Probe Ultrasonography

Henry C. Ho, MD, Jeffrey L. Tokar, MD,
and Irving Waxman, MD

CONTENTS

Abstract

High frequency ultrasound sonography (HFUS) utilizes probe catheters that operate at a higher frequency than standard endoscopic ultrasonography (EUS). These catheter probes can be passed down the channel of a standard endoscope, or sideview scope during endoscopic retrograde cholangiopancreatography (ERCP), to produce higher resolution ultrasound imaging of the gastrointestinal and pancreaticobiliary tracts. HFUS has an array of clinical applications, like EUS, including the examination of submucosal abnormalities and pancreatobiliary disease, as well as cancer staging. The improved imaging

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resolution of HFUS, however, results in a loss of imaging depth, thereby limiting its utility in defining deep tissue or distant structures along the GI tract. The extension of HFUS in the pancreaticobiliary tree is intraductal ultrasound (IDUS). IDUS has been shown to have indications in defining choledocholithiasis, evaluating biliary strictures, and local staging of cholangiocarcinoma. IDUS can also be applied as pancreatic IDUS and papilla of Vater IDUS, where it can be useful in the evaluation of pancreatic strictures, pancreatic adenocarcinoma, mucin producing tumors of the pancreas, and papillary tumors.

Key Words: Catheter probe, Probe ultrasonography, High frequency ultrasound sonography (HFUS), Intraductal ultrasound (IDUS), Pancreatic IDUS, Papilla of Vater IDUS

INTRODUCTION

Endoscopic ultrasonography (EUS) incorporates ultrasound technology into the tip of an endoscope to visualize the gastrointestinal wall and surrounding structures. EUS has been used to stage tumors of the gastrointestinal tract, pancreas, and bile ducts (1). Indeed, studies demonstrate that EUS is a highly accurate modality for staging the depth of tumor invasion. Unfortunately, there is difficulty in distinguishing inflammatory versus neoplastic processes via EUS (2). High frequency ultrasound sonography (HFUS) was therefore designed to improve imaging resolution. Typical echo-endoscopes operate from 5 to 20 MHz. HFUS probes, on the other hand, operate with higher frequency (12–30 MHz). HFUS has been demonstrated to produce images with improved resolution in comparison to standard EUS (0.07–0.18 mm) (3–6). One can imagine that more detailed imaging of mucosal and subepithelial lesions of the gastrointestinal tract and pancreaticobiliary tree can be achieved (5). Indeed, the superior definition of HFUS provides images of the wall structure layers resembling those seen on histology (7).

As with all ultrasound technology, the choice of frequency is a tradeoff between spatial resolution of the image and imaging depth: higher frequencies produce greater resolution but cannot image deeper into the tissue (8). In fact, the higher frequency image produced using HFUS usually results in a depth of penetration limited to 2–3 cm. Thus, HFUS probes are especially useful in evaluating tumor extension (T stage) of subepithelial lesions (9). The accuracy of staging superficial tumors of the esophagus, stomach, and colon with HFUS probes can be as high as 60–90% (2, 10–14). Moreover, HFUS has been particularly

attractive as the small caliber ultrasound probe (maximum diameter of 2.6 mm) can be passed through the biopsy channel of an endoscope without endoscope exchange (15). In addition, the ability to delineate tumor extension into the muscularis mucosa gives HFUS superior relevance in numerous clinical indications, particularly for tumors that can be cured by endoscopic mucosal resection or photodynamic therapy alone (16, 17).

INSTRUMENTS AND EXAMINATION TECHNIQUES

In general, HFUS probes can be classified by their working mechanism into mechanical or electronic catheters. At the tip of the catheter, mechanical probes have a single ultrasound transducer rotated by a cable, which transmits the signal to an ultrasound processor. When rotating, the ultrasound transducer produces a 360° image, perpendicular to the longitudinal axis of the HFUS catheter. These mechanical HFUS probes are available in various diameters (2–2.9 mm), frequencies (12–30 MHz), and lengths (1,700–2,200 mm) (18, 19). The mean imaging depths based on the 12, 20, and 30 MHz probes have been reported to be 29, 18, and 10 mm, respectively *(5, 6, 18–20)*. These catheters are also capable of linear scanning. Electronic catheters, on the other hand, consist of a probe that contains a number of fixed ultrasound transducers at their tip. These transducers transmit signals via microwires to the image processor. Thus, there is no rotating system; however, these electronic probes can be oriented radially or linearly. Most studies demonstrate experience with these probes in cardiovascular applications. Yet, there appears to be promise in gastrointestinal disease (18, 21, 22).

In order to utilize the HFUS catheter, a standard endoscope is negotiated through the gastrointestinal tract until the area of interest is reached. The HFUS catheter is then advanced through the biopsy channel of the endoscope and placed in contact with the target lesion. A number of techniques have been described to obtain adequate acoustic coupling between the HFUS catheter and the target lesion. The two methods most frequently used are the condom and the balloon techniques. These techniques appear to be especially useful in the esophagus and rectum (23, 24). In the condom technique, a latex condom is attached to the distal end of the endoscope. Unfortunately, the condom prevents visualization and air insufflation. Therefore, endoscopy must be performed prior to employing the condom. Once the condom is applied and the endoscope is advanced to the region of interest, the condom is filled with water through the biopsy channel. The HFUS

probe is then inserted and acoustic coupling is achieved. This technique can suffer from air pockets between the condom and the gut wall causing image degradation (23, 25).

In the balloon technique, a similar concept is used to improve acoustic coupling. In this method, the HFUS catheter is inserted into a latex sheath with a distal balloon that can be instilled with water. Again, air pockets lead to suboptimal image quality (26). If a double channel endoscope is used, however, the endoscopist can suction air pockets and inject water into the gut lumen through the second biopsy channel (27). The suctioning of air in the bowel can lead to collapse of the colon wall and subsequent obscuring of the anatomical relationships of interest. Water immersion over a miniprobe, then, may be the preferable method to decrease image distortion although this technique does not always appear to be necessary (28). There are several other subtleties in examination technique that can improve acoustic coupling. For example, prior to the procedure, the tip of the HFUS probe should be rotated to allow equal distribution of immersion oil that surrounds the transducer cap to maximize image quality. Some endoscopists have used submucosal injections below target lesions, particularly in esophageal and colorectal tumors to improve staging (29). More aggressive manipulation of target lesions such as actual biopsy, however, generally leads to greater artifact imaging. Therefore, the HFUS probe should be used prior to such procedures.

GASTROINTESTINAL WALL ANATOMY

Typical echo-endoscopes operate at frequencies that produce a five layer image of the gastrointestinal wall. The HFUS probe, on the other hand, can identify 9–11 layers in the stomach and five layers in the colon (10, 16, 17, 29, 30). In the stomach, the first (hyperechoic) and second (hypoechoic) layers correspond to the interface with the probe surface and mucosa. The third (hyperechoic) and fourth (hypoechoic) layers are the interface between the mucosa and submucosa. The fifth (hyperechoic) layer is the submucosa. The sixth (hypoechoic) layer represents the inner circular muscle layer. The seventh (hyperechoic) and eighth (hypoechoic) layers are the intramuscular connective tissue interface and outer longitudinal muscle layers, respectively. The ninth (hyperechoic) layer is the subserosa and serosa (Figs. 1 and 2). In the colon, the three layers of the muscularis propria can be visualized. The inner hypoechoic layer is the circular muscle; the middle hyperechoic interface represents the connective tissue; and the outer hypoechoic longitudinal layer is the muscle layer.

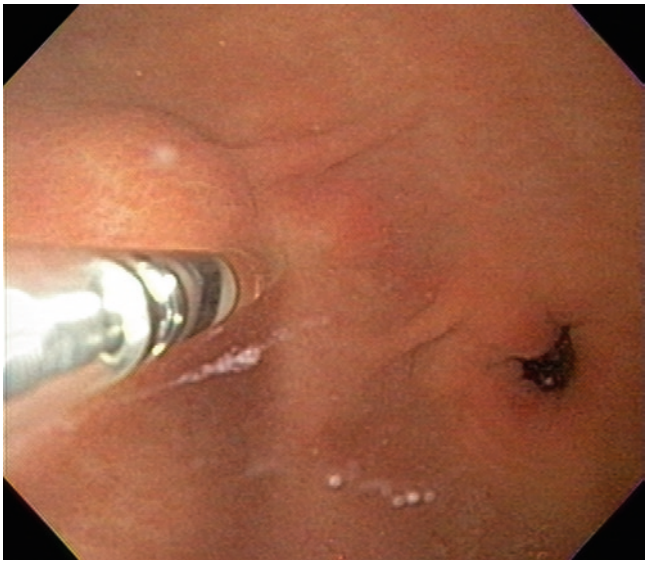

Fig. 1. Endoscopic view of a small, subepithelial mass in the gastric antrum being evaluated with a high-frequency ultrasound miniprobe.

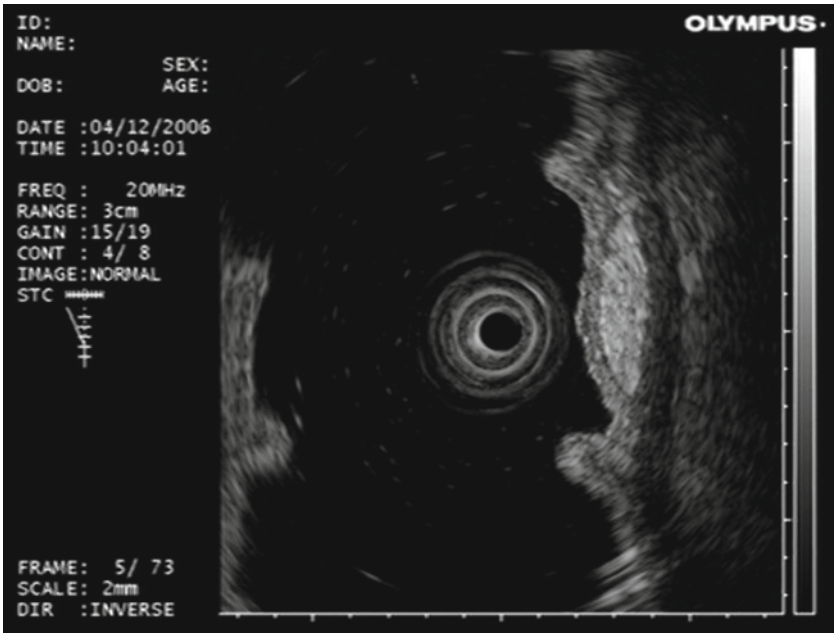

Fig. 2. Endosonographic imaging demonstrates an ovoid, hyperechoic, homogeneous mass in the third echolayer (submucosa) of the gastric antrum. The appearance is typical for a small lipoma.

CLINICAL INDICATIONS

Esophagus

The improved resolution and the ability of HFUS probes to traverse stenotic tumors, which may be inaccessible with dedicated echo-endoscopes, makes HFUS especially attractive in the evaluation of esophageal cancer (20). Indeed, the T staging accuracy of HFUS probes in this setting has been reported up to 85% (10, 17, 31, 32). The accuracy of standard EUS when compared with pathologic staging for superficial (T1) lesions shows a wide range from 50 to 90% (10, 33–35). HFUS probes, on the other hand, have been shown to improve the accuracy of T staging (T1 vs. T2) from 76 to 92% (Figs. 3 and 4) (10). One recent report does suggest, however, that HFUS has limited accuracy in detecting submucosal invasion in early esophageal cancer (36). In addition, the limited depth penetration of HFUS into surrounding tissues (~3 cm) precludes accurate assessment of nodal (N) stage (37). In one study, the accuracy of N staging in patients undergoing preoperative EUS for esophageal cancer was much worse with HFUS than with the standard radial-scanning echo-endoscope (48% vs. 90%) (38). The combined use of a balloon sheathed catheter may improve acoustic coupling and lead to more accurate staging with HFUS in esophageal cancer (23, 26, 27, 37). Unfortunately, HFUS also seems to have limited application in Barrett's esophagus. HFUS has been shown to have diminished accuracy in identifying invasive cancer in patients with high grade dysplasia or intramucosal carcinoma, even with endoscopically visible lesions (30). There are other clinical indications for HFUS in the esophagus including subepithelial lesions (Figs. 5 and 6). HFUS has also been in evaluating esophageal varices, specifically their radius and wall thickness without causing variceal compression (39–41). HFUS has also been useful in evaluation of motility disorders in the esophagus. Under HFUS, hypertrophy or in coordination of the circular and longitudinal muscles can be suggestive of achalasia, diffuse esophageal spasm, or nutcracker esophagus (42–44). Expansion of the esophageal wall and tissue layers (mucosa, submucosa, muscularis propria) has been demonstrated in the early diagnosis of eosinophilic esophagitis (45). In achalasia, the HFUS probe has been used to properly localize the lower esophageal sphincter for botulism toxin injection (46).

Stomach

HFUS has extensive applications beyond the esophagus in the gastrointestinal tract (Figs. 7 and 8). Some reports have indicated that

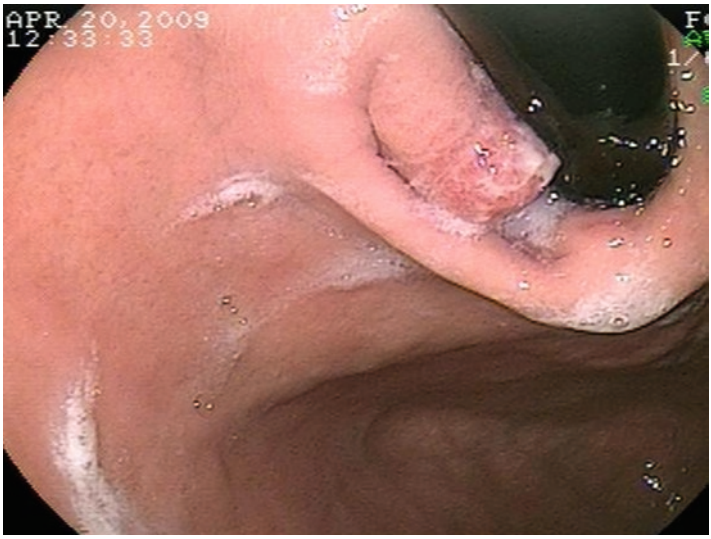

Fig. 3. Retrograde endoscopic view of a nodule involving the gastroesophageal mucosa.

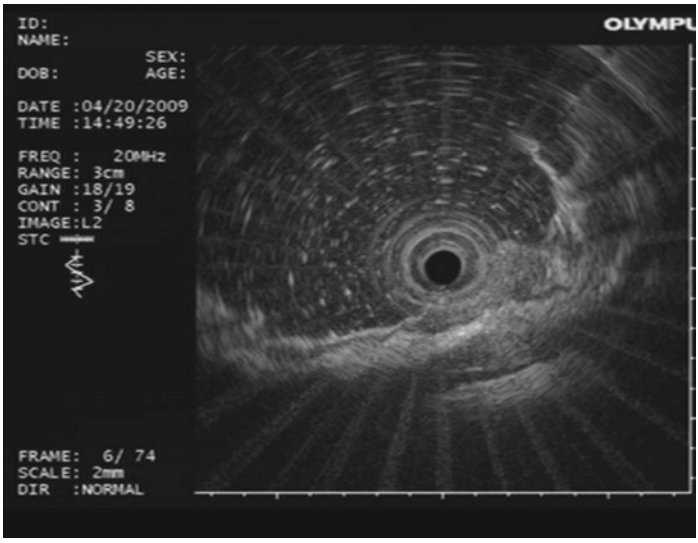

Fig. 4. Evaluation with a high-frequency ultrasound miniprobe demonstrates a hypoechoic mass arising from the second echolayer of the gastric mucosa (deep mucosa). No invasion of the third echolayer (submucosa) is visualized. Endoscopic mucosal resection confirmed a well-differentiated intramucosal adenocarcinoma.

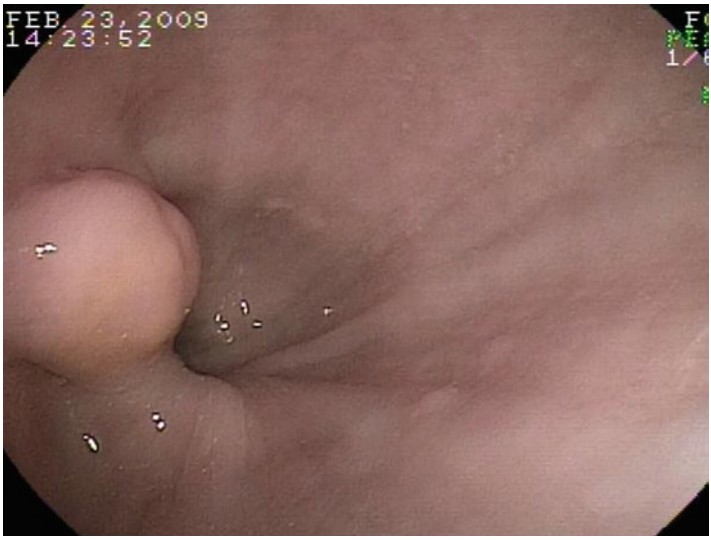

Fig. 5. Endoscopic view of an esophageal granular cell tumor.

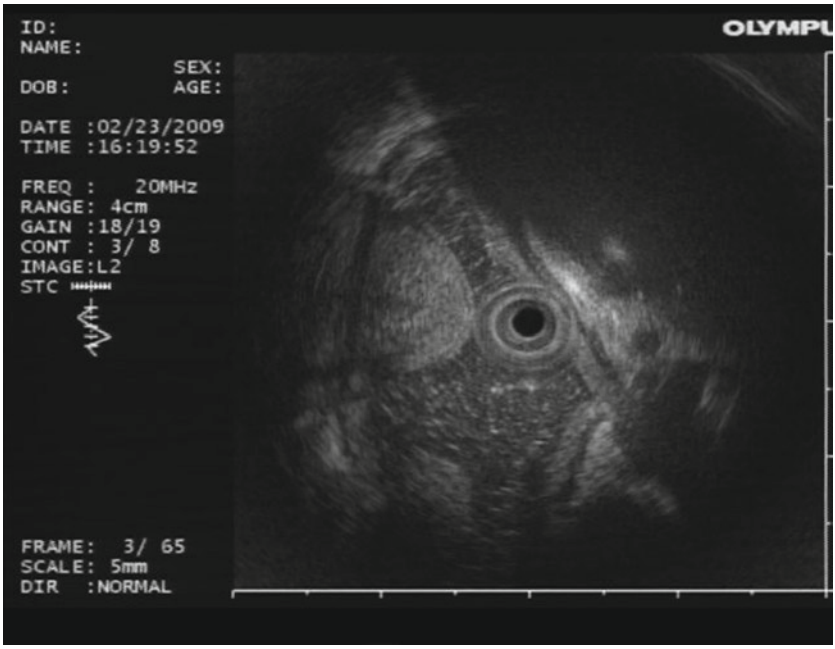

Fig. 6. Hypoechoic, homogenous, subepithelial mass localized to the third echolayer (submucosa) of the esophageal body.

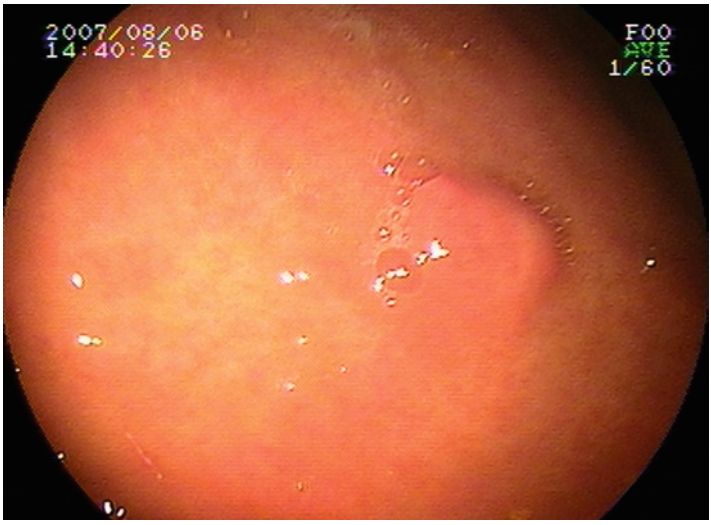

Fig. 7. Endoscopic view of a small subepithelial nodule in the gastric antrum.

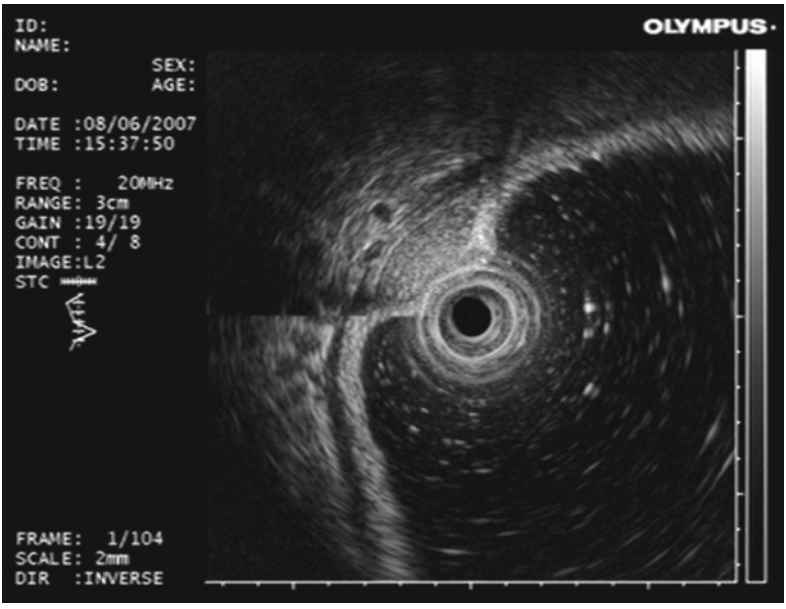

Fig. 8. Endosonographic imaging with a high-frequency ultrasound miniprobe demonstrates an ovoid mass in the third echolayer (submucosa). The submucosal location and shape of the lesion is suggestive of a lipoma, but the echotexture is less hyperechoic. Endoscopic resection demonstrated a submucosal myxoid angioma.

HFUS can aid in the diagnosis of gastric lymphoma, linitis plastica, gastric varices, and Menetrier's gastropathy (47). Under HFUS, lymphoma can be visualized as having thickened mucosa or submucosa with hypertrophic folds. Linitis plastica can appear with marked thickening of the mucosa, submucosa, and muscularis propria while Menetrier's gastropathy can appear sonographically with mucosal thickening and cyst formation (Figs. 9–12). One of the more useful applications of HFUS, though, appears to be T staging of early gastric cancer, particularly those confined to the mucosa or submucosa. The accuracy of T staging using HFUS has been reported as being up to 80% in comparison to 63% accuracy with conventional EUS (47–50). The limitation in depth penetration with HFUS appears to diminish the T staging accuracy in gastric cancer when the lesions invade deeper than 10 mm (51). Thus, subepithelial and well-differentiated lesions are better visualized. Indeed, ulcer scars, dilated glands, local edema, or fibrosis contribute to a large portion of staging errors (50). The HFUS catheters with 3-D imaging capabilities have been reported to have T staging accuracy of almost 90% in superficial gastric cancer (52). The improved accuracy in T staging with HFUS has proven useful in decision-making for endoscopic mucosal resection of early or superficial gastric cancer (53, 54) as early adenocarcinoma confined to the mucosa or submucosa has a 95% 5-year survival rate after resection (55).

Small Bowel and Colon

In the small bowel and colon, HFUS has been shown to be useful in the preoperative diagnosis of pathology such as leiomyoma, leiomyosarcoma, lipoma, lymphoma, and neuroendocrine tumors (56) (Figs. 13 and 14). There has also been evidence that HFUS can be used to assess the severity of active inflammatory bowel disease (57, 58). Some studies suggest that T staging accuracy with HFUS is similar to standard EUS in colorectal cancer (13). One of the largest reports on HFUS in this setting, however, found that tumor staging accuracy was fairly high at 76%. In particular, HFUS probes were more accurate for studying small and flat lesions (<15 mm) (14). In fact, one prospective study found that flat and superficial invasive tumors could be identified with 100% accuracy with HFUS (19). HFUS was even found to be more accurate than high magnification chromoendoscopy for differentiating T1 versus T2 disease (59, 60).

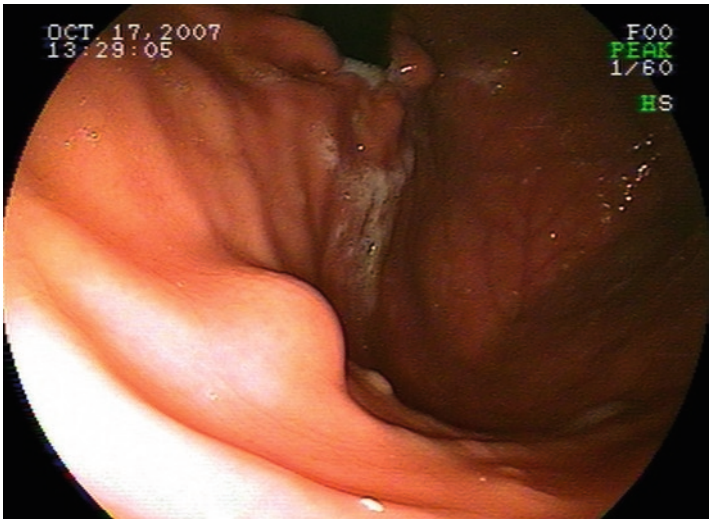

Fig. 9. Retrograde endoscopic view of a small subepithelial mass in the proximal gastric body.

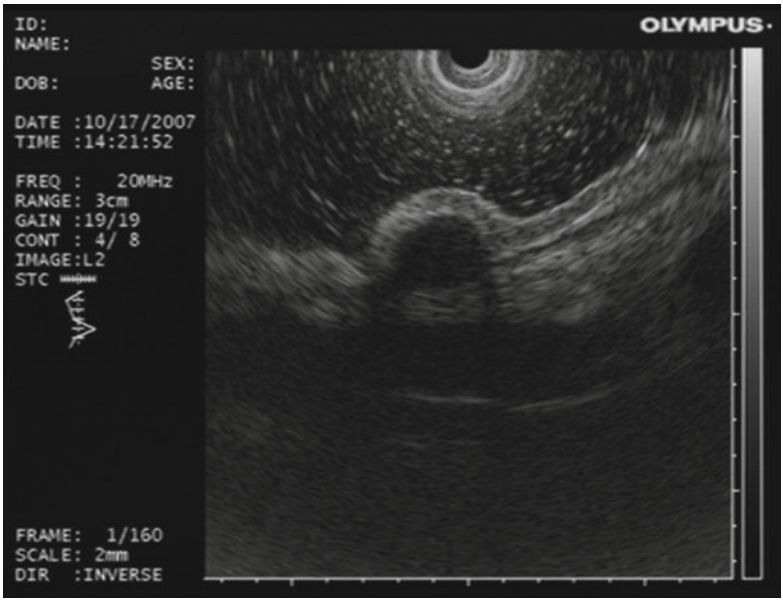

Fig. 10. Endosonographic imaging with a high-frequency miniprobe demonstrates a hypoechoic, homogeneous mass arising from the fourth echolayer (muscularis propria). The differential diagnosis includes a small leiomyoma versus gastrointestinal stromal tumor (GIST).

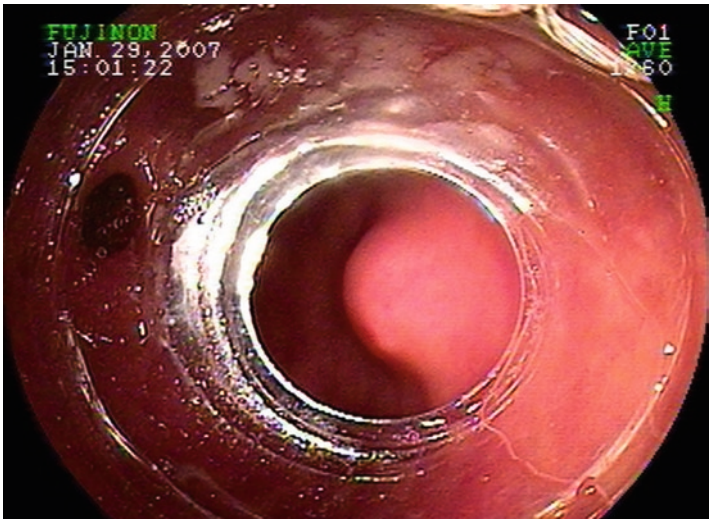

Fig. 11. Endoscopic view of a small, subepithelial mass in the gastric antrum. A clear plastic cap is affixed to the endoscope to facilitate endoscopic resection.

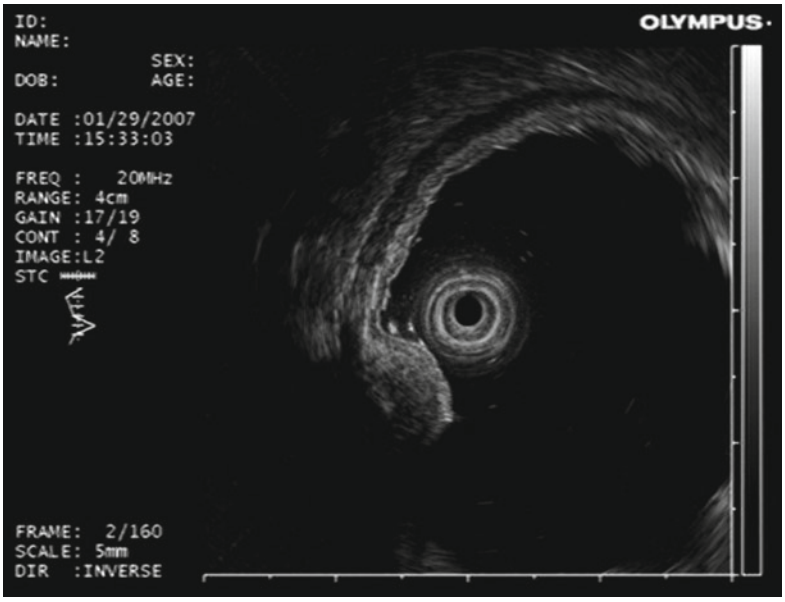

Fig. 12. Endosonographic imaging with a high-frequency miniprobe demonstrates a hypoechoic, mildly heterogeneous mass with indistinct margins in the third echolayer (submucosa). The appearance is consistent with heterotopic pancreatic tissue, "pancreatic rest," which was confirmed histologically. The punctate an-echoic (black) foci within the mass represent small pancreatic ductal structures.

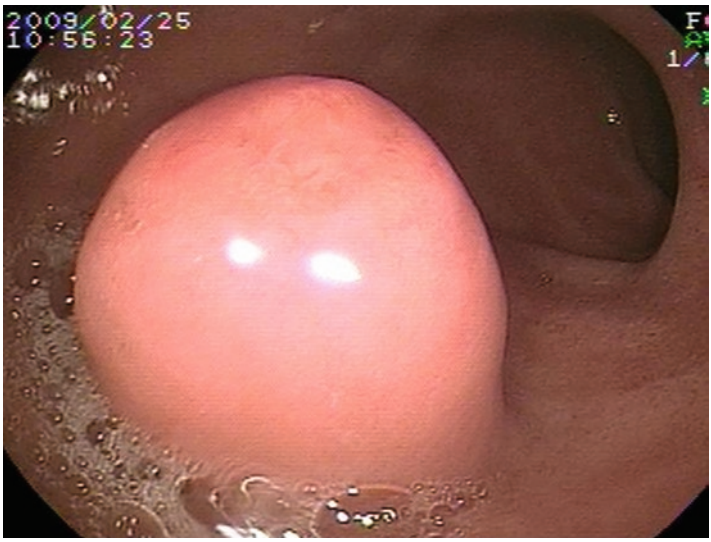

Fig. 13. Endoscopic view of a subepithelial mass in the duodenal bulb. Subepithelial lesions of this nature in the duodenal bulb are frequently found to be carcinoid tumors. However, note the subtle frond-like appearance to the mucosa at the surface of the mass, a feature not typical for carcinoid tumors.

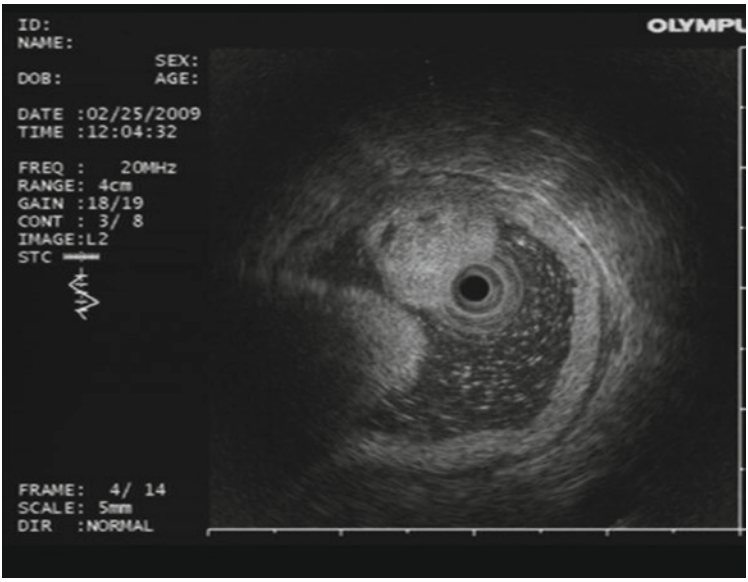

Fig. 14. Endosonographic imaging with a high-frequency miniprobe demonstrates a poorly defined, echogenic mass involving the third echolayer (submucosa). However, the precise echolayer of origin is difficult to determine. Endoscopic resection demonstrated a Brunner's gland adenoma. The small, round anechoic areas within the mass correspond to fluid-filled and dilated glands.

INTRADUCTAL ULTRASOUND

High frequency ultrasound catheters can also be passed over a guide wire into the bile and pancreatic ducts during endoscopic retrograde cholangiopancreatography (ERCP). This is known as intraductal ultrasound (IDUS). This method of ultrasonography utilizes wire-guided miniprobes in 5–10 F diameter with frequencies ranging from 12.5 to 30 MHz. IDUS creates images from within the duct lumen, whose tubular anatomy and surrounding bile and pancreatic fluid facilitates acoustic coupling.

TECHNICAL CONSIDERATIONS

The IDUS probes can be advanced by free cannulation or over a guidewire; they can be passed through a standard side-viewing endoscope or percutaneously (61–63). Cannulation with the IDUS miniprobe may be difficult without biliary sphincterotomy or use of a guide wire. In some early reports, endoscopic sphincterotomy was required in 10–15% of patients undergoing IDUS (63). New small caliber IDUS catheters, however, seem to permit cannulation without the need for sphincterotomy (62, 64, 65). Still, stenotic strictures may require dilation with a catheter or balloon. It should be noted that, in general, the IDUS procedure time, including catheter insertion and imaging time only adds about 5–10 min to the length of standard ERCP (63, 66). When using IDUS, the usual risks of biliary and pancreatic instrumentation apply, including pancreatitis, reported between 0.4 and 1.5% (63, 67, 68). Complications that are directly attributable to IDUS, however, are rare (62, 63, 66).

BILIARY TRACT ANATOMY

As with HFUS probes, there are different systems available to perform IDUS. Electronic systems use thin, flexible catheters that have no rotating parts. They are 1.1 mm in diameter and 3.5 F. They contain a ring of 64 transducer elements that produce a complete 360° image. The transducer ring detects signal from surrounding tissue and transmits them via microwires to the image processor. In the mechanical system, a single transducer is rotated via a wire producing a 360° image. There are many variations on this basic mechanical system. There are single use probes and multiuse catheters that can vary in design, including the presence of a water-filled protective housing or a water-filled transducer chamber. There are also newer mechanical probes that allow rotating sector and linear scanning.

In IDUS, the normal bile duct appears as either two or three layers, similar to what is visualized under standard EUS (69–72). The sphincter of Oddi appears as a hypoechoic circular thickening within the duodenal wall. When visualized as a two-layer structure, an internal hypoechoic layer represents the mucosa, muscularis propria, and fibrous layer of the subserosa. An outer hyperechoic layer represents the adipose layer of the subserosa, serosa, and interface echo between the serosa and surrounding organs. Unfortunately, it may be difficult to differentiate the fibromuscular layer from the perimuscular connective tissue. This may limit the ability to differentiate between T1 and T2 bile duct cancers although this distinction may not be clinically relevant (73). A third inner hyperechoic layer, representing the interface between the duct mucosa and bile, is occasionally visualized.

CLINICAL INDICATIONS

IDUS is useful in a variety of biliary tract disorders. The most common indications include the evaluation for choledocholithiasis and obstructive jaundice. IDUS is also useful for local tumor staging. In contrast to standard EUS, IDUS is often better in evaluating the proximal biliary system and surrounding structures like the right hepatic artery, portal vein, and hepatoduodenal ligament (69, 74, 75). Like HFUS, more distant structures are difficult to examine secondary to limited depth penetration.

Choledocholithiasis

IDUS has been well described in the evaluation of suspected choledocholithiasis. A number of imaging modalities are available to evaluate these patients, including transabdominal ultrasonography, computed tomography (CT), magnetic resonance (MR), ERCP, and EUS. Initial studies suggested a role for IDUS in patients with suspected choledocholithiasis who have a normal cholangiogram (76, 77). Subsequent studies revealed that the sensitivity of IDUS for suspected choledocholithiasis is superior to ERCP, EUS, or transabdominal ultrasonography (77–79). In some reports, the sensitivity of IDUS was even higher for detecting small stones (<5 mm) (78, 80). Despite the high sensitivity of IDUS for choledocholithiasis, many have questioned the clinical significance of residual sludge and stones observed in several of the aforementioned studies as these may have been small enough to pass spontaneous (81). However, IDUS has been demonstrated to distinguish stones from sludge and air bubbles, altering clinical management in

several studies (79). Unfortunately, the high cost and limited data supporting its utility will likely restrict the use of IDUS in evaluating suspected choledocholithiasis.

Bile Duct Strictures

IDUS has also been shown to distinguish benign from malignant biliary strictures based on bile duct anatomy and unique sonographic imaging characteristics. Features under IDUS that suggest malignancy include a hypoechoic mass (especially if infiltrating surrounding tissue), heterogeneity of the internal echo, notching or irregularity of the outer border, a papillary surface, or disruption of the normal bile duct structure (61, 66, 75, 82–84). There have been several series investigating the utility of IDUS in characterizing bile duct strictures. IDUS has been more accurate than EUS and better able to determine T stage and potential resectability (63). This appears to hold true especially for tumors at the hilum or mid-bile duct (66). IDUS has also been shown to be more accurate, sensitive, and specific when compared to ERCP with tissue sampling in making a final diagnosis (64). Indeed, in a series with patients with suspected malignant strictures but negative tissue sampling by ERCP, the combined use of IDUS resulted in sensitivity and specificity of 90 and 93%, respectively (85). The combination of IDUS and ERCP can improve diagnostic yield, as well. One study found that IDUS in conjunction with ERCP increased the accuracy of characterizing biliary strictures from 58 to 90% (86). A more recent report suggested that IDUS was able to accurately predict malignancy in 86% of patients with negative cytology and histology who were later proven to have malignancy. In fact, IDUS was superior in this setting to digital image analysis (DIA), fluorescence in situ hybridization (FISH), and composite DIA/FISH (87). Even if IDUS fails to provide a final diagnosis, it may be helpful in directing management. For example, some have suggested that identification of disruption of walls by a protruding tumor via IDUS, regardless of tissue sampling results, warrants surgical exploration.

Cholangiocarcinoma

The role of IDUS in primary sclerosing cholangitis is still being determined. IDUS can identify irregular foci within strictures, allowing for focused endoscopic transpapillary biopsy (88). This has not been proven to lead to an earlier diagnosis of cholangiocarcinoma, however

(68). Fortunately, IDUS has been shown to improve the accuracy of local tumor staging of bile duct carcinomas. IDUS is able to detect early lesions, characterize longitudinal tumor extension, and identify tumor spread to adjacent organs and major blood vessels with an accuracy of nearly 100% (69, 72, 75, 89). IDUS has been shown to accurately identify tumor invasion into the pancreatic parenchyma (72, 75, 90), portal vein (69, 72, 90, 91), and right hepatic artery (72, 74, 89, 90). IDUS is superior to standard EUS for T staging (72, 90, 92). In one report, when compared to operative findings, local tumor staging was accurate in 77% of patients with IDUS in comparison to only 54% of patients with EUS (63). The advantages of IDUS over EUS may be even greater for proximal bile duct tumors involving the mid-bile duct to bifurcation as the IDUS miniprobe allows further access (90). Unfortunately, with the limited depth penetration of IDUS, tumor extension outside of the hepatoduodenal ligament is difficult to assess. The use of IDUS in M-staging is therefore limited (69, 93).

Since bile duct carcinomas spread longitudinally, accurate determination of the extent of spread is important for planning operative intervention and margins of resection (94–99). Cholangiography is frequently used; however, this appears to be fairly inaccurate in this setting. In one study, IDUS was significantly more accurate than cholangiography in determining the longitudinal spread of the cancer toward the liver (84% vs. 47%) and toward the duodenum (96% vs. 43%) (62). This was confirmed in another report that cited IDUS as accurately determining the proximal extension of tumor in 92% of patients (61). The superiority of IDUS in comparison to cholangiography in assessing intraductal spread has been shown in other reports as well (75, 90).

It should be mentioned at this point that bile duct wall thickening may result from tumor spread or from peritumoral inflammation (61, 68, 75, 90, 100). This distinction cannot reliably be made with various noninvasive bile duct imaging, including IDUS (75, 89, 90, 101). Some echo-endoscopists have observed that inflammation typically causes symmetrical wall thickening in contrast to malignant infiltration that is typically asymmetric (61, 62). This distinction has not been universally observed, however (68). Another complicating factor in characterizing bile duct wall thickening is the effect of bile duct stents. Biliary stents have been shown to cause reactive changes that can lead to confusion, including overestimation of longitudinal tumor extension (62, 88, 100, 102). Unfortunately, bile duct stents are frequently required to decompress biliary obstruction. Therefore, it is generally recommended to perform IDUS prior to or within a few days of biliary decompression (62).

PANCREATIC INTRADUCTAL ULTRASOUND

Patients who present with signs or symptoms suggestive of a pancreatic neoplasm typically undergo initial transabdominal ultrasound or CT, which can reveal a pancreatic mass or fullness. Additional evaluation using endoscopic procedures such as ERCP and EUS may be required. There is growing evidence that pancreatic IDUS may be helpful for selected patients (67, 83, 103–105). The IDUS probe can usually be placed within the pancreatic duct without prior sphincterotomy (103, 106, 107). It may be difficult, however, to pass the probe into the proximal pancreatic duct since it can be tortuous. On pancreatic IDUS, the main pancreatic duct wall can appear as a single hyperechoic layer or up to three layers. The outer two layers, when visualized, will appear hyperechoic with an intervening hypoechoic layer (71, 103).

Pancreatic Duct Strictures and Pancreatic Adenocarcinoma

IDUS appears useful in characterizing whether pancreatic duct strictures are benign or malignant (83, 108). The accuracy of IDUS in characterizing pancreatic duct strictures has been reported up to 92% (67). In fact, one study demonstrated that IDUS was more sensitive and specific than EUS, CT, or ERCP. IDUS had 100% sensitivity versus 93, 64, and 86% sensitivity, respectively (83). IDUS has also been employed in the detection of pancreatic tumors in early stages. An echo-rich area surrounded by an echo-poor margin is fairly characteristic of pancreatic cancer (109, 110). Chronic pancreatitis, on the other hand, can appear as a ring-like echolucent band surrounded by a fine reticular pattern. The degree of heterogeneity has been described to be in proportion to the degree of fibrosis (83). In one large study, IDUS was found to be more sensitive and specific than EUS, CT, and ERCP in pancreatic imaging (67).

Mucin-Producing and Islet-Cell Tumors

IDUS also appears to have an emerging role in the evaluation of mucin producing tumors of the pancreas. Some of these lesions are premalignant or malignant and may undergo surgical resection. The appropriate diagnosis is crucial as these tumors have a better prognosis than ductal adenocarcinoma. Imaging studies such as transabdominal US, CT, and MR often inadequately differentiate between the cystic neoplasms. Initial experience suggests that EUS can be helpful, though IDUS may be

more accurate (111, 112). Furthermore, IDUS may be helpful in mucin-producing tumors of the ductal branches. For mucinous duct ectasia, IDUS can detect small lesions and determine the extent of intraductal spread and parenchymal invasion. In addition, IDUS can assess the extent of necessary surgery for patients with side-branch disease by identifying papillary tumor projections (67, 107, 113, 114). In one study, comparing IDUS with transabdominal US, CT, EUS, and pancreatoscopy by surgical and pathological confirmation for mucin-producing tumors of different origins, the detection rate of IDUS was superior (106). It should also be briefly mentioned that IDUS has been used with success in localizing pancreatic endocrine tumors (67, 105). These islet-cell tumors typically appear under IDUS as echo-poor, homogenous, well-delineated lesions. In one study, IDUS accurately determined the number of tumors in a patient with multifocal disease that was unrecognized under EUS (67).

PAPILLA OF VATER INTRADUCTAL ULTRASOUND

Lastly, it is worth mentioning the utility of IDUS in characterizing the size and extent of papillary tumors. IDUS has been shown to reliably distinguish the sphincter of Oddi muscle from the remainder of the papilla (115–118). IDUS, then, has great value in clearly visualizing the entire anatomy of the papilla. This was demonstrated in a prospective study of patients with papilla of Vater cancer that underwent surgical resection. IDUS was shown to accurately determine tumor extent at 88% in comparison to transabdominal US and CT, which only detected 9 and 6% of tumors, respectively (117). In another prospective study, IDUS compared favorably to EUS and CT in tumor visualization, diagnosis, and staging (116). Furthermore, in another study in patients with ampullary neoplasms, the accuracy of IDUS in T staging among patients who underwent endoscopic papillectomy was 100%. Overall, IDUS did appear to overestimate tumor staging; however, it appeared useful in therapeutic management (119). These studies indicate that IDUS may be the most accurate modality for diagnosis and local staging of tumors of the papilla of Vater.

FUTURE PROBE TECHOLOGY

The future of probe ultrasonography may lie in 3-D probes. These instruments are able to obtain up to 120 radial images per minute and produce 3-D figures. Initial reports suggest that 3-D EUS has been

accurate in delineating tumor volume and local invasion, with good explorer agreement and low interobserver variability *(*120–123*)*. By extension, some reports indicate that 3-D IDUS may better demonstrate biliary tract tumor extension *(*124–126*)*. In fact, 3-D IDUS may have an added advantage of decreased examination time as less time is spent characterizing relationships between lesions and surrounding structures (127).

CONCLUSION

In summary, continued advancements in ultrasound technology have led to the development of small caliber, catheter probes that can be passed through the accessory channel of a standard endoscope in HFUS or side-view scope in IDUS. These miniprobes operate with a higher frequency than standard EUS creating greater image resolution of mucosal and subepithelial lesions in the gastrointestinal tract and pancreatico-biliary tree. Indeed, HFUS appears to offer greater accuracy than standard EUS in T staging of early carcinoma confined to the mucosa or submucosa. As mentioned before, the greater imaging resolution of HFUS results in a loss of imaging depth. This can lead to impaired visualization of distant lymph nodes, and therefore compromised more distal nodal and metastatic staging. Despite these limitations, however, HFUS probes have allowed for more accurate evaluation of superficial tumors and subsequently have influenced therapeutic management such as endoscopic mucosal resection for early stage malignancies.

IDUS, on the other hand, appears to be an effective modality for diagnosing choledocholithiasis, evaluating biliary and pancreatic stenosis, and staging local carcinoma. IDUS can determine the etiology of bile duct strictures with a high sensitivity and specificity and significantly increase the diagnostic accuracy in comparison to other imaging studies or tissue sampling. As a result, IDUS is increasingly becoming an essential tool in the diagnostic work-up of patients with indeterminate biliary duct strictures. For patients with known malignant biliary strictures, IDUS has been shown to be superior to several other modalities in characterizing tumor extension. IDUS shows equal promise in pancreatic diseases, including pancreatic duct stenosis, small pancreatic tumors, intraductal papillary mucinous tumors, and neuroendocrine tumors. Clearly, high frequency ultrasound sonography has been validated in numerous clinical settings and has the potential for growth with further advancements in ultrasound technology.

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