Comparing endoscopic ultrasound-guided core biopsies of solid pancreatic and extrapancreatic lesions: a large single-operator experience with a new fine-needle biopsy needle

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Abstract

Background There has been a paradigm shift in tertiary centers from endoscopic ultrasound (EUS) fine-needle aspiration to EUS fine-needle biopsy (EUS-FNB) for tissue acquisition in solid lesions. While data exists on the use of FNB needles in solid pancreatic lesions, very few studies looked at the utility of FNB in solid extrapancreatic lesions. Our aim was to study and compare the technical success and feasibility of EUS-FNB in evaluating solid pancreatic and extrapancreatic lesions using a novel FNB needle.

Methods We performed a retrospective cohort study of patients with solid masses or lesions needing EUS-guided core biopsy at the University of Utah between May 2016 and November 2017. All core biopsies were obtained using an Acquire™ Fine Needle Biopsy Device (Boston Scientific Corporation, Natick MA, USA). Rapid on-site evaluation was performed by a board-certified cytopathologist in all cases.

Results One hundred thirty-two patients (87 male) were included. Ninety-nine (73.3%) of the lesions were located in the pancreas. All needle sizes (19 G, 22 G and 25 G) had similar yield. The mean number of passes needed was 2.28±0.7. EUS-FNB of the pancreatic lesions had a diagnostic accuracy of 97.9%, comparable to the 97.2% for the biopsied extra-pancreatic lesions. Only 3 of 132 cases needed re-biopsy at a later date. No immediate adverse events were reported.

Conclusion In this large, single-center study, EUS-FNB with a novel Franseen-design needle was proven to be an effective modality for tissue acquisition from both pancreatic and extrapancreatic solid lesions.

Keywords Fine-needle biopsy, core biopsy, pancreatic mass, extrapancreatic mass, endoscopic ultrasound

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Introduction

In the era of molecular profiling and personalized oncology, there is an increasing emphasis on obtaining histological samples with tissue cores for molecular and ancillary testing [1,2]. Since

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its introduction in 1992, endoscopic ultrasound (EUS) fine-needle aspiration (FNA) has shown increasingly better diagnostic accuracy with improved needle designs over the years. However, the aspirate obtained by FNA fails to provide information on tissue architecture and limits the ability to perform grade differentiation, molecular profiling, and other ancillary testing.

Fine-needle biopsy (FNB) needle technology has evolved rapidly during the last decade, paralleling the therapeutic indications for EUS. FNB specimens ideally provide preserved tissue architecture and a larger amount of tissue for any ancillary testing. A new Franseen-geometry, three-plane symmetric Acquire™ (Boston Scientific Corporation, MA, USA) FNB needle showed promising results in recent studies with small sample sizes. Most of the previous EUS-FNB studies looked primarily at solid pancreatic lesions, whereas very few extrapancreatic lesions were evaluated. Historically, the diagnostic accuracy of EUS-FNA is lower for extrapancreatic lesions than for pancreatic lesions, while only limited data are available from the use of EUS-FNB [3]. We performed a

retrospective study with a larger number of patients, comparing the performance of this new Franseen needle design in both pancreatic and extrapancreatic solid lesions.

Patients and methods

We evaluated a longitudinal retrospective cohort of patients with solid masses or lesions needing EUS-guided core biopsy at the University of Utah between May 2016 and November 2017. The Institutional Review Board at the University of Utah approved the study.

The medical records of all identified patients were reviewed manually. Patients with cystic lesions based on EUS and other cross-sectional imaging data were excluded from the study. Data points included, but were not limited to age, sex, location of the lesion, size of the lesion, endoscopic ultrasound findings, type of tissue acquisition (transesophageal, transgastric, transduodenal and transrectal), tissue acquisition techniques (slow pull, saline in the needle, fanning vs. suction), needle gauge, number of passes, technical success and final histopathologic diagnosis. Needle visibility/echogenicity was graded on a scale of 1-4, with 1 being highest and 4 being lowest. Technical success was defined as successful acquisition of the tissue with an FNB needle for adequate interpretation by a pathologist.

EUS-FNB with the Acquire™ Endoscopic Ultrasound Fine Needle Biopsy Device (Boston Scientific Corporation, Natick MA, USA) was performed using linear echoendoscopes (Fig. 1,2). All EUS-FNB procedures were performed by a single endosonographer (DGA) with over 15 years of experience at performing high-volume EUS. The technique used for tissue acquisition was to insert the needle into the target lesions and slowly remove the stylet manually during needle actuations ("slow-pull" technique). The same technique was used exclusively in this study for the sake of uniformity. Rapid on-site evaluation (ROSE) by a board-certified cytopathologist was performed in all cases. Pathologic material and reporting records were also reviewed for each case to confirm the number of needle passes needed to achieve diagnostic adequacy, the presence or absence of diagnostic material, and whether a definitive diagnosis could be derived from the specimen obtained.

Statistical analysis

Statistical analysis was performed using SPSS version 25 (SPSS Inc, Chicago, Ill). Baseline characteristics of the cohort, descriptive statistics, and continuous variables were presented as mean±standard deviation.

Results

A total of 132 patients, 87 (66%) male and 45 (34%) female were included in this study. The mean age of the study
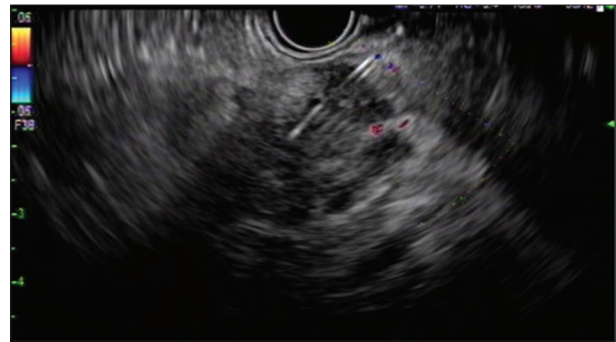
Figure 1 Endoscopic ultrasound image of a 19-G fine-needle biopsy needle used to obtain a core biopsy from a solid pancreatic head mass
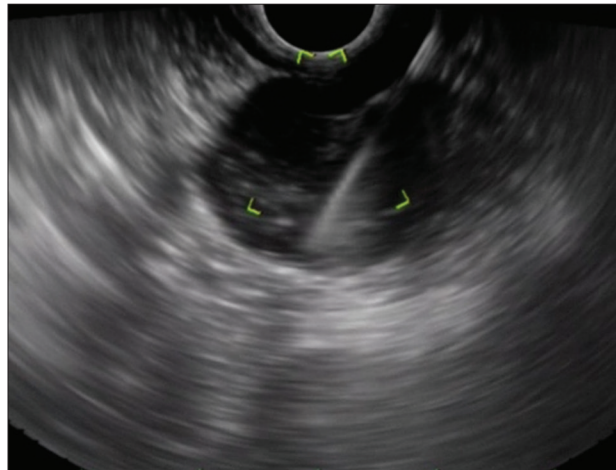
Figure 2 Endoscopic ultrasound image of a 22-G fine-needle biopsy needle used to obtain a core biopsy from an extrapancreatic, mediastinal lymph node

population was 63.5±13 years (Table 1). This was the first EUS biopsy of the target lesion in all patients.

Ninety-nine (73.3%) of the biopsied lesions were located in the pancreas and 36 (26.7%) were extrapancreatic in location. Of the pancreatic lesions, 60 (60.6%) were located in the head of the pancreas, 20 (20.2%) in the body, 12 (12.1%) in the tail, 4 (4%) in the uncinate process, and 3 (3%) in the neck of the pancreas. Three different gauges of Acquire™ biopsy needle were used: 130 (96.3%) lesions were biopsied with a 22 G needle, 3 (2.2%) with a 19 G needle, and 2 (1.5%) with a 25 G needle. The echogenicity of the needle was graded as 1 in all cases.

The transgastric approach was most commonly used, with 67 (49.6%) lesions accessed via this approach, followed by the transduodenal in 64 lesions (47.4%), transesophageal in 3 (2.2%), and transrectal in 1 (0.7%) (Table 2).

ROSE was performed by a board-certified pathologist in all cases. Our on-site pathologists used small samples of the core biopsy to make cytology slides to assess cellularity and adequacy. The majority of patients needed more than one pass to obtain an adequate specimen: 19 (14.4%) patients needed 1 pass, 68 (51.5%) two passes, 35 (26.5%) three passes, 9 (6.8%) 4 passes, and 1 patient needed 5 passes.

Table 1 Demographics and location of solid lesions studied by endoscopic ultrasound

Total number of patients	132
Total number of core biopsies obtained	135
Sex	
Male	87 (66%)
Female	45 (34%)
Lesion location	
Pancreatic	99 (73.3%)
Extrapancreatic	
Stomach	4 (2.9%)
Rectum	2 (1.4%)
Mediastinal lymph node	4 (2.9%)
Celiac lymph node	8 (5.9%)
Porta hepatis lymph node	6 (4.4%)
Peripancreatic lymph node	8 (5.9%)
Retroperitoneal lymph node	2 (1.4%)
Adrenal gland	1 (0.7%)
Location of pancreatic lesions	
Head	60 (60.6%)
Body	20 (20.2%)
Tail	12 (12.1%)
Uncinate	4 (4%)
Neck	3 (3%)

Table 2 Endoscopic ultrasound (EUS) fine-needle biopsy needle gauge, acquisition modality, number of passes needed and final diagnosis

Needle gauge	
22 G	130 (96.3%)
25 G	2 (1.5%)
19 G	3 (2.2%)
EUS modality	
Transesophageal	3 (2.2%)
Transgastric	67 (49.6%)
Transduodenal	64 (47.4%)
Transrectal	1 (0.7%)
Number of passes needed per patient	19 (14.4%)
1	68 (51.5%)
2	35 (26.5%)
3	9 (6.8%)
4	1 (0.8%)
5	
Need for re-biopsy	3 (2.3%)
Final diagnosis	
Pancreatic adenocarcinoma	74 (56%)
Gastrointestinal stromal tumors	6 (4.5%)
Neuroendocrine tumors	12 (9.1%) (all pancreatic)
Lymphoma	4 (3.0%)
Benign lesions	15 (11.5%) (5/15 pancreatic)
Pancreatic metastases	
Non-pancreatic metastatic lesions	7 (5.3%)
Non-pancreatic adenocarcinoma	7 (5.3%)
Non-diagnostic specimen	6 (4.5%)
Solid pseudo papillary tumor of pancreas	1(0.8%) (non-pancreatic)
	1 (0.8%)

The mean number of passes needed for an adequate sample was 2.28±0.7. Similar numbers of passes were needed for pancreatic (2.3±0.8) compared to extrapancreatic (2.3±0.6) lesions. Only 3 of 132 patients, with two pancreatic lesions and one extrapancreatic, needed re-biopsy at a later date. The overall diagnostic accuracy of the biopsied tissue was 97.7%. Biopsy samples from 128/132 patients (97%) were split for histological and cytological evaluation. Of the remaining 4 patients, two biopsies (1.5%) were sent for histological evaluation only and two for cytological evaluation only. No immediate adverse events were reported.

The final pathological diagnoses of the obtained biopsies were notable for pancreatic adenocarcinoma in 74 (56%), benign etiologies in 15 (11.5%), neuroendocrine tumors in 12 (9.1%), pancreatic metastases in 7 (5.3%), gastrointestinal stromal tumors in 6 (4.5%), lymphoma in 4 (3%), non-pancreatic metastases in 7 (5.3%), and non-pancreatic adenocarcinoma in 6 (4.5%). One of the specimens obtained was deemed non-diagnostic and the patient declined a re-biopsy. Benign etiologies included changes consistent with pancreatitis in 5 patients and benign adenopathy in 10 patients.

Comparing pancreatic to extrapancreatic sites, despite the 100% diagnostic yield based on ROSE, two pancreatic lesions and one extrapancreatic needed re-biopsy at a later date as the final pathology was indeterminate. Overall, FNB of the pancreatic lesions had a diagnostic accuracy of 97.9%, comparable to the 97.2% for extrapancreatic lesions (Table 3).

Discussion

Our retrospective study suggests that the use of core biopsy needles is an effective modality for tissue acquisition from both pancreatic and extrapancreatic solid lesions, and is the first study to specifically assess the value of a Franseen-tip needle when sampling extrapancreatic lesions FNA needles have an variable accuracy of 61% to 92% in pancreatic lesions, with significant heterogeneity among published studies [4-6]. Over the last decade, multiple Tru-Cut biopsy needles (e.g., Quick-Core: Cook medical, Limerick, Ireland) have been developed, improving sample procurement and offering a higher histological tissue yield [7,8]. With a diagnostic yield estimated to be between 52% and 95%, these needles were not superior to conventional FNA needles [9-13]. EUS-FNA quality indicators were proposed in 2015, with a diagnostic rate of malignancy for all pancreatic masses ≥70% and a sensitivity for malignancy among patients with pancreatic cancer ≥85% [14].

Recently there has been a paradigm shift in tertiary centers from EUS-FNA/Tru-Cut to EUS-FNB for tissue procurement; this was due to the improved diagnostic accuracy and the availability ofROSE [12]. Recent data on several new FNB needles have shown impressive tissue acquisition and a high rate of solid tissue cores available for more detailed analysis by pathology [15-17]. Earlier studies have shown that these needles are at least as good as standard FNA needles, while

Table 3 Comparison of endoscopic ultrasound fine-needle biopsies of pancreatic and extrapancreatic lesions

Characteristic	Pancreatic solid lesions	Extrapancreatic solid lesions
Number of lesions biopsied	99 (73.3%)	36 (26.7%)
Mean number of passes	2.3±0.8	2.3±0.6
Diagnostic yield based on ROSE	100%	100%
Patients needing re-biopsy after the final pathology read	2	1
Diagnostic accuracy	97.9%	97.2%
Immediate complications	None	None

ROSE, rapid on-site evaluation

they offer additional tissue for special stains with fewer needle passes overall [18]. While FNB sampling may obviate the need for ROSE, some in the cytology community still favor FNA over FNB [19]. Practices with regards to the need for ROSE in patients undergoing FNB remain unstandardized.

FNB sampling provides intact cores that provide better characterization of malignancy and improve the diagnostic accuracy for benign lesions. With extrapancreatic lesions (especially gastrointestinal stromal tumors, lymphoma, and neuroendocrine tumors), histology is crucial for reaching a diagnosis, as cytology alone cannot uniformly provide adequate architecture and cellular configuration [20,21]. In a prior study at our center, we compared the older reverse-bevel FNB needle to a standard FNA needle and found no significant difference in core tissue acquisition and diagnostic accuracy [22]. These findings were restated in a recent meta-analysis by Bang *et al* [11] which showed no significant difference between the reverse-bevel ProCore needles (22G/25G, Cook Endoscopy) and standard FNA needles (22 G/25 G) in terms of tissue acquisition and diagnostic accuracy. A few studies noted improved diagnostic yield with FNB of extrapancreatic lesions when compared to pancreatic lesions [23,24].

With the rapid evolution in needle technology, a new needle using a Franseen geometrical tip design (Acquire, Boston Scientific, Natick, MA) was recently introduced to maximize tissue capture and minimize fragmentation. In a recent study of 59 patients, using this needle for biopsy of only pancreatic solid lesions showed a high procurement yield and 98.3% diagnostic accuracy [25] This is comparable to our diagnostic accuracy of 97.9% for pancreatic and 97.2% for extrapancreatic lesions. Most of the FNB needle studies published to date focused primarily on pancreatic lesions, while only a few extrapancreatic lesions were evaluated. Our study is the first to specifically evaluate extrapancreatic solid lesions using the novel Franseen Acquire™ needle. Of the lesions evaluated in our study, 26.7% were extrapancreatic in location and FNB of these lesions showed comparable diagnostic accuracy without any adverse events.

The mean number of passes needed in previous studies ranged from 2.8-3.5 [16,18]. This is higher than the mean number of 2.28±0.7 passes needed in our study. Similar numbers of passes were needed for pancreatic (2.3±0.8) and for extrapancreatic (2.3±0.6) lesions. A study by Bang *et al* [26] reported a 3.3% rate of complications using a similar Franseen-design needle. Studies using 22/25 G SharkCore (Covidien, Sunnyvale, USA) needles showed increased bleeding associated with transduodenal biopsies, not observed in our study [27]. However, we encountered no procedure-related complications, similarly to Mitri *et al* [25].

Some limitations of our study should be noted, including its retrospective nature, single-center and single-operator design, with a possibility of selection bias. This study involved tissue acquisition by a highly experienced endosonographer, limiting its applicability to a real world environment. Given the lack of literature in this area, validated scoring systems were not used for cytology and histology specimens.

In this large, single-center study, EUS-FNB performed with a novel Franseen-type biopsy needle proved to be an effective modality for tissue acquisition from all solid lesions. We showed a very high histological and diagnostic yield, with equal effectiveness in both pancreatic and extrapancreatic lesions. Further evaluation with large, prospective, multi-center studies is needed to evaluate optimal needle diameter, the number of passes needed based on the biopsy site, and the need for ongoing ROSE.

Summary Box

What is already known:

- Fine-needle aspiration (FNA) has variable diagnostic accuracy and fails to provide information on tissue architecture
- The diagnostic accuracy with FNA is lower for extrapancreatic lesions than for pancreatic lesions
- Live donor LT (LDLT) has become the most promising alternative for the expansion of the organ pool for adult patients with HCC, but indications and criteria are still subject to debate

What the new findings are:

- This is the first study to specifically assess the value of a Franseen tip needle FNB for the sampling of extrapancreatic lesions
- All three needle sizes (19 G, 22 G and 25 G) had similar histological yield
- The novel Franseen-type needle showed equal effectiveness in both pancreatic and extrapancreatic lesions, with >97% diagnostic accuracy

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