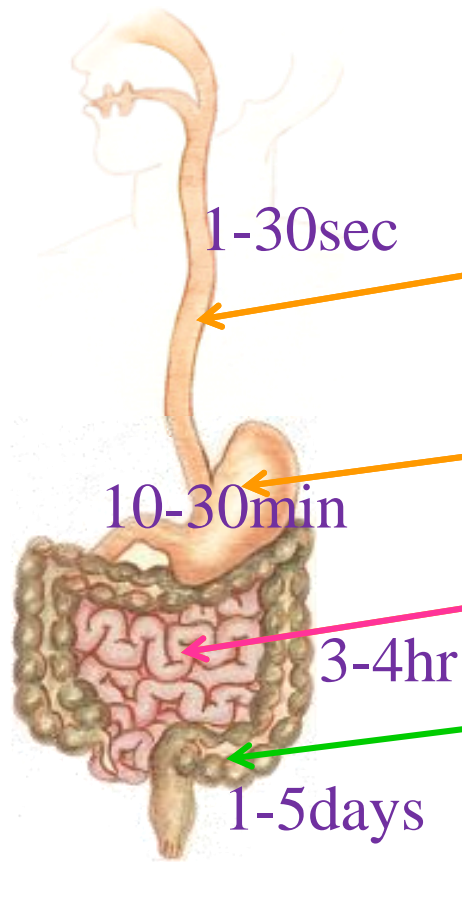


# Given Imaging

Rafi Nave - 2016



# Gastrointestinal System



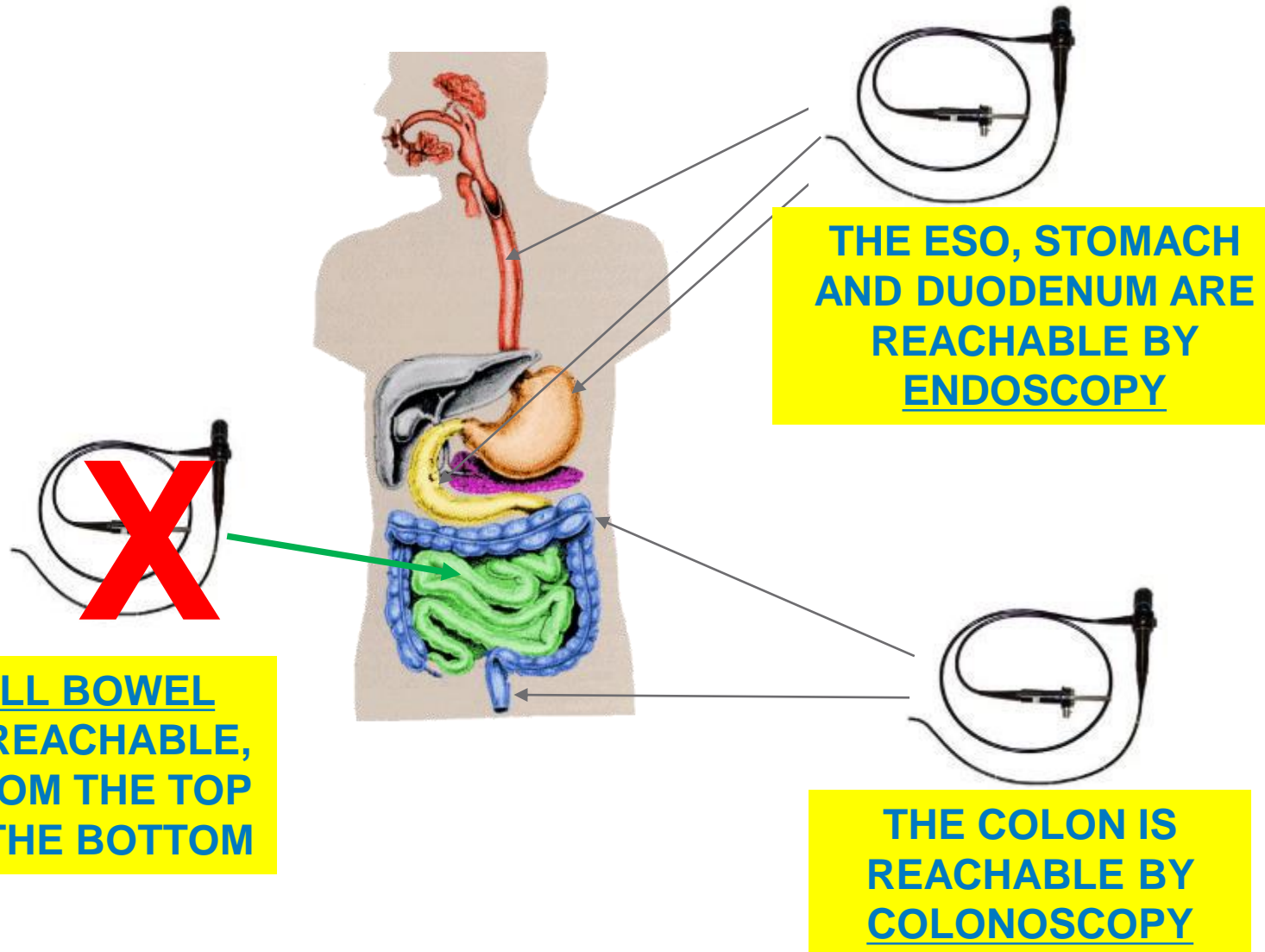
The diagram illustrates the human gastrointestinal tract. Arrows point from the transit time labels to the corresponding organs: 1-30sec to the esophagus, 10-30min to the stomach, 3-4hr to the small intestine, and 1-5days to the large intestine.

Organ	Major Tasks	Typical Length
<i>Esophagus</i> 1-30sec	Food transfer from mouth to Stomach	≈30 cm
<i>Stomach</i> 10-30min	Initial digestion of food (mechanical and enzymatic)	
<i>Small Intestine (Small Bowel)</i> 3-4hr	Absorption of nutrients	6-7 m
<i>Large Intestine (Colon)</i> 1-5days	Absorption of water & electrolytes. Temporary storage of residues	≈1.5 m

# ENDOSCOPY



## LIMITATIONS OF ENDOSCOPY



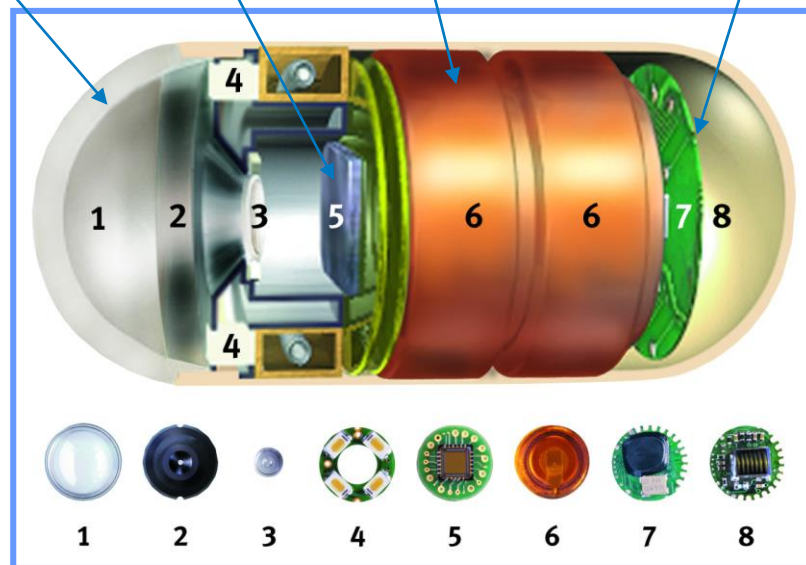
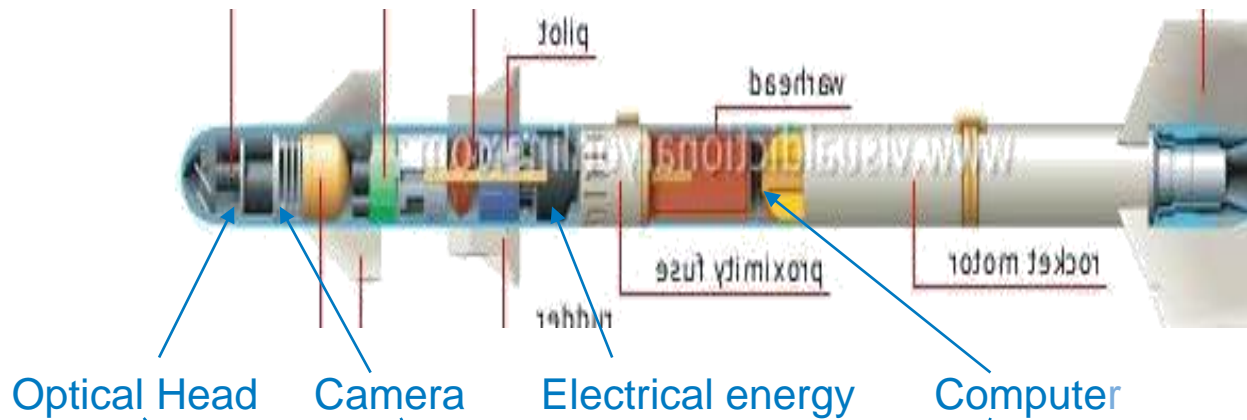
# BOSTON 1982



**Dr Eitan Scapa**  
**'Assaf Harofe' hospital**

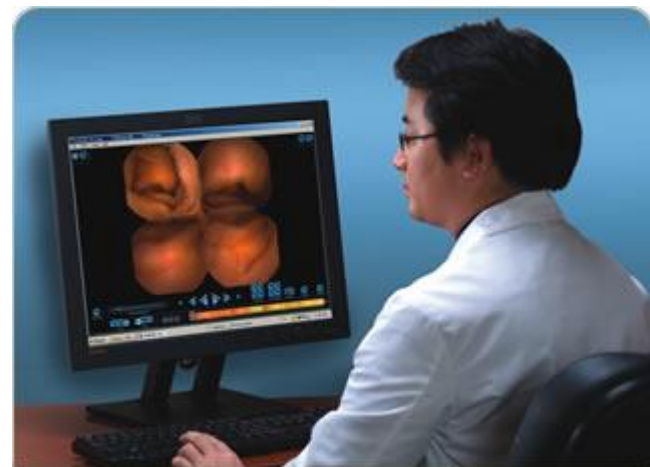
**Dr Gabi Idan**  
**RAFAEL**

# The Invention



Optical Head

# The system



*Pill cam*

692

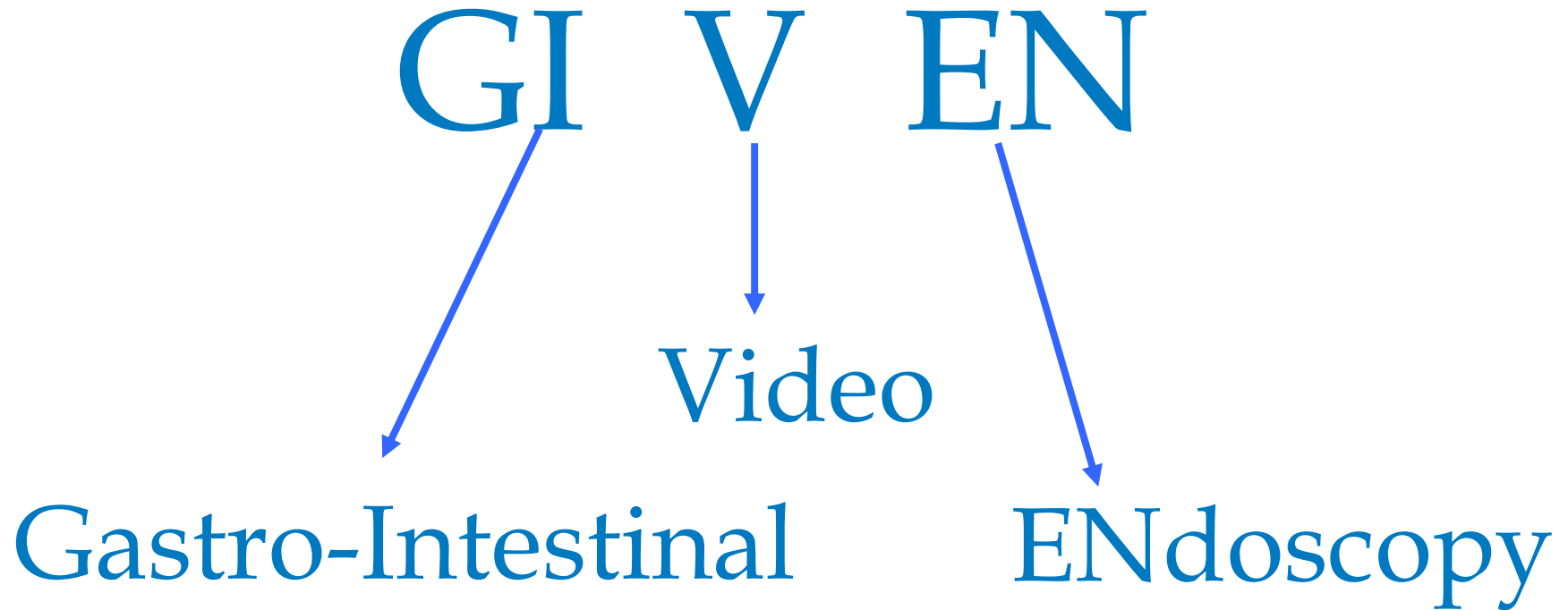
00:36:48

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PillCam™ SB

# Why “Given”?



# Comprehensive GI Diagnostic and Monitoring Solutions



- PillCam ESO 2
- Capsule endoscopy procedure for visualization of the esophagus



- The only capsule-based pH test for GERD
- Ambulatory pH testing gold standard



- PillCam SB 2
- Most widely used capsule endoscope for visualization of the entire small bowel
- The standard of care in numerous countries



Complete reflux diagnostic solution for both capsule and catheter-based testing



High-Resolution Manometry with physiology visualization and data analysis software for identification of motility disorders



- PillCam COLON 2
- Safe, minimally invasive, sedation-free, patient-friendly modality to visualize the colon and rectum



Ingestible, wireless motility capsule using sensor technology to measure pH, pressure and temperature from within the entire GI tract

PillCam COLON 2 not cleared for use in U.S.

# Recognized Industry Leader

## World Leader in Minimally-Invasive GI Diagnostics

~90% Market share world-wide. >95% share in the U.S.A.

One of the largest GI sales and marketing organizations in North America (nearly 100 sales and marketing professionals in the US alone)

~6,000 active PillCam customers<sup>1</sup>  
3,000 Americas, 1,000 APJ, 2,000 EMEA

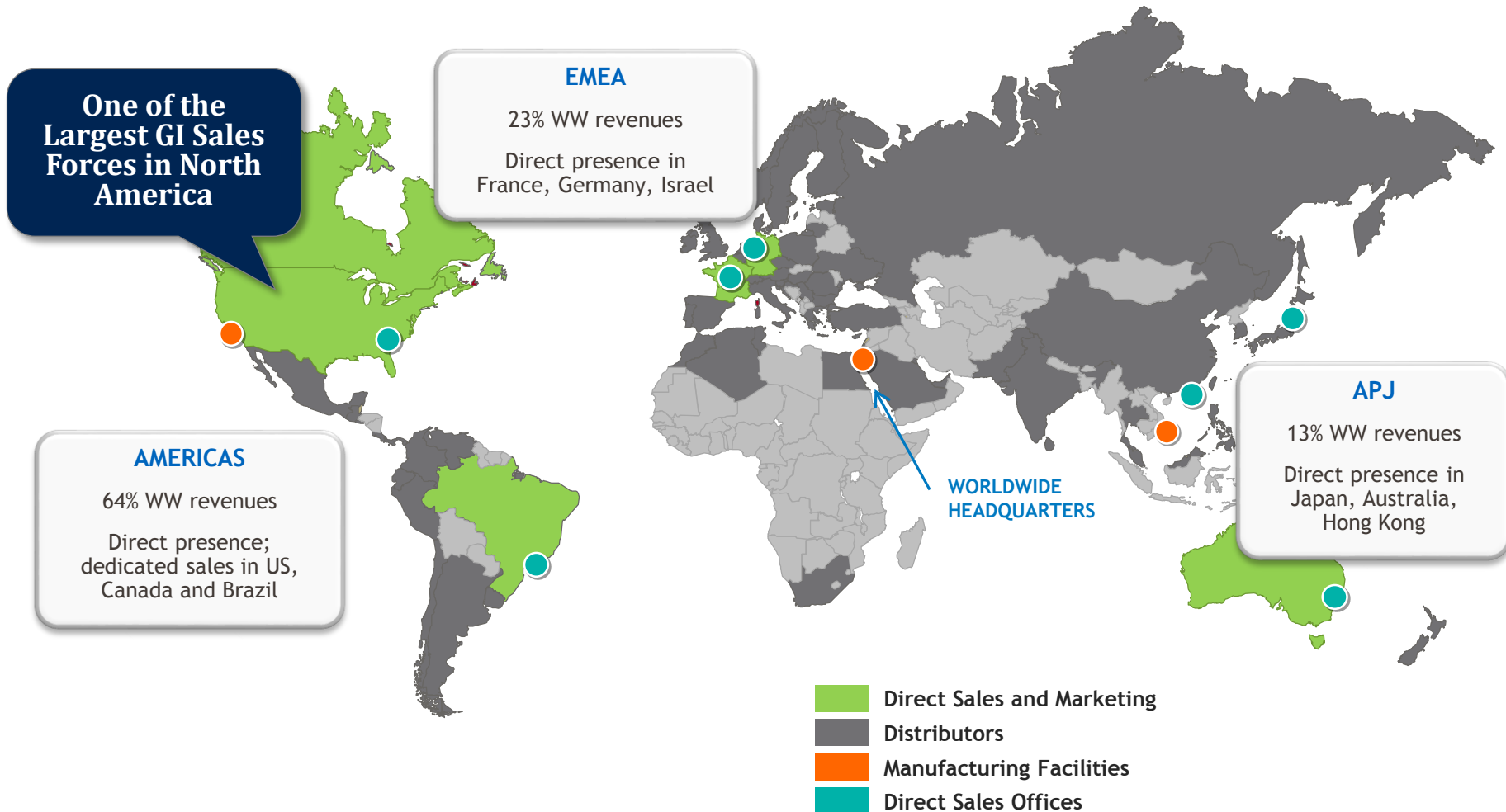
More than 2,000 PillCam and 300 Reflux & Manometry  
peer-reviewed publications

Strong IP: ~450 registered patents, ~250 pending patents

1. Refers to active customers, defined as those who have placed an order within the last 12 months.

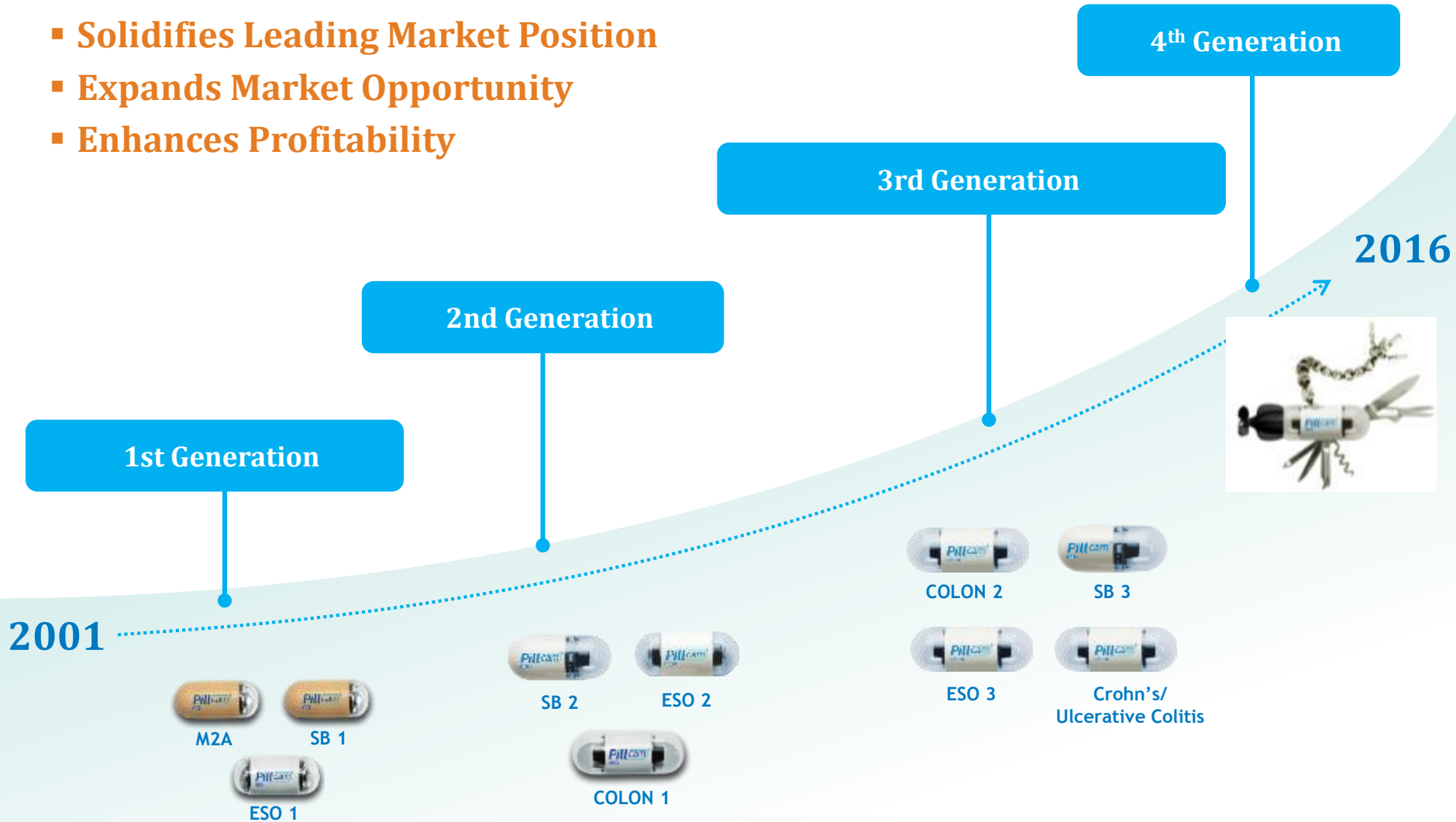
# Global Footprint Supports Growth

Direct sales and marketing in 9 countries; products available in 75 + countries

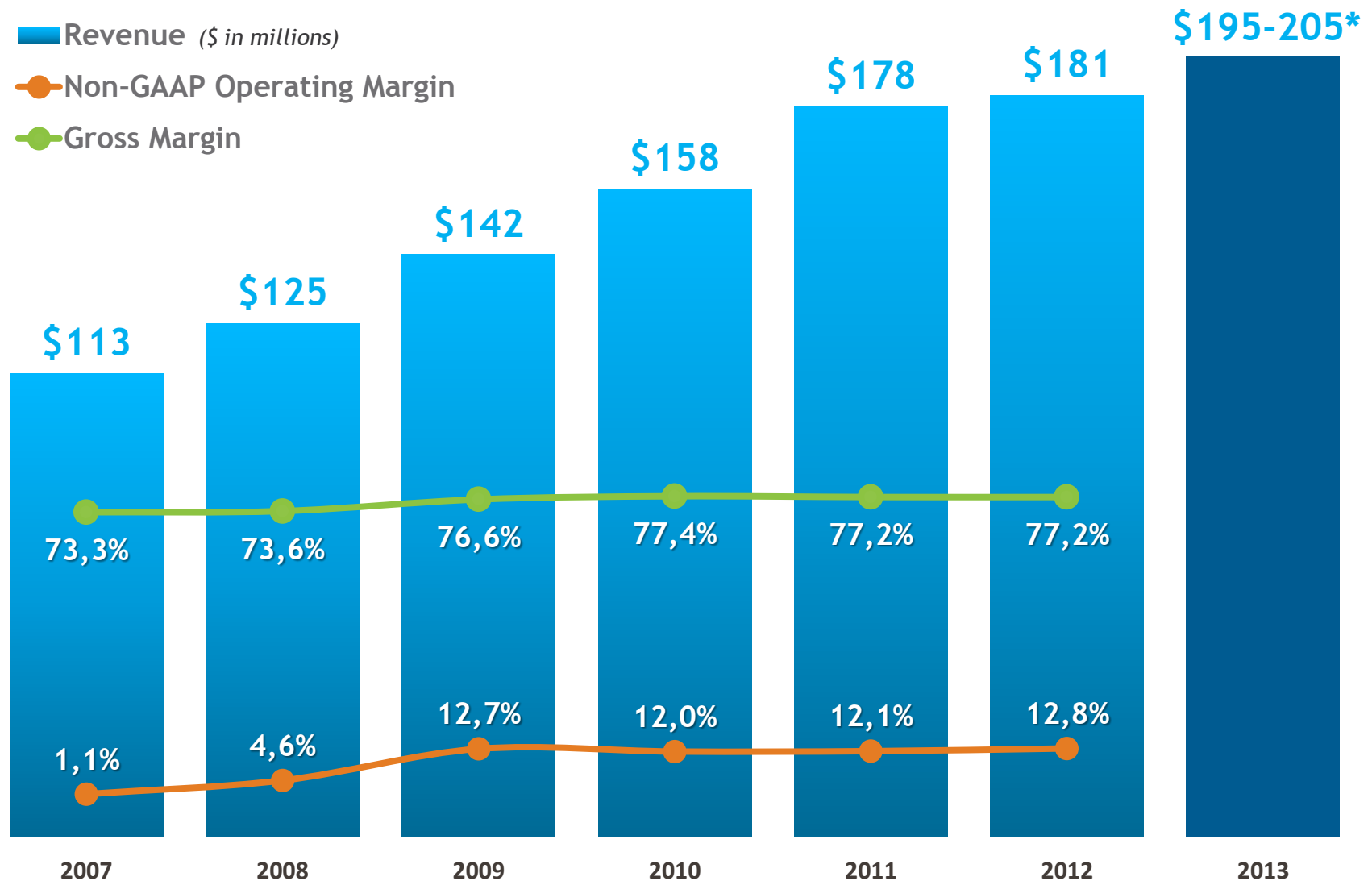


# Continuous Innovation of Capsule Endoscopy Franchise

- Solidifies Leading Market Position
- Expands Market Opportunity
- Enhances Profitability



# Demonstrated Revenue Growth and Profitability



\*Guidance



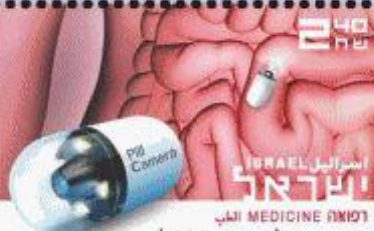




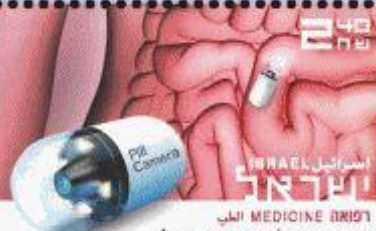


# 改变世界的以色列发明创造

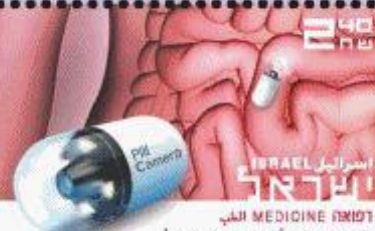
## חידושים ישראליים ששינו את העולם ISRAELI INNOVATIONS THAT CHANGED THE WORLD



רפואה MEDICINE ופדא  
חידושים ישראליים ששינו את העולם  
ISRAELI INNOVATIONS THAT CHANGED THE WORLD  
האינטקראד האסראלילאית התי גירד, ודג האלמ  
הטטיל 2010 דוד אל



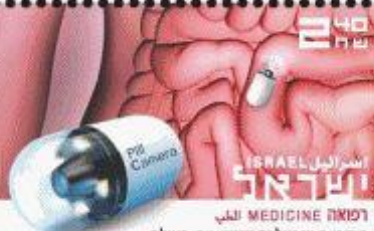
רפואה MEDICINE ופדא  
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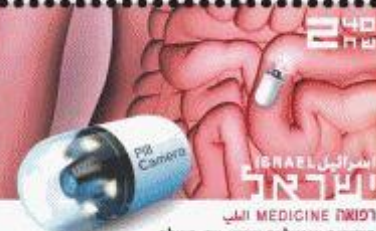


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הטטיל 2010 דוד אל



ביתן ישראל  
ISRAEL PAVILION  
以色列馆

EXPO  
2010  
SHANGHAI, CHINA



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# Given Imaging Products



# Flagship Product is Standard of Care

## PillCam SB

- Pioneer and market leader in small bowel visualization
  - PillCam SB
  - Seven generations of proprietary software
- PillCam SB is the standard of care for diagnosing small bowel disorders
  - ~2.5 million PillCam SB ingestions
  - Available in more than 80 countries
- Scientific backing
  - Over 100 sponsored clinical trials
  - Over 2,000 peer-reviewed articles



# Images from PillCam SB



Given Imaging Proprietary and Confidential

# PillCam SB Images



Normal Small Bowel



Crohn's Disease



Celiac Disease



Gastrointestinal  
Bleeding

# PillCam SB Meets a Critical Clinical Need

## ■ Patients

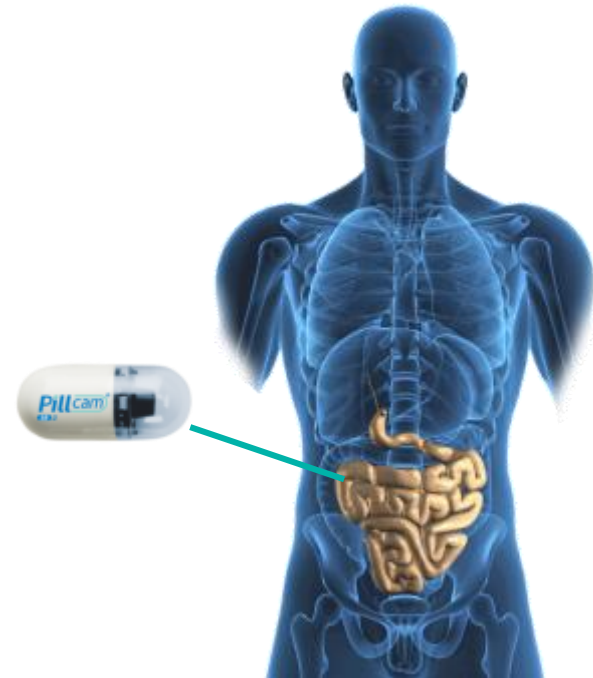
- Non-invasive
- No sedation
- Easy to administer and ingest
- No lost work time, instant recovery

## ■ Physicians

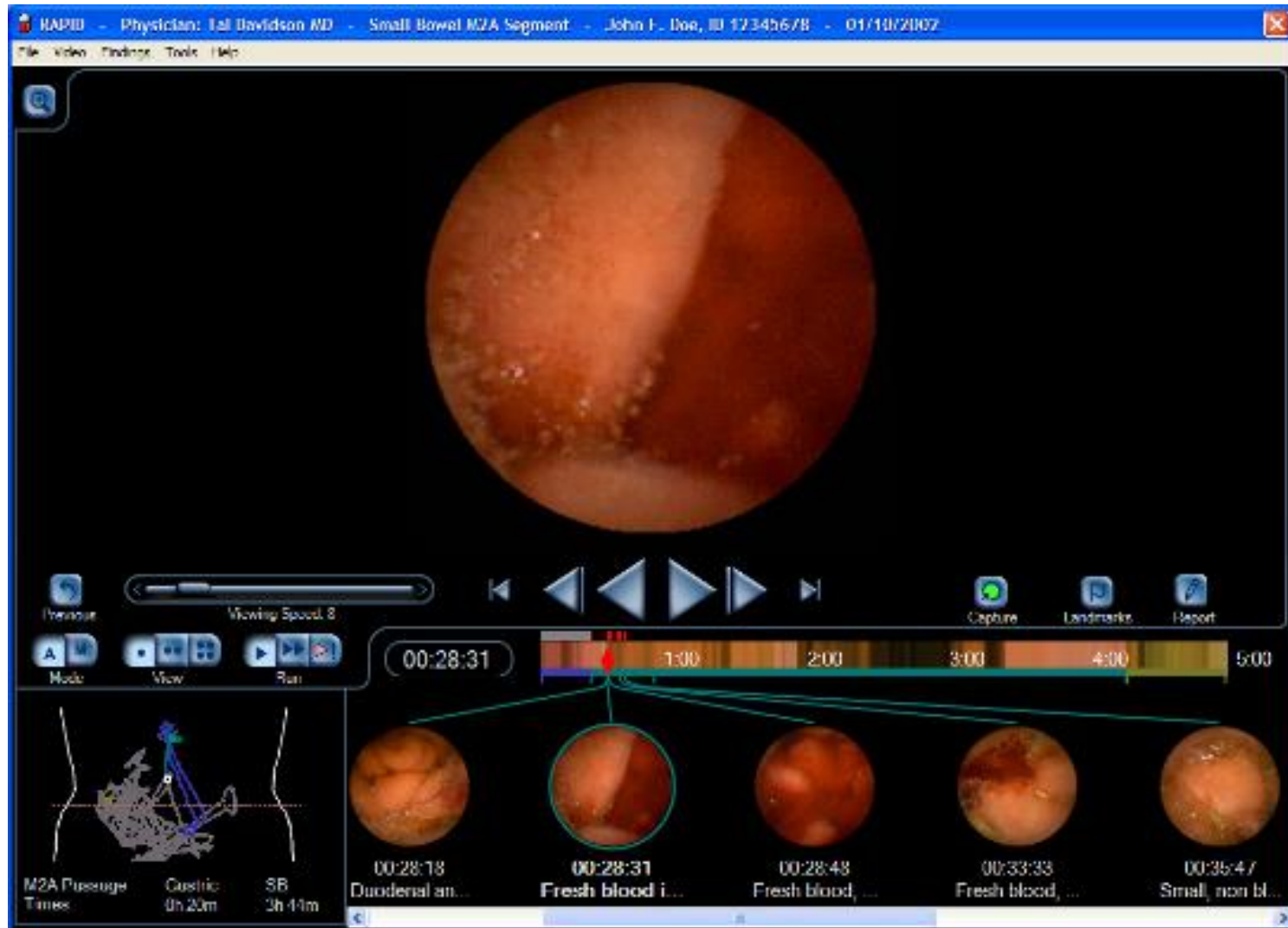
- Favorable reimbursement
- Average US reimbursement of \$945
- Reading time in 30 minutes or less

## ■ Broad Reimbursement Coverage

- Approximately 600 million worldwide with reimbursed access
- 220 million in the US reimbursed for OGIB and suspected Crohn's Disease
- 45 million in the US reimbursed for known Crohn's Disease



# RAPID – Reporting And Processing of Images and Data



# PillCam COLON 2



# Colon Cancer Facts

The second leading cause of cancer death WW with more than one million new cases and over 500,000 deaths annually:

## Europe

- 400,000<sup>1</sup> new cases of CRC each year
- 212,000<sup>1</sup> deaths in Europe each year

## U.S.

- 148,000<sup>2</sup> new cases each year
- 55,000<sup>3</sup> deaths annually

## Japan

- 98,000<sup>4</sup> new cases each year
- 43,354<sup>5</sup> deaths annually

### Source:

1. "Roadmap for a European Guideline in the Fight Against Colon Cancer." European Conference on Colon Cancer Prevention 2007.

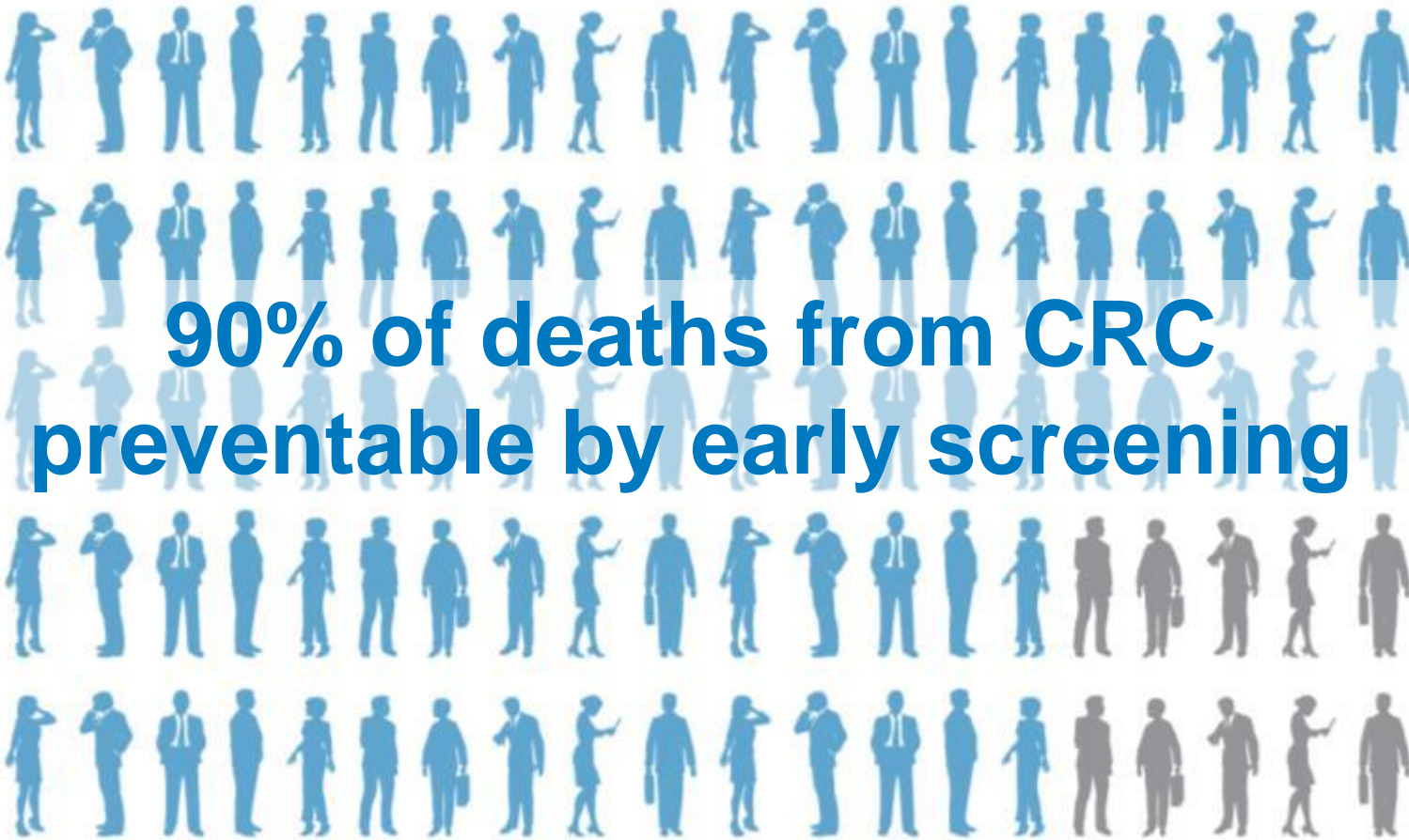
2. American Cancer Society, "What Are the Key Statistics for Colorectal Cancer?" March 2008.

3. "Colon and Rectal Cancer." National Cancer Institute. US National Institutes of Health, 2009.

4. Center for Cancer Control and Information Services. National Cancer Center, Japan – 2004 statistics

5. Center for Cancer Control and Information Services. National Cancer Center, Japan – 2004 statistics

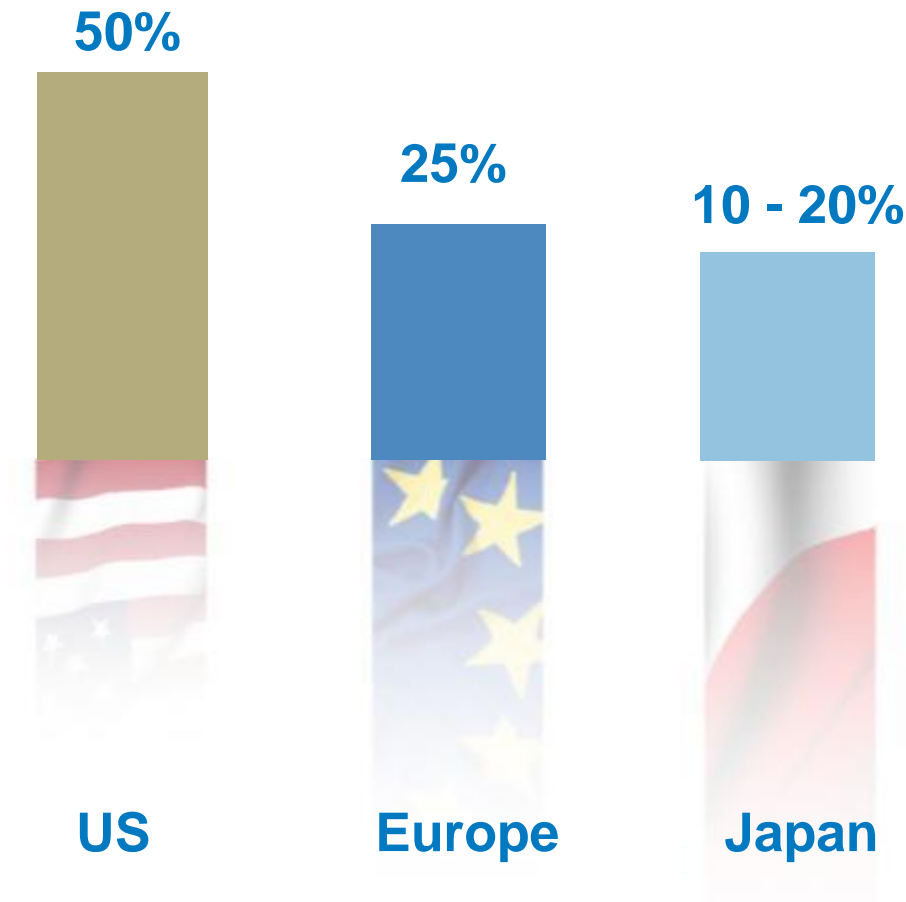
# Colon Cancer Facts



**90% of deaths from CRC  
preventable by early screening**

**450,000 Per Year should be alive**

# Colonoscopy Compliance Rates Remain Low



# PillCam COLON 2

- Patients who need repeat surveillance
- Patients unable or contraindicated for colonoscopy

**Saving Lives**



# Colorectal Cancer Facts

**1.2 million**  
new annual  
cases\*

**600,000**  
deaths  
annually\*

**~90% of deaths**  
can be prevented by  
early screening

- **Screening guidelines**

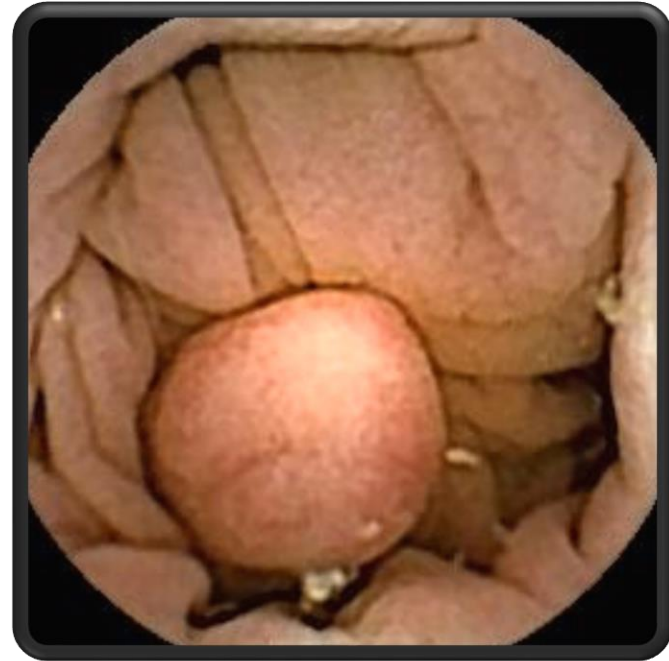
- In the US and major European countries, every adult >50 years should be screened
- In Japan, every adult >40 years should be screened
- Compliance 50-60% in US, <25% in Europe, Japan

- **Approximately 30 million colonoscopies per year globally**

\* Worldwide

Sources: GLOBOCAN 2008, Cancer Fact Sheet. John R, Ross H. *American Cancer Society & LIVESTRONG*. August 16, 2010, CDC, Shapiro et al., 2008, IMS and Millennium Research Group

# PillCam COLON Provides Excellent Visualization


















# PillCam<sup>TM</sup> COLON Views



# PillCam COLON2 Opportunity

## A Patient-Friendly Alternative

	Invasive	Sedation	Insufflation	Radiation	Bowel Prep
PillCam COLON 2					
Colonoscopy					
Virtual Colonoscopy					

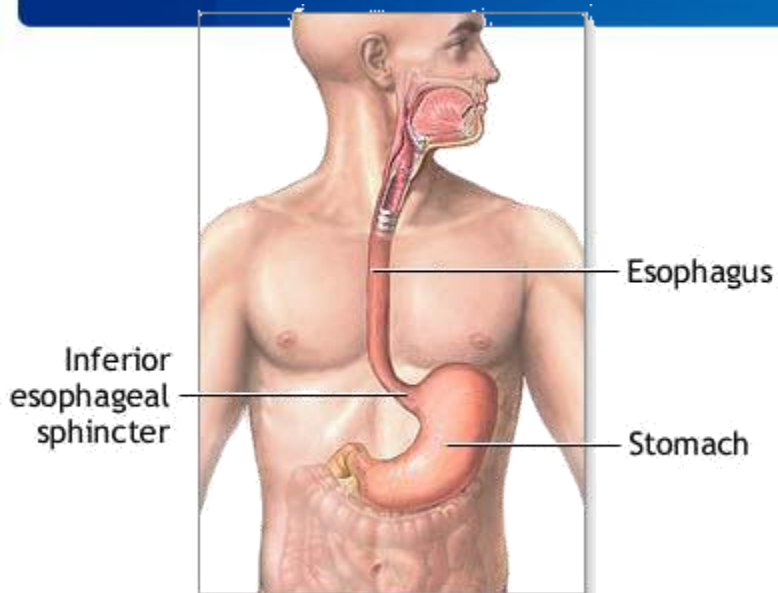
# PillCam™ ESO



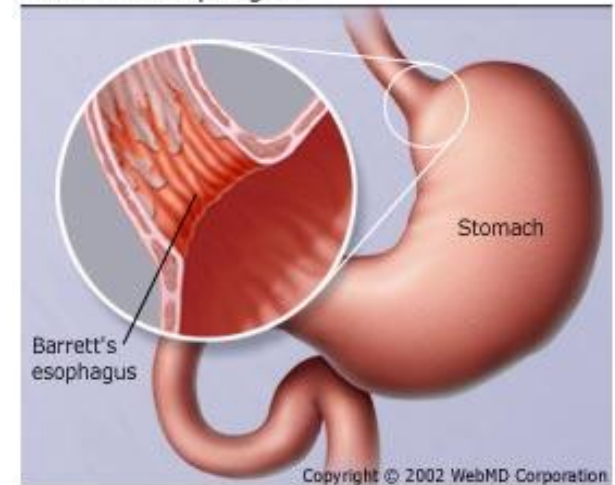
- For viewing of the esophagus walls
- Same size as SB capsule
- Short procedure
- Packaged like SB
- First line screening tool
- FDA cleared to market



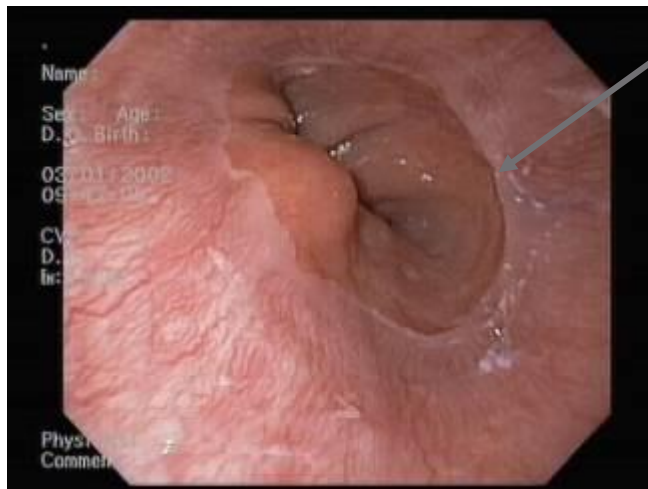
# PillCam™ ESO – the Needs



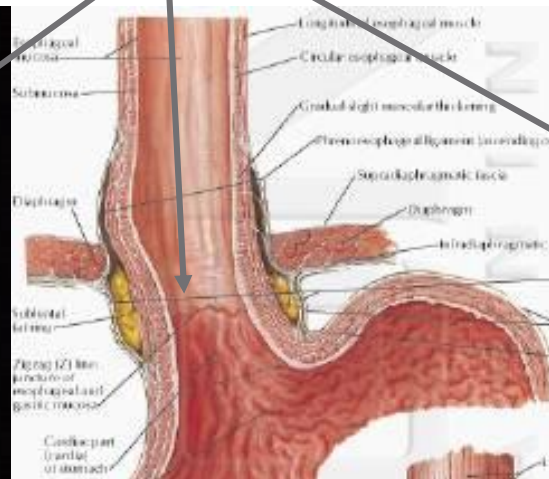
Barrett's Esophagus



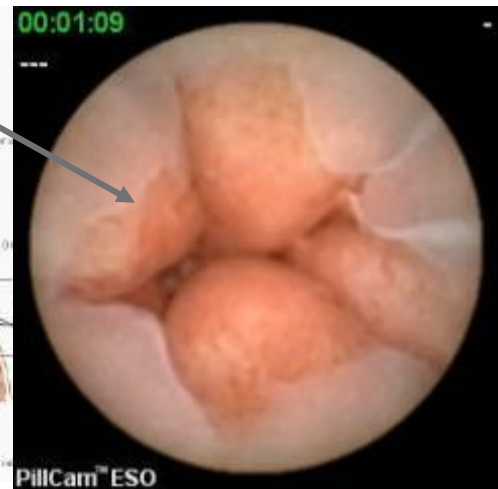
Z-line



Gastroscope



Anatomy



Capsule

# Beyond Imaging Capsules ...

## Continued focus on research and development activities

### ■ Next generation capsule endoscopes

- New capsules will have manoeuvring capabilities and applications in Molecular Diagnostics
- Additional potential applications include drug delivery and virtual biopsy



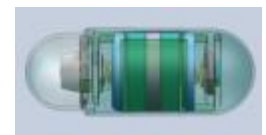
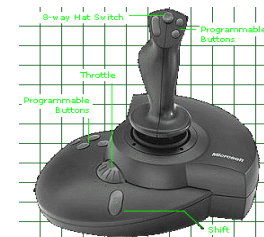
### ■ Use of magnetic guidance in new Voyager technology

- Enables greater movement precision and control of the capsule during the procedure
- Provides both automatic pilot and manual joystick movement control
- Enables treatment and biopsy
- Provides 3D measurement and reconstruction of the GI tract



### ■ Molecular Imaging

- Colon cancer screening / diagnosis
- Monitoring IBD patients



# Key Factors for Given's Success

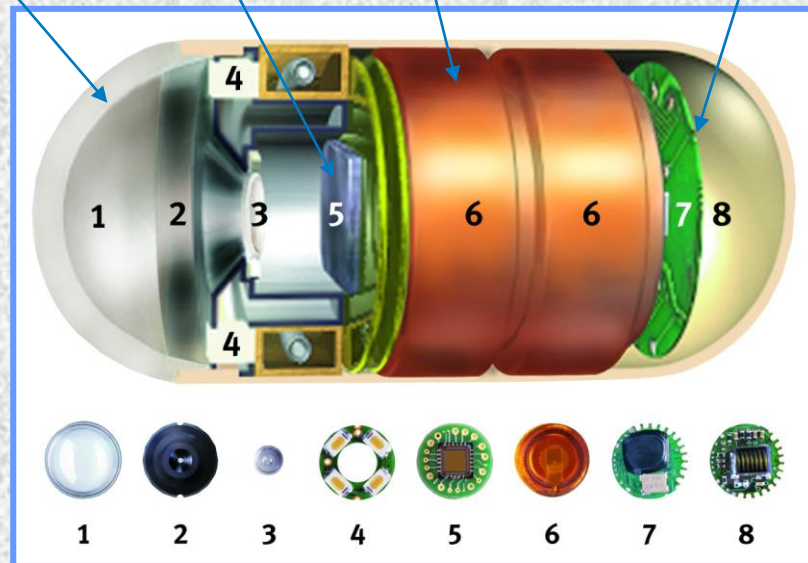
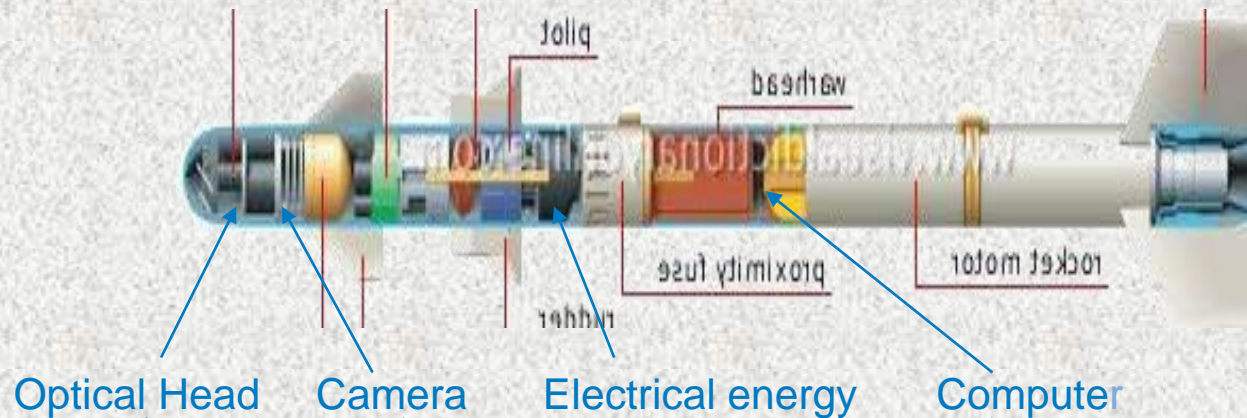
- A Market Need and a Technological Solution
- Passion and Drive to Save Lives
- Decision and Action to immediately go Global
- Hired the Best People we could find anywhere in the world (Initial Mgmt Team were from Israel, California, Atlanta, Germany, Argentina)
- Focus only half the resources of the company from day one on product, the other half on Processes
  - Clinical Studies
  - Regulatory Science Culture
  - Medical Advisory Groups
  - Regulatory Applications
  - Quality Culture
  - Reimbursement
  - Compliance and Improvement Culture

# Product Development & Innovation

*“They will beat their swords into plowshares and their spears into pruning hooks. Nation will not take up sword against nation, nor will they train for war anymore*

Isaiah 2:4 & Micah 4:3

# From military missile technology to the video endoscopic capsule



Optical Head

# The PillCam innovation historical time-line

**1981: Gabi Iddan meets Eitan Skapa M.D. and learns about the need to examine the small intestine.**

**1986: small CCD are available.**

**1990: small transmitters are available.**

**1992: The capsule concept was born.**

**1993: experiments begin, CMOS imager appears.**

**1994: patent application.**

**1995: ASIC transmitter appears.**

**1997: Given Imaging incorporated**

**2001: FDA granted**

**10 Years**

**20 Years**

# Idea to Reality

## Idea



## Concept

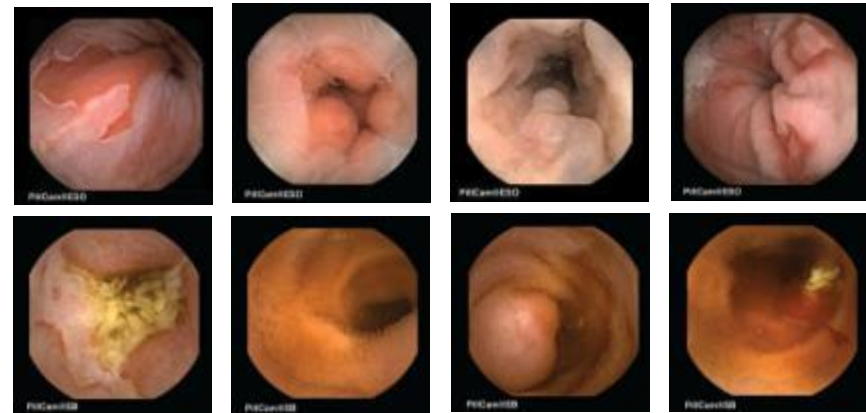


Fig.1: Early **non ingestible** wired devices with a 1/4" CCD used for testing the optics and the illumination

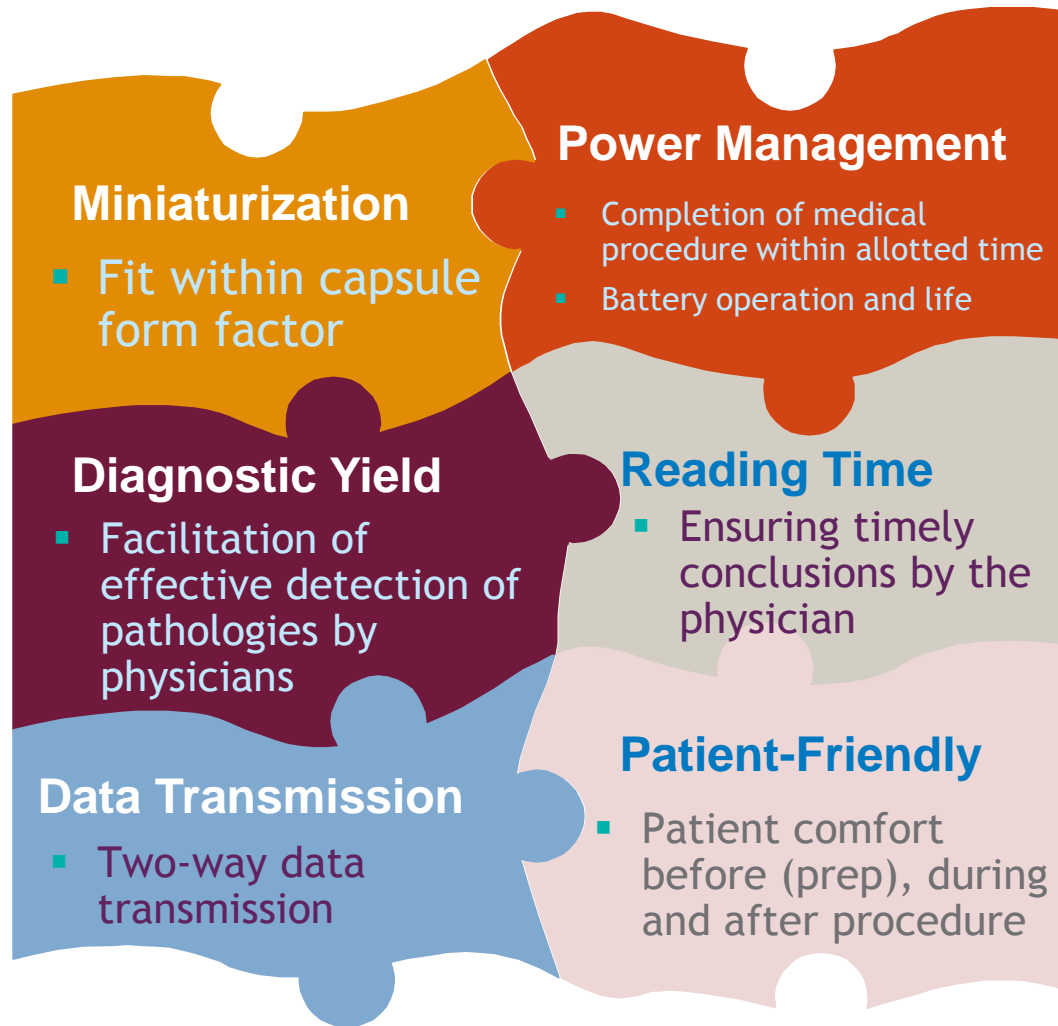
## Solution



## Result

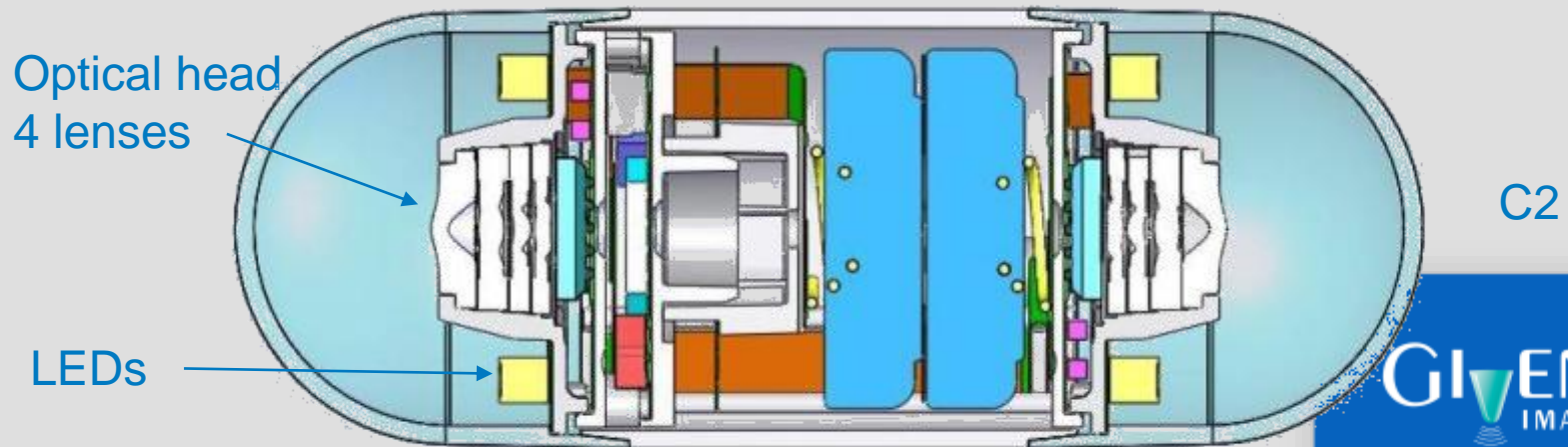
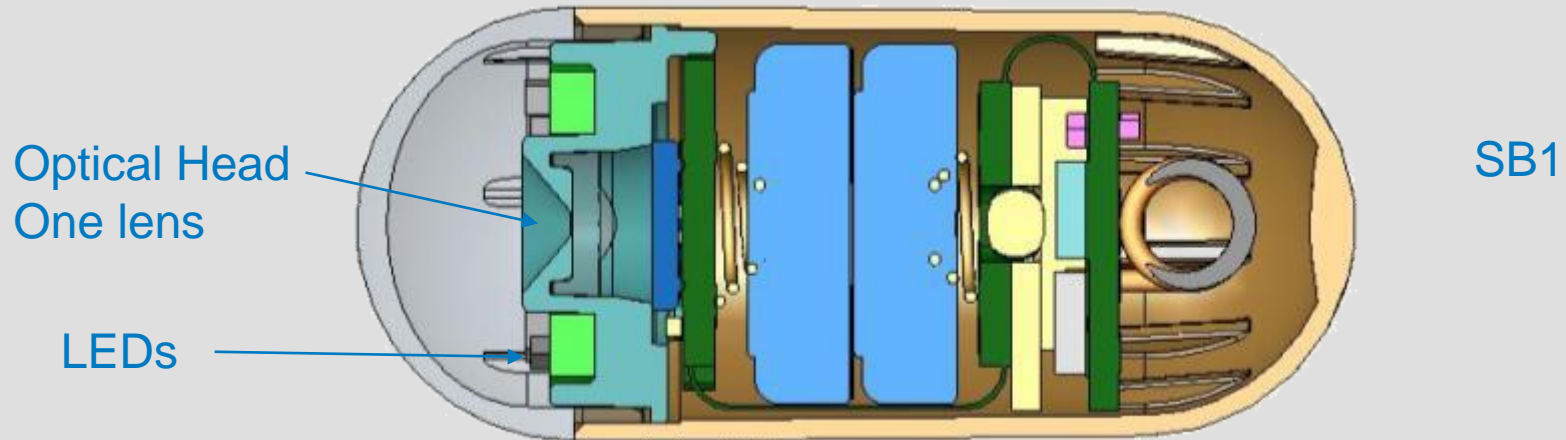


# Addressing the Main Challenges of Capsule Endoscopy



***The Gold Standard in Capsule Endoscopy***

# Improvements in capsules complexity



## Our products roadmap...



From visualization to therapy



2001

2007

## Beyond...

2001

2004

2007

2010

## Beyond...



# The Given – company sale story

- In 2013 Given was very successful!
  - Over 90% Market share
  - Outrageously profitable [ >80% product margin. 15% profit ]
  - Annual sales of 200M\$
  - 150M\$ in the bank
  - The Colon capsule was approved by FDA and PMDA and got reimbursement in Japan. Was on the verge of taking off!
  - A portfolio of new products in the making
- The Given management team was eager to continue leading the company towards future successes and growth.
- However, the key Shareholder ( close to 50% of shares ) was in severe need for cash and hence ‘put Given on the block’.
- Given’s management team cooperated with the process.

# The Given – company sale story

- During 2013 there were several encounters with potential buyers.
- All were impressed with the accomplishments and potential.
- But... an agreement did not materialize due to wide gap on the company valuation ( the sellers would not settle for less than 1B\$ ).
- Until, in early December, One of the earlier suitors, Covidien Corp, came back with a will to buy at 1B\$. This got the roller-coaster rolling!
- By February 2014 all regulatory, legal and other approvals were obtained. All necessary processes concluded and on Feb 28<sup>th</sup> 2014 - Given ceased to exist. All its shares were bought by Covidien and we became a wholly owned subsidiary.
- Following about a month of know-how transfer and pow-pow - in late March Covidien announced that it will let go the whole existing Given management team!
- End of story, for me and the great Given leadership team!

# What can we learn from the Given Imaging story?

- Necessity is mother of invention
- When there is an 'unmet need' - market penetration is much easier
- Success entails dealing with ALL aspects of the product/solution and business  
[ Engineering, Use case, pricing, regulation, reimbursement, distribution, KOLs, on-going innovation & collaborations ]
- No substitute to direct interaction with both users and customers
- Excellent people are key to success [ R&D, Mktg, Sales, Operations ( production ), Clinical affairs, Finance ]
- Desirably, maintain majority shares control/influence - to avoid early exit or other undesirable company actions

# Thank You!

