



# Optimizing colonic sampling

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Leuven Intestinal Failure and Transplantation (LIFT)  
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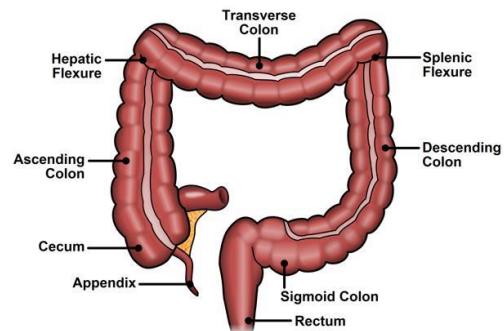
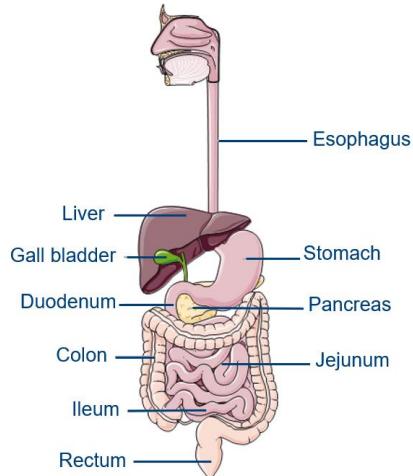


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## Overview

- **Introduction to the colon**
  - Anatomy and physiology
  - Diagnostic tools
- **Colonic drug disposition**
  - Relevance of colonic drug disposition
  - Traditional *in vivo* techniques
  - *In vivo* sampling
  - Application in drug disposition studies

# Anatomy



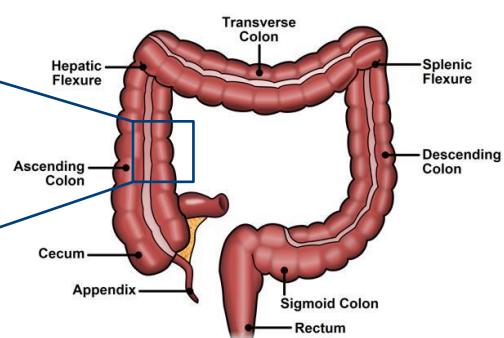
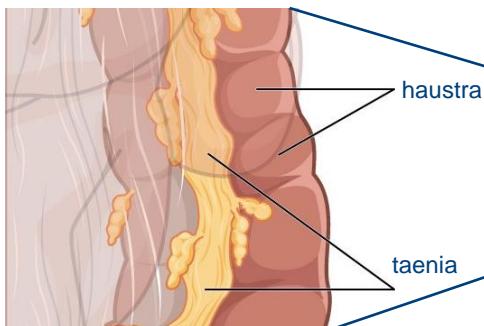
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# Anatomy

## Some facts:

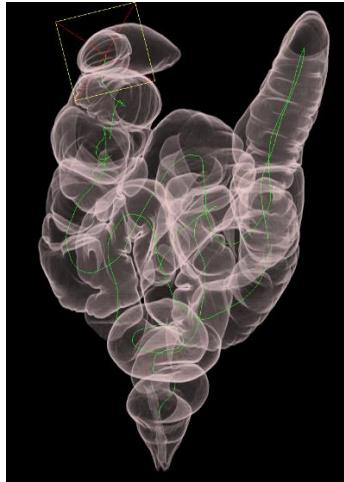
- Discontinuous longitudinal muscle: taeniae coli
- Tonic contractions of circular muscle: haustrations
- Colon is never empty >< rectum
- Length 80-150cm
- Highly variable shape



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# Anatomy



## Some facts:

- Discontinuous longitudinal muscle: taeniae coli
- Tonic contractions of circular muscle: haustrations
- Colon is never empty >< rectum
- Length 80-150cm
- Highly variable shape
- You can live without a colon

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# Diagnostic Tools: morphological

## Colonoscopy (with biopsies)



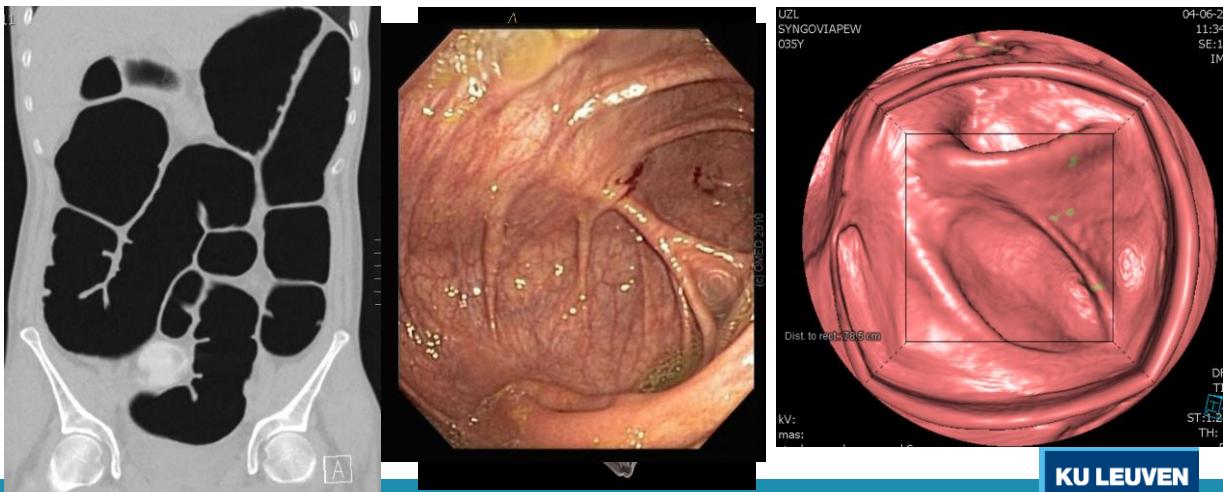
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# Diagnostic Tools: morphological

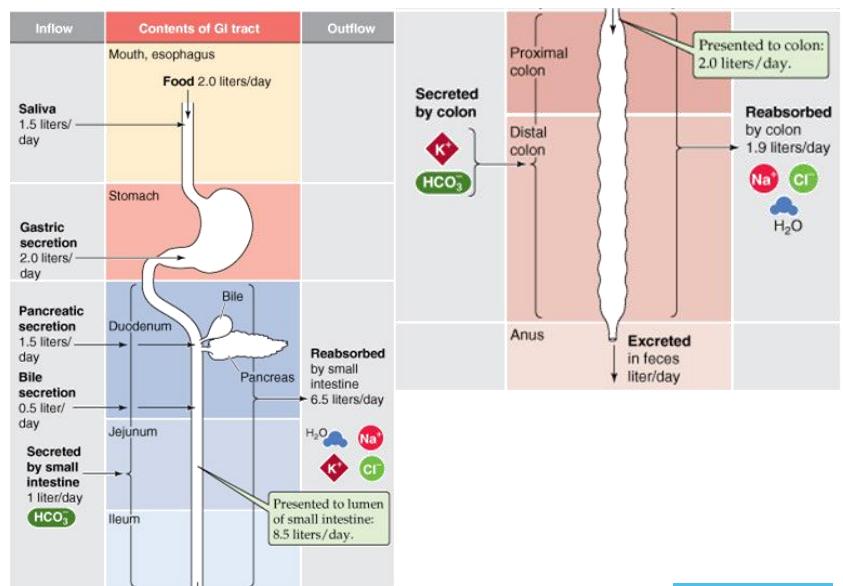
## Virtual colonoscopy



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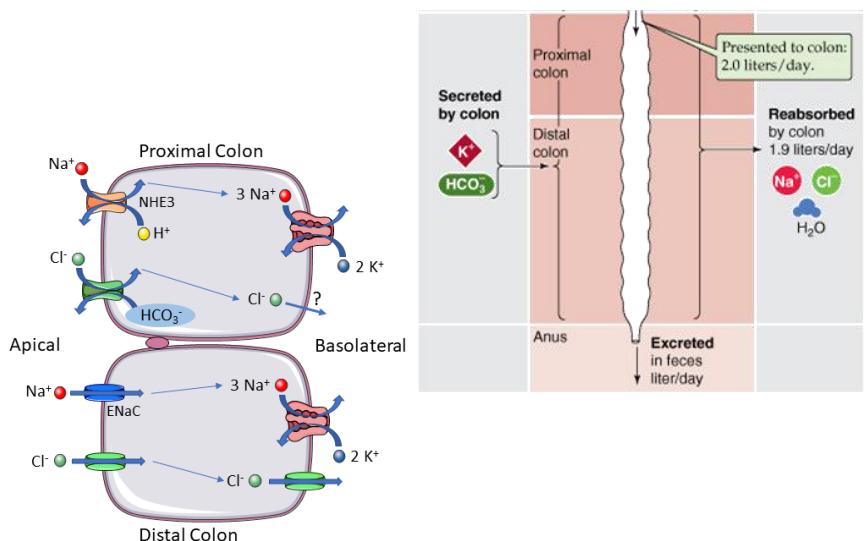
# Physiology

- Storage
- Desiccation (~ 1,9L/day)



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Vanuytsel T. Physiology of the Colon. in Steele's Colon and rectal surgery. In press

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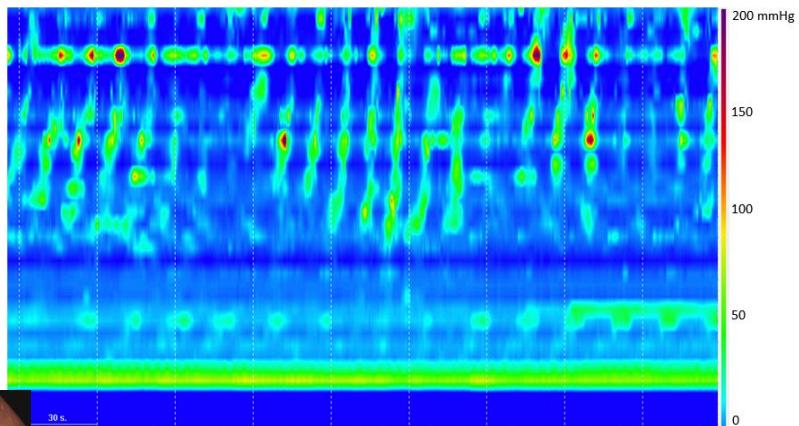
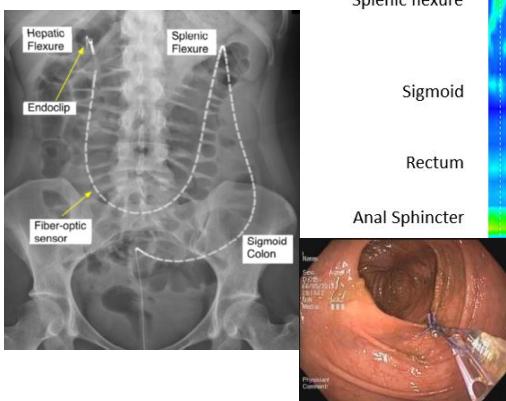
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# Physiology

Hepatic flexure

Retrograde motility patterns

200 mmHg



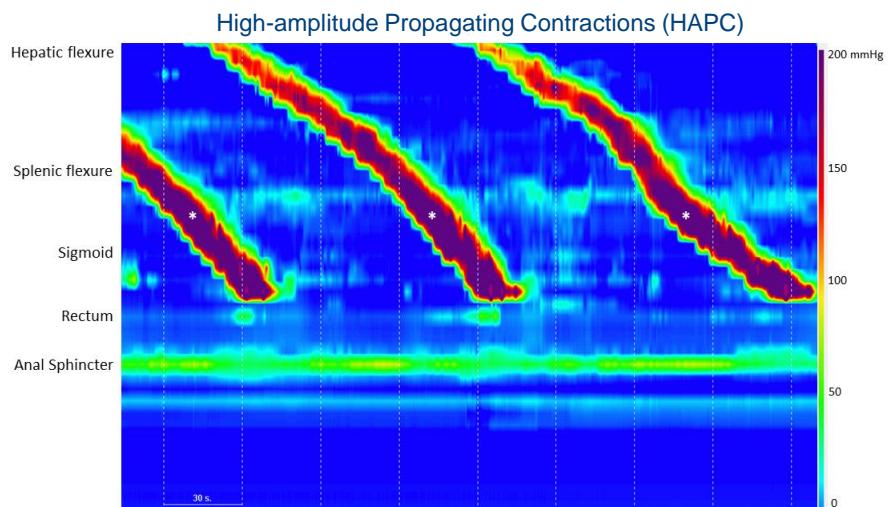
Vanuytsel T. Physiology of the Colon. in Steele's Colon and rectal surgery. In press

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# Physiology

- Storage
- Desiccation (~ 1,9L/day)
- Propulsion (16-89h transit)
- Defecation
- Fermentation



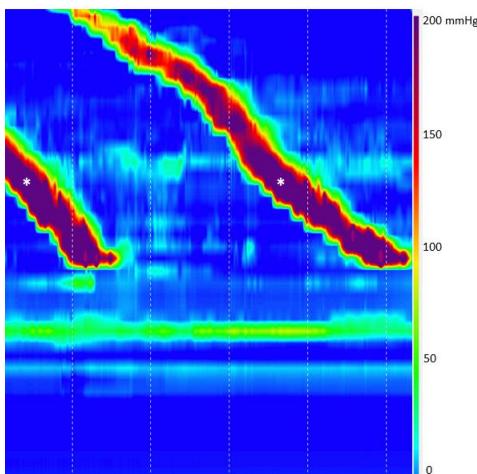
Vanuytsel T. Physiology of the Colon. in Steele's Colon and rectal surgery. In press

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## Diagnostic Tools: functional

**High-resolution manometry:** mainly research



**Pellet test:** daily clinical practice

10 pellets/day during 6 days; X-ray day 7  
Colonic transit = number of pellets x 2,4

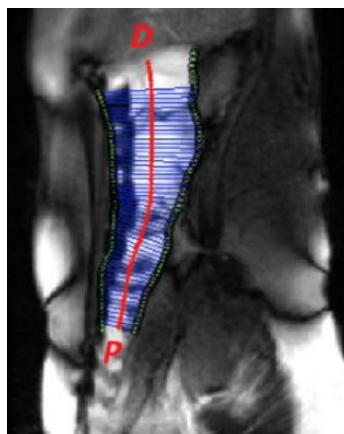


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# Diagnostic Tools: functional

**Colonic cine MRI:** mainly research



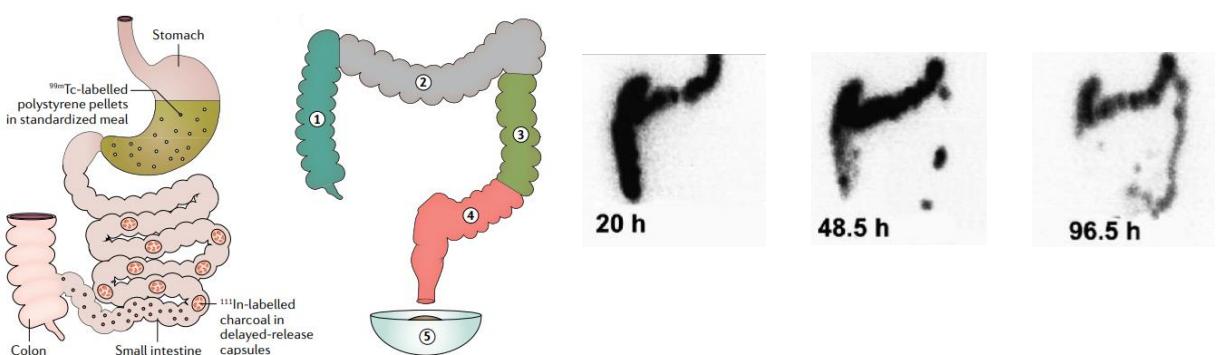
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Menys et al. Neurogastroenterol Motil 2019

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# Diagnostic Tools: functional

**Scintigraphy** (usually combined with small bowel)



Corsetti et al. Nat Rev Gastroenterol Hepatol 2019

Freedman et al. JNMT 2006

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## Colonic disease



Irritable Bowel Syndrome (IBS)



Inflammatory Bowel Disease (IBD)  
Crohn's disease  
Ulcerative Colitis



Colorectal tumors / polyps

Hypersensitivity  
Disturbed motility  
Immune activation  
Altered barrier function

Inflammation  
Altered barrier function

Cell proliferation

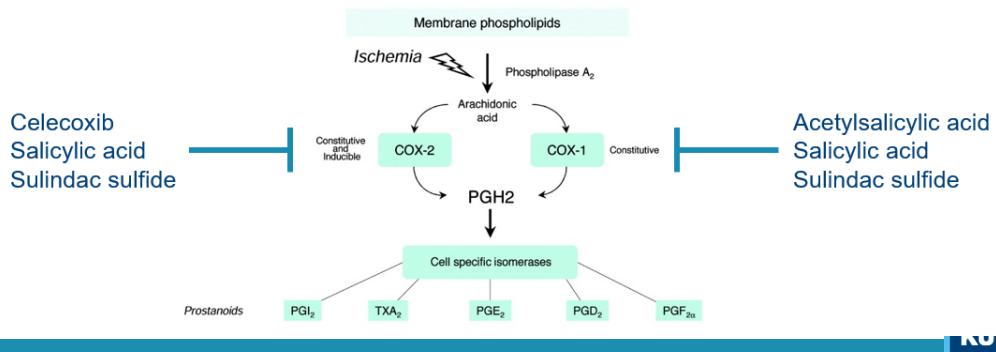
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# Chemoprevention of polyps

COX-inhibitors reduce polyp formation in patients at risk

Mechanism: reduction of angiogenesis  
induction of apoptosis



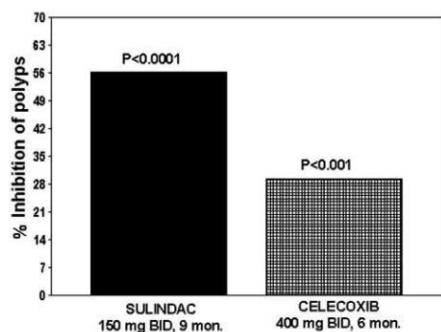
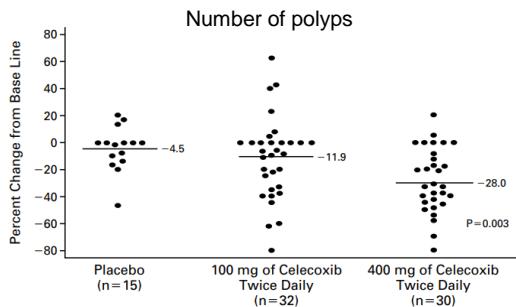
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# Chemoprevention of polyps

The New England Journal of Medicine

## THE EFFECT OF CELECOXIB, A CYCLOOXYGENASE-2 INHIBITOR, IN FAMILIAL ADENOMATOUS POLYPOSIS

GIDEON STEINBACH, M.D., PH.D., PATRICK M. LYNCH, M.D., J.D., ROBIN K.S. PHILLIPS, M.B., B.S., MARINA H. WALLACE, M.B., B.S., ERNEST HAWK, M.D., M.P.H., GARY B. GORDON, M.D., PH.D., NAOKI WAKABAYASHI, M.D., PH.D., BRIAN SAUNDERS, M.D., YU SHEN, PH.D., TAKASHI FUJIMURA, M.D., LI-KUO SU, PH.D., AND BERNARD LEVIN, M.D.

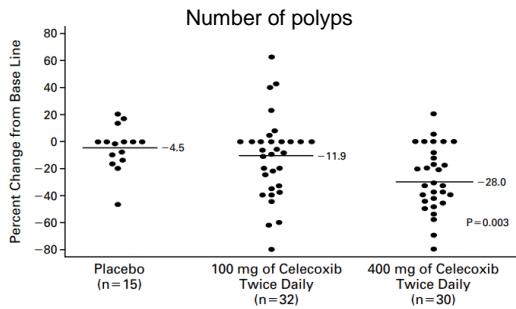


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Systemic side effects (GI, cardiac, renal)  
Suboptimal efficacy



Optimization of colonic disposition!



Poor understanding of current formulations!

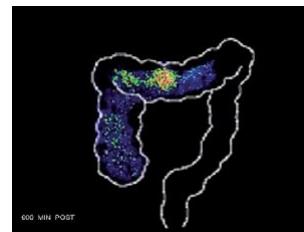
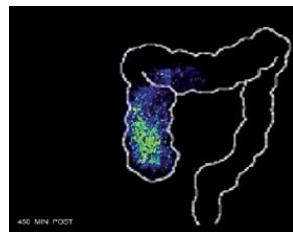
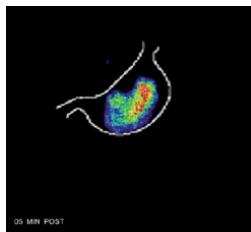
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Steinbach et al. N Eng J Med 2000

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# Scintigraphy of radio-labeled drug

Ketoprofen formulation



Indirect method!  
Local and tissue concentration of the drug?

Majumdar S. Gamma Scintigraphy 2016

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## In vivo colonic sampling



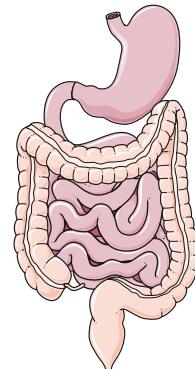
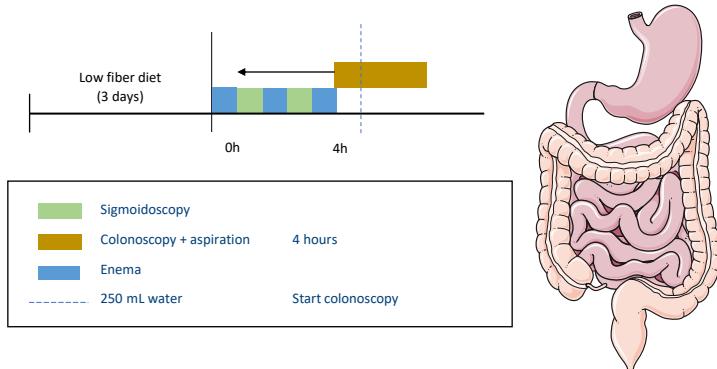
### Normal preparation:

- 3 days of low-fiber diet
- High-volume osmotic laxatives → Entirely flushes out colonic contents
- Conscious sedation + opioid analgesics → Reduces gastrointestinal motility

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## In vivo colonic sampling: preparation



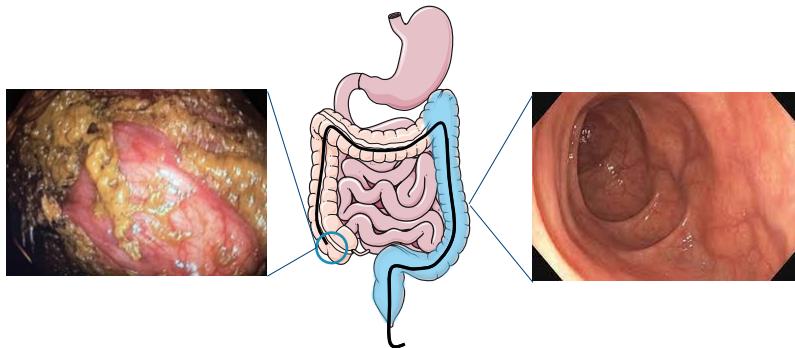
### Optimal cleansing method:

3 day low fiber diet (!)  
250 mL of water without soap or stimulant laxatives  
No sedation or analgesics!

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## In vivo colonic sampling: preparation



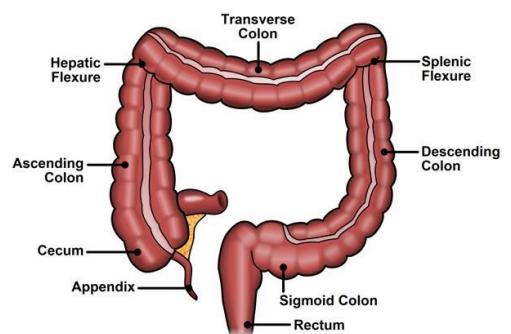
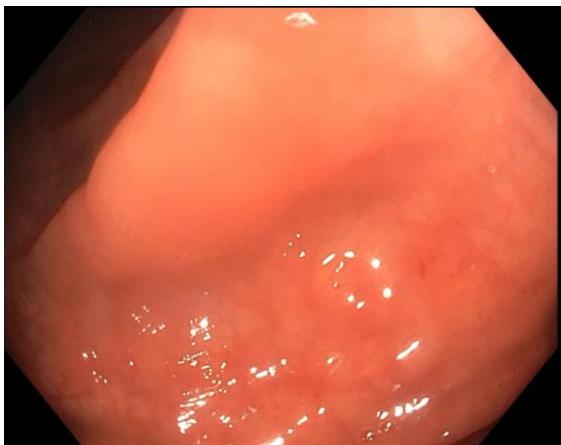
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## In vivo colonic sampling: colonoscopy

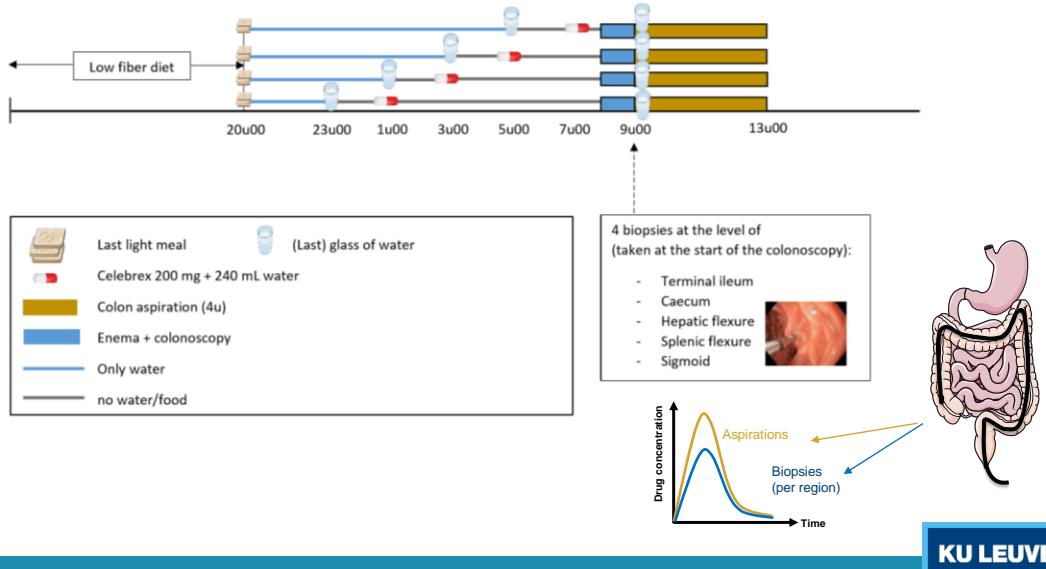


Total insertion duration: 4-10 minutes

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## In vivo colonic sampling: luminal sampling



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## In vivo colonic sampling: luminal sampling

Endoscopic polyp retriever



Salem sump tube



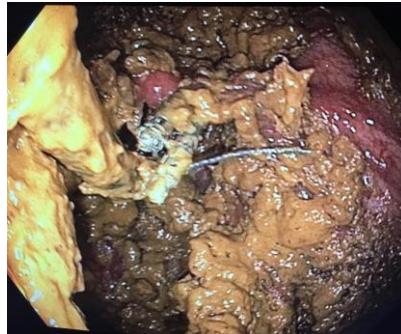
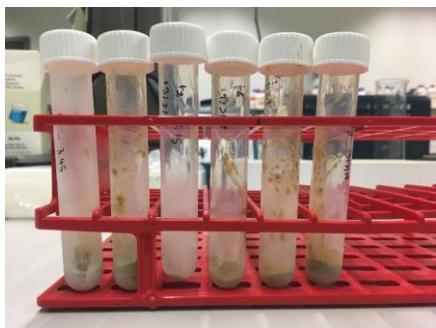
Faucher tube



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## In vivo colonic sampling: luminal sampling



Viscous contents  
Limited amount of fluid  
Long aspiration tube



**MISSION: IMPOSSIBLE**

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## In vivo colonic sampling: luminal sampling



Solution:

Aspiration through suction channel of the endoscope  
Limited to 1 sampling point per procedure

Viscous contents  
Limited amount of fluid  
Long distance aspiration tube

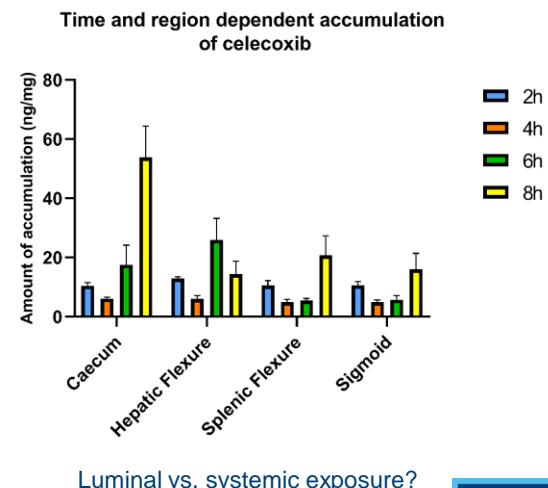
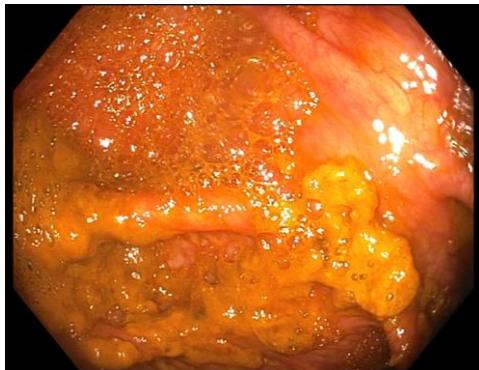


**MISSION: IMPOSSIBLE**

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## In vivo colonic sampling: tissue sampling



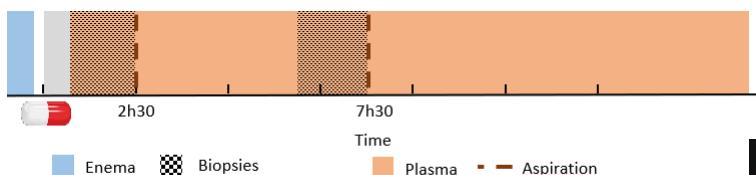
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## Application in disposition studies

Series of studies in healthy volunteers

First studies: two colonoscopies (early + late)  
biopsies every 15 minutes and 1 luminal aspiration at the end  
plasma sampling for 24h



Follow-up studies: one colonoscopy per formulation



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