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Original article

# CT in non-traumatic acute abdominal emergencies: Comparison of unenhanced acquisitions and single-energy iodine mapping for the characterization of bowel wall enhancement

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ABSTRACT

*Objectives:* To evaluate the benefit of unenhanced CT and single energy iodine mapping (SIM) to conventional contrast-enhanced CT for bowel wall enhancement characterization in an acute abdomen setting.
*Methods:* CT images from 45 patients with a suspected acute abdomen who underwent abdominopelvic CT from April 2018 to June 2018 were analyzed retrospectively by two independent radiologists. These patients had been referred by emergency department physicians in a context of acute abdominal pain and had a confirmed etiological diagnosis. Three image sets were evaluated separately (portal phase images alone; portal phase images and unenhanced images, portal phase images, and single energy iodine maps). Diagnostic accuracy and confidence were assessed. Quantitative analysis of bowel wall enhancement was also performed.
*Results:* The number of correct diagnoses increased by 8% and 12% with unenhanced images and 6% and 13% with SIM for readers 1 and 2, respectively, compared to the portal phase only. There was an improvement in the confidence of the etiological diagnosis with the number of certain diagnoses increasing from 23% to 100%, which was statistically significant for reader 2 and of borderline significance for reader 1 ($P$ = 0.002 and 0.052, respectively) when unenhanced phase and SIM were added. The inter-rater agreement improved when unenhanced and portal phase images were associated, compared to portal phase images alone (kappa = 0.652 [ICC=0.482−0.822] and 0.42 [ICC=0.241−0.607] respectively).
*Conclusion:* SIM and unenhanced images improve the reproducibility and the diagnostic confidence to diagnose ischemic and inflammatory/infectious bowel wall thickening compared to portal phase images alone
*Summary sentence:* The analysis of unenhanced and SIM images in association with portal phase images improves the reproducibility and the radiologist's confidence in the etiological diagnosis of acute non-traumatic bowel wall thickening in adults.
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## 1. Introduction

Bowel wall thickening in abdominal CT studies is a frequent, non-specific image finding common to various diseases (neoplasia, inflammatory bowel disease, infection, ischemia, etc.) (1). In patients with an acute abdomen, the etiology of bowel wall thickening can be particularly difficult to ascertain with potential implications in patient management [1]. Imaging features such as length of involvement, degree of thickening (e.g., normal values under 2−5 mm depending on the bowel segment and level of distention), symmetry, and attenuation pattern, as well as enteric abnormalities such pneumatosis intestinalis and peri-enteric abnormalities such portal venous gas, can help narrow the diagnostic possibilities [2-4]. In this context, enhancement pattern analysis is also important to further characterize bowel wall pathology [1,5-7].

Despite the undisputed role of CT in the detection and characterization of bowel wall thickening, which can be difficult to identify especially by bowel loop dilatation and the endoluminal gas artifact, there is no consensus on the benefit of unenhanced acquisitions in this context [8,9]. There is evidence suggesting that adding an unenhanced phase to the acquisition protocol improves the diagnosis accuracy significantly [10]. Contrast enhancement is an important feature for the differentiation between inflammatory, ischemic [11], and neoplastic causes as well as for the evaluation of the inflammatory activity [12] and the severity of the bowel ischemia [13]. Moreover, dual-energy CT-based iodine mapping has been advocated for evaluating bowel disease and may obliviate the need for an

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unenhanced acquisition [14]. This technique may allow a better visualization (and even quantification) of subtle differences in bowel wall enhancement in ischemic, inflammatory, and neoplastic pathologic processes [15,16]. However, the availability of dual-energy remains an issue along with the difficulties in protocol selection, data post-processing, and interpretation.

Single energy iodine mapping (SIM) became recently available for clinical application and is based on the non-rigid registration and subtraction of unenhanced and enhanced CT images [17]. SIM is an image post-processing technique that requires only the acquisition of pre- and post-contrast images, allowing quantification of iodine density in Hounsfield units (HU) and the generation of color iodine maps, which can be superimposed on the original images creating a single-photon emission computed tomography (SPECT) effect [18]. This technique can also be potentially combined with deep learning [19] to provide a systematic and semiautomatic approach to bowel wall thickening characterization. We hypothesize that an unenhanced phase and SIM subtraction could improve the evaluation of bowel wall thickening in patients with acute abdominal pain, increasing the radiologist's confidence in the differentiation of inflammatory and ischemic causes of bowel wall thickening.

## 2. Materials and methods

### 2.1. Study population

From April 2018 to June 2018, abdominal CT studies of 372 adults presenting nontraumatic abdominal pain were retrospectively evaluated (Fig. 1). Patients with prior surgery, trauma, and abdominal tumors were not included. Among these studies, 124 had both pre- and post-contrast acquisitions. SIM post-processing, however, was only feasible in 82 studies due to differences in the acquisition coverage between pre- and post-contrast phases. Then, we defined the bowel wall thickening as pathological beyond 3 mm, and 40 CT exams without bowel wall thickening were excluded. Among these patients, 25 had a confirmed final diagnosis (pathologic group): eight surgically confirmed bowel ischemia; six infectious colitis with positive coproculture; eight infectious colitis responding favorably to medical treatment on a seven-day clinical follow-up, and three patients with a prior diagnosis of Crohn's disease presenting an acute flare. Among the bowel ischemias evaluated, seven were transmural (e.g., three incarcerated hernias, three severe chronic atheromatosis, and two acute arterial occlusions). In the same period, a control group with 20 consecutive patients who consulted in the emergency room for acute non-traumatic abdominal pain without bowel wall thickening was formed. In this group, 11 patients had a normal CT evaluation, two had an iliopsoas abscess, three acute pancreatitis, two cholecystitis, one pyelonephritis, and one duodenal ulcer. Thus, the final study population was composed of 45 patients. In our institution, retrospective studies with standard imaging techniques with fully anonymized patient data analysis do not require ethics committee approval (IRB waived).

### 2.2. CT acquisition protocol

All images were acquired with a 320 detector-row CT scanner (Aquilion ONE, Canon Medical Systems, Ottawara, Japan) with the following parameters: 120 kV, mA modulation of with 150 mA minimum, collimation 0.5 second x 80 mm, FOV 35–50 cm, gantry rotation time of 0.5 second and a 512 × 512 matrix. Two acquisition phases were performed, one before contrast injection and one 80 s after contrast injection (portal phase) with 2 ml/kg Iodine (ULTRAVIST 370 mg/ml or XENETIX 350 mg/ml or VISIPAQUE 320 mg/ml or IOMERON 400 mg/ml) up to a maximum of 250 ml at 2.5 ml/s injection rate. All images were reconstructed using an iterative image reconstruction algorithm. Iodine maps were generated automatically at the scanner's workstation (Display console V8.3SP0204F Canon

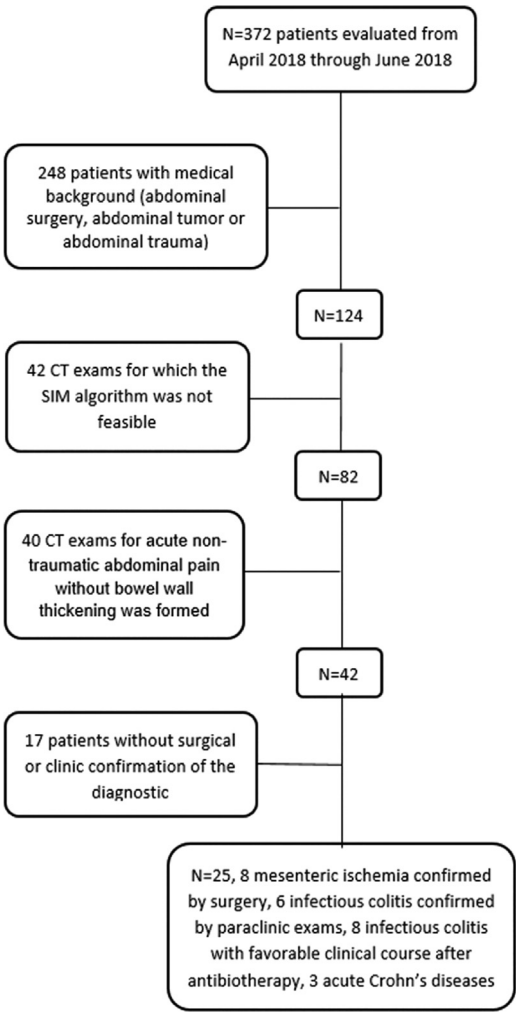


**Fig. 1.** Study flowchart shows patients selection.

Medical, Otawara, Japan) using the SUREsubtraction iodine mapping software, which applies a non-rigid registration algorithm to subtract pre- from post-contrast acquisitions on a pixel-by-pixel basis. The result is an iodine density gray-scale map in Hounsfield units (HU) that can be either used independently for quantitative analysis of the iodine distribution or generate a color-coded map to be overlaid to the unenhanced acquisition (nuclear medicine study effect) for visual analysis (Fig 2).

### 2.3. Quantitative iodine concentration assessment

All measurements were performed by a radiologist with three years of clinical experience with CT imaging on the portal phase, which was characterized by hepatic artery, portal vein, and antegrade hepatic vein enhancement [20].

For each patient in the study group, two free-hand regions-of-interest (ROI) contouring the bowel wall were drawn in the gray-scale iodine map on the portal phase and iodine density gray-scale map, one over the area of bowel wall thickening and a second over a normally appearing bowel segment distant to the pathologic bowel segment (Fig. 3). These ROIs were not necessarily in the same slice. The largest ROI possible was drawn and the ROI area was larger than 35 $mm^2$. Then the ROIs were copy-pasted onto both images for post-processing to assure ROI location was identical between the portal phase and gray-scale iodine mapping.

Slices depicting the bowel wall without partial volume effects and with a clear differentiation between the lumen and adjacent

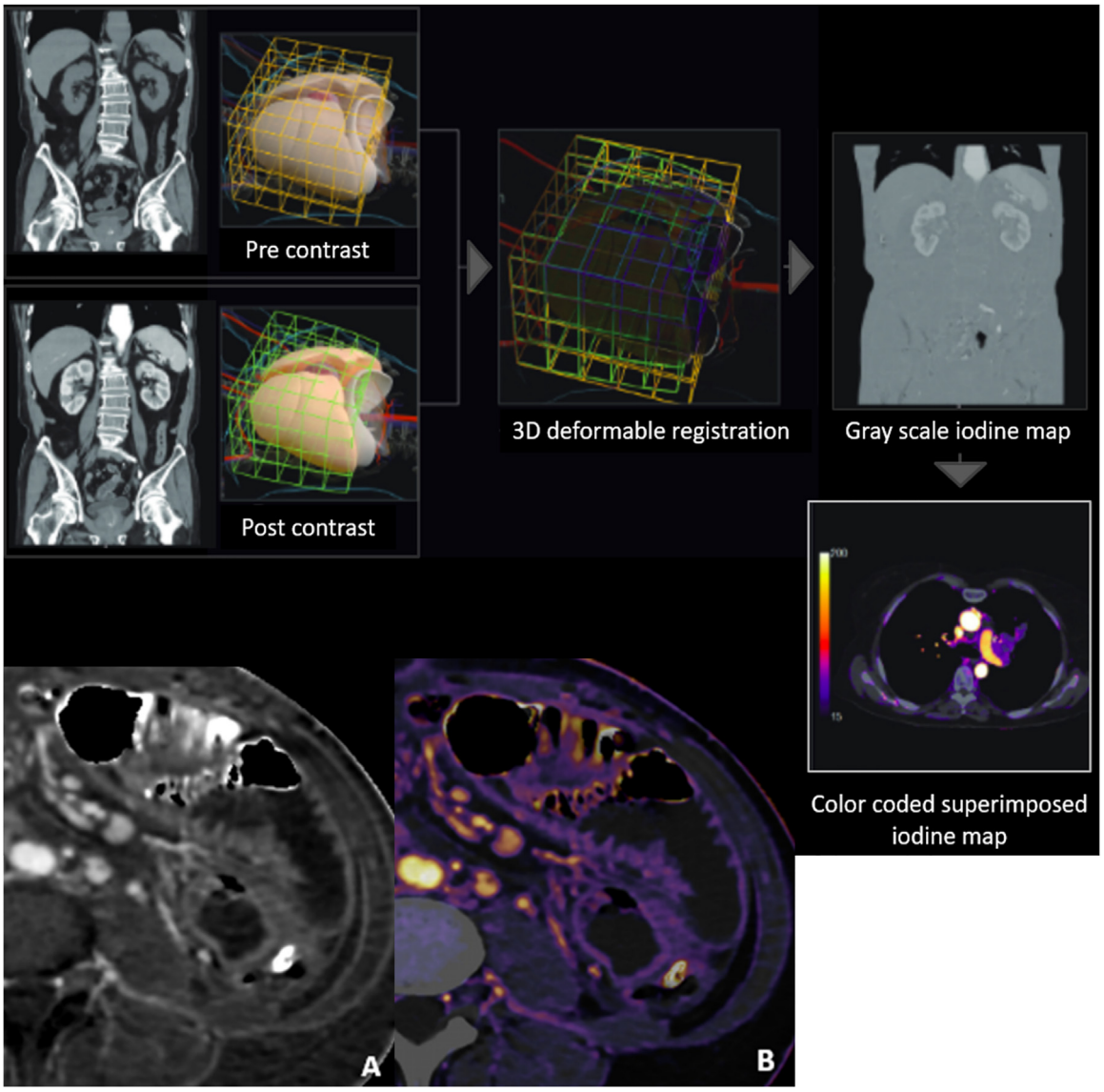


**Fig. 2.** Registration and iodine extraction. Subtraction iodine mapping utilizes pre- and post-contrast scans to isolate iodine signal. The key to obtaining results lies with an anatomically aware 3D derformable registration algorithm that compensates for patient motion which may occur between the two scans. The iodine signal is then color coded and superimposed on the post-contrast CTA images to facilitate the visualization of subtle differences in HU attenuation. For example, an abdominal CT with SIM pos-processing in our department with axial gray scale iodine map (A) and corresponding colored-scale iodine map (B).

structures were chosen for measurements. In the control group, a random segment of normally appearing bowel was analyzed using the same technique.

### *2.4. Visual iodine map assessment*

The radiological evaluation was performed by two different radiologists (to avoid memorization bias) with respectively 8 and 7 years of clinical experience with emergency CT imaging, blinded to the final diagnosis (readers 1 and 2, respectively).

Three readout sessions were performed, each at least two weeks apart:

- Portal phase images only
- Unenhanced and portal phase images
- Portal phase images and iodine color-coded map

For each CT study evaluated, one representative image was selected by the same radiologist who performed the bowel wall measurements to ensure that the same bowel wall segment was evaluated by both readers. The readers could not change the window setting and image zoom during analysis. This image clearly showed the pathologic bowel segment in the study group and normal bowel in the control group without partial volume effects. The order of patients was different in each imaging set with random distribution. Both readers had a few weeks to read and interpret the three sets.

Bowel wall thickening was diagnosed when the bowel wall measured over 3 mm for the small bowel and over 5 mm for the large bowel. Ischemic pathology was defined as bowel wall thickening with a delayed or absent enhancement. Infectious or inflammatory pathology were defined as bowel wall thickening associated with submucosal edema mesenteric fat stranding. The readers could not change the window setting and image zoom during analysis.

In each image selected, the target bowel segment was indicated for the readers to avoid bias by evaluating two different bowel sections. Then readers 1 and 2 classified the target bowel segment in each readout session as follows:

1) Inflammatory or infectious thickening
2) Ischemic thickening

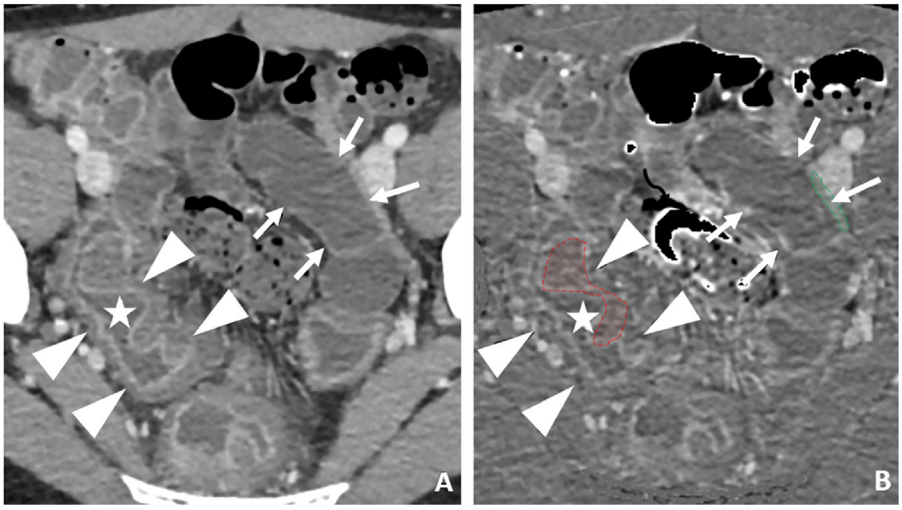


**Fig. 3.** ROI positioning technique in a 52-year-old man with Campylobacter colitis. Axial portal phase abdominal CT image (A) and corresponding gray-scale iodine map (B) depicting segments of bowel wall thickening (arrowheads) and normally appearing bowel wall (thin arrows). The bowel lumen in the pathologic segment is indicated by the star. Areas of misregistration artifact due to bowel movement (squiggly arrow) were avoided. Two free-hand ROI were positioned to delineate a portion of the bowel wall in both the pathologic (red free form ROI) and normally appearing (green free-form ROI) segments. The ROI were copy pasted onto both images for post-processing.

3) Normal bowel segment
4) Thickening of uncertain etiology.

The diagnostic confidence was assessed with the following scale:

1) Certain
2) Probably
3) Uncertain

The acquisition dose length product (DLP) in mGy*cm was evaluated with a 32 cm phantom.

### 2.5. Statistical analysis

Quantitative variables were described by using mean ± standard deviation [range]. Normal and pathologic bowel wall enhancement in HU was compared between the patient groups evaluated with the Wilcoxon or Mann-Whitney tests. The Mc Nemar test was used to evaluate the differences in the number of correct diagnoses in the different readout sessions performed. The threshold for statistical significance was set to $P < 0.05$. The sensitivity and specificity for detecting infectious/inflammatory or ischemic etiology were calculated for each reader and each readout session. "Thickenings of uncertain etiology" were considered as a false negative or false positive result according to the final diagnosis. Weighted kappa values were calculated to assess the inter-rater agreement. Kappa values were interpreted as follows: excellent (0.81–1.00), satisfactory (0.61–0.80), moderate (0.41–0.60), weak (0.21–0.40), or very weak (0.00–0.20). One-sided and two-sided 95% confidence intervals (CI) were calculated using the binomial exact method.

## 3. Results

There were 15 women and 10 men (F/M sex ratio 1.5) in the pathologic group with a mean age of 61 ± 19 [24–91] years, while in the control group, there were seven women and 13 men (F/M sex ratio 0.5) with a mean age of 63 ± 21 [21–100] years.

There were eight patients with mesenteric ischemia in the pathologic group and 17 with infectious or inflammatory bowel diseases. The patients with mesenteric ischemia were older than those with infectious or inflammatory pathology (mean age of 74 ± 17 [50–91] years and 48 ± 18 [24–91] years, respectively). The mean DLP of the portal and unenhanced phase acquisitions were 891 ± 215 [233–1656] mGy*cm and 775 ± 244 [233–1223] mGy*cm, respectively. Thus, adding an unenhanced acquisition to a final DLP of 1666 ± 459 [466–2879], which represents a mean 47% DLP increase.

### 3.1. Quantitative enhancement analysis

Quantitative analysis results are presented in Table 1. There was a statistically significant reduction ($P<0.0001$) in iodine gray-scale map density values between patients with bowel ischemia and controls (16±17 [0–54] versus 46±28 [9–119] HU) (Fig 3.). Interestingly, there was also a statistically significant increase in iodine distribution ($P = 0.04$) in normally appearing bowel segments in patients with mesenteric ischemia compared to controls (70±24 [35–102] versus 46±28 [9–119] HU, respectively). Iodine gray-scale maps did not show any statistically significant difference in iodine distribution between infectious or inflammatory bowel segments compared to controls ($P = 0.7$) (Fig. 4.) (42±16 [21–73] versus 46±28 [9–119] HU, respectively). There was also an increase in the enhancement of the parietal thickening of inflammatory origin in the portal phase and the iodine colored-map between inflammatory and ischemic origins (72±16 UH versus 56±32UH for the comparison in the portal phase) and (41±15UH versus 16±17UH for the colored iodine map). These differences, however, were only statistically significant on the colored iodine map assessment ($P = 0.001$).

The interobserver agreement for bowel wall thickening etiology was lowest when portal phase images were considered alone (Kappa = 0.42 [CI 0.241–0.607]). There was a slight increase in interobserver agreement when SIM was added (Kappa = 0.55 [CI 0.359–0.753]); however, the agreement in both these image sets was considered moderate. The combination of portal phase and unenhanced images yielded the best agreement (kappa = 0.652 [CI 0.482–0.822]), which was considered satisfactory.

### 3.2. Evolution of the number of correct diagnoses

The number of correct diagnoses for the differentiation between normal bowel, ischemic bowel, and infectious/inflammatory bowel obtained in each readout session is shown in Table 2. The number of correct diagnoses increased when an unenhanced acquisition and SIM were added to the evaluation (38 versus 33 and 34 versus 30 for readers 1 and 2, respectively) (Fig 5.). Compared to the analysis of portal phase images only, there was a nonsignificant 8% and 12%

**Table 1**
Quantitative enhancement analysis by bowel segment and by pathology. Comparison of enhancement in Hounsfield units (HU) on portal phase and gray-scale iodine maps.

| | Pathologic segment enhancement (HU) | Healthy segment enhancement (HU) | Variation of enhancement (HU) | P value |
|---|---|---|---|---|
| *Patient group* | | | | |
| Ischemic (Portal) | 56 ± 32 | 115 ± 19 | 59 ± 28 | $P < 0.05$ |
| Ischemic (Iodine map) | 16 ± 17 | 70 ± 26 | 54 ± 37 | $P < 0.05$ |
| Infec./Inflam. (Portal) | 72 ± 16 | 59 ± 16 | 13 ± 11 | $P = 0.0687$ |
| Infec./Inflam. (iodine map) | 41 ± 15 | 37 ± 11 | 4 ± 17 | $P = 0.0198$ |
| Control group | / | 57 ± 17 | / | $P = 0.03$ versus ischemia |
| Portal | / | 47 ± 28 | / | $P = 0.87$ versus inflammatory |
| Iodine map | | | | / |

Data presented in mean ± standard deviation.
Infec./inflam. = infectious or inflammatory bowel disease.

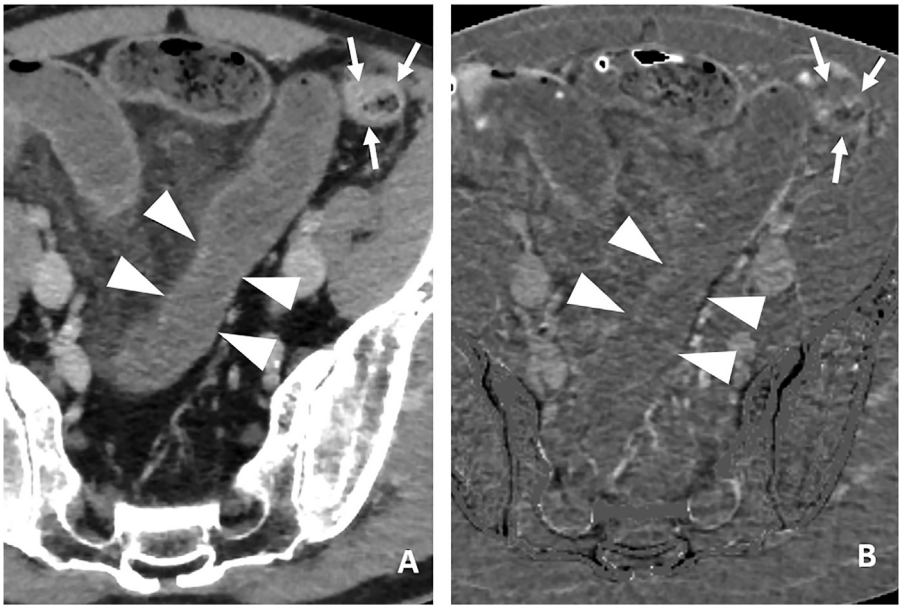


**Fig. 4.** 91-year-old woman with a surgically confirmed mesenteric ischemia. Axial portal phase CT image (A) and axial gray-scale iodine map (B) depicting segments of bowel wall thickening (arrowheads) and normally appearing bowel wall (thin arrows). Note the lower bowel wall enhancement in the pathologic segment measured at 31 HU compared to the normally appearing segment 83 HU.

increase in the number of correct diagnoses when unenhanced images were added for readers 1 and 2, respectively. The increase was 6% and 13% when SIM was added for readers 1 and 2 (Fig 6.). These differences, were not statistically significant ($P > 0.13$).

### 3.3. Radiologist's confidence analysis

The diagnostic confidence improved gradually from the portal phase-only readout to the portal phase - unenhanced readout to the portal phase - SIM readout. The number of patients with a certain diagnosis increased from 10 to 13 to 19 in these three readout sessions for reader 1, representing 23% and 90% increases, respectively, compared to the portal phase-only readout. These figures were 12, 20, and 24 for reader 2, representing 67% and 100% increases, respectively (Table 3). Compared to the analysis of portal phase images only, the number of uncertain diagnoses was lowest when SIM was added for both readers, two versus seven, and four versus 17 respectively for the reader 1 and 2. These differences were only significant for reader 2 ($P = 0.002$). For reader 1, the $P$ values were 0.5 and 0.052 when the portal phase-only readout confidence was compared to that of the unenhanced and SIM readouts. There was a reduction in the number of patients diagnosed with bowel thickenings of uncertain etiology when the portal phase-only readout was compared to the portal phase-unenhanced images readout (13–20% versus 9% for both readers). When SIM was associated with portal phase images, there were no patients with bowel thickening of uncertain etiology for both readers.

### 3.4. CT performance analysis

Concerning mesenteric ischemia's detection, the sensitivity and specificity were high regardless of the set of images studied and of the reader (75% [CI 0.45–1.05] –100% and 89% [CI 0.75–1.02]–100%, respectively). The diagnostic performance was lower for detecting inflammatory or infectious bowel wall thickening (sensitivity and specificity varying from 47% [CI 0.23–0.70] –76% [CI 0.55–0.96] and 83% [CI 0.66–0.99]–96% [CI 0.87–1.04], respectively, for the two readers) (Table 2). The addition of unenhanced images and SIM had a positive impact on CT diagnostic performance for the bowel wall thickening of inflammatory or infectious origin. For reader 1, the sensitivity increased when unenhanced and SIM images were added (76% [CI 0.55–0.96] versus 59% [CI 0.35–0.82] for portal phase only) without significative variation in the specificity. For reader 2, specificity increased when SIM was added (96% [CI 0.87–1.04] versus 85% [CI 0.69–1.00] for portal phase only), and sensitivity increased when unenhanced images were added (59% [0.35–0.82] versus 47% [IC0.23–0.70] for portal phase only).

**Table 2**
Etiologic diagnostic performance of bowel wall thickening in the three readout sessions performed and sensitivity and specificity by reader and by session.

| ISCHEMIC DETECTION | TP | TN | FP | FN | Se | CI | Sp | CI |
|---|---|---|---|---|---|---|---|---|
| *Reader 1* | | | | | | | | |
| Portal phase only | 8 | 33 | 4 | 0 | 100% | [1] | 89% | [0.75–1.00] |
| Portal phase + unenhanced phase | 8 | 35 | 2 | 0 | 100% | [1] | 95% | [0.85–1.00] |
| Portal phase + SIM | 8 | 34 | 3 | 0 | 100% | [1] | 92% | [0.8–1.00] |
| *Reader 2* | | | | | | | | |
| Portal phase only | 6 | 37 | 0 | 2 | 75% | [0.45–1.05] | 100% | [1] |
| Portal phase + unenhanced phase | 8 | 37 | 0 | 0 | 100% | [1] | 100% | [1] |
| Portal phase + SIM | 8 | 33 | 4 | 0 | 100% | [1] | 89% | [0.75–1.00] |
| INFLAMMATION DETECTION | TP | TN | FP | FN | Se | CI | Sp | CI |
| *Reader 1* | | | | | | | | |
| Portal phase only | 10 | 15 | 2 | 7 | 59% | [0.35–0.82] | 88% | [0.73–1.00] |
| Portal phase + unenhanced phase | 13 | 15 | 3 | 4 | 76% | [0.55–0.96] | 83% | [0.66–0.99] |
| Portal phase + SIM | 13 | 18 | 3 | 4 | 76% | [0.55–0.96] | 86% | [0.7–1.00] |
| *Reader 2* | | | | | | | | |
| Portal phase only | 8 | 24 | 4 | 9 | 47% | [0.23–0.70] | 85% | [0.69–1.00] |
| Portal phase + unenhanced phase | 10 | 26 | 2 | 7 | 59% | [0.35–0.82] | 93% | [0.81–1.00] |
| Portal phase + SIM | 8 | 27 | 1 | 9 | 47% | [0.23–0.70] | 96% | [0.87–1.00] |

(TP = true positive; TN = True negative; FP = false positive; FN = false negative; Se= sensitivity; Sp = specificity; CI = confidence interval).

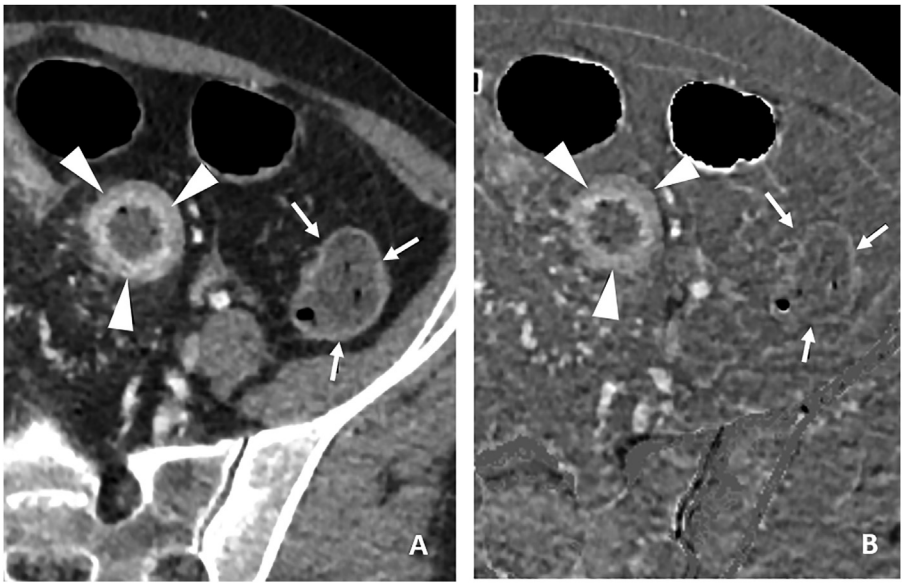


**Fig. 5.** 52-year-old woman with a clinical diagnosis of Crohn's disease presenting an acute flare. Axial portal phase CT image (A) and axial gray-scale iodine map (B) depicting segments of bowel wall thickening (arrowheads) and normally appearing bowel wall (thin arrows). Note the higher bowel wall enhancement in the pathologic segment measured at 98 HU compared to the normally appearing segment 85 HU.

## 4. Discussion

The analysis of unenhanced phase images led to an improvement in inter-reader reproducibility for the etiological diagnosis of bowel wall thickening compared to evaluating portal phase images alone (Kappa = 0.652 versus 0.42, respectively). Moreover, there was an improvement in the etiological diagnosis's confidence with the number of certain diagnoses increasing from 23% to 100%, which was statistically significant for reader 2 and of borderline significance for reader 1. The association of unenhanced and SIM also led to an 8 −13% increase in the number of correct etiological diagnoses with a slight improvement in the diagnostic performance for both readers. No patients were diagnosed with bowel wall thickening of uncertain etiology when SIM was associated for both readers. These results are explained by the fact that an unenhanced phase and SIM provide a referential to the reader to evaluate the enhancement of the bowel wall, improving confidence and reproducibility. In addition, SIM color maps are reconstructed automaticaly and almost instantaneously after image acquisition. The presented results suggest a benefit in considering unenhanced images and SIM combined with portal phase images for the characterization of bowel wall thickening in patients with acute abdominal pain.

CT image post-processing based on registration and subtraction (similar to SIM) is currently used for multiple purposes in various organs and systems as an alternative to dual-energy with improved scanner's diagnostic performance reported in the literature [21–24]. For bowel wall thickening characterization, quantitative analysis of bowel wall enhancement showed statistically significant differences between pathologic and normally appearing bowel segments (e.g., no thickening) of patients with bowel ischemia, which could be related to reactive bowel hyperperfusion. Quantitative analysis was not useful to differentiate infectious or inflammatory bowel wall thickening. SIM post-processing, however, provides similar data than dual-energy CT, which allows quantification of bowel wall

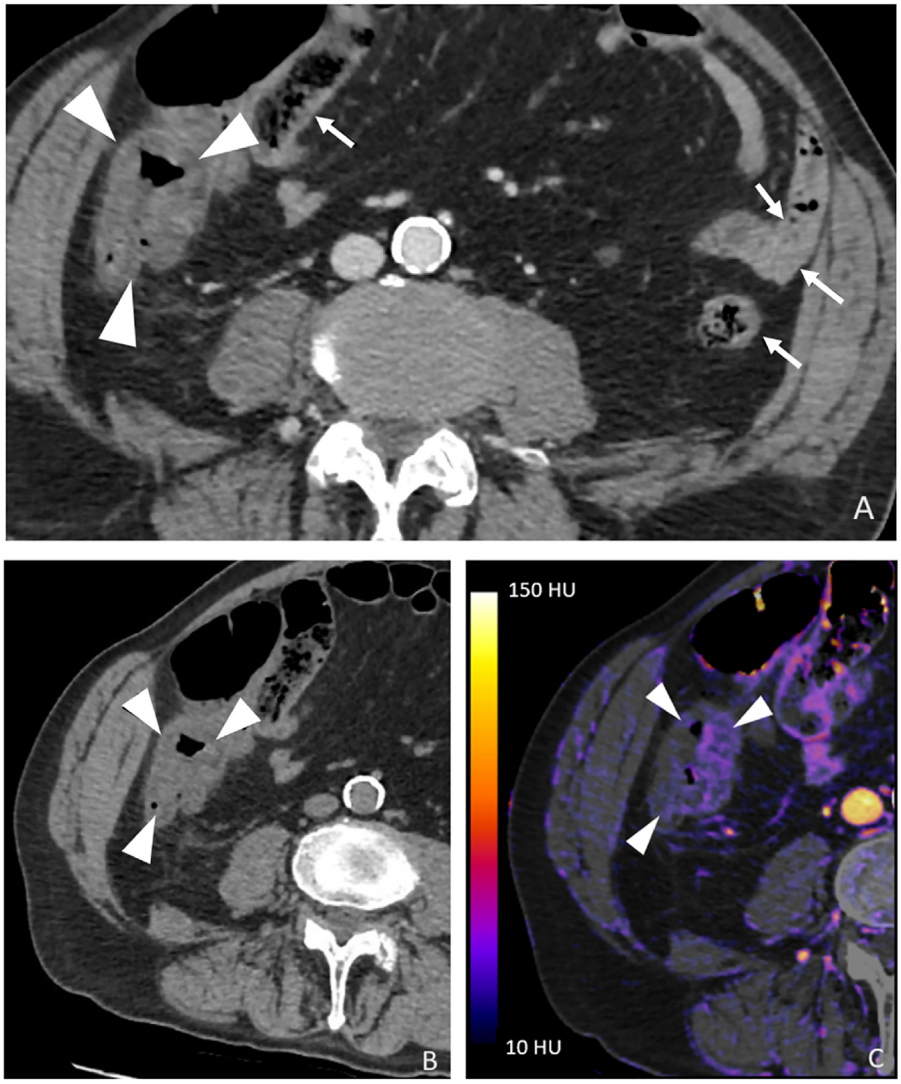


**Fig. 6.** 63-year-old male included diagnosed with uncomplicated cholecystitis and no pathologic bowel wall thickening. A) Axial CT image in the portal phase showing mild bowel wall thickening at the caecum (arrowheads), which appears to show an increased enhancement compared to adjacent bowel loops (thin arrows). This led both readers to diagnose an inflammatory thickening in the portal-phase only readout. B) Corresponding unenhanced phase image, showing a mild spontaneous hyperdensity of the caecum (arrowheads). Despite this fact, when images A and B are compared, it seems there an increased enhancement in the caecum. Both readers maintained the diagnosis of inflammatory thickening in this readout. C) Corresponding single-energy iodine map (SIM) showing iodine density in both the caecum (arrowheads) and adjacent bowel loops (thin arrows). Note that iodine density is similar in all depicted bowel loops. In the readout including SIM, both readers diagnosed this patient as normal.

**Table 3**
Quantitative analysis of radiologist's confidence for each reader regarding the three sets of images (portal phase only, portal phase + unenhanced and portale phase + SIM). Comparison of the number of certain diagnostics according to the phases studied.

| Diagnostic confidence | Certain | Probably | Uncertain |
|---|---|---|---|
| Reader 1 | | | |
| Portal phase | 10 | 28 | 7 |
| Portal phase + unenhanced | 13 | 23 | 9 |
| Portal phase + colored iodine map | 19 | 24 | 2 |
| Reader 2 | | | |
| Portal phase | 12 | 16 | 17 |
| Portal phase + unenhanced | 20 | 19 | 6 |
| Portal phase + colored iodine map | 24 | 17 | 4 |

enhancement and a more conspicuous detection of bowel enhancement differences favoring the application of artificial intelligence-based diagnostic assist methods [14,15]. SIM post-processing technique could also be applied to virtual pre-contrast images reconstructed using monochromatic imaging techniques, which can be obtained without an increase in the delivered dose to the patient [21]· [25]. SIM data could also be applied to composite scoring systems for bowel ischemia in association with clinical data, blood lactate levels and other signs of bowel hypoperfusion.

Peristalsis, patient respiration and motion between pre- and post-contrast acquisitions could hamper the diagnostic performance of SIM. As image registering was performed with a non-rigid algorithm, motion influence does not appear as visual artifacts, since this algorithm ensures that all the pixels in pre- and post-contrast images are matched prior to subtraction. Rather motion reduces the measured amplitude of density variation between pre- and post-contrast acquisitions as part of the enhancement is "interpreded" as motion by the algorithm, reducing the sensitiviy of SIM [22]. Beam hardening artifacts may also have an impact on the quality of SIM images. The improvement of registering and image reconstruction algorithms [26] with deep-learnig based approaches are currently being tested in clinical practice and may help overcome some of these issues [27].

Various limitations of this study should be acknowledged. The study population was small as this was a pilot study, and only patients with a confirmed etiologic diagnosis of bowel wall

thickening were included. Only surgically confirmed mesenteric ischemia patients were included, which constitutes a selection bias as most cases were of severe transmural necrosis and may impact diagnostic performance. The readers evaluated a single representative image and could not change the window setting and image zoom during analysis, which might also influence diagnostic performance. However, the impact of these biases was limited given the study design that compared the performance of three image sets in the same population. The study design also allowed for the prevention of memory bias, with a random distribution of patients in each set and a time gap for the reading [28]. Measurements were performed by a single reader and further studies in large populations are necessary to assess the reproducibility of quantitative analysis with SIM. Four different types of iodinated contrast agents (e.g., depending on local availability) with slight variations in the iodine concentration (320–400 mg/ml) were used, which might have impacted quantitative enhancement analysis. There was no direct comparison between SIM data and dual-energy data in this study. The reproducibility of ROI placement was not evaluated in this study.

## 5. Conclusion

The analysis of unenhanced and SIM images in association with portal phase images seemed to procure a beneficial effect on the reproducibility and confidence of the etiological diagnosis of adults with acute non-traumatic bowel wall thickening compared to the analysis of portal phase images alone. The best diagnostic performance was reached when SIM was associated with portal phase which supports further evaluation of this technique in larger studies.

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## Declaration of Competing Interest

None.

## CRediT authorship contribution statement

**Sophie Boyer:** Data curation, Formal analysis, Investigation, Writing – review & editing. **Charles Lombard:** Formal analysis. **Ayla Urbaneja:** Formal analysis. **Céline Vogrig:** Formal analysis. **Alain Blum:** Methodology. **Pedro Augusto Gondim Teixeira:** Conceptualization, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing.

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