRC

Kaminski et al. NEJM 2010

- Poland, n=45,026 patients
- Colonoscopists 186
- Stratified results

<u>ADR</u>	<u>Interval CRC (per 100,000)</u>
<11%	34
11-19.9%	24
<u>≥20%</u>	~2

# Polyp Targets

## Size Considerations

- **Most do not progress**
  - 50-70% get polyps
  - 6% get CRC
- **Small (5-9mm) & diminutive (<5mm)**
  - Controversial targets
  - Hard to predict natural hx
  - Relevant because of lengthy (10 yr) colonoscopy screening interval
- **Large ( $\geq 1$ cm)—consensus targets**
  - Risk of HGD & CRC increases exponentially with size above 1cm

# Premalignant Polyp Types

- **Adenoma**

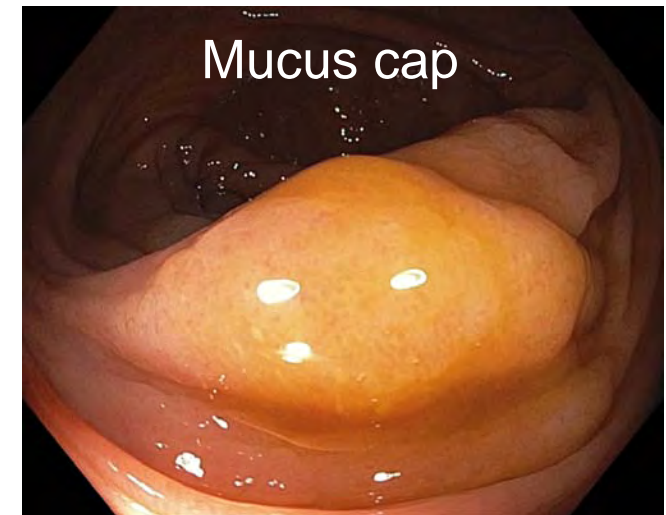
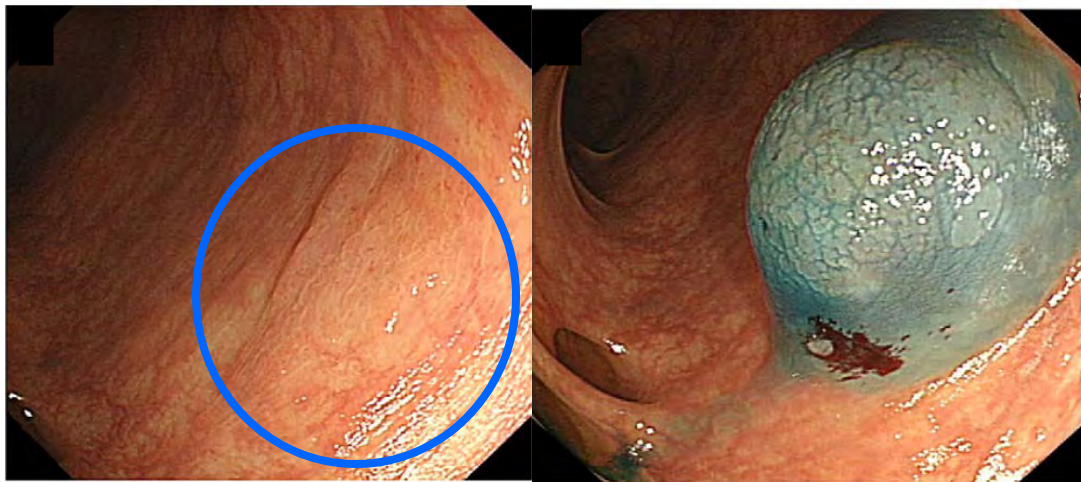
- Tubular (T), villous (V), tubulovillous (TV)
- **“Advanced” if  $\geq 1\text{cm}$ , V, or TV**

- **Serrated**

- Hyperplastic
- Sessile serrated polyp (*BRAF* + meth)
- Traditional serrated polyp (*KRAS* + meth)
- **“Advanced”? (if  $\geq 1\text{cm}$ )**

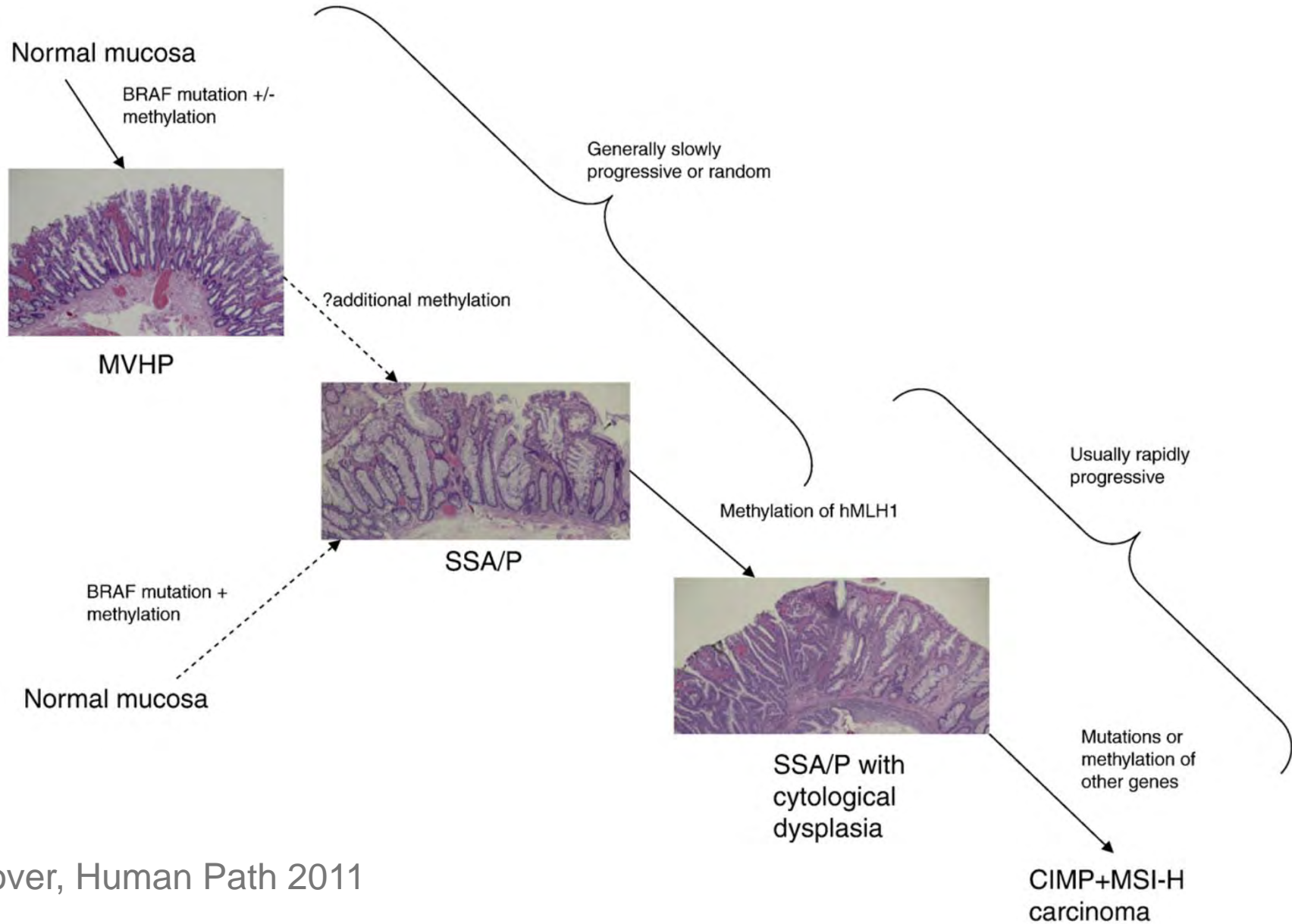
## Sessile Serrated Polyps

- Precursors for ~1/3 of CRC
- Now account for ~1/3 of advanced polyps
- R>>L
- Detection requires mindfulness & a trained eye

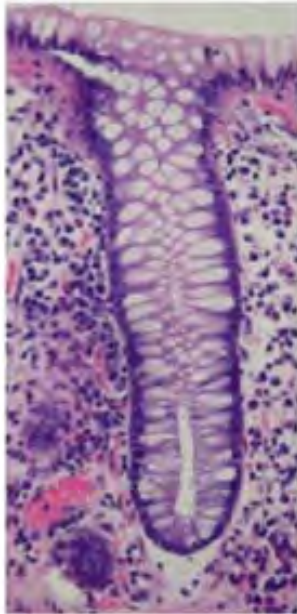


Images courtesy of  
Drs Rex & Won Kee Song

# Serrated Polyp Pathway to CRC

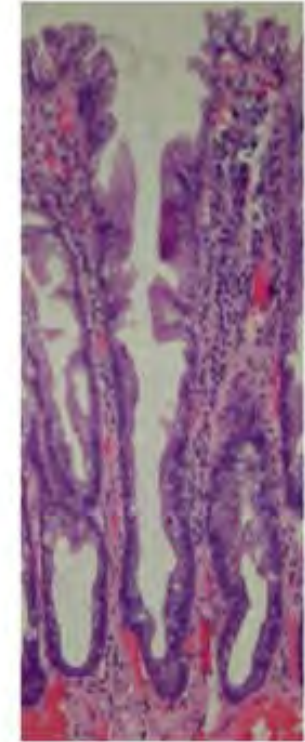


## Hyperplastic Polyp



### Normal Crypt

- Prolif at base
- Cells mature toward lumen

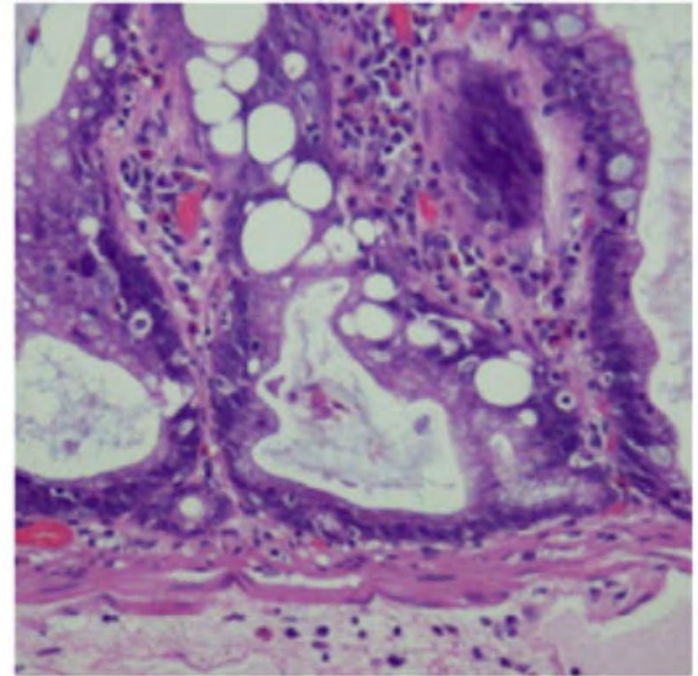
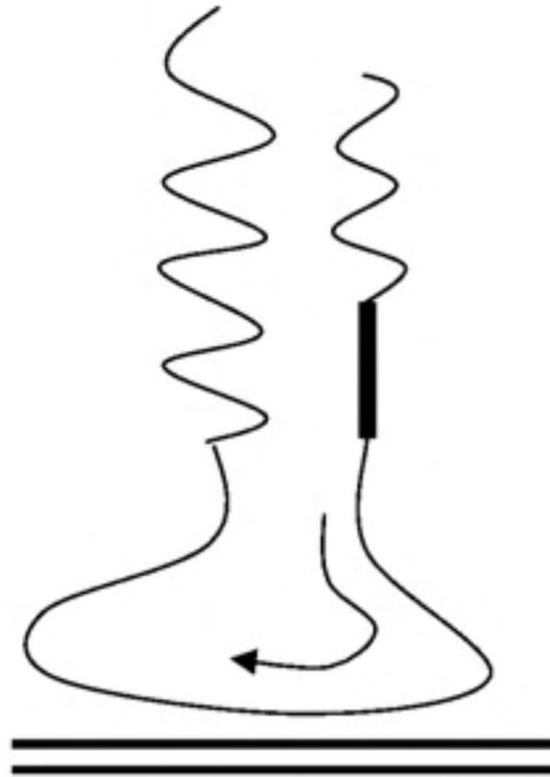
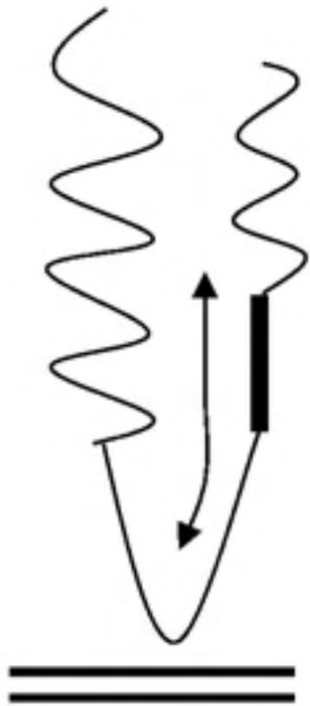


### Hyperplastic Polyp

- Expanded basal prolifer
- Cells mature toward lumen
- ↓ apoptosis = serrations

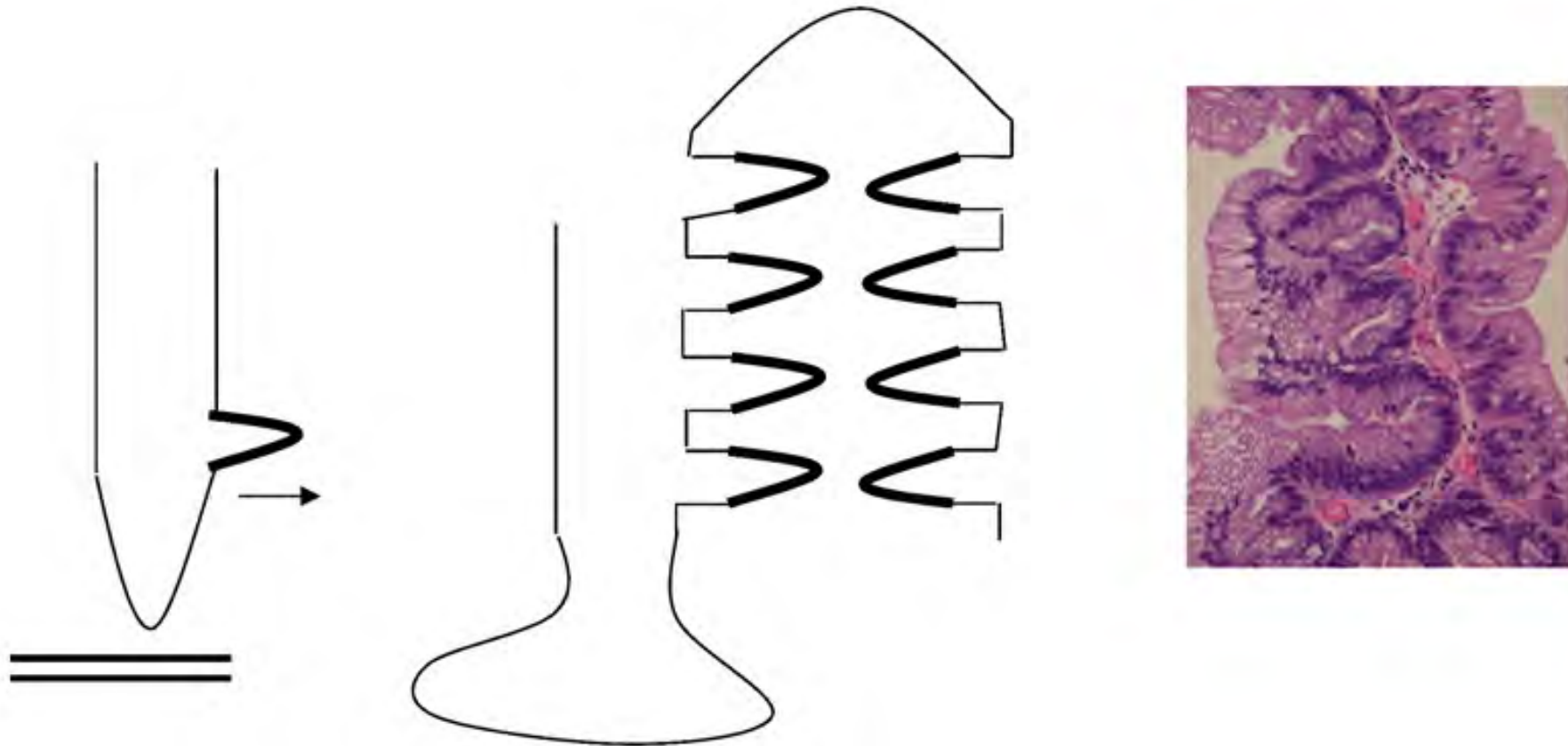


## Sessile Serrated Polyp



- Proliferative zone moves up side of crypt
- Movement of mature cells all directions

## Traditional Serrated Polyp



- Emergence of proliferative zones on side of crypt
- Multiple ectopic crypts form

# Polyp Targets

	Type*	Site	Detection Barrier
<b>Pedunculated</b>	AD	L>R	<b>Surface exposure</b>
<b>Sessile</b>	AD,S	Both	
<b>Flat</b>	AD,S	R>L	<b>Surface exposure + Lesion discrimination</b>
<b>Depressed**</b>	AD	R>L	

\*AD = adenoma, S = serrated polyp

\*\*Rare, disproportionate HGD

# The “Mozart Effect”

3x increase  
in polyp  
detection

O’Shea, ACG Meeting 2011



## Methods Intended to Enhance *Surface Exposure*

- Insertion to cecum
- Bowel prep & cleansing
- ~~Wide angle endoscopy~~
- Cap-assisted colonoscopy
- Through-the-scope  
retroscopes
- Retroflexion



**Better views of  
flexures & prox  
sides of folds?**

## Bowel Preparation

*Lebwohl et al. GIE 2011*

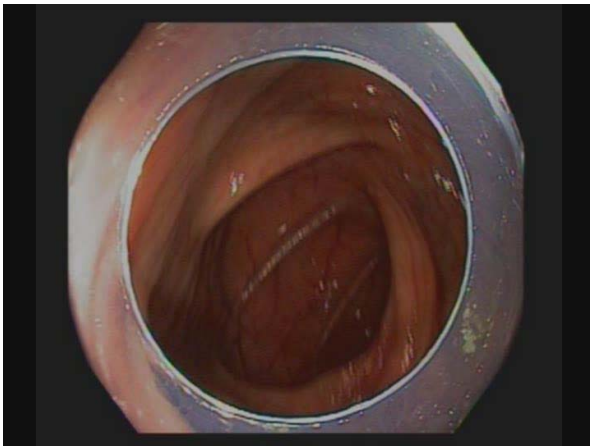
From 12,787 colonoscopies,  
24% had suboptimal prep (poor/fair)



Among those who had repeat colonoscopy  
with optimal prep <3yrs\*

Adenomas	42%
Adv adenomas	27%

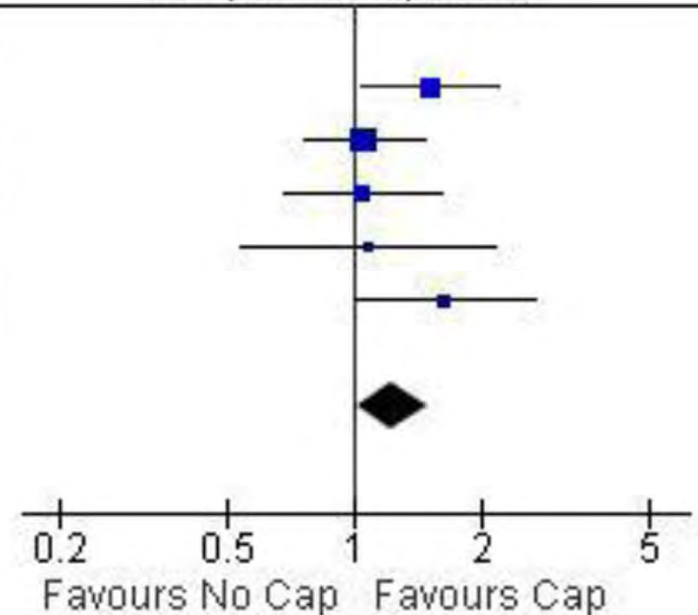
\* not seen on index colonoscopy with poor prep



# Polyp Detection with Cap-assisted Colonoscopy (CAC): Meta-analysis

Wani et al (DDW 2012)

Study	Weight	Odds Ratio		Year	Odds Ratio	
		M-H, Random, 95% CI	Year		M-H, Random, 95% CI	
Matsushita 1998		Not estimable		1998		
Kondo 2007	25.5%	1.51 [1.04, 2.19]		2007		
Harada 2009	32.5%	1.05 [0.76, 1.46]		2009		
Tee 2010	19.7%	1.05 [0.69, 1.60]		2010		
Dai 2010	7.5%	1.08 [0.54, 2.15]		2010		
Lee 2011	14.8%	1.64 [1.01, 2.68]		2011		
<b>Total (95% CI)</b>	<b>100.0%</b>	<b>1.23 [1.02, 1.49]</b>				



	<b>CAC</b>	<b>Std Colo</b>
<b>All polyps</b>	<b>40%</b>	<b>36%</b>
<b>Adenomas</b>	<b>32%</b>	<b>34%</b>

# Through-the-Scope Retrosopes

## Gains in polyp detection rates

- Uncontrolled studies ~10%
- RCT (Leufkens GIE 2011)
  - All adenomas 7%
  - Adv adenomas 2%



## Issues

- Distraction from 2 simultaneous images
- Creation of blind spots
- Lens cleaning
- Suctioning impaired
- Procedure time ↑
- Cost & reimbursement

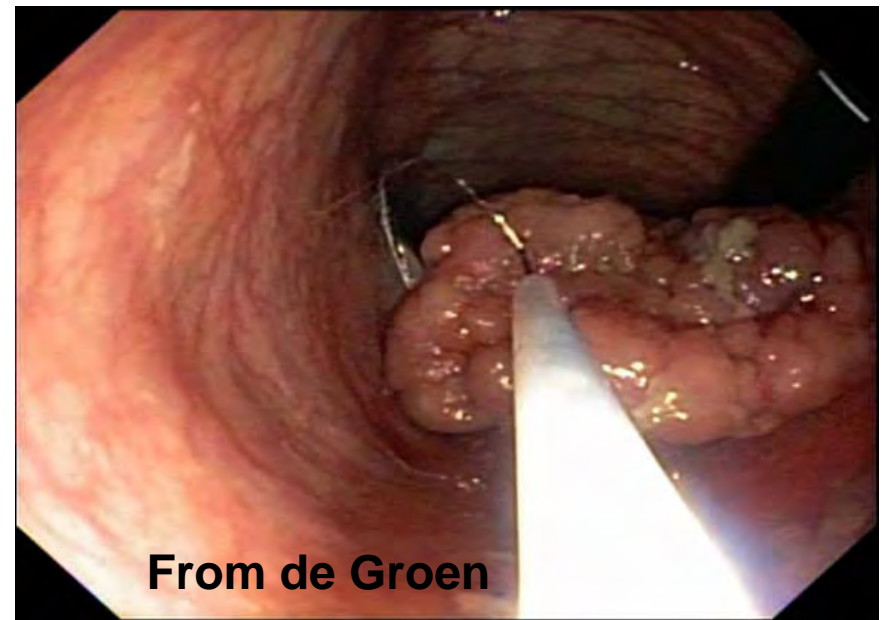
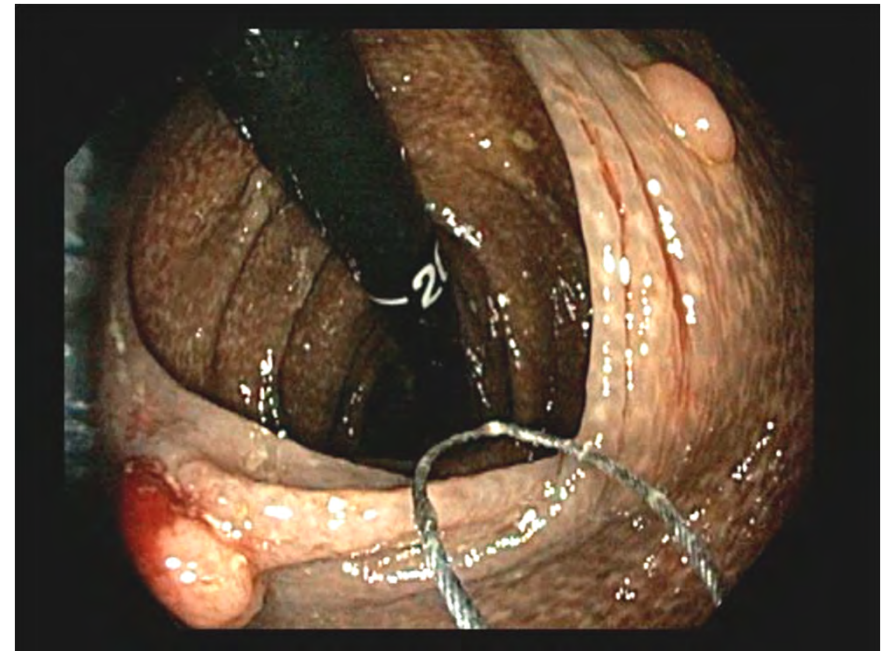
Adapted from Dr Doug Rex



# Proximal Colon Retroflexion



From de Groen



From de Groen

# Additional Polyp Yield with Retroflexion

## Hewett & Rex, GIE 2011

### Study

- 1000 consecutive patients
- 2 experienced colonoscopists
- Forward-viewing colonoscopy with removal of all polyps → then retroflex exam

### Results

- Successful retroflexion 95%, safe
- Additional adenoma yield

<b>Any</b>	<b>9.8%</b>
<b>Advanced</b>	<b>4.4%</b>

# Methods Intended to Enhance *Lesion Discrimination*

## Tools

- Chromoendoscopy
- Narrow band imaging (NBI)
- High definition (HD)

*Opportunity/need for optical innovations that better highlight flat/depressed lesions*

## Individual Performance/Skill

- Mindfulness, recognition clues, education
- Optimal metrics

## Chromoendoscopy

- **Modest (~10%) increase in detection of small polyps** (Randomised studies: Kahi 2010 (US), Pohl 2011 (Germany))
- **But, tedious, nonspecific, and ↑ time + cost**
- **Thoughts**
  - Impractical for general CRC screening
  - Helpful to define flat lesions
  - Important role in IBD surveillance



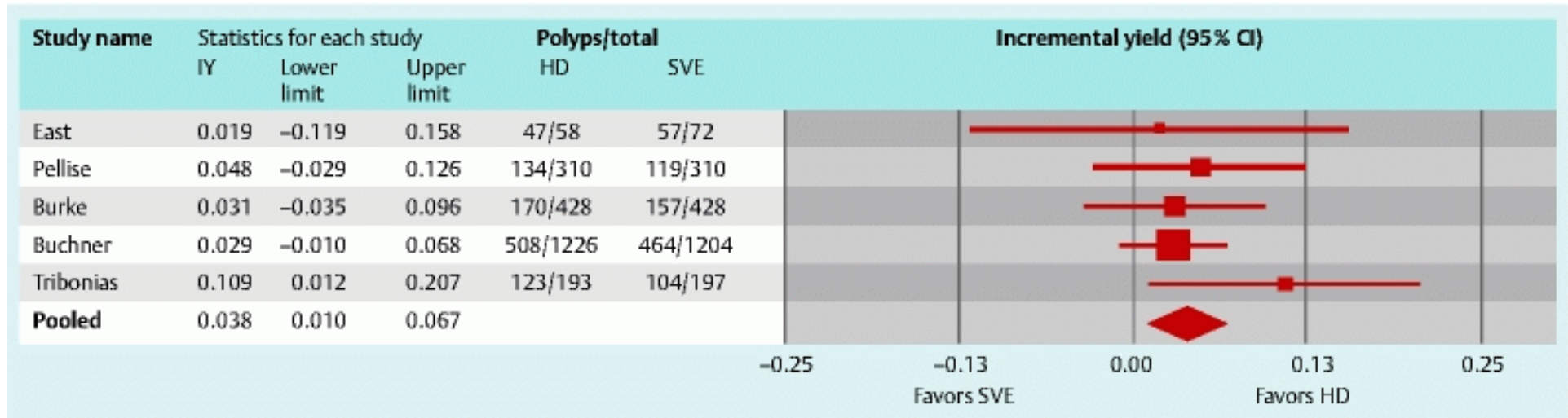
## NBI vs White Light

### Meta-analysis of Randomized Studies

Study	Pts with adenoma NBI	Pts with adenoma WLE	adenoma/pt NBI	adenoma/pt WLE	O.R. NBI vs WLE
Rex 2007 N=217	65%	67%	1.86	1.82	0.90 (0.61-1.34)
Adler 2007 N= 198	23%	17%	0.33	0.26	1.27 (0.88-1.84)
Inoue 2008 N=122	42%	34%	0.84	0.55	1.55 (1.14-2.11)
Pooled	44%	41%	1.06	0.96	1.23 (0.93-1.61)

Van den Broek et al. GIE 2009;69:124 (Adapted from Dr. Mike Wallace)

# HD vs Standard Colonoscopy Meta-analysis



## Increase adenoma detection by HD

**Any** 3.5%

**Advanced** (no increase)

Subramanian et al Endoscopy 2011;43:499 (Adapted from Dr. Mike Wallace)

# Metachronous & Interval CRC

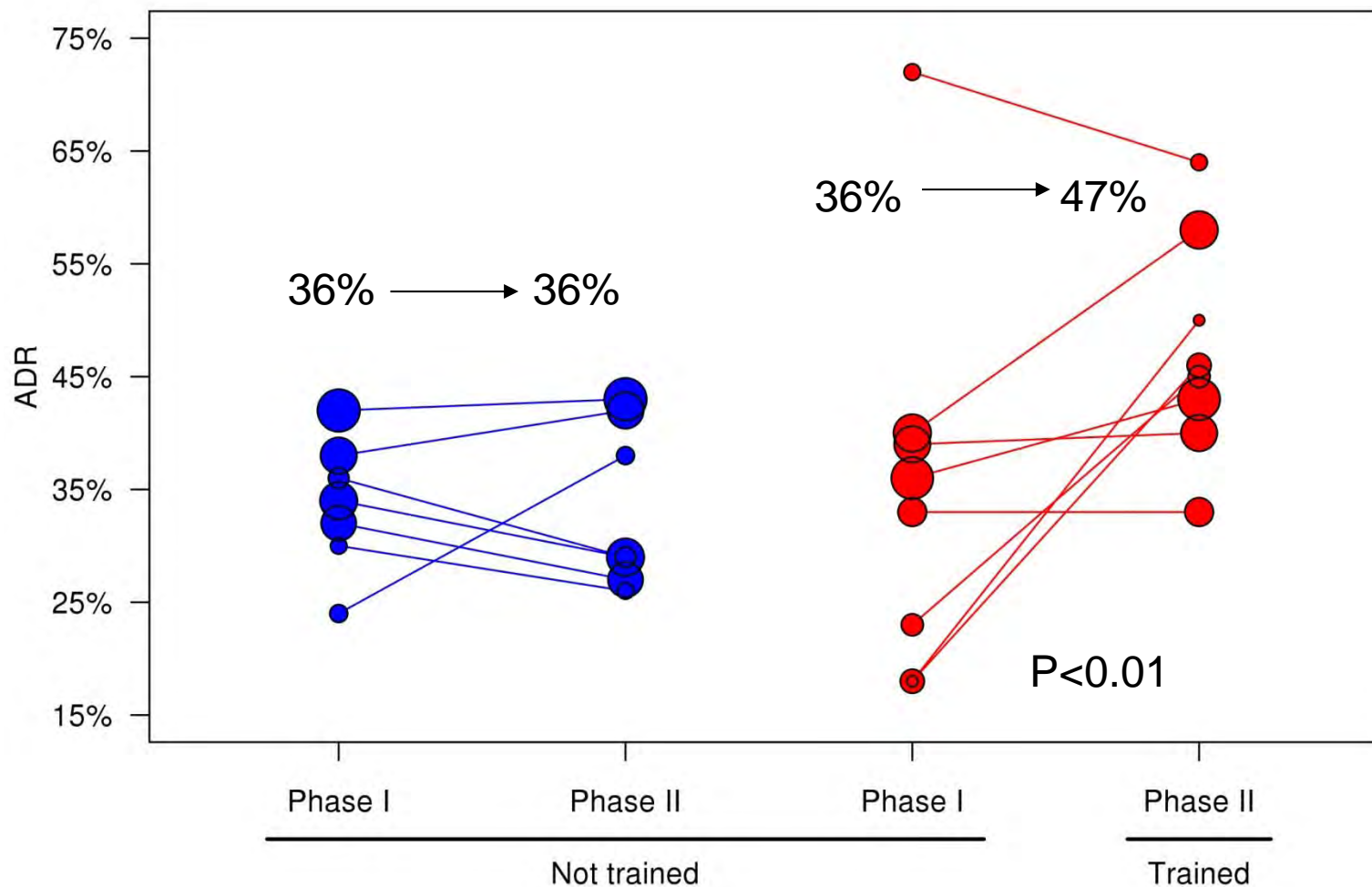
## *Program Failures*

- Metachronous CRC incidence (%)

	<i>Years post-resection</i>				
	<u>3</u>	<u>5</u>	<u>6</u>	<u>10</u>	<u>20</u>
Bonvier 2008	--	1.8	--	3.4	7.2
Mulder 2012	1.1	--	2	3.1	--

- Interval CRC
  - 30-50% of CRC in screen/surveillance programs not detected soon enough or at all
  - R>L
- Potential causes and solutions
  - Non-compliance
  - Missed lesions
  - New lesions

# Effect of Didactic Sessions on ADR





# Quality Metrics

- **Ultimate metric: Interval CRC**

- **Surrogate measures**

  - Precursor targets

    - Adenoma detection rate (ADR)
    - Polyps per patient rate

  - Technical elements

    - Cecal intubation rate, withdrawal time, etc

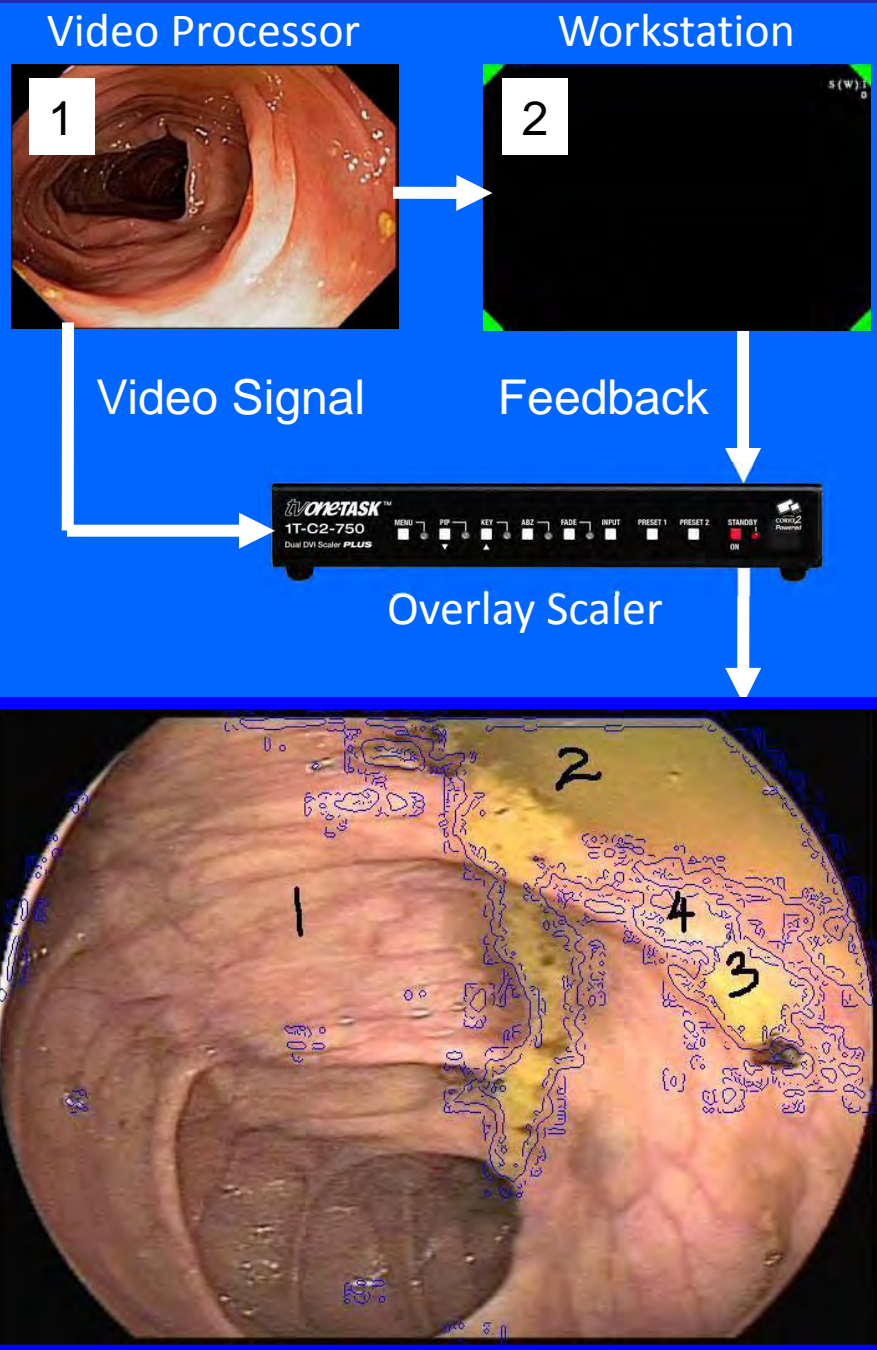
  - Aggregate quality score

    - **Real-time computer systems**

# Real-time Quality Analysis and Feedback

- Clear frame
- Retroflexion
- Circumferential inspection
- Withdrawal time
- Stool/fluid (score & map)

From Dr Piet de Groen, Mayo Clinic



# EndoMetric Report

## Prototype for Colonoscopy

Overall Quality Score

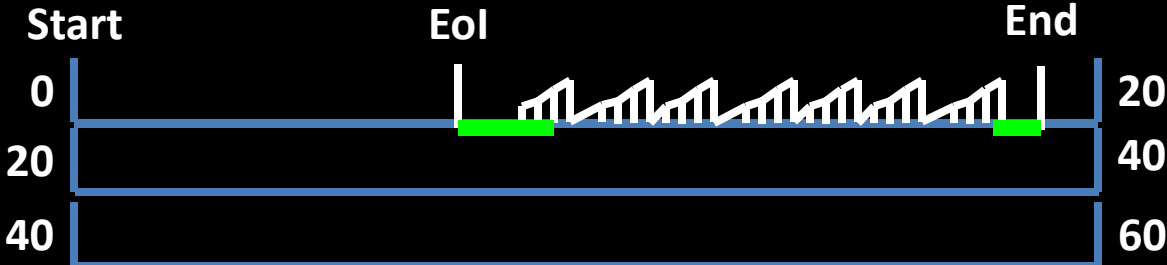


Preparation Score **8** (Min-Max)

Cleaning Score **8** (Min-Max)

Spiral Score **7** (0-∞)

Image Eol



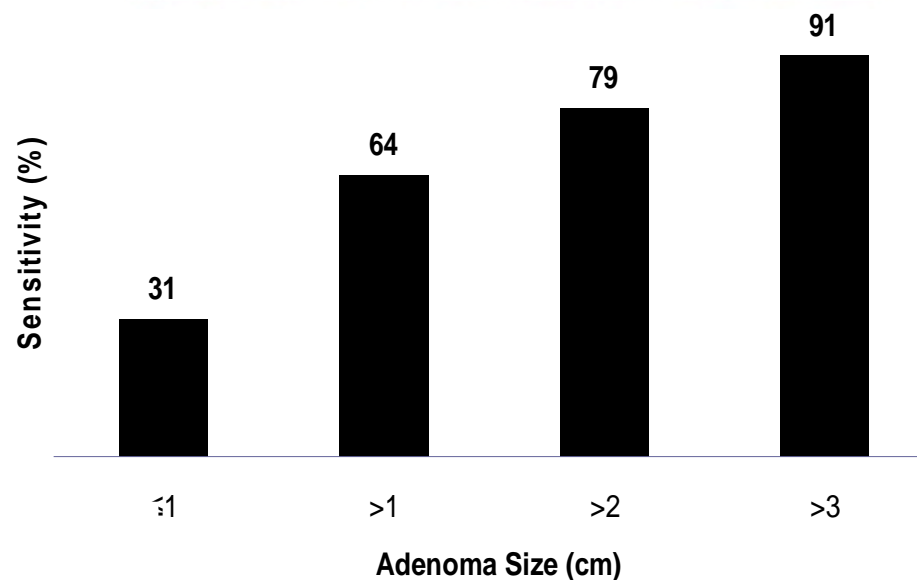
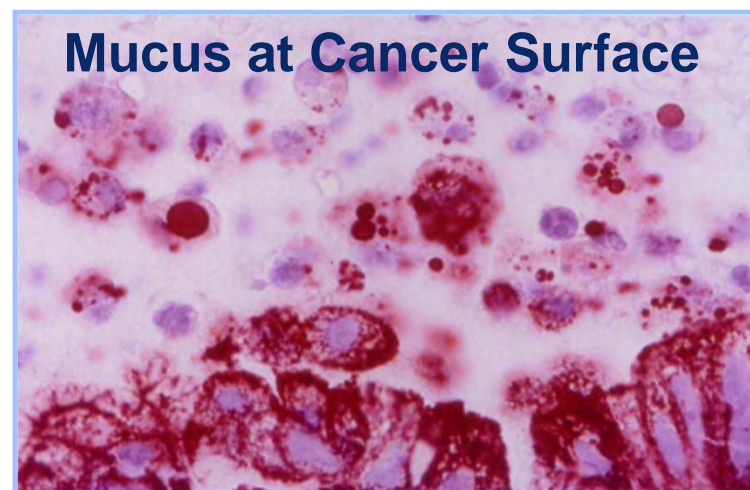
Retroflexion: 

Insertion Time (min): Total **8** Clear **6**

Withdrawal Time (min): Total **10** Clear **7**

# Stool DNA Testing

- Biologically rational
- Noninvasive
- No cathartic prep
- No diet or med restriction
- Can be mailed
- Not affected by site\*
- High sensitivity for both CRC (85-98%) & precancer\*
- Primary screen + interval test



\*Ahlquist et al. Gastroenterology 2012,  
Lidgard et al, DDW 2012

# Interventions for Polyp Detection

## Potential to Increase Yield?

**Capture the unscreened** **40-50%**

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**Reduce operator variation** **15-20%**  
e.g. training & metrics

**Optimize longitudinal program** **10%**

**Retroflex routinely** **5-10%**

**Perfect preparation** **5-10%**

**Use ancillary tools** **0-10%**

e.g. NBI, CAC, TTS retroscope

## Summary

- **Colonoscopy is operator-dependent, and quality varies widely**
- **Polyp miss rates highest on right**
- **Impact: population screen capture > quality/skill > ancillary tools**

***Clear opportunities to improve polyp detection***