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## REVIEW ARTICLE

# Intestinal Ultrasound and its Application as Point-of-Care Procedure for Diagnosing and Detecting Inflammatory Bowel Disease and Related Complications: A Narrative Review

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## ABSTRACT

Inflammatory bowel disease, comprising Crohn's disease and ulcerative colitis, defines as an idiopathic, chronic, relapsing, inflammatory disease affecting the gastrointestinal tract and leading to chronic damage. Endoscopy with biopsies is considered the gold standard for inflammatory bowel disease diagnosis, whereas magnetic resonance for Crohn's disease extension and complication assessment. However, colonoscopy is an invasive procedure, while magnetic resonance is relatively not easily accessible for patients; thus, the need for a reliable, accessible and non-invasive way to perform inflammatory bowel diseases diagnosis and monitoring in the tight control era, like intestinal ultrasound is. Compared to endoscopy and magnetic resonance, ultrasound has shown reliable diagnostic accuracy in assessing Crohn's disease diagnosis and evaluation of localisation, extension and complications. On the other hand, intestinal ultrasound is emerging as a valid tool also for ulcerative colitis severity and extension assessment. Moreover, performing ultrasonography in a point-of-care setting can guide the clinician in driving the diagnostic and therapeutic pathway, thus accelerating clinical decisions. As a novelty, point-of-care intestinal ultrasound performed with pocket devices could represent a promising item for the future of physical examination in outpatient or inpatient examination. The need for reproducibility of intestinal ultrasound among sonographers has emerged as a key-point in inflammatory bowel disease research field: the development of new scores for the evaluation of disease severity together with an intensive dedicated trainship could potentially reduce the differences between clinicians reporting. Accordingly, our aim was to perform a narrative review about the application of intestinal ultrasound in Crohn's disease and ulcerative colitis diagnosis and monitoring. Furthermore, technical aspects of this imaging technique and its application in a point-of-care setting through traditional and handheld sonographers were explored.

**Keywords:** *IBD, Crohn, Ulcerative colitis, diagnosis, intestinal ultrasonography, POCIUS.*

## Introduction

Inflammatory bowel disease (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC), defines as an idiopathic, chronic, relapsing, inflammatory disease possibly affecting any part of the gastrointestinal tract in CD and colonic wall continuously from the rectum in UC. Over the last few years, their incidence and prevalence have arisen across the globe, resulting in areas with "compounding prevalence" or "acceleration in incidence"<sup>1</sup>. Thus, the need for a reliable and accessible way to perform IBD diagnosis and monitoring has become a priority to direct the diagnostic path efficiently and avoid time-consuming and expensive procedures.

The use of laboratory biomarkers, such as C-reactive protein (CRP) and faecal calprotectin (FC), together with clinical symptoms, does not accurately provide comprehensive information about disease extent and severity<sup>2</sup>. Indeed, due to the transmural involvement of the bowel wall in CD and the submucosal in UC, cross-sectional imaging techniques comprising magnetic resonance (MRI), computed tomography (CT) and intestinal ultrasound (IUS) are considered a precious resource for suggesting or completing an IBD diagnosis and evaluating the disease course with possible extramural complications, even though endoscopy with biopsies remains mandatory<sup>3-5</sup>. In this context, IUS has been gaining attention, being a non-invasive, cost-effective, reliable tool for IBD evaluation without needing bowel preparation or contrast media. Nonetheless, performing IUS in a point-of-care setting (POCIUS), such as completing a routine physical examination, can ameliorate IBD-related outcomes, thus ensuring an earlier diagnosis and prompt therapy beginning<sup>6-8</sup>. Due to the increasing interest in POCIUS, some training programs, such as the International Bowel Ultrasound Group (IBUS Group), were born to standardise imaging reports and facilitate communication between physicians.

The aim of this review is to explore the technical aspects of IUS applied in a point-of-care setting (POCIUS) and its role in IBD diagnosis and detection of complications with traditional and handheld sonographers. Moreover, the topic of the standardisation and optimisation of reporting IUS in IBD will be explored.

## Methods

A narrative review with the findings obtained from research on the previously exposed topic on the PubMed database was performed. Our search terms, including medical subject headings (MeSH)

were included as follows and combined using the set operators AND or OR: "Inflammatory bowel disease" "IBD" "Crohn's disease" "Post-operative recurrence" "ulcerative colitis" "intestinal ultrasound" "Point of care ultrasound" "POCUS" "bowel ultrasound". Original articles, abstracts, systematic reviews, meta-analyses in English language, and references from the most relevant articles and ClinicalTrials.gov were selected. All studies underwent preliminary screening through title and abstract assessment.

## Results

### TECHNICAL ASPECTS OF INTESTINAL ULTRASOUND PERFORMING AND REPORTING

Performing IUS does not need fasting conditions. It can be generally conducted with two probes, a low-frequency (1-5 MHz) convex and a high-frequency (6-13 MHz) linear probe. The first provides a panoramic overview of the abdomen; the second ensures a specific visualisation of bowel wall layers. The bowel wall consists of 5 layers: superficial mucosal layer (hyperechoic), deep mucosal layer (hypoechoic), submucosal layer (hyperechoic), muscular layer (hypoechoic), serosa layer (hyperechoic). The practical aspects of the IUS examination are not yet well established; thus, it generally depends upon each centre. The most common approach is searching for left iliac vessels and psoas muscle as a reference point for the sigmoid colon, then tracking each colonic segment till caecum and terminal ileum recognition. Aftermath, an entire abdomen scan through multiple linear movements should be performed to ensure a global evaluation of possible complications. During the examination, the probe should be fanned with different grades of compression to identify air and all bowel layers; at least two 90-degree rotations at the splenic and hepatic flexure are needed to follow the colonic structure<sup>9,10</sup>.

The intramural findings that should be reported in an IUS examination are the following<sup>11</sup>:

- Bowel wall thickness, measured in two planes from the superficial mucosal layer to the serosal layer, has a pathological finding of > 3mm for both the ileal and colonic walls;
- Colour Doppler signal, measured at the most thickened bowel segment and reported at least with the intramural and/or extramural signal presence;
- Bowel wall stratification, considered normal, focally or extensively lost.
- Presence or absence of haustrations, ulcers, peristaltic movements and significant/persistent stenoses.

About the extramural findings, they should generally be reported as the presence or absence of enlarged inflammatory lymph nodes, mesenteric fat inflammation, free fluid, fistula (< 2 cm diameter hypochoic tract generally starting from bowel wall and extending through mesentery towards other bowel loops, bladder, or urogenital tract and abscesses (irregular anechoic lesions with posterior wall enhancement without vascularisation signals).

Using oral or intravenous contrast media agents has extensively been proposed and studied. Although it can add some information to basal IUS, it can make the examination more invasive and time-consuming, thus reducing its cost-effectiveness.

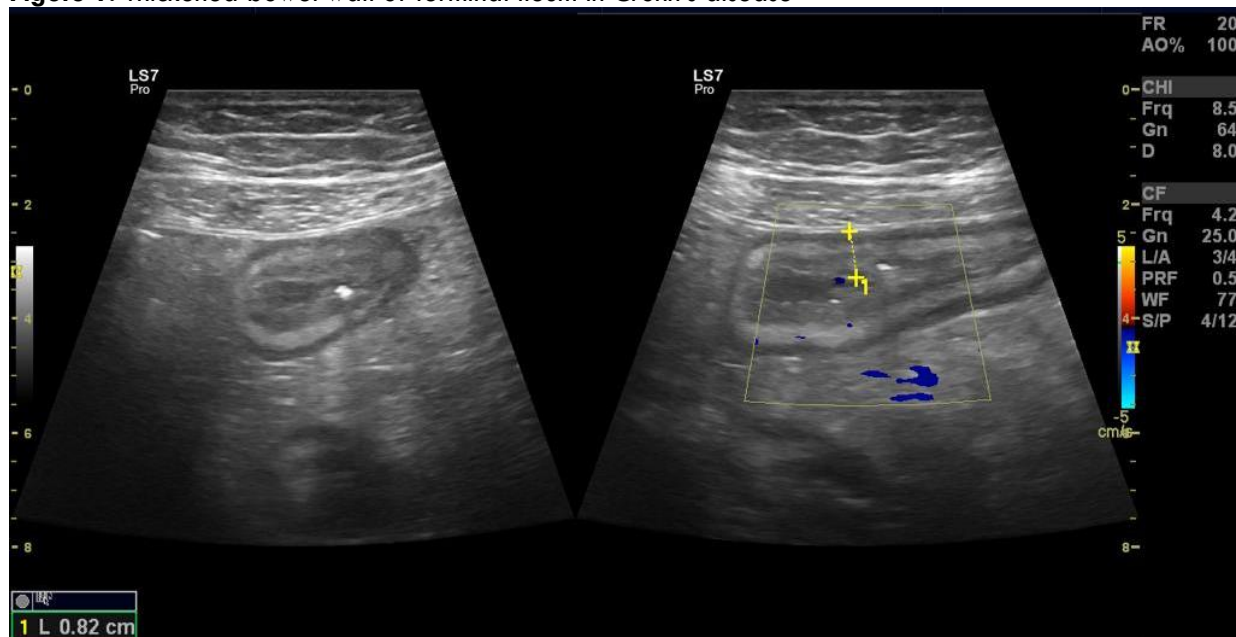
Some technical aspects can limit the reliability of the IUS examination. First, the patient's body status, especially when obesity is present, can reduce the correct visualisation of abdominal organs. Secondly, given that rectum is the most affected colonic part in UC, its "deep" and pelvic anatomic position represents a further limitation for the complete reliability of disease evaluation due to difficulty reaching it during the exam<sup>11</sup>.

#### INTESTINAL ULTRASOUND IN THE DIAGNOSIS OF CROHN'S DISEASE

The role of IUS in CD diagnosis in patients with symptoms suggesting IBD has been well-analysed through literature. The diagnostic accuracy of IUS for patients without an established diagnosis of CD is summarised in Table 1, Figure 1. Sensitivity and specificity were assessed in 11 studies<sup>12-20</sup>; results ranged from 57% to 100% for the first and 91.9%

to 100% for the second. The comparison between IUS and MRI<sup>18</sup> showed no difference in terms of sensitivity (94% for IUS vs 96% for MRI) and specificity (97% for IUS vs 94% for MRI) with overlapping confidence intervals, although MRI performed better than IUS for disease extension. In a systematic review conducted by Calabrese E. et al.<sup>21</sup>, where the sensitivity and specificity for the US were respectively 79.7% (71.9-87.5%, CI 95%) and 96.7% (95.1-98.4%, CI 95%). However, as shown in the METRIC study conducted in 2018 by Taylor et al.<sup>22</sup>, MRE performed better than IUS for ileal CD presence detection (97% vs 92%; p=0,025), while IUS performed better than MRE for colonic disease detection (73% vs 64%; p=0,202) in terms of sensitivity. In the same study specificity of MRE and IUS were not statistically different (96% vs 84%; p=0.054 for ileal CD and 96% vs 96%; p=1,000 for colonic CD). The latter is the only randomised control trial (therefore, the most methodologically correct study) regarding the use of ultrasound for CD diagnosis. Accordingly, IUS can be considered a reliable tool for the first-level examination of patients with clinical and laboratory findings suggestive of IBD. Performing ultrasound in a point-of-care setting can drive the diagnostic and therapeutic pathway in different clinical conditions, such as IBD, bowel infections, IBS, acute diverticulitis or bowel cancer. This tool's high specificity can help physicians exclude IBD in patients with non-specific gastrointestinal symptoms and negative laboratory findings. Conversely, in patients with sonographic features highly suggestive for IBD, it can support a second level imaging technique prescription or an endoscopic examination.

**Figure 1.** Thickened bowel wall of terminal ileum in Crohn's disease



**Table 1.** Sensitivity and specificity of IUS in suspected CD compared to endoscopic evaluation

Study	Year	Study Design	Comparison	Segment	No. of Patients	Sensitivity (%)	Specificity (%)
<b>Maconi<sup>12</sup> et al.</b>	1996	Prospective	IC, radiology, histology	Ileum, colon	110	89.1	94
<b>Astegiano<sup>13</sup> et al.</b>	2001	Prospective	IC, radiology, clinical evaluation	Ileum, colon	313	74	98
<b>Parente<sup>14</sup> et al.</b>	2002	Prospective	IC, radiology, surgery	Ileum, colon	296	93.4	97.3
<b>Pascu<sup>15</sup> et al.</b>	2004	Prospective	IC	Ileum, colon	37	82	97
<b>Pallotta<sup>16</sup> et al.</b>	2005	Prospective	IC, radiology, surgery, clinical evaluation	Jejunum, ileum	148	57; 94.3	100; 98
<b>Rispo<sup>17</sup> et al.</b>	2005	Prospective	IC, radiology	Ileum	106	92	97
<b>Castiglione<sup>18</sup> et al.</b>	2013	Prospective	IC	Ileum, colon	234	94	97
<b>Pallotta<sup>19</sup> et al.<sup>^</sup></b>	2013	Prospective	IC, radiology, clinical evaluation	Jejunum, ileum	51	75	100
<b>Rispo<sup>20</sup> et al.*</b>	2022	Prospective	IC, radiology	Ileum, colon	85	87.5	91.9

**IUS: intestinal ultrasound; CD: Crohn's disease; IC: ileocolonoscopy . <sup>^</sup>Study conducted on children\*IUS has been performed with Handheld device**

#### INTESTINAL ULTRASOUND IN DEFINING CROHN'S DISEASE LOCALISATION AND EXTENSION

The role of IUS in defining disease localisation is reported in the studies summarised in Table 2. Those findings confirm ultrasound's reliability with a ranging sensitivity and specificity of 73-96% and 67-98%<sup>12,14,15,18,23-29</sup>. In a systematic review conducted by Panes et al.<sup>30</sup> in 2011, the overall sensitivity and specificity were found to be 84% and 94%. The diagnostic accuracy of IUS did not

significantly differ from MRE in a study conducted by our group<sup>18</sup>, where sensitivity and specificity for CD location for ultrasound were 73% and 92%. Subsequently, Calabrese E. et al.<sup>21</sup> analysed the sensitivity and specificity of IUS in detecting anatomical lesions for each bowel wall segment: they were 55.6% and 98.5% for jejunal lesions, 92.7% and 88.2% for ileal lesions, 81.8% and 95.3% for colonic lesions.

**Table 2.** Sensitivity and specificity of IUS in assessing CD localisation

Study	Year	Study Design	Comparison	Segment	No. of Patients	Sensitivity (%)	Specificity (%)
<b>Maconi<sup>12</sup> et al.</b>	1996	Prospective	IC, enteroclysis	Ileum and colon	110	89	94
<b>Reimund<sup>23</sup> et al.</b>	1999	Prospective	IC, enteroclysis	Ileum and colon	74	83	67
<b>Bru<sup>24</sup> et al.</b>	2001	Prospective	IC	Ileum and colon	68	83	87
<b>Parente<sup>14</sup> et al.</b>	2002	Prospective	IC, enteroclysis	Ileum and colon	296	93	97
<b>Parente<sup>25</sup> et al.</b>	2003	Prospective	IC, enteroclysis, CT, surgery	Ileum and colon	487	77	95
<b>Pascu<sup>15</sup> et al.</b>	2004	Prospective	IC	Ileum and colon	37	74	97
<b>Parente<sup>26</sup> et al.</b>	2004	Prospective	IC, enteroclysis	Small bowel	102	96	98
<b>Martinez<sup>27</sup> et al.</b>	2009	Prospective	IC, enteroclysis, CT	Small bowel and colon	30	91	98
<b>Castiglione<sup>18</sup> et al.</b>	2013	Prospective	IC, MRE, surgery	Small bowel and colon	234	73	92

Study	Year	Study Design	Comparison	Segment	No. of Patients	Sensitivity (%)	Specificity (%)
Rispo <sup>28</sup> et al.	2017	Prospective	IC, MRE	Small bowel and colon	71	78	94
Allocca <sup>29</sup> et al.	2018	Prospective	IC, MRE	Ileum and colon	60	88	96

IUS: intestinal ultrasound; CD: Crohn's disease; IC: ileocolonoscopy; MRE: magnetic resonance enterography

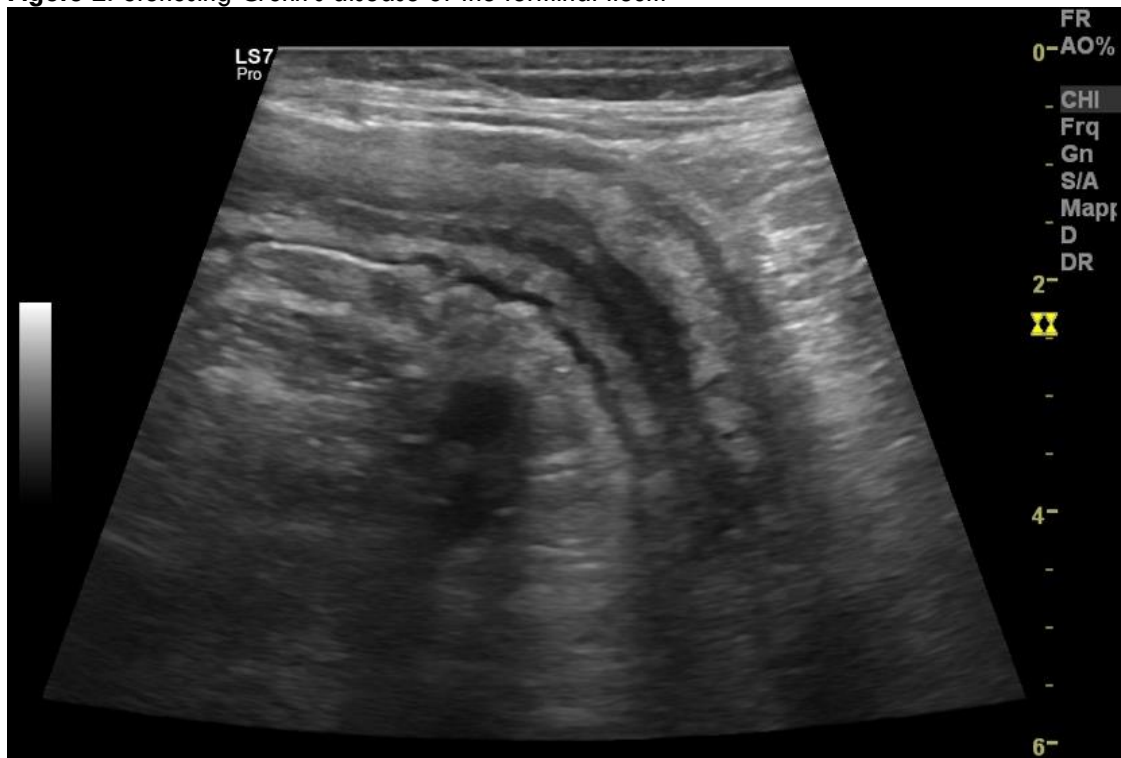
On the other hand, the evaluation of disease extension differs from the disease location. In a study conducted by our group in 2013<sup>18</sup>, the concordance between IUS and MRI regarding disease extension was moderate ( $r=0.69$ ); this result was more evident when the disease involved longer ( $> 30$  cm) ileal segments. The concordance between the two procedures seems to become higher when IUS is performed with oral contrast administration (SICUS), as stated in the studies conducted by Pallotta et al.<sup>16</sup> and Calabrese E. et al.<sup>31</sup>. According to the results from the METRIC study<sup>22</sup>, IUS has a sensitivity of 29% and a specificity of 61% in evaluating disease extension in both ileal and colonic involvement. At the same time, MRE had a sensitivity of 44% ( $p=0.002$ ) and a specificity of 80% ( $p=0.337$ ). Those results are worse if only colonic extension evaluation (17% sensitivity) is considered. Hence, considering IUS accuracy in determining CD location and extension, applying it in routine IBD clinical assessment and early disease evaluation is advisable. Certainly, the evaluation of disease extension has limited value compared to MRI.

## INTESTINAL ULTRASOUND IN DEFINING COMPLICATED CROHN'S DISEASE

### Strictures

Crohn's disease patients can develop small bowel and, less commonly, colonic strictures (Figure 2) It usually causes obstructive symptoms, and the detection of this complication requires either an intensive medical treatment escalation or surgery. However, up to 20% of small bowel strictures in CD does not cause any symptom<sup>32</sup>. Thus, early detection of this kind of complication is crucial in CD diagnosis and monitoring; IUS can help physicians identify them with minimal additional time if performed correctly, as well as for other CD complications. The accepted definition for luminal stenoses at cross-sectional imaging and ultrasound comprises the presence of a fixed luminal narrowing associated with an upstream loop dilation  $\geq 3$  cm<sup>11</sup>. Intestinal ultrasound has a sensitivity and specificity in detecting stenosis compared to surgery of 75-100% and 0-91%, respectively<sup>33-37</sup>. A complete overview of this evaluation is available in Table 3.

Figure 2. Stenosing Crohn's disease of the terminal ileum



**Table 3.** Sensitivity and specificity of IUS in assessing CD strictures

Study	Year	Study Design	Comparison	Us Techniques	No. of Patients	Sensitivity (%)	Specificity (%)
Gasche <sup>33</sup> et al.	1999	Prospective	Surgery	US	213	100	91
Kohn <sup>34</sup> et al.	1999	Prospective	Surgery	US	44	75	89
Pallotta <sup>35</sup> et al.	2012	Prospective	Surgery	US/SICUS	49	80	75
Onali <sup>36</sup> et al.	2012	Prospective	Surgery	SICUS	15	92	0
Kumar <sup>37</sup> et al.	2015	Prospective	Surgery	SICUS	67	88	88

IUS: intestinal ultrasound; CD: Crohn's disease; SICUS: small intestine contrast ultrasonography

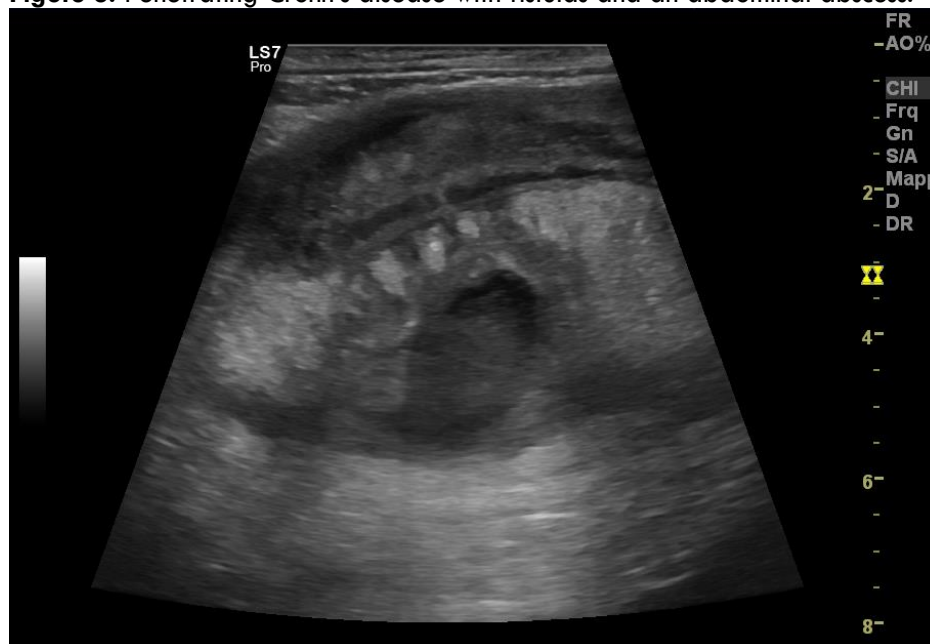
Three out of five studies applied SICUS<sup>35–37</sup>, which seems to perform better than IUS in detecting strictures. According to Panes et al.<sup>30</sup>, IUS's pooled sensitivity and specificity are 79% and 92%, even though not all the studies considered surgery as a reference standard. The concordance of IUS and other radiologic techniques, such as MRE, was evaluated by our group in 2013<sup>18</sup>: the results showed fair concordance ( $k=0.082$ ;  $p=0.01$ ) between those two techniques in detecting small bowel stenoses. Therefore, IUS can be considered a reliable tool for detecting stenotic complications of CD. However, as for the other imaging techniques, it has never been demonstrated a role in stenosis characterisation. Indeed, knowing its nature (either inflammatory or fibrotic) could be a turning point for CD management in decision-making. An attempt in this direction has been made by describing BWS: in a study conducted by Maconi et al.<sup>38</sup>, the loss of stratification in the bowel wall was related to inflammatory stenosis, while a stratified pattern suggested a stenotic disease behaviour. The latter results, although promising, have not been studied in deeper, probably due to the subjectivity of the choice of the different stratification patterns. The use of elastography and contrast-enhanced

ultrasound (CEUS) seems promising in this field, despite the small sample size of studies and different methodologies in measurement<sup>39</sup>.

### Abscesses

After stenoses, the formation of abscesses is one of CD's most common extramural complications (Figure 3). On ultrasound, these are described as an ill-defined inflammatory mass without concrete walls and with peripheral and internal CDS<sup>11</sup>. The role of IUS in abscess detection has been extensively analysed in the literature. The sensitivity and specificity of IUS ranged from 80% to 100% and 80% to 96%, using surgery as the comparator in three out of four studies<sup>12,29,33,36,38</sup>. Results are summarised in Table 4. In the study conducted by Maconi et al. in 2003<sup>38</sup>, CT performed better than IUS in detecting abscesses (92% CT vs 87% IUS for diagnostic accuracy): both techniques failed to detect “deep” abscesses, such as interloop, appendicular and mesenteric ones, according to the systematic review conducted by Calabrese E. et al.<sup>21</sup>, IUS's overall sensitivity and specificity was 86.5% (95% CI; 83.3%–88%), while the specificity was 94.5% (95% CI, 87.9%–100%).

**Figure 3.** Penetrating Crohn's disease with fistulas and an abdominal abscess.



**Table 4.** Sensitivity and specificity of IUS in assessing CD abscesses

Study	Year	Study Design	Comparison	Us Techniques	No. of Patients	Sensitivity (%)	Specificity (%)
Maconi <sup>12</sup> et al.	1996	Prospective	Endoscopy, enteroclysis	CT, US	110	83	94
Gasche <sup>33</sup> et al.	1999	Prospective	Surgery	US	213	100	92
Maconi <sup>38</sup> et al.	2003	Prospective	Surgery	US	625	80	93
Onali <sup>36</sup> et al.	2012	Prospective	Surgery	SICUS	15	100	80
Allocca <sup>29</sup> et al.	2018	Prospective	IC, MRI	IUS	60	100	96

**IUS: intestinal ultrasound; CD: Crohn's disease; CT: computed tomography; MRI: magnetic resonance imaging**

Regarding the concordance between MRI and IUS, in the study conducted by our group in 2013<sup>18</sup>, it was excellent ( $k=0.88$ ;  $p=0.01$ ). Hence, IUS can be considered a reliable tool for detecting abscess formation in CD.

#### Intrabdominal fistula

The evaluation of intrabdominal fistulas is a crucial point for IUS. These are defined as a hypoechoic duct with < 2 cm diameter (differentiating them from perienteric abscesses) with or without gas filling; additionally, the fistula site and organ involvement (entero-enteric, entero-cutaneous and enterovesical) should be reported<sup>11</sup>. According to

the results summarised in Table 5, the sensitivity of ultrasound without oral contrast administration ranges from 60% to 87%<sup>12,29,33,35,36</sup>; those results improve when SICUS is performed. In more recent works, the global sensitivity of IUS (either with or without oral contrast) was 70.1% (95% CI, 59.7%–80.6%), while the specificity was 95.6% (95% CI, 92.5%–98.8%)<sup>21</sup>. Moreover, IUS showed no good concordance with MRI regarding fistula detection ( $k=0.67$ ;  $p=0.01$ )<sup>18</sup>. However, in a more recent prospective study including 60 CD patients, IUS showed a sensitivity of 100% and a specificity of 98% in detecting fistulas with 98% diagnostic accuracy compared to MRI<sup>29</sup>.

**Table 5.** Sensitivity and specificity of IUS in assessing CD fistula

Study	Year	Study Design	Comparison	Us Techniques	No. of Patients	Sensitivity (%)	Specificity (%)
Maconi <sup>12</sup> et al.	1996	Prospective	Endoscopy, CT, enteroclysis	US	110	66	96
Gasche <sup>33</sup> et al.	1999	Prospective	Surgery	US	213	87	90
Pallotta <sup>35</sup> et al.	2012	Prospective	Surgery	SICUS	49	96	90.5
Onali <sup>36</sup> et al.	2012	Prospective	Surgery	SICUS	15	60	88
Allocca <sup>29</sup> et al.	2018	Prospective	IC, MRI	IUS	60	100	98

**IUS: intestinal ultrasound; CD: Crohn's disease; CT: computed tomography; IC: ileocolonoscopy; MRI: magnetic resonance imaging**

#### IUS in post-operative recurrence detection

Crohn's disease patients require surgery in up to 70% of cases in ten years, and disease recurrence after bowel resection can occur in up to 90% without therapy within five years<sup>40</sup>. Although it is not possible to talk about a proper "diagnosis", early detection of CD post-operative recurrence (POR) is crucial for IBD management. Colonoscopy with biopsies within 6-12 months after surgery<sup>41</sup> remains the gold standard for POR detection, but IUS shows good accuracy in its recognition<sup>42</sup>. Moreover, IUS can help the physician accelerate its early identification and introduce or escalate

therapy faster. In 1998, Andreoli et al.<sup>43</sup> first described IUS as a reliable first-line tool to detect CD POR, despite the machine performance of that time: in their study conducted on 41 patients, they found a sensitivity of 81%, a specificity of 86%, and a diagnostic accuracy of 83% for BWT > 5 mm in detecting recurrence compared to endoscopy.

Rispo et al.<sup>44</sup> compared the diagnostic accuracy of IUS with endoscopy one year after surgery: they found sensitivity, specificity, positive predictive value and negative predictive value, respectively of 79%, 95%, 95%, and 80%. Furthermore, a cut-

off of BWT > 5 mm differentiated mild from severe endoscopic recurrence (Rutgeerts score i1-2 vs i3-4) with excellent agreement with endoscopy ( $k=0.90$ ).

In 2008, Castiglione et al.<sup>45</sup> conducted a prospective study on 40 patients who had undergone surgery. After one year of follow-up, IUS, SICUS and IC were executed: the sensitivity and specificity of IUS and SICUS were comparable (77% and 94% for IUS, 82% and 94% for SICUS) with a cut-off of BWT > 3 mm without statistically significant different results. On the other side, a cut-off of 5 mm for IUS and 4 mm for SICUS showed an excellent AUROC in the detection of severe POR, both with a diagnostic accuracy of 97%. The threshold values differ between the two techniques because the oral contrast agent flattens the bowel wall, thus making it thinner.

On the other side, Calabrese E. et al.<sup>46</sup> found a significant correlation ( $r= 0.67$ ;  $p < 0.0001$ ) between BWT evaluated with SICUS and Rutgeerts score, defining CD recurrence in the presence of BWT > 3 mm for at least 4 cm length at the perianastomotic area, bowel dilation > 2.5 cm and bowel stricture defined as < 1 cm bowel lumen diameter.

In 2016, Onali et al.<sup>47</sup> reported a five years' experience sensitivity and specificity for SICUS of 98% and 75% for SICUS performed one year after surgery. However, BWT was not correlated with clinical outcomes at the end of the follow-up.

In a systematic review and meta-analysis conducted by our group in 2018<sup>42</sup> including ten eligible studies and 536 patients, IUS showed a sensitivity and specificity of 82% and 88% in determining POR; furthermore a cut-off of BWT  $\geq 5.5$  mm predicted a severe POR (Rutgeerts score i3-i4) with a sensitivity and specificity of 83.8% and 97.7%.

Furthermore, in a 2021 retrospective study on 201 patients by Dal Piaz et al.<sup>48</sup>, IUS recurrence and BWT  $\geq 4$  mm predicted surgical recurrence with an OR = 6.04 and 2.58, respectively. The latter results support the routine use of IUS and SICUS in clinical practice for POR detection within one year after surgery, especially in the first months, in order to detect early recurrence. However, large prospective studies involving IUS as a point-of-care test after CD surgery are mandatory to determine its actual influential role in POR evaluation.

#### INTESTINAL ULTRASOUND IN ULCERATIVE COLITIS DIAGNOSIS

The utility of IUS in UC has been gaining attention over the last few years. Whilst its utility in defining

disease extension and activity is well known, IUS has not been proven reliable for diagnosing UC. The findings from the literature show an overlap regarding sonographic findings among the most common conditions affecting the colon, such as UC, colonic CD, radiation, infectious and ischaemic colitis<sup>25,49-51</sup>. Even though some studies report a marked BWT associated with colonic CD, this finding can not reliably distinguish it from a severe UC. Hence, IUS can represent a valuable tool during everyday practice for recognising colonic disease, thus guiding an indication by the physician to an early endoscopic examination, which remains the gold standard for UC diagnosis together with biopsy sampling<sup>4</sup>. Except this, IUS has a limited role as a point-of-care test for diagnosing UC, thus not furnishing features attributable to this condition.

#### INTESTINAL ULTRASOUND IN ULCERATIVE COLITIS EXTENSION

Since IUS cannot provide specific features for UC diagnosis, it is a reliable tool for defining disease extent and severity. Already in 1992, Schwerk et al.<sup>52</sup>, in a prospective study including 30 patients diagnosed with UC, found a 100% sensitivity for IUS in detecting extensive colitis, 95% for left colitis and 50% for rectal disease. Other studies subsequently confirmed the latter results regarding diagnostic accuracy<sup>15,25</sup>. In 2018, Allocca et al.<sup>53</sup> found a good correlation between UC extension measured with IUS and endoscopy (0.660, 95% CI: 0.474-0.790,  $p < 0.0001$ ). Subsequently, Kinoshita et al.<sup>54</sup> demonstrated a moderate concordance between IUS evaluation and endoscopy for all colonic segments except for the rectum ( $k=0.33$ ). As well as rectal and perianal involvement for CD is poorly assessed with transabdominal ultrasound, rectal visualisation in UC is limited by its distance from the abdominal wall. Thus, Sagami et al. proposed<sup>55</sup> adopting trans-perineal ultrasound (TPUS) approach for rectal involvement evaluation in UC. According to the results coming from the latter study, BWT < 4mm measured with TPUS was an independent predictor for endoscopic and histologic healing in the rectum ( $p < 0.05$ ).

#### INTESTINAL ULTRASOUND IN ULCERATIVE COLITIS DISEASE ACTIVITY

During the last few years, the growing evidence for the reliability of IUS in UC activity evaluation has made spreading its use and literature interest. Several studies assessed endoscopic disease severity and activity according to heterogenic criteria<sup>15,56-59</sup>; findings are summarised in Table 6. Bozkurt et al.<sup>56</sup> in 1996 first evaluated UC activity through ultrasound: among the 36 patients diagnosed with UC, BWT > 4 mm and BWS were considered features correlated with endoscopic and



histological severe activity ( $p < 0.01$ ). Subsequently, an increasing number of studies have been conducted. To date, the need for standardisation in the definition of UC activity has led to the proposal of unified scores. In 2018, Allocca et al.<sup>53</sup> developed a score and externally validated it in 2020 as Milano Ultrasound Criteria (MUC)<sup>58</sup>: a MUC score  $> 6.2$  was the cut-off best correlated with a Mayo endoscopic score (MES)  $\geq 2$  [sensitivity 0.85, specificity 0.94; AUC 0.902 (95% CI 0.772–0.971)]. In 2021, Bots et al.<sup>59</sup> defined and

internally validated the UC-IUS index as a score showing a strong correlation with endoscopic disease activity (MES  $r = 0.830$ ;  $p < 0.001$ , Ulcerative Colitis Endoscopic Index of Severity UCEIS  $r = 0.759$ ;  $p < 0.001$ ). Therefore, UC activity can be assessed through IUS with a good correlation with endoscopic activity. In this clinical setting, IUS has gained attention: however, the evaluation of UC activity in a point-of-care setting is more closely related to the monitoring phase than the diagnostic.

**Table 6.** Studies assessing UC activity compared to endoscopy

Study	Year	Study Design	Comparison	No of Patients	Results
Bozkurt <sup>56</sup> et al.	1996	Prospective	IC, CRP	88	Three grades based upon BWT $> 4$ mm, BWS and haustration
Pascu <sup>15</sup> et al.	2004	Prospective	IC, CRP	24	Four levels based upon BWT $> 3$ mm, CD and BWS
Antonelli <sup>57</sup> et al.	2011	Retrospective	IC, CRP	51	BWT $> 4$ mm
Allocca <sup>53</sup> et al.	2018	Prospective	IC	53	BWT $> 3$ mm, CD, BWS, lymph nodes mesentery inflammation
Kinoshita <sup>54</sup> et al.	2019	Prospective	IC, barium studies, clinics	173	Four grades based upon BWT and BWS $k = 0.43-0.70$ , $p < 0.01$
Allocca <sup>58(P202)</sup> et al.	2021	Prospective	IC	43	MUC ( MUC = $1.4 \times \text{BWT} + 2.0 \times \text{CD}$ ) $> 6.2$
Bots <sup>59</sup> et al.	2021	Retrospective	IC	345	UC-IUS (0-7) = BWT $> 2$ mm + CD + haustration + fat wrapping $k = 0.61$ ; $p < 0.001$
Rispo <sup>69</sup> et al.*	2023	Prospective	IUS, IC	86	BWT $> 3$ mm, CS and BWS; MUC.

**UC:** ulcerative colitis; **IC:** ileo-colonoscopy; **CRP:** C-reactive protein; **BWT:** bowel wall thickness; **BWS:** bowel wall stratification; **MUC:** Milan Ultrasound Criteria; **UC-IUS:** Ulcerative Colitis Intestinal Ultrasound\***IUS** has been performed with Hand-held device

### Reproducibility and scoring

The reproducibility of the technique remains one of the most crucial key-point for defining the role of IUS in IBD management. In 2008, Fraquelli et al.<sup>60</sup> demonstrated good-to-excellent reproducibility among expert sonographers ( $k$  values for BWT ranged between 0.7 and 1). Subsequently, other studies confirmed those results and added new data: De Voogd et al.<sup>61</sup> found a strong intraclass correlation coefficient (ICC=0.96) for BWT in UC, with substantial results also for CDS ( $k = 0.63$ ). However, the need for standardisation in non-expert centres was noticeable. Thus, a need for standardisation of exam execution has given rise to the development of training courses, like the one from the International Bowel Ultrasound Group (IBUS), to educate physicians in the oriented performance of IUS. Furthermore, the need for a unique way to communicate the findings and correlate them with disease activity made it necessary to develop eco-graphic activity scores. Two scores have been developed for CD: Novak et

al.<sup>62</sup> in 2021 presented a Delphi consensus which defined the International Bowel Ultrasound Segment Activity Score (IBUS-SAS), calculated through BWT, i-fat, CDS and BWS, and showed an ICC of 0.97 (0.95–0.99,  $p < 0.001$ ). Moreover, Allocca et al.<sup>63</sup> elaborated bowel-US-score (BUSS), calculated using the following formula  $\text{BUSS} = 0.75 * \text{BWT} + 1.65 * \text{CDS}$ . BUSS significantly correlated with endoscopic activity ( $r = 0.55$ ;  $p < 0.01$ ), and the cut-off of 3.52 discriminated between endoscopically active and non-active disease. Nonetheless, the same cut-off predicted disease course at 12 months, determining patients group at higher risk of treatment escalation ( $p < 0.001$ ) and need for surgery ( $p < 0.001$ ).

Regarding UC, the MUC score was analysed in the above paragraph. Also of note is the predictive value of this score: in a prospective study on 98 UC patients followed-up for a median time of 1.6 years, MUC score and MES well correlated at baseline ( $r = 0.653$ ;  $p < 0.001$ ) and lower

cumulative probability of treatment escalation, the need of corticosteroids, hospitalisation and colectomy were found among patients who had  $MUC \leq 6.2$  at baseline as compared to patients with  $MUC > 6.2$  ( $p < 0.05$ )<sup>64</sup>.

Hence, IUS scores are a well-established way to express disease activity and severity, nonetheless, to drive therapeutic decisions based on the predictor value of ultrasound findings.

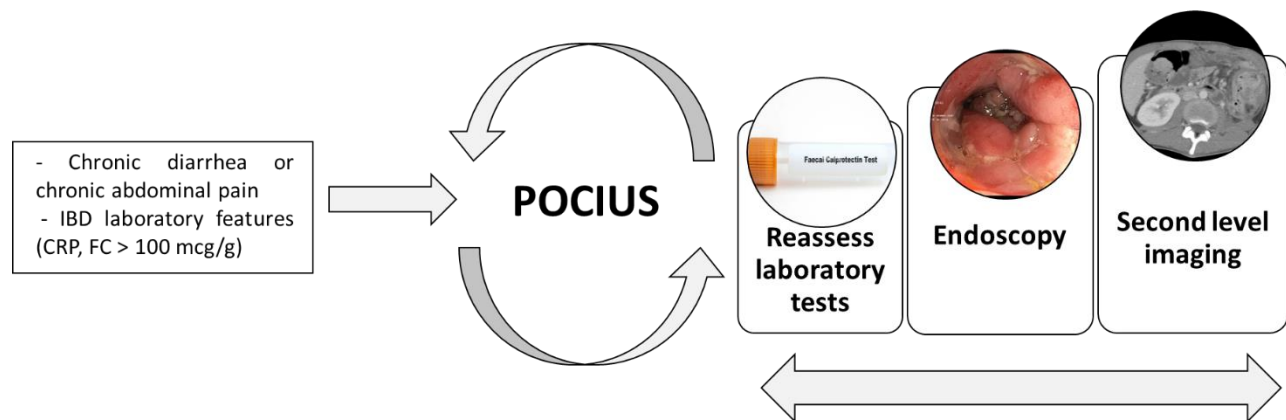
#### Point-of-care Intestinal Ultrasound (POCIUS) with handheld sonographers

As already highlighted, performing IUS in a POC setting represents an impacting way to complete physical examinations during outpatient visits. With the spreading use of handheld pocket probes, POC ultrasound can increase the accuracy of daily clinical activity, as already done in cardiologic and emergency scenarios<sup>65-68</sup>. Thus, a new discipline called "echoscopy" has been named by the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) as a targeted ultrasound examination directed to the specifically interested suspected disease site. In the attempt to apply those concepts to the IBD study, in a pilot

cohort study, our group recently assessed the diagnostic accuracy of handheld IUS (HHIUS) in detecting CD, compared with MRI, finding fair agreement and no significant differences in diagnostic accuracy between the two techniques (89.41% for HHBS vs 92.94% for MRE;  $p = n.s.$ )<sup>20</sup>. Furthermore, a substantial agreement was demonstrated between HHIUS and MRI in the assessment of CD location ( $k = 0.81$ ;  $p < 0.01$ ) and evaluation of stenoses ( $k = 0.75$ ;  $P < 0.01$ ), abscesses ( $k = 0.68$ ;  $P < 0.01$ ) and fistulas ( $k = 0.65$ ;  $P < 0.01$ ). On the other hand, a significant underestimation of HHIUS in CD extension assessment ( $r = 0.67$ ;  $P < .01$ ) has been found. As done for CD, HHIUS was applied also to UC management, comparing it to traditional IUS in the MUC score evaluation for UC. No statistically significant results between the two techniques were found between the assessment of BWT, CDS, BWS and MUC score evaluation<sup>69</sup>.

Hence, handheld POCIUS can be considered a valuable tool in IBD diagnosis, speeding up the definitive diagnosis, driving a therapeutic decision and optimising resources (Figure 4).

**Figure 4.** POCIUS positioning in IBD suspicion.



#### Conclusions

Current literature suggests IUS as an accurate, safe, cost-effective tool for IBD diagnosis, localisation, and behaviour evaluation. During the last decades, its role has evolved from a first-line tool for suspicious IBD and the definition of active vs non-active disease to a finished imaging technique that the physician can count on in IBD management. Indeed, IUS is emerging with a double role: a point-of-care test to speed up clinical and therapeutic decision-making in everyday practice; moreover, an ideal tool for evaluating IBD in the entirety of the bowel wall.

In conclusion, it is reasonable to state that IUS is a compulsory tool in Gastroenterology Units for evaluating patients with suspected IBD in a point-of-care setting, given its high diagnostic accuracy. Its use can ameliorate disease management for standard physical examination integration and in settings where endoscopy or second-level imaging is not firmly necessary.

Certainly, gastroenterologists need to train extensively to acquire the essential IUS expertise and unify how the technique is performed. Furthermore, handheld sonographers can help increase the use of IUS as a point-of-care test.

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