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Future directions in endoscopic ultrasound-guided tissue acquisition

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ABSTRACT

Endoscopic ultrasound-guided tissue acquisition (EUS-TA) is safe and has a high diagnostic yield. Multiple factors affect the outcome of EUS-TA such as operator experience, procedure technique, needle-type, and cytopathologist training and experience. There have been numerous advances aiming to increase the diagnostic yield of EUS-TA. These include novel devices, modified tissue acquisition techniques, enhancements in EUS imaging, improved tissue processing methods, and increasingly frequent molecular and genetic testing of acquired tissue. Importantly, recent advances in personalized medicine may require greater amounts of tissue to be acquired to guide subsequent oncotherapy. As a result of all these new developments, several additional questions have arisen including defining the precise role of EUS-guided fine-needle biopsy, the optimal technique for EUS-TA, and standardization of tissue processing protocols. This review discusses recent advances and future directions regarding EUS-TA.

1. Introduction

Over the last 4 decades, the role of endoscopic ultrasound (EUS) has gradually evolved from a tool used initially for visual inspection to one capable of tissue acquisition to an increasingly therapeutic intervention. EUS-guided tissue acquisition (EUS-TA) was initially described in 1991, in a patient with pancreatic cancer [1]. This was an important development for the diagnosis and staging of various gastrointestinal cancers. Although it is typically superior to other modalities such as percutaneous ultrasound, computed tomography-guided fine-needle aspiration (FNA), or endoscopic retrograde cholangiopancreatography for tissue acquisition, EUS-TA is not without limitations and several areas for improvement can be identified. This review will discuss the unmet needs and current state of EUS-TA, focusing on recent developments and future directions.

2. Variables affecting EUS-TA performance and current limitations

A multitude of factors can affect the outcome of EUS-TA (Table 1): the competency and experience of the endosonographer; staff experience and quality of specimen preparation; cytopathologist experience and availability; the type, location and size of the targeted lesion; needle size (19 G, 22 G, or 25 G) and device used (FNA vs fine-needle biopsy [FNB]); the FNA technique used including suction method (wet suction, dry suction, or "capillary" technique); use of needle fanning; and the number of passes obtained. There has been a gradual refinement of EUS-TA over the years with the development of new devices and techniques, changing attitudes regarding the need for and use of rapid on-site cytopathology evaluation (ROSE), and improvements in endoscopic training, tissue processing methods, and cytopathology interpretation.

Despite these numerous advances, several limitations remain regarding EUS-TA. The procedure has a steep and prolonged learning curve and concerns have been raised regarding the adequacy of current advanced endoscopy programs in training competent fellows [2]. Furthermore, the specificity of EUS-TA is high but the reported sensitivities have been rather variable. The false negative rate ranges from 5%-23% for pancreatic masses [3,4], 33%-42% for pancreatic cystic neoplasms [5,6], and 2%-11% for lymph nodes [7,8]. In addition, the need for on-site specimen evaluation is uncertain. Although ROSE may not be needed in high-volume centers [9], it may provide significant benefit in centers with less experience and lower adequacy rates ($<90\%$) [10]. In the absence of ROSE, an increased number of FNA passes may be needed to achieve a confirmatory diagnosis [2,11]. The success of EUS-FNA also relies on the experience of the cytotechnician, as formal training in cytopathology is associated

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Table 1
Potential factors affecting endoscopic ultrasound-guided tissue acquistion.

Endosonographer training and experience
Endoscopy unit staff experience/quality of specimen preparation
Cytopathologist training and experience
Lesion type
Lesion location
Lesion size
Needle gauge
Needle type (aspiration vs biopsy)
Sampling technique during EUS-TA (fanning, # of passes)
Suction technique during EUS-TA (wet suction, capillary technique, etc)
Number of passes obtained

with higher diagnostic accuracy and lower number of passes to yield a diagnosis [12]. Finally, until recently, EUS-TA could not reliably provide tissue architecture or adequate material for secondary testing such as immunohistochemistry (IHC) or molecular or DNA testing.

The ideal scenario for EUS-TA should be somewhat similar to obtaining a biopsy during routine endoscopy. The technique should be simple and easy to apply with a short learning curve, thereby reducing the effect of operator experience and center volume on the success of the procedure. The procedure should be safe with a high diagnostic yield and adequate amount of tissue acquired to assess architecture and to perform secondary analyses such as IHC and molecular and DNA or RNA testing. The number of required passes should be minimal and ROSE should not be needed in order to improve efficiency and reduce procedure costs.

2.1. Effect of advances in needle size and design

Traditionally FNA needles have been used to perform EUS-TA. The FNA needles are available in 3 different sizes—19 G, 22 G, or 25 G needles. The size or gauge of FNA needle is possibly the most extensively studied predictor of diagnostic accuracy in EUS-TA. Although several comparative studies have shown no difference in performance between the needles, subtle differences have been noted. A meta-analysis including nearly 1,300 patients undergoing EUS-FNA of solid pancreatic masses found a higher sensitivity (93%) for the 25 G FNA needle when compared to the 22 G FNA needle (85%) [13]. The larger 19 G FNA needle is more technically challenging to use than smaller gauge needles, especially when sampling uncinate lesions via a transduodenal route, and has not provided improved results. Similarly, older generation Trucut-FNB needles had limited adoption owing to a lack of flexibility, a variably reliable spring loading mechanism, their large size (19 G) and a high failure rate via the transduodenal route. Although the 25 G needle is excellent for diagnosis, multiple passes may be required to obtain adequate tissue for cell block and tissue architecture cannot be determined [14].

In comparison, FNB needles have several potential advantages over FNA needles. These include the ability to obtain adequate tissue to perform molecular testing to improve diagnostic accuracy and predict treatment response as well as the ability to assess tissue architecture and perform IHC. Several new FNB needles have become commercially available with various different designs to obtain “core specimen.” The ProCore needle (Cook Medical, Winston-Salem, NC) has a reverse bevel design, such that tissue can be obtained during retrograde movement of the needle through the tissue. The needle also has side holes to facilitate exit of air and movement of tissue in the needle. The Acquire needle (Boston Scientific Corp, Natick, MA) has a “three-point” design with 3-pronged cutting edge. The SharkCore needle (Medtronic Inc, Boston, MA) has a “fork tip” needle design with 6 cutting surfaces and an opposing catch bevel. FNB needles may not increase the diagnostic yield compared to FNA needles for pancreatic masses [15] but they appear to provide more tissue and require fewer passes to obtain adequate tissue [16]. For nonpancreatic masses, however, the diagnostic yield was greater for EUS-FNB needles compared to EUS-FNA needles [17]. A more detailed discussion of the comparison between the types of needles was discussed in Chapter 2 (Cytology versus Histology).

One area where advancements in EUS-TA could significantly improve patient care is in the evaluation and characterization of pancreatic cystic lesions. EUS-FNA with pancreatic cyst fluid analysis can potentially aid in distinguishing between mucinous and nonmucinous cysts. However, in a significant proportion of cases, the diagnosis remains uncertain owing to equivocal cyst fluid analysis results. The feasibility of obtaining a biopsy of the pancreatic cyst wall was initially shown in 2 cases in which pancreatic cystoscopy using a fiberoptic Spyglass probe was performed followed by biopsy of the cyst wall using an ERCP forceps inserted through a 19 G FNA needle [18]. A new forceps has recently been introduced (“Moray micro Forceps,” US Endoscopy, Mentor, OH) specifically designed to obtain a biopsy of the pancreatic cyst wall via a 19 G FNA needle. Multiple recent case reports have shown the feasibility and safety of these forceps in diagnosing various pancreatic cystic neoplasms, especially in cases with nondiagnostic cyst fluid analysis results [19-21]. The details of the Moray micro forceps and its performance characteristics are discussed in Chapter 1.

Other techniques for obtaining cyst wall tissue include performing EUS-FNB of the cyst wall and repeat cyst wall puncture after cyst fluid aspiration using an EUS-FNA needle. In a series of 10 patients, EUS-FNB of the cyst wall using a 19 G Trucut-FNB needle [22] was shown to provide cyst diagnosis in 70% and altered clinical management by avoiding surgery in 3 of 4 patients (75%) planning to undergo surgery. In another study, following cyst aspiration with an EUS-FNA needle, the cyst wall was punctured by a to-and-fro movement of the needle. This technique improved the diagnostic yield of cytology by 29% [23].

2.2. Effect of advances in EUS-TA technique

The technique of EUS-FNA has also evolved from the traditional advancement of the needle with or without a stylet into the lesion, followed by a to-and-fro technique with suction achieved by negative pressure from a syringe. Newer methods include the wet suction technique, slow pull stylet or “capillary” technique, and “fanning” of needle within the lesion during specimen acquisition. An interesting observation by Attam et al led to the description of wet suction technique [24]. The “wet suction” technique involves preflushing the needle with 5 cc of normal saline to remove the column of air in the needle lumen after removing the stylet. The needle hub is attached to a 10 cc syringe filled with about 3 cc of normal saline and maximal suction applied. The needle is then advanced into the targeted lesion and FNA is performed in a routine manner. This technique was shown to have significantly greater cellularity and diagnostic yield when compared to traditional FNA technique using air suction [24]. The authors hypothesized that a column of normal saline would coat the inner lining of the needle lumen and facilitate movement of cells and prevent clogging of the needle lumen. In a proof of concept study, the mechanism of superiority of wet suction technique was explained on the basis of fluid dynamic principles [25]. Because water is less compressible than air, a column of normal saline in the needle lumen would lead to greater amount of suction at the needle tip compared to air. Simulation using a 3-dimensional computational fluid dynamic model showed that the length of aspirated tissue was much longer when