VHJOE is an interactive online journal utilizing a powerful tool: the Visible Human Interactive Atlas. This web-based application, developed by the Center for Human Simulation, provides unparalleled views of human anatomy. By loading models of selected organs, and manipulating an image plane, unique images of human anatomy are created realtime and loaded into your browser window.
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EUS Movies in VHJOE

The next advance in the development of VHJOE has occurred. We are now able to accept and publish movies with VHJOE articles. This will provide a powerful tool to demonstrate image acquisition from EUS and endoluminal digital technology. Click on Video Clip 1 [online only] to view the video clip from the article titled “Insulinoma Unmasked by Bariatric Surgery” by J. Deutsch, M. Slag, and J. Streitz in this issue of VHJOE. Click on Video Clip 2 [online only] to see a moving image of the bile duct from the Visible Human database.

Video clips are most conveniently viewed using the newest versions of Internet Explorer browsing software and a Pentium IV processor, but should also be viewable with most current computer software and hardware. Contributing authors are encouraged to submit video files with their articles. These video files can be in any digital format or on SHVS tapes. Video files should be emailed to pubvhjoe@uchsc.edu as separate attachments from the article text file. All patient identification should be deleted from the video clips.

With this next step, we hope that the VHJOE becomes a dynamic and interactive device in which to expand one’s knowledge in EUS visualization, technical skills, and pertinent interactive anatomy. Additionally, our expert review columns are a place where one can turn for practical advice on the role of EUS in clinical medicine. This issue features an article by Dr. Richard Erickson titled “Endoscopic Ultrasound-Guided Fine Needle Aspiration of the Pancreas.” Dr. Erickson provides useful technical tips on the safe and effective use of EUS-FNA of pancreatic disorders.

Finally, we want to continue to emphasize interactions with the Visible Human anatomy database. Figure 1 is a linked image in the Visible Human database showing the SMV as it transverses the pancreatic head. Please click on this image to enter the database at this image. If you cannot interact, make sure you have installed the prerequisite downloads. (This is found under “Install Interactive Atlas.”)
Primary Splenic Artery Aneurysm Diagnosed by EUS

Introduction: A 44-year-old male was referred for EUS evaluation of pancreatic mass.

Methods for EUS Capture: EUS examination was performed with the Pentax FG-32UA linear array echoendoscope at 5 MHz. Images were obtained using a Sony thermal printer and subsequently scanned and saved in .jpg format.

Case: A 44-year-old male presented to an emergency room with a severe attack of epigastric pain associated with nausea and vomiting. He also gave a history of recurrent, episodic upper abdominal pain over the past ten years, occurring about twice a year. He had undergone an upper endoscopy in the past as work up for this abdominal pain, which was reportedly negative.

Past medical history was negative except for distant appendectomy and tonsillectomy. He was on no medications. Family history was non-contributory. He was a non-smoker and drank alcohol only occasionally.

Physical examination was unremarkable. The abdomen was non-tender and there was no bruise, palpable mass, or organomegaly.

Laboratory studies revealed a slightly elevated WBC at 13.1. Electrolytes and liver function tests were within normal limits. Serum amylase was elevated at 641 U/L (normal 30-110 U/L). An abdominal ultrasound was performed and revealed a 7 cm retroperitoneal inhomogeneous hypoechoic mass in the left upper quadrant. It was unclear whether this lesion was arising from the left adrenal or the pancreas. The patient subsequently had a CT of the abdomen that confirmed the presence of a homogeneous mass lesion with rim enhancement in the left upper quadrant, most likely arising from the pancreatic tail (Figures 1 and 2). No abnormal lymphadenopathy or ascites was noted. The patient was then referred for EUS evaluation and possible EUS-guided FNA of this mass lesion.

Linear array EUS identified a 72 mm by 60 mm inhomogeneous hypoechoic round mass lesion with smooth margins in the region of the pancreatic tail (Figure 3). Along the anterior edge of the lesion was a 30 mm by 25 mm anechoic structure which carried an arterial doppler signal (Figures 4, 5, and 6). This was demonstrated on EUS to be an aneurismal dilatation of the splenic artery as it could be followed continuously back to the celiac trunk medially and to the spleen laterally. A 7 mm by 6 mm hyperechoic shadowing area of calcification was within the aneurysm (Figure 7). This mass lesion was displacing the splenic vein posteriorly without invading it. It was felt that the “mass” most likely represented a contained hematoma or a pseudoaneurysm, rather than a pancreatic mass. Thus, fine needle aspiration of the lesion was not performed.

The patient was referred for surgical resection of the splenic artery aneurysm. A distal pancreatectomy and splenectomy were necessary since the lesion could not be separated from the pancreatic tail. After further dissection, a defect 1 cm in length was found in the splenic artery leading into the aneurysm. On final surgical pathology, the “mass” lesion was confirmed to be a large hematoma; the resection portion of the pancreas and the spleen were normal.

Discussion: Primary splenic artery aneurysm is an uncommon vascular pathology, with incidence of 0.01% to 0.2% reported at autopsy series (1-3). It accounts for up to 60% of all visceral artery aneurysms (1,4). There is a female predominance, with the mean age of presentation at 52 years (1, 5-8). They are usually saccular, and the majority of them are located in the mid to distal splenic artery. (1, 6-8). The pathogenesis of splenic artery aneurysm is not fully understood. However, there are close associations with medial fibroly dysplasia, multiple pregnancies, portal hypertension, liver transplant, and splenomegaly. Atherosclerosis and inflammation are often seen histologically; although they are most commonly secondary events resulting from primary degeneration of the media.

Most patients are asymptomatic, with aneurysm found incidentally on imaging studies. Up to 20% may present with epigastric or left upper quadrant abdominal pain (1, 9). Occasionally, the aneurysm can erode into an adjacent viscus or into the pancreatic duct and presents as gastrointestinal hemorrhage (3). Rupture of the aneurysm causes severe abdominal pain and hypovolemic shock. The initial rupture may be tamponaded within the lesser sac, with free intraperitoneal hemorrhage ensuing in minutes to hours. This double-rupture phenomenon allows valuable time for diagnosis and surgical intervention.

The reported risk of rupture varies from 3% to 10%, with a significant mortality rate of 36% after rupture. The risk of rupture is much higher during pregnancy and results in a
Introduction: Insulinoma is a rare condition associated with severe hypoglycemia and occasionally with hyperphagia. This is the first case report that we are aware of in which an insulinoma was unmasked by gastric bypass surgery.

Methods for EUS Capture: SVHS recording was digitally captured using Dazzle Movie Star software. EUS was performed with a Pentax EG3630UR solid state radial EUS at 7.5 MHz.

Case: A 48-year-old woman with chronic obesity underwent bariatric surgery with creation of a stapled gastric pouch and roux-en-y gastroenterostomy. Prior to her surgery, she had a craving for sweets but could sleep through the night without eating. She had otherwise felt well prior to her surgical procedure.

The surgery was uncomplicated. However, on the sixth postoperative day, she developed hemiparesis. A neurological and vascular evaluation was performed, and a patent foramen ovale was found. The patient was anticoagulated.

The patient had two similar events in the two following weeks, and, during an emergency room evaluation, after an overnight fast, was found to have a blood sugar of 24 mg/dl. A simultaneous insulin level was 6.2 micro IU/ml (nl 1.4-14) and C-peptide was 740 pmol/l (nl 170-900). She was given intravenous glucose with resolution of her hemiparesis.

She was transferred to our hospital for further evaluation. The patient had no prior medical problems. Her only medications at the time of evaluation were aspirin.
Although some subjects with insulinoma have normal body weight, which are usually benign but often quite symptomatic (1, 2). The patient's symptoms have totally resolved, and postoperative blood sugar levels have remained normal.

Figure 4A and 4B. Representative Visible Human images and an entry into the Visible Human database are shown in Figures 2A-2C. The patient underwent EUS. The forward viewing Pentax solid-state instrument was advanced to the gastric-jejunal anastomosis but could not be passed through this narrowed area. Therefore, scanning was done through the gastric remnant at 7.5 mHz. A 1.1 cm by 1.1 cm hypoechoic mass was found in the pancreas adjacent to the splenic artery (Video: Video Clip 1; Images: Figures 1A and 1B). Representative Visible Human images and an entry into the Visible Human database are shown in Figures 2A-2C.

The patient was taken to surgery, and her pancreas explored. The tumor was not initially palpable but was ultimately found underneath the retrogastric Roux-en-y limb using intraoperative ultrasonography (Figure 3). It was removed by enucleation uneventfully. Pathology revealed a completely resected insulinoma. Histology and chromogranin stains are shown in Figure 4A and 4B.

The patient’s symptoms have totally resolved, and postoperative blood sugar measurements have remained normal.

Discussion: Insulinomas are rare tumors which are usually benign but often quite symptomatic (1, 2). Although some subjects with insulinoma have normal body habitus (3), hyperphagia can result from the patient’s attempts to alleviate symptomatic hypoglycemia. This causes some subjects with insulinoma to gain weight (4, 5).

The evaluation of subjects in which insulinomas are considered generally begins with biochemical screening. Laboratories suggestive of insulinoma include hypoglycemia with inappropriately elevated insulin and C-peptide levels as well as a negative evaluation for oral hypoglycemic agents (1-5).

Our case report has the typical biochemical features that suggest insulinoma. As part of the initial evaluation, CT scanning was performed to look for a mass. Although this is often done, CT is notoriously poor at localizing insulinomas (6). EUS has become the preferred method to image the pancreas when insulinoma is suspected, and in this case, EUS identified the tumor after a normal CT scan, despite the limitations imposed from previous anti-obesity surgery. At the time of surgical resection, the addition of intraoperative ultrasonography (11) made surgical removal possible with minimal morbidity despite the altered anatomy.

The most interesting aspect of this case was the manner of presentation. The patient presented with significant neurologic symptoms following anti-obesity surgery. This suggests to us that the insulinoma had been effectively palliated by the patient through overeating, and only when her caloric intake was curtailed, did she suffer the effects from her tumor. As far as we are aware, this is the first case in which anti-obesity surgery unmasked an insulinoma and suggests that evaluation for hypoglycemia may be useful in the evaluation of subjects with morbid obesity.

References:
type-2 diabetes mellitus and morbid obesity. 


\textbf{Review} || Richard A. Erickson MD, FACP, FACG

\textbf{Endoscopic Ultrasound-Guided Fine Needle Aspiration of the Pancreas}

\textbf{Introduction:} Few clinical problems warrant as much urgency for definitive diagnosis as pancreatic masses. Because of its unique diagnostic capabilities, endoscopic ultrasound (EUS) and EUS-guided fine needle aspiration (EUS-FNA) have become important tools in the evaluation of pancreatic masses (1-7). The first commercially available radial echoendoscopes were introduced in Japan (8) and Europe (9) in the mid to late 1980s. Although radial instruments were used for fine needle aspiration (10), EUS-FNA did not become technologically practical until the early 1990s (11) when linear echoendoscopes were introduced. This introduction generated ultrasonic images parallel to the instrument over the exit port of the biopsy channel. With this modification, objects exiting the biopsy channel of the endoscope (e.g., a needle) could be followed and guided into lesions in “real-time.” Very soon after the introduction of linear echoendoscopes, the first report of EUS-FNA of the pancreas appeared (12) and, shortly thereafter, of EUS-FNA of a pancreatic cancer (13). Since 1994, there have been numerous series reporting on the safety, technique, and yield of EUS-FNA of the pancreas (4, 6, 10, 14-24). This review will focus on our current understanding of the utility, technique, and safety of EUS-FNA of the pancreas.

\textbf{Body:}

\textit{Utility of EUS-FNA of the Pancreas}

The foremost indication for EUS-FNA of the pancreas is for the definitive diagnosis of pancreatic masses. Approximately 90% of pancreatic neoplasms are adenocarcinomas, another 5% are cystic lesions, and some 2-5% are neuroendocrine tumors (25). The remainder are metastatic lesions to the pancreas, primarily from renal cancer, lung cancer, and lymphomas. Because cystadenocarcinomas (26) and neuroendocrine tumors (27) of the pancreas have a significantly better prognosis than pancreatic adenocarcinoma, accurate cytologic preoperative identification can significantly alter the subsequent management of these patients (28).

As an imaging modality, many series (1, 3-6) have demonstrated that EUS is superior to CT, MRI, and ERCP (29) in the diagnosis of pancreatic diseases and especially neoplasms. Detection rates for pancreatic cancer using EUS, even lesions less than
3 cm, have been consistently in the range of 95-100%. However, the superiority of EUS for pancreatic pathology detection is being continually challenged by the technologic advances in CT and MRI imaging, although well-controlled, head-to-head trials of comparable patients are still scare (30). Positron emission tomography (PET) also may play a significant role in pancreatic cancer detection, especially in looking for occult pancreatic malignancies or metastatic disease (31). However, just finding an imaging abnormality is often not enough to determine subsequent management of patients with pancreatic masses. The rational for attempting to obtain a cytologic diagnosis of most pancreatic masses has been detailed elsewhere (1, 32). When combined with FNA capabilities, EUS has the powerful advantage over all other imaging techniques of being able to immediately sample any suspicious lesions seen in the pancreas. The one area where malignancies can be still easily missed by EUS, even with EUS-FNA, is in the setting of underlying chronic pancreatitis (3, 6, 12, 18, 23, 33-35). No single or combination of imaging modalities has yet proven accurate in definitively determining when a patient with chronic pancreatitis has developed pancreatic cancer. This clinical dilemma may have to await continued progress in the molecular diagnosis of cancer (36, 37).

**Technical Considerations**

The technique of EUS-guided FNA has been described in detail elsewhere (19, 23) but basically involves passing an 18 to 22 gauge metal needle through the biopsy port of a linear echoendoscope under real-time guidance into an endosonographically visualized pancreatic mass, associated lymph node, liver metastasis, or fluid collection. The needle is then moved back and forth 5 to 10 times through the lesion with varying degrees of suction applied to it. The specimen is then deposited on a cytology slide(s) for immediate fixation and staining and cytopathologic examination. Since its initial inception, there have been significant technologic advances in needle technology and are now at least three manufacturers of effective disposable and semi-disposable EUS-FNA needles. There are also new innovative devices such as spring activated needles to help penetrate firm lesions and cutting needles to provide small cores of tissue to try and perhaps improve diagnostic accuracy (38). Biopsy most distant disease first: Because the specificity of a cytologic diagnosis of malignancy is almost 100%, in performing

EUS-FNA for pancreatic neoplasms, a general guiding principle is to try to cytologically confirm the most advanced stage of the tumor. Thus, during EUS-FNA of pancreatic masses, needle aspiration should first be done of any potentially metastatic disease in the liver (Figures 1-4) or in the peritoneum (ascites), then any distant pathologic lymph nodes, then regional nodes, and, finally, if these are negative, the primary mass can be aspirated. In addition to cytopathologically documenting the most advanced degree of the patient’s tumor stage, EUS-FNA of malignant liver lesions is usually easier than pancreatic mass FNA in that it only takes 1 to 2 needle passes for a positive cytology. Likewise, lymph nodes usually only require 1 to 4 passes to obtain a cytologically positive diagnosis (17, 23, 39-41).

Cytopathology interaction: The yield of EUS-FNA of primary pancreatic malignancies has been reported to run from 80-93% (4, 6, 10, 14-21, 23). Obtaining a high yield of positive diagnoses in pancreatic EUS-FNA is very dependent on FNA technique and the active involvement of a cytopathologist. Most very active EUS-FNA centers have a cytopathologist on site to provide immediate feedback on the adequacy and preliminary cytocologic diagnosis (10, 14, 15, 18-21, 23). Live feedback from a cytopathologist results in about a 10% increase in the yield of a positive diagnosis (17, 21, 23).

Where to aspirate a pancreatic mass: Choosing what part of a pancreatic mass to aspirate is something of an art that comes with experience in aspirating these lesions. The most difficult pancreatic masses to aspirate are those located near the uncinate portion of the pancreas where it can be very hard to direct the needle around the second and third portion of the duodenum to enter the lesion. Novice endosonographers are also surprised by how much force it may take to make an FNA needle penetrate deeply into the typical pancreatic adenocarcinoma because of the surrounding desmoplastic reaction. The usual temptation is to biopsy deep into the center of a mass; however, this may yield only necrotic debris with few intact tumor cells. EUS-FNA of the edge of the tumor may yield only peritumor pancreatitis (Figures 5A and 5B). The best yield of diagnostic cells usually seems to come from 1 cm to 2 cm deep to the echolucent margin of the tumor (Figures 5B-7). Color flow Doppler can be used prior to EUS-FNA to help avoid vessels overlying the proposed path of the aspiration needle such as are seen when there is underlying portal vein or splenic vein obstruction.
Number of EUS-FNA passes: Most pancreatic EUS-FNA series report taking an average of three to four needle passes to make a definitive cytopathologic diagnosis of pancreatic cancer. The major determinant of the number of EUS-FNA passes needed to diagnose pancreatic adenocarcinoma is the differentiation of the tumor (23). Some well-differentiated tumors may take over ten separate passes to obtain enough diagnostic material. Although, performing this many passes may be frustrating for the endoscopist and cytopathologist, the consequences of a non-diagnostic aspirate may mean more procedures, including unnecessary surgery, for the patient. If a cytopathologist is not available to immediately assess the slides, then five to six passes of the lesion are recommended (23). However, this approach may produce non-diagnostic EUS-FNAs 15-20% of the time.

Aspiration tips: The ideal EUS-FNA specimen should produce just a few drops of slightly serosanguinous fluid, perhaps with a few particles of tissue visible within the specimen. If an aspirate just looks like pure blood, it is less likely to have much diagnostic material within it. Whether to use hard suction or minimal suction on the aspiration needle is a matter of preference in pancreatic EUS-FNA. My own approach is to use moderate suction initially for pancreatic masses (5 ml of suction in a 10 ml syringe). If I get a bloody aspirate with this approach, I make subsequent passes with minimal or no suction. Often just pulling back the needle trocar about 10 cm with each stroke or two of the needle in the tumor will provide enough suction to retrieve a diagnostic specimen. Whether using larger needles will increase diagnostic yields with the same degree of safety as 22 gauge needles is still unclear (38). Sometimes a few additional passes are needed to provide the cytopathologist with adequate material for special cytoplogic analyses (Figures 6 and 7). This most commonly occurs when the initial EUS-FNA suggests that the tumor may be something other than a pancreatic adenocarcinoma such as a lymphoma, islet cell tumor, or metastatic tumor. Lymphoma diagnosis by cell surface markers depends on obtaining enough viable tumor cells preserved in a special medium (42). Sometimes a few additional passes may be frustrating for the endoscopist, but one of these diagnoses is suspected, then the EUS-FNA may result in an equivocal cytopathologic diagnosis for lack of adequate material for special processing.

EUS-FNA of Cystic Pancreatic Masses: EUS-FNA of cystic pancreatic lesions is different than for solid lesions. About 75% of cystic pancreatic lesions are pseudocysts (43). The goal of EUS and EUS-FNA is to differentiate truly benign lesions such as pseudocysts and serous cystadenomas from precancero us lesions such as mucinous cystadenomas (44) and intraductal papillary mucinous tumors (IPMT) (45) of the pancreas from frankly malignant cystadenocarcinomas (Figures 1 and 3). There are a number of studies demonstrating the endosonographic characteristics of these various cystic lesions (44-46); however, EUS-FNA continues to play a role especially in examining the suspicious multiplecystic pancreatic cystic lesion. Obtaining a diagnostic cytology from malignant cystic lesions by just aspirating the cyst contents is low yield. If there is any solid component to the wall of a pancreatic cyst, this should be aspirated aggressively after draining the cyst contents. Chemical analysis of the cyst fluid has been studied extensively. Only an elevated cyst fluid carcinoembryonic antigen (CEA) seems to have any consistent predictive power in identifying likely mucinous cystadenomas and cystadenocarcinomas (44).

EUS-FNA for benign disease: EUS-FNA for benign disease other than pancreatic cystic lesions is still in its infancy. Although it appears to be safe, pancreatic EUS-FNA does not appear to add significantly to the diagnostic accuracy of EUS for chronic pancreatitis (47).

Complications of EUS-Guided Fine Needle Aspiration: The overall complication rate of pancreatic EUS-FNA appears to be about 1-2% (4, 6, 10, 14-21, 23, 48), similar to that reported with CT, ultrasound-guided FNA, or biopsy. The major complications reported with EUS-FNA are bleeding, pancreatitis, and infection. Only one death has been reported to date with pancreatic EUS-FNA (10) which was uncontrollable bleeding after EUS-FNA using a radial echoendoscope. Extraluminal bleeding can actually be observed while doing EUS-FNA as an expanding echo-poor lesion adjacent to the aspirated lesion (49). In my own experience, bleeding is especially likely when the patient has portal hypertension from portal vein or splenic vein obstruction from the pancreatic neoplasm or when aspirating metastatic renal carcinoma to the pancreas (Figures 8-11). Pancreatitis after EUS-FNA is most likely to occur in patients already being evaluated for recurrent pancreatitis and when the FNA needle is passed through more than 2 cm to 3 cm of normal pancreas to obtain a specimen. Fortunately, bacteremia following EUS-
FNA is quite uncommon (50); however, EUS-FNA of cystic pancreatic lesions has a higher risk of infectious complications (48). Because of this risk, broad-spectrum intravenous antibiotics during aspiration followed by a few days of oral antibiotics are routinely given for EUS-FNA of cystic pancreatic lesions. The risk of cancer seeding by EUS-FNA appears to be very low. I know of only one anecdotal case of documented EUS-FNA peritoneal seeding after aspirating a cystadenocarcinoma (Goldin SB, personal communication). Supporting the low incidence of peritoneal seeding with EUS-FNA is a recent interesting abstract (51) which reported a significantly lower incidence of peritoneal carcinomatosis after EUS-FNA of pancreatic cancers compared to percutaneous FNA.

**Summary:** In conclusion, EUS-guided FNA has high sensitivity, specificity, and diagnostic accuracy that are comparable to that of mediastinoscopy and trans-bronchial FNA, and allows sampling of nodes that cannot be easily obtained with the other methods. When mediastinal adenopathy due to lung cancer is suspected from imaging studies, it can serve as a first-line means to obtain a definitive tissue diagnosis, and can safely and efficaciously provide the staging information that is so critical in guiding therapy. Compared to EUS/FNA of the pancreas, transesophageal EUS/FNA of mediastinal lymph nodes is technically much easier, and should allow physicians new to EUS/FNA to still maintain a high diagnostic accuracy despite a relative lack of expertise.

**References**

The majority of these neoplasms are immunohistochemical staining. should be avoided in most cases, unless the leiomyoblastoma, and leiomyosarcoma phenotypic origin of these neoplasms stromal tumor (GIST) to indicate that the correct terminology is now gastrointestinal muscle cell types. Therefore, the preferred and now be classified into several subtypes based (6-11). These submucosal stromal tumors can neoplasms is possibly the interstitial cell of Cajal smooth muscle, these tumors were originally only about 1% of all gastrointestinal tumors gastrointestinal tract. However, they comprise most common submucosal tumors of the B

Figure 1: Submucosal antral tumor.

Figure 2: Umbilicated GIST in gastric fundus.

asymptomatic and are discovered incidentally during endoscopic or radiologic examinations. They occur in equal frequency in men and women, generally after the fifth decade (1-5). The overlying mucosa usually appears smooth and normal at endoscopy (Figure 1). Large tumors may outgrow their blood supply, ulcerate, and present with gastrointestinal bleeding (Figure 2). GISTS may also present with obstructive symptoms, especially if they are located at the cardia (Figure 3) or near the pylorus. Pain and weight loss, often associated with very large GISTS, are symptoms that suggest malignancy. However, benign GISTS may also be large and the differential diagnosis is clinically difficult. Histologic diagnosis of GIST is usually not possible by endoscopic biopsy because these neoplasms are located below the submucusa and are quite firm.

The differentiation of benign and malignant GISTS is difficult even after the tumor has been surgically resected. Pathological series have reported a malignancy rate of 13 to 56% in resected tumors (1-5) A combination of pathological criteria, which includes size of neoplasm, mitotic rate (> 4 mitoses per high

**Stromal Tumors**

**Body:** Mesenchymal tumors are the most common submucosal tumors of the gastrointestinal tract. However, they comprise only about 1% of all gastrointestinal tumors (1-3). Based on a histological resemblance to smooth muscle, these tumors were originally referred to as leiomyomas, leiomyoblastomas, and leiomyosarcomas (1-5). This terminology continues to be commonly used. Detailed structural studies using immunohistochemical staining with molecular markers have demonstrated that the cel of origin of these neoplasms is possibly the interstitial cell of Cajal (6-11). These submucosal stromal tumors can now be classified into several subtypes based on differentiation into neuronal and/or smooth muscle cell types. Therefore, the preferred and correct terminology is now gastrointestinal stromal tumor (GIST) to indicate that the phenotypic origin of these neoplasms may be uncertain. The terms leiomyoma, leiomyoblastoma, and leiomyosarcoma should be avoided in most cases, unless the tumor has been extensively characterized by immunohistochemical staining.

The majority of these neoplasms are...
power field are associated with malignancy), tumor cell necrosis, increased cellularity, cellular atypia, and invasion into adjacent organs are used to help diagnose malignancy (11, 25, 29).

Because large tumors may be benign and tumors with a low mitotic rate may metastasize, even expert pathologists cannot predict the behavior of all GISTs after resection.

Endosonography (EUS) has become an invaluable imaging modality for the clinical diagnosis of GIST and for differentiating these neoplasms from other submucosal lesions (12-16). At EUS, GISTs are characterized by a hypoechoic appearance (Figure 4) and can be seen to originate from the fourth hypoechoic endosonographic layer (muscularis propria). They are generally ovoid or elliptical in shape but may be multilobular or pedunculated.

EUS features that should be characterized when imaging a GIST include regularity of the extraluminal border (Figure 5), presence of cystic spaces (Figure 6), echogenic foci (Figure 7), heterogeneity and size (17-20). An irregular extraluminal border (Figure 8) is likely associated with an invasive tumor, cystic areas likely represent cellular necrosis, and echogenic foci are likely caused by fibrosis (17). These histopathological features along with size are criteria that are used to diagnose malignancy. The corresponding EUS features along with endosonographic measurements of size also appear to be able to differentiate benign GISTs from malignant ones. If multiple EUS features are present in a large GIST (>3 or 4 cm), then the neoplasm is likely malignant, and if a GIST is < 3 cm in size, homogeneous, and smooth, it is likely benign. The behavior of a GIST that is < 4 cm in size and contains one or two of the EUS features is difficult to predict. One must remember that the EUS interpretation of these features is dependent on the endosonographer and is subject to a fair degree of inter-observer variability (17).

Multiple investigators have attempted to use EUS guidance to obtain diagnostic histological material (21-24). Unfortunately, fine needle aspiration of these lesions has not been very successful. Firstly, because they are very firm, a large amount of force is required to penetrate the neoplasm with a narrow gauge needle. Secondly, the neoplasms may be fibrotic and it may be difficult to obtain cytological material by aspiration. Finally, because the diagnosis of malignancy is dependent on histology and architecture, even if an adequate cytological specimen is obtained by EUS guided fine needle aspiration, a reliable diagnosis of a benign GIST cannot be made. A guillotine needle that permitted endoscopic biopsies of GISTs and obtained a core specimen was developed (21). However, it did not gain popularity probably because of concern for bleeding and difficulty in use. A recent pilot investigation (25) demonstrated that immunohistochemical staining using CD34, c-kit, and Ki-67 labeling index was able to diagnose GISTs preoperatively but the diagnosis of malignancy in this study was still based on tumor size and mitotic index. Other investigators confirm these results in larger studies, then this methodology might provide a pre-operative method for the histological diagnosis of GISTs. Large bore and Trucut needles being developed for EUS use may further enhance the ability to obtain a core of tissue from within these firm neoplasms. However, given that pathologists have difficulty in determining the behavior of a GIST even after the entire specimen has been resected, it remains unclear whether improved techniques for obtaining tissue under EUS guidance will improve clinical decision making.

Surgical resection is the only treatment that is effective for symptomatic GISTs. Surgery should also be performed on incidental GISTs that are large or have several EUS features associated with malignancy. GISTs that appear benign at EUS can be safely observed. The frequency with which characteristically benign asymptomatic lesions should be re-imaged has not been determined but is likely in the order of several years. It is difficult to decide what to recommend to patients who have GISTs that are indeterminate at EUS. These management decisions should be made on a case-by-case basis. Gastric tumors that are amenable should probably be re-imaged for laparoscopic excision, if the patient is a good surgical candidate. Esophageal GISTs are more likely to be benign and should probably be left alone, provided that they are not symptomatic. Excision of duodenal tumors requires a more aggressive approach and should only be attempted when there is a high suspicion of malignancy. Colonic and rectal GISTs are unusual. Excision of small rectal GISTs may sometimes be possible using a transanal approach. Until recently, therapy of metastatic GISTs was largely ineffective. However, the discovery that a large number of GISTs are malignant because of the presence of a mutated c-kit gene (26-28) and the availability of a specific chemotherapeutic agent that targets this oncogene has led to remarkable advances in the chemotherapy of this uncommon gastrointestinal malignancy.

References
7. Ueyama T, Guo K-J, Hashimoto H, Daimaru Y, Enjoji M. A clinicopathologic and immunohistochemical study of gastrointestinal
The purposes of this study were to develop a noninvasive method for measuring intravascular pressure, and to develop a model of esophageal varices that can be used to test this pressure measurement device. The authors concluded that the variceal pressure measuring device developed for this study measured intravascular pressure in a model varix with a low percent error and high correlation to the actual pressures. Intraobserver and interobserver variability was low.

This study validates in a variceal model the ability of a modified EUS miniprobe to measure pressure in esophageal varices. Since EUS is now established as a method of imaging, EUS guided FNA with ability to get a tissue diagnosis, EUS may also be a useful in the future for physiological measurements such as variceal pressure measurement in a minimally invasive way. The results from this group are very promising and further research in this area would be beneficial.

Figure 8: Multilobular, heterogeneous, GIN with irregular outer border.

EUS in the Literature || Manoop Bhutani MD

The aim of this prospective, blinded study of patients with rectal cancer, was to assess the impact of preoperative staging on treatment decisions and compare the tumor (T) and nodal (N) staging performance characteristics of pelvic computed tomography (CT), rectal endoscopic ultrasonography (EUS), and EUS FNA. The authors concluded that preoperative staging with EUS results in more frequent use of preoperative neoadjuvant therapy than if staging was performed with CT alone.

The addition of FNA only to EUS improved the management of one patient, whereas FNA did not significantly improve N staging accuracy over EUS alone. FNA seems to offer the most potential for impacting management in those patients with early T stage disease, and its use should be confined to this subgroup of patients. EUS is more accurate than CT for determining T stage of rectal carcinoma.

This study is a good case in point that every lymph node or mass lesion seen by EUS that could potentially be subjected to EUS should not be punctured, but rather a decision should be made on a case to case basis based on the potential clinical impact of the EUS guide FNA.