Pancreatic Endoscopic Ultrasound

Pancreatic Endoscopic Ultrasound:

Current Practice and Clinical Applications

Edited by

Leonardo Sosa Valencia
and Lee L. Swanström

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This book has mainly images in gray scale pattern from internal echographic multi slices of the human body but there are some images with doppler, elastography, histology and of the digestive tract mucosa in color that due to publication policies are printed in gray scale, however the digital version keeps the original format of all the images' characteristics.

PREFACE

Endoscopic ultrasound (EUS) has gradually acquired a major and indisputable place for the examination of the pancreas. This is essentially for anatomical reasons, EUS being able to explore as closely as possible the whole of this rather hidden organ. The position of EUS has been reinforced in recent years, both for diagnosis – thanks to recent advances in imaging technologies and tissue acquisition techniques – but also for treatment, thanks to new devices for drainage of ducts and cysts or for ablation of pancreatic tumors or cysts.

It is certain that the EUS revolution is the most impressive and the most useful for the pancreas. I admit to being enthusiastic and fascinated by a clever EUS examination of the pancreas, when, for example, the expert is able to see the precise relationship between the pancreatic duct and an endocrine tumor in 3 dimensions, or to conduct a meticulous and complete staging of a cancer of pancreatic head, or position a needle with millimeter precision, or analyze all the details of a cystic lesion. It's really about piloting around and within the pancreas, thanks to the technology but also to the expert's ability to localize himself in 3 dimensions and skillfully handle the probe. This combination of technology and human adaptability is very specific to pancreatic EUS.

It is therefore quite logical that a book be devoted exclusively to the place of EUS in the pathology of the pancreas, in particular cancer. This book covers all the subjects, from the technique which must be well codified for the exploration to be complete, to a chapter on the future of pancreatic EUS. This book also gives the floor to surgeons and radiologists on the role they attribute to EUS. And finally, it should be emphasized that this book focuses on training and quality criteria, very important elements to codify and implement, because everyone knows that the performance of EUS is relatively operator dependent.

I have no doubt that this book, developed with recognized experts, will become a reference book for endoscopists wishing to learn or complete their training in pancreatic EUS. It took the passion of Leonardo Sosa Valencia and Lee Swanström for this technique to launch and lead this project to

completion and to bring together energies and expertise. This is a book generated by enthusiasts and scientists.

I am not likely to be mistaken in predicting a long life for pancreatic EUS and therefore a long life for this book which will certainly not fail to evolve in the future.

Thierry Ponchon MD,
Lyon University, France, past president of ESGE

ACKNOWLEDGMENTS

Lee and Leo would like to acknowledge the valuable time and effort of the authors of this book, world experts who are united by their love of Endoscopic Ultrasound, developed more than 30 years ago and still misunderstood by many people worldwide. Thank you as well to all the patients who had EUS and contributed to enlarging our knowledge and developing the skills expressed in the content of these chapters. And finally, thanks to all the doctors and persons who will use these 370 pages to advance their understanding and provide better care for their patients and themselves.

CHAPTER ONE

HOW TO PERFORM PANCREATIC EUS WITHOUT MISINTERPRETING THE PANCREAS: CRITICAL ANATOMY ASSESSMENT AND TRICKS

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Introduction

Pancreatic cancer (PC) is one of the leading causes of cancer-related mortality. Early diagnosis of pancreatic tumors plays a fundamental role in the cancer management by recognition of patients who are potential surgical candidates. Improvements in radiological imaging and in endoscopy expertise - including endoscopic ultrasound (EUS), endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic stenting techniques - have had a significant impact in the diagnostic evaluation, staging and

management of PC, which commonly requires a multidisciplinary approach involving radiology, endoscopy, medical oncology and surgery.

EUS is an endoscopic imaging modality that uses an ultrasound transducer on the tip of the flexible endoscope that provides a detailed and high-resolution spatial imaging of the pancreas comparable to CT or MRI. Linear EUS provides imaging in the same plane as the shaft of the endoscope, whereas radial EUS generates images in the plane perpendicular to the shaft of the endoscope. Since its first introduction into clinical practice in 1980, EUS has established itself as an important diagnostic tool for a wide range of pancreatic diseases. One of the earliest successful applications was the detection of small pancreatic neoplasms (under 2 cm in size), where EUS has been shown to be as sensitive as magnetic resonance imaging (MRI), computed tomography (CT) or abdominal ultrasound (US)[1]. EUS provides very high-resolution imaging for the identification and evaluation of small pancreatic masses and cysts due to the proximity of the EUS transducer to the pancreas (including the digestive wall, from a few mm to a few cm), obtained by positioning the transducer in the esophago-gastric junction (EGJ), body and antrum of the stomach, bulb and second portion of the duodenum. This also eliminates the effect from artifacts produced by intestinal gas and fat that often compromises other imaging modalities.

PC screening is recommended for high-risk individuals including those with familial pancreatic cancer (direct relatives) and those with known germline genetic mutations for the development of pancreatic cancers (STK11/LKB1, PRSS1/SPINK1, p16/ CDKN2A, MLH1, MSH2, MSH6, TP53, APC, ATM, BRCA1, BRCA2, PALB2, MEN1, VHL, NF1 and TSC1/TSC2) with the following related syndromes: *Peutz-Jeghers, Hereditary Pancreatitis, Familial Atypical Multiple Mole Melanoma, Lynch Syndrome, Ly-Fraumeni, Familial Adenomatous Polyposis, Ataxia Telangiectasia Mutated, Breast/ ovarian cancer syndromes, Multiple Endocrine Neoplasia type 1, Von Hippel-Lindau disease, Neurofibromatosis type 1, Tuberous sclerosis*. Non-invasive imaging (such as MRI and CT scan) and minimally invasive imaging with EUS are the first-line screening tools for this high-risk population[2], however screening indications are controversial today due to the costs and relative rarity of PC.

EUS is probably more sensitive, specific and accurate in the detection of pancreatic lesions than high-quality cross-sectional imaging. Numerous studies (n=23) have shown high sensitivity (92%–100%), specificity (89%–100%) and accuracy (86%–99%) of EUS in the detection of pancreatic malignancies which is higher than that of CT scan, particularly for small

diameter pancreatic lesions[3]. In a systematic review of 66 studies, EUS has been shown to be the most sensitive and specific investigation technique in identifying pancreatic lesions under 2 cm when compared to other imaging modalities[4].

Kurihara *et al* proposed a study to evaluate the utility of EUS in the early diagnosis of PC. CT and MRCP detected main pancreatic duct (MPD) stenosis in several cases, but seldom detected tumors. EUS on the other hand had a high detection rate for early-stage tumor lesions. Therefore, cases with main pancreatic duct dilation or stenosis, especially with tumors that cannot be identified on CT and MRI, should be offered EUS examination with the added benefit of fine needle biopsy (FNB).

The advantages of EUS over cross-sectional images for detecting small pancreatic masses (0.5–2 cm) and its ability to perform EUS-guided fine needle aspiration (EUS-FNA) or fine needle biopsy (EUS-FNB) are of paramount importance for confirmation of tissue diagnosis whenever histology is required for clinical management.

Pancreatic EUS examination

To obtain the benefits of EUS pancreatic diagnostics, a quality exam must be performed. It is critical to image the entire pancreatic gland. The body and tail of the pancreas are more effectively imaged through the posterior wall of the stomach. This transgastric approach also provides images of the genu (neck) of the pancreas. Regarding complete examination of the pancreatic head, it is necessary to place the transducer in three different positions within the duodenum: the apex of the duodenal bulb (the apical view), directly opposite the papilla ("kissing the papilla"), and slightly distal (1-2cms) to the papilla to visualize and include the lower part of the head and the uncinate process with the superior mesenteric vessels (artery and vein).

A systematic approach, based on stations, is of assistance for obtaining pancreatic imaging, especially by endoscopists who are learning, or who have limited experience with EUS. Despite these stations being the same for radial and linear endosonography, the images produced are different and the techniques for maneuvering the echoendoscope are different for each modality. Some doctors prefer to evaluate the head and the uncinate process from the duodenal bulb and/or the gastric antrum because passing to the second part of the duodenum represents a perforation risk, however this technique limits the complete pancreatic evaluation and in some overweight

patients this could contribute to missing lesions or a particular pathology, leading to a false negative exam. Correct but safe duodenal positioning should always be taught to practitioners because difficulties are encountered with the different anatomical shape of the genus superior.

The procedure (radial and linear) is performed with the patient in left lateral position under sedation in some countries and in decubitus dorsalis and under general anesthesia in other countries.

Radial EUS examination

The radial echoendoscope produces images in cross sectional orientation. Therefore imaging is usually easier to interpret because the images are orientated in a similar way to CT scan. The pancreatic body and tail are best examined from the stomach while pancreatic head and uncinate process are best examined from duodenum. Table 1 summarizes the basic scanning positions, visualized regions and the corresponding landmarks[1].

Table 1: Stations and landmarks for orientation and scanning in EUS examination of the pancreas
PV=Portal vein, SMV= superior mesenteric vein

Station	Visualized regions	Landmarks
Stomach (antrum and lower-middle body)	Pancreatic body; pancreatic tail	Splenic vessels; left kidney; superior mesenteric vessels; celiac trunk; left adrenal gland, aorta
Duodenal bulb (D1)	Pancreatic head; pancreatic body; common bile duct; gallbladder	PV; SMV; splenic vein
Descending part of duodenum (D2)	Pancreatic head; pancreatic genu; major papilla; gallbladder	Aorta; inferior vena cava; superior mesenteric vessels; PV

A radial EUS examination starts at the first station, adjacent to the EGJ. The left lobe of the liver is readily seen when the probe is in this EGJ position.

The scope should be rotated clockwise (rotation to the right) until the aorta is oriented to the 6 o'clock position. Figure 1.

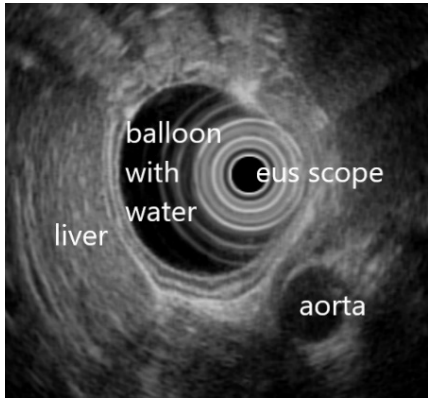


Figure 1: first EUS station at EGJ position.

The scope is next advanced, following the aorta, until the take-off of the celiac trunk is seen, which is traced until it bifurcates into the hepatic artery, which can be seen on the left side of the screen and the splenic artery on the right side of the screen. Once the splenic artery is detected, one can follow it with a slight clockwise turn and withdrawing of the scope. This movement ne to visualize the pancreatic body and tail all the way to the splenic hilum. Figure 2. The main pancreatic duct can be visualized with a back-and-forth movement of the scope.

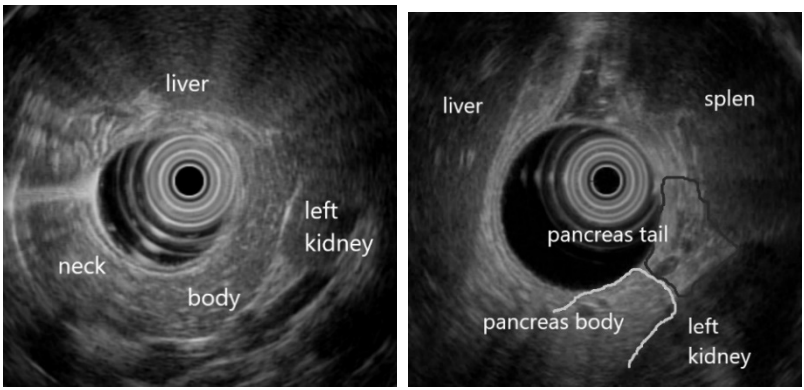


Figure 2: first EUS station.

At the splenic hilum, one can next follow the splenic vein back to the neck of the pancreas with a counterclockwise torsion and scope advancing movement. The splenic vein can be traced from the splenic hilum back to the splenic and portal vein (PV) confluence. Figure 3.

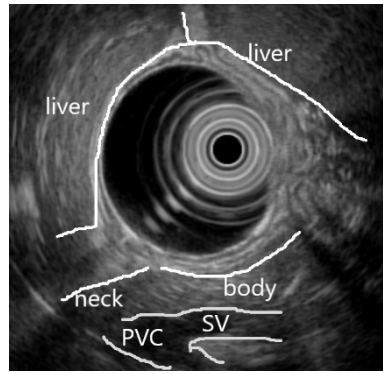


Figure 3: Following the splenic vein, first station.

The second station is located in the gastric antrum, with the scope oriented in the direction of the anterior wall and lower gastric curvature. This station is not specifically designed to assess the pancreas itself, but it is a useful window to screen the liver hilum and gall bladder to rule out stones, polyps or masses, which is an essential component of the pancreatic exam. Figure 4.

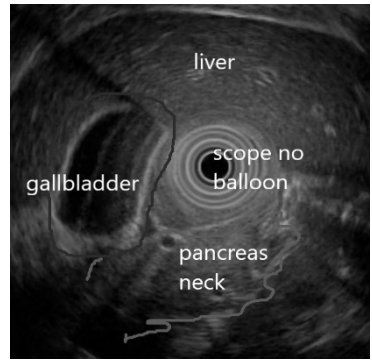


Figure 4: second station at the antrum.

The third station begins in the duodenal bulb, transducer oriented towards the anterior wall at the transition to the second portion of the duodenum.

The scope is introduced into the duodenal bulb, where one aspirates all the air and fills the transducer balloon

with water. The examination is performed while slowly withdrawing the scope. The liver will usually come into view from the upper left-hand corner of the screen and the gallbladder will be visualized between the scope and the liver. Figure 5. The PV will be visualized in the lower left-hand portion of the screen and the pancreatic head will be located between the scope and PV. The bile duct is visualized as a tubular, doppler-negative, structure between the PV and the scope. This area may also include an image of the PD as a tubular structure, likewise without Doppler signals.

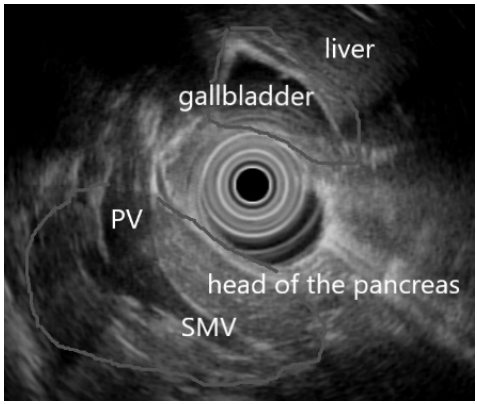


Figure 5: third station at the duodenal bulb.

The fourth station is obtained from the second portion of the duodenum. Advance the tip of the scope to the apex of the duodenal bulb. Then rotate the “right/left” knob gently to the right and reduce the scope back to the short scope position as in ERCP. With a slightly right torque and maximum “up” tip deflection, we can identify the aorta which is usually located on the left side of the screen. Slowly withdraw the scope at this juncture and the uncinate process and head of the pancreas will be seen at the 6 o’clock position. Figure 6. From this position, it is possible to obtain a detailed examination of the pancreatic head and uncinate process. The major papilla can also be examined, particularly if one fills the duodenal lumen with de-aerated water (without air bubbles). Figure 7.

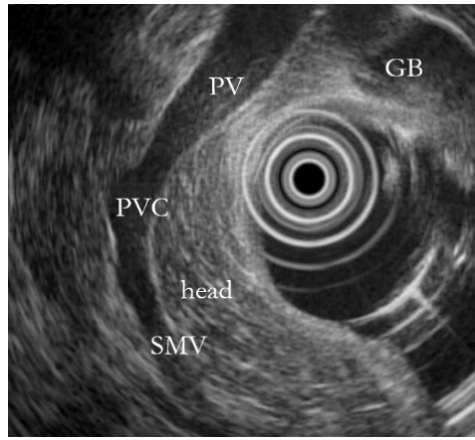


Figure 6: station 4 at second duodenum.

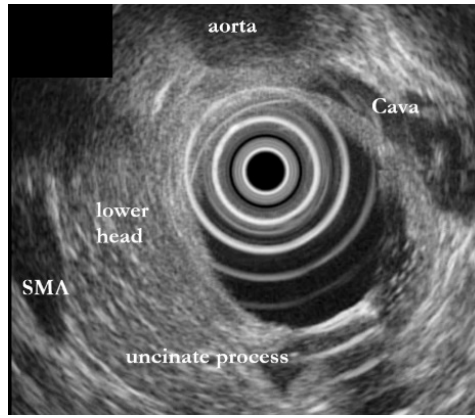
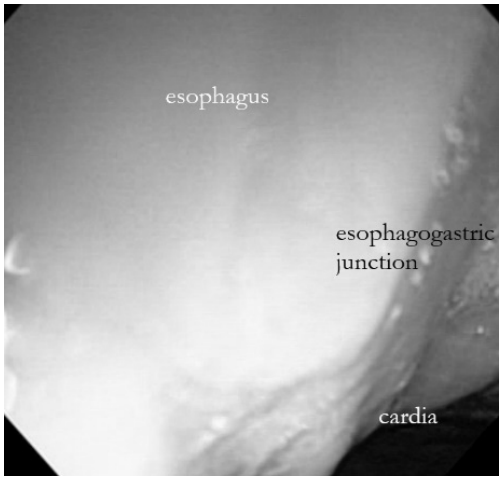


Figure 7: station 4 at the mayor papilla level.

Linear EUS examination

In linear echoendoscopes, the ultrasound signals are transmitted in a curvilinear manner. As with all aspects of linear array imaging, gentle clockwise and counterclockwise torquing is mandatory throughout the examination to obtain complete imaging. Left and right tip deflection is complementary, but actually of less importance when the linear echoendoscope is used.

First locate the aorta and celiac trunk at the starting point, which usually at the EGJ. As in radial EUS, pancreatic examination with linear scope is carried out in three positions: the stomach, duodenal bulb and the descending duodenum. Once the scope enters the EGJ, the left lobe of liver is readily visible. By rotating the scope clockwise (rotation to the right), the hepatic vein, inferior vena cava and the abdominal aorta can be seen. Figure 8a. At this stage, move the echoendoscope in and out to locate the celiac trunk take off. Follow the celiac trunk by advancing the scope slightly to identify the splenic artery. Once the splenic artery is identified, rotate the scope clockwise and slightly withdraw it to follow the artery to the splenic hilum. Using these positions, a close and detailed examination of the pancreatic neck, body and tail can be obtained. Figure 8b.



Picture 8a: endoscopic view of the station number 1.

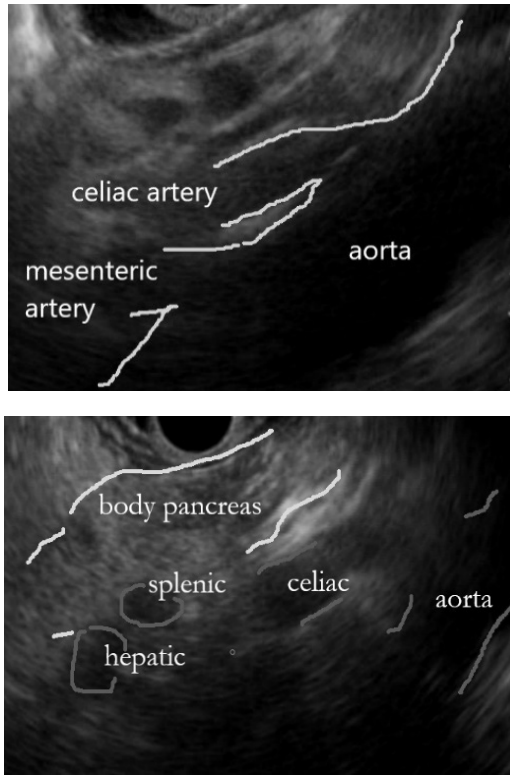


Figure 8b: linear echographic view in station number 1

Next trace the splenic vein back to its origin by anti-clockwise rotation and slight scope advancement, in order to see the splenic vein joining the superior mesenteric vein (SMV) to form the PV. Further anti-clockwise rotation will allow the identification of the PD and common bile duct (CBD), as well as the surrounding pancreatic head.

Inserting the scope into the duodenal bulb usually produces better images of the pancreatic head. After entering the duodenal bulb, rotate the scope clockwise to identify the three luminal structures, i.e., PV, bile duct and common hepatic artery. Figure 9.

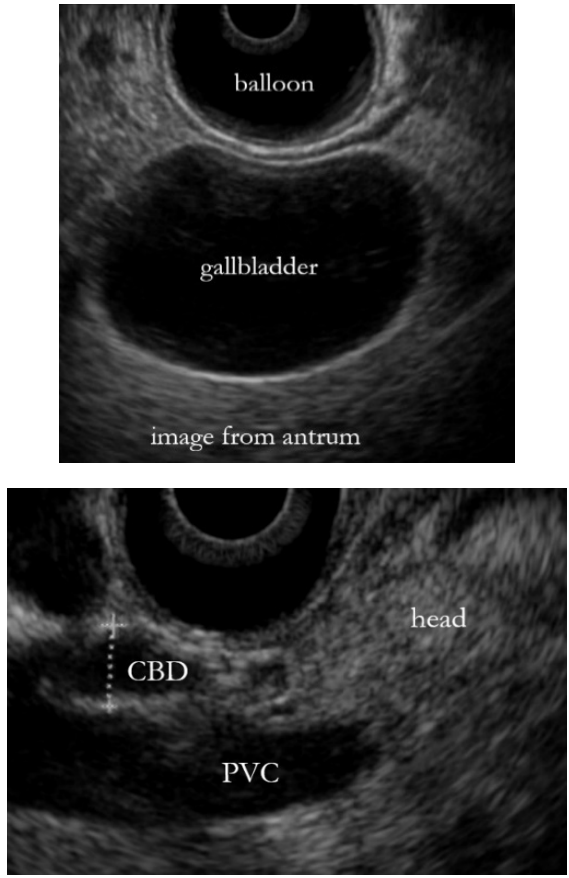


Figure 9: second and third stations from antrum and duodenal bulb respectively.

Follow along the PV to the confluence of SMV to obtain a detailed examination of the pancreatic head. In the case of a carcinoma of the head of the pancreas (HOP), assessment for any vascular invasion can only be seen from this position. Fig 10a.

Introduce the linear scope gently into the descending duodenum (second part), and perform a shortening maneuver similar to ERCP, to reduce the scope and then rotate it clockwise to see the aorta and inferior vena cava. Then, follow the aorta by slowly withdrawing the scope to observe the lower part of the pancreatic head and uncinate process, which is located between the aorta and the transducer Fig 10b.

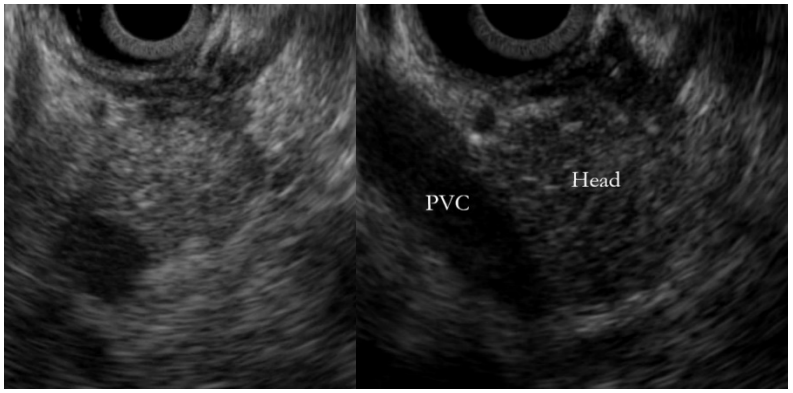


Figure 10a: station 4.

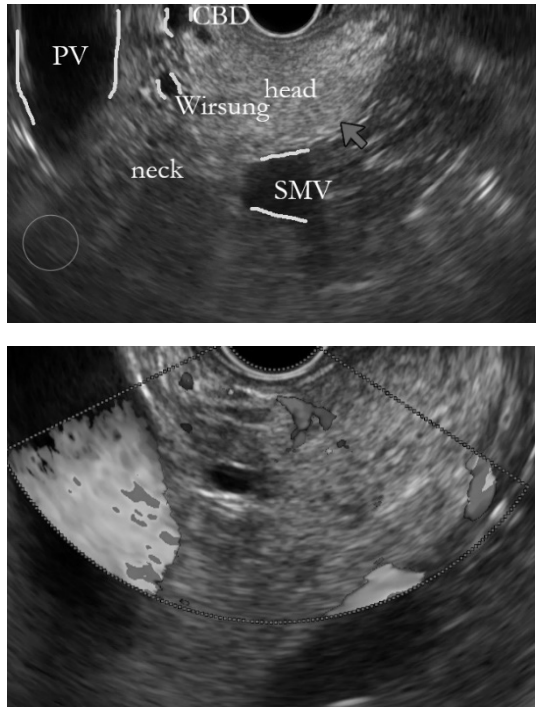


Figure 10b:station 4.

From this station it is important to locate the pancreatic-biliary confluence that will lead to the major duodenal papilla. Figure 11.

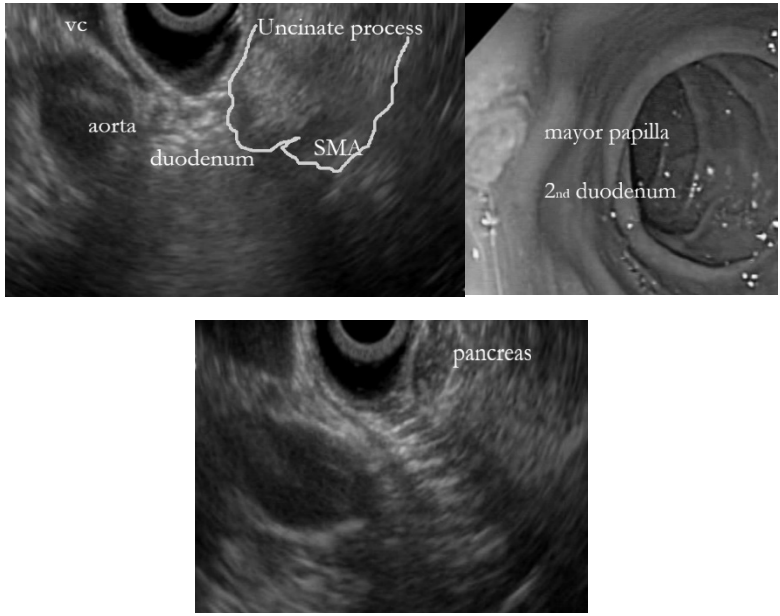


Figure 11: station number 4 next to the mayor papilla.

In such a station-based approach, if the endosonographer does not see the typical landmarks that characterize the station during the procedure, one should return immediately to the starting point for that station and repeat the standard maneuvers. A particular station should be examined as many times as is required to make the endosonographer comfortable that the examination is complete. Sometimes, despite repeated attempts, one cannot achieve the imaging goals of a particular station. In this case, the endosonographer should continue the examination by going to other stations and then return later to the difficult station. Often, the return examination is successful.

It is important that the endosonographers is familiar with the eco patterns of normal and abnormal anatomical structures and organs, especially of the pancreatic paryncyma. This will help a lot to identify structures in each station. There is a tremendous amount of anatomic variation between humans, particularly for the vascular tree, which makes learning the stations

more difficult, moreover there are difrences in the location of the gastroesophageal junction, and the size and shape of the stomach and the duodenum, all of which lead to navigation dificulties for endosonographers. It is important to concentrate on learning the endoscopic views of the stations in the first part of the learning curve. Only experienced endosonographers are capable of doing EUS with very little endoscopic visulaization. Remember as well that air is the first enemy of a good echographic images throughout the procedure.

Helpful tricks to remember

- These manual skill technics are taught in South American and European countries like France and Spain, however in Italy and some Asiatic countries the screen orientation is exactly the opposite, therefore right is left and left is right. Even the needle enters the field on the left side of the screen compared to the right side in Brazil.
- Also, some countries use very little or no water instilled into the latex balloon, where others use constant water infusion in different quantities, which can be very helpful to provide stability in the duodenum (bulb and descending portion). A clear beautiful echography image will only be accomplished if all air is absent and a close, intimate contact of the tip of the scope and the gastrointestinal wall is obtained.
- We strongly recommend the use of the balloon for all EUS even if minimal water is used, because the very small channels at the tip of the echoendoscope are easily contaminated if they are in direct contact with the patient's secretions. Due to their very small diameter, they are almost impossible to clean properly.
- Movements of the scope tip should be done gently to avoid artifacts and false images which are very common at the beginning of one's training.
- The scope tip should not be fixed by using the wheel brakes like in ERCP, to avoid false contact. The smoother the movements of the right-hand wrist and the left-hand scope control is, the better the views of the targeted zones will be.
- Remember the patient's breathing movement are not similar in all cases, there are anatomic differences in the stomach and duodenum of patients and even intestine motion varies greatly between patients depending on comorbidities and diseases. Navigation within the digestive tract with the echoendoscope is more difficult than with a regular gastroscope due to the need to avoid air or CO2 insufflation

for the ultrasound imaging. In a gastroscopy the air-water button/piston is constantly used to improve the quality of the endoscopic image, on the other hand, while doing EUS, this button is seldom touched. This endoscopic habit is difficult to break when learning EUS. Navigation is primarily performed using the echographic anatomic images after the early learning stage.

- Echographic patterns exist for each normal organ that is evaluated with EUS. These grey scale patterns are similar to abdominal percutaneous echosonographic examinations. These patterns should be memorized by reviewing many still and video recordings in order to improve station recognitions and EUS orientation.

Post-procedure management

Post-procedure management should mainly focus on monitoring for potential complications. Despite an increasing range of indications, complications of diagnostic EUS remain low. The main complications of EUS include perforation, bleeding and bacteremia. The reported complication rate of pancreatic EUS is 0.03% and the reported complication rate of EUS-guided FNA is around 1–2%[5].

Diagnostic EUS procedures are performed regularly under sedation and as an outpatient procedure. Patients are usually closely monitored in the recovery area after the procedure for 1 hour (and 2 hours for EUS-FNA procedures). In some countries, EUS is performed under general anesthesia with and without endotracheal intubation according to the patient's comorbidities.

For interventional EUS, post-procedure management should be individualized and will depend on the type of intervention performed. Patients should be closely monitored immediately post procedure for evidence of bleeding, perforation, leaks and sepsis especially when advanced interventions like EUS-guided pseudocyst drainage or biliary drainage have been carried out.

Tips, tricks and pitfalls of pancreatic EUS examination

Although EUS has been shown to be superior to CT in detecting small pancreatic tumors it should be kept in mind that the consequences of missing a lesion on an EUS can result in patient death. There are circumstances in which false-negative EUS examinations are more common. In a multi-

center study involving nine experienced endosonographers, the presence of chronic pancreatitis, a diffusely infiltrating carcinoma, a prominent ventral/dorsal split, and a recent episode of acute pancreatitis (<4 weeks) were associated with a higher incidence of missed pancreatic cancer on the initial EUS examination[6]. A follow up EUS should therefore be scheduled in 8 to 12 weeks if clinical suspicion for pancreatic tumor remains high despite an initially unrevealing EUS examination.

Detection of small pancreatic tumors may still be challenging at times using conventional EUS imaging. Novel diagnostic EUS imaging techniques such as contrast enhanced harmonic EUS (CEH-EUS) and elastography can further improve the detection and characterization of small pancreatic lesions. In CEH-EUS, an ultrasound contrast agent composed of microbubbles is injected intravenously to highlight the slow-flowing intra-tumoral vessels. Pancreatic cancer most commonly appears as a hypo-enhanced lesion on CEH-EUS, also for cystic wall evaluation as seen in Figure 12.

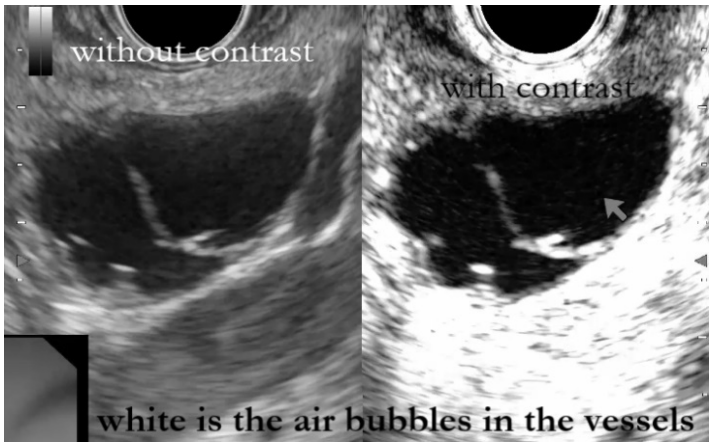


Figure 12: Contrast enhanced EUS of pancreatic cystic lesion.

Elastography allows real-time assessment of the stiffness of a suspected lesion. In general, malignant tumors are noted to be stiff, while normal tissue or a benign lesion is generally noted to be soft on elastography Figure 13. Theses technics will be explained later.

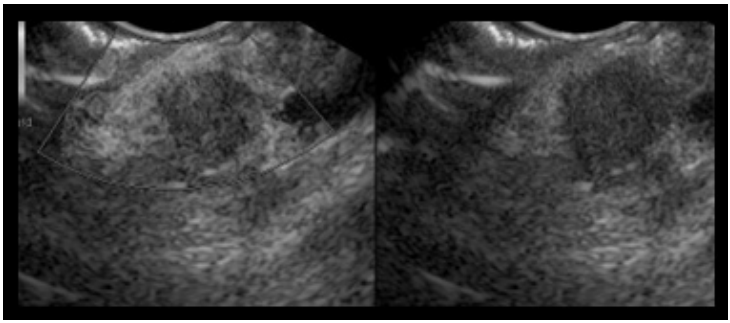


Figure13: neoplastic lesion with blue color.

Common mistakes during pancreatic EUS examination

1 - Failing to understand the anatomical structure of the pancreaticobiliary region

Sometimes the lobular architecture of the pancreas is so pronounced that it can be mistaken for chronic pancreatitis. Pancreatic echogenicity on ultrasound is normally equal to or slightly greater than that of the liver however, increased echogenicity in the pancreatic parenchyma is not uncommon and can be mistaken for chronic pancreatitis during EUS examination. Hyperechoic pancreatic changes are frequently encountered in elderly and obese patients and understanding the possible variations in pancreatic echo structure and echogenicity is fundamental for accurate EUS diagnosis. The lack of pancreatic parenchyma calcifications and especially the presence of a normal pancreatic duct can help exclude chronic pancreatitis.

On EUS, the ventral part of the uncinate process is often hypoechoic in appearance and may be mistaken for a hypoechoic focal lesion. However, the absence of clear margins and a nondilated CBD and pancreatic duct may help differentiate the ventral anlage from a pancreatic tumor.

EUS is of great value for the diagnosis of bile duct stones, but it can be challenging in the presence of a periampullary diverticulum, particularly if it is large and obstructed with debris. Intra diverticular papilla can also confuse the operator because of air artifacts that can produce a false stone-like image leading to unnecessary endoscopic retrograde cholangiopancreatography (ERCP). Filling the duodenum with water so that the papilla is submerged and free of air bubbles can avoid this issue.

2 - Choosing the correct echoendoscope

Examination of pancreatic tail lesions are traditionally accessed through the gastric fundus by following the aorta until the coeliac take-off is seen, at which point it bifurcates into the hepatic and splenic artery. Once the splenic artery is detected, it can be followed with a slightly clockwise rotation and withdrawal of the scope. This movement allows complete examination of the pancreatic body and tail up to the splenic hilum. However, in some cases (about 20%), the pancreatic tail is separated from the gastric wall and cannot be fully explored, especially with a radial scope. Several studies show that the lowest sensitivity of EUS for detecting pancreatic lesions is in the tail (37–40%) compared with the body (79%) and the head (83–92%)[7]. In some clinical situations (unexplained acute pancreatitis, intraductal papillary mucinous neoplasm [IPMN] follow-up, secretory syndrome with normal conventional imaging or screening for a genetic predisposition for pancreatic neoplasia syndrome), a linear scope would be preferred for a pancreatic body–tail exploration.

3 - Having the incorrect position to reach the target lesion during EUS-guided tissue acquisition

When performing EUS-FNA or FNB the EUS transducer should be placed as close as possible to the target lesion. The uncinate process is difficult to reach when excessive torquing of the echoendoscope in the second part of the duodenum is necessary. Another difficult location to reach is near the fornix and greater curvature of the stomach, in which case the long position of the echoendoscope in the stomach can be helpful—in this case, the needle can push the stomach wall away and a rapid and strong push of the needle is needed to pass the gastric wall. Diverticula or interposing vessels can (and should) be avoided by slight modification of the transducer position to puncture the gastrointestinal wall away from the vessels, followed by redirecting the needle towards the target lesion. In such awkward duodenal positions, the use of thinner FNA needles (25 Gauge) offers a technical advantage.

Previous surgery, especially gastrectomy or pancreatectomy, can make the detection of pancreatic lesions difficult. The surgical procedure and type of gastrointestinal anastomosis should be reviwed before starting the EUS procedure.