

Application of Endorectal Ultrasound in Evaluation of Anorectal Diseases

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INTRODUCTION

In the early 1980s, ERUS was initially introduced to clinical practice to evaluate the prostate^[1]. In 1985, Hildebrandt *et al*^[2] firstly introduced ERUS as a method to stage rectal carcinoma. Since then, it has been used in the diagnosis of various anorectal diseases and disorders. By utilizing 3-dimensional (3D) ERUS, high spatial resolution mechanically rotating endoprobe and other new techniques, it is possible to diagnose the anorectal diseases in multilane and significantly improved the imaging of anorectal diseases. Over the past three decades, ERUS has been progressively used and now considered to be an integral part of the investigation of various anorectal diseases^[3].

Techniques

ERUS can be performed with either blind, rigid probes or flexible echoendoscopes. (Figure 1) Several frequencies are available. While high frequencies have better resolution to evaluate the rectal wall and sphincter complex, lower ones are helpful to exam the mesorectum or deep lesions. Intravenous sedation is not necessary but is optional if the patient cannot tolerate the procedure. Patients with rectal diseases should prepare the rectum with fleets enema in advance, because fecal material can distort the images obtained and reduce the accuracy of diagnose. However, bowel preparation is not necessary for patients with anal diseases. ERUS are usually performed in left lateral decubitus position. Supine lithotomy position or prone position can also be used if needed. Radial positions around the anus are referenced with respect to a clock face. Thus, 12 o'clock represents anterior side, 3 o'clock represents left side, 6 o'clock represents posterior side, and 9 o'clock represents right side. Prior to the procedure, careful inspection of the perianal area followed by a digital examination is essential. A digital rectal examination should be performed to assess sphincter tone or palpate the lesion. If the lesion is palpable, the location, distance from the anal verge, fixation and mobility of the lesion should be

ABSTRACT

Endorectal ultrasound (ERUS) has become an acknowledged technique for imaging anal sphincters, rectum and pelvic floor in the patients with different kinds of anorectal diseases. ERUS can accurately depict internal sphincter (IS) and external sphincter (ES). Therefore, it is valuable in the diagnosis of faecal incontinence and perianal fistulae. Besides, it is reliable for staging rectal tumors, even after neoadjuvant therapy, and is widely used in the surveillance of rectal cancer patients. The paper mainly reviews the indications and application of ERUS in clinical practice, and some new developments of ERUS.

Key words: Endorectal ultrasound; Anorectal diseases; Diagnosis; Rectum; Ano

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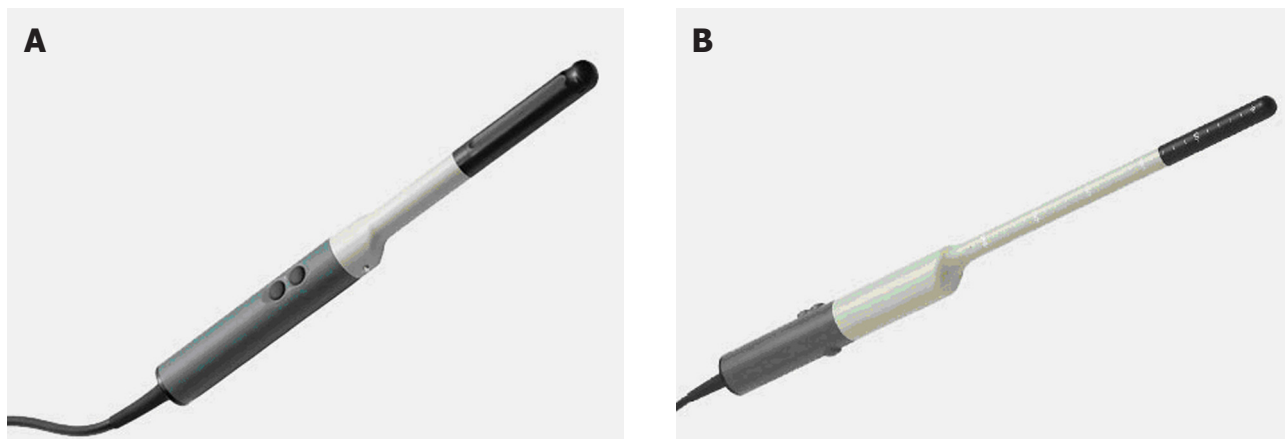


Figure 1 Rigid probes of ERUS. (A) Bi-planar endoprobe, frequency range: 4-12MHz, detailed high resolution biplane with 6.5 cm linear and convex views (180°). (B) Three dimensional endoprobe, frequency range: 6-16MHz, 360 degree real-time scanning with ability to form a three dimensional data cube of the anorectum. (Cited from <http://www.bkmed.cn/>).

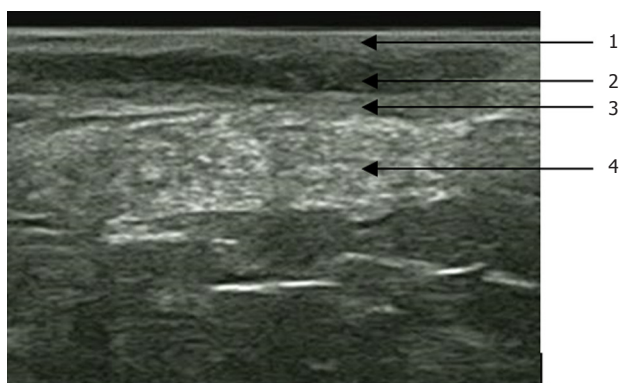


Figure 2 ERUS image of normal anal canal. 1: subepithelial tissues (isoechogenic); 2: IS (hypoechoic); 3: longitudinal muscle (variable echogenic); 4: ES (variable echogenic).

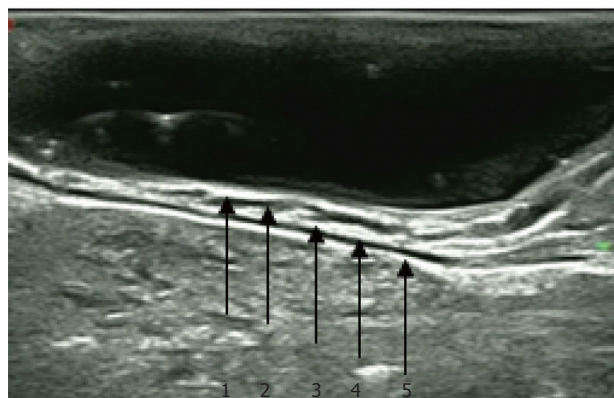


Figure 3 US image of rectum. 1: interface of the condom/covering balloon/water bath and mucosa (hyperechoic); 2: deep mucosa and muscularis mucosa (hypoechoic); 3: Submucosa (hyperechoic); 4: muscularis propria (hypoechoic); 5: interface between the serosa and perirectal fat (hyperechoic).

described. The probe with a condom protected is then slowly inserted and advanced into the rectum. During this procedure, the anorectal angle should be remembered. When accessing rectal tumors, the probe should advance over the lesion to achieve satisfactory imaging over the length of the lesion and fully observe the mesorectum around the lesion. When accessing anal canal diseases, the probe should be slowly withdraw down the anal canal. When the lesion is located in the rectal ampulla, special water filled balloons should usually be applied. The balloon is filled with sufficient water, which compress the lesion and removes the air from the rectum. In most cases, 50-60 mL of water is enough, but it should be adjusted according to the rectal diameter^[3]. Instead of the standard water-balloon filling technique, Wang *et al*^[4] developed a novel technique by injecting the coupling gel into the rectum directly. The amount of gel was usually 100-150 mL, depending on filling degree of the rectum. The gel helped the probe pass through the tumoral stenosis of rectum, minimized compression and distortion of the tumors, and improved visualization of the rectal wall and tumor. Moreover, it is much easier to perform and less expensive. ERUS with color or power Doppler imaging may offer additional information in detecting and characterizing rectal neoplasm and inflammatory, distinguishing perirectal lymph nodes from vessels, and differentiating tumor/fistulas recurrence from postsurgical fibrosis^[5,6].

Normal anatomy and morphology

In anatomy, the rectum is separated into the anus, anal canal and ampulla. In clinical, the last two parts are separated into the lower,

middle and upper third rectum. The anal verge, which is the upper anal margin located at lowest point of the ES (anal verge), is a principal landmark for all other rectal measurements. Because of the different tissue-dependent reflection of the ultrasound, ERUS can easily show the structure of anal sphincter, rectum and mesorectum.

The anal canal: The normal anatomy of anal canal consists of 4-layer structure with subepithelial tissues (isoechogenic), IS (hypoechoic), longitudinal muscle (variable echogenic) and ES (variable echogenic) (Figure 2)^[7,8].

The ampulla of rectum: Typically, five layers of the rectal wall can be seen on ERUS: three hyperechoic and two hypoechoic ones. From inner to outermost layer, they are as follows: interface of the condom/covering balloon/water bath and mucosa (hyperechoic), deep mucosa and muscularis mucosa (hypoechoic), submucosa (hyperechoic), muscularis propria (hypoechoic), and interface between the serosa and perirectal fat (hyperechoic). The perirectal fat has mixed echogenicity and perirectal lymph nodes (hypoechoic) may occasionally be seen (Figure 3)^[9].

CLINICAL APPLICATION

Benign disease

Because ERUS can accurately depict the IS and ES with high

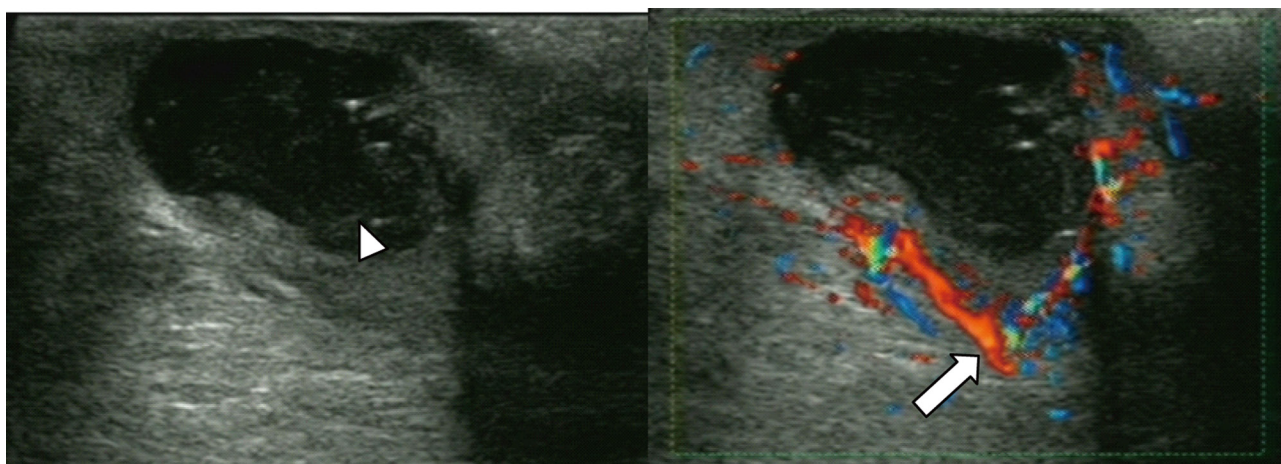


Figure 4 A 47-year-old male patient with perianal abscess. (A) On ERUS perianal abscess appeared as hypoechoic area with internal echoes of cellular debris (white arrow head). (B) Color Doppler showed no signal of the hypoechoic area, but abundant blood flow signal of the boundary (white arrow).

resolution, it plays an important role in the diagnosis of benign diseases, such as faecal incontinence and inflammatory conditions.

Faecal incontinence: Although faecal incontinence may be the result of several causes, the highly prevalent reason is anal sphincter injury, as a result of consequence of obstetrical trauma, anorectal surgery or accidental injury^[10].

ERUS is the best choice for imaging the morphology of the anal sphincter, and can recognize defects that are responsible for faecal incontinence. At present, patients with faecal incontinence should firstly take a test of ERUS to identify whether they have sphincter defects and those patients may benefit from surgical repair. Common sphincter disruption because of vagina delivery often relates to ES injury, especially anterior ES. Injuries caused by trauma, most commonly by surgery, often relate to isolated IS injury. Neurologic degeneration and other uncertain reasons may cause sphincter atrophy^[11,12].

Hussain *et al*^[13] classified anal sphincter damages as localized scarring, generalized scarring, localized defects, fragmentation, and atrophy. Replacement of muscle fibers by scar tissue cause localized or generalized scarring, which appears as mixed echogenicity on ERUS. The discontinuity in the ring structure is defined as sphincter defects. An IS defect appears as an interruption in the hypoechoic ring, and ES defect appears as a break, usually hypoechoic in the normal texture of the echogenic muscle ring. Sometimes, some defects may be hyperechoic and of mixed echogenicity. Fragmentation of the anal sphincter is recognized by two or more fragments in the axial plane^[14]. An extreme thinning of the sphincter fibers or a generalized fatty infiltration could be considered as the sign of sphincter atrophy or degenerative. The thinning of the sphincter or heterogeneous increased echogenicity on ERUS can indirectly indicate the sphincter atrophic or degenerative is present^[15]. Generally, the thickness of anterior muscle of the mid-anal canal is 10-15 mm, but should not less than 6 mm. However, at older ages, ES muscle could be thinner^[16]. Recently, some studies found that 3D-ERUS could provide more information on the anal sphincters than traditional 2D-ERUS and might be able to measure sphincter accurately to predict the presence of ES atrophy^[17].

The anterior ES of female is much shorter than that of the male, and this normal anatomical characteristic may be confused with an ES defect. Besides, at the lower canal level, the triangular hypoechoic anococcygeal ligament on the axial images posterior should not be mistaken for a sphincter defect^[14]. Female may suffer from undetected anal defects after childbirth which might be associated

with subsequent faecal incontinence. ERUS is also helpful in the early diagnosis of this defect, which might help in the prevention of anal incontinence^[18,19].

ERUS presents sphincter defects accurately and patients can thus be carefully selected for sphincter repair. Moreover, ERUS is also useful for patients who have a failed surgery repair with persistent faecal incontinence. Repeat repair following exactly imaging the sphincter can improve continence.

Inflammatory conditions: Infection in small intersphincteric anal glands basically located at the dentate line often results in perianal abscess and fistula in ano^[20]. Perianal inflammatory diseases are often with Crohn's disease. Nearly one third of all Crohn's disease patients suffer from perianal fistulas or abscesses^[21].

(1) Perianal abscesses: Most perianal abscesses are evident on clinical examination. Suitable recognition and prompt drainage is the routine therapeutic schedule. Although the presence of an abscess is strongly suspected, it cannot be correctly recognized on clinically physical examination. Under these circumstances, ERUS can provide important information in confirming and recognizing an abscess. Abscess usually appears as anechoic or hypoechoic areas (with internal echoes of cellular debris), and often surrounded by hyperechoic borders (Figure 4, 5)^[13]. ERUS can be used to distinguish inflammation from abscess, which is helpful for the clinicians to choose between medical and surgical treatment. When an abscess is suspected, ERUS should identify its relationship with the ano and detect whether a fistula has existed^[22]. Moreover, ERUS can assist in preoperatively puncturing abscesses. A retrospective study showed that 3D-ERUS could add information for 69% of patients with abscess and assisted in planning and performing endocavity drainages of deep pelvic fluid collections^[23,24].

(2) Fistula in ano: Fistula in ano occurs in about 10 per 100000 individuals and it is a common benign anal disease seen in clinical^[25]. The most comprehensive and practical classification in use today is the Parks classification. Parks *et al*^[26] found that they were able to assign all fistulas into one of four groups: intersphincteric (low or high) type (45% of cases), transsphincteric (low or high) type (30%), suprasphincteric (high) type (20%) and extrasphincteric (high) type (3%) (Figure 6). But it should be proposed that Parks did not describe submucosal fistula (low), which are extremely superficial and do not involve the sphincter at all.

Fistulas may originate below or above the dentate line, and then are classified as low or high. In clinical practice, fistulas are

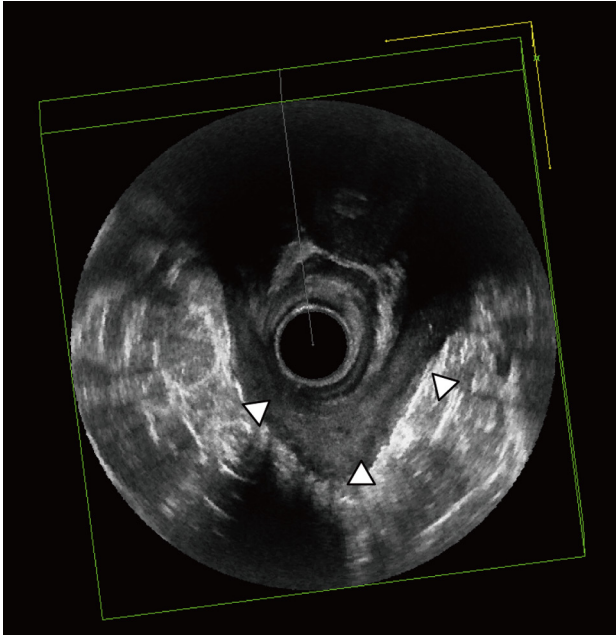


Figure 5 A 26-year-old male patient with horseshoe abscess, US showed hypoechoic area (white arrow heads) of horse shoe shape.

also classified as either simple or complex. A simple fistula is a superficial, intersphincteric, or low transsphincteric fistula, which has only one opening, has no perianal abscess or rectovaginal fistula. And a complex fistula is high, has multiple external openings, and has a perianal abscess or a rectovaginal fistula^[27].

Surgery is the main effective treatment for fistula in ano. Regardless of seemingly adequate surgery, anal fistula has a tendency to recrudescence. Moreover, if fistula anatomy is delineated incorrectly or an occult abscess or secondary fistula is missed, the fistula cannot be completely cured and highly to recurrence. It is now gradually acknowledged that preoperative imaging can help identify abscess and accessory tracts that are easy unidentified^[28]. MRI is the gold standard of imaging the fistula tracts. It is reported that MRI guided surgery helps reduce postoperative recurrence by 75% in patients with complex disease. However, because of financial constraints, some patients were not possible to undergo MRI. ERUS is a viable alternative to MRI^[28]. Preoperative ERUS for fistula in ano is able to identify the internal opening and the fistula tracts. Besides, relationship to the muscles and surrounding areas and anatomic integrity of the anal sphincter could also be evaluated by ERUS.

ERUS sign of fistula is continuous linear structure. Fluids present within the tract appear to be hypoechoic and air within the fistula appears to be hyperechoic. The criteria for the internal opening include hypoechoic gap in the subepithelial area, a defect in the IS, and a hypoechoic area in the intersphincteric space. In clinical, a tract extending up to the subepithelial area is rarely seen, although the opening is usually positioned right at the probe surface. A hypoechoic focus in the intersphincteric space that abuts the internal sphincter is a common indirectly sign for the presence of the internal opening. The depiction of fistulas by ERUS permits accurate classification, which plays an important role in surgical planning. ERUS has a good accuracy in identifying intrasphincteric and transsphincteric tracts, however, extrasphincteric, suprasphincteric, and secondary supralevator or infralevator tracts might be missed owing to the limited depth of penetration^[29].

In a preoperative study, by comparing ERUS with intraoperative

findings for simple fistula in ano, ERUS detected the presence of the fistula in most cases (95.3%, 61/64) and the accuracy of ERUS for detecting the site of fluid collection was 86.9%^[28]. For complex fistulas, 3% hydrogen peroxide solution could be injected directly into the canal from the external opening. The hydrogen peroxide will then fill the tract and produce hyperechoic gas, allowing visualization of entire course of the fistula, including its relation to the internal and external sphincters and the levatorani muscle. A subsequent study found that diagnostic accuracy was improved after hydrogen peroxide injection was used^[30]. 3D-ERUS might be more accurate than ERUS in assessing the fistula tracks and the internal opening, because it could depict the fistula in different angles^[31]. West *et al.*^[32] combined the use of 3D-ERUS and hydrogen peroxide to evaluate the fistula with a high accuracy. Buchanan *et al.* found no significant difference between 3D-ERUS and hydrogen peroxide enhanced 3D-ERUS in classifying internal openings (90% vs 86%), primary tracks (81% vs 71%), and secondary tracks (68% vs 63%). However, gas made primary tracks more conspicuous for 32% of those detected and secondary tracks for 46%, suggesting that hydrogen peroxide may be helpful in difficult cases^[33]. Recently, transperineal ultrasound is reported helpful to diagnose fistula in some circumstances, for example, the patients with rectum stenosis, anal canal distortion, rectovaginal fistula or complex fistula^[34,35].

In addition, ERUS can be performed in the operating room, so the surgeons can be accurately informed the fistula tract anatomy. ERUS can also be helpful puncture the abscesses. ERUS-guided drainage of deep pelvic abscesses could be considered in carefully selected patients as adjunctive or alternative treatment to surgery, especially for the patients with comorbidities^[24].

Some studies have found that ERUS to be useful, while others found it to be no better than digital rectal examination. Much of the discrepancy may be owing to the operator's experience. But beyond that, for fistula ERUS has some undoubtedly limitations: (a) without sufficient penetration a tendency to miss ischioanal and supralevator infections; (b) ERUS cannot distinguish recurrent fistulas or infections from postoperative fibrosis, for they are both hypoechoic; (c) gas produced by hydrogen peroxide within the tract may cause acoustic shadowing that mimics an extension^[36].

(3) Perianal fistula Crohn's disease: Crohn's disease (CD) is a chronic inflammatory disease of the gastrointestinal tract. Perianal fistula is one of the major complications of CD, which is also an indicator as a more aggressive phenotype of CD^[37]. It is estimated that about 20-26% of patients with CD have perianal fistulas and most of the fistulas are complex^[38,39]. Accurate and early detection of the presence of fistulas is the key to control the disease. Utilizing diagnostic imaging is the best means to identify the early signs of perianal fistulas or abscesses formation and ERUS and pelvic MRI are known as the most useful modalities^[36]. When ERUS is performed, it is of vital importance to accurately identify the fistulas, the presence of secondary extension and the presence of abscess. The use of 3D-ERUS and addition of hydrogen peroxide and transperineal ultrasound can help display complex fistulas, especially for the perianal fistula CD^[40,41].

ERUS is an available tool to monitor the effect of treatment in the therapy of perianal CD. Medicines such as Infliximab, is effective in the treatment of perianal CD. In result, early assessment of treatment response can be essential evidence for the following therapy^[42]. Overall, utilizing ERUS in the longitudinal surveillance of perianal fistulas improve outcomes for patients with CD^[43].

Some studies tried to use ERUS to differentiate CD from fistula in ano. They identified a thin hypoechoic edge branched or the presence

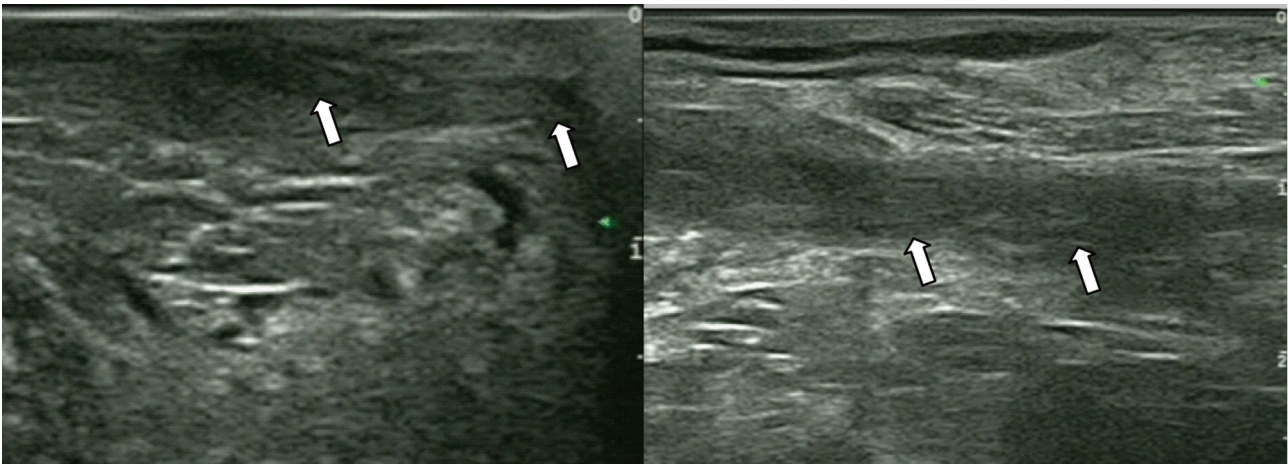


Figure 6 US image of fistulas (white arrows), (A) A 33-year-old female patient with intersphincteric fistulae. US showed continuous hypoechoic linear structure in the intersphincter (B) A 47-year-old male patient with extrasphincteric fistulae. US showed continuous hypoechoic linear structure outside the ES.

of hyperechoic debris within a fistula or bifurcation of a fistula complex as the sign of CD fistula, which had a good specificity, positive predictive value and negative predictive value^[44,45].

In conclusion, ERUS can better optimize the outcomes for fistulas, especially for CD patients.

Others benign diseases: Some studies reports that ERUS may have an important role in assessing endometriosis infiltrating the rectum^[46,47]. ERUS has also been performed in anorectal diseases without a direct clinic impact, such as constipation, haemorrhoids and anal fissure. But by now ERUS has no place in the clinical work-up with these diseases^[48].

Neoplasm

In Western countries, colorectal cancer is the second most common reason of cancer-related deaths, and nearly 30% of these cancers arise in the rectum^[49]. Among the colorectal cancers, 98% are adenocarcinomas^[50]. Generally, tumors located within 12 cm of the anal verge are defined as rectal tumor^[51].

Adenocarcinomas: For treating rectal carcinoma, it is essential to have adequate preoperative imaging, because accurate staging can influence the therapeutic strategy, type of surgery, and candidacy for preoperative neoadjuvant therapy.

The treatment and prognosis of rectal cancer is mainly determined by its local stage. Accurate staging of rectal cancer should describe depth of invasion, presence of malignant lymph node and relationship with the mesorectal fascia (MRF). Above all, assessment of the cancer invasion through the bowel wall remains the primary and most important factor in treatment of patients with rectal cancer^[52].

Classically, rectal tumors are staged according to TNM stage. ERUS is highly accurate in the assessment of the T stage and N stage^[53]. But, this classification is only appropriate to adenocarcinomas, not benign or other tumors such as sarcoma, lymphoma, carcinoids and melanoma.

(1) T stage: Since 1985, Hildebrant *et al*^[2] firstly used ERUS to stage rectal cancer. ERUS has become the primary method for loco regional staging of rectal cancer. Nowadays, ERUS is the most accurate modality for depicting local depth of invasion of rectal cancer into the rectal wall layers (T stage)^[52,54].

Rectal carcinoma appears on ERUS as a hypoechoic lesion with abundant blood signals that abruptly interrupts the normal sequence of layers. And morphology the lesions is various according to their

classifications. Ultrasonographic staging of tumor depth is denoted by the prefix "u". An uT1 tumor is confined to the submucosa with no extension to the muscularis propria. Complete disruption of the submucosa, penetrating the muscularis propria, indicates an uT2 tumor. An uT3 tumor extends through the muscularis propria into the perirectal tissue. An uT4 tumor is diagnosed by invasion of adjacent organs or the pelvic wall (Figure 7, 8)^[55,56]. However, for cancer located within anal canal, the staging system is based on whether the tumor involve IS or ES. When the tumor involve the IS with no extension to the intersphincter, it is an uT2 tumor. When penetrating the intersphincter, it is an uT3 tumor. An uT4 tumor is diagnosed by invasion of ES^[57].

A meta-analysis evaluating all ERUS studies from 1980 to 2008 involving 5039 patients with rectal cancer showed that the pooled sensitivity of ERUS for T stage is high (approximately 88-95%). For T1, the sensitivity and specificity of ERUS is 87.8% and 98.3%, and the corresponding data are 80.5% and 95.6% for T2, 96.4% and 90.6% for T3, and 95.4% and 98.3% for T4^[58]. In our center, we evaluated 31 patients with rectal cancer without preoperative neoadjuvant chemo radiation therapy by ERUS, the diagnostic accuracy of T1, T2, T3, and T4 staging for ERUS was 93.55%, 93.55%, 87.10%, and 100%. The overall accuracy was 93.55%. These results show good agreement with data from literatures.

Transanal endoscopic microsurgery (TEM) and endoscopic submucosal dissections have been widely used for patients with early rectal cancer because they can preserve the postoperative defecation function. But these surgeries require accurate assessment whether tumor has breached to the submucosa. It has been reported that ERUS is accurate at predicting early disease than other imaging modalities, because of its higher anatomical resolution. Glancy *et al*^[59] reported a prospective study with 62 patients underwent TEM. They found that the accuracy of ERUS at detecting early disease was 95%, and only 5% were over staged, and with no case under staged.

But, in some cases, ERUS might over stage T2 tumors as T3 tumors, because ERUS cannot precisely distinguish an irregular outer rectal wall due to inflammation or real transmural tumor extension^[58,60].

(2) N stage: For the patients with rectal cancer, the malignant lymph nodes in the perirectal fat adversely affect the prognosis and survival. Suspected lymph node metastases are a strong indication for preoperative treatment^[61]. In TNM stage for the rectal cancer, N

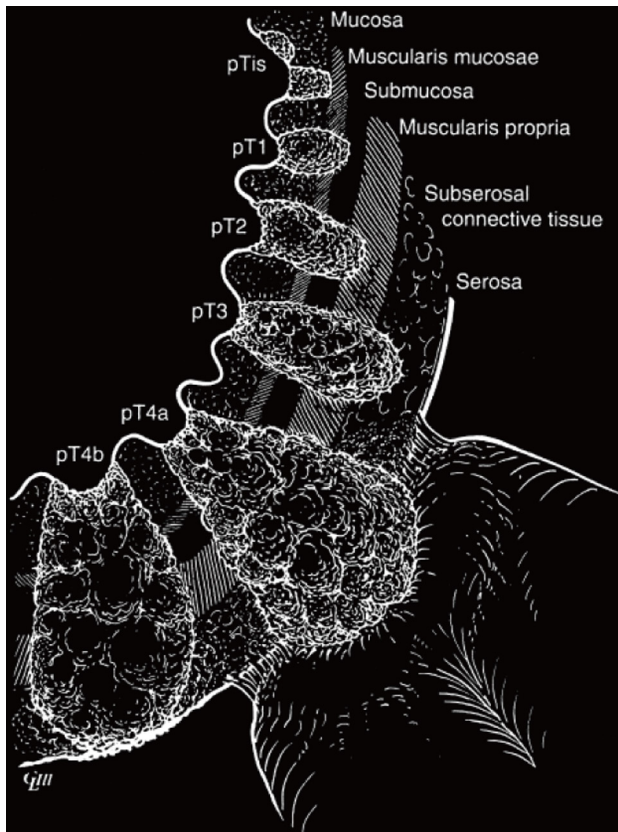


Figure 7 Depiction of the subdivision of the pT category; a T1 tumor is confined to the submucosa; a T2 tumor completely disrupts the submucosa and penetrates the muscularis propria; a T3 tumor extends through the muscularis propria into the perirectal tissue; a T4 tumor is diagnosed by invasion of adjacent organs or the pelvic wall. (Cited from American Joint Committee on Cancer Prognostic Factors Consensus Conference, Cancer 2000).

stage is influenced by the number of metastatic lymph nodes. One to three malignant lymph nodes in perirectal fat are defined as N1 stage, while more than 3 malignant lymph nodes are defined as N2 stage^[53]. However, nowadays, N stage of the rectal cancer remains an unsolved difficulty, because the lack of proper radiological criteria for nodal metastatic changes in the pelvis. Although radiological criteria for the lymph node invasion varies among investigators, the most common criteria is that nodes with diameter large than 5mm should be considered invasion^[62]. ERUS is better at evaluating lymph nodes in the distal and middle thirds of the rectum. The sonographic criteria for malignant lymph nodes consist of size greater than 5mm, irregular margins, mixed echogenicity, and spherical rather than ovoid or flat shape, with size as the most crucial factor^[52].

Generally, ERUS is not as accurate for predicting N stage as for T stage. The lower accuracy of N stage is attributed to the observation that up to 50% of the malignant nodes are less than 5mm in diameter^[62]. Brown *et al.*^[63] evaluated 284 nodes in rectal cancer with use of high spatial resolution MR imaging with histopathologic comparison. Using the criteria of size greater than 3 mm, the sensitivity and specificity for nodal detection was 78% and 59%; using 5 mm, was 42% and 87%; using 10 mm, was 3% and 100%. Because lymph nodes can harbor micro metastasis or minimetastasis, which does not always change uniform or size of the lymph nodes. Besides, the reactive swollen lymph nodes could be mistaken as malignant. On ERUS, the small blood vessels, urethra, and seminal vesicle can also simulate metastatic lymph nodes, but by moving the

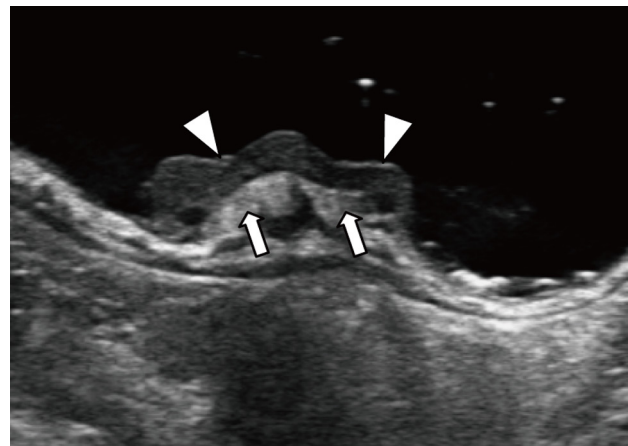


Figure 8 A 41-year-old male patient with rectal tumor (white arrow heads). On ERUS, the tumor was confined to the submucosa (white arrow), thus staged as an uT1 tumor.

transducer to outline the linear course or by color/power Doppler, they can easily be distinguished.

To improve the accuracy, the size of the lymph nodes should be measured in different planes on ERUS to ensure the size is measured in largest diameter. Besides 3D-ERUS is helpful by visualizing lymph nodes at different angles. When necessary, ERUS FNA of lymph nodes can help to confirm diagnosis.

A meta-analysis involved more than 2700 patients of 35 studies showed that the sensitivity of ERUS in diagnosing nodal involvement in rectal cancer was 73.2% and it had a specificity of 75.8%^[64]. In many studies the accuracy of MRI also has not shown very high accuracy rate (70-76% for the diagnosis of metastatic lymph nodes^[65]). When assessing N stage, some studies reported that ERUS has demonstrated accuracy of approximately 70-75% for evaluating malignant nodal compared to CT (55-65%) and MRI (60-65%)^[9,66]. Because ERUS has a higher anatomical resolution, it might detect lymph node metastasis more accurately, but limited field of view imprisons its applications.

(3) MRF (Mesorectal Fascia): Preoperative radiochemotherapy (RCT) is the standard treatment recommended for patients with locally advanced rectal cancer. But neoadjuvant therapy is usually associated with potential toxicity, early postoperative complications, and long-term dysfunction, such as fecal incontinence and sexual dysfunction^[67].

After total mesorectal excision (TME) pathologic involvement of the conferral resection margin (CRM) is a prognostic factor associated with high local recurrence and poor survival^[68]. Studies have reported that patients with free CRM predicted by MRI can undergo TME alone without preoperative RCT, which resulted in a low risk of local recurrence. Besides, patients can avoid overtreatment with preoperative RCT^[69].

Therefore, in order to make the suitable therapeutic strategy, one of the objectives of preoperative imaging workup is to accurately assess the CRM before treatment. When the tumor was within 1mm of the MRF on imaging modalities, pathologic CRM was considered involved^[70,71].

Although MRI has become the gold standard to assess the relationship between tumor and MRF, the accuracy of MRI in low anterior rectal cancer decreases because of thin anterior perirectal fat tissue. In addition, the anterior rectal tumors have a higher risk of a positive resection margin compared with posterior tumors^[72].

Phang *et al.*^[70] firstly demonstrated that ERUS has good agreement

with MR to evaluate MRF below the pelvic cul de sac in rectal cancer. In that study, the posterior aspect of the vagina or seminal vesicles and prostate is defined as the anterior MRF. The lateral and posterior MRF is between the perirectal mesorectal fat and pelvic sidewall parietal fat. Thus following the anterior MRF, the lateral and posterior MRF may be indirectly recognized as an interface between 2 relative high/low echo densities in the lateral fat. Another study showed that ERUS can help MRI in predicting CRM involvement in anterior rectal cancer, especially at the lowest third of the rectum, with a high negative predictive value (97.2%), allowing the selection of patients with free CRM for direct TME surgery without preoperative RCT^[73].

(4) Tumor height and tumor size: The tumor height should be measured from the lowest point of the tumor attached to the wall to the anal verge. The low rectal cancer, defined as within 5 cm of the anal verge, is especially for a higher risk of recurrence. Tumors more than 10 cm from the anal verge are high rectal cancers and tumors located between 5-10 cm are middle rectal cancers. In clinic, tumor length is commonly used to assess tumor size, but tumor volume may offer more information.

(5) Extramural tumor growth or depth: From some clinicians' view, it is more important to measure the depth of extramural spread in the mesorectal fat than to ascertain the T stage, since a T2 tumor has the same prognosis as a T3 tumor with less than 1 mm spread. Moreover, a T3 tumor with minimally invasion has a favorable prognosis than advanced T3 tumor. ERUS, especially 3D-ERUS is able to accurately demonstrate the extramural tumor depth^[55,74,75].

(6) Neoadjuvant therapy: Locally advanced rectal cancer is recognized by rectal tumors with transmural extension (T3/T4) or tumor involving lymph nodes (N1/N2). Primary surgery is no longer the only treatment. For patients with advanced tumors, neoadjuvant treatment may be a more suitable choice. To shrink the tumor size and downstage the tumor are the potential advantages of preoperative treatment, which enhance the rate of resectability and facilitate sphincter-saving surgery. As a result, it may reduce local recurrences, and possibly improve long-term survival^[67,76,77].

Among the benefits, downsize and downstage of the tumor are most important for the prognosis. ERUS is one of the best modalities to image the rectal cancer after neoadjuvant treatment. However, after neoadjuvant treatment, imaging staging of the rectal cancer becomes difficult, because irradiated tissues is significantly changed by radiotherapy and the fibrotic tissues could influence the correct interpretation of images. On ERUS, the fibrotic outcomes and the neoplastic tissue both appears as hypoechoic and it is difficult to distinguish between them, which results to a low accuracy between 47% and 62% for T stage after neoadjuvant treatment, and over staging is common. The same problem also occurs with MRI. Many studies have proved that ERUS is still the most accurate method to determine neoplastic wall infiltration and lymph node involvement even after RCT^[78,79]. After neoadjuvant treatment, the status of the lymph nodes remains a problem; ERUS and MRI both have a low accuracy to evaluate metastatic lymph nodes after neoadjuvant^[80].

For the correctly restaging rectal cancer after neoadjuvant treatment, it is of vital importance to choose the correct time between the end of neoadjuvant therapy and the procedure of ERUS. To reduce the risk of artifacts, ERUS is recommended to be performed at least 30 days and maximum 60 days after the end of neoadjuvant therapy. Besides, an accurate comparison between US images before and after treatment is also helpful^[78,81].

(7) ERUS-guided fine needle aspiration and trucut needle biopsy: ERUS-guided fine needle aspiration (ERUS-FNA) was applied to

enhance diagnostic accuracy by obtaining tissue samples for cytological and/or histological examination. ERUS-guided trucut needle biopsy (ERUS-TCB) is to acquire larger tissue samples, to evaluate the tissue architecture or permit immunohistochemical staining. In general, while ERUS-TCB could provide more prognostic information, ERUS-FNA may be much safer for avoiding damaging other important structures around the lesion^[82,83].

Studies have proved that ERUS-FNA and/or TCB could improve therapeutic and clinical schedule and are useful techniques to evaluate patients with rectal and perirectal lesions, especially for the subepithelial tumor^[84].

Boo *et al.*^[85] performed ERUS-FNA and/or ERUS-TCB in 11 patients with rectal or perirectal lesions for whom conventional diagnostic could not provide definitive diagnoses, and 10 out of 11 patients finally obtained correct diagnoses. Meanwhile, no serious complications were evident.

In our center, we performed ERUS-TCB (18G, Pajunk, German) in 16 patients who were discovered anorectal lesions by CT, MRI or endoscope but without conclusive diagnosis. All the specimens were adequate for histology and consistent with surgical pathology or follow-up results. And no complication happened. In our study, we also performed ERUS-TCB of lymph nodes to help confirm diagnosis of benign or malignant nodes (Figure 9). In 2 patients with rectal cancer in early T stage (both are T1 and confirmed by the postoperative pathology), MRI and ERUS found both of them had only one lymph node larger than 5 mm in the mesorectum. While MRI and ERUS could not draw conclusive diagnosis whether the nodes were malignant, we successfully performed ERUS-TCB of the lymph nodes and the histology studies proved both were benign. Finally, without preoperative neoadjuvant therapy, they accepted TEM and TME, respectively. Therefore, both patients avoided excessive neoadjuvant therapy or surgery.

Generally, ERUS-FNA and/or TCB are useful in the diagnosis and clinical therapeutic plan in patients with rectal and perirectal lesions.

(8) Surveillance: In the first two years after surgery, the rectal cancer patients have higher rates of local recurrence. Studies also have found that patients undergoing low anterior resection of rectal cancer generally are more likely to recurrent than in other place of rectum. The patients with rectal cancer, especially for the low anterior tumor, should be carefully followed up for the detecting a surgically curable recurrence of the rectal cancer at 3-6 months intervals for the first 2 years after resection. ERUS has been proved as an accurate technique to detect recurrent rectal tumor, with ERUS guided biopsy being able to provide tissue confirmation^[86-88].

Other rectal masses: Other types of neoplasm may happen in anorectum, such as polyps, squamous cell carcinomas, neuroendocrine tumors, lymphomas, anorectal melanoma, and gastrointestinal stromal tumor (GIST).

These neoplasms appear various echo and pattern on ERUS. For example, polyps appear as a neoplasm with a root grown in the surface of the mucosa (Figure 10). There are no criteria on ERUS right now to distinguish the polyps from adenocarcinomas and biopsy is still needed. Besides, squamous cell carcinomas also appear as a hypoechoic mass resembling rectal adenocarcinomas on ERUS. Neuroendocrine tumors usually appear as small, mobile, submucosal nodules or focal areas of submucosal thick. Lymphomas are rare, and can be a primary lesion or a secondary infiltration of the large intestine, which characteristically involves the deeper layers of the intestine wall. GIST is the most common mesenchymal tumor that originates in the alimentary tract. On ERUS, a GIST appears as a hypoechoic mass (Figure 11). ERUS



Figure 9 A 70-year-old male patient with rectal tumor (T1). A suspected malignant lymph node (white arrow head) with 6mm in diameter was biopsied with an 18 G trucut needle.



Figure 10 A 78-year-old male patient with polyps. US showed an isoechoic neoplasm with a root (white arrow) grown in the surface of the mucosa.

can evaluate the neoplasm of rectum before treatment to acquire very useful prognostic information, especially for staging and follow up of squamous cell carcinomas. The depth of squamous cell carcinomas invasion should be noted to determine whether the lesion is confined to the submucosa or invades the adjacent muscle or perirectal fat^[22]. Chemoradiation as primary therapy is the main therapeutic plan for squamous cell carcinomas, and surgical resection is reserved for RCT failures. Gleevec is effective in the treatment of rectal GIST. ERUS is very helpful for the follow up of this neoplasm during the treatment of RCT, because it can identify or exclude persistent or recurrent disease. Needle core biopsies under ultrasound guidance can be obtained to identify the persistent masses or abnormalities following treatment^[89].

Under the enteroscope, intramural lesions or extramural compression from a pathologic process or an anatomic aberration causing subepithelial compression appear as a rectal subepithelial lesions. ERUS and biopsies guided by ERUS have been showed useful for investigation rectal subepithelial lesions, for example, stromal tumor, neuroendocrine carcinoma, diploma, and other distant malignancies such as ovarian carcinoma^[83].

NEW TECHNIQUES AND DEVELOPMENTS

3D-ERUS

In 1999, 3D-ERUS was firstly reported to be used to assess the

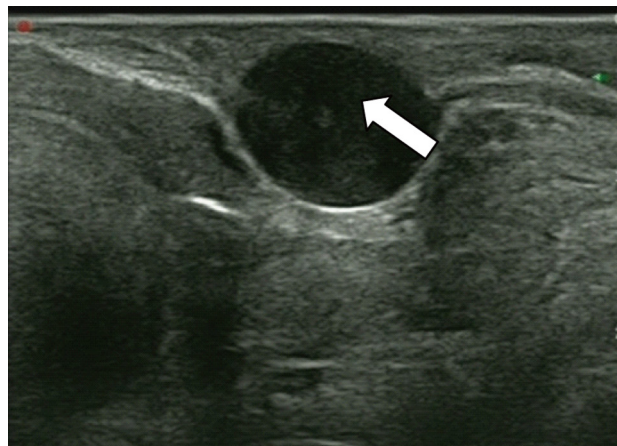


Figure 11 A 40-year-old female patient with GIST. US showed a hypoechoic mass with clear boundary (white arrow).

anal anatomy^[90]. Nowadays, 3D probes are widely used. A 3D reconstruction is usually based on a high number of parallel transaxial image acquired by using a mechanically rotating endoprobe. A 3D volume displayed as a cube consists of a series of closely spaced 2D images. The 3D cube can then be freely rotated and to show the defects at different angles and present more information out of the data.

3D-ERUS is a valuable technique for assessing anorectal disorders, because it allows multiplanar imaging of the rectum and anal sphincters, and providing additional data than 2D-ERUS that in many cases which have changed the operative approach^[31].

On the basis of published studies, the accuracy of 3D-ERUS shows superior to 2D-ERUS in the diagnosis of anorectal diseases. Kim *et al*^[91] evaluated 86 consecutive rectal cancer patients by 2D and 3D ERUS. The accuracy of the T-stage for 3D-ERUS is 78% and 69% for 2D-ERUS, and the accuracy of the N-stage for 3D-ERUS is 65% and 56% for 2D-ERUS. Besides, 3D-ERUS has greatly contributed to the understanding the normal anorectal anatomy and definition of the anorectal region, for example, the physiologic sphincter gaps of healthy women^[31]. Additionally, 3D-ERUS allowed a correct evaluation of the MRF and the degree of mesorectum involvement precisely in patients with rectal cancer, which was not possible with 2D-ERUS images. All of these advantages make a difference on therapeutic decision making for patients with anorectal diseases.

Elastography

Elastography is a technique based on B-mode scanning during compressions. Because elastography could differentiate the stiffness of normal and pathological tissue non-invasively by ultrasound, it can provide good information of the consistency of the tissue of interest. Recently, it has been widely applied on the liver, breast and thyroid gland^[92-94].

Elastography of the ERUS has been used in faecal incontinence, inflammatory bowel disease and staging of carcinoma^[95-97]. Mezzi *et al*^[97] evaluated 20 patients with rectal cancer by ERUS elastography. They found that the elastography images showed a discreet correlation (65%) in the staging of advanced lesions; and post-radiotherapy disease persistence could be correctly (100%) confirmed by elastography score. Waage *et al*^[95] used ERUS elastography to discriminate adenoma from adenocarcinomas, where the sensitivity, specificity and accuracy resulted to be high. Whether ERUS elastography can improve preoperative T and N staging or not remains to be investigated in more studies. A recent study suggested that ERUS elastography could assess

the stiffness of the rectal and perirectal tissue and help to differentiate CD from UC, which could not accurately, assessed using standard diagnostic techniques^[98].

Elastography of the ERUS seems to be a promising new diagnostic tool in the field of rectal disease, and further study on a larger cohort of patients is needed to definitely assess the role of it.

Contrast-enhanced ultrasound (CEUS)

Angiogenesis regulation is gradually applied in the fight against cancer. By inhibiting new vessel formation, anti-angiogenic therapy inhibits factors can cut-off the source of nutrients and oxygen of the tumor. An earlier imaging indication of the treatment efficacy of this new therapy is important.

Some clinical studies proved that CEUS can provide early indication of tumor response to anti-angiogenic therapy. However, there are few studies about whether CEUS can assess the rectal cancer response to anti-angiogenic therapy^[99,100].

In current, all the imaging modalities cannot accurately detect the local recurrence of rectal cancer. Because imaging modalities, such as CT, MRI, and ERUS cannot distinguish recurrent lesions from artifacts caused by fibrosis scarring, granulation tissue and inflammation. Cui *et al* believed contrast-enhanced ERUS is not interfered by the artifacts and tried using it to differentiate a postoperative tissue proliferation from local recurrence^[101].

CONCLUSION

ERUS is easy to learn and perform, and is a patient friendly technique. It has greatly influenced the diagnosis and treatment of many anorectal diseases and disorders. It not only makes a major contribution in the assessment of benign diseases such as faecal incontinence, abscess and fistula, but also accurately evaluates the rectal neoplasm and greatly influences the management strategy. The main limitation of ERUS is that the technique requires a learning curve and the accuracy of ERUS depends on the experience of the operator. Besides, limited tolerance of patients, and limited depth of the transducer also restrict its utilizing in some cases.

CONFLICT OF INTEREST

There are no conflicts of interest with regard to the present study.

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