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

PillCam Crohn’s

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Crohn’s Disease
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
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

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

- Clinical remission: N=52
- Clinical and biomarker remission: N=21 (40.4%)
- Deep remission: N=7 (13.4%)
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**
  - Hazard ratio: 12.4 (4.1-38)
  - P < 0.0001

- **Total score**
  - Hazard ratio: 9.4 (3.2-27)
  - P = 0.0002

**Worse VCE score (at visit 1)**
- Youden point > 400
- AUC = 0.84

**Total VCE score (at visit 1)**
- Youden point > 585
- AUC = 0.82
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’Haens¹, ², Löwenberg¹, Samaan¹, ², Franchimont³, Ponsioen¹, van den Brink¹, Fockens¹, Bossuyt⁴, Amininejad³, Rajamannar², van Gossum³

*Clin Gastroenterol Hepatol 2015*

- **Multicenter 40 patients** with known Crohn’s Disease (colon ± 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® 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”
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
- Recorder (DR 3)
- PillCam® Software v 9.0
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)
  - ![Clear liquids](image)

- **7 pm – 9 pm**
  - Ingest 2L of PEG
  - (ingest over 2 hours)
  - ![PEG](image)

- **Continue with clear liquids**
  - ![Clear liquids](image)

## Day of Procedure

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>7 am – 9 am</strong></td>
<td>Ingest 2L of PEG (ingest over 2 hours)</td>
</tr>
<tr>
<td><strong>10 am</strong></td>
<td>Ingest PillCam™ Crohn’s capsule</td>
</tr>
<tr>
<td><strong>1 hour later</strong></td>
<td>10 mg metoclopramide</td>
</tr>
<tr>
<td><strong>At small bowel detection</strong></td>
<td>180 mL oral sulfate solution added to 300 mL of water</td>
</tr>
<tr>
<td><strong>Drink additional 1L of water</strong></td>
<td>(resume clear liquids)</td>
</tr>
<tr>
<td><strong>3 hours later</strong></td>
<td>90 mL oral sulfate solution added to 150 mL of water</td>
</tr>
<tr>
<td><strong>Drink additional 1L of water</strong></td>
<td></td>
</tr>
<tr>
<td><strong>2 hours later</strong></td>
<td>– 10 mg bisacodyl suppository</td>
</tr>
<tr>
<td><strong>2 hours later</strong></td>
<td>– Light meal</td>
</tr>
</tbody>
</table>

*Not required for all patients*
this is what one may see.............
Pillcam™ software
READ THE STUDIES WITH GREATER EFFICIENCY

Assessment of disease activity by segment
- Small bowel defined by progress vs. time
- Optional sub-segments provide more detailed analysis

Graphical representation of data from the GI Table for analysis and comparison
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.
4. **Stricture**: Existence of a stricture.
PILLCAM™ CROHN'S CAPSULE

DISEASE EVALUATION METHODOLOGY

- Complete evaluation of all the 3 small bowel segments and the colon:
  
  - Most Common Lesion (MCL)
  - Most Severe Lesion (MSL)

  - Disease Extent:
    - 30-60% (1/3 SB)
    - 0% (1/3 SB)
    - >60% (1/3 SB)
    - 10-30% (Colon)

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

GI TABLE

GI MAP
# PILLCAM CROHN'S CAPSULE

## REPORT SCREEN

![Image of the PillCam CROHN's Capsule Report Screen]

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

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### Prior Report

**Capsule Endoscopy Report**

- **Reason for Referral:**
  - Long-standing CD patient with recent re-flux of disease.
  - Baseline assessment of mucosal status due to newly initiated biological therapy.
- **Patient Data**
  - Name: Patient Patient
  - ID: 123456
  - Birth Date: 1965/06/01
  - Gender: Male
  - Note: Capsule ID
  - Procedure Date: 6/30/2012

#### Procedure Information and Findings:

- Diffuse disease involvement of the SB and colon. Continue biological therapy with reassessment of mucosal responses in 1 year.

### Summary and Recommendations:

- Diffuse disease involvement of the SB and colon. Continue biological therapy with reassessment of mucosal responses in 1 year.

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**TABLE 1**

<table>
<thead>
<tr>
<th>SEGMENT</th>
<th>MOST SEVERE LESION</th>
<th>TYPICAL SEVERITY</th>
<th>EXTENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>SB I</td>
<td>2 - Moderate</td>
<td>1 - Mild</td>
<td>10%-30%</td>
</tr>
<tr>
<td>SB II</td>
<td>1 - Mild</td>
<td>1 - Mild</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>SB III</td>
<td>2 - Moderate</td>
<td>2 - Moderate</td>
<td>30%-60%</td>
</tr>
<tr>
<td>Colon</td>
<td>3 - Severe</td>
<td>1 - Mild</td>
<td>10%-50%</td>
</tr>
</tbody>
</table>

- Disease: Diffuse disease involvement of the SB and colon. Continue biological therapy with reassessment of mucosal responses in 1 year.

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**Signatures**

(Please provide signatories for the report.)
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 over time

- Jan 2012: 6MP, 100mg
- Jan 2013: Infliximab, 400mg
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,1 Debra J. Helper, MD,2 Ian M. Gralnek, MD, MSHS,3 Iris Dotan, MD,4 Ignacio Fernandez-Urrien, MD,5 Adi Lahat, MD,6 Pramod Malik, MD,7 Gerard E. Mullin, MD,8 Bruno Rosa, MD9

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

#### TABLE 6. Detection rate per segment

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

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

<table>
<thead>
<tr>
<th>Characteristics of active Crohn’s disease in the proximal small bowel</th>
<th>Number of subjects (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcers other than aphthous-type lesions</td>
<td>25 (83.3%)</td>
</tr>
<tr>
<td>Aphthous ulceration</td>
<td>16 (53.3%)</td>
</tr>
<tr>
<td>Inflammatory stricture</td>
<td>6 (20.0%)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>2 (6.7%)</td>
</tr>
</tbody>
</table>
“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
### Purpose of study
assess positive/negative agreement for lesions in the SB & colon comparing PillCam SBC capsule versus IC plus MRE in symptomatic or asymptomatic subjects with known CD and mucosal disease.

### Study design
Multicenter, Prospective, Randomized Study

### Number of patients
352 /~30-40 sites

### Patients population
Patients > 8 years with active CD and mucosal disease on clinical evaluation

### Study Procedures
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.

### Follow up
Q3 M

### Duration of study
~3 years
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