

# The new era in IBD Capsule Endoscopy- comprehensive disease monitoring with a single capsule

## PillCam Crohn's

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Sheba - Academic Medical Center Hospital



# Crohn's Disease Anatomic Distribution

CD

## Anatomic Distribution

Freq. of involvement  
most least

Small bowel alone 33%

Ileocolic 45%

Colon alone 20%

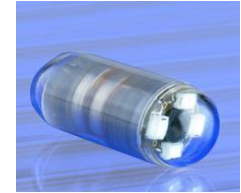


# Capsule Endoscopy in CD

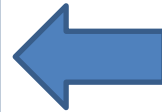
- Suspected CD- role well established → primary tool after a negative IC when no obstruction is suspected
- Known CD- ?????? Limited to unexplained bleeding/symptoms after all other tools have been exhausted

**ECCO guidelines 2013, ESGE guidelines 2016**

# Good reasons for bowel evaluation in established CD:

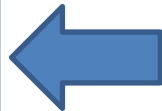


- Disease activity & severity
- Disease distribution/extent
- complications



Stratify patients to  
Low versus High risk

- Disease activity & severity
- Mucosal healing



Therapeutic plan  
Treat to target concept

- Before treatment
- After treatment
- After surgery



Prognosis

# Lessons from the initial results of the IIRN trial in known CD- a 3y prospective study

## Primary goal:

- + To examine if periodic CE, in conjunction with MRE, Inflammatory markers, and immunology phenotyping can predict imminent flares and complications in CD patients in remission or with mild activity

## Secondary goals:

- + To evaluate the prevalence of active inflammation, mucosal healing and deep remission in CD patients using biomarkers, CE and MRE
- + Evaluate the impact of CE and MRE on disease re-classification

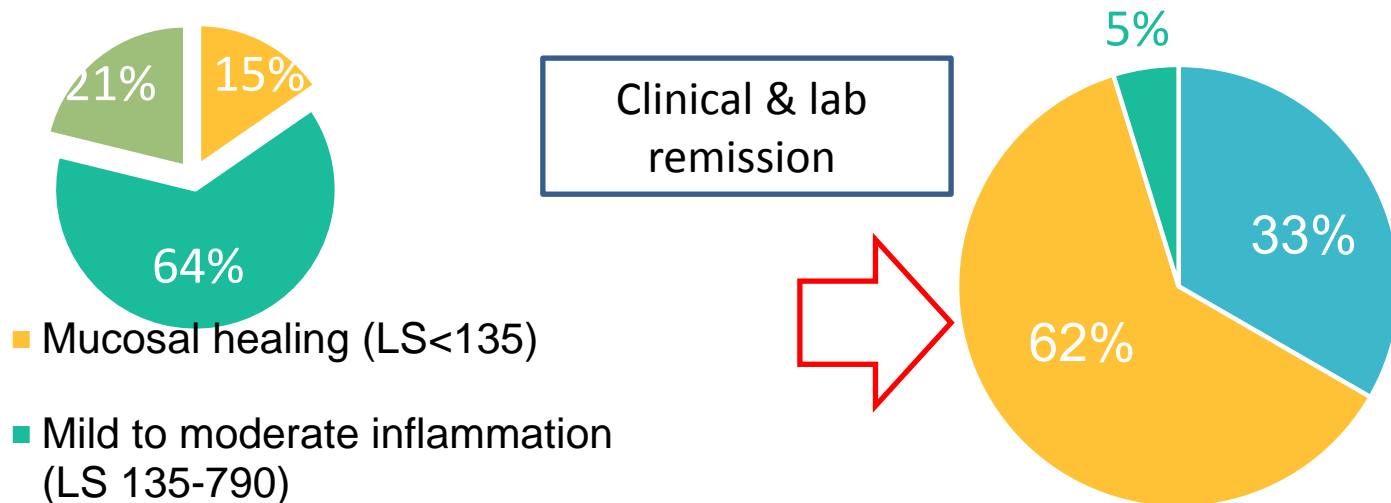
# What have we learned from the initial results of the IIRN trial in known CD??

## Safety

- All capsules reached the cecum (SB3) or toilet (CC2)- all together **240** capsules...
- No cases of VCE retention
- **100% full small bowel examination**

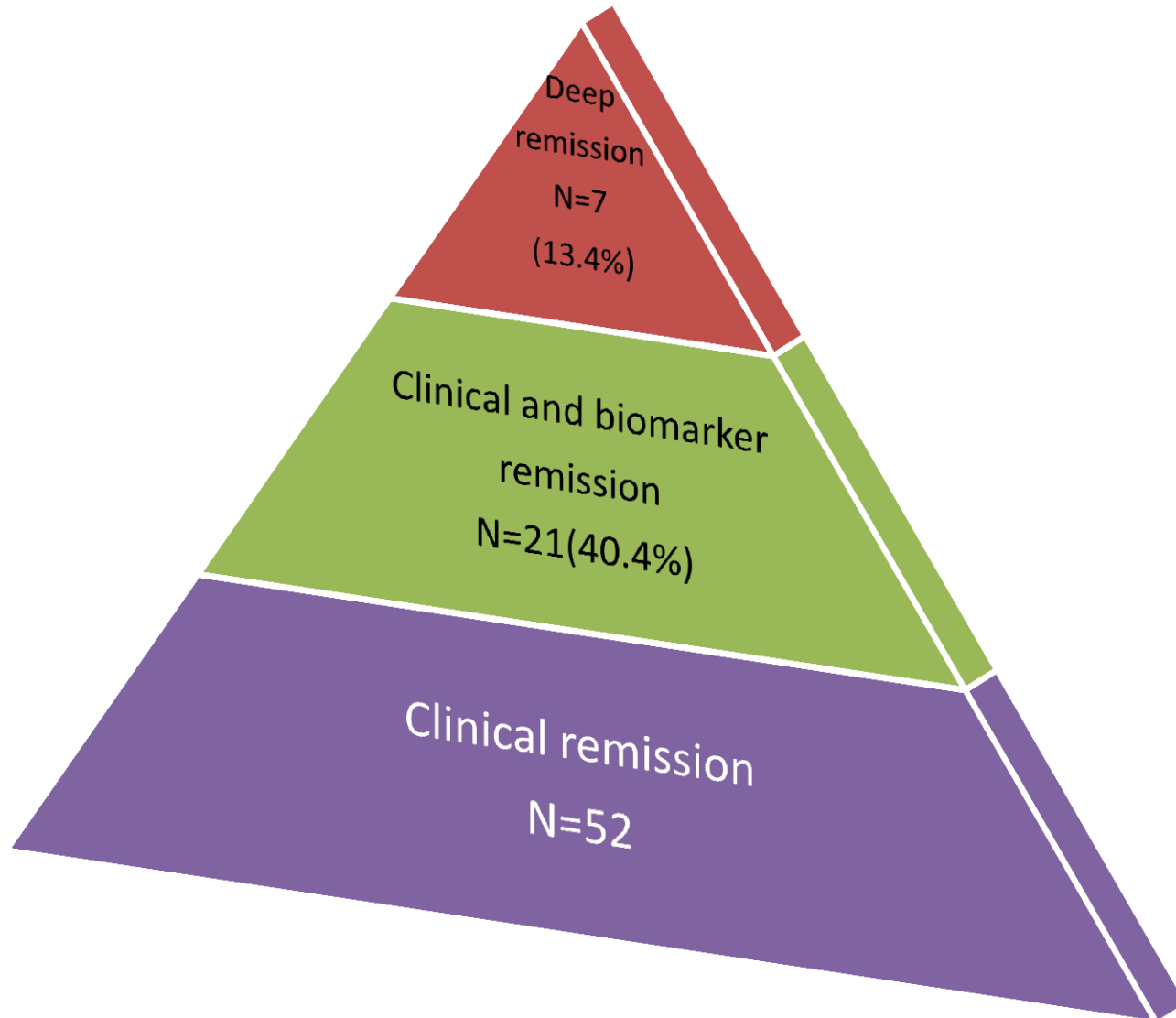
# What have we learned from the IIRN?- disease activity

- Small bowel inflammation, is severely under-estimated by current techniques. Such inflammation was disclosed by CE in > 70% of patients in clinical remission, many with normal CRP & Calprotectin (i.e. Lab remission)



- These findings may greatly impact our understanding of how best to alter the natural history of CD  
(Kopylov, Am J Gastroenterol 2015)

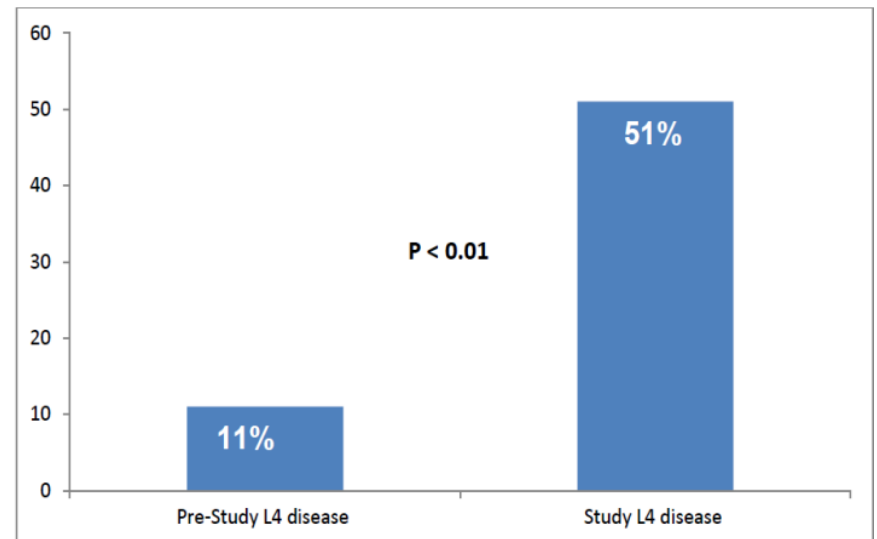
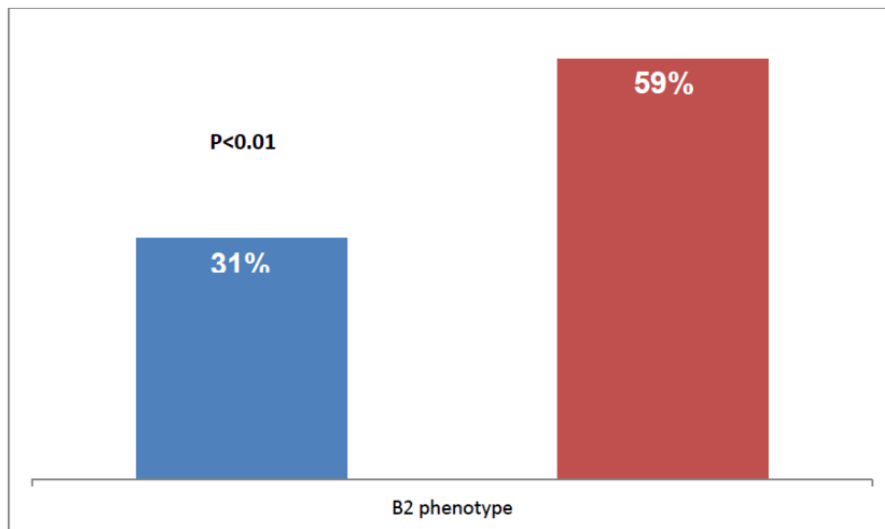
# How frequent is small bowel mucosal healing?





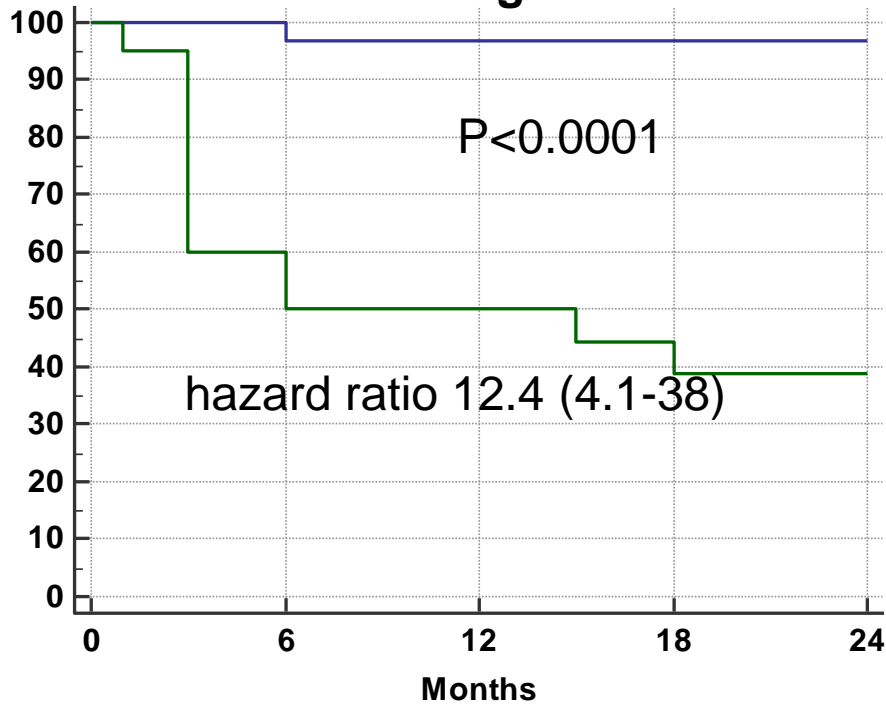
# What have we learned from the IIRN trial in known CD?- Phenotype change

- MRE and CE can re-classify the original phenotype of CD in 2/3 of patients, which may impact management decisions

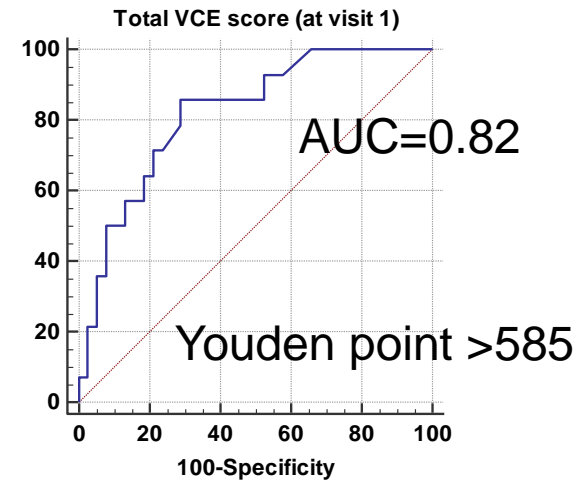
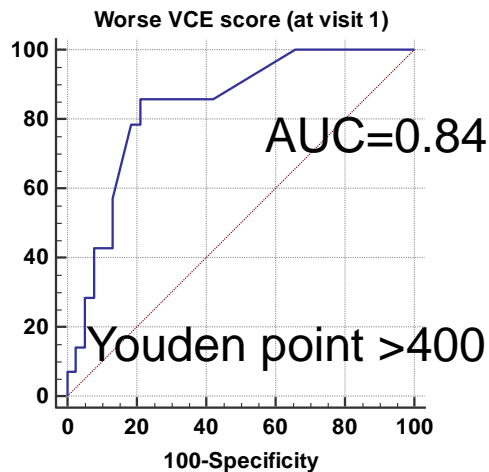
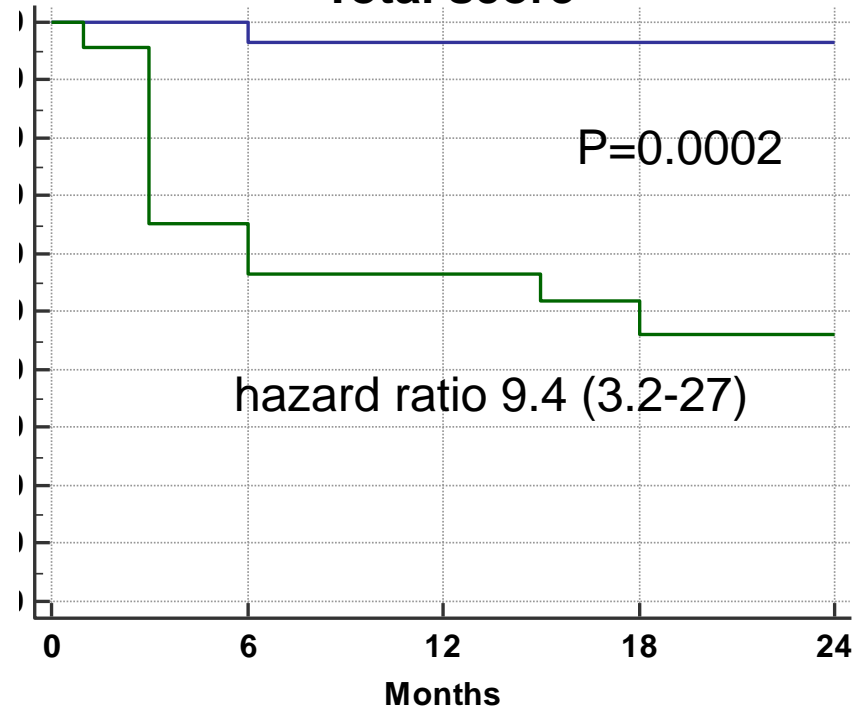


# Refined Lewis score predicts prognosis better

Baseline elevated capsule **LS>400**  
at worse segment



Baseline elevated capsule **LS>585**  
Total score



# Insights....


- This findings lead to the concept that one needs one PillCam to view the entire gut
- Up till a few months there was only one way of doing that- early activation of PillCam Colon2

# PCCE-2 in CD: pan-enteric capsule for a pan-enteric disease

## Safety and Feasibility of Using the Second-Generation Pillcam Colon Capsule to Assess Active Colonic Crohn's Disease

D'Haens<sup>1, 2</sup>, Löwenberg<sup>1</sup>, Samaan<sup>1, 2</sup>, Franchimont<sup>3</sup>, Ponsioen<sup>1</sup>, van den Brink<sup>1</sup>, Fockens<sup>1</sup>, Bossuyt<sup>4</sup>, Amininejad<sup>3</sup>, Rajamannar<sup>2</sup>, van Gossum<sup>3</sup>

Clin Gastroenterol Hepatol 2015

- **Multicenter 40 patients** with known Crohn's Disease (colon  $\pm$  SB)
- **PCCE-2**  **IC then same or next day**

- CCE shows moderate to strong correlation with endoscopy
- CCE underestimates disease severity vs. Colonoscopy
- CCE was better tolerated. No adverse events, no cases of capsule retention

# PillCam COLON 2<sup>©</sup> in Crohn's disease: A new concept of pan-enteric mucosal healing assessment

**12 patients**, active L3 disease

IC + small bowel capsule endoscopy at diagnosis

Inflammatory (B1) Phenotype

10 patients on azathioprine ± biologic

Corticosteroid-free remission (HBI < 5)

Follow-up ≥ 1 year

- PCCE-2 was used to assess pan-enteric MH
- MH- defined as Lewis Score < 135 in the SB
- No ulcers / erosions in the colon



Medtronic “picked the glove”

# Pillcam™ Crohn's capsule

## INDICATIONS FOR USE

The PillCam Crohn's capsule is intended for visualization of the **small bowel** and **colonic** mucosa

in adults and children from eight years of age.

- To visualize & monitor lesions that may indicate Crohn's disease - suspected or known



# PillCam Crohn's- product "package"

- Crohn's capsule
- Sensor belt & sensor array



- PillCam® Software v 9.0

- Recorder (DR 3)



# Pillcam™ Crohn's system

## FEATURES

**PillCam™ Crohn's** : PAN-INTESTINAL TOOL FOR A PAN-INTESTINAL DISEASE.



❑ 344 degree field of view

✓ **172 degrees per head**

❑ 256x256 image resolution

❑ Adaptive Frame Rate (AFR) technology increases the rate of image capture from **4 to 35 frames** per second based on the speed of the capsule.

Capsule transmits at 4 fps until AFR is activated at small bowel detection

❑ 3 SB and colon segments **according to length**



# Pillcam™ Crohn's patient Regimen

## Day 1 Prior

Begin clear liquid diet  
(Approximately 1L of clear liquids should be consumed throughout the day)



7 pm – 9 pm  
Ingest 2L of PEG  
(ingest over 2 hours)



Continue with clear liquids



## Day of Procedure

**7 am – 9 am**  
Ingest 2L of PEG  
(ingest over 2 hours)



**10 am**  
Ingest PillCam™  
Crohn's capsule



**1 hour later**  
10 mg metoclopramide



**At small bowel detection**  
180 mL oral sulfate solution  
added to 300 mL of water  
Drink additional 1L of water  
(resume clear liquids)



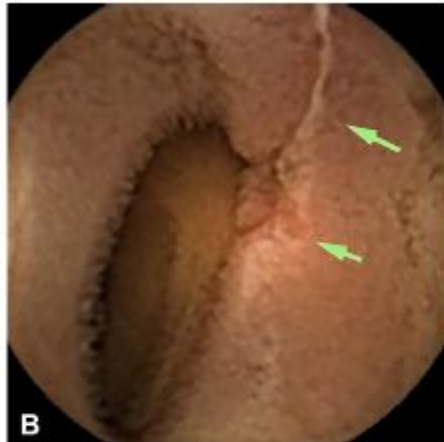
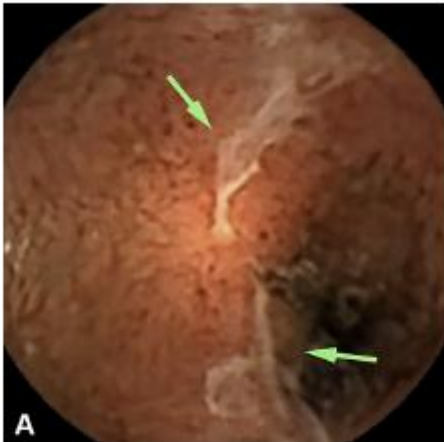
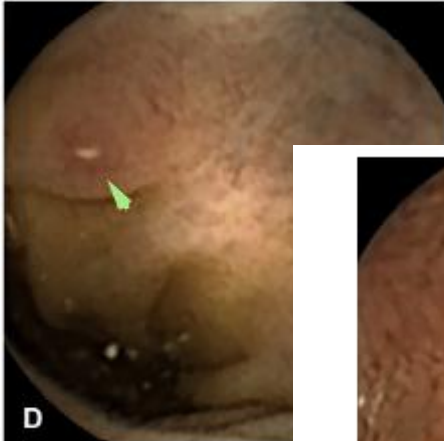
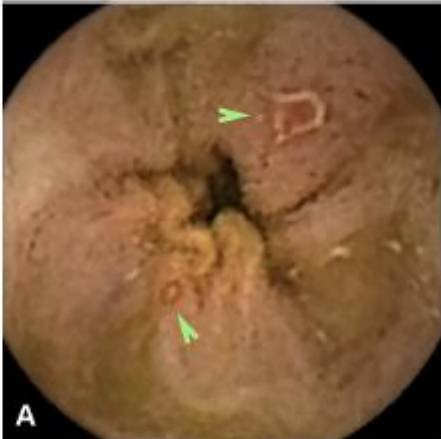
**3 hours later**  
90 mL oral sulfate solution  
added to 150 mL of water  
Drink additional 1L of water



**2 hours later – 10 mg bisacodyl suppository**  
**2 hours later – Light meal**

★ Not required for all patients

this is what one may see.....



# Pillcam™ software

READ THE STUDIES WITH GREATER EFFICIENCY

GI Table

SEGMENT	MOST SEVERE LESION	TYPICAL SEVERITY	EXTENT	IMAGES
SB I	2	2	30%-60%	<input type="radio"/>
SB II	3	1	<10%	<input type="radio"/>
SB III	2	2	10%-30%	<input type="radio"/>
Colon	3	3	>60%	<input type="radio"/>

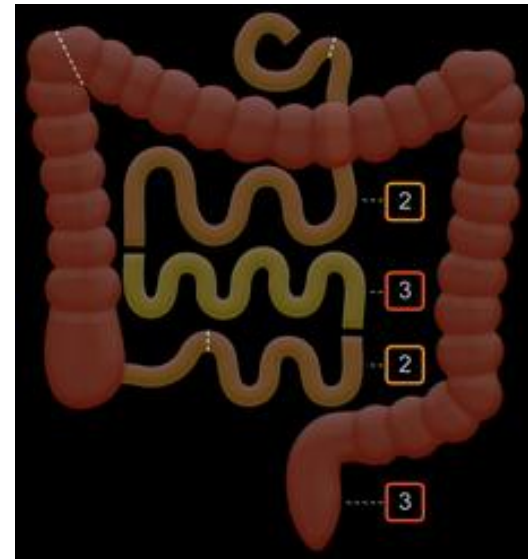
SUB SEGMENTS

Duo.	Involved	R. Colon	Involved
TI	Involved	L. Colon	Involved

Assessment of disease activity by segment

- Small bowel defined by progress vs. time
- Optional sub-segments provide more detailed analysis

GI Map



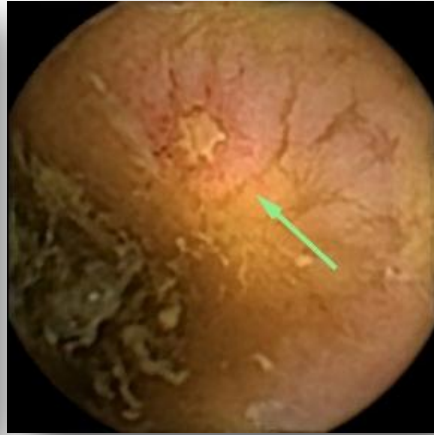
Graphical representation of data from the GI Table for analysis and comparison

# PILLCAM™ CROHN'S CAPSULE

## LESION SEVERITY



Mild - 1



Moderate- 2



Severe - 3



Stricture- S

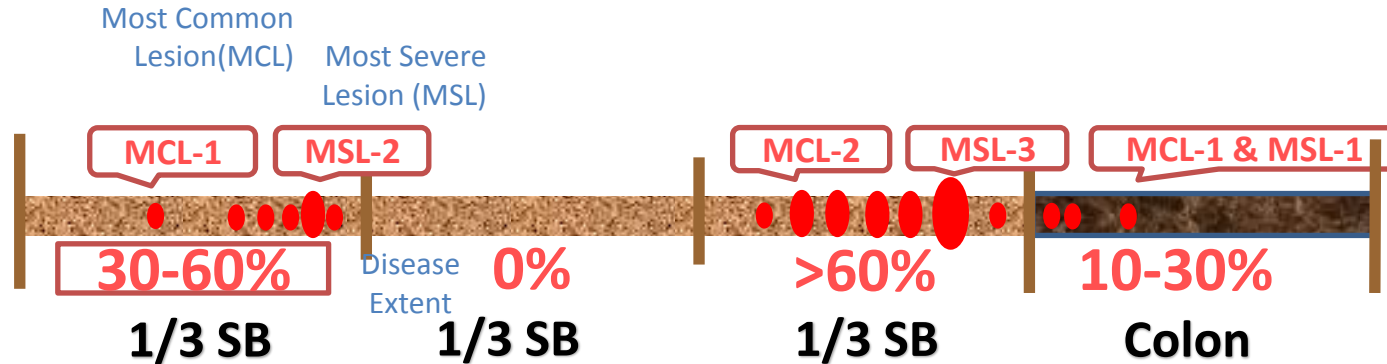
### LESION SEVERITY RATING:

1. **Mild:** Superficial, small ulcer or erosion.
  2. **Moderate:** Intermediate ulcer in terms of size and depth.
  3. **Severe:** Prominent ulcer (size & depth) with either circular, longitudinal, "kissing", fissuring or "cobblestone" morphology.
- S. **Stricture:** Existence of a stricture.

# PILLCAM™ CROHN'S CAPSULE

## DISEASE EVALUATION METHODOLOGY

- Complete evaluation of all the 3 small bowel segments and the colon:



- In order to filled by segment the GI table and obtain a GI MAP

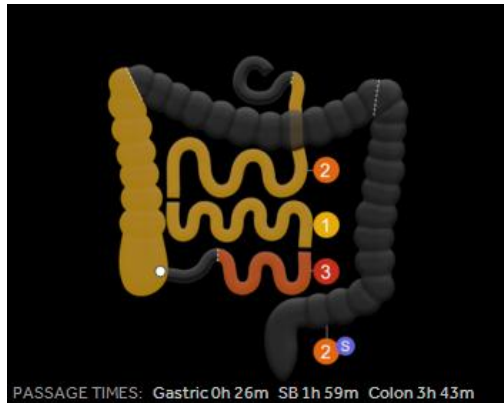
SEGMENT	MSL	MCL	EXTENT %	IMAGES
SB I	2	1	10 - 30	<input type="checkbox"/>
SB II	1	1	0 - 10	<input type="checkbox"/>
SB III	3	2	30 - 60	<input type="checkbox"/>
Colon	2	1	0 - 10	<input type="checkbox"/>

SUB SEGMENTS

Duo.	Not Involved	TI	Not Involved
R. Colon	Involved	L. Colon	Not Involved

COMMENTS

GI TABLE



GI MAP

# PILLCAM CROHN'S CAPSULE

## REPORT SCREEN

Click **Compare Report** to view prior report summary

The screenshot displays the PillCam Desktop Software interface. The main window is titled "PillCam SBC - Patient Patient, ID 123456 - 12/30/2012". The interface is divided into several sections:

- Top Bar:** Includes "File", "Save", and "PillCam SBC - Patient Patient, ID 123456 - 12/30/2012".
- Navigation:** "PREPARE", "VIEW", and "REPORT" buttons.
- Tools:** "De-Identify", "Electronically Sign Reports", "Preview", "Save", "Print", "Export", "Compare Tables", "Treatment Over Time", "Save Clips/Images", "Save Video Segment", "Save Joined Segment", "Lewis Score", and "Atlas".
- Report Summary:** A table showing segment details and a 3D anatomical diagram of the colon with numbered regions (1, 2).
- Reason for Referral:** "CD follow-up after introduction of biological therapy".
- Procedure Information and Findings:** "mild inflammation in SB2, SB3 with moderate severity lesions. No inflammatory lesions in the colon."
- Summary and Recommendations:** "Diffuse disease involvement of the SB and colon. Continue biological therapy with re-assessment of mucosal responsiveness in 1 year."

A "PRIOR REPORT" pop-up window is open, titled "Capsule Endoscopy Report". It contains the following information:

- Patient Data:** Patient Name: Patient Patient, ID: 123456, Birth Date: 10/26/1975, Gender: Male, Capsule ID: 4RYJAA5, Procedure Date: 6/30/2012.
- Reason for Referral:** Long-standing CD patient with recent re-flare of disease. Base-line assessment of mucosal status due to newly initiated biological therapy.
- Patient Data:** Small bowel passage time: 1h 12m, Colon passage time: 0h 46m.
- Procedure Information and Findings:** Mild to moderate involvement of the SB, with duodenal involvement and TI involvement. Severe disease in the distal left colon.
- GI Table:**

SEGMENT	MOST SEVERE LESION	TYPICAL SEVERITY	EXTENT
SB I	2 - Moderate	1 - Mild	10%-30%
SB II	1 - Mild	1 - Mild	<10%
SB III	2 - Moderate	2 - Moderate	30%-60%
Colon	3 - Severe	Stricture	1 - Mild

Sub-segments: Duodenum: Not Involved, Right Colon: Involved, Terminal Ileum: Involved, Left Colon: Involved.

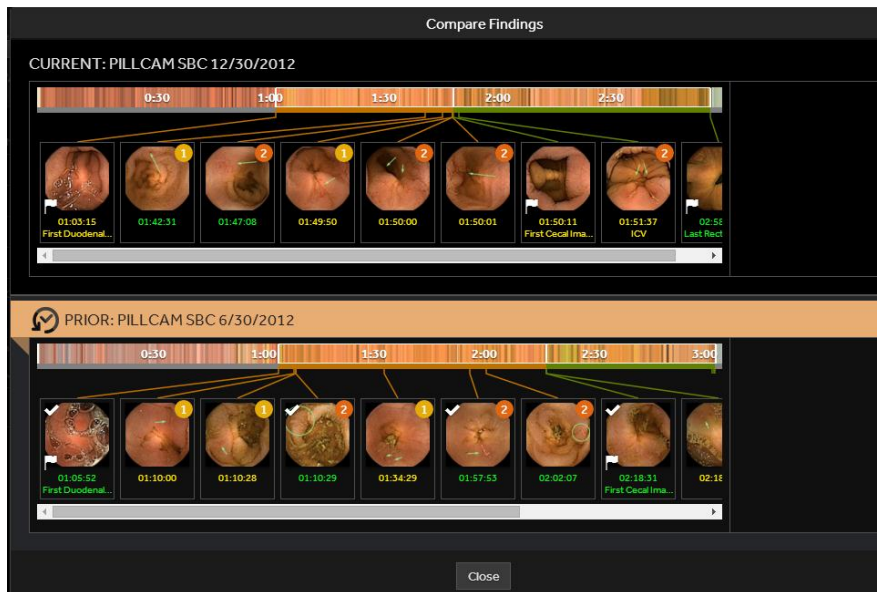


# Pillcam™ Crohn's system

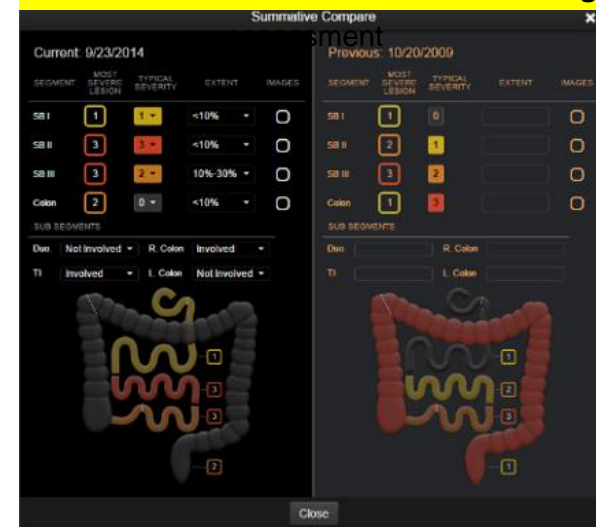
## FEATURES

### PillCam™ Software V9:

Software enables a quantitative assessment of disease progression **over time** to evaluate Rx effectiveness & MH of the SB and colon **with a single capsule**.



The "GI MAP" and "GI table"  
a Graphical representation of :  
**Treatment Over Time & Mucosal Healing**



# Comparing treatment overtime

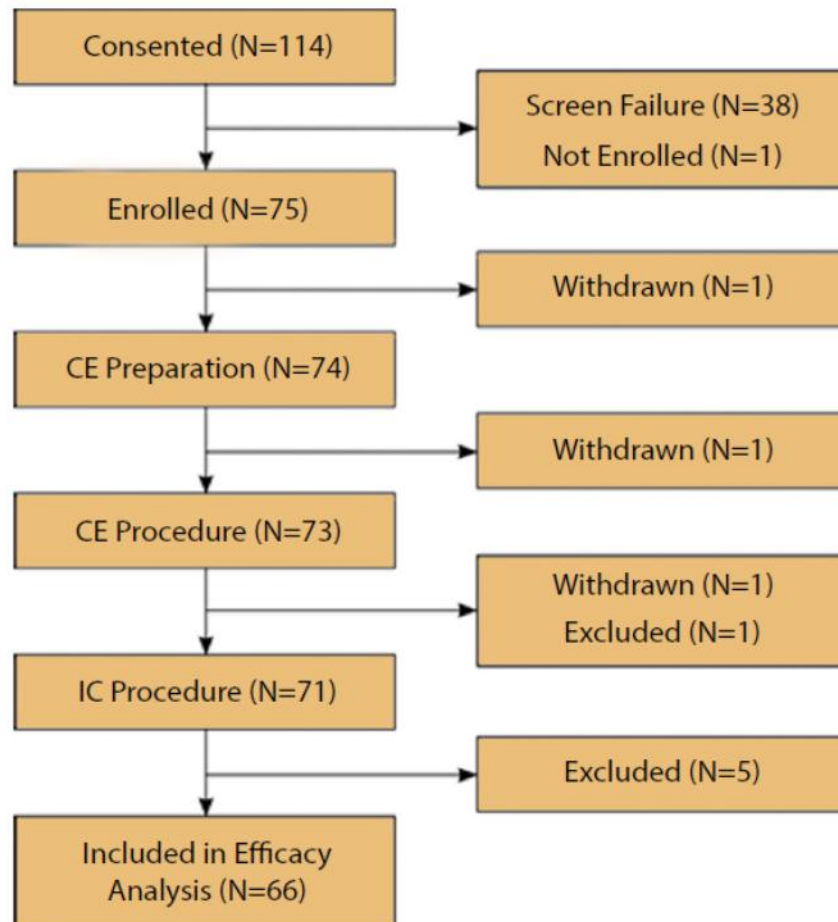




# Comparing diagnostic yield of a novel pan-enteric video capsule endoscope with ileocolonoscopy in patients with active Crohn's disease: a feasibility study

Jonathan A. Leighton, MD,<sup>1</sup> Debra J. Helper, MD,<sup>2</sup> Ian M. Gralnek, MD, MSHS,<sup>3</sup>  
Iris Dotan, MD,<sup>4</sup> Ignacio Fernandez-Urien, MD,<sup>5</sup> Adi Lahat, MD,<sup>6</sup> Pramod Malik, MD,<sup>7</sup>  
Gerard E. Mullin, MD,<sup>8</sup> Bruno Rosa, MD<sup>9</sup>

Scottsdale, Arizona; Indianapolis, Indiana; Baltimore, Maryland, USA; Afula, Tel Aviv, Israel; Navarra, Spain; Guimarães, Portugal



# Detection rates

**TABLE 6. Detection rate per segment**

Segment	Subjects with active lesions (n)	Capsule detection rate (%)	IC detection rate (%)	Capsule-IC detection rate (%)	95% CI† detection rate (%)
Ileum*	46	70	54	16	3-26
Cecum	23	38	26	12	-2 to 26
Ascending colon	27	36	34	2	-9 to 12
Transverse colon	22	30	24	6	-3 to 16
Descending/sigmoid Colon	27	39	31	8	-3 to 16
Rectum	20	29	25	4	-3 to 16

IC, ileocolonoscopy; CI, confidence interval.

\*The terminal ileum using the capsule was defined as the video segment 10 minutes before the cecum was reached. Thus, it may include mucosa of the more proximal small bowel.

†Based on the Wald interval method for paired proportions.

**TABLE 8. Characteristics of active Crohn's disease in subjects with proximal small-bowel disease**

Characteristics of active Crohn's disease in the proximal small bowel	Number of subjects (n = 30)
Ulcers other than aphthous-type lesions	25 (83.3%)
Aphthous ulceration	16 (53.3%)
Inflammatory stricture	6 (20.0%)
Bleeding	2 (6.7%)

# “PIANO” study-proof of concept

- Multicenter prospective feasibility study
- 50 patients (10 from each center)
- Mainly **known CD** (69%); UC- 10%; **susp. CD**- 21%
- **Technical issues:**
  - Completion rate
  - Reading time
  - Quality of images
- **Patients issues:**
  - Convenience of patients & operators
  - Safety

# “PIANO” study-results

- 68 screened; 54 recruited (14 patency failures); **49** ingested the capsule (5 withdrew consent)
- **All** 49 patients **completed** the study
- **All** capsules reached the **toilet**, most while photographing
- **Reading time-** much shorter than PillCam C2 for CRC/polyps
- **Excellent quality** pictures

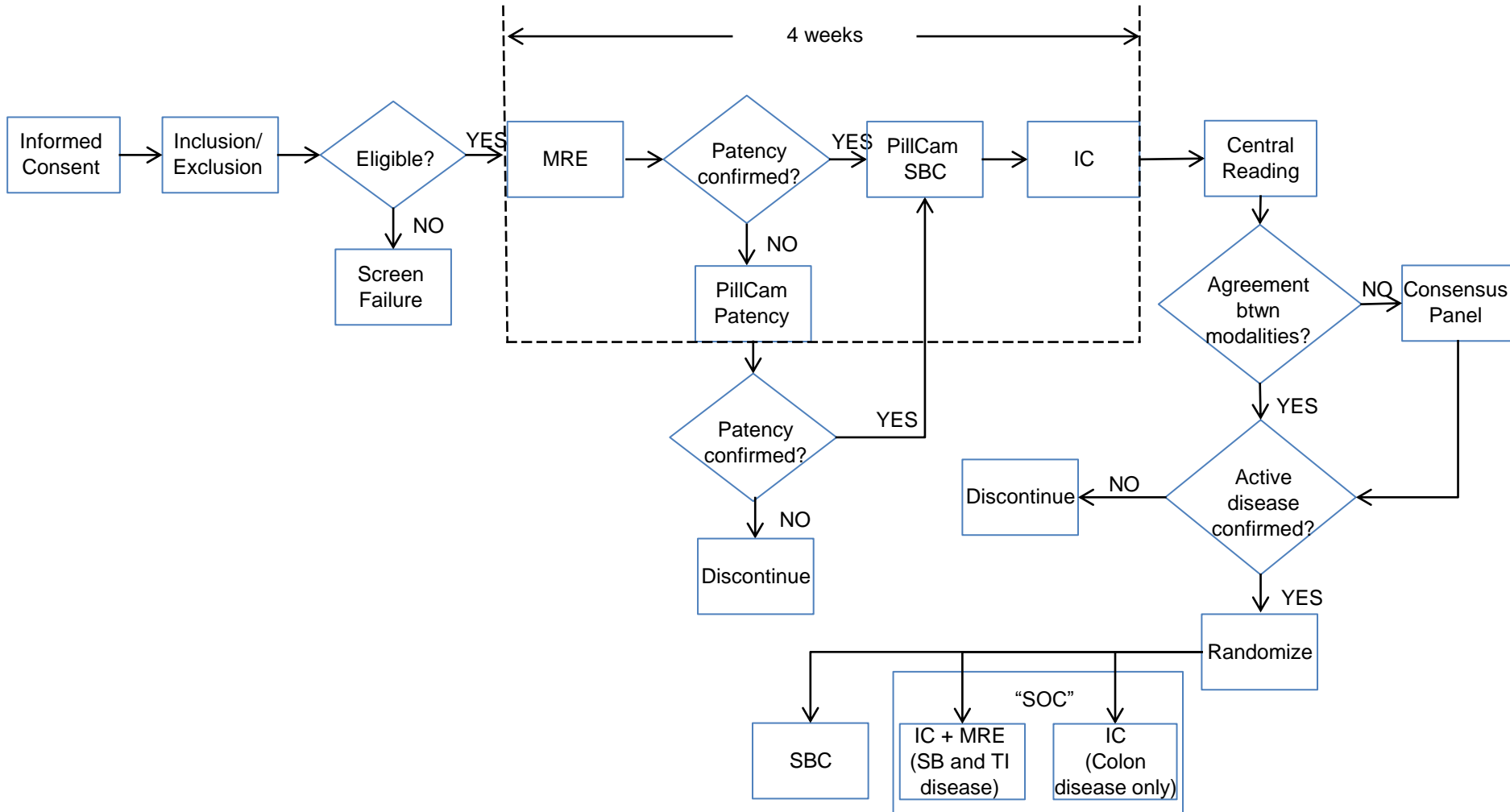
# Summary

- The new pan-enteric capsule is **safe** in patients with IBD
- It may have an **important role** in assessing pan enteric **MH**
- The new software allows follow up and comparison over time
- The capsule's role as a screening tool to patients with suspected CD needs further evaluation

# The Blink study- starting soon....

<b>Purpose of study</b>	<b>assess positive/negative agreement for lesions in the SB &amp; colon comparing PillCam SBC capsule versus IC plus MRE in symptomatic or asymptomatic subjects with known CD and mucosal disease.</b>
<b>Study design</b>	<b>Multicenter, Prospective, Randomized Study</b>
<b>Number of patients</b>	<b>352 /~30-40 sites</b>
<b>Patients population</b>	<b>Patients &gt; 8 years with active CD and mucosal disease on clinical evaluation</b>
<b>Study Procedures</b>	<b>All enrolled subjects will undergo IC, MRE and PillCam SBC imaging at baseline evaluation. Those with confirmed disease will be 1:1 randomized to either the PillCam SBC group or the Standard of Care group for the follow-up. Subjects followed at q3 months with additional imaging studies based on randomization taking place at 6 and 12 months.</b>
<b>Follow up</b>	<b>Q3 M</b>
<b>Duration of study</b>	<b>~3 years</b>

# Study flow



**This will teach us a lot about the role of SBC capsule versus standard of care techniques- regarding sensitivity ,safety, costs and possibly outcomes**



So, the future is bright.....  
Thanks for your attention