Endoanal Ultrasound in Perianal Fistulae and Abscesses

Arjan Paul Visscher, MD and Richelle JF Felt-Bersma, MD, PhD

Abstract: Endoanal ultrasound is a technique that provides imaging of the anal sphincters and its surrounding structures as well as the pelvic floor. However, endoanal magnetic resonance imaging (MRI) is preferred by most physicians, although costs are higher and demand easily outgrows availability. Endoanal ultrasound is an accurate imaging modality delineating anatomy of both cryptoglandular as well as Crohn perianal fistula and abscess. Endoanal ultrasound is comparable with examination under anesthesia and equally sensitive as endoanal MRI in fistula detection. When fistula tracts or abscesses are located above the puborectal muscle, an additional endoanal MRI should be performed. Preoperative imaging is advocated in recurrent cryptoglandular fistula because a more complex pattern can be expected. Endoanal ultrasound can help avoid missing tracts during surgery, lowering the chance for the fistula to persist or recur. It can easily be performed in an outpatient setting and endosonographic skills are quickly incremented. Costs are low and endoanal ultrasound has the potential to improve outcome of patients with both cryptoglandular and fistulizing Crohn disease; therefore, it values more attention.

Key Words: perianal fistulae, anorectal abscesses, anorectal imaging, endoanal ultrasound

(*Ultrasound Quarterly* 2015;31:130–137)

A simple perianal abscess is the acute phase manifestation of cryptoglandular disease. It results from infection of 1 of the 6 to 10 rudimental anal glands that extend from the anal crypts. A perianal fistula represents the chronic phase of the same anorectal disease process. Perianal fistulae are a common benign anorectal condition, with a prevalence of 1 per 10,000, mostly affecting men in their 40s.[1] Perianal sepsis (abscesses and fistulae) can have several non–cryptoglandular causes including Crohn disease, chronic fissures, pilonidal sinus, hidradenitis suppurativa, Bartholin gland abscess, tuberculosis, human immunodeficiency virus, actinomycosis, anal carcinoma, or hematologic malignancies.[2] However, cryptoglandular disease accounts for more than 90% of patients. Treatment is surgical and efficiently eradicating perianal sepsis while preserving anal sphincter integrity is the main goal. Preoperatively missed tracts are considered a main reason for recurrence.[3,4] Therefore, assessing the exact fistula pattern in relation to patient-specific anatomy is mandatory before performing definitive surgery. Preoperative imaging can help delineate fistula pattern, guiding surgical treatment without compromising the anal sphincter complex. An imaging modality often used for this purpose is endoanal ultrasound (EAUS). A rotating probe with a 3-dimensional 360-degree radius and a frequency between 5 and 16 MHz is introduced into the anal canal up to the distal part of the rectum. The technique was introduced 25 years ago by urologists evaluating the prostate. It was easy to learn and perform without causing more discomfort than routine digital examination. Other specialists incorporated it into their clinical practice, and by clarifying perianal anatomy, it increased insights regarding anal pathology. Current clinical indications for EAUS are fecal incontinence for the detection of anal sphincter defects and atrophy, perianal disease to assess fistula and abscess pattern, as well as anorectal carcinoma for staging and follow-up. This review will focus on the clinical relevance of EAUS concerning cryptoglandular as well as Crohn perianal abscesses and fistulae.

Received for publication May 29, 2014; accepted September 9, 2014.

From the Department of Gastroenterology and Hepatology, VU University Medical Center, Amsterdam, the Netherlands.

The authors declare no conflict of interest.

Reprints: Arjan Paul Visscher, MD, PhD, Department of Gastroenterology and Hepatology, VU University Medical Center, PO Box 7057, 1007 MB Amsterdam, the Netherlands (e-mail: ap.visscher@vumc.nl).

ANAL ANATOMY

The anal canal is 2- to 4-cm long, starting at the most distal part of the anorectal ring, at the puborectal (PR) muscle, and extending down to the anal orifice. The dentate line is a wavy line, which divides the upper two thirds and lower one third of the anal canal. Proximal to the dentate line, pain sensation is negligible because innervation is sympathetic and parasympathetic. Below the dentate line, however, nerve supply is somatic, making the tissue highly sensitive, which is important to know when examining the anal canal. Immediately proximal to the dentate line, the mucosa has 8- to 14-fold called the columns of Morgagni. It represents the funneling of the rectum because it narrows into the anal canal. The anal glands empty into the anal crypts just at the base of these columns of Morgagni. Glands sometimes extend through the internal anal sphincter (IAS), and when its ducts are blocked, an anal abscess or fistula can arise.

Because of lack of air in the anal canal, the anus lies tightly around the endoprobe and outstanding images can be obtained with EAUS. The reproducibility of endosonographic findings has been thoroughly investigated in healthy volunteers.[5–9] Further studies established basic endosonographic anatomy through comparing findings with anatomical preparations.[10,11]

The muscles surrounding the anal canal are important for maintaining continence. The subsequent layers that can be identified with EAUS are the mucosa/submucosa, the IAS, the intersphincteric groove, the external anal sphincter (EAS), and the PR muscle. The submucosa is portrayed as a mixed echogenic structure and is partly collapsed by pressure of the endoprobe.[11] Its thickness increases slightly with age,[12] which is caused by physiological distal displacement plus enlargement of the anal cushions,[13] and has been found to a larger extent in

internal hemorrhoids.[14] The mucosa/submucosa cannot be identified separately with the frequencies used.

The IAS is the thickened continuation of the circular smooth muscle layer of the rectum. This muscle ends above the external sphincter and is important for passive continence. It is a 1- to 3-mm–thick involuntary muscle, which appears as a black hypoechoic band on EAUS.[10,15,16] It is possible to partially divide the internal sphincter by fistulotomy without causing significant incontinence. However, anterior or posterior division can lead to leakage of stool because of the creation of an oval-shaped defect, known as a keyhole deformity. The IAS increases in thickness and echogenicity with age, both in patients[17,18] and in healthy volunteers.[15,19] Histological evidence suggests that aging-induced sclerosis of the IAS is responsible for this finding.[20] The muscle thickness is not related to sex, body weight, or length.[19]

The EAS is a 4- to 10-mm–thick voluntary skeletal muscle.[7,12,15] In women, the external sphincter is thinner and shorter anteriorly, making it more vulnerable to obstetric anal sphincter injury.[6,15] Besides being related to sex, thickness is also correlated to body weight, with thicker muscles in heavier persons,[15] and age, with thinner muscles in older patients.[21] Because of the structure of striated muscle, the external sphincter appears as a band of mixed echogenicity on EAUS. Proximally, the EAS weaves itself into the PR and levator ani muscles. Distally, it ends slightly past the IAS. As a result, an intersphincteric groove can be palpated on digital examination. This intersphincteric groove can be made visible during EAUS; however, its importance is controversial.[6,7,11,15,22]

Endoanal ultrasound of the anal canal identifies these layers and structures. The PR muscle is, in almost all cases, easily visualized and can serve as a point of orientation: it appears as a V-shaped echogenic band, which slings dorsally around the rectum (Fig. 1A). The figures were made using a 3-dimensional EAUS (3D-EAUS) B-K Medical system (see the EAUS Imaging section), which was standardly set at 7 MHz. When withdrawing the probe, the echogenic band is closing anteriorly, thus forming the EAS (Fig. 1B). Figures 1C and 1D represent the lateral and coronal views, respectively.

Other anatomical structures that can be seen using EAUS are the anococcygeal ligament (posterior), the levator ani, the transverse perineal muscles, the ischiocavernosus muscles, the urethra, and the pubic bones.[9,15] The anococcygeal ligament appears as an hypoechoic triangle and causes narrowing of the external sphincter.[6] The levator ani comprises 3 parts: the mentioned PR muscle, the iliococcygeus muscle, and the pubococcygeus muscle.

The normal rectum measures 11 to 16 cm in length, with a maximum diameter of 4 to 5 cm. On EAUS, the normal rectal wall is 2- to 3-mm thick and composed of the same 5-layer structure as the entire digestive tract. It is generally filled with some remainders of fecal material or air. These circumstances can make it challenging to obtain an optimal acoustical surrounding. Infusion of water into the rectum using a flexible plastic cannula is a manner in which imaging quality can be improved. When EAUS is not possible because of extreme anal stenosis, pain, or an asymmetrical anal canal, vaginal endosonography can be performed as an alternative.[23]

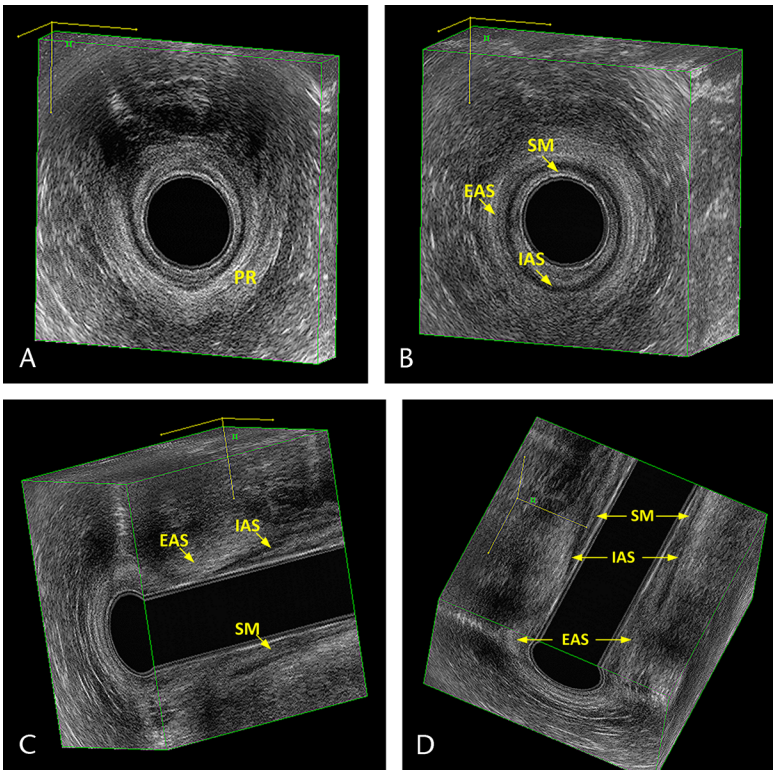

FIGURE 1. A, Anal endosonography. Normal anatomy of the anal sphincter and PR muscle in 3-dimensional imaging. Frontal view of PR muscle. B, Anal endosonography. Normal anatomy of the anal sphincter and PR muscle in 3-dimensional imaging. Frontal view of the anal sphincters and submucosa. C, Anal endosonography. Normal anatomy of the anal sphincter and PR muscle in 3-dimensional imaging. Lateral view. D, Anal endosonography. Normal anatomy of the anal sphincter and PR muscle in 3-dimensional imaging. Coronal view. SM indicates submucosa. Figure 1 can be viewed in color online at www.ultrasound-quarterly.com.

CLASSIFICATION

In cryptoglandular disease, nearly all abscesses originate in the intersphincteric space. From here, they can migrate up, down, or circumferentially around the anal canal. Abscesses are classified according toward where they have extended as superficially perianal, intersphincteric, ischiorectal, or supralevatoric. In approximately 50% of patients undergoing surgical incision and drainage of an abscess, a fistula will develop. Perianal fistulae are classified in relation to the striated muscle structures they surpass as submucosal (15%), intersphincteric (24%), transsphincteric (58%), suprasphincteric (3%), or extrasphincteric (<1%) (Fig. 2).[24] It is a slightly adapted version of the surgical classification first described by Parks et al,[25] which lacked submucosal fistulae. These are located superficially and do not involve the anal sphincter complex. Intersphincteric fistulae are characterized by a course through the intersphincteric space without penetrating the EAS. Transsphincteric fistulae breach through the external sphincter, pass into the ischiorectal fossa, and find their way to the perianal skin. They are often subcategorized into low and high transsphincteric fistulae, depending on the amount of external sphincter involvement. Suprasphincteric fistulae surpass the musculus puborectalis, move into the ischiorectal fossa, and reach the perianal skin. Extrasphincteric fistulae have no relation to the sphincter complex and are found after prior fistula surgery or in non–cryptoglandular disease.

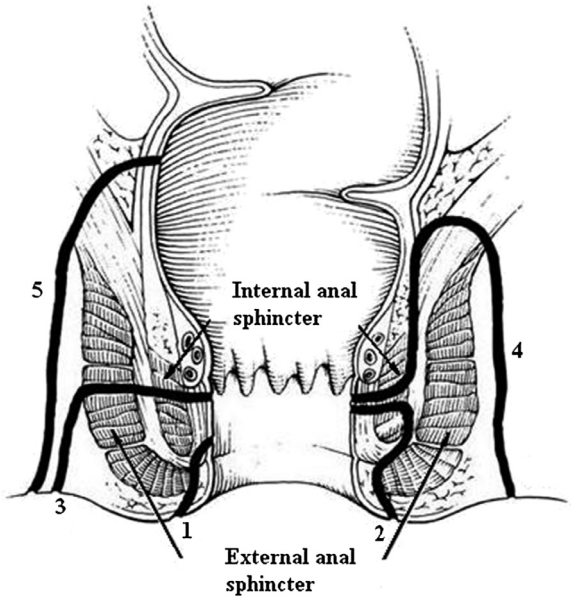

FIGURE 2. Perianal fistula classification: 1, submucosal (15%); 2, intersphincteric (24%); 3, transsphincteric (58%); 4, suprasphincteric (3%); and 5, extrasphincteric (1%). Adapted from the study of Schwartz et al.[71] Adaptations are themselves works protected by copyright. So in order to publish this adaptation, authorization must be obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

EAUS IMAGING

Probes

Endoanal ultrasound is performed with a transrectal ultrasound probe. The rigid rotating endoprobes with a 360-degree view are preferable. Rigid mechanical probes are provided by Bruel & Kjaer Medical (Herlev, Denmark) and Aloka (7.5–12.5 MHz; Tokyo, Japan). We used a 3D-EAUS system (Hawk type 2050; B-K Medical, Naerum, Denmark) with a rotating endoprobe with 2 crystals, covering 2 to 6 MHz (focal range, 2–4.5 cm; diameter, 1.7 cm), producing a 360-degree view. During recording, the crystals are automatically pulled back using an internal puller, allowing longitudinal distances to be measured. Endoanal ultrasound uses frequencies between 2.5 and 16 MHz. Images are formed by reflection at the interfaces of 2 structures; part of the signal is transmitted and part is reflected. Reflections from deeper structures are weaker because of greater signal attenuation. This can be corrected through changing the megahertz frequency; lower frequencies (2.5 MHz) penetrate better into deeper layers and superficial structures are better visualized with higher frequencies (16 MHz).

Performing EAUS

In our department, the patient is positioned in the left lateral decubitus position with the anus at the very edge of the bed, allowing movement of the probe by the operator. Before introducing the probe, a digital rectal examination is performed to rule out possible abnormalities (stenosis, painful lesions, or a tumor). To optimize conductance and for hygienic reasons, the rigid probe is covered by a condom filled with ultrasound gel. The probe is then covered with lubrication gel and gently introduced into the anus up to the distal part of the rectum. Important landmarks are the prostate, the vagina, and the PR muscle. Anorectal anatomy, as described previously, can be visualized when withdrawing the probe from the distal rectum into the anal canal. When there is loss of contact with the anal canal due to an asymmetrical anus or the presence of air, reverberation can occur. Reverberation is an artifact because of mismatch of acoustic impedance at an interface. When there is a loss of contact with the mucosa, the ultrasound probe's first (and essentially only) interface is with air or air-containing anal debris, which produces near-total difference in acoustic impedance, and no sound waves travel into the anal wall; in addition, only reverberation artifact is propagated. Some reverberation artifact occurs even when there is normal contact with the anal mucosa because there is always some acoustic impedance mismatch. Improving acoustic qualities by gently maneuvering the probe solves this problem.

EAUS in Anal Fistula

To reduce the risk for postoperative fecal incontinence and recurrence, it is important to identify the precise anatomic course of the fistula in relation to the anal sphincters and to be informed about preoperative anal pressures as well as the possible anal sphincter defects. Conventional 2-dimensional EAUS (2D-EAUS) was introduced in 1989 by Law and Bartram[6] as "a quick and minimally invasive technique for obtaining high resolution images of the anal canal and surrounding structures."

Using the technique for the evaluation of perianal fistula was first reported later that same year.[26]

Additional studies reported accuracy rates up to 94% regarding primary fistula tract classification[26–30] and rates up to 93% regarding location of the internal opening.[28] Cho[31] published 3 criteria identifying the site of the internal opening, increasing accuracy up to 94%. Although fistula assessment is possible with digital examination and probing, anatomic accuracy is higher using EAUS.[27,31,32]

The advent of hydrogen peroxide (HP) as a contrast agent, which was first described by Cheong et al[33] in 1993, further increased accurate classification up to 95%[3,34,35] (Figs. 3 and 4A, B). With this technique, HP is gently introduced into the external fistula opening using a flexible cannula, illuminating the fistula tract after the formation of gas bubbles within the lumen. Without HP, the fistula tract appears as a hypoechoic or mixed echoic band and an abscess appears as a hypoechoic to anechoic region, so do enlarged glands, large blood vessels, or the anococcygeal ligament posterior in the distal anal canal. After introduction of HP, fistulous tracts and connecting cavities become brightly hyperechoic on EAUS. Another advantage is that HP makes it possible to differentiate between scar tissue and fistula tract. It is a safe, reliable, and economic procedure for the assessment of perianal fistulae.

Although 2D-EAUS proved to be helpful in the early days of EAUS imaging, it had some shortcomings. Images were produced in a transaxial scanning plane, and therefore, the only way to extend scanning in the proximal-distal direction was to move the probe farther in or out of the anal canal or rectum. The first report of 3D-EAUS for the assessment of anorectal anatomy appeared in 1999 by Konerding et al.[36] In 3D-EAUS, multiple parallel 2-dimensional ultrasound images are synthesized into a 3-dimensional data set. Three-dimensional EAUS has been compared with other imaging techniques regarding the assessment of fistula detection. A prospective trial (including 25 symptomatic patients of which 17 were men; mean age, 41 years) comparing preoperative fistula assessment using 2D-EAUS and 3D-EAUS with evaluation under surgery (evaluation under anesthesia [EUA]) concluded that 3D-EAUS was more accurate in delineating the primary tract and the internal opening compared with 2D-EAUS.[37]

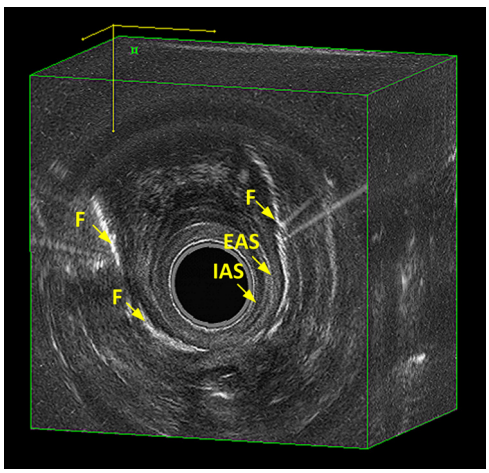

FIGURE 3. Anal endosonography of a cryptoglandular fistula. Frontal view of a patient with a high transsphincteric (3) and partly extrasphincteric (5) horseshoe fistula after infusion of HP through the external fistulous opening. Both anal sphincters have been damaged after several fistula operations. Measured in hours of the clock, the IAS is almost completely missing from 4- up to 9-o'clock position. F indicates fistula tract. Figure 3 can be viewed in color online at www.ultrasound-quarterly.com.

EAUS Versus Magnetic Resonance Imaging

Ever since the late 1980s, the use of magnetic resonance imaging (MRI) has also proven to be highly accurate in evaluating fistulae.[38] However, MRI is costly and the demand can easily outgrow availability, resulting in longer waiting lists for patients. Several studies determined agreement between EAUS and endoanal MRI in the preoperative assessment of perianal fistulae; however, results are not unambiguous.[4,39–44] One prospective study compared both modalities with EUA in 21 symptomatic patients (aged 26–71 years) with cryptoglandular perianal fistula.[43] Observers were blinded for each other's findings and assessed fistulae characteristics separately. The median time between 3-dimensional peroxide-enhanced EAUS (3D-HPUS) and endoanal MRI was 66 days. The medium time between imaging modality and EUA was 154 days. Agreement regarding classification according to Parks et al[25] was 81% for 3D-HPUS and EUA and 90% for endoanal MRI and EUA as well as for 3D-HPUS and endoanal MRI. On circular secondary tracts, agreement was 67% for 3D-HPUS and EUA, 57% for endoanal MRI and EUA, as well as 71% for 3D-HPUS and endoanal MRI. For linear secondary tracts, rates were 76% for 3D-HPUS and EUA, 81% for endoanal MRI and EUA, as well as 71% for 3D-HPUS and endoanal MRI. Regarding location of an internal opening, agreement was 86% for 3D-HPUS and EUA as well as for endoanal MRI and EUA and 90% for 3D-HPUS and endoanal MRI. Agreement between 3D-HPUS and endoanal MRI was excellent, especially regarding fistula classification and locating the internal opening. Both modalities showed good agreement with EUA, and the authors concluded that both 3D-HPUS and MRI were reliable for preoperative perianal fistula evaluation.

In another study of 40 patients (aged 21–70 years), anatomical agreement and patient preference were determined.[44] Interval between 3D-HPUS and endoanal MRI was shorter than 14 days. Both methods agreed in 88% on fistula tract classification, in 90% on location of the internal opening, in 78% regarding secondary tracts, and in 88% on the presence and location of fluid collections. There was no significant difference between discomforts experienced and in patient preference for 1 procedure over the other.

Two older studies comparing EAUS and endoanal MRI in the assessment of perianal fistula concluded MRI to be more accurate.[40,42] However, contrast enhancement using HP was not yet performed in those years.

In patients with Crohn disease, 1 prospective study comparing EAUS and MRI found EAUS to be more accurate in detecting anorectal abscesses and much more accurate than MRI regarding the evaluation of complex fistulae.[39] Another study comparing EAUS with a 10-MHz probe to body coil MRI found comparable results between both modalities.[4] Schwartz et al[41] performed one of the largest prospective

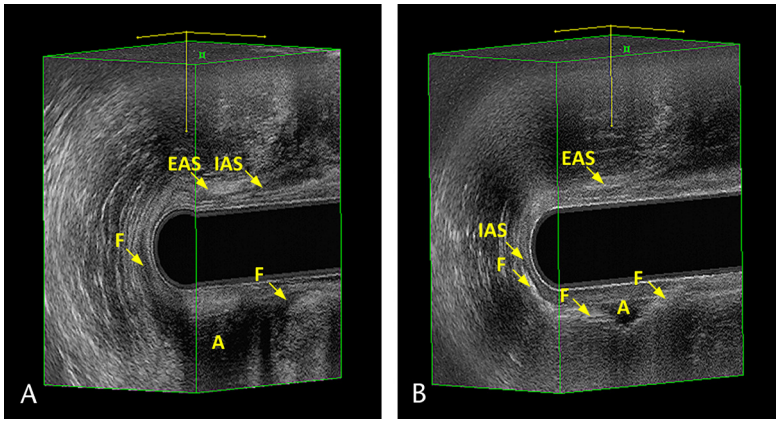

FIGURE 4. A, Anal endosonography of a patient with Crohn disease. Frontolateral view without infusion of HP shows a large intersphincteric abscess with connecting transsphincteric (3) fistula tract. B, Anal endosonography of the same patient with Crohn disease. The tract becomes hyperechoic after infusion of HP, revealing a high transsphincteric (3) pathway. A indicates abscess; F, fistula tract. Figure 4 can be viewed in color online at www.ultrasound-quarterly.com.

studies evaluating EAUS, MRI, and EUS and concluded all modalities to be accurate for determining fistula anatomy in perianal Crohn disease. Accuracy reached 100% when any 2 tests were combined.

Three-dimensional HPUS and endoanal MRI are highly accurate techniques for assessing perianal fistulae; yet, most of the studies mentioned previously used EUA as a criterion standard. Yet, there is evidence that questions that standard.

One study investigated the predictive value of preoperative body coil MRI in 37 patients with surgically proven perianal fistulae.[45] Minimum follow-up was 14 months (range, 14–39 months). Surgery was performed without the surgeon having access to the fistula characteristics assessed using MRI. Outcome was considered unsatisfactory if further surgery was required. Magnetic resonance imaging–derived fistula characteristics made better predictions regarding patient outcome than findings during EUA did.

Another prospective study evaluating 3D-HPUS and EUA revealed secondary fistula tracts in 2 patients during 3D-HPUS that were not found during EUA. Both patients developed a recurrent fistula, suggesting that these branches were actually present at the time of 3D-HPUS.[3]

A similar conclusion was reported in a study of 23 patients undergoing EAUS and body coil MRI for preoperative anal fistula assessment. In the 2 patients with recurrent fistula, EAUS showed an extension and/or abscess, which was not identified during EUA. For body coil MRI, the corresponding number was 3.[4]

To minimize the risk for missing fistulous tracts during surgery, it seems wise not to consider EUA and surgery alone as the criterion standard but to supplement information on precise fistula pattern using preoperative 3D-HPUS or MRI.

The outcomes of the studies mentioned previously vary, which may be explained by the different imaging techniques used. With EAUS, better results were reported when a linear or biplane endoanal probe was used[39,41] and 3D-HPUS also improved imaging quality.[43,46] Most of the MRI studies mentioned previously used a phased array body coil.[4,39,40] This technique has the advantage of providing additional information on structures farther away from the anal canal. However, reliable distinction between fistula tract and blood vessels can be difficult. When the objective is obtaining information on anal sphincter anatomy and perianal region, endoanal coil MRI has been demonstrated to be more accurate.[43] In both simple and more complex perianal fistulae, the internal opening, the primary tract, and fluid collections were more accurately detected using endoanal coil MRI. However, in correctly identifying fistula extension located subcutaneously or above the musculus levator ani, phased array body coil MRI was superior.[47]

Regarding EAUS performance, it is important to recognize that many of the available studies did not use HP, which could have improved results.[33,35,48–51] With EAUS, it can be challenging to distinguish between scar tissue and active fistulae. Adding HP helps discriminate the fistulous tract from the surrounding non–fistulous tissue, increasing accuracy up to 30%.[3,52] As described previously, EAUS and MRI can be considered equally accurate in the preoperative assessment of perianal fistulae. However, in high fistula tracts or abscesses that cannot be followed more proximally with EAUS, a phased array body coil MRI seems advocated. In patients with anal fibrosis or severe anal pain, endoanal imaging may be impossible. In these cases, a vaginal endosonographic approach is a good alternative for women. Otherwise, a body coil MRI can be performed.

FISTULA COMPLEXITY

Cryptoglandular Disease

Determining the likelihood of fistula complexity before surgery is important for whether additional anorectal imaging is necessary. One study of 115 patients with cryptoglandular fistula undergoing fistula surgery investigated the diagnostic value of measuring the distance between external opening and anal orifice to evaluate its relation to fistula complexity. The mean (SD) distance in simple fistula was 2.8 (0.689) cm compared with 4.4 (0.526) cm in complex fistula. Higher age and prior operation were also related to fistula complexity.[53] Identification of these patients can select the cases that should have specific sophisticated preoperative workup such as EAUS. Another study investigated the frequency in which different types of fistulae were present in 81 patients with cryptoglandular fistulae (never operated, n = 48; recurrent, n = 33).[54] All patients were

assessed through clinical examination and using 3D-HPUS. All never operated fistulae were intersphincteric or transsphincteric, and a secondary tract was found in 5%. Recurrent fistulae were suprasphincteric or extrasphincteric in 15%, and secondary tracts were present in 27%. Therefore, never operated fistulae might not require any special preoperative workup because there is a very small chance of fistula complexity, which is in contrast to a recurrent fistula where preoperative 3D-HPUS is advocated to delineate exact fistula pattern and avoid unnecessary iatrogenic anal sphincter damage.

Crohn Disease

Abscesses and fistulae are the most common first presentation of perianal Crohn disease.[55] A study in 41 patients assessing fistula classification using 3D-HPUS showed that only 22% of fistulae were single intersphincteric or transsphincteric tracts.[49] Single suprasphincteric or extrasphincteric tracts were present in 12%, rectovaginal and anovaginal fistulae were present in 32%, and secondary tracts were seen in 34% of the patients. In this cohort, 78% of the patients had a complex fistula. Three-dimensional HPUS is highly accurate for delineating the anatomy of complex perianal fistula[52] and for determining the site of the internal fistula opening.[31] However, not all Crohn fistulae are complex; especially on first presentation, it can be difficult to differentiate Crohn disease from cryptoglandular fistulae. To discriminate between the 2, a specific Crohn ultrasound fistula sign has been suggested.[56] It is characterized by the presence of a hypoechoic fistula tract with a surrounding hyperechoic area containing a thin hypoechoic edge. Another 3D-EAUS study suggested Crohn fistulae to have secondary tracts more often, be wider, and have more fistulous hyperechoic debris.[57] Furthermore, degree of hyperechoicity is proposed to be a sign of inflammatory activity of the fistula tract, or of perianal disease activity as a whole.[58,59] More recently, a large 3D-EAUS study confirmed the presence of Crohn ultrasound fistula signs to be a feature of Crohn disease but not cryptogenic fistulae. Therefore, when in doubt, the presence of these Crohn-related features would more likely mandate colonoscopy with mucosal biopsy in selected patients.[60]

EAUS in Crohn Disease

The introduction of biologicals gave physicians the first treatment that could potentially result in complete cessation of perianal fistula drainage in patients with Crohn disease. However, the refractory nature of the disease was highlighted by the first maintenance trials using infliximab and adalimumab. During infliximab treatment, healing of the external opening precedes fistula tract healing, which contributes to abscess formation and fistula recurrence after discontinuation of treatment. Several studies have monitored treatment response using EAUS through observing what was happening to the internal fistula tract at different time point during the healing process.

One EAUS study documented fistula tracts at baseline and after 3 infusions of infliximab (5 mg/kg) in 8 patients with Crohn disease.[61] Patients with vaginal or perineal fistulae did not clinically respond to therapy, whereas patients with perianal fistulae improved considerably. Yet, in all patients, fistulous remainders could still be demonstrated 4 weeks after the last infliximab infusion.

In another study of 30 patients with Crohn disease and perianal or rectovaginal fistulae, 3 infusions of infliximab (5 mg/kg) were given at weeks 0, 2, and 6. Patients underwent EAUS at weeks 0 and 10. Fifteen patients showed closure of the external fistula opening at week 10; yet, EAUS showed full tract disappearance in only 5 patients. Those with a persisting internal tract on EAUS were at higher risk for fistula recurrence.[62] Rectovaginal fistulae had a poorer response (29%) compared with perianal fistulae (59%).

A double-blind placebo-controlled 3D-HPUS study of 24 patients evaluated the effect of combined ciprofloxacin and infliximab treatment.[46] The patients received infliximab (5 mg/kg) at weeks 6, 8, and 12 and were randomly assigned to receive 500 mg of ciprofloxacin twice daily or a placebo for 12 weeks. The patients treated with ciprofloxacin tended to respond better; however, 3D-HPUS improved in only 3 of the 8 patients with a clinical response.

A retrospective study of 21 patients with perianal Crohn disease evaluated the effect of an EAUS protocol where it served as a clinical guideline for combined medical and surgical therapy.[63] All patients underwent baseline EAUS and received maximal medical treatment with infliximab (5 mg/kg), immunosuppressives (6-mercaptopurine, azathioprine), and antibiotics (Ciproxin). Sixteen (76%) patients maintained long-term cessation of drainage, with a median follow-up of 68 weeks (range, 35–101 weeks). Of the 11 patients in whom EAUS showed no persistent fistula activity, 7 patients maintained fistula closure without recurrence after having discontinued their infliximab treatment. The remaining 4 patients continued infliximab to maintain remission of luminal disease.

A prospective study evaluated the efficacy of combined treatment with infliximab and setons for complex perianal fistulae in 9 patients with Crohn disease using EAUS.[64] Setons were removed in 8 patients after a mean (SD) of 30 (16) weeks when EAUS provided evidence of a fully healed fistula tract. Infliximab was discontinued in 6 patients, with a mean (SD) follow-up of 20 (9) months; 5 patients with a clinical and endosonographic response were still without recurrence.

Therefore, short-term treatment with infliximab and/or antibiotics does not induce disappearance of fistulous tracts in Crohn disease, irrespective of therapeutic response. Further combined medical and/or surgical therapy needs to be evaluated to reach structural internal healing of these fistulae. Besides its accuracy in the assessment of fistulae and abscesses in Crohn disease,[46,61–63,65–70] 3D-HPUS might identify patients who can discontinue treatment without recurrence and would therefore be an excellent technique for following these fistulae rather than using MRI each time. However, disease severity is a clinical assessment and is based on both clinical and imaging studies.[70]

CONCLUSIONS

Endoanal ultrasound is a highly accurate tool for the assessment of perianal fistulae in both cryptoglandular and Crohn disease, which can easily be performed in an outpatient setting. The results are comparable with MRI, examination under anesthesia, and surgery, especially when using peroxide as contrast enhancement. In cryptoglandular disease, EAUS should be performed in recurrent fistula because complexity

can be expected and preoperatively mapping the exact fistula pattern can help prevent recurrence. In perianal fistulizing Crohn disease, EAUS can provide reliable end points in the clinical assessment and has the potential to improve outcome of patients. When more proximal fistulae or abscesses are suspected, an additional MRI should be performed.

REFERENCES

1. Abcarian H. Anorectal infection: abscess-fistula. *Clin Colon Rectal Surg*. 2011;24(1):14–21.
2. Sainio P. Fistula-in-ano in a defined population. Incidence and epidemiological aspects. *Ann Chir Gynaecol*. 1984;73(4):219–224.
3. Poen AC, Felt-Bersma RJ, Eijsbouts QA, et al. Hydrogen peroxide-enhanced transanal ultrasound in the assessment of fistula-in-ano. *Dis Colon Rectum*. 1998;41(9):1147–1152.
4. Gustafsson UM, Kahvecioglu B, Aström G, et al. Endoanal ultrasound or magnetic resonance imaging for preoperative assessment of anal fistula: a comparative study. *Colorectal Dis*. 2001;3(3):189–197.
5. Eckardt VF, Jung B, Fischer B, et al. Anal endosonography in healthy subjects and patients with idiopathic fecal incontinence. *Dis Colon Rectum*. 1994;37(3):235–242.
6. Law PJ, Bartram CI. Anal endosonography: technique and normal anatomy. *Gastrointest Radiol*. 1989;14(4):349–353.
7. Nielsen MB, Hauge C, Rasmussen OO, et al. Anal sphincter size measured by endosonography in healthy volunteers. Effect of age, sex, and parity. *Acta Radiol*. 1992;33(5):453–456.
8. Nielsen MB, Pedersen JF. Changes in the anal sphincter with age. An endosonographic study. *Acta Radiol*. 1996;37(3 Pt 1):357–361.
9. Tjandra JJ, Milsom JW, Stolfi VM, et al. Endoluminal ultrasound defines anatomy of the anal canal and pelvic floor. *Dis Colon Rectum*. 1992;35(5):465–470.
10. Sultan AH, Nicholls RJ, Kamm MA, et al. Anal endosonography and correlation with in vitro and in vivo anatomy. *Br J Surg*. 1993;80(4):508–511.
11. Gerdes B, Köhler HH, Zielke A, et al. The anatomical basis of anal endosonography. A study in postmortem specimens. *Surg Endosc*. 1997;11(10):986–990.
12. Papachrysostomou M, Pye SD, Wild SR, et al. Significance of the thickness of the anal sphincters with age and its relevance in faecal incontinence. *Scand J Gastroenterol*. 1994;29(8):710–714.
13. Loder PB, Kamm MA, Nicholls RJ, et al. Haemorrhoids: pathology, pathophysiology and aetiology. *Br J Surg*. 1994;81(7):946–954.
14. Poen AC, Felt-Bersma RJ, Cuesta MA, et al. Anal endosonography in haemorrhoidal disease: do anatomical changes have clinical implications? *Colorectal Dis*. 1999;1(3):146–150.
15. Sultan AH, Kamm MA, Hudson CN, et al. Endosonography of the anal sphincters: normal anatomy and comparison with manometry. *Clin Radiol*. 1994;49(6):368–374.
16. Papachrysostomou M, Pye SD, Wild SR, et al. Anal endosonography in asymptomatic subjects. *Scand J Gastroenterol*. 1993;28(6):551–556.
17. Schäfer R, Heyer T, Gantke B, et al. Anal endosonography and manometry: comparison in patients with defecation problems. *Dis Colon Rectum*. 1997;40(3):293–297.
18. Emblem R, Dhaenens G, Stien R, et al. The importance of anal endosonography in the evaluation of idiopathic fecal incontinence. *Dis Colon Rectum*. 1994;37(1):42–48.
19. Burnett SJ, Bartram CI. Endosonographic variations in the normal internal anal sphincter. *Int J Colorectal Dis*. 1991;6(1):2–4.
20. Klosterhalfen B, Offner F, Topf N, et al. Sclerosis of the internal anal sphincter—a process of aging. *Dis Colon Rectum*. 1990;33(7):606–609.
21. Murad-Regadas SM, Regadas FS, Rodrigues LV, et al. Effect of vaginal delivery and ageing on the anatomy of the female anal canal assessed by three-dimensional anorectal ultrasound. *Colorectal Dis*. 2012;14(12):1521–1527.
22. Lunniss PJ, Phillips RK. Anatomy and function of the anal longitudinal muscle. *Br J Surg*. 1992;79(9):882–884.
23. Poen AC, Felt-Bersma RJ, Cuesta MA, et al. Vaginal endosonography of the anal sphincter complex is important in the assessment of faecal incontinence and perianal sepsis. *Br J Surg*. 1998;85(3):359–363.
24. Rosa G, Lolli P, Piccinelli D, et al. Fistula in ano: anatomoclinical aspects, surgical therapy and results in 844 patients. *Tech Coloproctol*. 2006;10(3):215–221.
25. Parks AG, Gordon PH, Hardcastle JD. A classification of fistula-in-ano. *Br J Surg*. 1976;63(1):1–12.
26. Law PJ, Talbot RW, Bartram CI, et al. Anal endosonography in the evaluation of perianal sepsis and fistula in ano. *Br J Surg*. 1989;76(7):752–755.
27. Deen KI, Williams JG, Hutchinson R, et al. Fistulas in ano: endoanal ultrasonographic assessment assists decision making for surgery. *Gut*. 1994;35(3):391–394.
28. Lengyel AJ, Hurst NG, Williams JG. Pre-operative assessment of anal fistulas using endoanal ultrasound. *Colorectal Dis*. 2002;4(6):436–440.
29. Cataldo PA, Senagore A, Luchtefeld MA. Intrarectal ultrasound in the evaluation of perirectal abscesses. *Dis Colon Rectum*. 1993;36(6):554–558.
30. Lindsey I, Humphreys MM, George BD, et al. The role of anal ultrasound in the management of anal fistulas. *Colorectal Dis*. 2002;4(2):118–122.
31. Cho DY. Endosonographic criteria for an internal opening of fistula-in-ano. *Dis Colon Rectum*. 1999;42(4):515–518.
32. Choen S, Burnett S, Bartram CI, et al. Comparison between anal endosonography and digital examination in the evaluation of anal fistulae. *Br J Surg*. 1991;78(4):445–447.
33. Cheong DM, Nogueras JJ, Wexner SD, et al. Anal endosonography for recurrent anal fistulas: image enhancement with hydrogen peroxide. *Dis Colon Rectum*. 1993;36(12):1158–1160.
34. Ratto C, Gentile E, Merico M, et al. How can the assessment of fistula-inano be improved? *Dis Colon Rectum*. 2000;43(10):1375–1382.
35. Navarro-Luna A, García-Domingo MI, Rius-Macías J, et al. Ultrasound study of anal fistulas with hydrogen peroxide enhancement. *Dis Colon Rectum*. 2004;47(1):108–114.
36. Konerding MA, Dzemali O, Gaumann A, et al. Correlation of endoanal sonography with cross-sectional anatomy of the anal sphincter. *Gastrointest Endosc*. 1999;50(6):804–810.
37. Gravante G, Giordano P. The role of three-dimensional endoluminal ultrasound imaging in the evaluation of anorectal diseases: a review. *Surg Endosc*. 2008;22(7):1570–1578.
38. Fishman-Javitt MC, Lovecchio JL, Javors B, et al. The value of MRI in evaluating perirectal and pelvic disease. *Magn Reson Imaging*. 1987;5(5):371–380.
39. Orsoni P, Barthet M, Portier F, et al. Prospective comparison of endosonography, magnetic resonance imaging and surgical findings in anorectal fistula and abscess complicating Crohn's disease. *Br J Surg*. 1999;86(3):360–364.
40. Lunniss PJ, Barker PG, Sultan AH, et al. Magnetic resonance imaging of fistula-in-ano. *Dis Colon Rectum*. 1994;37(7):708–718.
41. Schwartz DA, Wiersema MJ, Dudiak KM, et al. A comparison of endoscopic ultrasound, magnetic resonance imaging, and exam under anesthesia for evaluation of Crohn's perianal fistulas. *Gastroenterology*. 2001;121(5):1064–1072.
42. Hussain SM, Stoker J, Schouten WR, et al. Fistula in ano: endoanal sonography versus endoanal MR imaging in classification. *Radiology*. 1996;200(2):475–481.
43. West RL, Zimmerman DD, Dwarkasing S, et al. Prospective comparison of hydrogen peroxide-enhanced three-dimensional endoanal ultrasonography and endoanal magnetic resonance imaging of perianal fistulas. *Dis Colon Rectum*. 2003;46(10):1407–1415.
44. West RL, Dwarkasing S, Felt-Bersma RJ, et al. Hydrogen peroxide-enhanced three-dimensional endoanal ultrasonography and endoanal magnetic resonance imaging in evaluating perianal fistulas: agreement and patient preference. *Eur J Gastroenterol Hepatol*. 2004;16(12):1319–1324.
45. Spencer JA, Chapple K, Wilson D, et al. Outcome after surgery for perianal fistula: predictive value of MR imaging. *AJR Am J Roentgenol*. 1998;171(2):403–406.
46. West RL, van der Woude CJ, Hansen BE, et al. Clinical and endosonographic effect of ciprofloxacin on the treatment of perianal fistulae in Crohn's disease with infliximab: a double-blind placebo-controlled study. *Aliment Pharmacol Ther*. 2004;20(11–12):1329–1336.
47. deSouza NM, Gilderdale DJ, Coutts GA, et al. MRI of fistula-in-ano: a comparison of endoanal coil with external phased array coil techniques. *J Comput Assist Tomogr*. 1998;22(3):357–363.

48. Sudol-Szopinska I, Szczepkowski M, Panorska AK, et al. Comparison of contrast-enhanced with non-contrast endosonography in the diagnostics of anal fistulas. *Eur Radiol*. 2004;14(12):2236–2241.
49. Sloots CE, Felt-Bersma RJ, Poen AC, et al. Assessment and classification of fistula-in-ano in patients with Crohn's disease by hydrogen peroxide enhanced transanal ultrasound. *Int J Colorectal Dis*. 2001;16(5): 292–297.
50. Buchanan GN, Bartram CI, Williams AB, et al. Value of hydrogen peroxide enhancement of three-dimensional endoanal ultrasound in fistula-in-ano. *Dis Colon Rectum*. 2005;48(1):141–147.
51. Nagendranath C, Saravanan MN, Sridhar C, et al. Peroxide-enhanced endoanal ultrasound in preoperative assessment of complex fistula-in-ano. *Tech Coloproctol*. 2014;18(5):433–438.
52. Kim Y, Park YJ. Three-dimensional endoanal ultrasonographic assessment of an anal fistula with and without H(2)O(2) enhancement. *World J Gastroenterol*. 2009;15(38):4810–4815.
53. Becker A, Koltun L, Sayfan J. Simple clinical examination predicts complexity of perianal fistula. *Colorectal Dis*. 2006;8(7):601–604.
54. Sloots CE, Felt-Bersma RJ, Poen AC, et al. Assessment and classification of never operated and recurrent cryptoglandular fistulas-in-ano using hydrogen peroxide enhanced transanal ultrasound. *Colorectal Dis*. 2001;3(6):422–426.
55. Lewis RT, Maron DJ. Anorectal Crohn's disease. *Surg Clin North Am*. 2010;90(1):83–97.
56. Zawadzki A, Starck M, Bohe M, et al. A unique 3D endoanal ultrasound feature of perianal Crohn's fistula: the 'Crohn ultrasound fistula sign'. *Colorectal Dis*. 2012;14(9):e608–e611.
57. Blom J, Nyström PO, Gunnarsson U, et al. Endoanal ultrasonography may distinguish Crohn's anal fistulae from cryptoglandular fistulae in patients with Crohn's disease: a cross-sectional study. *Tech Coloproctol*. 2011;15(3):327–330.
58. Losco A, Viganò C, Conte D, et al. Assessing the activity of perianal Crohn's disease: comparison of clinical indices and computer-assisted anal ultrasound. *Inflamm Bowel Dis*. 2009;15(5):742–749.
59. Caprioli F, Losco A, Viganò C, et al. Computer-assisted evaluation of perianal fistula activity by means of anal ultrasound in patients with Crohn's disease. *Am J Gastroenterol*. 2006;101(7):1551–1558.
60. Zbar AP, Horesh N, Bucholtz V, et al. Are there specific endosonographic features in Crohn's patients with perianal fistulae? *J Crohns Colitis*. 2013;7(6):490–496.
61. van Bodegraven AA, Sloots CE, Felt-Bersma RJ, et al. Endosonographic evidence of persistence of Crohn's disease-associated fistulas after infliximab treatment, irrespective of clinical response. *Dis Colon Rectum*. 2002;45(1):39–45.
62. Ardizzone S, Maconi G, Colombo E, et al. Perianal fistulae following infliximab treatment: clinical and endosonographic outcome. *Inflamm Bowel Dis*. 2004;10(2):91–96.
63. Schwartz DA, White CM, Wise PE, et al. Use of endoscopic ultrasound to guide combination medical and surgical therapy for patients with Crohn's perianal fistulas. *Inflamm Bowel Dis*. 2005;11(8):727–732.
64. Guidi L, Ratto C, Semeraro S, et al. Combined therapy with infliximab and seton drainage for perianal fistulizing Crohn's disease with anal endosonographic monitoring: a single-centre experience. *Tech Coloproctol*. 2008;12(2):111–117.
65. Schratter-Sehn AU, Lochs H, Vogelsang H, et al. Endoscopic ultrasonography versus computed tomography in the differential diagnosis of perianorectal complications in Crohn's disease. *Endoscopy.* 1993;25(9):582–586.
66. Schratter-Sehn AU, Lochs H, Handl-Zeller L, et al. Endosonographic features of the lower pelvic region in Crohn's disease. *Am J Gastroenterol*. 1993;88(7):1054–1057.
67. Solomon MJ. Fistulae and abscesses in symptomatic perianal Crohn's disease. *Int J Colorectal Dis*. 1996;11(5):222–226.
68. Van Outryve MJ, Pelckmans PA, Michielsen PP, et al. Value of transrectal ultrasonography in Crohn's disease. *Gastroenterology.* 1991;101(5): 1171–1177.
69. Solomon MJ, McLeod RS, Cohen EK, et al. Anal wall thickness under normal and inflammatory conditions of the anorectum as determined by endoluminal ultrasonography. *Am J Gastroenterol*. 1995;90(4):574–578.
70. Lew RJ, Ginsberg GG. The role of endoscopic ultrasound in inflammatory bowel disease. *Gastrointest Endosc Clin N Am*. 2002;12(3):561–571.
71. Schwartz DA, Pemberton JH, Sandborn WJ. Diagnosis and treatment of perianal fistulas in Crohn disease. *Ann Intern Med*. 2001;135(10): 906–918.