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## LA TECNOLOGIA NELLA DIAGNOSI DEI DISTURBI FUNZIONALI

### Manometria High-Resolution del Colon

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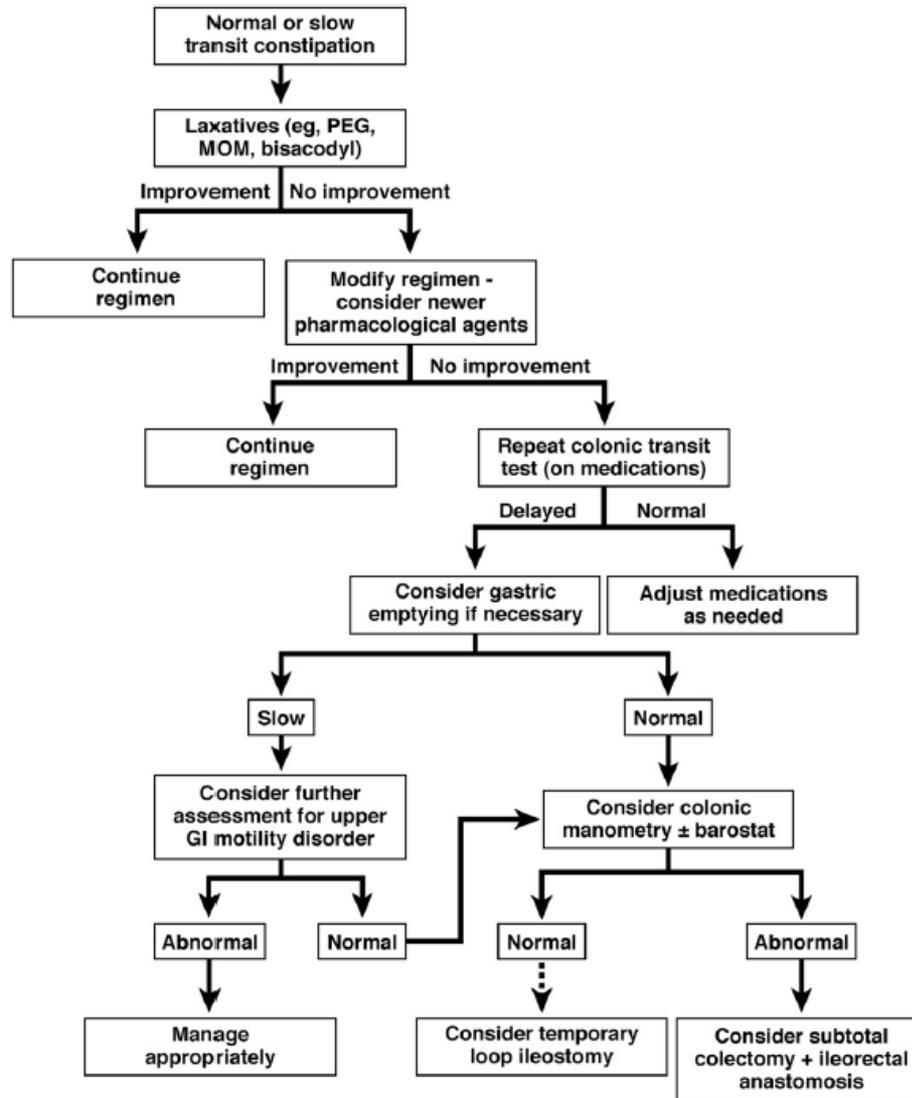
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SINGEM





# What is the clinical indication for colonic manometry in adults?



# The first translational consensus on colonic motility



Consensus  
colonic  
motility  
meeting  
Leuven  
Sept 2016



Maura Corsetti and Marcello Costa, Gabrio Bassotti, Adil Bharucha, Osvaldo Borrelli, Phil Dinning, Carlo Di Lorenzo, Jan Huizinga, Marcel Jimenez, Nick Spencer, Robin Spiller, Satish Rao, Roger Lentle, Marc Benninga and Jan Tack.

**“The first time that basic scientists, gastroenterologists, pediatricians met with the aim of reviewing the current literature in order to find an agreement on terminology and definition of colonic motor patterns”**

Corsetti M, Nature Reviews (in press)



# What is the clinical indication for colonic manometry in children?

In children, colonic manometry is currently indicated to discriminate between colonic neuromuscular disorders and functional constipation to guide the surgical approach in those patients refractory to conventional medical treatment, to evaluate the colonic involvement in children with chronic intestinal pseudo-obstruction, to determine whether a diverted colon is suitable for reconnection, and to clarify the underlying mechanisms responsible for the persistence of symptoms after surgery for either Hirschsprung's disease or other anorectal abnormalities

HAPCs are generally classified based on their distance of propagation: fully propagating, when HAPCs reach the sigmoid colon; partially propagating, when HAPCs stop at the level of the splenic flexure or the descending colon; absent, when no HAPCs are observed in the entire colon

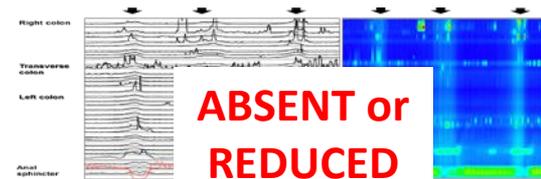
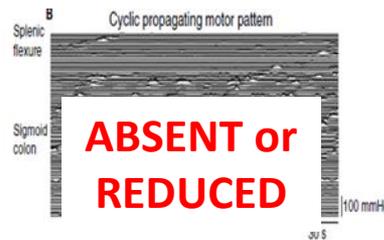
Their presence suggests intact colonic neuromuscular function and studies based on the characteristics of HAPCs have been found to be predictive of medical and surgical outcome



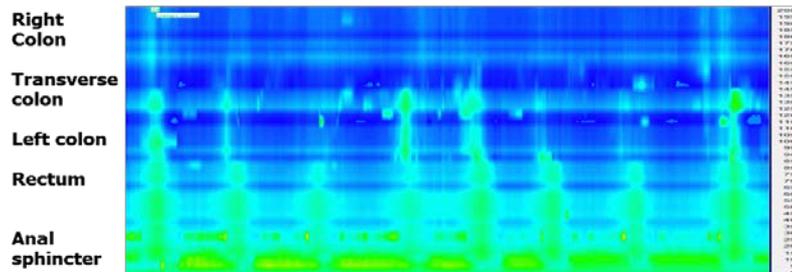
**Why the colonic transit time is not enough?**

# The colonic motility in patients with slow-transit functional constipation as measured by HRM

**FASTING AND POSTPRANDIAL PERIOD**



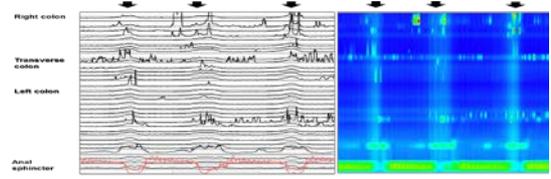
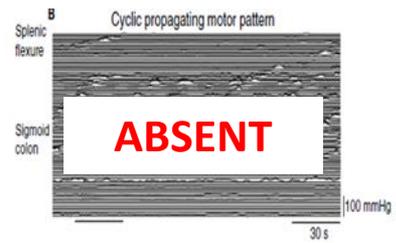
**RESPONSE TO STIMULANT LAXATIVE (BISACODYL)**



**Slow transit:  
Absence or reduction of both non-propulsive and propulsive colonic motility**

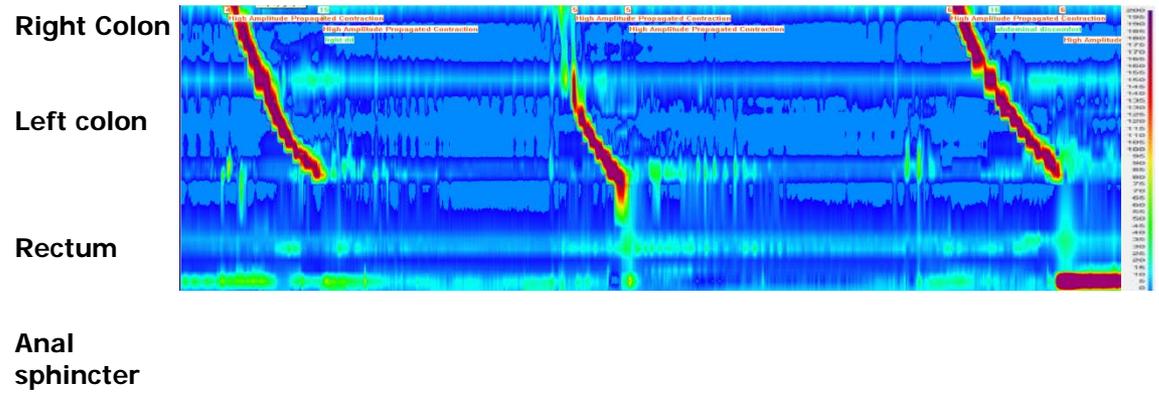
# The colonic motility in patients with slow-transit IBS-C as measured by HRM

**FASTING AND POSTPRANDIAL PERIOD**

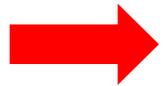


vs HS

**RESPONSE TO STIMULANT LAXATIVE (BISACODYL)**



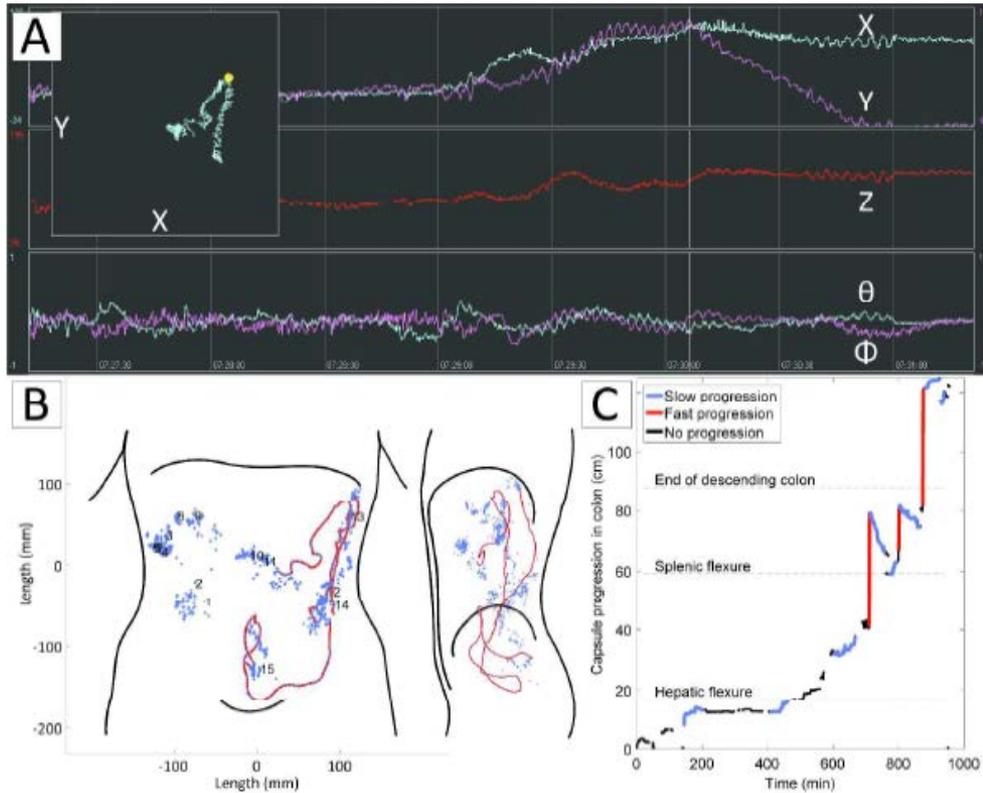
vs HS



**Slow transit:**  
**Increased non-propulsive and decreased propulsive colonic motility**



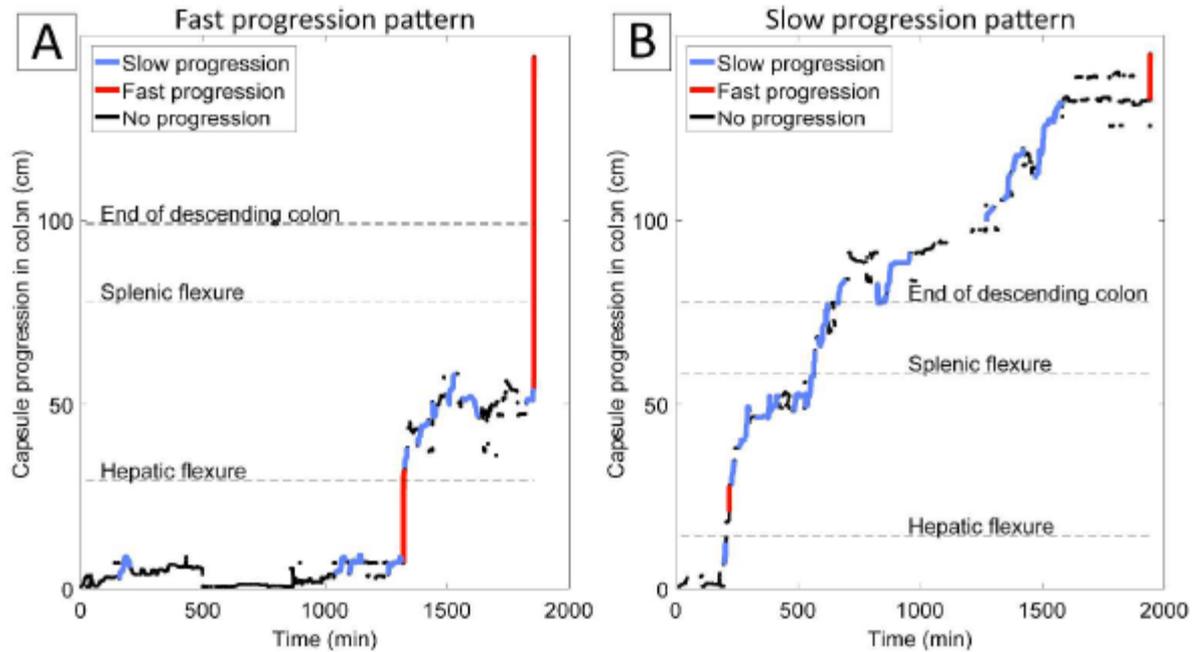
# The lesson of the electromagnetic capsule



What does this capsule measure?



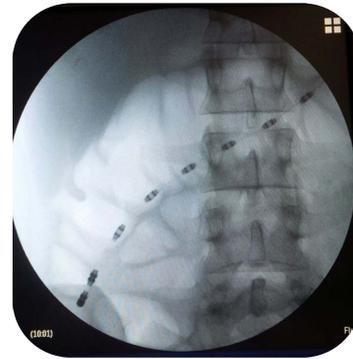
# The lesson of electromagnetic capsule



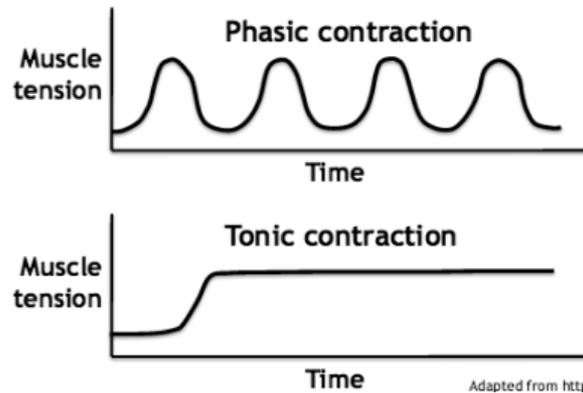
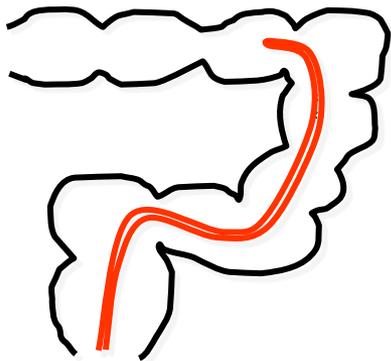


**What did we learn from colon HRM?**

# How do we perform the colon HRM?

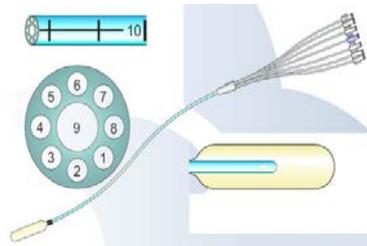
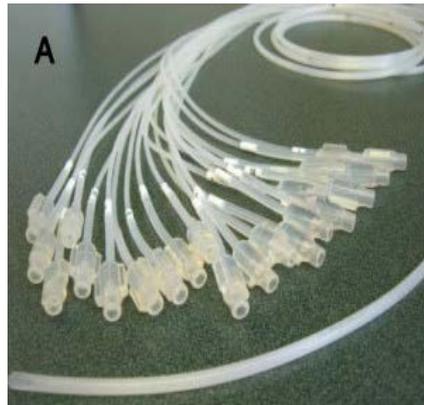


# What does the colon HRM measure?



# How can we measure colonic motility with HRM?

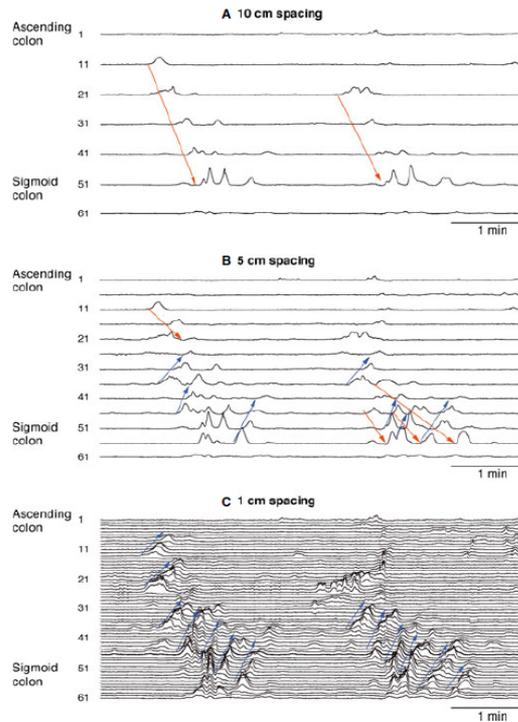
## Water-perfused



## Solid state catheters



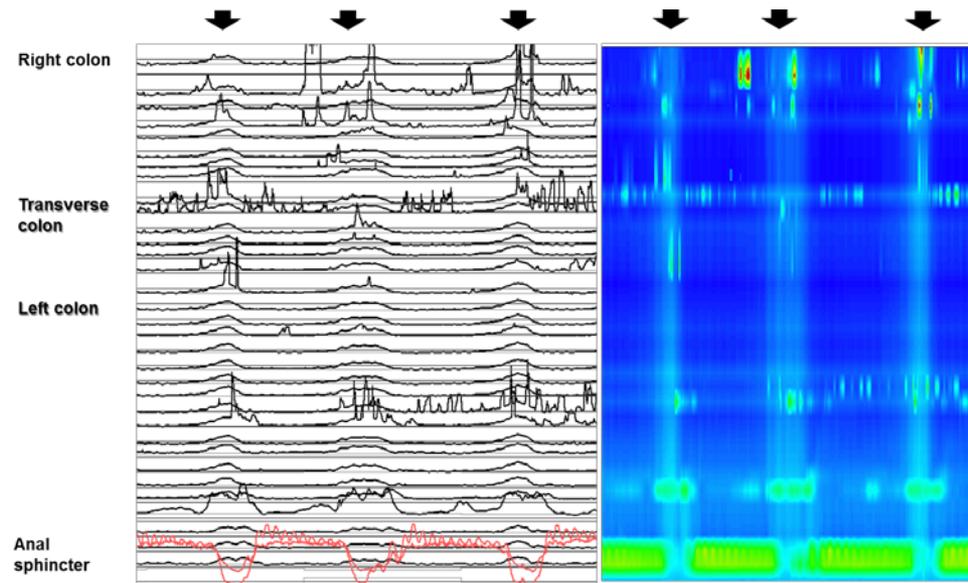
# Why do we need the HRM to study colonic motility?



Dinning P, Neurogastroenterol Mot 2013

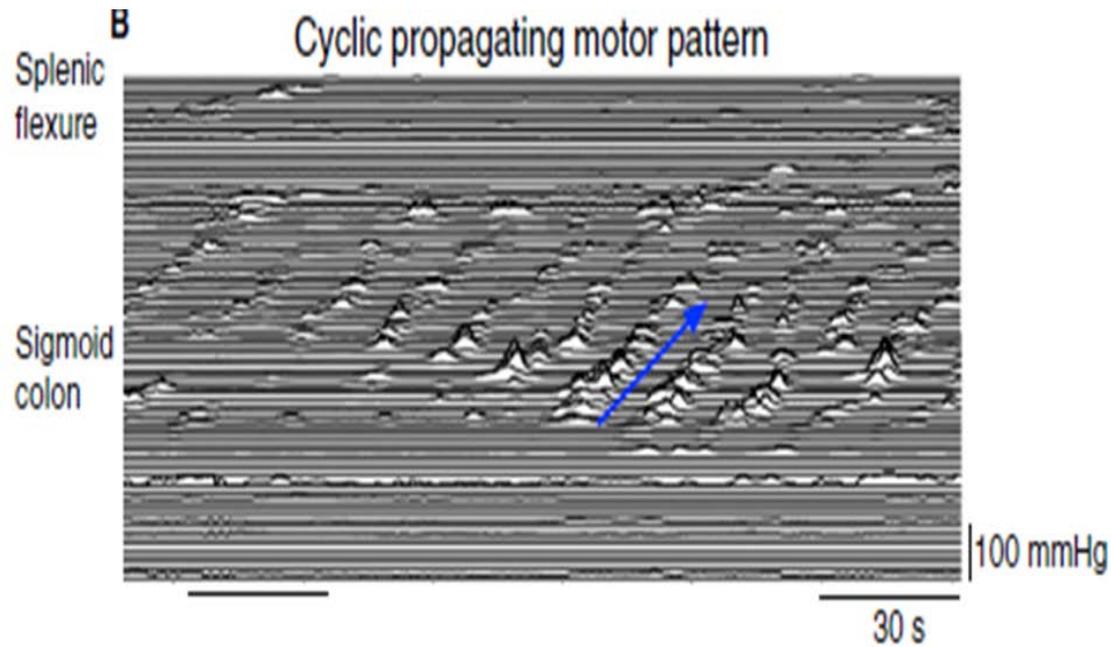
**What are the colonic motor patterns recorded in humans?**

# Pancolonic pressurizations as the more frequent colonic motor pattern in health



Corsetti M, Am J Gastroenterol 2017

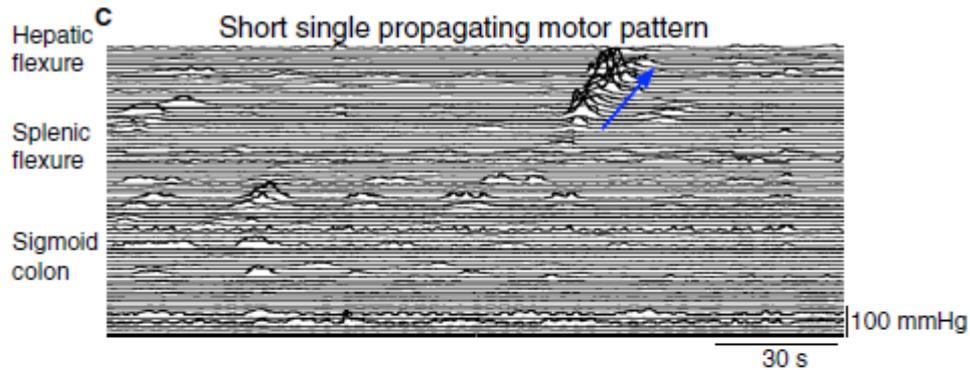
# Cyclic motor pattern as the most frequent **propagating** motor pattern in health



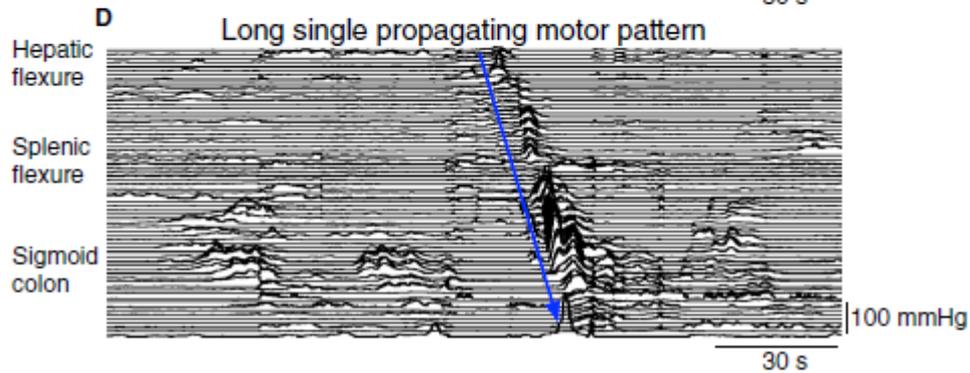
Dinning P, Neurogastroenterol Mot 2014



# Short and long single motor pattern

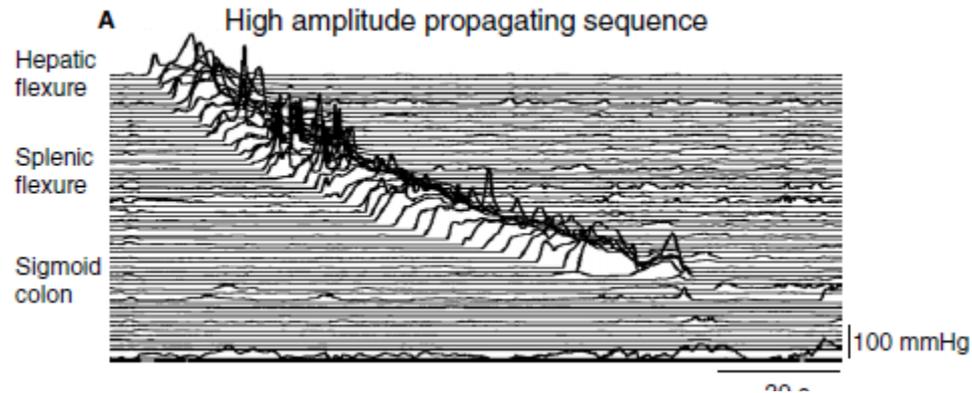


24% of all propagating motor patterns



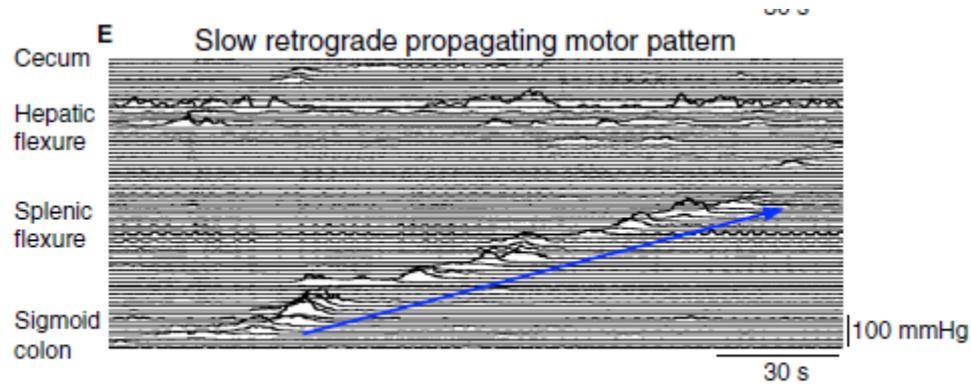


# High amplitude propagating contractions



**1% of all propagating motor patterns**

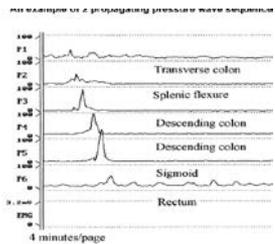
# Slow retrograde propagating motor pattern



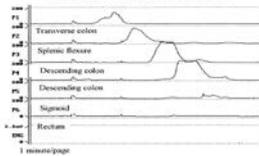
**0.4% of all propagating motor patterns**

# The colonic motility in health

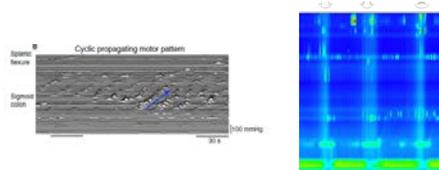
At awakening time



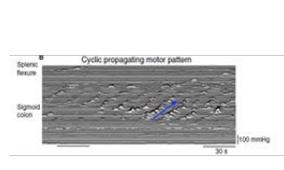
An example of specialized propagating pressure wave that propagated from channels F1-F4 and started in the rectosigmoid region (channels F5 and F6).



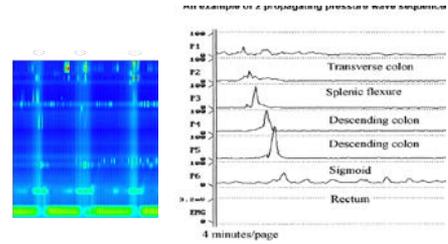
Pre-prandial period



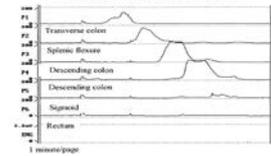
Post-prandial period



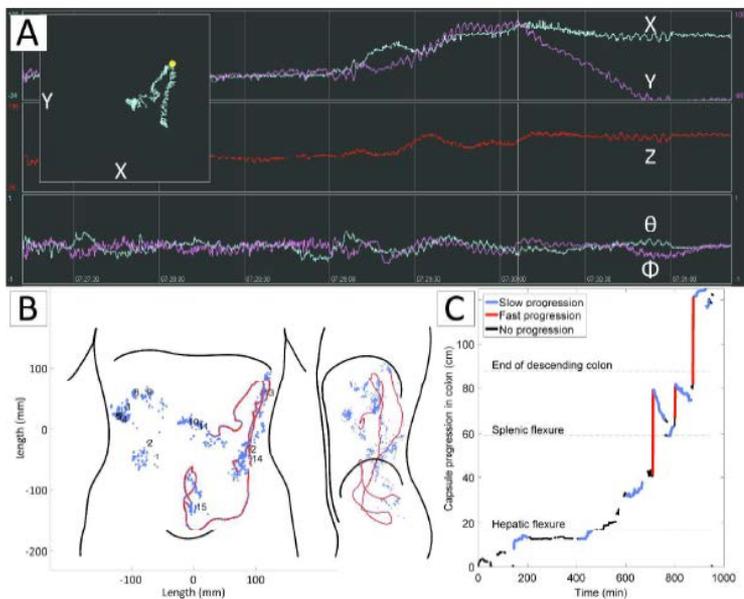
About 2 hours after the meal



An example of specialized propagating pressure wave that propagated from channels F1-F4 and started in the rectosigmoid region (channels F5 and F6).



# The lesson of the electromagnetic capsule



What does this capsule measure?

# The colonic motility as studied by the electromagnetic capsule

**Table 1.** Colonic motility parameters in healthy volunteers (n=34)

		Cecum & ascending	Transverse	Descending	Sigmoid & rectum	All colon
<i>Movement patterns</i>						
Long fast antegrade (seen in 94% of rec.)	(no.)	0 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)	2 (1-4)
	(cm)	10.4 (8.5-17.0)	11.7 (7.7-22.6)	13.6 (8.8-17.1)	10.4 (10.2-13.8)	20.8 (10.4-36.2)
Fast antegrade (seen in 88% of rec.)	(no.)	0 (0-1)	0 (0-1)	0 (0-1)	1 (0-1)	2 (1-4)
	(cm)	4.2 (4.1-5.9)	8.2 (4.3-9.7)	4.6 (4.4-8.6)	4.4 (4.1-10.7)	13.0 (8.5-21.0)
Slow antegrade (seen in 100% of rec.)	(no.)	1 (1-2)	3 (2-5)	1 (0-2)	1 (1-2)	7 (5-11)
	(cm)	7.1 (4.1-11.6)	13.8 (10.2-20.4)	8.1 (4.1-12.6)	8.3 (4.2-12.2)	33.2 (19.9-48.7)
Slow retrograde (seen in 65% of rec.)	(no.)	0 (0-1)	0 (0-1)	0 (0-0)	0 (0-1)	1 (0-2)
	(cm)	4.3 (4.0-8.0)	4.1 (4.0-13.2)	4.4 (4.1-9.6)	4.1 (4.1-5.6)	8.1 (4.6-15.4)
<i>Capsule transit characteristics</i>						
Colonic transit time	(hours)	4.2 (1.3-10.3)	4.0 (2.0-8.0)	0.9 (0.2-2.2)	6.0 (2.1-12.0)	18.2 (15.2-26.7)
Total velocity	(cm hour <sup>-1</sup> )	3.0 (1.8-9.8)	6.5 (3.4-11.0)	19.7 (3.6-127.0)	4.3 (1.8-8.2)	4.4 (2.6-6.0)
Disp. at fast velocity	(% of length)	46.1 (11.2-78.0)	39.0 (9.2-61.6)	67.6 (0.0-100.0)	68.6 (36.0-80.4)	51.6 (36.0-67.1)
No capsule movement	(% of time)	85.7 (74.0-92.8)	76.8 (61.6-83.6)	69.7 (3.4-89.5)	85.5 (57.0-92.4)	81.8 (74.5-87.3)
Colon length	(cm)	21.2 (15.8-25.7)	34.0 (28.5-37.2)	19.2 (15.0-25.9)	32.6 (26.5-38.9)	110.2 (96.8-122.4)
<i>Data quality</i>						
Missing data	(% of time)	3.8 (0.0-11.0)	3.7 (0.9-9.5)	0.0 (0.0-12.9)	4.4 (1.4-12.9)	6.4 (4.3-10.2)
Missing trajectory	(% of length)	18.6 (3.0-52.8)	29.8 (7.9-47.2)	18.8 (3.2-42.0)	43.5 (30.3-55.9)	35.1 (24.4-45.9)

# New understanding of colonic motility

# The first translational consensus on colonic motility



Consensus  
colonic  
motility  
meeting  
Leuven  
Sept 2016

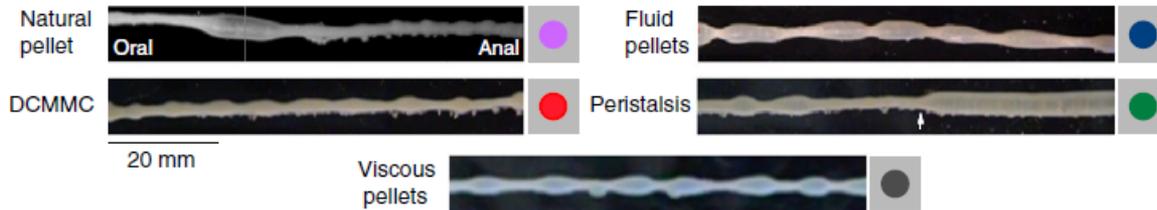
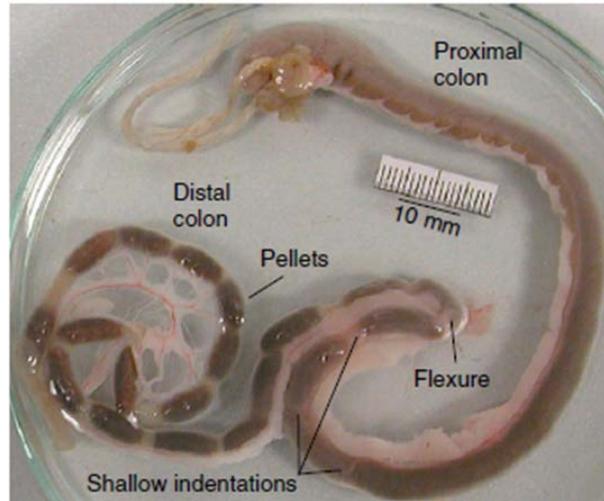


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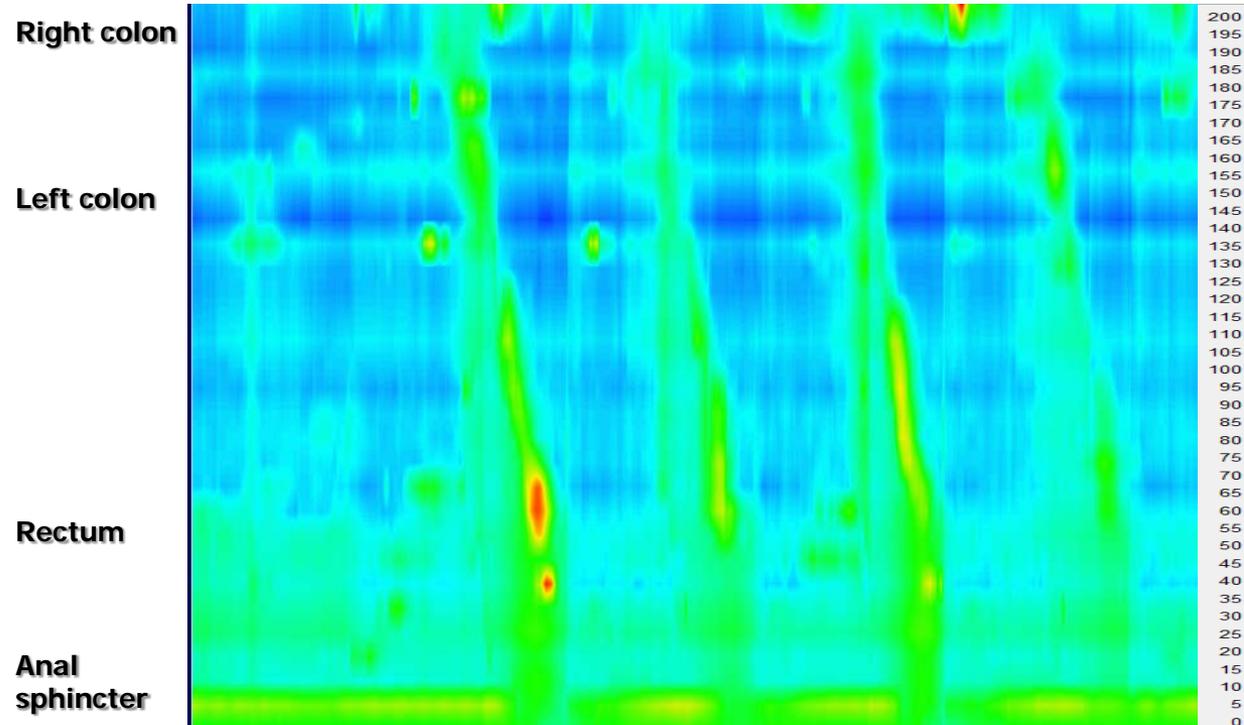
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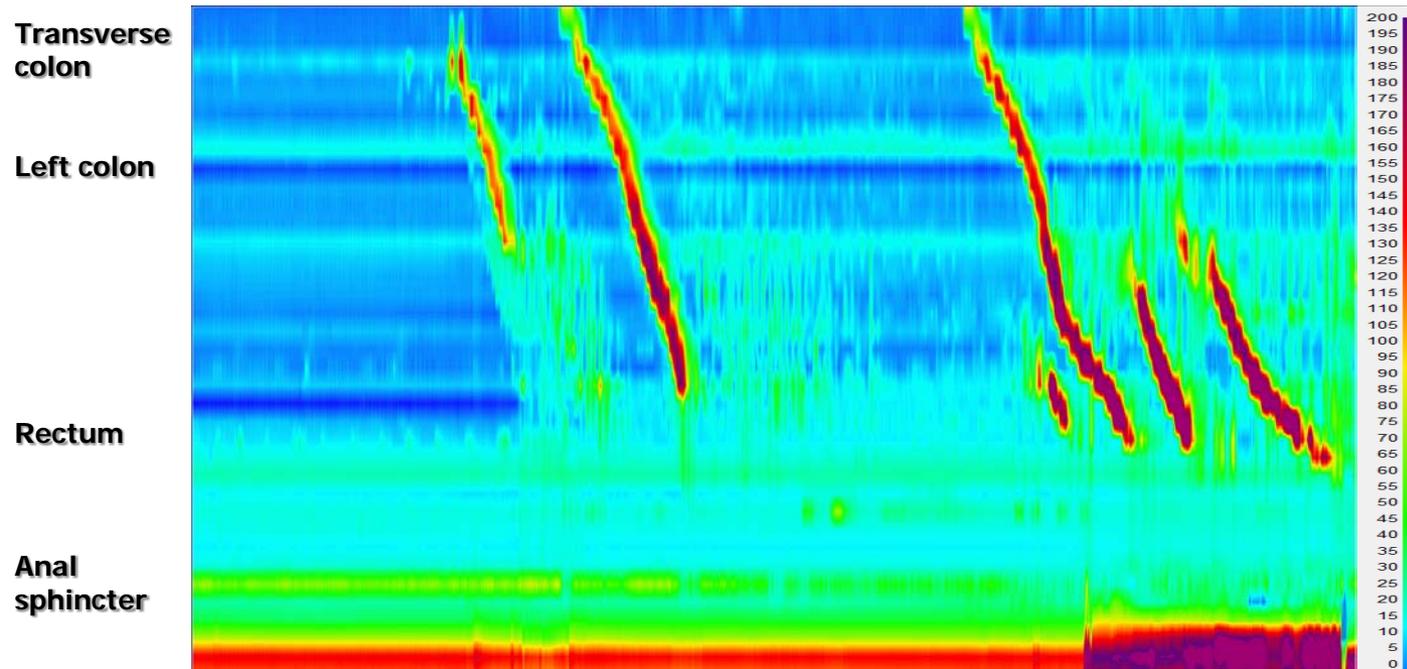
# The content-dependent neuromechanical loop



# The long distance low-amplitude propagating contraction as response to liquid colonic content

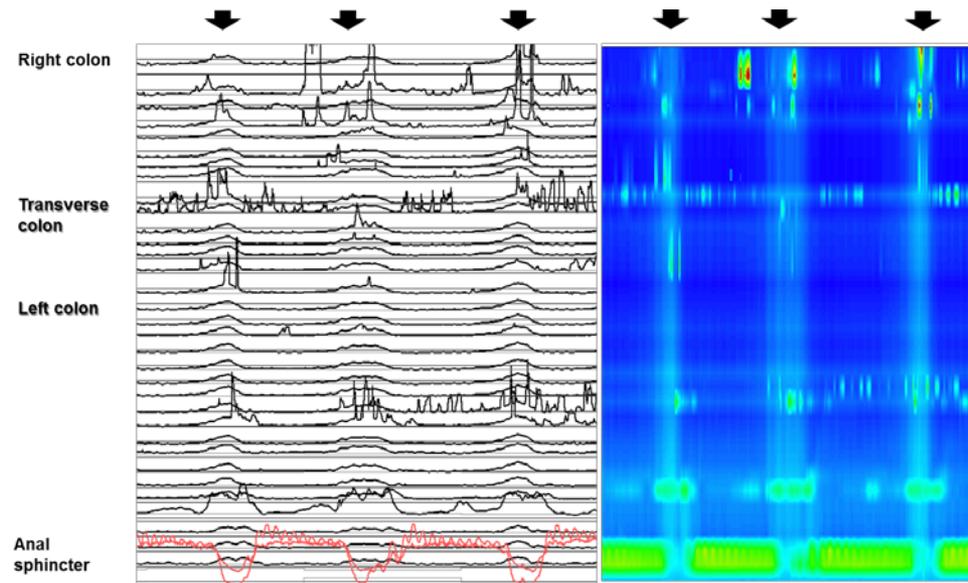


# The high-amplitude propagating contractions as response to solid colonic content



Corsetti M, Nature Reviews (in press)

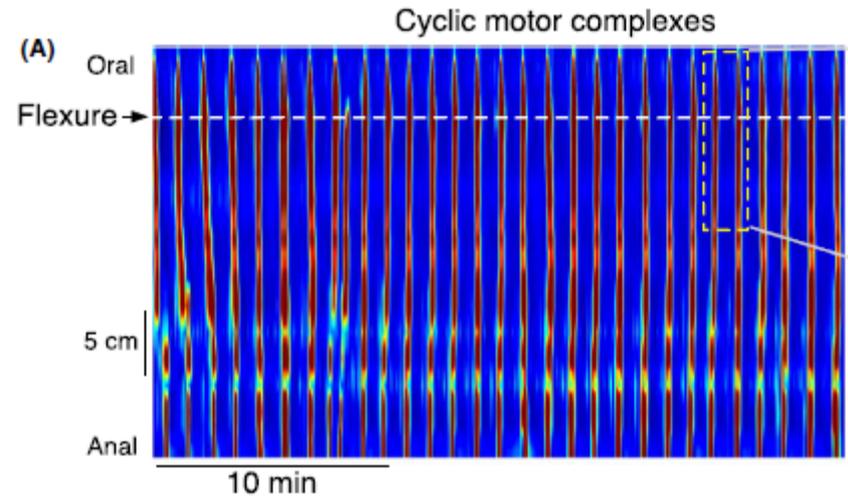
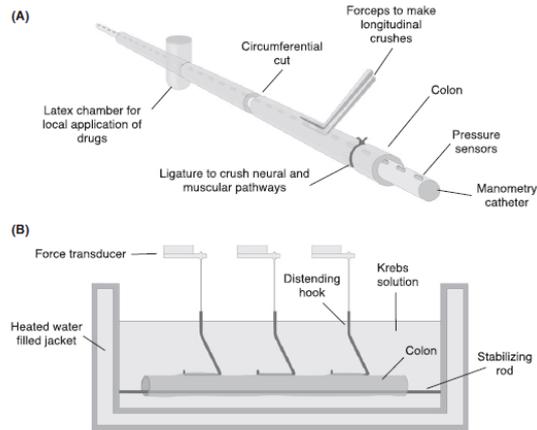
# Pancolonic pressurizations as the more frequent colonic motor pattern in health



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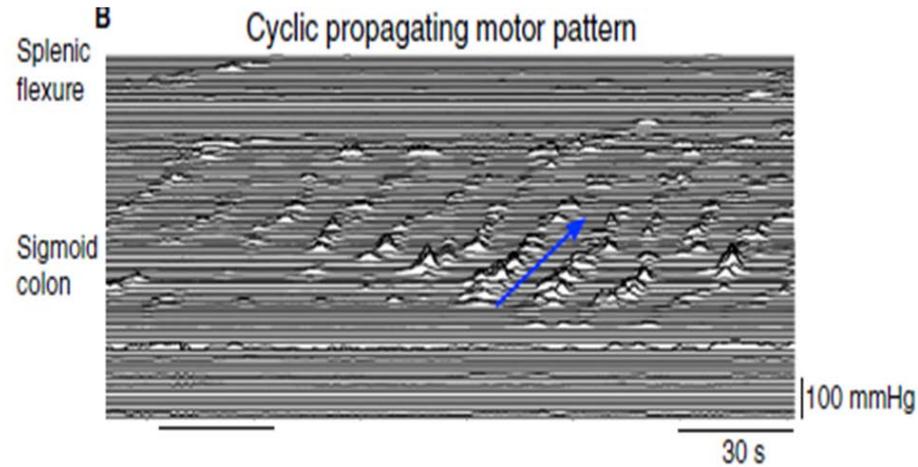
# Pancolonic pressurizations as colonic motor response to maintained distension

In animal studies...



**What do we know about the pharmacological modulation of these colonic motor patterns?**

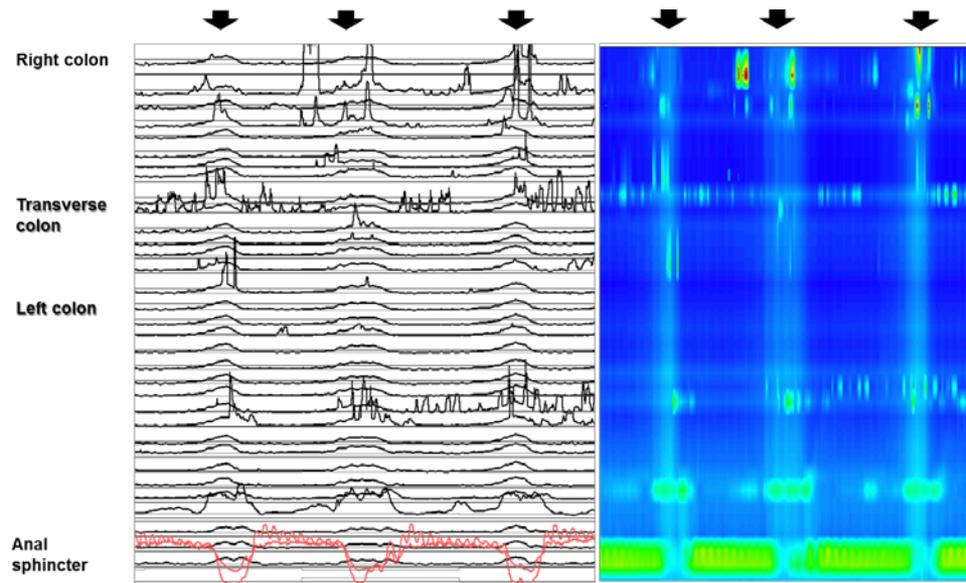
# Cyclic motor pattern



This motor pattern increases after the meal.

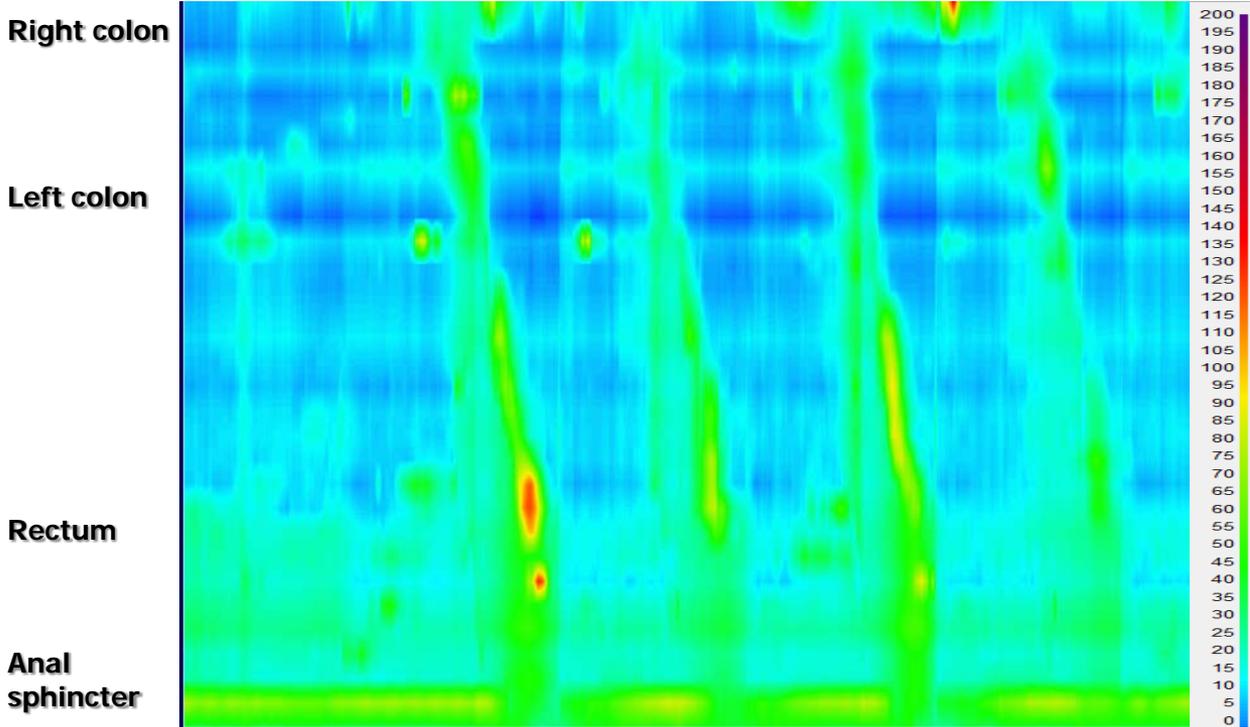
Is this activity increased by ondansetron? by codein?

# Pancolonic pressurizations or simultaneous pressure increases



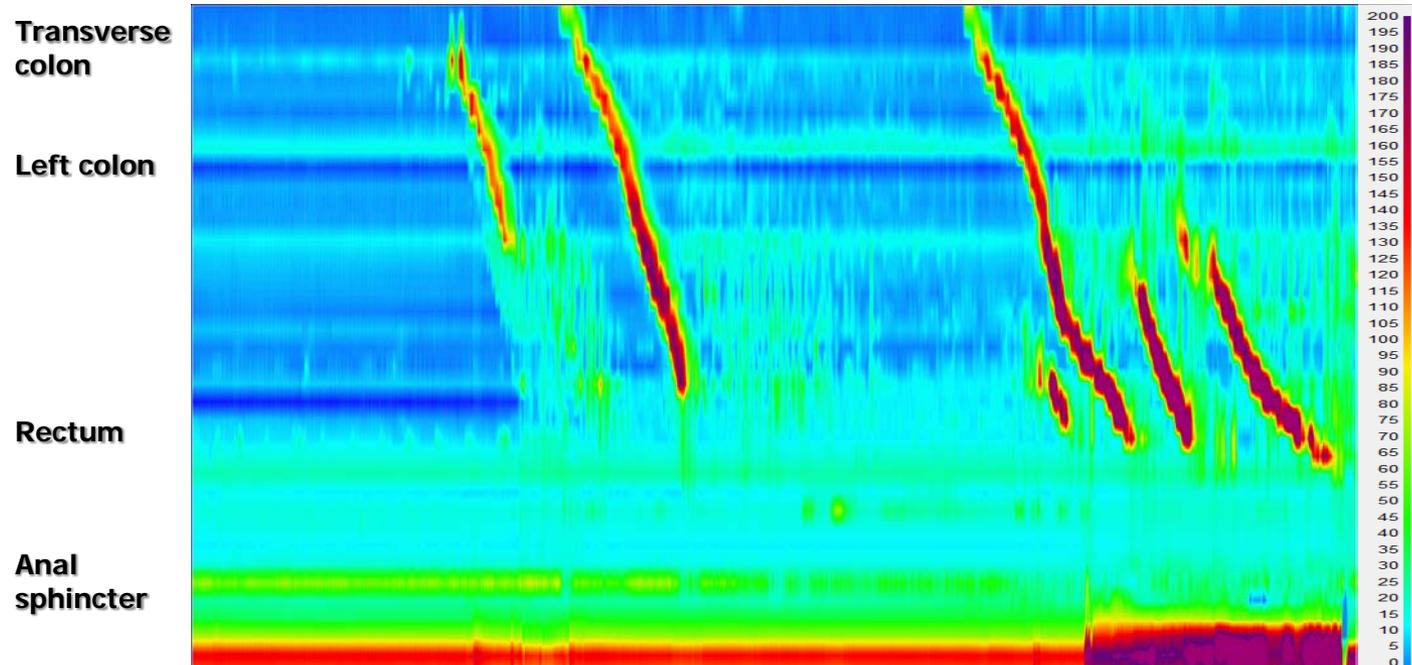
This colonic motor pattern is increased by meal, prucalopride and neostigmine

# The long distance low-amplitude propagating contraction



This colonic motor pattern is increased by linaclotide and PEG....but are these contractions simply pancolonic pressurations in presence of liquid contents?

# The high-amplitude propagating contractions



This colonic motor pattern is increased by meal (1-2 hours after the meal), by adrenergic alpha-2 receptor antagonist yohimbine (i.v.), glycerol (i.c.), oleic acid (i.c.), bisacodyl (i.c and p.o.).

This colonic motor pattern is inhibited by lidocaine (i.c.) and phloroglucinol (i.v.)

**Are we able to differentiate healthy subjects from patients or to predict treatment response?**



# Summary of colon HRM in health and disease

Author	Year	Catheter type	No. sensors	Sensor spacing (mm)	Anesthetic used	Recording time (hours)	Healthy adults (number)	Patient type (number)	Meal (kcal)	Chemical response (type)	Other
<i>Adult studies</i>											
De Schryver <sup>1</sup>	2003	WP	12	10-100	Midazolam	6	10	STC (10)	900	Bisacodyl	—
Dinning <sup>2</sup>	2012	FO	72	10	General anesthesia	8	—	STC (6)▼	—	—	Sacral Nerve Stimulation
Patton <sup>3</sup>	2013	FO	72	10	General anesthesia	8	—	FI (11)	—	—	Sacral Nerve Stimulation
Dinning <sup>4</sup>	2013	FO	72	10	General anesthesia	2	9*	STC (11) FI (11)	—	—	—
Dinning <sup>5</sup>	2014	FO	72	10	Midazolam Fentanyl	4	10*	—	700	—	—
Dinning <sup>6</sup>	2015	FO	72	10	Midazolam Fentanyl	4	12*	STC (14)	700	—	—
Vather <sup>12</sup>	2016	FO	36	10	Midazolam Fentanyl	4	12*	AR (15)	700	—	—
Dinning <sup>9</sup>	2016	FO	72	10	Midazolam Fentanyl	2	—	STC (4)	—	—	Colonic motility recorded in vivo & ex vivo
Miner <sup>10</sup>	2016	SS	40	25	Not specified	12	—	Constipation (12)	+	Prucalopride	—
Lin <sup>7</sup>	2017	FO	72	10	Midazolam Fentanyl	4	9*	—	700	—	—
Chen <sup>16</sup>	2017	SS	36	10	No Sedation	10	5	IBS (9); Constipation (15)	+	—	—
Corsetti <sup>13</sup>	2017	SS	40	25	Midazolam pethidine	7	17	STC (10)	314	Prostigmine/ Bisacodyl	—
Vather <sup>19</sup>	2018	FO	36	10	Midazolam Fentanyl	4	—	Hemicolectomy (8)	—	—	Pre-, intra-, postoperative colon motility
<i>Pediatric studies</i>											
Giorgio <sup>8</sup>	2013	WP	20	25	Propofol	4	—	STC (18)	—	Bisacodyl	—
El-Chammas <sup>7</sup>	2014	SS	36	20-40	Not specified	?	—	Constipation (10)	+	Bisacodyl	—
Wessel <sup>15</sup>	2016	WP	36	15	General anesthesia	5	12*	Constipation (18)	400-700	Bisacodyl	—
Borrelli <sup>11</sup>	2016	WP	20	25	Propofol	3	—	STC (103)	—	Bisacodyl	—
Koppen <sup>18</sup>	2017	SS	36	30	General anesthesia	5	—	Constipation (4)▼	+	Bisacodyl	—
Arbizu <sup>14</sup>	2017	SS	36	30	Midazolam	2 × 4 hour over 2 days	—	Constipation #	+	Bisacodyl	—



# Some considerations for future studies

The only solid state HRM catheters for colonic manometry available are those with 1 cm spaced 36 sensors (evaluation of segments of the colon with difficult concurrent study of anal sphincter) allow or with 2/2.5 cm spaced 40 sensors. **But...**

Water perfused catheters with different number of sensors are available in the market. **But...**

Most of the centres are currently using CO<sub>2</sub> during colonoscopy placement of the colonic catheter

Most of the centres are currently trying to avoid the use of conscious sedation medications other than midazolam

Ongoing discussion about standardization of the colonic manometry: bowel preparation (oral/water enemas), meal (high/low calories), duration of recording, colonic stimulation with intraluminal administration of bisacodyl

The colonic HRM has improved our understanding of colonic motility.

However it has not added useful information for clinical practice.

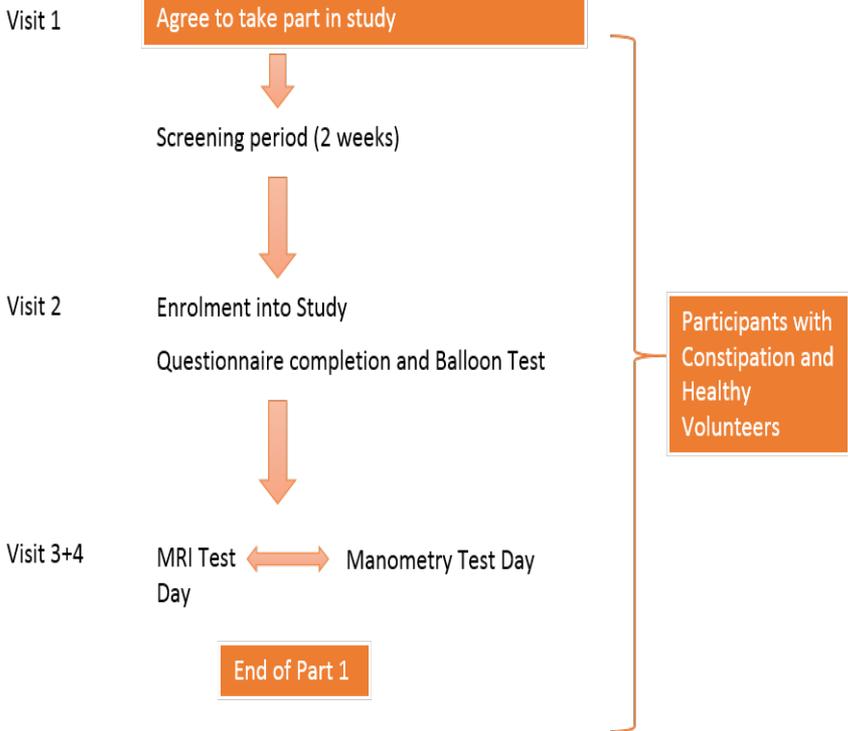
The procedure needs to be standardised across different centres.

We need larger and multicentre studies to evaluate whether this technique has a clinical role in guiding the management of patients.

**Are other non-invasive techniques the solution?**

# The RECLAIM study

- Participants are screened for eligibility ( 2 week period)
- Then undergo balloon expulsion test (for obstructed defecation)
- MRI and Manometry Test then undertaken in random order
- Stool samples and colonic biopsies taken



- **Currently recruiting at both sites!**
- **Nottingham:**
  - 8/20 HV Completed
  - 18/40 Patients Completed
- **London:**
  - 18/20 HV Completed
  - 2/40 Patients Completed



# Some tracings from the ongoing RECLAIM study

