Compendium of **Gastrointestinal Ultrasonography in Inflammatory Bowel Diseases**

TRUST

TRansabdominal Ultrasonography
of the bowel in Subjects with IBD
To monitor disease activity

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This compendium belongs to the TRUST initiative. The purpose of the TRUST studies was to analyze and define GIUS parameters as surrogate markers for disease activity, which allow individual monitoring of disease course and treatment response in IBD

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Compendium of **Gastrointestinal Ultrasonography**

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Preface

Dear Colleagues,

In recent years, ultrasonography has become an important diagnostic tool in monitoring patients with Crohn's disease. A variety of trials have shown that gastrointestinal ultrasonography (GIUS) of the large and small bowel in patients with Crohn's disease and ulcerative colitis has at least the same diagnostic significance as other imaging tools such as MRI. In addition, several trials have recently been published on the role of intestinal ultrasound to monitor ulcerative colitis. The advantage of ultrasonography over other imaging modalities is that it is readily available and inexpensive, and results are highly reproducible.

The treatment targets in inflammatory bowel diseases (IBD) are evolving and experts emphasize the need for objective monitoring of disease activity like the Stride recommendations (Peyrin-Biroulet L et al. 2015). In this context, GIUS was described in a recent publication as an "underused resource with potential paradigm-changing application" (Bryant RV et al. 2018). Since GIUS allows the accurate localization and characterization of inflammatory infiltration of the bowel wall layers and of peri-gut abnormalities, its use should not be limited to diagnostic purposes, but may be of great value in disease monitoring and therapy management in the "treat-to-target" era. Furthermore, GIUS is well recognized by international guidelines (Maaser C et al. 2018), although there is a lack of standardization and a general agreement with regard to the definition of the GIUS parameters so far. However, up to now there are only few European countries where ultrasound is performed by gastroenterologists themselves.

The present booklet is summarizing the important educational steps of the workshop on GIUS that is intended to introduce IBD specialists into this fascinating technique. The most important steps in learning GIUS are outlined and important characteristic sonographic features of the small and large bowel of Crohn's disease patients are demonstrated. The book contains a variety of ultrasound pictures as well as illustrated images with detailed comments to provide a quick overview of ultrasound features in IBD. In addition to the practical experience during the hands-on workshops on ultrasound in IBD patients, the book will enable the reader to transfer parameters of ultrasound into clinical practice and to localize and characterize IBD pathology in patients. For those readers interested in an even more intense training as well as interaction with GIUS experienced IBD gastroenterologists, we recommend visiting the website of the International Bowel Ultrasound Group (https:// www.ibus-group.org).

We would like to thank the authors for their excellent contribution. **We are convinced that this book will help beginners in bowel sonography to understand ultrasound anatomy and to characterize pathological features in IBD patients. It is desirable that this booklet will help to implement bowel ultrasonography as a standard procedure for IBD patients in clinical practice.**

We hope you will have the same fun in reading the chapters and in learning bowel ultrasonography as we had.

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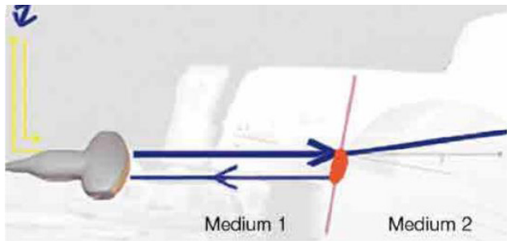
1. Technical principles of ultrasonography

1.1 Image generation

The visualization of structures using ultrasound technology is based on the measurement of the run time and intensity of reflected acoustic waves. The applied waves have a frequency of 2–10 MHz, thereby exceeding the audio spectrum of humans.

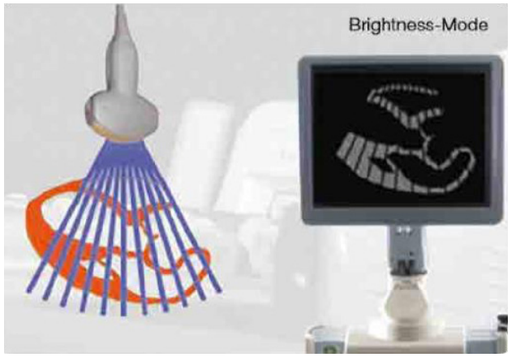
To generate visual information from acoustic waves, an ultrasound image is produced in the following way:

A piezoelectric crystal, such as quartz, which nowadays often comprises plastic with crystalline components, oscillates, when an alternating current is applied. The resulting acoustic beam is partly reflected by the penetrated tissue and deflected back to the crystal, producing an electric signal on impingement (in contrast to its emission).



The acoustic beam is thereby reflected, especially by the interfaces of media of varying acoustic densities – the greater the difference in density, the stronger the reflection.

In the case of the widely used echo-impulse method, a roughly 1-ps-short electrical impulse is applied to the crystal, generating a short ultrasonic signal. The crystal is then switched to receive mode. The run time of the acoustic beam, from its emission to its return, permits a measurement of the depth of the structure reflecting the signal based on acoustic velocity; the intensity of the incoming acoustic beam is also measured. This intensity is influenced by the strength of the reflection (e.g. gallstone = strong, portal vein = weak) or by the attenuation of the acoustic beam in the tissue.



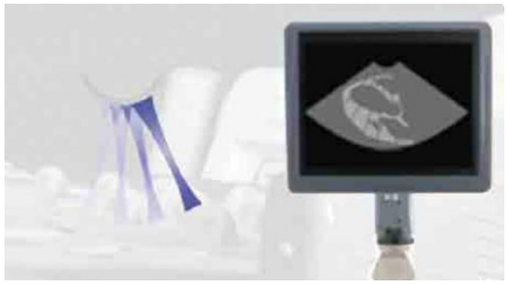
The signal generated using this technology can be visualized as a pixel in the standard B-mode method of abdominal ultrasound procedures. Its position reflects the location of the object, and the intensity of the measured acoustic beam is visualized by means of brightness. By arranging and interconnecting several crystals next to one another, not only one single pixel, but several pixels can ultimately be generated in order to produce a two-dimensional image. In such a way, today's complex electronic image processing methods (Beam Forming, Tissue Harmonic Imaging (THI), Compounding) represent a decisive improvement in image quality and resolution.

Both the penetration depth and resolution capability of the ultrasound depend very much on frequency and wavelength. High-frequency (and thus shorter wavelength) ultrasounds have a high resolution capability, though the acoustic beams are attenuated to a greater extent in the tissue, thereby limiting the depth of penetration. Low-frequency ultrasound, on the other hand, can penetrate further into the tissue but – on account of its longer wavelength – the localized resolution potential is lower.

Technical designs today comprise low-frequency mostly curved transducers and high-frequency mostly linear transducers.

High-frequency ultrasound scanners are mostly constructed as parallel scanners or linear array devices in which the crystal elements are arranged next to one another in a straight line. The result is a rectangular sectional image in which the resolution is roughly the same across the entire depth of penetration. The frequencies usually range from 5 to 13 MHz.

In contrast, the crystals of curved array transducers are arranged next to one another in a curved pattern. As a result, they produce fan-shaped images covering an angle of 60-90°. The fan effect of the ultrasonic beams causes the resolution potential to be reduced on a deeper pane, allowing for a larger acoustic field. The frequencies usually range from 3 to 7 MHz.

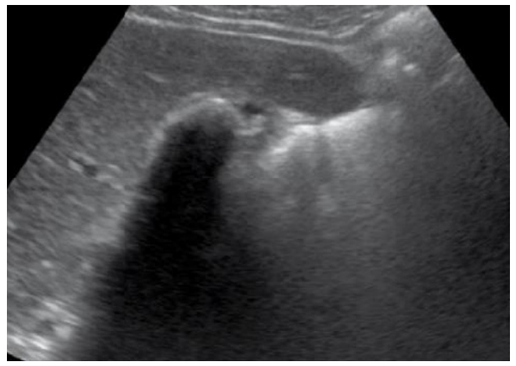


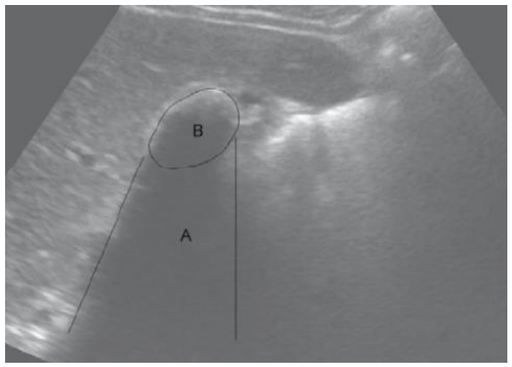
1.2 Common artefacts

The penetration potential of the ultrasonic signal varies considerably depending on tissue properties. Bone, for example, is an almost impenetrable tissue with a high degree of reflection and absorption. On account of the large impedance jump, air equally reflects almost 100% of the ultrasound signal, whereas fluids (e.g. in the gall or urinary bladder, or blood vessels) conduct the ultrasound signal without any major losses.

Bones, air or solid concrements, such as in the gall bladder, therefore often attenuate the ultrasound signal, resulting in "dorsal acoustic shadows". This basically artificial phenomenon can be used to distinguish between concrements and soft-tissue density lesions (e.g. gallstones versus gall bladder polyps).

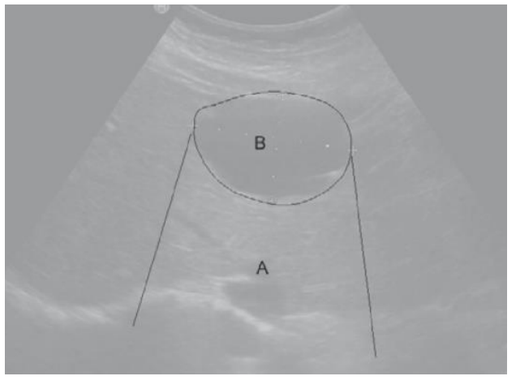
Attenuation of the signal can be compensated in the ultrasound device by amplifying the intensity of signals with a long run time, i.e. from a greater depth, provided that the attenuation is uniform. As a rule, the operator can control such amplification manually and modify the conditions accordingly.





Dorsal acoustic attenuation (A) in cholecystolithiasis with large concrement (B)

Localized decreases in density (e.g. fluid-filled gall bladder, larger blood vessels, cysts or abscesses) thereby result in an amplified ultrasound signal, since the calculated, "anticipated" attenuation from the remaining penetrated tissue fails to materialize. This is referred to as "dorsal acoustic enhancement".

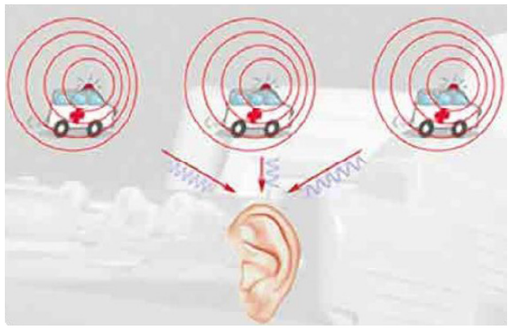


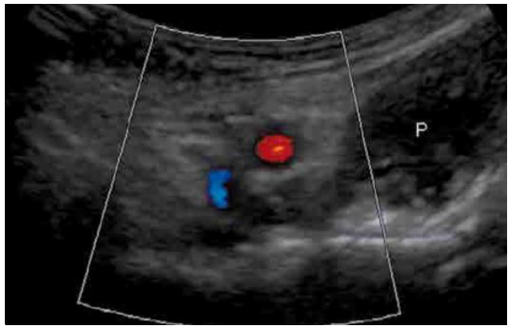
Dorsal acoustic enhancement (A) in hepatic cyst (B)

1.3 Doppler ultrasonography

According to the doppler effect reported in the 19th century by JC. Doppler, a change in distance from an acoustic source produces a change in frequency to the observer. The frequency increases as the distance lessens, whereas it decreases as the distance becomes greater. As the reflecting tissue on ultrasound acts as an acoustic source, this effect can be utilized for diagnostic purposes.

Consequently, Doppler ultrasonography allows the flow of the blood in the vessels to be quantified; the most commonly used color-coded Doppler ultrasound method presents the flow signals on a standard B-mode image in red (flowing towards the ultrasound scanner) or blue (flowing away from the ultrasound scanner). The intensity of the Doppler signal depends on the angle of flow in relation to the ultrasound scanner: it will be minimal at a right angle, and maximal in the direction of the ultrasound. The method is used to quantify the flow of blood (e.g. in portal vein or deep vein thrombosis), but also to differentiate between cystic (unperfused) lesions and truncated blood vessels with a cyst-like appearance on the 2D image. The Doppler technique is also used for ultrasound examination of the bowel, as a measure of metabolic activity, and is utilized, among others, by the Limberg score (see below).





Doppler signal in external iliac artery (red) and vein (blue)
P: psoas muscle

1.4 Contrast-enhanced ultrasonography

Contrast-enhanced ultrasonography (CEUS) was established several years ago as a method for assessing vascularization of solid organs, unexplained masses, and for examining the intestine. The low-energy ultrasonic waves produced by harmonic CEUS cause the oscillation of microbubbles, the electronically processed frequency of which can be used to generate images. The microbubbles are retained in the blood vessels; in other words, vascularization is depicted with the contrast agent.

The intensity of the contrast enhancement, as well as absorption and clearance behavior, are important parameters in CEUS.

1.5 Elastography

Elasticity of tissues can be measured and visualised with modern ultrasound devices. The tissue deformations that result from the acoustic energy lead to shear waves, expanding sideways. Their speed can be measured and visualised in a color-coded manner similar to color Doppler ultrasonography or quantified without image generation, depending on the exact type of elastographic data generation.

1.6 Adverse effects

Many years of experience in the diagnostic application of ultrasound methods have not produced any evidence of direct cell damage or an indirect risk to the patient as a result of tissue hyperthermia. Furthermore, no adverse effects have been reported as a result of repeated or prolonged examinations. Regarding safety of bowel ultrasonography in pregnant patients, no increased risk has been documented for the unborn child.

2. General information on abdominal ultrasonography

Ultrasound examination of the solid abdominal organs does not entail adverse effects and has, for many years, been an established method of diagnosis. The earlier generations of ultrasound, which were of a lower resolution, were also a safe and reliable means of differentiating between solid and cystic lesions. Tumors of the liver, kidneys and pancreas, cysts in the liver and kidneys, as well as gallstones and renal calculi, are the typical findings that can be identified with reliable diagnostic accuracy by transabdominal ultrasound. Pleural effusions or free intra-abdominal fluid are easy to define, and obstructions in the biliary or urinary tracts are readily identifiable.

Today, ultrasonography is a readily and rapidly available method – emergency diagnostics would now be unthinkable without it, and it is of invaluable assistance to clinicians in the documentation of clinical findings.

Further possibilities emerged over time with Doppler ultrasonography – in particular, the color-coded Doppler ultrasonography (CCU), which is easy to perform in everyday clinical practice and can take the form of either a Pulsed-Wave Doppler (PWD) or Continuous-Wave Doppler (CWD). Today, perfusion of the liver, spleen and kidneys can be visualized and quantified, as can the large and also smaller intestinal blood vessels. Furthermore, CCU also permits rapid and reliable differentiation of truncated blood vessels from unperfused, hypoechoic structures in a two-dimensional image.

Because the spatial resolution of Doppler ultrasonography is limited, however, contrast-enhanced ultrasonography (CEUS) has become an increasingly important method for in-depth assessment of organ perfusion and delimitation of unclear lesions based on perfusion properties. It permits precise imaging of perfusion disorders such as ischemia of the kidneys and spleen, but also differentiation between benign and malignant intrahepatic lesions, for example. Furthermore, increased perfusion as a result of inflammation can be identified by CEUS.

Using the ultrasound scanners available today, it is easy to obtain images of the motility, caliber and wall structures of the large and small bowel, with delimitation of the mucosal, submucosal and muscular layers.

3. General information on gastro-intestinal ultrasonography (GIUS)

For a long time, the outcome of treatment for chronic inflammatory bowel disease (IBD) was measured primarily on the basis of the patient's clinical symptoms. In recent years, mucosal healing has increasingly become the objective. As this generally involves the stressful procedure of colonic irrigation and endoscopy, particularly for patients with Crohn's disease, there is a need for straightforward diagnostic alternatives that are free of adverse effects.

Sectional imaging with computer tomography (CT) is readily available but limited due to its high level of radiation exposure. Magnetic resonance imaging (MRI), when performed by an experienced radiologist, delivers reliable data; on account of the often long waiting times for an appointment and considerable cost, however, this procedure is not practical for the purposes of routine diagnostics and especially not for regular follow-up. Moreover, the patient must return for the examination and for discussion of the results.

Gastrointestinal ultrasonography (GIUS) is a simple and quick diagnostic method that is now widely used in the German and Italian speaking regions and is now becoming a standard diagnostic tool in various IBD centers throughout the world, e.g. Australia, Canada and Israel.

In the ECCO guideline on diagnostics of IBD, intestinal ultrasonography has received a clear role at initial diagnosis, to monitor treatment response, as alternative to detect postoperative recurrence as well as to detect complications (Maaser C et al. 2018).

GIUS is useful when making the initial diagnostic decision as well as later for monitoring of IBD treatment. Apart from the fact that it is readily available, the minimal stress and, in particular, the lack of radiation to which the patient is exposed during the scan are positive factors of the use of bowel ultrasound. Today's technological standards permit high-resolution imaging of the bowel's mural stratification with assessment of the mucosal, submucosal and muscular layers, along with reliable delimitation of the inflammatory processes. Furthermore, submucosal pathologies, especially in a transmural disease such as Crohn's, can be visualized more clearly using ultrasound than with endoscopic imaging. In fact, such pathologies are very difficult to identify by endoscopy. In addition, complications of IBD such as stenoses, abscesses or fistulas, are often easily accessible with ultrasound assessments and monitoring.

Point-of-care GIUS performed by gastroenterologists:
- improves clinicians assessment of disease activity;
- alters management strategies for IBD patients;
- improves patients understanding of disease, motivation and compliance;
- is patients' preferred investigative modality;
- provides a valuable, relatively inexpensive and non-invasive tool that contributes to improved outcomes for IBD patients" (Friedman AB et al. 2018).

Gastrointestinal ultrasonography is useful

- for initial diagnosis
- for monitoring the therapeutic response
- if relapse is suspected
- to detect complications (fistula, abscess, etc.)
- for cancer surveillance under immunosuppression (including assessment of the liver, spleen, lymph node status)
- if an extraintestinal manifestation is suspected (nephro-/cholangiolithiasis, primary sclerotic cholangitis)
- to detect postoperative recurrence

Reasons for gastrointestinal ultrasonography

- easy and quick to perform
- can be conducted by the attending specialist during an outpatient appointment
- no preparation required on the part of the patient
- infinitely repeatable
- minimal cost
- assessment of the entire intestinal wall and extra-luminal processes possible
- as a real-time procedure, assessment of peristalsis and differentiation of stenoses from functional status possible
- interventions such as abscess drainage can be performed under ultrasound guidance
- no exposure to radiation

Arguments from critical colleagues:

Time-consuming

Our response: While a full ultrasound at a patient's initial appointment may certainly take some time, a follow-up scan to check for symptoms or prior findings will take just a few minutes.

Difficult to learn

Our response: As with many other methods, a certain degree of training is required in order to learn how to perform bowel ultrasonography; this also applies to a lot of other examinations, such as colonoscopy or MRI.

Quality and outcome dependent on examiner

Our response: As many of the aspects of bowel ultrasonography entail a subjective assessment of the imaging information, an ultrasound does of course depend on the examiner; this applies in the exact same way to numerous other methods (e.g. MRI enteroclysis, endoscopy).

Topographically precise reproduction of the images is difficult

Our response: As imaging standards are lacking at present, topographically precise reproduction of the ultrasound images is difficult; this is all the more reason to encourage performance of the procedure by the attending specialist.

4. Technical requirements, preparation & conduction of the scan

In principle, any device capable of performing Doppler sonography can be used for bowel ultrasonography. A high-frequency (usually linear) and low-frequency sector array transducer should be available.

The scan does not have to be performed on an empty stomach, though food intake can considerably influence the perfusion of the bowel wall. If this is an essential parameter for assessing the course, attention should be paid to ensure similar conditions at each examination.

The patient is positioned supine. So as to gain a better initial impression and not overlook any deeper-lying structures and abscesses, an orienting ultrasound should first be performed using the low frequency probe.

Intestinal air is often thought to be a disruptive factor but can actually be very helpful to identify bowel segments. For better bowel distension, oral contrast (250-400 cc of bowel prep solution) can be applied (SICUS). This can especially be helpful to increase the sensitivity to detect small bowel strictures other than of the terminal ileum and to detect postoperative short fibrotic anastomotic strictures. However, this procedure usually requires an additional 20-30 min and a number of patients dislike the bowel prep solution.

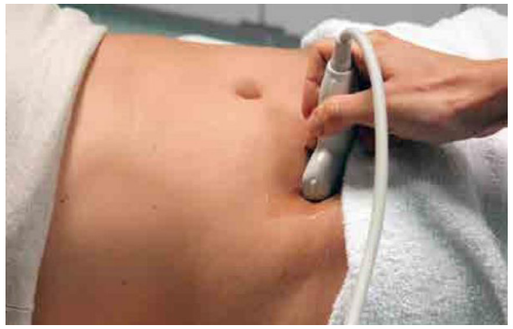
Following the scan with a low-frequency probe identifying larger pathologies such as abscesses, one should change to the high frequency probe for detailed examination of the bowel. At the beginning of every bowel ultrasound, it is very important to optimize the settings. The easiest way to do this is to start either in the very left or right quadrant of the abdomen identifying the psoas muscle, iliac vessels and the pelvic bone, followed by optimizing the penetration depth, gain and focus. The bowel should not be evaluated unless these settings have been optimized as otherwise there is the danger of missing important pathologies.

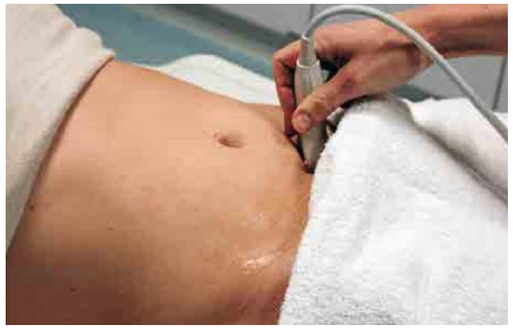
In very obese patients, however, the reduced penetration depth of the high-frequency transducers means that, to some extent, the imaging will be unsatisfactory or the investigation can only be performed with the low frequency probe.

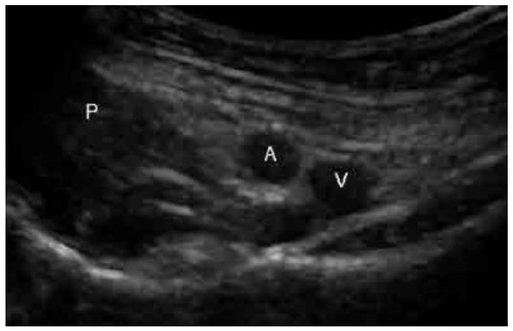
This compendium focusses on bowel ultrasonography. However, a routine abdominal ultrasonography including liver, biliary tracts, kidneys, spleen and lymph nodes is helpful to identify complications of IBD as well as signs of malignancy during disease course under possible immunosuppressive medication.

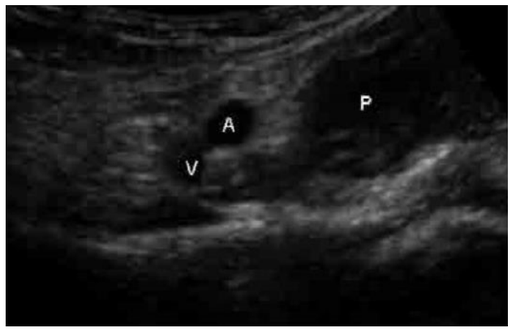
Examination procedure:

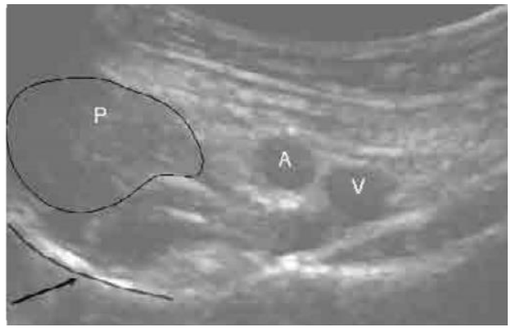
1. Location of landmarks in the left and right lower abdomen: iliac wing, psoas muscle, iliac artery and vein. Important: use these landmarks to optimize the penetration depth, focus and gain.

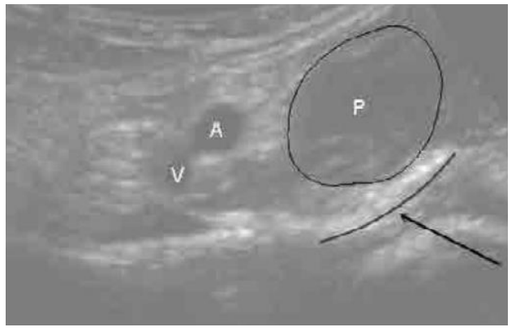








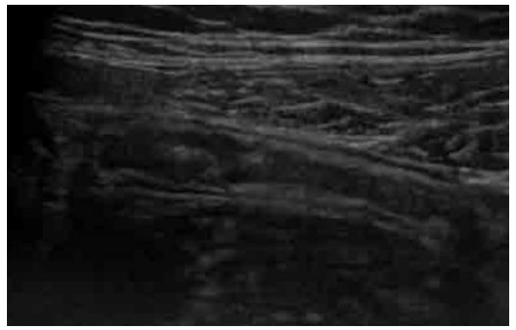


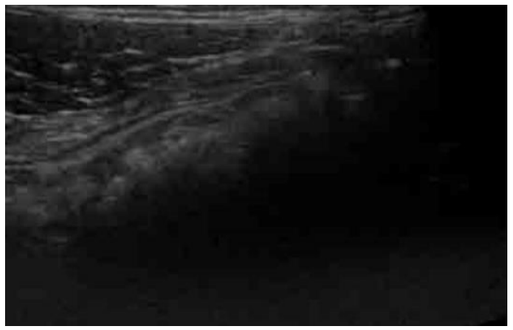


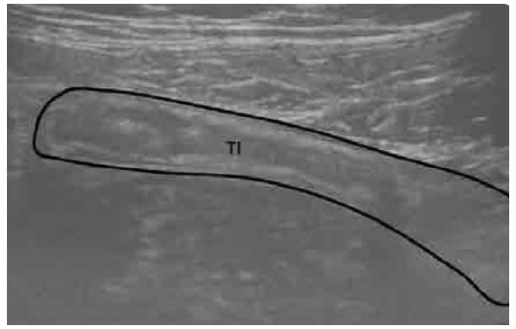
Landmarks in the right and left lower abdomen: A: Iliac artery, V: Iliac vein, P: Psoas muscle, arrow: Iliac wing

2. Slowly tilt the transducer cranially; the terminal ileum will appear on the right and sigmoid on the left (repeat optimization of image settings).

3. On either a transverse or longitudinal plane, move along the descending colon or terminal ileum and ascending colon, respectively. In the flexure region, visualization is often more difficult and usually only possible from the direction of the flank. In addition the descending colon can sometimes be more easily identified and examined from the flank than from ventrally.







Terminal ileum (TI) and sigmoid (S), I: Intraenteric air

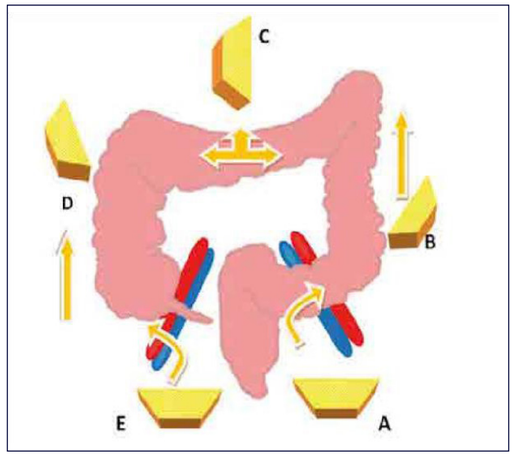
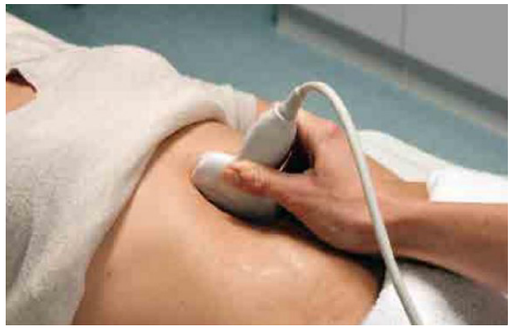
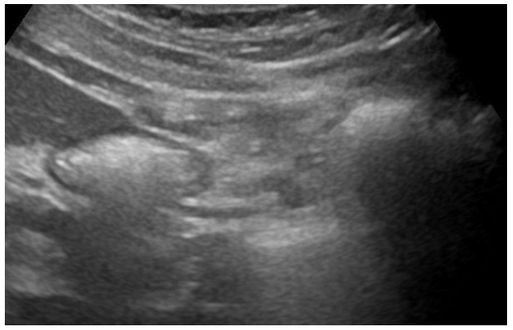


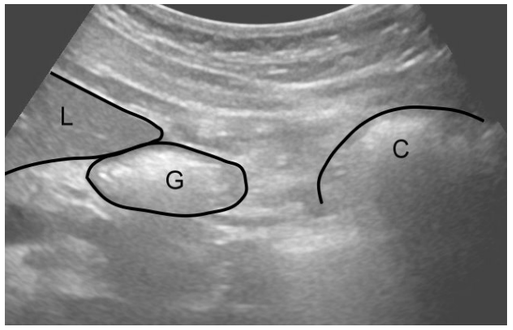
Diagram of examination procedure for ultrasonography of the large bowel

4. In the longitudinal upper abdominal plane, locate the gastric cockade at the lower margin of the liver. From here, slowly proceed caudally until the transverse colon comes into view. Looking for the artifacts due to intraluminal air often helps to identify the transverse colon. The position may be extremely caudal in some patients.



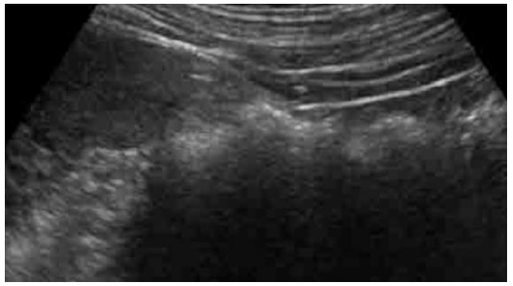


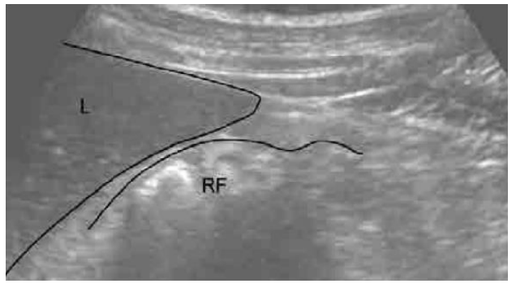
5. Move on laterally to the left and right and follow If the transverse colon. If the transverse colon disappears from view, start again from the gastric cockade.

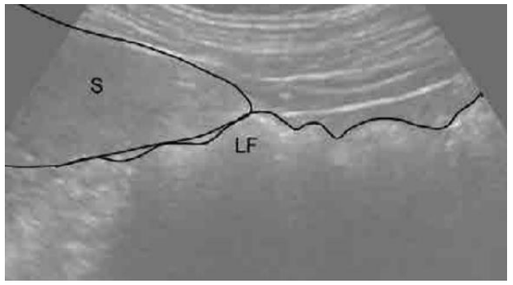


Landmarks in the epigastrium: Liver (L), gastric cockade (G), transverse colon (C)

6. The right and left flexures are often easy to visualize from the flank; the liver will be on the right and lower extremity of the spleen on the left as a contact point of the respective flexure.

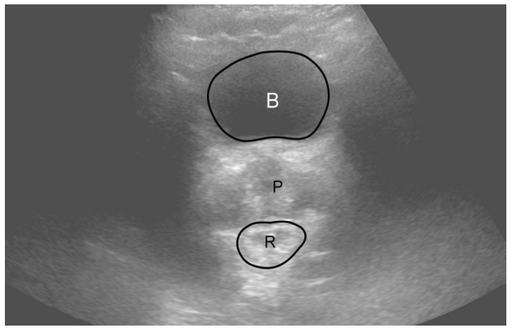






Liver (L) and right flexure (RF) seen from the right flank as well as spleen (S) and left flexure (LF) seen from the left flank

7. If the urinary bladder is not empty, the rectum may be visible through the bladder



The rectum may be visible through the bladder. B: Bladder, P: Prostate, R: Rectum

8. Now scan the small bowel with the sector transducer over the entire abdomen.

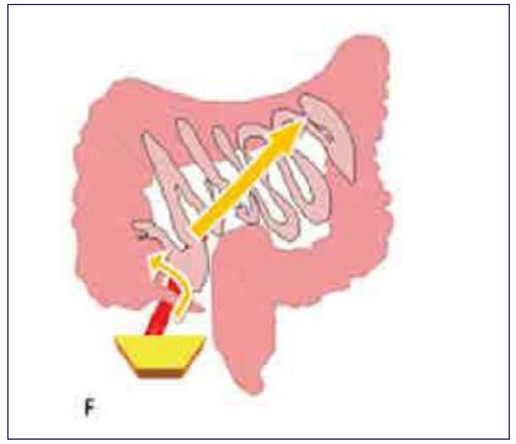


Diagram of examination procedure for ultrasonography of the small bowel

9. The sigmoid, as well as terminal ileum and any remarkable section of the intestine previously scanned with the sector transducer, should also be examined using the high-frequency probe, following the pattern described above.

5. Bowel ultrasonography – what can be seen?

Mural stratification and thickness

The mural stratification of the bowel can be easily differentiated using a high-frequency transducer. The entire thickness of the bowel wall in a healthy individual can reach 3 mm. The typical layers, from the inside outwards, are: entry echo – hypoechoic lamina mucosa – hyperechoic submucosa – hypoechoic muscularis propria – hyperechoic serosa.

Intestinal lumen

In a normal case, the small bowel has a total diameter of 3 cm; toxic megacolon exists above a diameter of 5.5 cm. Furthermore, the Kerckring folds in the small bowel and haustration in the large bowel are frequently visible and useful as landmarks. If there is a question concerning possible stenosis, in particular, dynamic ultrasound over the course of time can often help to distinguish a fixed stricture from contraction-induced constrictions.

Peristalsis

Ultrasonography is the ideal method for assessing peristalsis, because it permits to observe movement over time. Examples of pathological findings are absent peristalsis in paralytic ileus, non-propulsive peristalsis in mechanical ileus, and piano-key phenomenon. In particular, a motile small bowel can be differentiated from a somewhat inactive large bowel and the almost inactive appendix.

Paraintestinal structures

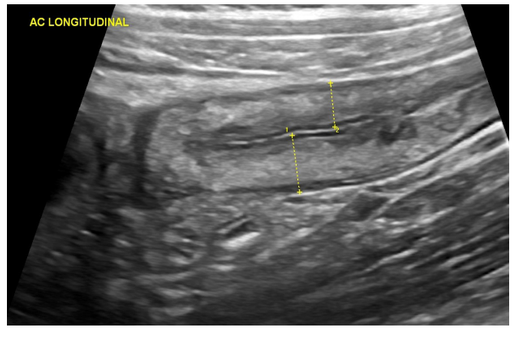
Thickening of the mesenteric adipose tissue, lymph node enlargements or free intra-abdominal fluid, are further characteristic and important aspects to be observed when assessing intra-abdominal inflammatory activity. They are often concomitant reactions of the paraintestinal structures.

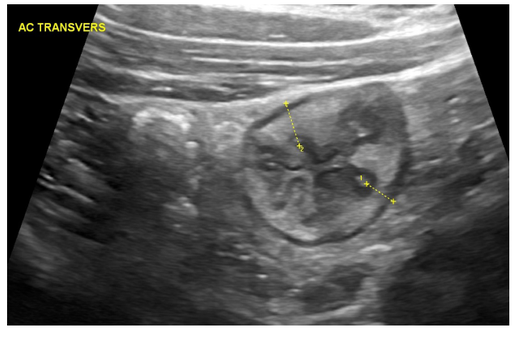
What needs to be assessed?	
1. Mural thickness	Terminal ileum < 2 mm normal, colon < 3 mm normal
2. Echogenicity	Hyperechoic bowel wall/ hypoechoic bowel wall
3. Mural stratification	Preserved/ lost
4. Mesenteric adipose tissue reaction	Pale gray cuff surrounding the bowel, slightly pinnate
5. Mesenteric lymphadenopathy	Enlarged lymph nodes in direct proximity to the inflamed area of the bowel
6. Stenosis	Signs: · No peristalsis · No expansion on motility · Linear air bubbles
7. Prestenotic dilatation	· Non-propulsive peristalsis · Widening of bowel prior to stenosis
8. Subileus/ ileus	· Non-propulsive peristalsis? · Kerckring folds visible? · Step-ladder pattern? · Enlarged fluid-filled bowel loop?
9. Fistula	· Hypoechoic projections from bowel wall · Air bubble within the hypoechoic tract
10. Abscess	· Hypoechoic, irregularly defined formation in direct proximity to the inflamed section of bowel, with air bubbles (hyperechoic signals)
11. Ascites	Free fluid between bowel loops?
12. Vascularization	Doppler ultrasonography in inflamed bowel wall (possible classification: Limberg score I-IV)

How to measure bowel wall thickness?

To get reproducible results, bowel wall thickness should be measured at representative points. Bowel wall thickness is measured from the serosa to the lumen, last of which can easily be identified if there is an air reflex inside the bowel. To avoid measurement errors by measuring within folds, which may occur by measuring in a transverse section, it is recommended to measure in a longitudinal section of the bowel, while one has to avoid tangential sections of the bowel in this case. Multiple measurements to calculate average values can help.

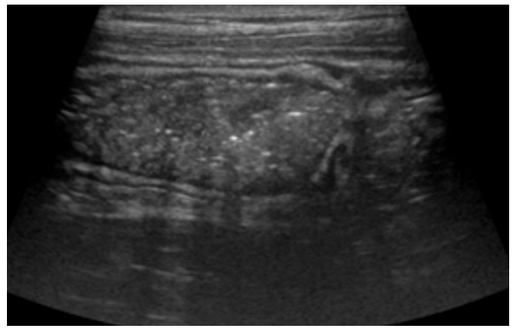
Moreover, the location of measurement should be documented by text or pictogram.



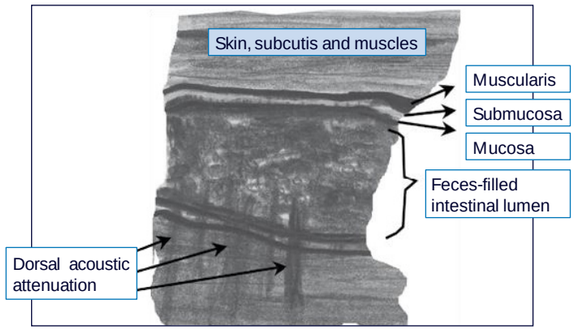


1. Mural thickness
(normal term. ileum < 2 mm, colon < 3 mm)

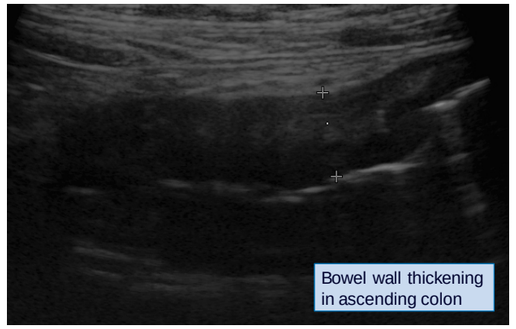
a) Normal bowel wall

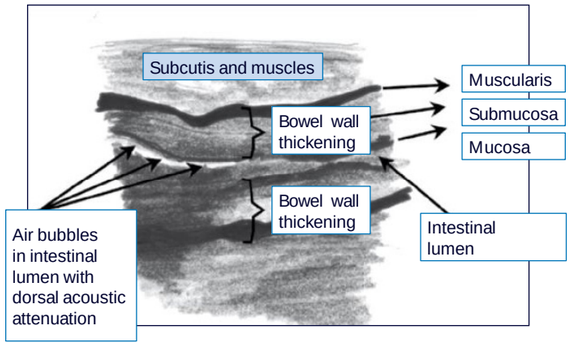


Normal ileum



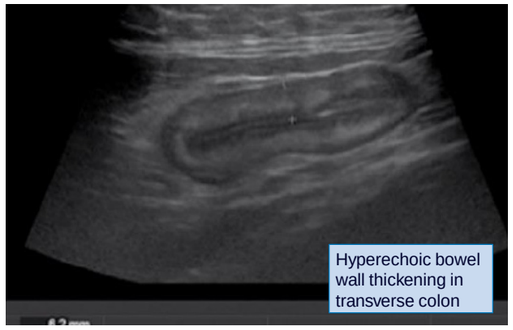
b) Thickened bowel wall

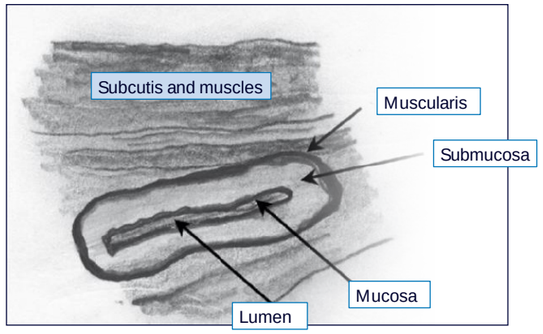




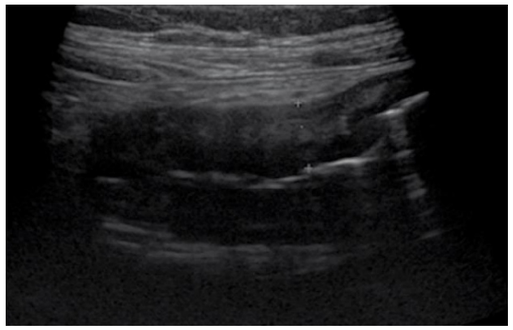
2. Echogenicity

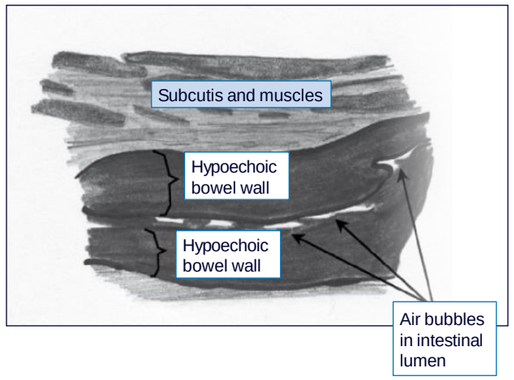
a) Hyperechoic bowel wall



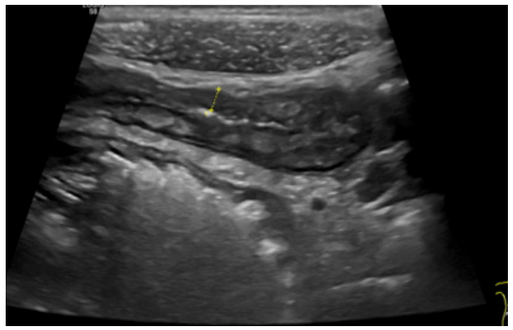


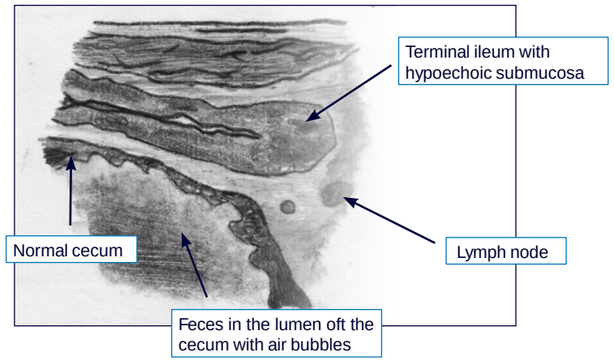
b) Hypoechoic bowel wall





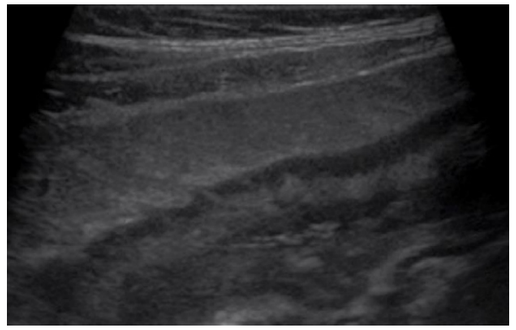
3. Mural stratification

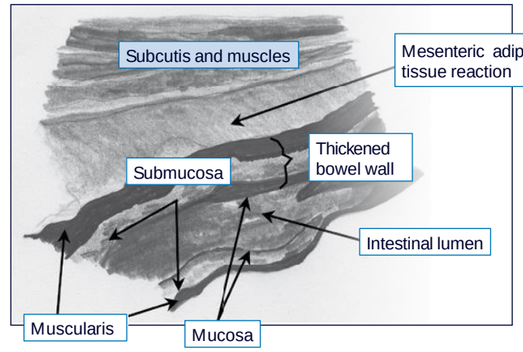


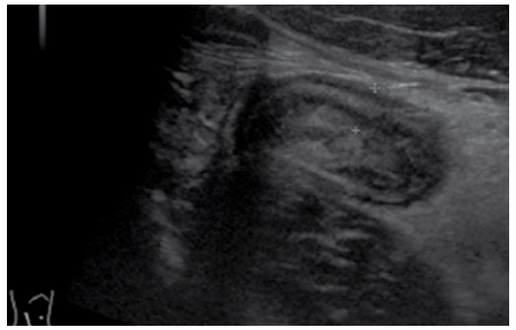


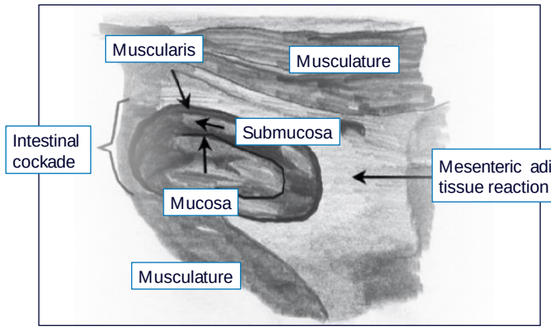
4. Mesenteric fibro-fatty proliferation

The mesenterium appears more hyperechoic with a hyperechogenic line adjacent to the muscle; the tissue appears swollen, often with some streaking.

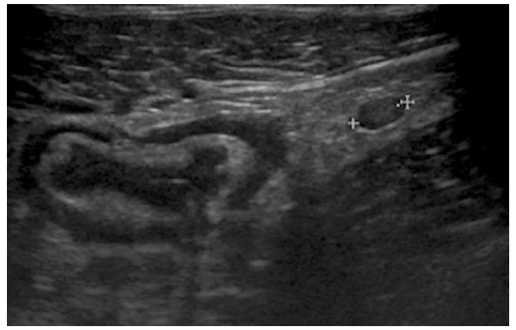


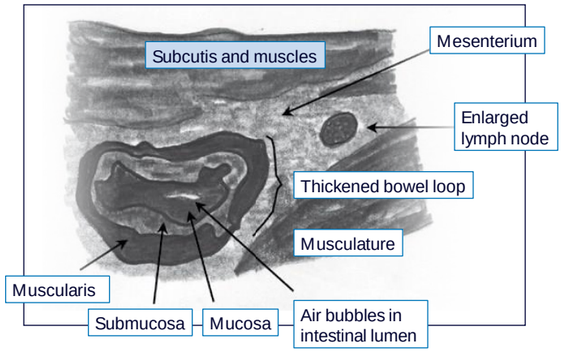






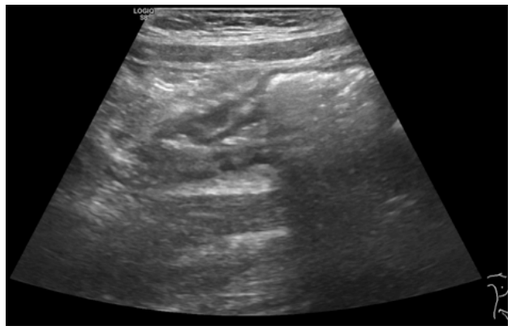
5. Mesenteric lymphadenopathy

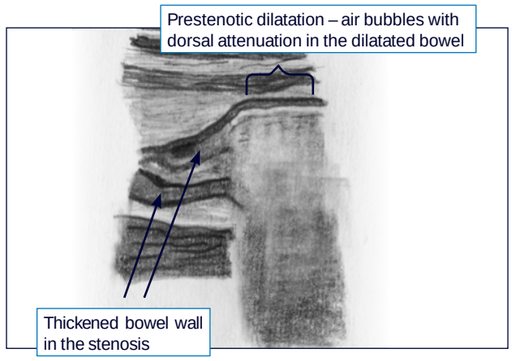




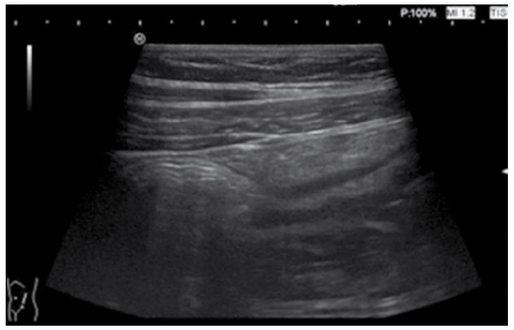
6. Is there any stenosis?

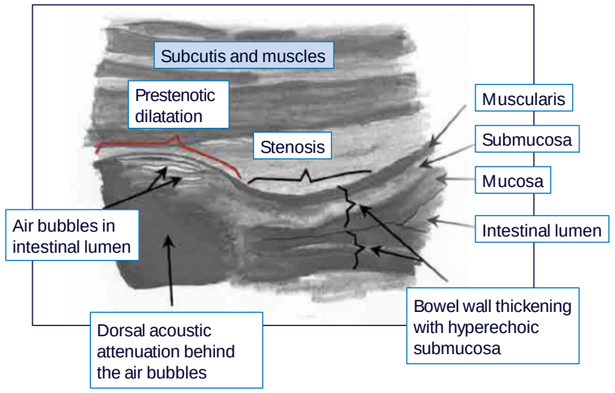
- Prestenotic peristalsis
- No stenotic peristalsis
- No extension of bowel wall with incoming peristaltic wave/motility
- Linear air bubbles in stenosis





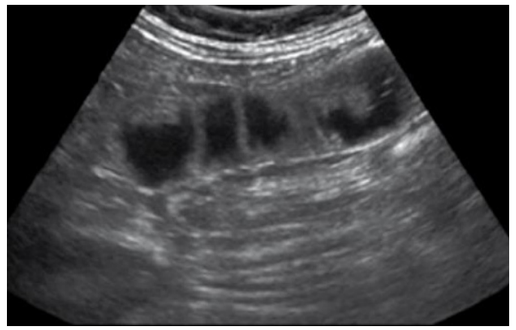
7. Is there any prestenotic dilatation?

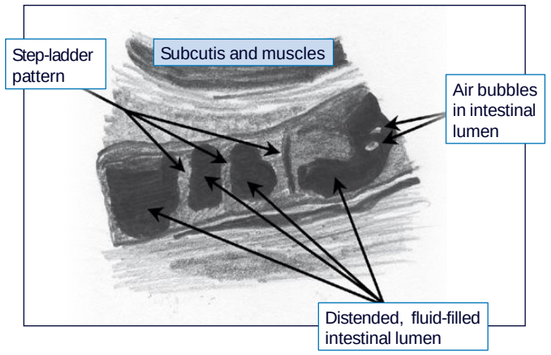




8. Subileus/ ileus

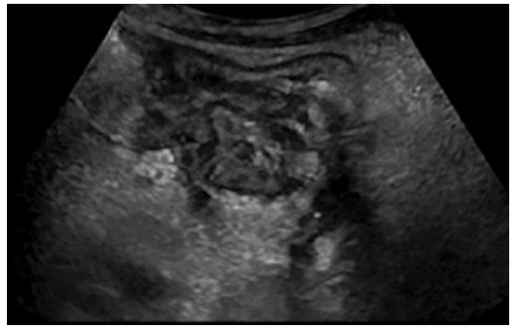
- Distended, fluid-filled bowel loop?
- Kerckring folds visible?
- Piano-key phenomenon/step-ladder pattern?
- Non-propulsive peristalsis? (final evaluation needs to be done looking while at a moving image instead of a still image)





9. Fistula

If the bowel wall is not entirely visible and there is image interference, look for hypoechoic projections which partly contain air bubbles.



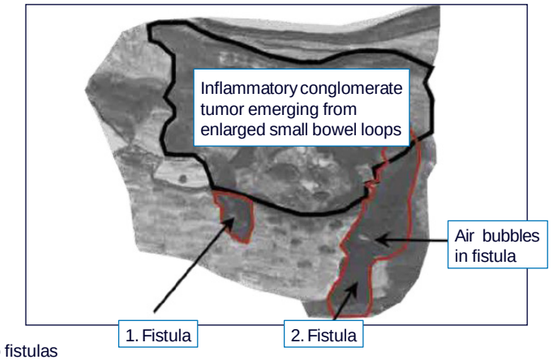
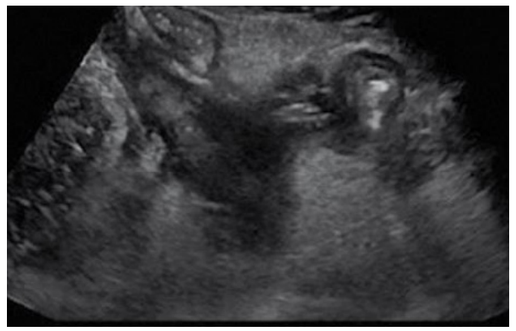


Image example: conglomerate tumor in right lower abdomen with two fistulas



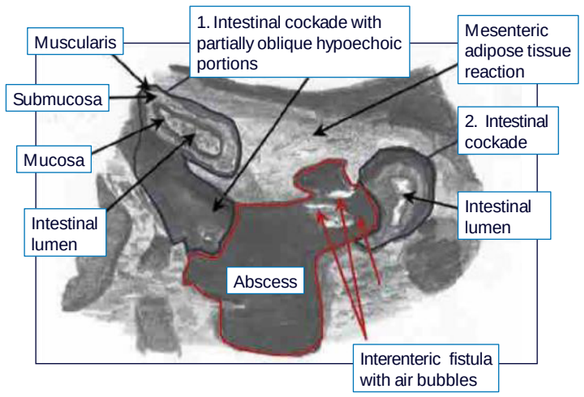
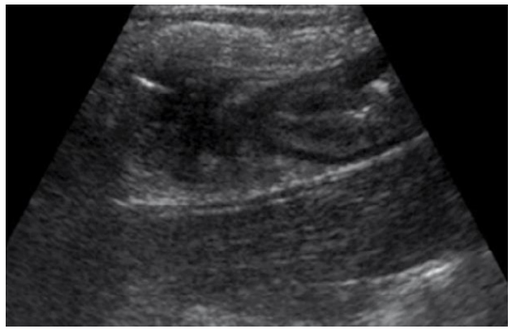
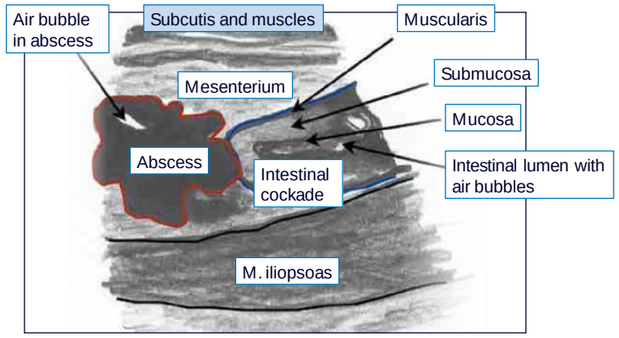


Image example: Interenteric fistula with abscess

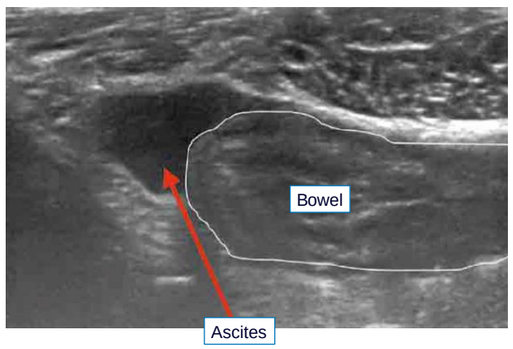
10. Abscess





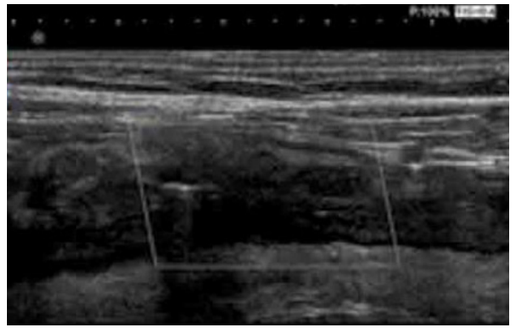
11. Ascites

Hypoechoic area of free fluid between bowel loops, often appearing as small points (like a triangle). Ascites is never round, and the interstices between the bowel loops are filled.

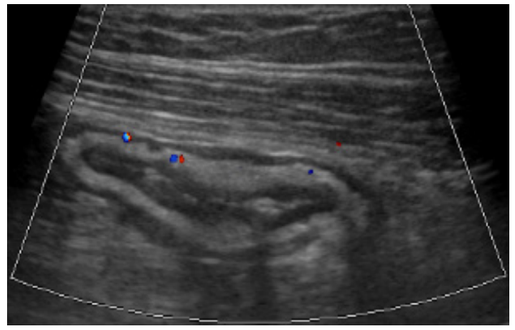


12. Vascularization

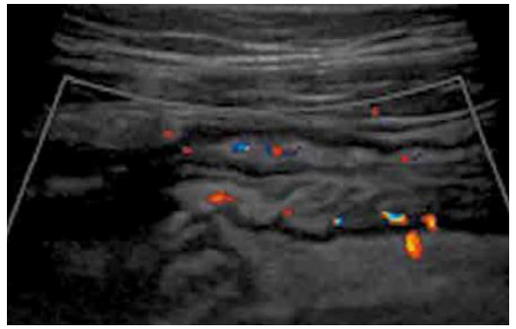
Extent of perfusion of the bowel wall, e.g. using the Limberg score



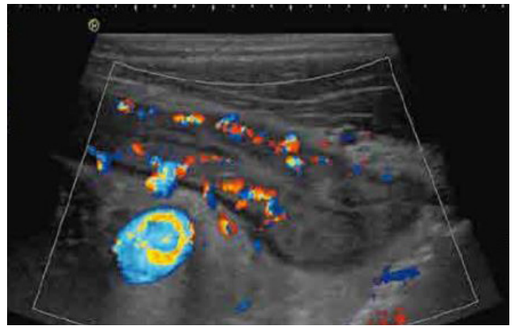
Limberg I: thickened bowel wall (hypoechoic, sometimes also hyperechoic submucosa, partially absent stratification) **without intramural blood vessels**



Limberg II: thickened bowel wall (hypoechoic, sometimes also hyperechoic submucosa, partially absent stratification) with detection of short segments of blood vessels in the bowel wall



Limberg III: long segments of blood vessels in a uniformly thickened wall



Limberg IV: long segments of blood vessels visible, some of them continuing into the mesenterium

6. Bowel ultrasonography in Crohn's disease with case histories

A. General considerations concerning bowel ultrasonography in Crohn's disease

In general, Crohn's disease shows more pronounced sonomorphological changes than ulcerative colitis, due to its transmural character. The inflammatory mural thickening and imbibition of the adipose tissue, as well as ascites and lymphadenopathies, are often very distinctive. Additional color Doppler can be added to differentiate mainly inflammatory from mainly fibrotic thickened bowel wall. In such a case, an additional color Doppler scan is helpful for determining any vascularization of the thickened portions of the bowel wall, since this is related to clinical activity. Moreover, due to discontinuous involvement (segmental wall thickening) and the possible spread into the entire gastrointestinal tract, assessment of the site of the inflammatory changes and relationship to anatomical landmarks is crucial. Terminal ileitis as well as colon involvement is easier to assess than lesions in the rectum and proximal small bowel; for example, inflammatory portions of remaining small bowel can, in fact, be easily identified on ultrasound. Assigning them to a precise section of the small bowel is generally much more difficult compared to an affected colon due to the frequent lack of landmarks.

In addition to the aforementioned sonomorphological changes in parts of the bowel modified by inflammation, complications of Crohn's disease such as fistulas, abscesses and stenoses, in particular, can be identified by ultrasonography with high sensitivity and specificity. Furthermore, by measuring perfusion, a distinction can be made between an acute episode and a fibrotic stage. In contrast to an acute episode, perfusion in a fibrotic stage is normal or decreased. However, it is often very difficult to make the important distinction between inflammatory and fibrotic stenosis. Contrast-enhanced ultrasonography may be of potential use over the further course of the disease. When differentiating between inflammatory conglomerate tumors and abscess formation, for example, ultrasound contrast imaging is of great value.

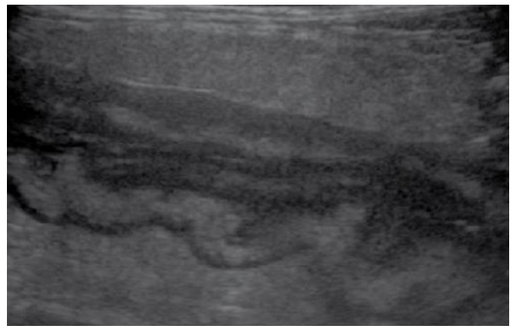
In addition studies are currently evaluating the role of elastography to distinguish inflamed from fibrotic bowel wall.

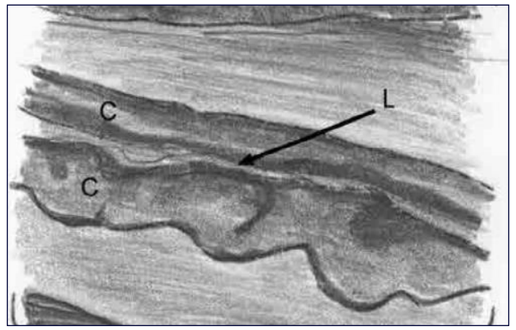
As illustrated in the patient case histories below, bowel ultrasonography has become an important non-invasive method – not only for the purposes of initial diagnosis and detecting complications, such as the development of fistulas and abscesses, but also for monitoring the therapeutic response and detecting relapses.

B. Examples of the use of bowel ultrasonography in Crohn's disease

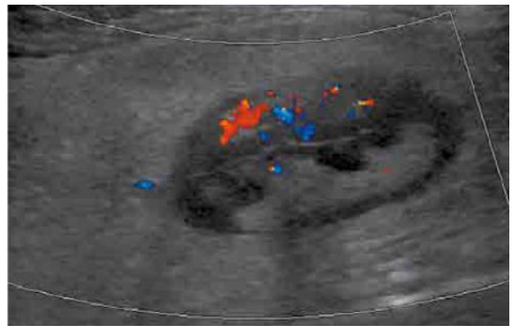
1. Initial diagnosis of Crohn's disease

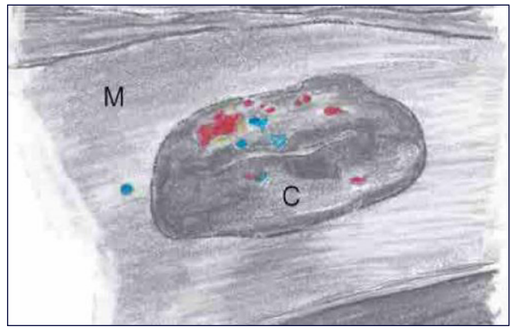
- 21-year-old female patient
- Watery/pulpy, bloody diarrhea
- Painful defecation and lower abdominal pain
- Onset of symptoms about 4 weeks previously, increasing in intensity
- No significant diseases in the past
- Examination: active bowel sounds, tenderness in the left lower abdomen, no abdominal guarding
- Laboratory values: leukocytes 5.44/nl, CRP 25.4 mg/dL





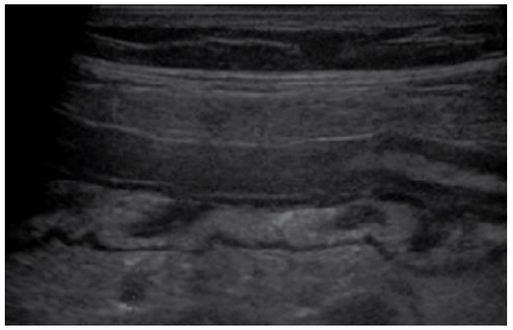
Marked thickening of colon wall, C: colon wall, L: intestinal lumen

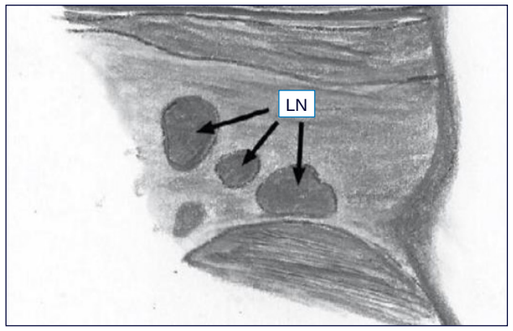




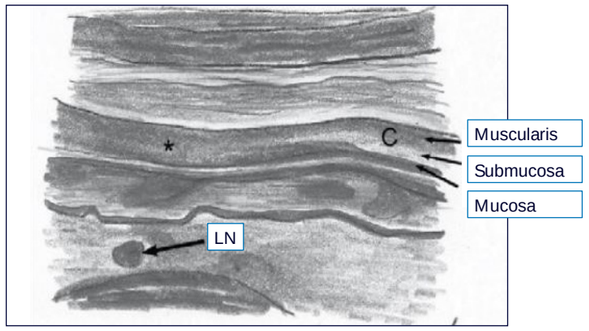
M: mesenteric adipose tissue reaction with clear hyperfusion
C: colon wall

Outcome of diagnostic procedure: colonoscopy the following day – Diagnosis: Crohn's disease





Enlarged intra-abdominal lymph nodes (LN)

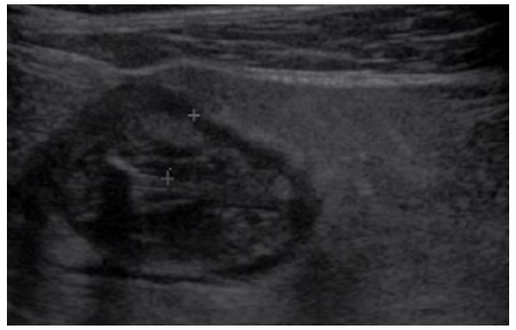


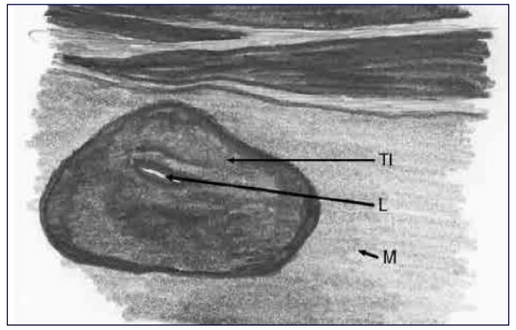
C: colon wall, with partial loss of stratification (*), LN: Lymph node

Acute colitis on endoscopy

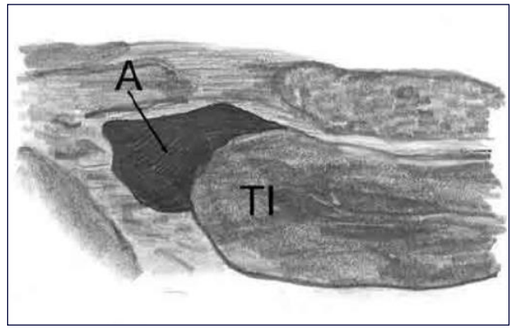
2.a. Acute episode of known Crohn's disease

- 25-year-old female patient known to have Crohn's disease with terminal ileitis
- Treatment with azathioprine for 1 year with deep remission
- Recurrence with increasing paroxysmal abdominal pain and stool frequency
- Examination: tenderness in the right lower abdomen, no abdominal guarding, active bowel sounds
- Laboratory values: leukocytes: 10.8/nl, platelets: 220/nl, CRP: 42 mg/dL
- Stool test for pathogenic bacteria and C. diff. negative
- Fecal calprotectin: 789 mg/ kg





Cockade sign, clearly thickened bowel wall, TI: Terminal ileum, L: Intestinal lumen, M: Mesenteric adipose tissue reaction

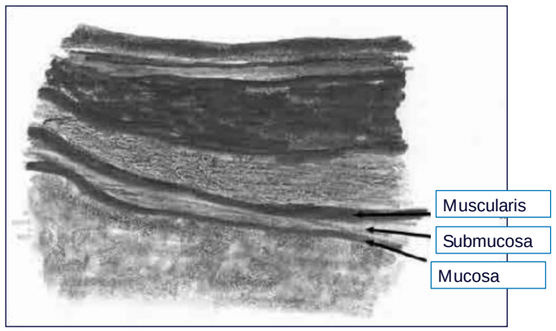


Some interenteric ascites (A), TI: Terminal ileum

Current diagnosis: Acute episode of known Crohn's disease, suspected azathioprine-resistant course

2.b. Therapeutic response and follow-up

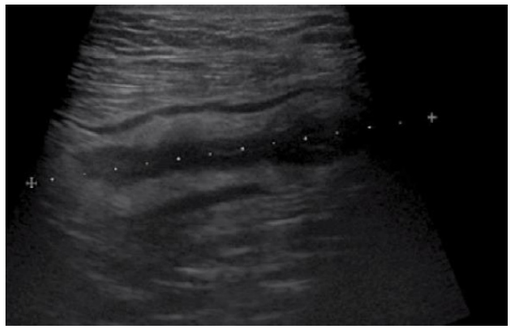
- Patient described above (2.a) reattended with no clinical symptoms 3 months after induction of anti-TNF therapy

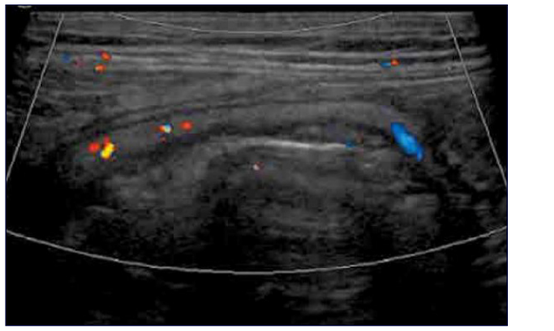


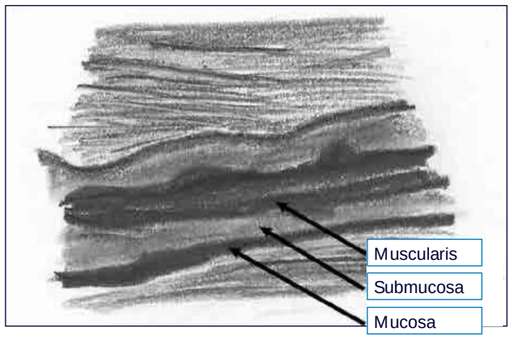
Clear improvement in findings with a still moderately enhanced bowel wall of the terminal ileum

3. Follow-up in clinically asymptomatic patients

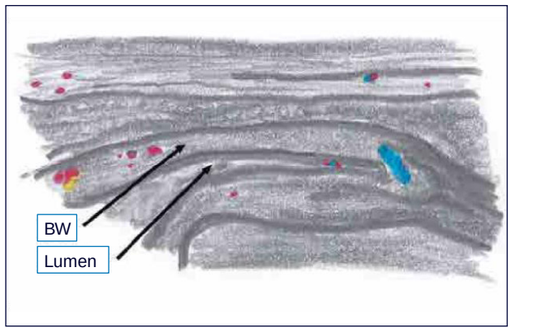
- Crohn's, first diagnosed 2002
- Treatment discontinued by patient 6 months ago, therapy with natural remedies commenced
- First re-attendance for repeat assessment: patient reports feeling clinically well
- Examination: Slight tenderness in the upper abdomen, bowel sounds unremarkable
- Laboratory values: leukocytes: 5/nl, CRP: 3.5 mg/dL, fecal calprotectin: 120 mg/kg







Clear thickening of bowel wall

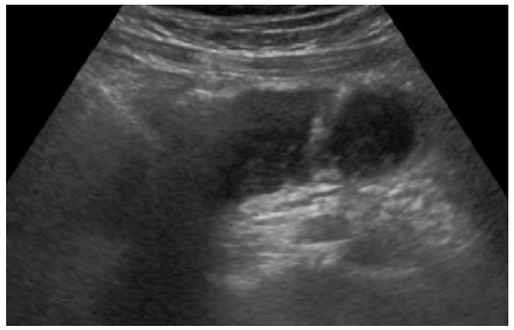


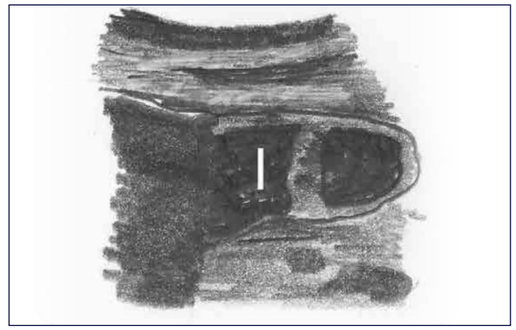
Increased perfusion (BW: Bowel wall)

Recommendation to resume anti-inflammatory therapy

For detection of complications
4.a. Subileus:

- 16-year-old male patient, suspected elsewhere 3 months ago to have mild florid Crohn's disease with terminal ileitis, first diagnosis, no small bowel diagnostics
- Currently, emergency attendance with marked abdominal pain, nausea and vomiting
- Examination: high-pitched bowel sounds, taut abdomen
- Laboratory values: blood count unremarkable, CRP: 85 mg/dL



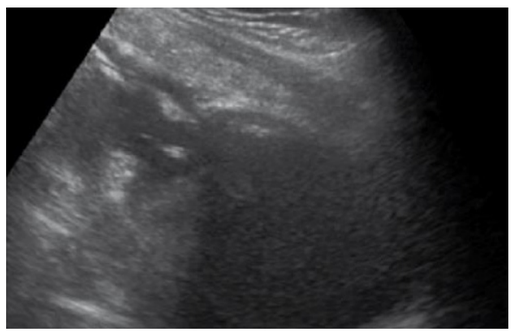


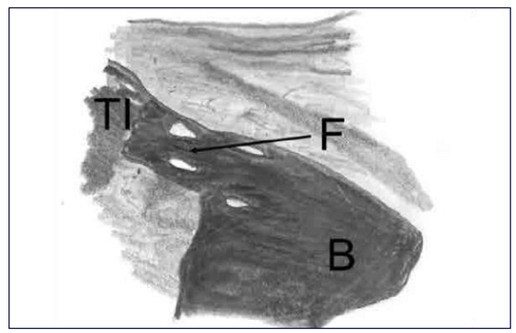
I: Ileum, filled with fluid, bowel wall very thin. On a moving image, onset of oscillating peristaltic movement

Consequence: further diagnostic procedures focusing on small bowel

4.b. Enterovesical fistula

- 19-year-old female patient, known Crohn's disease with ileitis
- Ongoing azathioprine therapy
- Emergency attendance with chills and fever, paroxysmal pain in the right lower abdomen, subfebrile temperatures
- Examination: Heart and lungs unremarkable, slight febrile temperatures, tenderness in the right lower abdomen, otherwise no indicative findings
- Laboratory values: leukocytes: 18/nl, CRP: 64mg/dL,
- Urine status: leukocytes > 500, bacteria +++



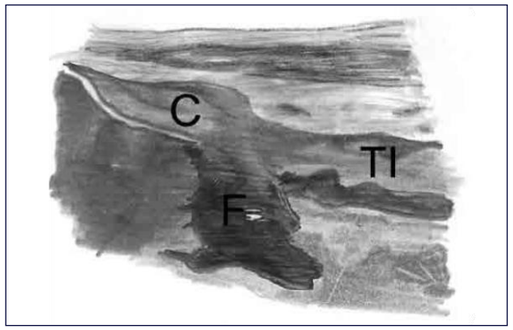


Enterovesical fistula. TI: Term. ileum, B: Urinary bladder, F: Fistula

Consequence: surgical intervention

4.c. Retroperitoneal fistula with abscess

- Known Crohn's ileitis, no treatment at present
- First attendance at IBD center due to recent recurrent fever and abdominal pain
- Laboratory values: blood count unremarkable, CRP 15 mg/dL



Retroperitoneal fistulation in the region of the ileocecal valve;
C: Cecum, TI: Terminal ileum, F: Fistula with abscess

Consequence: surgical intervention

4.d. Stenosis

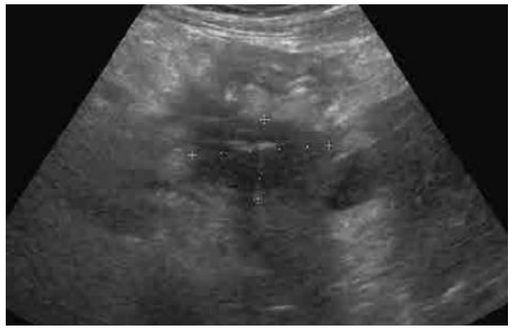
- 27-year-old male patient with known Crohn's disease diagnosed 3 years ago
- Treatment with budesonide for terminal ileitis was finished in remission
- Patient presents with postprandial abdominal pain
- Laboratory values: blood count and CRP normal
- Loss of weight due to reduced food intake because of abdominal pain

Wall thickening of the ileum with prestenotic dilatation

Consequence: Improvement of symptoms upon fasting and steroid therapy

4.e. Conglomerate

- 25-year-old female patient, 4-5 liquid stools per day since 3 weeks
- Similar episode one year ago ended limiting itself
- No known diseases
- Oral aphthous disease since 1 week
- Strong postprandial pain
- Stool sample negative for pathogenic bacteria and C. diff.
- Poppy seed test: negative



In the right lower abdomen tumor mass of unclear origin, initially suspicion of abscess

Consequence: further diagnostic with colonoscopy and MRI

Contrast enhanced ultrasonography shows fistula tracts; while abscesses were suspected on MRI, these could be excluded with contrast enhanced ultrasonography

Consequence: treatment with antibiotics and steroids

7. Bowel ultrasonography in ulcerative colitis with case histories

When performing an ultrasound scan in a patient with ulcerative colitis, the following criteria for bowel ultrasonography should be noted:

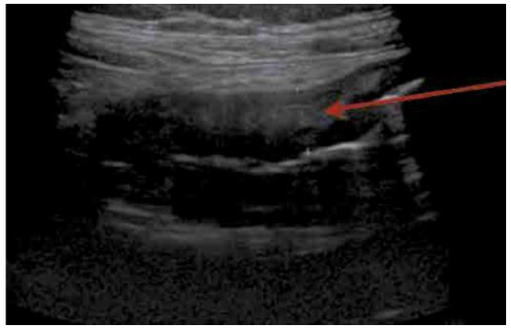
- Indication signs of acute inflammation?
- Is the spread limited to the left side of the colon or are further areas affected?
- Chronic changes? (inner tube appearance/absent haustration?)

It must be remembered, however, that the extent of the inflammation can be underestimated, since the inflammatory changes in ulcerative colitis are often limited to the mucosa. Hence, the sonomorphological changes are mostly not as pronounced as they are in Crohn's disease. Irrespective of an unremarkable ultrasound, further diagnostic measures such as sigmoidoscopy and measurement of fecal calprotectin should be instigated if the symptoms are suggestive of an acute episode despite normal findings on ultrasound.

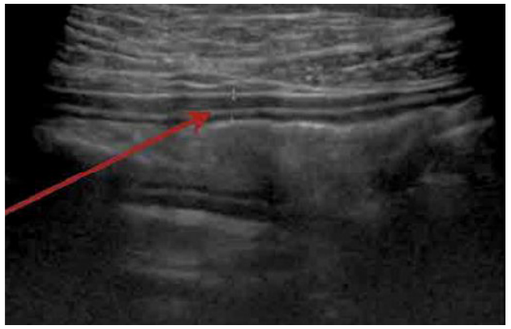
Nevertheless, there are often sonomorphological signs of inflammatory bowel wall thickening which can be used as a basis for individual follow-up. Even if there is sonomorphological evidence of severe pancolitis, the course can be easily assessed under pharmacological therapy. Healing of the mucosa will progress proximally to distally, and in many cases can be ascertained using sonomorphology:

Example:

- 28-year-old female patient with acute episode of ulcerative colitis (first diagnosed 4 years ago)
- Bloody diarrhea for 10 days with paroxysmal abdominal pain
- Leukocytes: 13.5/nl, CRP 13 mg/dL



Acute episode: hypoechoic mural thickening of sigmoid colon (8 mm)

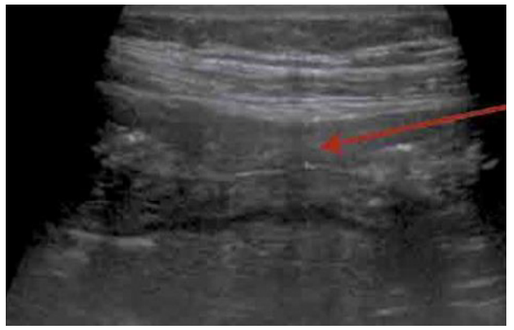


Whereas colitis is present on the left, the mural stratification in the right colon is, at the same time, preserved with only mild signs of inflammation (2.9 mm)

If there are chronic changes in the colonic mucosa, they can to some extent also be seen on ultrasonography. The phenomenon of loss of haustration as well as the resulting inner-tube be visualized, and an expansion in hyperechoic submucosa is often visible.

However, complications of ulcerative colitis such as toxic megacolon, ascites formation and intestinal perforation can also be seen on ultrasound. To this end, an ultrasound examination can easily be used as a non-invasive method for follow-up.

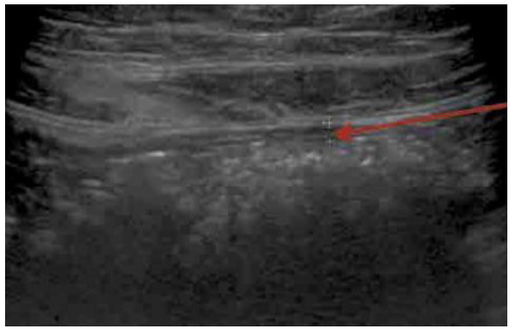
Acute episode: hypoechoic mural thickening in the sigmoid with increased perfusion (Limberg III)



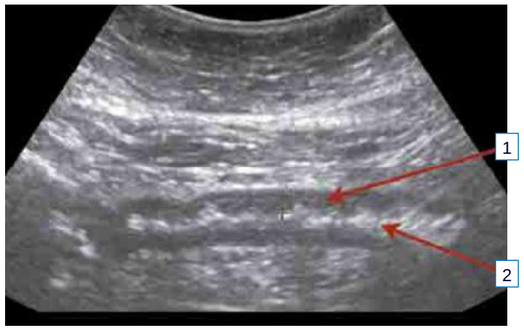
Bowel wall after 2 weeks of therapy (becoming lighter, mural thickness decreasing: 5.1 mm)

Warning:

When performing ultrasound examinations on patients with ulcerative colitis with acute symptoms, it is important to remember that the mentioned condition cannot distinguish from an acute episode of infectious colitis (e.g. EHEC, CMV or Clostridium difficile). If atypical symptoms give rise to doubts concerning an acute episode, further diagnostic measures should be undertaken.



Bowel wall normal again after 4 weeks of therapy (1.8 mm)



1. Chronic left-sided colitis: enlarged bowel wall, lack of haustration
2. Hyperechoic intestinal lumen

8. Complementary diagnostic ultrasonography

A) Doppler ultrasonography

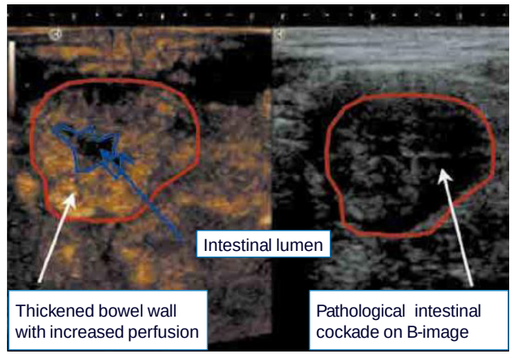
Crohn's disease, in particular, entails hypervascularization of the inflamed bowel wall that is easy to identify on a color-coded B-image. The Limberg score was developed in order to permit a semi-quantitative assessment. It demonstrates a significant correlation with clinical activity (measured as CDAI) (Limberg B 1999). The radiomorphological increase in perfusion of the bowel wall and surrounding mesenterium is assessed using this method (see page 23).

However, consideration should be given to the fact that perfusion signals can be disrupted by peristalsis and patient movement, or may even appear as artifacts due to movement.

From a technical point, to detect the small intramural vessels, Doppler intensity should be increased until blooming artifacts occur and then be reduced slightly.

B) Contrast-enhanced ultrasonography (CEUS)

Contrast-enhanced ultrasonography can be performed to visualize the inflamed portions of the colon wall. Its significance in the diagnosis of chronic inflammatory bowel diseases is the subject of current scientific research. As far as can be judged at present, it appears that it may improve the assessment of disease activity (Wilkens R et al. 2018, Socaciu M et al. 2015, Girlich C, et al. 2012). Furthermore, the procedure appears to facilitate the differentiation between inflammatory and fibrotic intestinal stenoses, since the uptake of contrast agent is greater in the former than in the latter (Kratzer W et al. 2002, Ripollés T et al. 2013). Contrast-enhanced ultrasonography is certainly of value when differentiating between abscess formation and inflammation (Ripollés T et al. 2013). In the former, there is a noticeable absence of contrast agent in the area of the abscess after administration, whereas perfusion is visible in inflamed tissue. It also can be used to visualize the full extent of a fistula if injected into the fistulous tract. In the near future, the use of contrast-enhanced bowel ultrasonography will certainly become more widespread as experience and clinical evaluation develop. To perform CEUS, contrast agent is injected via a cubital vein catheter, followed by a saline flush. Perfusion characteristics are then evaluated instantly during the examination.



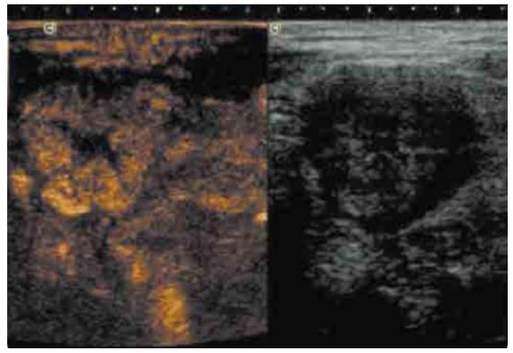
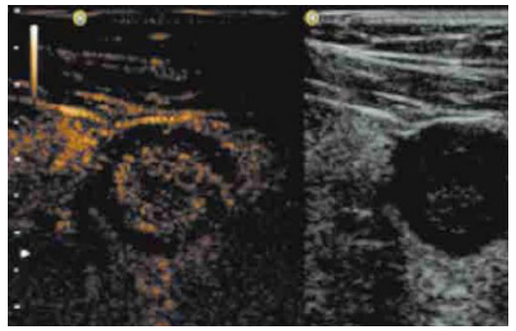


Image example: acute inflammatory mural changes with extensive contrast agent influx (increased perfusion within the scope of acute inflammation)



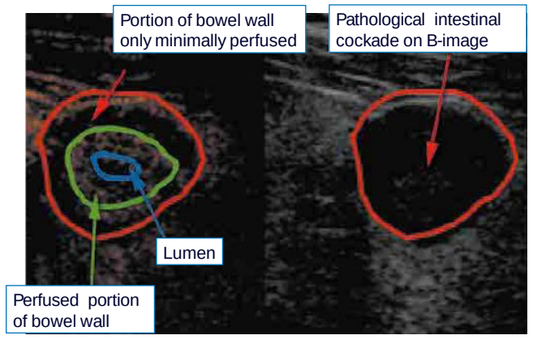


Image example: Crohn's disease with chronic fibrotic course and inadequate response to pharmacological therapy: little uptake of contrast agent after application

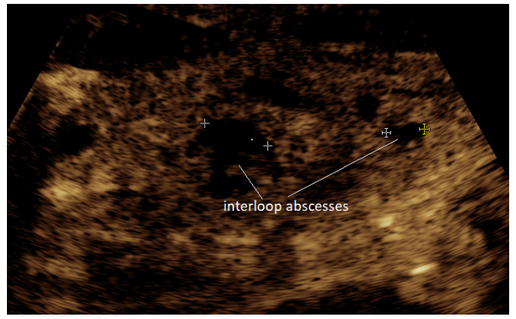
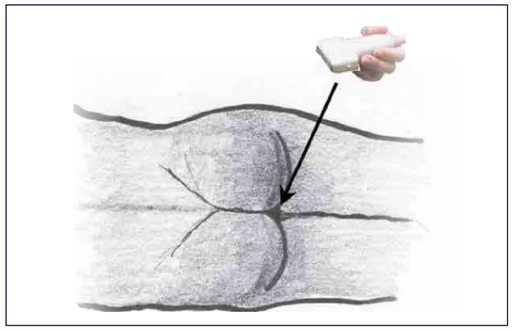


Image example: two small interloop abscesses, wich show no enhancement during contrast enhanced ultrasonography

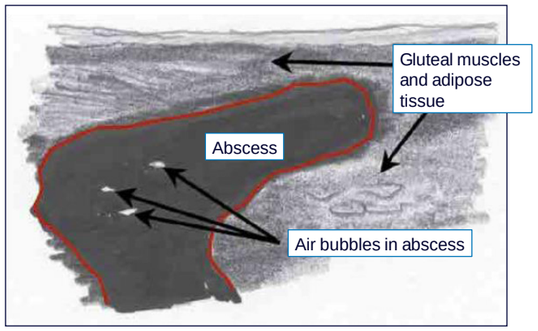
C) Perineal ultrasonography

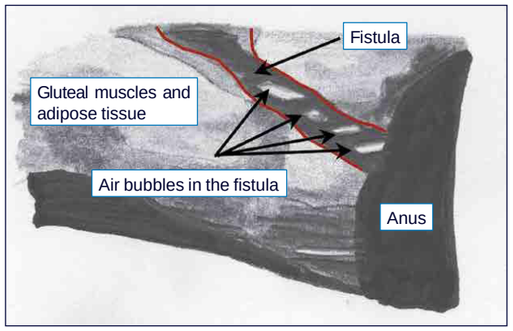
In the presence of an anal fistula associated with Crohn's disease, perineal ultrasound can help in estimating the extent of the fistulation and detecting small abscesses.

In doing so, either a curved or a linear transducer can be used. For reasons of hygiene, the transducer should be placed in a protective cover (such as a surgical glove filled with ultrasound gel).



Example: Gluteal abscess in Crohn's disease





Example: Anal fistula in Crohn's disease

9. How can one learn intestinal ultrasonography if this is not part of the national training curriculum?

First of all, there is no guideline available on how many intestinal ultrasonography examinations are needed to be performed in order to become an expert. Much depends on the background knowledge on general abdominal ultrasonography, local expertise, e.g. is there a knowledgeable colleague on hand with whom to discuss problems or questions. Naturally, knowledge of the terminology is essential. Several excellent, recent publications are available on the subject, for example:

Maconi G et al. EFSUMB Recommendations and Clinical Guidelines for Intestinal Ultrasound (GIUS) in Inflammatory Bowel Diseases. Ultraschall Med. 2018 Jun;39(3):304-317.

Bryant RV et al. Gastrointestinal ultrasound in inflammatory bowel disease: an underused resource with potential paradigm-changing application. Gut. 2018 May;67(5):973-985.

Atkinson NSS et al. How to perform gastrointestinal ultrasonography: Anatomy and normal findings. World JGastroenterol. 2017 Oct 14;23(38):6931-6941.

Nylund K et al. EFSUMB Recommendations and Guidelines for Gastrointestinal Ultrasound. Ultraschall Med. 2017 Jun;38(3):273-284.

Kucharzik T, Maaser C Intestinal ultrasound and management of small bowel Crohn's disease. Therap Adv Gastroenterol. 2018;11:1-13.

Kucharzik T et al. Use of Intestinal Ultrasound to Monitor Crohn's Disease Activity. Clin Gastroenterol Hepatol. 2017;15:535-542.

The next step is to learn the basics and, after that, obtain extensive hands-on practice. One option is to participate in the IBUS 3-step training curriculum. During the first module, colleagues learn the basic skills: setting up the instrument, how to find the bowel and what to look for during a 3-day hands-on workshop. During the second module, participants work for a 4-week rotation at an IBD GIUS expert center, performing and documenting GIUS on a daily basis and finishing this part with a practical exam. The third and last module is an advanced IUS course taking place during the annual spring ECCO meeting. More detailed information is available under

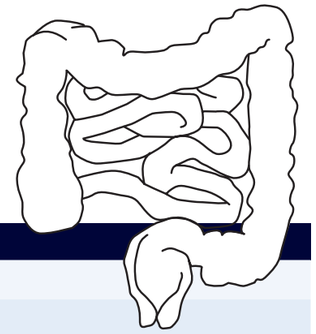
www.ibus-group.org

10. Bowel ultrasonography reporting form

With respect to documentation of bowel US findings, reproducible images are as important as structured and clear reports. Moreover, structured reports help to perform structured investigations, ensuring that no pathologies are missed.

The following form proposes a system for a structured bowel ultrasound report. Diagram of affected segments:

Diagram of affected segments:



Bowel ultrasonography report					
Sigma:					
Pathologic segment: ¨ no ¨ yes (if yes, continue with the following)					
	Bowel wall thickened:	¨ yes	¨ no	max.: ___ mm	
	Bowel wall stratification intact:	¨ yes	¨ partial	¨ no	
	Bowel wall perfusion:	¨ normal	¨ enhanced Limberg: ___		
	Mesenteric proliferation:	¨ yes	¨ no		
	Lymph nodes:	¨ yes	¨ no, largest in diameter: ___ mm		
	Free fluid:	¨ yes	¨ no		
Descending colon:					
Pathologic segment: ¨ no ¨ yes (if yes, continue with the following)					
	Bowel wall thickened:	¨ yes	¨ no	max.: ___ mm	
	Bowel wall stratification intact:	¨ yes	¨ partial	¨ no	
	Bowel wall perfusion:	¨ normal	¨ enhanced Limberg: ___		
	Mesenteric proliferation:	¨ yes	¨ no		
	Lymph nodes:	¨ yes	¨ no, largest in diameter: ___ mm		
	Free fluid:	¨ yes	¨ no		
Transverse colon:					
Pathologic segment: ¨ no ¨ yes (if yes, continue with the following)					
	Bowel wall thickened:	¨ yes	¨ no	max.: ___ mm	
	Bowel wall stratification intact:	¨ yes	¨ partial	¨ no	
	Bowel wall perfusion:	¨ normal	¨ enhanced Limberg: ___		
	Mesenteric proliferation:	¨ yes	¨ no		
	Lymph nodes:	¨ yes	¨ no, largest in diameter: ___ mm		
	Free fluid:	¨ yes	¨ no		

Ascending colon:					
Pathologic segment: ¨ no ¨ yes (if yes, continue with the following)					
	Bowel wall thickened:	¨ yes	¨ no	max.: ___ mm	
	Bowel wall stratification intact:	¨ yes	¨ partial	¨ no	
	Bowel wall perfusion:	¨ normal	¨ enhanced Limberg: ___		
	Mesenteric proliferation:	¨ yes	¨ no		
	Lymph nodes:	¨ yes	¨ no, largest in diameter: ___ mm		
	Free fluid:	¨ yes	¨ no		
TI:					
Pathologic segment: ¨ no ¨ yes (if yes, continue with the following)					
	Bowel wall thickened:	¨ yes	¨ no	max.: ___ mm	
	Bowel wall stratification intact:	¨ yes	¨ partial	¨ no	
	Bowel wall perfusion:	¨ normal	¨ enhanced Limberg: ___		
	Mesenteric proliferation:	¨ yes	¨ no		
	Lymph nodes:	¨ yes	¨ no, largest in diameter: ___ mm		
	Free fluid:	¨ yes	¨ no		
Small bowel other than TI:					
Pathologic segment: ¨ no ¨ yes (if yes, continue with the following)					
	Bowel wall thickened:	¨ yes	¨ no	max.: ___ mm	
	Bowel wall stratification intact:	¨ yes	¨ partial	¨ no	
	Bowel wall perfusion:	¨ normal	¨ enhanced Limberg: ___		
	Mesenteric proliferation:	¨ yes	¨ no		
	Lymph nodes:	¨ yes	¨ no, largest in diameter: ___ mm		
	Free fluid:	¨ yes	¨ no		
Complications:					
a. Stricture ¨ yes ¨ no length: ___					
b. Fistula ¨ yes ¨ no					
c. Abscess ¨ yes ¨ no					
Details: _____					
_____					
Other findings:					
_____					
_____					
Summary of findings and conclusions:					
_____					
_____					

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