

The difference in histological yield between 19G EUS-FNA and EUS-fine-needle biopsy needles

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ABSTRACT

Background and Objective: EUS-guided fine-needle biopsy (EUS-FNB) with acquisition of tissue core is possible with the use of 19G fine-needle aspiration (FNA) and dedicated biopsy needles. Published data of direct comparisons between biopsy needles are more limited compared to the abundant data comparing EUS-FNA with EUS-FNB. We performed a retrospective study to determine the difference in histologic yield between 19G FNA needle and EUS-FNB needles in patients with solid masses. **Materials and Methods:** Consecutive patients who underwent EUS-FNB of solid masses from January 2014 to July 2018 were identified from a database. The difference in histologic yield between needles was analyzed. **Results:** A total of 159 patients underwent 179 EUS-FNB procedures (median of 2 needle passes [range: 1–4]). The use of 19G FNA, 19G, 20G, and 22G FNB needles allowed acquisition of a histologic core in 67.4% (29/43), 72.5% (29/40), 82.1% (46/56), and 75.9% (22/29), respectively ($P = 0.368$). A significant difference in the yield of histologic core was detected when 19G FNA needle was compared with 22G Acquire™ FNB needle (67.4% [29/43] vs. 94.1% [16/17], $P = 0.032$). The presence of histologic core was significantly associated with a positive diagnosis (95.6% vs. 30.2%, $P < 0.0001$). **Conclusion:** EUS-FNB with acquisition of histologic core improved the diagnostic yield. Dedicated FNB needles appeared to achieve a higher yield of histologic core compared to 19G FNA needles.

Key words: Aspiration, biopsy, cytology, endoscopic ultrasound, histology, needles

INTRODUCTION


EUS-FNA has an excellent diagnostic yield and safety profile.^[1] In a meta-analysis that examined the diagnostic accuracy of EUS-FNA for staging mediastinal lymph nodes in patients with lung cancer, the sensitivity was 83% (95% confidence interval [CI]: 78%–87%) and the specificity was 97% (95% CI: 96%–98%).^[2] In another meta-analysis that focused on EUS-FNA of pancreatic masses, the sensitivity for diagnosing the

correct etiology was 86.8% (95% CI: 85.5%–87.9%) and the specificity was 95.8% (95% CI: 94.6%–96.7%).^[3] Although excellent diagnostic accuracy can be achieved by cytology in most instances, there may be a need for histology in specific circumstances such as the acquisition of more tissue to allow more detailed examination and immunostaining, the need for tissue architecture as part of the diagnostic evaluation as

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How to cite this article: Ang TL, Li JW, Kwek AB, Thurairajah PH, Wang LM. The difference in histological yield between 19G EUS-FNA and EUS-fine-needle biopsy needles. *Endosc Ultrasound* 2019;8:255-60.

Access this article online	
Quick Response Code: 	Website: www.eusjournal.com
	DOI: 10.4103/eus.eus_12_19

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Received: 2018-11-05; **Accepted:** 2019-02-05; **Published online:** 2019-05-09

in the case of gastrointestinal stromal tumor (GIST), lymphoma or autoimmune pancreatitis, and as a salvage diagnostic tool when there is nondiagnostic cytology.

EUS-guided fine-needle biopsy (EUS-FNB) with the procurement of histological core tissue was initially feasible only using a 19G Trucut biopsy device (Quick-Core®, Cook Medical Inc., Winston-Salem, North Carolina, United States) that was cumbersome to use.^[4] Data have demonstrated that histological core tissue can be obtained using standard 19G FNA needles.^[5] In recent years, biopsy needles have been developed by modification of the needle tip design to allow tissue procurement, such as the Procore® (Cook Medical Inc., Winston-Salem, North Carolina, United States),^[6] Acquire™ (Boston Scientific, Natick, MA, USA),^[7] and Sharkcore™ (Medtronic, Dublin, Ireland)^[8] needles. These needles are just as easy to use as standard FNA needles and have been shown to achieve excellent histologic and diagnostic yield.^[6-8] In particular, randomized studies have shown the superiority of these biopsy needles to the now obsolete Trucut biopsy needle^[4] and to FNA needles in the evaluation of submucosal lesions.^[9] Even in the context of pancreatic masses, where cytology is usually sufficient to make a diagnosis of malignancy, a recent meta-analysis has reported that EUS-FNB can improve histologic and diagnostic yield, decrease number of needle passes, and obviate the need for rapid on-site cytological evaluation (ROSE).^[10] A recently published randomized trial confirmed that diagnostic cell block could be achieved in >90% of patients with solid pancreatic masses using the new-generation FNB needles, thus obviating the need for ROSE.^[11]

Currently, published data of direct comparisons between biopsy needles^[11,12] are more limited compared to the abundant data comparing EUS-FNA with EUS-FNB.^[10] As part of a clinical audit of the quality of EUS-guided tissue acquisition at our center, we examined the difference in histologic yield between 19G FNA needle and EUS-FNB needles of different sizes in patients with solid masses.

MATERIALS AND METHODS

Setting and trial design

This was a single-center retrospective comparative study conducted at the Department of Gastroenterology and Hepatology, Changi General Hospital, Singapore. The study period was from January 2014 to July 2018. The

study was approved by the institutional review board. All patients gave consent for EUS-FNB and consent for the use of anonymized data for academic purposes.

Study population

The inclusion criterion was all patients referred for EUS-FNB of solid masses with size of at least 10 mm and either a 19G FNA needle or a dedicated FNB needle was used. Patients were excluded if the lesion was predominantly cystic, or when EUS-FNB could not be performed due to coagulopathy, inability to access the lesion with the echoendoscope, or inability to puncture the lesion due to the presence of interposed blood vessels.

Choice of needles

The choice of needles was at the discretion of the endoscopist. The needles used included a standard 19G FNA needle (either Echotip® needle from Cook or Expect™ needle from Boston Scientific), the Procore® needles from Cook (19G, 20G, 22G, and 25G), and 22G Acquire™ needles from Boston Scientific.

EUS-fine needle biopsy technique^[1]

EUS-FNB was performed using a curvilinear echoendoscope by credentialed endoscopists (TLA, ABEK, PHT) or under the direct supervision of a credentialed endoscopist in the case of procedures performed by trainees. The procedures were performed under moderate sedation using a combination of intravenous midazolam and fentanyl. The solid lesion was visualized using EUS and punctured under real-time ultrasonic guidance with the application of suction by attachment of a syringe with negative pressure. The number of needle passes was at the discretion of the endoscopist. The material obtained was expressed onto glass slides by reinsertion of the stylet, and the material was sent for both cytology and histology assessments. This process may be repeated, as per standard clinical practice, if the on-site assessment by the endoscopist was that inadequate tissue had been obtained. There was no ROSE by pathologists or cytotechnicians.

Pathology

An experienced gastroenterology pathologist (LMW) blinded to the type of needle used reviewed all the processed pathology specimens. Core biopsy specimens were immediately placed in formalin and subsequently embedded in paraffin. Tissue blocks were stained by hematoxylin and eosin, and additional immunohistochemistry studies were performed as

needed. Specimens were assessed for total specimen length and for adequacy to provide both a histologic diagnosis and desired immunohistochemical studies. For the histological core to be considered adequate, the following criteria must be met: (1) length of at least 15 mm for liver biopsy and at least 3 mm for tissue from other sites (the length is measured off glass slide); (2) adequacy to provide histologic diagnosis; and (3) adequacy for desired immunohistochemical studies.

Study definitions

When there was surgical resection of the lesion, the surgical histopathological specimen was considered the gold standard. In the absence of surgical resection, diagnostic histology (with immunohistochemistry if performed) or cytology provided by EUS-FNA was considered the gold standard. When diagnostic histology or cytology was not available, a benign diagnosis was confirmed by clinical follow-up (≥ 6 months) and other imaging tests to ensure that no malignancy developed over the course of time.

Statistical analyses

The primary outcome measure was adequacy of histologic core. Secondary outcome measures were the difference in diagnostic yield between histology and cytology and between biopsy sites. Categorical parameters including gender, type and location of masses, technical success, adequacy of histologic core, and diagnostic accuracy were compared by Chi-square test or Fisher's exact test. Continuous variables including age, size of mass, follow-up period, number of needle passes, and adequacy of specimens were compared by the Student's *t*-test or Wilcoxon rank sum test. For all calculations, biopsies with insufficient specimens were considered nondiagnostic biopsies. Statistical analysis was performed using SPSS software (version 20.0; SPSS, Chicago, IL, USA).

RESULTS

A total of 159 patients (male 94/159; mean age 63 years [range: 33–103]) were referred for EUS-FNB during the study. A total of 179 EUS-FNB procedures were performed. The main target sites for EUS-FNB were pancreatic masses (72; 40.2%), gastric submucosal tumors (49; 27.4%), and lymph nodes (27; 15.1%). Patient demographics and clinical information are summarized in Table 1. Needles used for EUS-FNB included 19G FNA needles (43), Procore[®] biopsy

Table 1. Patient demographics and clinical data

Characteristics	Population (n = 159)
Mean age, year (standard deviation)	62.91 (12.393)
Gender, n (%)	
Male	94 (59)
Female	65 (41)
Biopsy sites, n (%):	Total number of lesions = 179
Pancreatic mass	72 (40.2)
Stomach wall	49 (27.4)
Lymph nodes	27 (15.1)
Liver mass	12 (6.7)
Oesophagus wall	6 (3.4)
Duodenum wall	4 (2.2)
Bile duct mass	3 (1.9)
Gallbladder mass	1 (0.6)
Left adrenal mass	1 (0.6)
Porta hepatis mass	1 (0.6)
Rectum wall	1 (0.6)
Retroperitoneal mass	1 (0.6)
Thyroid mass	1 (0.6)

SD: Standard deviation

needles (19G: 40; 20G: 57; 22G: 12; 25G: 10), and Acquire[™] biopsy needles (22G: 17).

The median number of needle passes used for biopsy was 2 (range: 1–4). Where feasible, aspirates were sent for both histology and cytology as part of the diagnostic evaluation. The median number of cytology slides sent was 6 (range: 0–19, with 13/179 [7.3%] having only histological specimens sent).

There was a trend for FNB needles to achieve a higher yield of histologic core [Figures 1-4] compared to 19G FNA needles [Table 2]. The 19G FNA, 19G, 20G, 22G, and 25G FNB needles obtained histologic core in 67.4% (29/43), 72.5% (29/40), 82.1% (46/56), 75.9% (22/29), and 90% (9/10), respectively ($P = 0.358$). A significant difference in the yield of histologic core was detected only when the 19G FNA needle was specifically compared with 22G Acquire[™] needle (67.4% [29/43] *vs.* 94.1%, [16/17]; $P = 0.032$). The 10 cases in which 25G FNB needles were used were all pancreatic masses. The histologic yield was significantly lower for EUS-FNB of gastrointestinal (GI) wall lesions (61.7%; 37/60) compared to EUS-FNB of pancreatic masses (86.1%; 62/72) and other non-GI wall lesions (78.7%; 37/47), $P = 0.004$.

The presence of histologic core was significantly associated with a positive diagnosis (95.6% *vs.* 30.2%, $P < 0.0001$). The diagnostic yield was significantly lower for EUS-FNB of GI wall (61.7%; 37/60) compared to

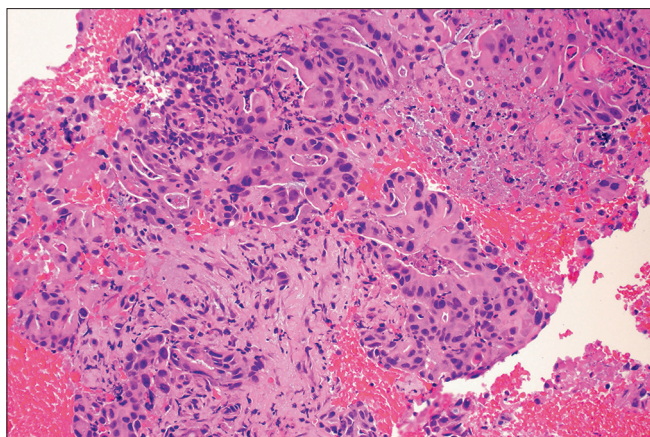


Figure 1. H and E section (×200) of EUS-guided pancreatic biopsy showing invasive adenocarcinoma, moderately differentiated, associated with desmoplastic stroma and tumor necrosis

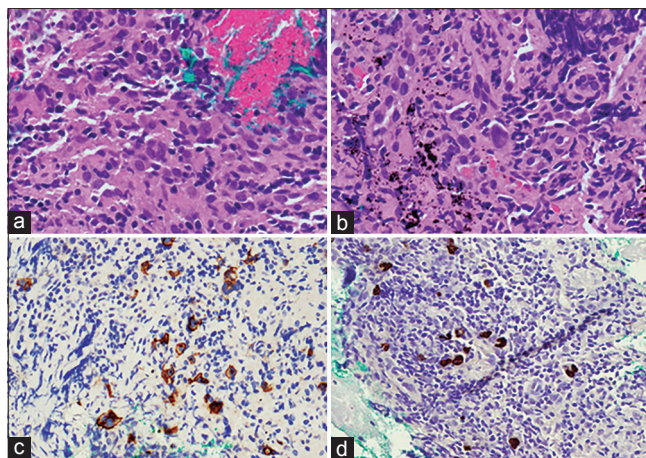


Figure 2. (a) H and E section (×400) of EUS-guided lymph node biopsy showing poorly formed granuloma in association with (b) atypical enlarged hyperchromatic cells that are positive for (c) CD30 (×200) and (d) EBER (×200) on immunohistochemical studies, suggestive of lymphoma. A subsequent excision biopsy of the lymph node was reported as non-Hodgkin lymphoma

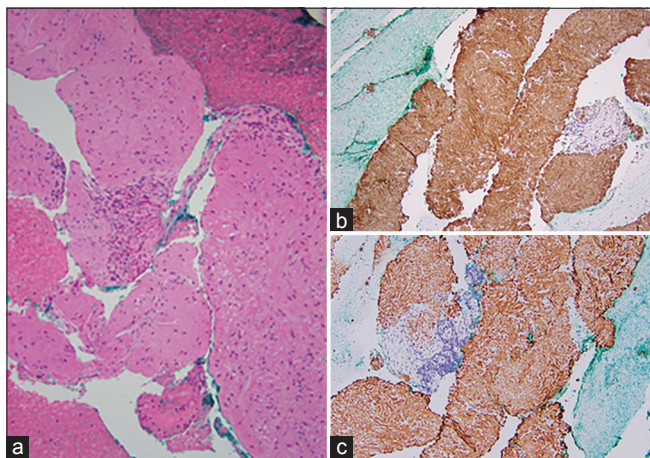


Figure 3. Spindle-shaped tumor cells are identified on the (a) H and E section (×100) of EUS-guided biopsy from a gastric lesion. No mitosis or necrosis was seen. On immunohistochemical studies, these were positive for (b) smooth muscle actin and (c) desmin, consistent with a leiomyoma

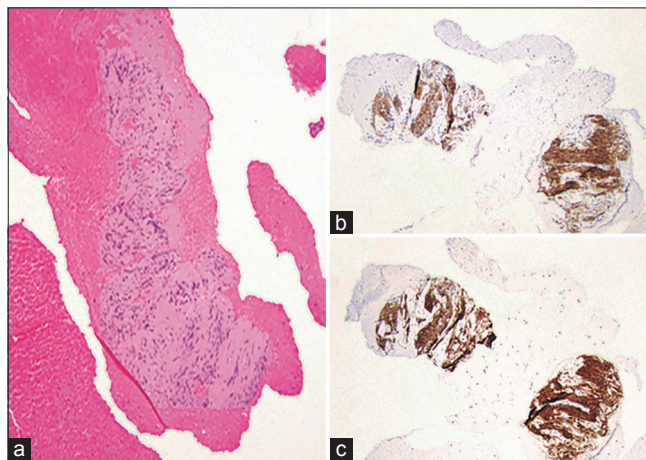


Figure 4. (a) H and E section (×100) of EUS-guided biopsy from “duodenal/gastric” lesion showing gastrointestinal stromal tumor, spindle cell type, with positive (b) CKIT and (c) DOG1 immunoreactivity

Table 2. Histological yield of EUS-biopsy needles

Needle type	Number	Histology available (%)
19G FNA needle	43	67.4
19G Procore needle	40	72.5
20G Procore needle	57	82.1
22G Procore needle	12	50
22G Acquire needle	17	94.1
25G Procore needle	10	90

FNA: Fine-needle aspiration

EUS-FNB of the pancreas (91.7%; 66/72) and other non-GI wall sites (85.1%; 40/47), *P* < 0.001.

DISCUSSION

Most studies have compared the diagnostic yield between EUS-FNA and EUS-FNB. These studies sometimes produced conflicting results due to the

study power, the definition of the primary endpoints, and the nature of the lesions biopsied. For instance, studies investigating the diagnostic yield of EUS-FNA in the context of malignant pancreatic masses often have excellent results as cytology was usually adequate for the diagnosis of pancreatic adenocarcinoma and thus would not highlight the importance or relevance of obtaining tissue for histology assessment.^[3] While clinical endpoints such as diagnostic accuracy are important, they do not highlight important technical details which must be considered when evaluating the effectiveness of EUS-FNB needles.

First, many centers employ the use of ROSE to increase the diagnostic accuracy of EUS-FNA. Several studies have indeed shown increased diagnostic

yield when EUS-FNA was used in conjunction with ROSE.^[13-16] A recent meta-analysis by Khan *et al.*,^[17] however, demonstrated that the use of EUS-FNB needles resulted in improved diagnostic yield in the absence of ROSE. All patients in our study undergoing EUS-FNB did not have ROSE. A relatively high yield of histologic core was achieved in our study, which in turn was significantly associated with a positive diagnosis. This supported the role of EUS-FNB needles in obviating the need for ROSE, thus decreasing the overall actual financial and manpower costs of the procedure despite the higher cost of an individual FNB needle.^[18] This is especially important as the need for EUS-guided tissue acquisition increases, and the manpower to support ROSE may not be available in every institution, particularly in nonacademic centers. The same meta-analysis also highlighted that EUS-FNB required fewer needle passes to establish the diagnosis compared to EUS-FNA, and this finding is also supported by other studies.^[9,10] The median number of needle passes required per lesion was 2 in our study, which was consistent with the figures published in the literature for EUS-FNB needles to date. Requiring fewer needle passes per lesion translates into a shorter procedure time and may potentially decrease the risk of procedure-related adverse events. These are key advantages in a real-world setting as they impact on the efficiency of the running of an endoscopy center and the cost per procedure.

Second, the presence of a histologic core is essential for diagnosis in most nonpancreatic lesions such as GIST and lymphoma, as tissue architecture is needed for diagnostic evaluation. Moreover, even in the case of pancreatic malignancies, immunohistochemical and tissue staining can only be performed on histological cores, which may become more important in the era of individualized therapy. Most pathologists are also generally less familiar with the interpretation of cytology and would prefer the presence of histologic core tissue for evaluation, especially in difficult diagnostic cases. The yield of histologic cores from published large multicenter series ranges between 88% and 90%.^[6,7,19,20] The findings from our study showed high rates of histologic cores obtained with the use of EUS-FNB needles, with no statistical difference between needles of different designs and sizes. Hence, our study adds to the data supporting the use of EUS-FNB needles to obtain histologic cores. As highlighted in the results section of the paper, the procurement of histologic cores was

associated with increased diagnostic yield. This was consistent with the results from a recent multicenter study by Cheng *et al.*,^[21] where diagnostic failure in nonpancreatic lesions was significantly higher with EUS-FNA compared to FNB.

Third, although larger FNA needles may in theory yield histologic cores, a study by Iwashita *et al.*^[5] showed that 19G FNB needles were superior to 19G FNA needles in obtaining histologic core and in histological accuracy. Moreover, larger needles are stiffer than the smaller 20, 22, and 25G FNB needles, and this may make procurement of tissue technically more challenging, especially when performing EUS-FNB through a transduodenal approach. EUS-FNB needles overcome the size limitation with their unique cutting surfaces to obtain histologic cores, as described earlier.

We acknowledge our study limitations. It was retrospective and was a single-center study. With regard to the former limitation, the data from all EUS procedure were captured and maintained prospectively in a registry in our institution. The number of patients and procedures involved in our single-center study was comparable to that from other published multicenter series, and the data reflected results obtained in the real-world setting.^[6,7,19,20]

Indeed, given the fact that diagnostic yield may be influenced not just by the needle used but also the level of experience of the endoscopist, one of the strengths of this study was that variability from this was kept to a minimum compared to studies involving several centers where the experience and training of the endoscopist may vary greatly. Furthermore, published data comparing different EUS-FNB needles were limited.^[11,22,23] These limited studies only evaluated FNB needles with similar gauges or solely at solid pancreatic lesions. Our study was novel in analyzing differences in performance of EUS-FNB across different needle sizes with a large bore 19G FNA needle acting as a control. Moreover, we also captured and analyzed data of EUS-FNB from pancreatic and nonpancreatic lesions, thus evaluating the differences in performance of the various EUS-FNB needles in greater detail and over a wider range of clinical scenarios than other published studies to date.

CONCLUSION

EUS-FNB with acquisition of histologic core improved the diagnostic yield. Dedicated FNB needles appeared

to achieve a higher yield of histologic core compared to 19G FNA needles.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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