Techniques of Endoscopic Ultrasound-Guided Fine Needle Aspiration

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Introduction

Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is an essential diagnostic tool and currently the most accurate technique for tissue diagnosis of tumors and lesions of the gastrointestinal (GI) wall and adjacent organs. It can safely provide, both, cytological and histological samples from mural and extra-mural lesions within reach of the linear echoendoscope. In daily GI practice, it is most commonly used for pancreatic masses and cysts as it is the best method for sampling pancreatic lesions. Implementation of EUS-FNA in GI practice has significantly improved the diagnostic sensitivity and specificity for pancreatic cancer [1]. The overall current sensitivity, specificity, and diagnostic accuracy of EUS-FNA for the diagnosis of malignant pancreatic neoplasms are 77–95%, 96–100%, and 79–97%, respectively [2]. A recent study using medicare data to investigate changing trends in tissue acquisition in pancreatic disease found out that over the span of 5 years (2006–2010), use of EUS-FNA increased approximately to 70% in the USA [3].

Depending on the target lesion, EUS-FNA provides adequate cytological or histological material in 70–100% of cases [2, 4–7]. However, the reported high success and diagnostic accuracy rates of EUS-FNA is mostly operator-dependent, and endoscopist experience is the most critical factor for obtaining these results [8, 9]. Proper training of endosonographers increased the accuracy of EUS-FNA from 33 to 91% in one study; and EUS-FNA errors during the initial learning phase were primarily due to inadequate specimens [10]. Therefore, similar to many other complicated interventions, proficiency in EUS-FNA also requires learning the useful technical details and tips from all available sources. This chapter mainly reviews the current literature for EUS-FNA and provides up-to-date information on patient selection, technical details, equipment, and diagnostic accuracy.

Case Study

Initial Presentation

A 72-year-old woman presented with a history of periumbilical pain, abdominal bloating, and discomfort over the past 4 weeks. Physical examination and basic laboratory tests, including blood count, biochemistry, urine analysis, and plain abdominal X-ray, were unremarkable. She was given symptomatic treatment at a nearby hospital but admitted again 4 weeks later with increased symp-

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toms. A transabdominal ultrasonography (US) and then CT scan demonstrated significant retroperitoneal adenopathy from the aortic bifurcation up to the celiac axis. A right inguinal lymph node biopsy was performed, which was unremarkable. A bone marrow aspirate, biopsy, and a bone scan were also unremarkable. An MRI of the abdomen again confirmed retroperitoneal adenopathy. Ultimately, patient was referred to a tertiary center for an EUS-FNA of abdominal lymph nodes given the high suspicion of non-Hodgkin lymphoma.

Is This An Appropriate Indication for EUS-FNA, and What Impact Does EUS-FNA Have on Management of This Patient?

EUS-FNA is generally safe and reliable with a low complication rate. However, the cost effectiveness and possible risks and benefits should always be weighed carefully before the procedure. The procedure is indicated if the results will potentially impact patient management. If there is an alternative method for diagnosis, which is safer and reliable, it should be the first priority. The indications and contraindications of EUS-FNA are summarized in Table 23.1.

In our case, the patient had unexplained diffuse abdominal lymphadenopathy. Evaluation of unexplained periluminal lymphadenopathy is among the important indications of EUS and EUS-FNA. Before an FNA procedure, the patient first needs a diagnostic EUS to assess for a possible mediastinal or abdominal lesion, which may be related to lymphadenopathy.

EUS and EUS-FNA may have an important impact in the management of this patient. The procedures will likely provide a tissue diagnosis. Furthermore, the risk of EUS-FNA of enlarged lymph nodes is relatively low.

Case Continued

The patient underwent a diagnostic EUS with a linear array echoendoscope. Many malignant-appearing, round, hypoechoic lymph nodes with well-defined margins were visualized in the aortopulmonary window, the paraesophageal mediastinum, and the mediastinal periaortic region. The largest measured 10 by 10 mm in maximal cross-sectional diameter (Fig. 23.1). A round, well-defined, hypoechoic and homogenous, 20 mm by 20 mm in maximal cross-sectional diameter mass was identified in the pancreatic

Table 23.1 Indications and contraindications of EUS-FNA

Indications
Primary diagnosis of pancreatic masses
Differentiation of cystic pancreatic lesions
Evaluation of unexplained periluminal lymphadenopathy
Diagnosis of gastrointestinal intramural lesions
Staging of digestive and pulmonary malignancies
Sampling of peritoneal and pleural fluid
Contraindications
Risks outweigh the expected benefits
Results would not affect patient management
Lesions that cannot be visualized clearly
Lack of informed consent or cooperation of the patient
Uncorrectable coagulopathy (INR >1.5) or thrombocytopenia ($<50{,}000/\mu l$)
Under thienopyridines therapy
Relative contraindications
Failure of control of needle position
Biliary obstruction without prior decompression
Luminal stenosis
Venous collaterals in the path of the needle tract

EUS endoscopic ultrasound, *FNA* fine needle aspiration

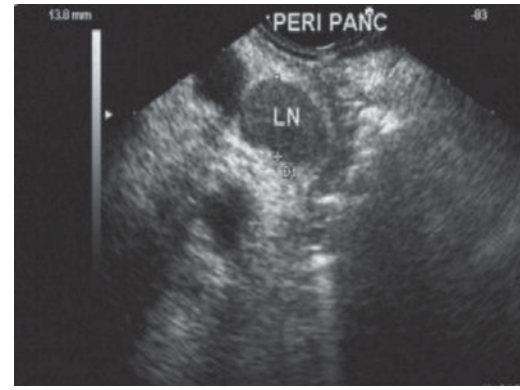

Fig. 23.1 Round, hypoechoic, and well-defined lymph node in peripancreatic area

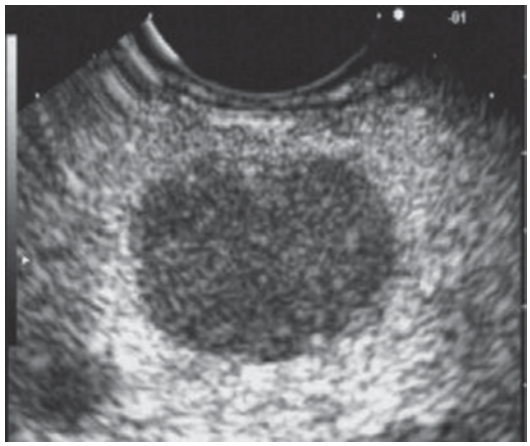

Fig. 23.2 A round, well-defined, hypoechoic and homogenous, 2 cm in maximal diameter mass in the pancreatic body

body (Fig. 23.2). The mass appeared atypical for pancreatic adenocarcinoma. There was no sign of significant endosonographic abnormality in the left lobe of the liver.

Does the Patient Still Need EUS-FNA and Which Lesion Should Be Sampled?

This patient had a pancreatic mass and diffuse lymphadenopathy. The EUS findings were not typical for a pancreatic adenocarcinoma. However, a pancreatic cancer with diffuse metastasis still remained in the differential diagnosis. The atypical imaging findings of diffuse lymphadenopathy also raised suspicion of pancreatic lymphoma. As management of these two conditions differ, a definite cytological or histological diagnosis was necessary to guide treatment of the patient at this stage, and EUS-FNA of both the lymph nodes and pancreatic mass was required. The first EUS-FNA should always target the lesion, which likely represents the most advanced stage of malignancy. This approach will help prevent subsequent seeding.

When sampling a suspected pancreatic cancer is indicated, EUS-FNA should be the first-line procedure. It has significant advantages over percutaneous US or CT-guided biopsies [11, 12]. EUS and EUS-FNA are superior for detecting early malignancies, obtaining cytologic material, and minimizing the risk of tissue seeding. EUS-FNA may diagnose a potentially resectable mass or pancreatic metastasis, and exclude other pancreatic tumors such as lymphoma or neuroendocrine tumor, in addition to benign disease such as chronic or autoimmune pancreatitis.

A preoperative diagnostic EUS-FNA is controversial in patients who are good surgical candidates with a high suspicion of pancreatic adenocarcinoma. The negative predictive value of EUS-FNA for pancreatic cancer is approximately 70%; thus, a negative result cannot rule out malignancy with adequate reliability [13–15]. Therefore, routine preoperative EUS-FNA of potentially resectable pancreatic adenocarcinomas is not generally advised. However, in cases where other types of pancreatic malignancies (e.g., neuroendocrine tumors, lymphomas, metastatic disease) are suspected, EUS-FNA is indicated to assist in planning appropriate management.

What Is the Preparation for EUS-FNA?

Initial planning and preparation for EUS-FNA is similar to other endoscopic interventions. Prior to starting the procedure, the medical history and records of the patient should be reviewed with all necessary laboratory and radiological tests, and then informed consent should be obtained after discussing the indication, benefits, and risks of the procedure with the patient and the family. The diagnostic success of EUS-FNA is highly related to the preparation of the patient and instruments as well as the expertise of the whole endoscopy team. Therefore, each step of the procedure needs to be carefully planned and executed with the entire team. The risk of bacteremia is rare and similar to other endoscopic procedures. As such, prophylactic antibiotics are not routinely recommended [16]. Serious infectious complications have only been reported after EUS-FNA of cysts (e.g., pancreatic and mediastinal) and the American Society for Gastrointestinal Endoscopy (ASGE) guideline recommends periprocedural antibiotics only in these patients [17, 18].

EUS alone, without FNA, is a low-risk procedure for bleeding, but EUS with FNA is classified as a high-risk procedure. There is no need to stop aspirin, thienopyridines including clopidogrel or warfarin for patients undergoing a low-risk procedure for bleeding [19]. Aspirin may be continued even in patients undergoing EUS-FNA of solid lesions, but clopidogrel should be discontinued 7–10 days prior to the procedure. Warfarin should be stopped 2–5 days before the procedure in all patients who are scheduled for EUS-FNA and restarted within 24 h after the procedure. A bridge therapy with low molecular weight heparin should be considered in patients with higher risk conditions for thromboembolic event [19]. These decisions regarding antiplatelet agents and anticoagulants should be discussed with the patient's cardiologist and/or neurologist prescribing those medications.

Sudden movements during FNA may lead to injury of adjacent structures and effective sedation of patients is important for a complication-free procedure. Sedation may be provided with intravenous conscious sedation (IVCS) or with monitored total anesthesia during EUS-FNA. A recent study compared the impact of IVCS and general anesthesia (GA) on diagnostic yield of EUS-FNA in patients with pancreatic mass [20]. Anesthesiologist-delivered GA was associated with a significantly higher diagnostic yield of EUS-FNA compared to IVCS. The authors commented that GA may improve EUS-FNA yield by improving patient cooperation and stillness during the procedure. There was no difference in the complication rates between the groups.

Before proceeding with EUS-FNA, a complete diagnostic EUS should be performed to evaluate the lesion and adjacent structures to allow adequate staging and in order to choose the optimal needle tract. A radial EUS examination is usually suggested for areas other than the pancreas, but selecting the radial or linear scope for diagnostic EUS depends on the endoscopist's experience. The linear echoendoscope provides complete visualization of the pancreas. After the target lesion is identified, the scope should be placed in a stable position adjacent to the lesion, and if possible, within the projected plane of the needle path. Doppler function should be utilized to exclude an interposed vessel between the transducer and the target lesion.

Once the target lesion is localized and an appropriate position is achieved, the needle catheter device is advanced through the biopsy channel to begin the puncture. The location of the target lesion affects the difficulty of the procedure. In general, transduodenal FNA is difficult, while transgastric is easier and transesophageal easiest.

What Factors Impact the Choice of Needle Type and Size?

EUS-FNA is classically performed with 19-, 22-, and 25-gauge (G) aspiration needles from several manufacturers (Table 23.2 and Fig. 23.3). There is no optimal needle size for EUS-FNA, and each size may have advantages and disadvantages depending on the location and type of lesion. Larger diameter needles do not increase the risk of the procedure, and no significant difference in com-

Table 23.2 Commercially available fine-needle aspiration and biopsy needles

Type of needle	Available sizes (G)	Device	Manufacturer
Aspiration	19, 22, 25	Expect	Boston Scientific
		EchoTip Ultra	Cook Medical
		EzShot2	Olympus
		SonoTipII	Medi-Globe
		BNX system	Covidien
		Clearview	Conmed
Trucut biopsy	19	Quick-Core	Cook Medical
Core biopsy	19, 22, 25	Echotip Procore	Cook Medical
Aspiration flex	19	Expect flex	Boston Scientific

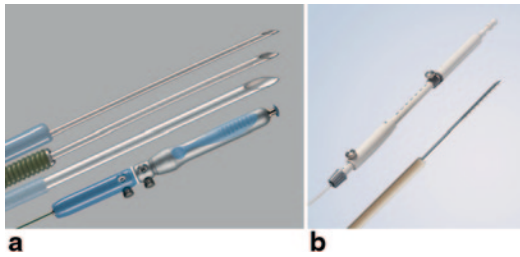

Fig. 23.3 Fine-needle aspiration needles in different type and sizes. (Cook Medical Inc. and Olympus Inc)

plication rates has been shown among the different sized FNA needles [6]. The 19G needle is the stiffest and may be difficult to manipulate in the duodenum where the scope is sharply angulated. For this reason, technical failure rate is higher with 19G needles used for pancreatic head lesions [21, 22]. Although the 19G needle may obtain tissue fragments from suspected tumors and potentially increase diagnostic accuracy, it may cause more trauma and bloodier samples. Conversely, a 25G needle offers ease of use and less risk of a bloody aspirate [23]. The 25G needle may be particularly useful for difficult pancreatic head lesions [24]. Several prospective studies have compared the 22G and 25G needles for their performance, diagnostic accuracy, and safety [7, 25, 26]. In general, diagnostic yield and complications appear comparable between the 22G and 25G needles [27, 28]. Endoscopists should be familiar with all needle sizes and choose the size based on the flexibility needed, the size which may provide optimal tissue yield, and the safest size for a particular location and type of lesion.

A new 19G aspiration needle made of nitinol with enhanced flexibility (Expect flex, Boston Scientific, Marlborough, MA, Fig. 23.4) was designed to overcome the limitations of current 19G needles. A recent study demonstrated successful tissue acquisition adequate for cytological assessment in all 38 patients (100%), which included transduodenal passes, and therapeutic interventions were also effective in 12 patients [29]. In another pilot study with this needle, EUS-FNA was successful in all eight cases with six involving the pancreatic head, and adequate specimen was obtained with a mean of 1.2 passes [30].

Fig. 23.4 A new 19G aspiration needle made of nitinol with enhanced flexibility (Boston Scientific)

To obtain adequate histologic samples and overcome some limitations of EUS-FNA, EUS-fine needle biopsy (EUS-FNB) has been performed with a 19G Tru-cut biopsy needle (TBN) (Fig. 23.5). The needle consists of a 5 mm stylet tip, an 18-mm specimen tray, a 19G internal cutting sheath, the outer catheter sheath, and the handle portion. It permits procurement of tissue specimen automatically with a spring-loaded handle mechanism. The needle is advanced to the target lesion with the handle in the retracted firing position. The specimen tray is inserted into the target lesion and the handle is pressed forward until resistance is felt. The specimen tray and cutting sheath are visualized within the target tissue with distinct echo features. Increased pressure on the handle fires the device, moving the cutting sheath quickly over the tray to acquire a tissue sample. Straightening the echoendoscope and needle, proper device orientation, and targeting the lesion are important technical details when using this needle. By preserving the tissue architecture, this needle may be more helpful for the diagnosis of specific conditions such as gastrointestinal stromal tumors, lymphomas, well-differentiated neoplasia, neuroendocrine

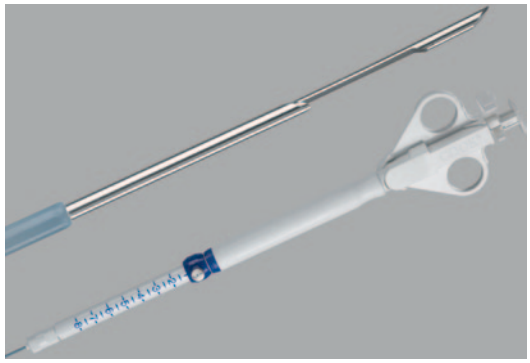

Fig. 23.5 19G Tru-cut EUS biopsy needle (Cook Medical Inc.). *EUS* endoscopic ultrasound

tumors, and autoimmune pancreatitis. However, the rigidity of the needle limits its usage especially in difficult locations such as duodenal bulb, fundus, and antrum [22].

Recently, 19G, 22G, and 25G biopsy needles were designed with a cutting knife (Procore, Cook Medical, Fig. 23.6, Table 23.2). The flexibility of the 22G and 25G core needles may offer advantages in difficult locations. Several recent studies compared the diagnostic yield of 22G aspiration needles with 22G core needles for solid lesions of the pancreas and gastrointestinal tract with inconclusive findings. Depending on the study, the diagnostic yield of the 22G aspiration needle was equal, superior, or inferior to the 22G core biopsy needle [6, 7, 28]. Procore needles may require fewer passes compared to aspiration needles. The diagnostic yield on the first pass of the 22G Procore needle was approximately twice compared to the 22G aspiration needle [31]. Downsides of the core needles include their greater expense and need for additional training and technical assistance. A new core needle (SharkCore fine needle biopsy, Covidien) is now available in 19G, 22G, and 25G with a unique design of 6 cutting surfaces, and needs study to determine its utility and place within the current armamentarium of aspiration and biopsy needles. Both types of needles may offer advantages and may prove more useful in different lesions and individuals. Table 23.3 summarizes suggested needle type and size according to specific characteristics of the case.

In our case, the mediastinal and peripancreatic lymph nodes were suitable for EUS-FNA. For better staging and to prevent subsequent seeding, the first EUS-FNA should target the lesion, which likely represents the most advanced stage of malignancy. Thus, the mediastinal lymph nodes were targeted first by a transesophageal approach. For lymph node aspiration, 22G and 25G needles may be easiest to use. The mass in the pancreatic

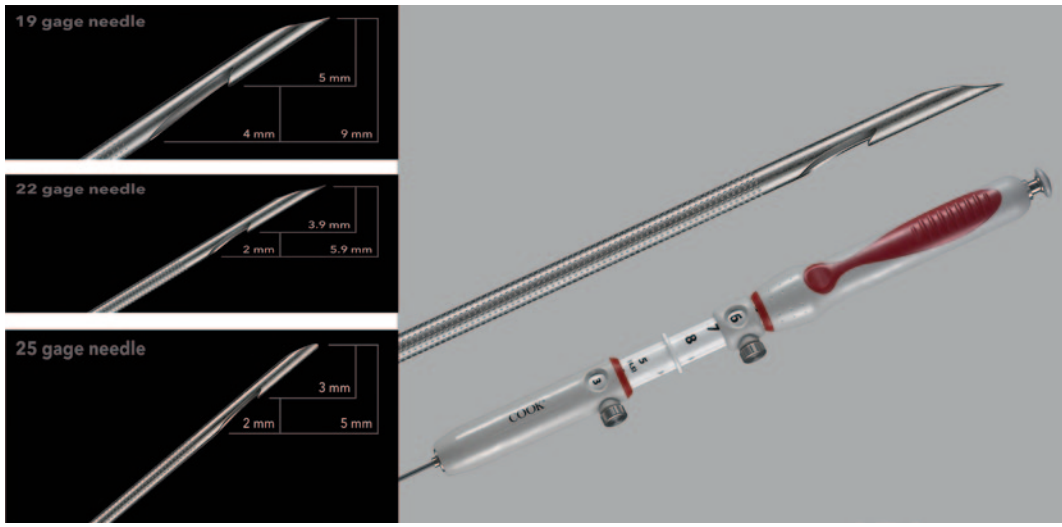

Fig. 23.6 Procore EUS biopsy needle in different sizes. (Cook Medical Inc.). *EUS* endoscopic ultrasound

Table 23.3 Suggested EUS-guided aspiration or biopsy needle according to lesion and patient characteristics

Characteristics	Suggested needles
Access	22 and 25G for transduodenal approach 19 and 22G for transgastric and transesophageal puncture
Location	22 and 25G for pancreatic head, neck, and uncinate 19 and 22G for other locations
Cellularity and diagnostic yield	22 and 25G for pancreatic head and uncinate 19G for other locations (possible more cells obtained)
Nature of the lesion	For lesions with a high suspicion of GIST, lymphoma, and metastatic tumor, Trucut and core biopsy needles. Alternative: 19G aspiration flex
On-site cytopathology	Aspiration needles. If on-site evaluation is not available, core needles and 19 G aspiration flex may be better
Ancillary studies and histological samples	Core biopsy needles. Alternative: 19G aspiration needle and 19G aspiration flex
Contamination and bleeding	Smaller gauge needles (possible decreased contamination and risk of bleeding)
Cost effectiveness	Aspiration needles
Safety	No definite data, but 19G aspiration and Trucut possibly more traumatic

body was accessed transgastrically. For atypical lesions, a larger needle to obtain tissue fragments for histology may be more helpful for diagnosis. Considering all these factors, starting with a 22G for the lymph nodes and then a 19G for the pancreatic mass or using a 22G aspiration needle for both lesions are reasonable choices in this case. EUS-FNB with a 22G Procore needle for both the lymph nodes and pancreatic mass may be an alternative, especially for atypical lesions, and if Rapid Onsite Evaluation (ROSE) is not available.

How Is EUS-FNA Performed?

Most single-use EUS-FNA needles are very similar in design and operation [32]. They consist of a hollow metallic needle inside a semirigid protective sheath with a plastic rigid cylinder handle containing a port (Figs. 23.3, 23.4, 23.6). From the port, there is a solid removable stylet inside the needle to enhance its rigidity during puncture and to prevent clogging the needle tip with intestinal mucosa. The port is also used to attach a vacuum syringe. The handle is attached to the accessory channel of the echoendoscope via a Luer Lock to stabilize the system during use. Markings at 1 cm intervals on the handle enable to set and monitor the depth of the needle. The maximum needle length from the tip of the echoendoscope is usually 8–9 cm. The handle has a stopping device to set the maximum needle excursion. This safety mechanism helps to keep the needle within the limits of the target lesion. To facilitate the passage of multiple needles through a single delivery catheter, a new system called BNX (Beacon Needle Exchange) has been developed (Beacon Endoscopic, Covidien) (Fig. 23.7). The system has the ability to remove the needle from the sheath and place different sized needles through the same sheath to perform multiple passes. The aim of the system is to increase the diagnostic yield of EUS-FNA with low cost and

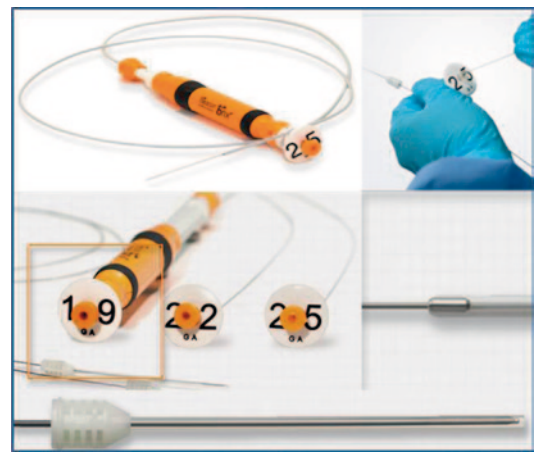

Fig. 23.7 Beacon needle exchange FNA system with multiple size needles and delivery device (Beacon Endoscopic, Covidien). *FNA* fine needle aspiration

increased efficiency, but no clinical study has been published yet about the effectiveness of this system.

After the target lesion is identified and the scope placed into a stable and proper position for the lesion, the needle system is inserted through the working channel of the echoendoscope and advanced to the tip of the scope with the lesion in close proximity. To achieve the proper position, the transducer of echoendoscope should contact the luminal wall firmly near the target lesion, and the lesion should be within the potential direction of the needle in order to perform FNA without difficulty, which is usually at the 6 o'clock position on the EUS screen. Slow movements of the echoendoscope and using the up and down knob and the elevator may help to achieve the proper position and to set the needle angle. Straightening the tip of the echoendoscope is especially important when puncturing lesions located in the pancreatic head. It may be difficult to pass the needle system if the echoendoscope is angulated. In this situation, instead of pushing the system by force, the endoscopist should reduce the scope to a straight position, insert the needle system completely, and then reposition the scope at the target lesion. The use of small gauge needles reduces the difficulty of passing the needle through an angulated scope.

After the needle system is completely inserted into the channel, it is firmly screwed onto the biopsy channel and the needle stop is set to limit the maximum distance that the needle can be advanced. The stylet inside the needle may prevent contamination of the needle tip during puncturing the intestinal wall; although, recent studies have questioned the benefit of using a stylet [33, 34]. If the stylet is used, it is withdrawn slightly before advancing the needle into the target tissue to facilitate entry and then may be readvanced to remove any potential tissue clogging the tip of the needle. Transgastric puncture sometimes may be difficult due to the thicker and redundant gastric wall. Suctioning the gastric wall and advancing the needle with a brisk but controlled, forceful maneuver may overcome this problem.

The needle is always advanced into the target lesion under direct EUS guidance. To avoid excessive needle excursion, the palm of the right hand grasps the handle with the last three fingers and the movable part is controlled by the thumb and index finger. The elevator of the scope can help deflect the needle with small adjustments. After the lesion is punctured properly, the stylet may be removed completely or left inside the needle. If a vacuum syringe is used, the stylet is removed completely after puncturing the lesion and a 10 ml vacuum syringe is affixed to the handle port for permanent suction. Then, the needle is moved back and forth about 5–10 times through the lesion to shear-off cells under sonographic control. If a vacuum suction syringe is not used, the stylet is retracted slightly inside the needle and the needle passed through the lesion. Before withdrawing the needle from the lesion, 5–10 ml of suction may be applied for a few seconds. The endoscopist should be careful to keep the needle inside the lesion and to turn the suction off before withdrawing the needle from the lesion. After the procedure has been completed, the needle is removed from the scope and the aspirant is expressed onto a slide or container. An air-filled 10 ml syringe or stylet through the needle can be used to express the aspirate from the needle tip. After all the material is evacuated from the needle, it is cleansed and rinsed in sterile saline or alcohol by aspiration and flushing. Then it is reassembled for the next pass.

The overall experience with EUS-FNB is limited compared to EUS-FNA. Suction or stylet use is not suggested when using a 19G needle or core biopsy needle since it might increase the bloodiness of specimens. Repeated insertion of the needle into the same area should be avoided. Multiple biopsies may increase bleeding, and more than three passes is usually not suggested. The needle may be moved back and forth within the lesion 2 or 3 times.

How Can We Increase Diagnostic Yield of EUS-FNA?

Small technical tricks and details during EUS-FNA may increase diagnostic yield and success of the whole procedure. A "fanning" technique

involves advancing the needle into different areas within the lesion to secure cells from, both, the center and periphery of the mass (Fig. 23.8). A recent study has shown that this FNA technique was superior to the standard approach because fewer passes were required for diagnosis, and there was a trend towards increased diagnostic accuracy (96 vs. 77 %, $p = 0.05$) [35].

The use of 5–10 ml of suction for a few seconds before withdrawing the needle from the target lesion may increase cellular yield. A prospective randomized controlled trial showed that EUS-FNA of solid masses using suction yielded significantly higher sensitivity and negative predictive value for diagnosis without increasing bloodiness [36]. However, another study found that applying suction during FNA of lymph nodes did not improve diagnostic accuracy and increased specimen bloodiness compared to without suction [37]. It may be suggested to start EUS-FNA of solid lesions without suction but add further passes with suction if the cellular yield is inadequate. The European Society of Gastrointestinal Endoscopy (ESGE) technical guideline recommends using suction for EUS-FNA of solid masses/cystic lesions and not using suction for lymph nodes [38].

The number of needle passes to obtain cytologically adequate samples is unclear. ROSE may decrease the number of passes [39]. If on-site cytopathology is not available, 4–6 passes for a mass lesion, 3–4 passes for a lymph node, 5 for subepithelial lesions, and 2–3 for liver lesions is generally suggested to optimize diagnostic yield [37, 40]. Directing the needle to different parts of the lesion with each pass may increase the quality of sample. Advancing the needle repeatedly through the same tract may result in bloodier samples with decreased quality. Moreover, targeting the periphery of large lesions may also increase the diagnostic yield since the central areas are usually associated with necrosis.

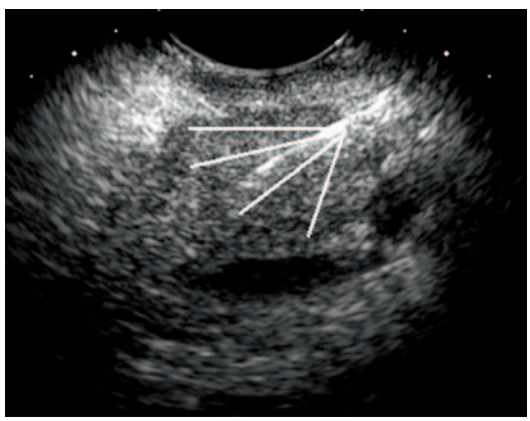

Fig. 23.8 Fine needle aspiration of a pancreatic mass and schematization of "fanning" technique

What If Enough Material Cannot Be Aspirated or Cytology Shows Inconclusive Results?

When confronted with nondiagnostic or indeterminate cytology, the patient should be reevaluated carefully. If there is a high clinical and/or imaging suspicion of cancer, the next step may be surgery.

If a cytological diagnosis is essential for management, patients can undergo repeat EUS-FNA. The diagnostic yield for repeat EUS-FNA of suspected pancreatic cancer ranged between 27 and 82 % in different studies [41–43]. The rate of repeat FNA varied among the centers from 5 to 10 % [41–43].

One of the important factors to increase diagnostic yield of FNA is ROSE of the cytological material. Nearly all published studies have demonstrated advantages of on-site cytopathology during EUS-FNA [44]. The use of ROSE for EUS-FNA decreases the number of patients who require a repeat procedure [41]. ROSE increases the diagnostic yield of EUS-FNA approximately 10–15 to 92 % sensitivity and 100 % specificity [45]. However, despite data supporting ROSE, widespread use remains limited due to restricted availability beyond academic and specialized centers, and low reimbursement rates.

Using a core needle to obtain a histological sample may be another option. Adequate histological samples may overcome the problem with limited use of ROSE. Core histology specimens may enable tissue profiling and cell culture as molecular-targeted agents and biological

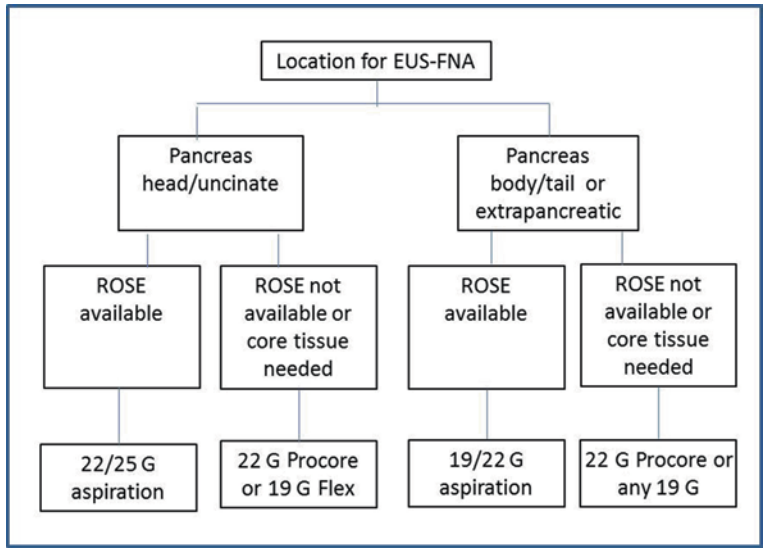

Fig. 23.9 An algorithm for needle type and size choices based on location of lesion, availability of ROSE, and need for core tissue

therapies are assuming more importance in the treatment of GI cancers. EUS-FNB can be performed during the same EUS session if FNA failed or ROSE showed inconclusive results after three or four passes. If ROSE is not available, using a core needle to procure a histological sample may increase diagnostic yield. A recent, multicenter prospective study showed that EUS-FNB with a 22G Procore needle produced a sample suitable for histological evaluation in 88.5 % of the cases after only one needle pass [46]. No study has evaluated the value of using a Procore needle during the same session following failed EUS-FNA or inconclusive ROSE results. However, this seems a more efficient option than repeating EUS-FNA. We suggest an algorithm for choosing needle type and size based on location of the lesion, ROSE availability, and desire for core tissue (Fig. 23.9).

Case Continued

Two passes into a mediastinal lymph node were performed using a 22G aspiration needle (Fig. 23.10). ROSE was available, and the smear was positive for malignant cells. The lymph node was diagnosed as a metastatic large cell carcinoma. Then, the pancreatic mass was targeted with the 22G aspiration needle and after two passes, ROSE showed positive malignant cells consistent with high grade adenocarcinoma. Subsequent cytological diagnosis confirmed the ROSE results. The patient was diagnosed with an advanced stage pancreatic adenocarcinoma and referred to oncology for chemotherapy.

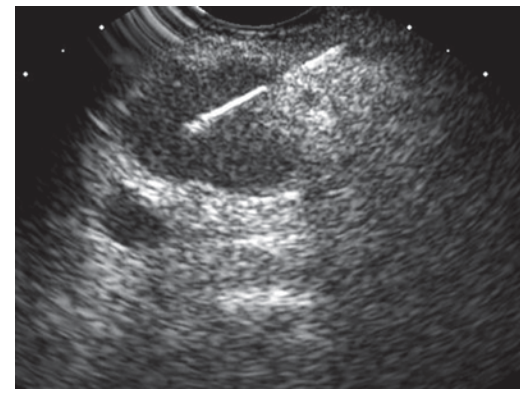

Fig. 23.10 EUS-FNA of lymph node in the patient. *EUS* endoscopic ultrasound; *FNA* fine needle aspiration

EUS-FNA for Cystic Lesions

Cystic lesions of the pancreas show a wide spectrum of demographic, morphological, and histological characteristics. The accurate diagnosis and discrimination of these lesions are very important because of the presence of malignancy or tendency to develop malignancy over time in some pancreatic cysts. Clinically, mucinous (intraductal papillary mucinous neoplasm (IPMN), mucinous cystic neoplasm (MCN)), and nonmucinous cysts (pseudocysts and serous cystadenoma) must be distinguished. Cross-sectional imaging tests and EUS alone are often inadequate to accurately differentiate between benign or malignant and mucinous or nonmucinous cysts. EUS-FNA is currently the most helpful procedure for the differentiation and clinical management of these patients [47–49].

EUS-FNA of pancreatic cystic (Video 23.1) lesions needs extra care compared to solid lesions. Complications including infection, bleeding, and pancreatitis have been reported more frequently following EUS-FNA of cystic lesions compared to solid masses [38, 50, 51]. Prophylactic antibiotics are usually recommended for patients undergoing FNA of pancreatic cysts. The aspiration of all cyst contents may minimize the risk of infection and maximize diagnostic yield. The tip of the needle should be carefully maintained within the cyst lumen since wall abrasion may lead to bleeding during complete evacuation of the cyst. The largest and most accessible locule should be targeted in multilocular cysts. A solid component associated with the cyst should increase the suspicion of malignancy and be targeted for FNA. Due to the high viscosity of mucinous fluid, a 22G or 19G aspiration needle is more appropriate for cyst aspiration; however, a 25G needle may also be used for small (<2 cm) nonmucinous cysts or a transduodenal approach. The 19G needle may aspirate viscous fluid more efficiently and allows the use of novel instruments such as cytobrushing and confocal probes. The new 19G Flex needle may offer the large diameter of a 19G needle while providing a more flexible device for accessing head lesions.

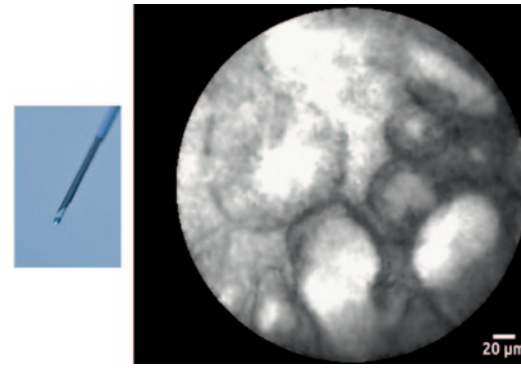

Fig. 23.11 Confocal laser endomicroscopy miniprobe on *left*, and papillary structures in a patient with IPMN on *right. IPMN* intraductal papillary mucinous neoplasm

Occasionally, debris or clot may block the needle tip and interfere with cyst aspiration. Clot, mucin globules, and septations should be avoided during FNA. The stylet may be used to dislodge adherent or obstructing material from the needle tip and/or channel by advancing the stylet through the needle.

After EUS-FNA, cyst fluid is routinely evaluated for gross appearance, amylase levels, CEA, and cytology. Genetic mutations (*KRAS* and *GNAS*) may aid in the diagnosis in select cases [52]. Recently, a confocal laser endomicroscopy miniprobe (nCLE) has been developed for use during EUS-FNA to visualize cyst wall and epithelium directly (Fig. 23.11). Preliminary studies of pancreatic cystic lesions showed promising cyst wall imaging findings to differentiate mucinous and nonmucinous cysts [53]. A pilot study reported 100% specificity to diagnose mucinous pancreatic cysts by nCLE with 3% rate of pancreatitis [54]. Further studies are needed to ascertain the contribution of nCLE for diagnosing cystic pancreatic lesions.

What Are Complications of EUS-FNA and How Can they Be Avoided?

EUS-FNA is generally a safe procedure with low incidence of complications. The most frequent complications are infection, bleeding, and acute

pancreatitis. The frequency and severity of complications vary according to the type of lesion and endosonographer experience. Most studies reported a procedure-related complication rate between 0.5 and 3.5%. A systematic review pooling 10,941 patients from 51 articles reported an approximately 1% overall morbidity rate for EUS-FNA [50]. The mortality rate attributable to EUS-FNA was 0.02%. The morbidity rate was significantly higher in prospective studies compared to retrospective studies (2.44 vs. 0.35% for pancreatic mass and 5.07 vs. 2.33% for pancreatic cysts). Therefore, complication rates may be underestimated in retrospective studies.

The most important risk factors for complications include endosonographer inexperience and FNA of cystic lesions [38, 50, 51]. Cysts are more prone to infection and bleeding. Antibiotic prophylaxis typically with a fluoroquinolone is administered routinely before and for 3–5 days after aspiration of any cystic lesion [38]. In large prospective series using antibiotic prophylaxis, 0–1.4% rate of infectious complications have been reported [17, 55]. Multiple passes into a cyst may increase risk of infection. Therefore, the goal of cyst aspiration is to completely drain the cyst contents to minimize risk of infection and maximize diagnostic yield. Aspiration of simple mediastinal cysts is contraindicated and indicated only when the cyst appears atypical or complex to rule out malignancy. There is no clear evidence that EUS-FNA of solid lesions may cause bacteremia and infectious complications.

A single-center study including 327 procedures of solid pancreatic lesions reported 3.4% post-procedural adverse event [56]. Multivariate analysis showed that pancreatic lesions less than 2 cm in diameter and neuroendocrine tumors were associated with more frequent complications. These results have not been confirmed by other studies.

Rates of acute pancreatitis after EUS-FNA range from 0.26 to 2% in different studies [17, 57, 58]. No significant risk factors were identified for post-EUS-FNA pancreatitis. A history of recent pancreatitis appeared to be a potential risk factor in one study [58]. If there is not a clear indication that may change clinical management, it is best to avoid EUS-FNA in the setting of recent pancreatitis.

Self-limited minor bleeding without clinical findings may occur following EUS-FNA of solid lesions, but clinically significant extra-luminal bleeding is very rare [59, 60]. Bleeding is more frequent and may cause significant consequences in FNA of cystic lesions. The rate was reported as 6% in a prospective study [61]. A gradually expanding hyperechoic area within the cyst after needle puncture is an important finding indicative of bleeding. In these cases, the procedure should be stopped and a short course of antibiotic is suggested. EUS-FNA should not be performed in patients with uncorrectable coagulopathy or on antiplatelet agents [62].

Less frequent complications have been reported after EUS-FNA in case reports and most were not directly related to FNA. Tumor cell seeding following EUS-FNA has been reported in a few cases. The actual risk of this is unknown, but significantly lower compared to percutaneous CT or US-guided FNA [63].

Key Points

- EUS-FNA should be performed if the results will impact patient management.
- Endosonographer experience, availability of adequate equipment, expertise of endoscopy staff, effective sedation, and quality of cytological examination are key factors for success.
- The location, route of access, nature of the lesion, need for histologic sample, and availability of rapid onsite evaluation (ROSE) should be considered when deciding the type and size of needle to use.
- Procore biopsy needles can obtain histologic samples, which may decrease the number of passes necessary for diagnosis and may be a better choice when ROSE is not available.
- The use of a stylet does not seem to impact diagnostic yield. Suction may help increase cellular yield. The “fanning” technique likely improves diagnostic accuracy.

- Complication rates may be higher in EUS-FNA of cystic lesions; and thus, require extra care compared to solid lesions.

Conflict of Interest The authors declare no conflict of interest.

Financial Disclosures None

Video Caption

Video 23.1 EUS-FNA of pancreatic cyst

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