



**Università  
di Brescia**

Dipartimento di Scienze Cliniche e Sperimentali

Dottorato di Ricerca in  
«Intelligenza Artificiale in Medicina e Innovazione  
nella Ricerca clinica e metodologica»

*Coordinatore: Prof. Domenico Russo*



# AI-assisted intestinal ultrasound to assess post-operative recurrence and predict clinical outcomes in Crohn's disease

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CICLO XL

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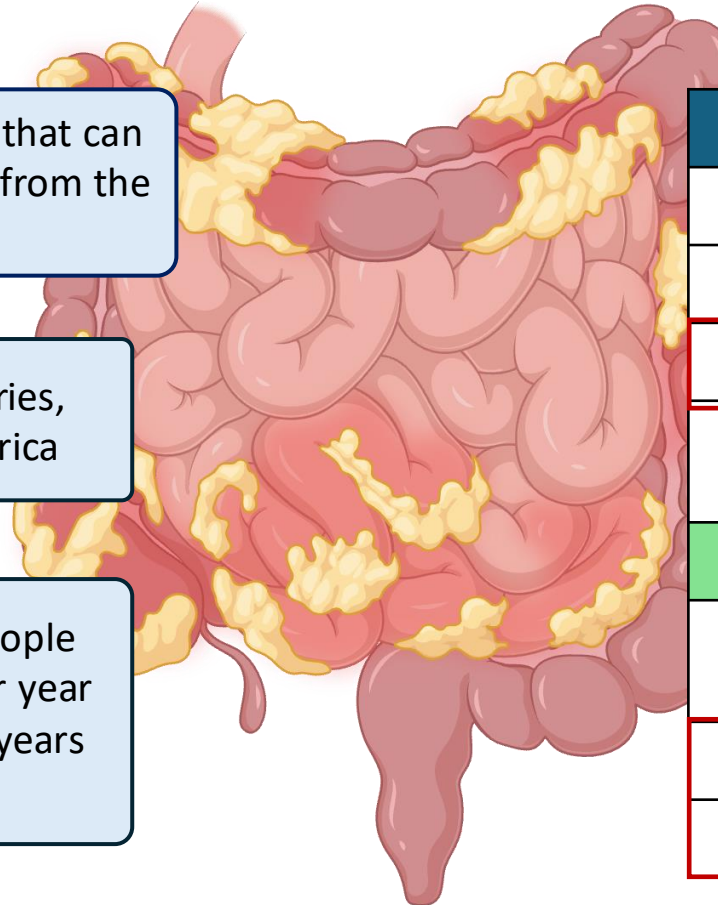
Co-Supervisor: Prof. Marietta Iacucci – APC Microbiome Ireland; Department of Medicine and Health; University College Cork

# Crohn's disease

Chronic inflammatory bowel disease (IBD) that can affect any part of the gastrointestinal tract from the mouth to the anus.

More common in industrialized countries, particularly in Europe and North America

- **Prevalence:** > 200–300/100,000 people
- **Incidence:** 3–20/100,000 people per year
- **Peak onset:** 25-35 years and 50-60 years
  - **M = F**



| Location  |                                                                                 |
|-----------|---------------------------------------------------------------------------------|
| <b>L1</b> | Terminal ileum (ileal disease) – 30-40%                                         |
| <b>L2</b> | Colon (Crohn's colitis) - 20-30%                                                |
| <b>L3</b> | <b>Ileocolonic disease – 40-50%</b>                                             |
| <b>L4</b> | Upper gastrointestinal tract (alone or associated with other locations) – 5-15% |
| Phenotype |                                                                                 |
| <b>B1</b> | Non-stricturing, non-penetrating (inflammatory) – 55-75%                        |
| <b>B2</b> | <b>Stricturing disease – 15-25%</b>                                             |
| <b>B3</b> | <b>Penetrating/fistulizing disease – 10-20%</b>                                 |

# Monitoring tools for POR

## ⌚ Disease onset & Diagnosis

## ⌚ Within 10 years after diagnosis

## ⌚ Within 1 year after index surgery

### Clinical (symptoms)

### Biomarkers

- CRP
- Faecal calprotectin

### Cross-sectional imaging

- CTE
- MRE

### Ileal and Ileo-Colonic Involvement

Relapsing-Remitting Episodes



### Fibrostenotic Disease Pattern

Progressive Strictureing



### Index surgery

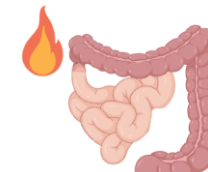
Ileo-Caecal or Ileo-Colonic Resection



~50% of patients

### Postoperative Recurrence

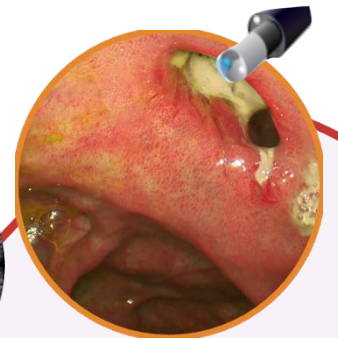
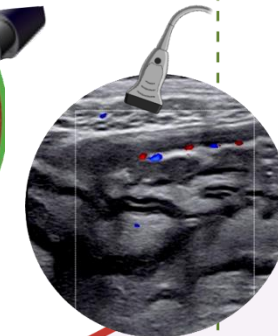
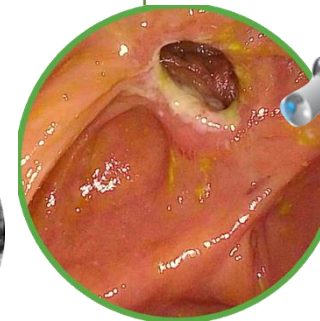
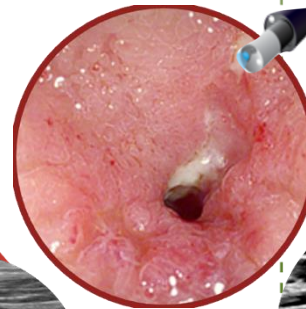
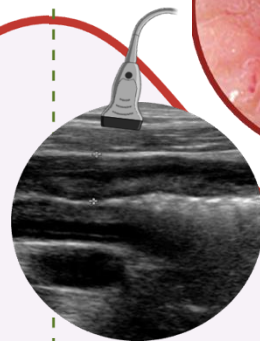
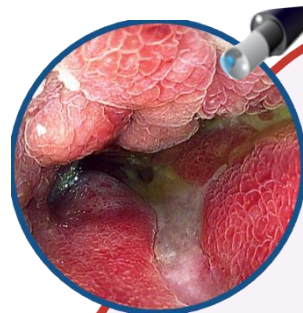
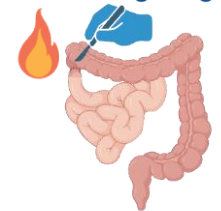
Endoscopic Recurrence with Subclinical Progression



~ 75% of patients

### Need for second surgery

Symptomatic Complications Necessitating Surgery



Endoscopy with biopsies (Rutgeerts score) – Gold standard

Intestinal ultrasound

# Intestinal ultrasound

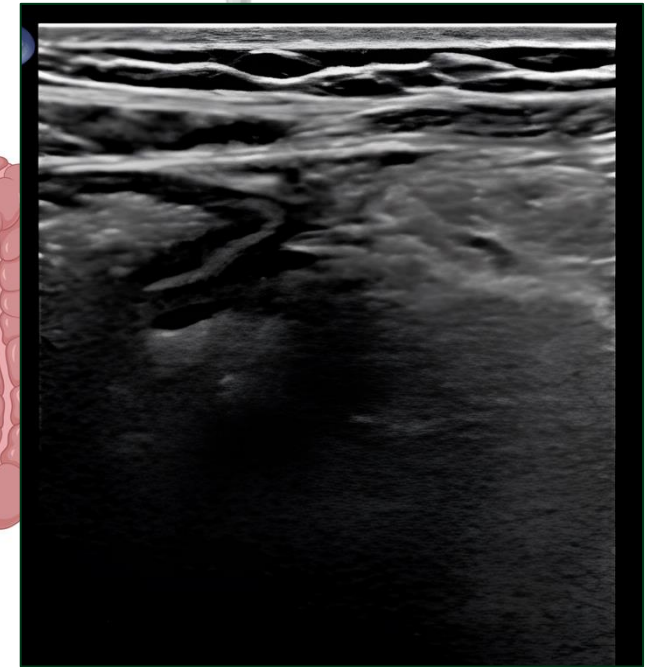
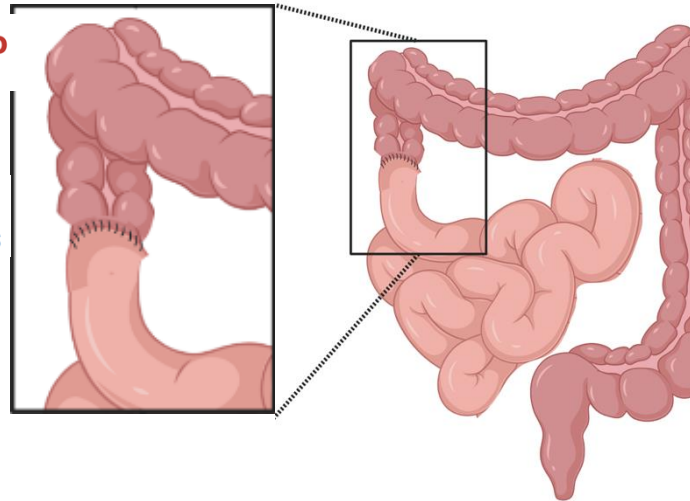
Intestinal ultrasound is an accurate non-invasive tool to assess and monitor post-operative recurrence in CD



Colon prox to anastomosis

Ileo-colonic anastomosis

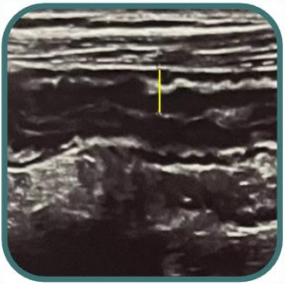
neo-TI



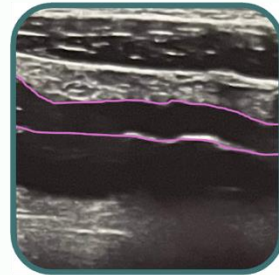
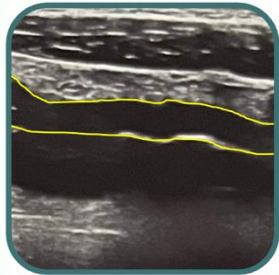
# IUS assessment in IBD

## Intestinal features

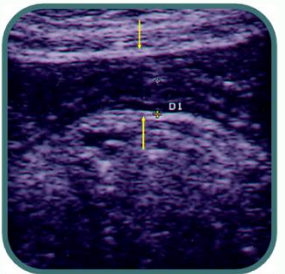
### Bowel wall thickness



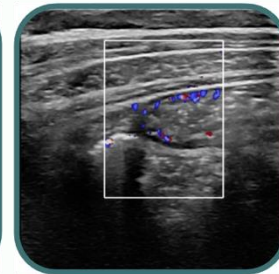
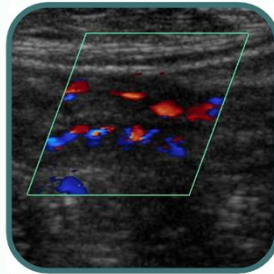
### Bowel wall stratification



### Stenosis



### Bowel wall vascularization

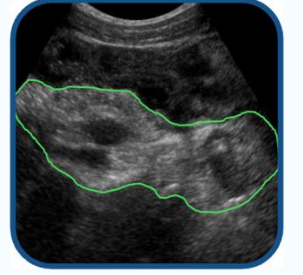


## Extraintestinal features

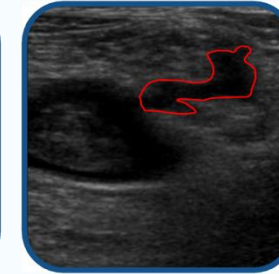
### Lymph nodes



### Inflammatory mesenteric fat (iFAT)



### Fistula



### Abscesses



## IUS scoring systems in CD

| IUS score        | Calculation                                                                                    | BWT                                                             | BWS                                                                            | CDS                                                                                                                                        | iFAT                                       |
|------------------|------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|
| <b>IBUS-SAS</b>  | $4 \times \text{BWT (mm)} + 15 \times \text{iFat} + 7 \times \text{CDS} + 4 \times \text{BWS}$ | Normal $\leq 3$ mm<br>Active $> 3$ mm                           | 0 – Normal<br>1 – Uncertain<br>2 – Focal $\leq 3$ cm<br>3 – Extensive $> 3$ cm | 0 – Absent<br>1 – Short signals<br>2 – Long signals inside the bowel<br>3 – Long signals inside and outside the bowel                      | 0 – Absent<br>1 – Uncertain<br>2 – Present |
| <b>SUS-CD</b>    | BWT + CDS                                                                                      | 0 – $< 3$ mm<br>1 – 3-4.9 mm<br>2 – 5-7.9 mm<br>3 – $\geq 8$ mm |                                                                                | 0 – Absent or single vessels<br>1 – 2-5 vessels/cm <sup>2</sup><br>2 – $> 5$ vessels/cm <sup>2</sup>                                       |                                            |
| <b>BUSS</b>      | $0.75 \times \text{BWT (mm)} + 1.65 \times \text{CDS}$                                         | Normal $\leq 3$ mm<br>Active $> 3$ mm                           |                                                                                | 0 – Absent<br>1 – Present                                                                                                                  |                                            |
| <b>Simple-US</b> | BWT (mm) + CDS                                                                                 | Normal $\leq 3$ mm<br>Active $> 3$ mm                           |                                                                                | 0 – Absent<br>1 – 1-2 points/cm <sup>2</sup><br>2 – 3-5 points/cm <sup>2</sup><br>3 – $> 5$ points and vessels outside the intestinal wall |                                            |



**No IUS score for POR has been yet developed**

**Crucial to better classify early changes predictive of POR, especially when endoscopy is not feasible**

| IUS score | Calculation                    |
|-----------|--------------------------------|
| IBUS-SAS  | $4 \times BV$<br>$4 \times BV$ |
| SUS-CD    | BWT                            |
| BUSS      | $0.75 \times$                  |
| Simple-US | BWT                            |

| iFAT                                       |
|--------------------------------------------|
| 0 – Absent<br>1 – Uncertain<br>2 – Present |
|                                            |
|                                            |
|                                            |



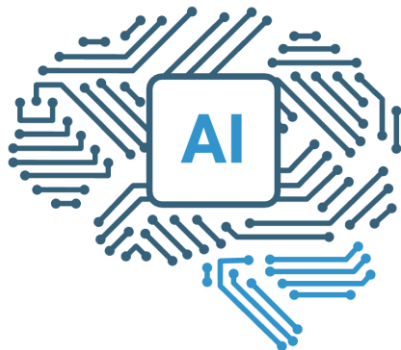
No dedicated IUS score for POR



Challenging assessment of anastomosis for altered anatomical landmarks



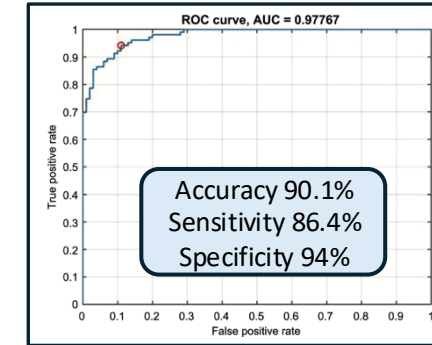
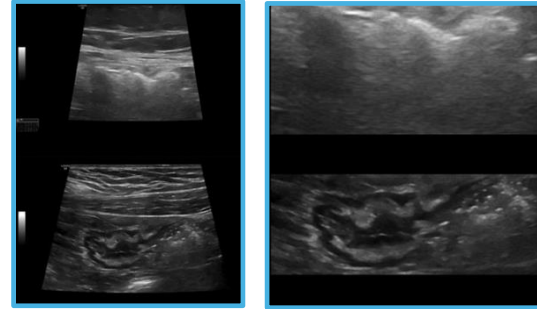
Significant learning curve and interobserver variability even among experts



# Preliminary AI models in IUS

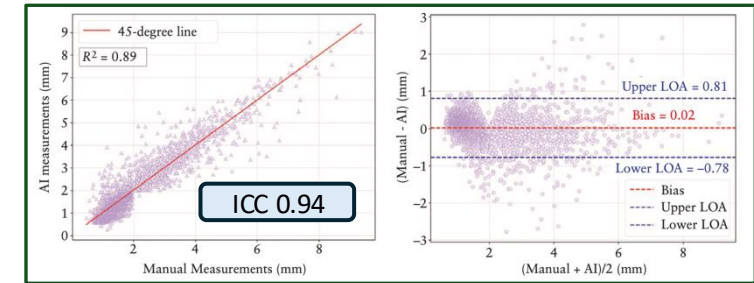
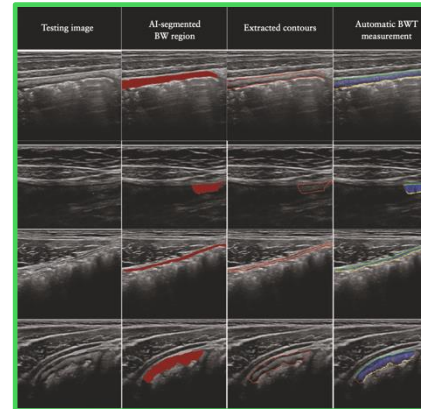
- CNN module to distinguish abnormal from normal BWT (>3 mm)
- 1008 images (50% normal, 50% abnormal)
  - 805/203 training/classification

Carter D, et al. *Inflamm Bowel Dis*. 2023



- Fully automated analysis to distinguish between abnormal and normal BWT (2 mm) in 260 pediatric IBD pts
- 4565 images (1478/3087 abnormal/normal)

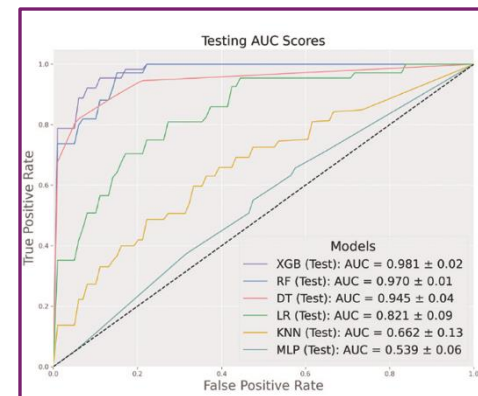
Kumaralingam L, et al., *J Crohns Colitis*. 2025



|                 | Manual measurement (mm) | Automatic measurement (mm) |
|-----------------|-------------------------|----------------------------|
| <b>Abnormal</b> | 3.05 (2.49-4.01)        | 3.18 (2.54-4.12)           |
| <b>Normal</b>   | 1.30 (1.12-1.52)        | 1.19 (0.97-1.48)           |

- Radiomic-based and CNN-based models to distinguish between normal and abnormal images (BWT >3 mm or modified Limberg score  $\geq 1$ )
  - 125 images (33% abnormal)

Gu P, et al., *Crohns Colitis* 2024



|                               | Accuracy (95% CI) | Sensitivity (95% CI) | Specificity (95% CI) |
|-------------------------------|-------------------|----------------------|----------------------|
| <b>XG boost</b>               | 0.94 (0.90-0.97)  | 0.94 (0.87-0.99)     | 0.94 (0.89-0.99)     |
| <b>Decision tree</b>          | 0.90 (0.85-0.95)  | 0.94 (0.87-0.99)     | 0.88 (0.81-0.95)     |
| <b>Random forest</b>          | 0.87 (0.83-0.91)  | 0.63 (0.43-0.83)     | 0.97 (0.93-0.99)     |
| <b>Logistic regression</b>    | 0.83 (0.75-0.92)  | 0.68 (0.52-0.85)     | 0.88 (0.76-0.99)     |
| <b>K-nearest neighbor</b>     | 0.69 (0.65-0.73)  | 0.41 (0.29-0.53)     | 0.82 (0.76-0.88)     |
| <b>Multi-layer perceptron</b> | 0.66 (0.61-0.71)  | 0.28 (0.01-0.61)     | 0.81 (0.60-0.99)     |

## Aims

Develop a **novel IUS score** to **predict early post-operative recurrence** and **long-term clinical outcomes**

Develop a **novel AI** model for

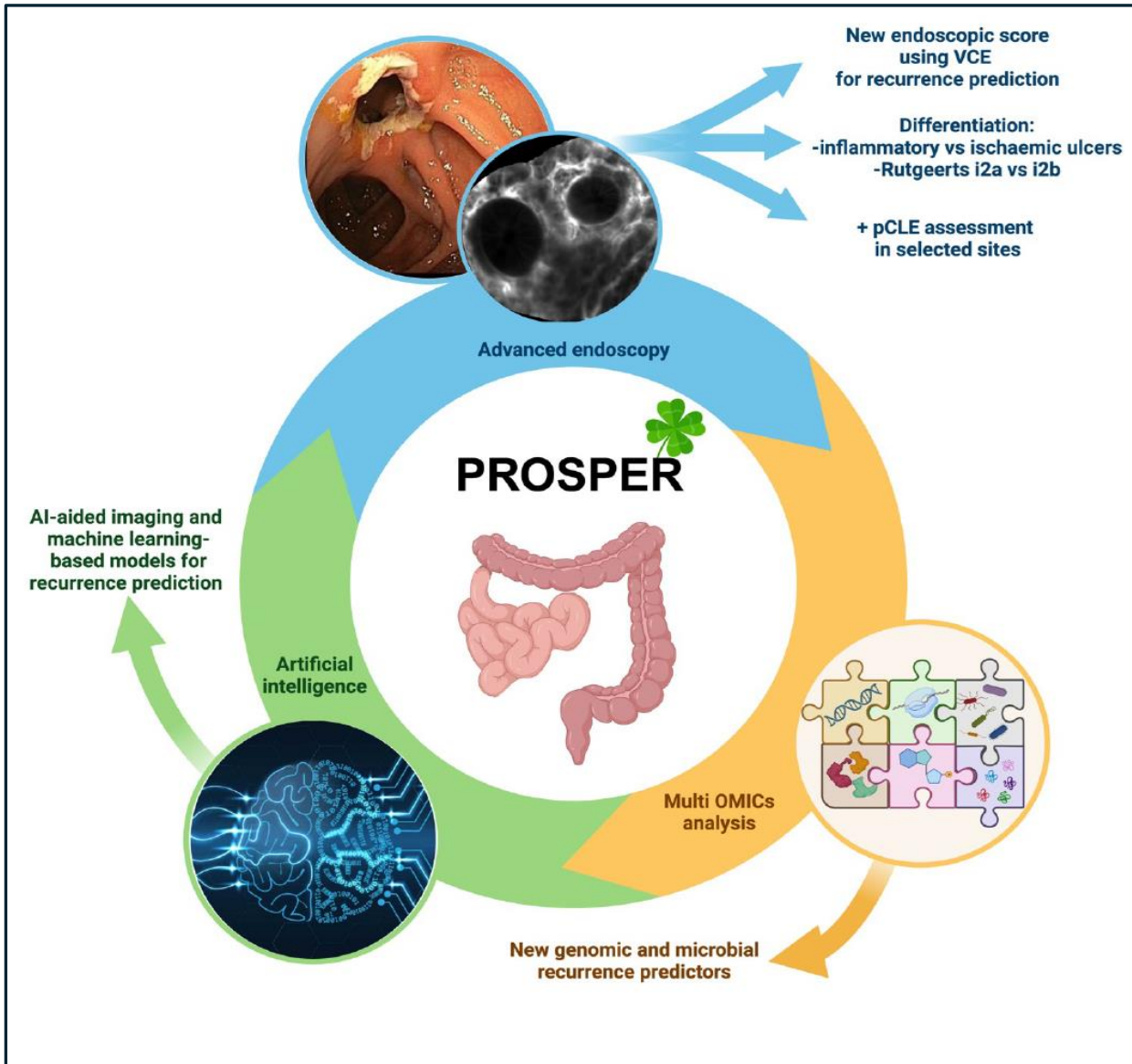
Bowel wall detection

Identification of **anatomical segments** (ileum; anastomosis; colon)

Evaluation of most relevant features of PROSPER-IUS score:

- **Bowel wall thickness**
- **Bowel wall stratification**
- **Bowel wall vascularization**
- **Lymph nodes**

# Endoscopic multimodal assessment using advanced imaging integrated AI to predict recurrence in post-operative Crohn's Disease - PROSPER



**International multicenter prospective study**

**Chief Investigator - Prof. Marietta Iacucci (UCC)**

# Study workflow

Enrollment

CD patients undergoing  
ileo-colonic resection

Faecal calprotectin  
assessment

Within 3 months after surgery

*FC <150 ug/g*

*FC >150 ug/g*

VISIT 1

3 months after surgery

US/MRI  
Blood and Stool samples

→ Colonoscopy + biopsies  
US/MRI  
Blood and Stool samples

VISIT 2

6 months after surgery

→ Colonoscopy + biopsies  
US/MRI  
Blood and Stool samples

US/MRI  
Blood and Stool samples

IUS videos and still  
images of neoterminal  
ileum, anastomosis and  
colon in longitudinal  
and transverse section

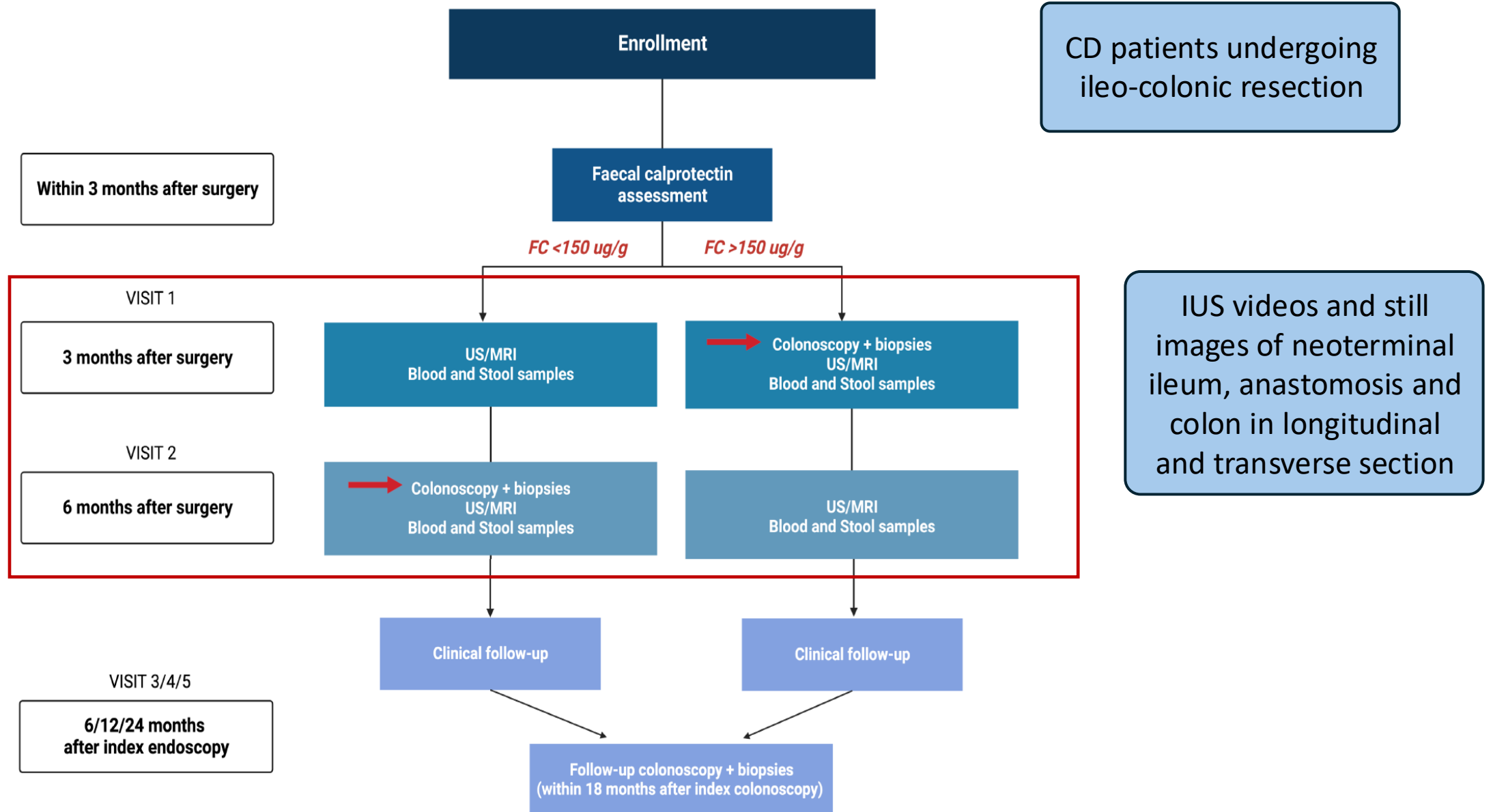
Clinical follow-up

Clinical follow-up

VISIT 3/4/5

6/12/24 months  
after index endoscopy

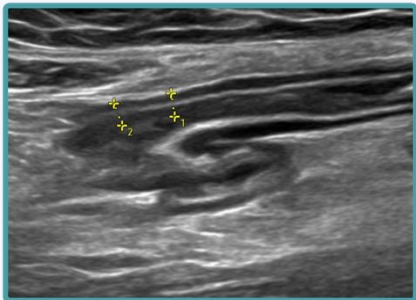
Follow-up colonoscopy + biopsies  
(within 18 months after index colonoscopy)



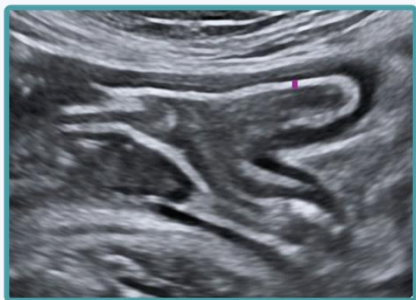
Selected features for PROSPER-IUS score

Intestinal features

Bowel wall thickness  
(mm)

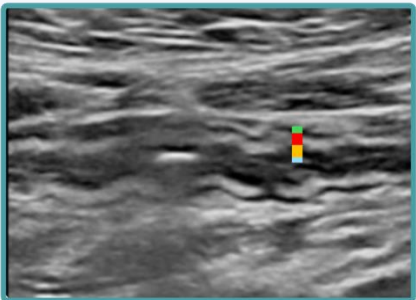


Submucosal thickness  
(mm)



Bowel wall stratification

Normal  
Focal disruption  
Extensive disruption

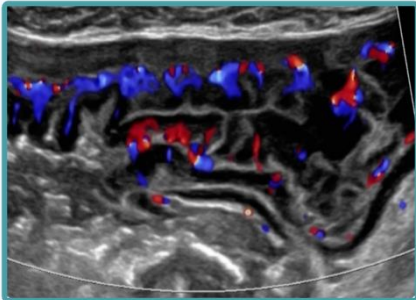


Ileal motility

Normal/abnormal

Bowel wall vascularization

Modified Limberg score



Strictures

Present/Absent

2 on-site expert consensus

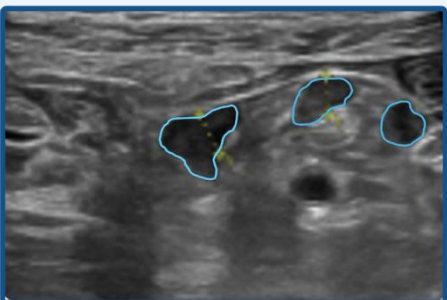
Assessment of 10 videos:

- Neoterminal ileum
- Anastomosis
- Colon

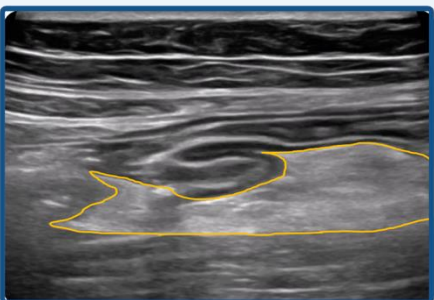
Final online survey reaching **75% agreement** for feature selection

Extraintestinal features

Mesenteric lymphadenopathy



Inflammatory mesenteric fat (iFAT)



Present/Absent

Abscesses



Free fluid



Fistula



## Inter-rater agreement for PROSPER-IUS features

|                                   | Ileum             |         |           | Anastomosis      |         |           | Colon            |         |           |
|-----------------------------------|-------------------|---------|-----------|------------------|---------|-----------|------------------|---------|-----------|
|                                   | K (95% CI)        | P value | Agreement | K (95% CI)       | P value | Agreement | K (95% CI)       | P value | Agreement |
| <b>BWT</b>                        | 0.61 (0.33-0.89)  | <0.001  | Good      | 0.53 (0.25-0.86) | <0.001  | Moderate  | 0.93 (0.83-0.99) | <0.001  | Very good |
| <b>Submucosal thickness</b>       | 0.52 (0.24-0.86)  | <0.001  | Moderate  | 0.46 (0.19-0.83) | <0.001  | Moderate  | 0.91 (0.79-0.98) | <0.001  | Very good |
| <b>Bowel wall stratification</b>  | 0.94 (0.85-1)     | 0.001   | Excellent | 0.88 (0.66-0.92) | 0.001   | Excellent | 0.96 (0.89-1)    | 0.001   | Excellent |
| <b>Bowel wall vascularization</b> | 0.88 (0.5-0.98)   | 0.001   | Excellent | 0.88 (0.37-0.96) | <0.001  | Excellent | 0.96 (0.89-1)    | 0.09    | Excellent |
|                                   | <b>K (95% CI)</b> |         |           | <b>P value</b>   |         |           | <b>Agreement</b> |         |           |
| <b>Ileal motility</b>             | 0.57 (0.06-0.77)  |         |           | 0.001            |         |           | Moderate         |         |           |
| <b>iFAT</b>                       | 0.6 (0.38-0.61)   |         |           | <0.001           |         |           | Moderate         |         |           |
| <b>Lymph nodes</b>                | 0.66 (0.49-0.67)  |         |           | <0.001           |         |           | Substantial      |         |           |
| <b>Stenosis</b>                   | 0.99 (0.97-1)     |         |           | 0.0001           |         |           | Excellent        |         |           |
| <b>Fistulas</b>                   | 1 (1-1)           |         |           | 0.0001           |         |           | Excellent        |         |           |
| <b>Abscesses</b>                  | 1 (1-1)           |         |           | 0.0001           |         |           | Excellent        |         |           |
| <b>Free fluid</b>                 | 0.99 (0.98-1)     |         |           | 0.001            |         |           | Excellent        |         |           |
| <b>Spiculates</b>                 | 0.99 (0.97-1)     |         |           | 0.0001           |         |           | Excellent        |         |           |

**Table.** PROSPER-IUS interobserver agreement for intestinal and extraintestinal IUS features



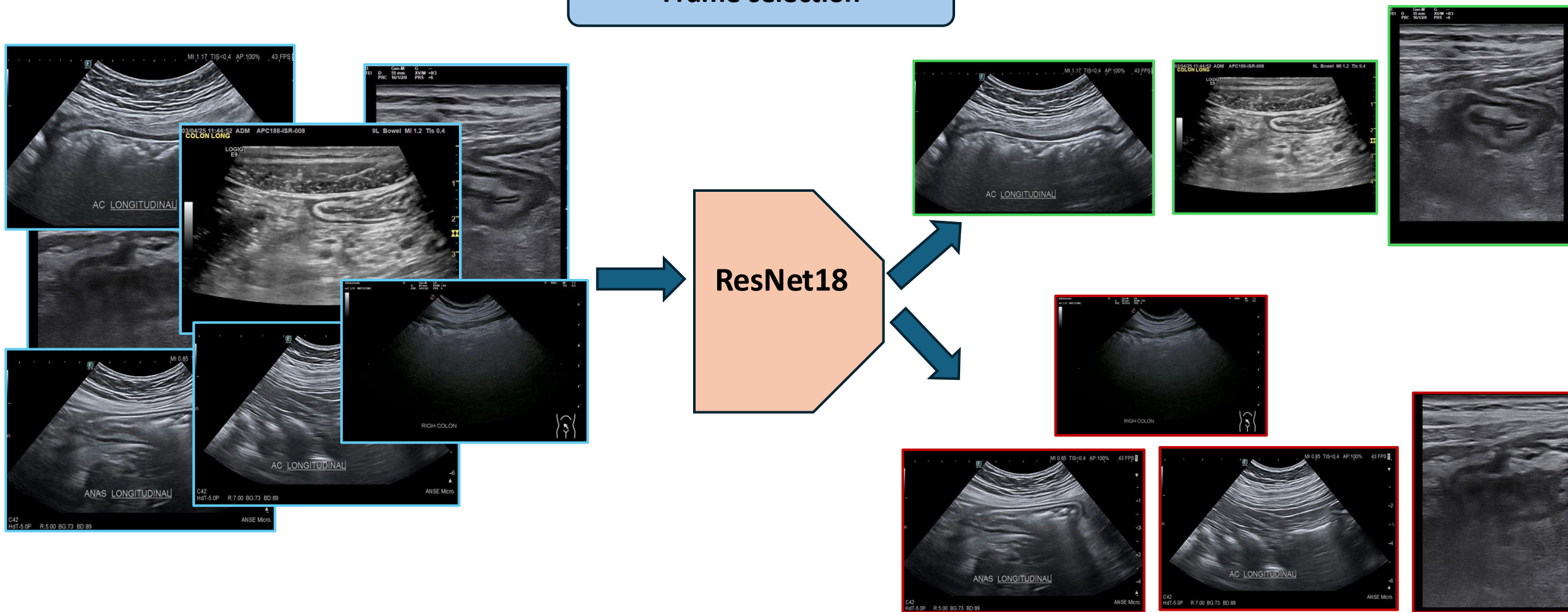
Good-to-excellent agreement for most features



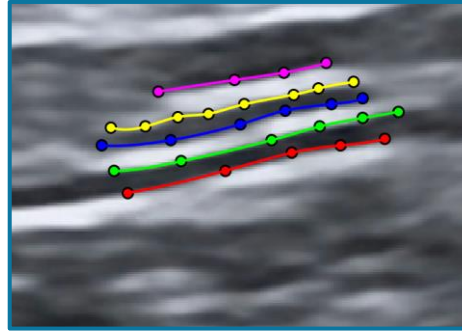
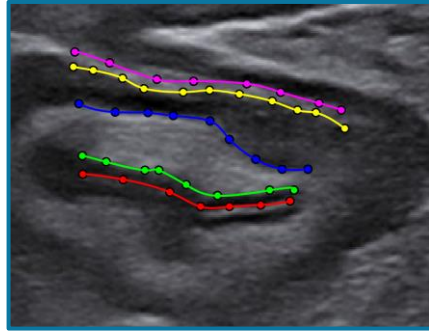
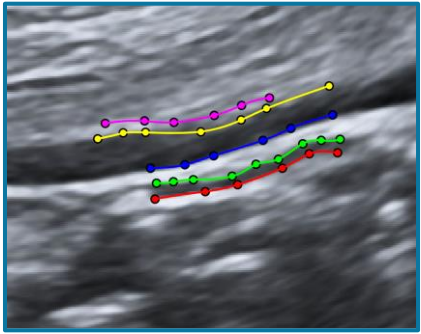
# AI model development

- 341 manually selected frames from 33 videos neoterminal ileum, anastomosis, colon (longitudinal and transverse sections)
- 80-20 Train-test split: 272 frame train, 69 frames test

## Frame selection

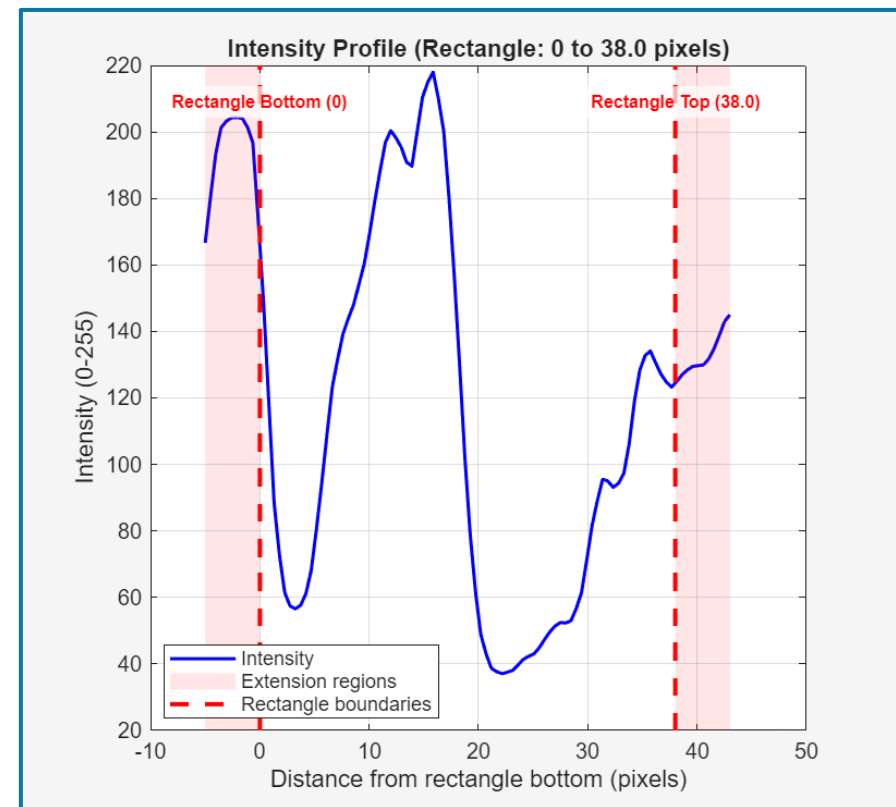
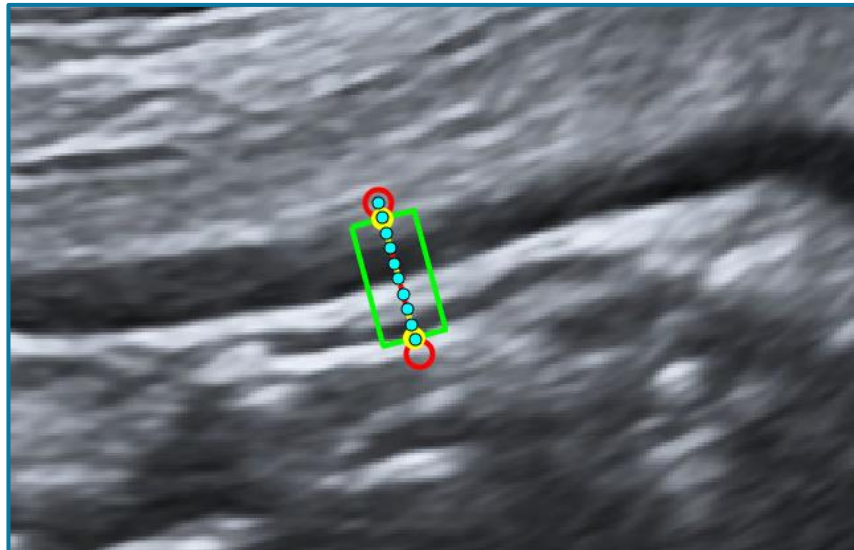


## Region of interest detection



Manually annotated bowel wall layers

## Wall layer profile extraction



## Preliminary results

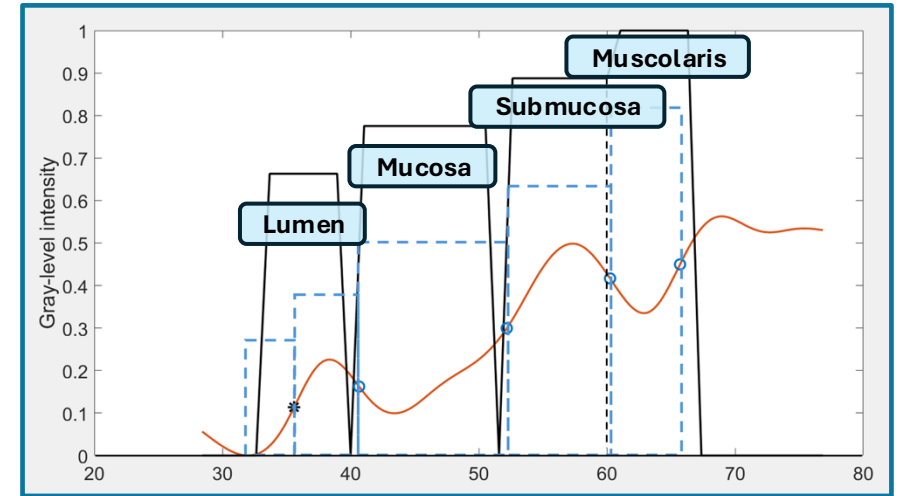
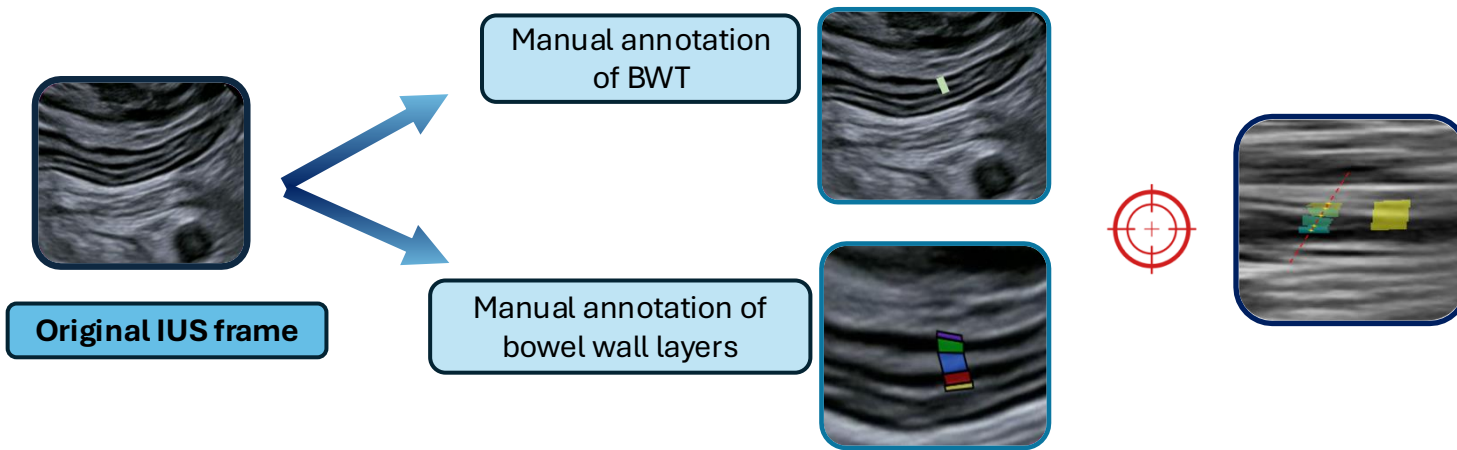
## Detection of informative frames

|           |                 | Manual          |             |
|-----------|-----------------|-----------------|-------------|
|           |                 | Non informative | Informative |
| Automatic | Non informative | 20              | 9           |
|           | Informative     | 0               | 40          |

| Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI)     | NPV (95% CI)       | Accuracy (95% CI) |
|----------------------|----------------------|------------------|--------------------|-------------------|
| 100.0 (91.2-100.0)   | 69.0 (50.8-82.7)     | 81.6 (68.6-90.0) | 100.0 (83.9-100.0) | 87.0 (77.0-93.0)  |

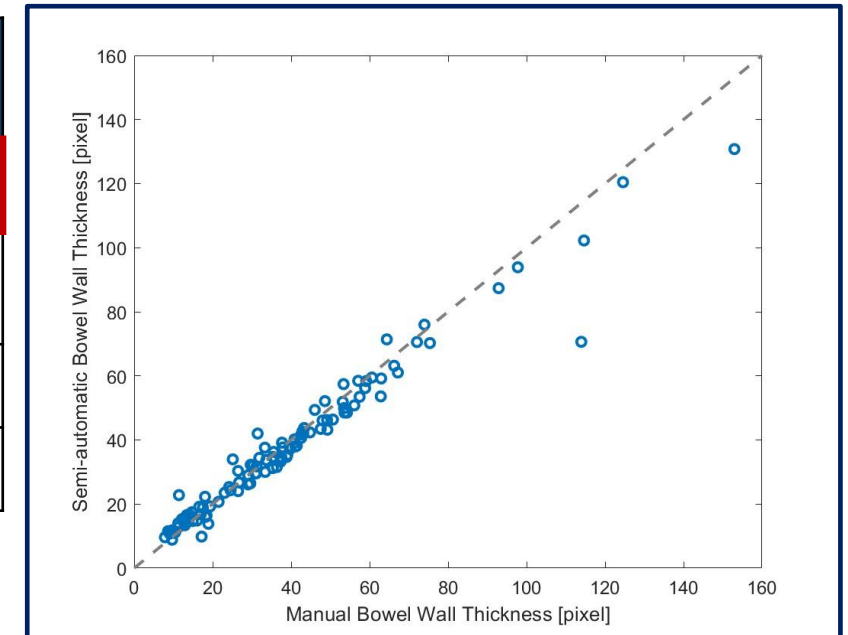
## Preliminary results

## Automated assessment of bowel wall layers



|                           | Correlation ( $\rho$ ) | Mean Absolute Error (pixels) | Mean Percentual Error (%) | Number of frames |
|---------------------------|------------------------|------------------------------|---------------------------|------------------|
| <b>Overall</b>            | 0.98                   | 3.4                          | 10.5                      | 109              |
| <b>Neo-terminal ileum</b> | 0.98                   | 2.8                          | 12.4                      | 38               |
| <b>Anastomosis</b>        | 0.99                   | 3.9                          | 10.0                      | 40               |
| <b>Colon</b>              | 0.98                   | 4.9                          | 9.2                       | 31               |

**Excellent correlation between manual and automated BWT measurements**



## Next steps

**Real-world validation** of the **PROSPER-IUS score** evaluating its ability to predict endoscopic remission and long-term clinical outcomes

**Implementation** of the **AI model** with:

- Segmentation of ileum, anastomosis, colon
- Bowel wall vascularization (Limberg score)
- Lymph nodes detection

Implementation and validation of the AI model in **predicting clinical outcome**

## Expected final study population

225 Patients

IUS at 3 time-points (3, 6, 18 months after surgery)

675 expected IUS videos

## Abstracts

- M Iacucci, I Zammarchi, B Verstockt, et al., P0279 Automated bowel wall layer assessment in post-operative Crohn's Disease: the Prosper study, *Journal of Crohn's and Colitis*, Volume 20, Issue Supplement\_1, January 2026, jjaf231.460, <https://doi.org/10.1093/ecco-jcc/jjaf231.460>
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- Presented at DDW (Digestive Disease Week) 2026 (2°-5° May 2026 – Chicago)

## Review

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# AI-assisted intestinal ultrasound to assess post-operative recurrence and predict clinical outcomes in Crohn's disease

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