INVESTIGATIONS: ORIGINAL ARTICLE

Pilot study comparing a novel EUS-guided motorized biopsy needle technique with traditional sampling

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Background and Aims: Improving tissue acquisition in core samples using EUS-guided fine-needle biopsy sampling (EUS-FNB) for histologic diagnosis and tumor molecular profiling is needed for the era of precision medicine. However, sample quality is impacted by needle type, number of throws, and technique. Currently, all commercially available biopsy needles are manually operated. This pilot study is the first to compare Precision (Limaca Medical, Ein HaEmek, Israel), a new motorized EUS-FNB device programmed to drive controlled axial tissue cutting and synchronized high-speed rotational coring to optimize tissue acquisition and physician control, with SharkCore (Medtronic Corp., Minneapolis, MN) using a traditional manual technique.

Methods: Patients with solid pancreas tumors were eligible for enrollment. Each patient's target lesion was sampled by both Precision and SharkCore. Procedure measures were number of passes and throws, diagnostic yield, and histologic scores.

Results: Nine patients were enrolled. The average tissue sampling time using Precision was 3.87 minutes compared with 5.64 minutes with SharkCore ($P = .001$). Average Precision throws were 5 compared with 55 for SharkCore ($P = .00002$). The diagnostic yield was similar in both arms. However, the average histologic score of Precision was higher (4.6/5) compared with SharkCore (3.2/5, $P = .002$).

Conclusions: EUS-FNB is the method of choice for tumor data acquisition. The initial results of this pilot study suggest an automated motorized needle biopsy sampling approach may lead to more consistent histologic quality along with the ability for molecular profiling of tumors with fewer throws and passes reducing average procedure time. Future larger studies are needed to validate these findings. (iGIE 2023;■:1-5.)

Linear EUS allows for the visualization, characterization, and diagnostic sampling of subepithelial lesions of the GI tract in addition to adjacent structures such as the pancreas, liver, and lymph nodes. EUS-guided FNA (EUS-FNA), first developed in the early 1990s, obtains cytologic material of lesions under investigation to aid in diagnosis and management. EUS-FNA improved the diagnostic capabilities of EUS to provide tissue sampling of lesions previously only sampled by more invasive means.[1]

The emergence of multiple EUS-guided fine needle biopsy sampling (EUS-FNB) needles to obtain core specimens within the past decade has further improved the diagnostic accuracy and histologic adequacy of sampling.[2-5] EUS-FNB may even eliminate the need for on-site cytopathic evaluation.[4-6] Greater histologic sampling also allows for the analysis of molecular and tumor markers using genome sequencing, which can risk stratify malignancies and aid in the choice of chemotherapeutic or other treatment agents including immunotherapy in the era of personalized "precision medicine."[7-9] Therefore, innovations that can improve the efficiency and effectiveness of EUS-guided core tissue sampling are of current clinical relevance to improve patient care. Here we present a novel method of EUS-FNB tissue acquisition with a motorized, automated approach compared with the traditional manual technique.

EUS-FNB has gained popularity over EUS-FNA for tissue sampling within the GI tract and of adjacent structures. Prior studies have shown that EUS-FNB compared with EUS-FNA was almost twice as likely to obtain a tissue sample with histologic adequacy with a low adverse event rate and demonstrated a reduced need for additional diagnostic procedures.[2] Three different needle types for EUS-FNB are currently commercially available. The ProCore (Cook Medical, Bloomington, IN) needle is a reverse-bevel core needle. The SharkCore (Medtronic Corp., Minneapolis, MN) needle is a fork-tip needle that has an additional second sharp tip on the opposite side of the needle lumen compared with the reverse-bevel core needle designed to enhance the amount of tissue sampling during each pass. The Acquire (Boston Scientific, Marlborough, MA) needle

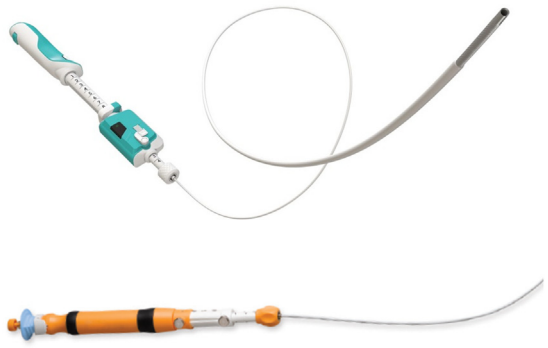

Figure 1. Precision (*top*) and SharkCore (*bottom*) EUS biopsy devices.

is a Franseen-tip needle that has a crown tip with 3 cutting edges, again designed to increase the amount of tissue acquisition during each needle pass.[1] Tissue sample quality is impacted by several factors including needle type, number of passes in and out of the endoscope, number of stabs or throws made during each pass, and technique of the endosonographer. The diagnostic sampling of these 3 needle types has been compared in previous studies with mixed results, with some studies suggesting 1 manual needle type is superior and other studies showing no significant differences.[5,10-15]

Although all commercially available EUS-FNB needle types require manual operation and advancement of the needle into the tissue for sampling, generally using a high number of throws of the needle into the target lesion, the Precision (Limaca Medical, Ein HaEmek, Israel) EUS-guided biopsy device is motorized and automated while the operator maintains control over tissue targeting and depth of advancement. Precision is a motorized EUS biopsy device programmed to drive controlled axial tissue cutting and synchronized high-speed rotational coring in a predefined ratio to optimize tissue acquisition and physician control (Fig. 1). This novel device has been developed to extract intact core tissue quality and quantity per throw, with minimal fragmentation of the biopsy samples, which improves standardization of tissue sampling as well as the ability to perform genomic and molecular tumor profiling (Fig. 2). We performed a crossover design pilot study comparing procedural and histologic outcomes between Precision and traditional manual needle sampling.

METHODS

Study design

We conducted a pilot study using a single-center crossover design at Rambam Hospital (Haifa, Israel) that was approved by the local institutional review board. Inclusion criteria were patients who were scheduled for diagnostic EUS aged ≥18 years and were able to provide written informed consent to be enrolled in the study. Patients excluded from the study were those who had an underlying medical condition contraindicating EUS diagnostic sampling, increased risk for postprocedure bleeding (including use of anticoagulants, international normalized ratio >1.5, or platelet count <50,000), and pregnant or lactating patients.

Patients undergoing EUS for solid pancreas masses who met these criteria were enrolled in the pilot study in a consecutive manner. Each patient enrolled in the study had the same lesion sampled by both the novel 19-gauge motorized needle (Precision) and a 22-gauge manual needle (SharkCore) biopsy sampling method. Per protocol, the tissue sampling with the manual needle was performed first followed by the motorized needle. The number of needle passes and throws and the time for each procedure were also recorded. Each biopsy sample was given a histologic score from 1 to 5 by a pathologist who was blinded to the needle type used to obtain each specimen (1 = poor sample, nondiagnostic yield; 5 = excellent sample, complete diagnostic yield).

EUS motorized biopsy technique

The initial technique for the motorized device was identical to the manual EUS needles. The echoendoscope was advanced by the proceduralist toward the lesion under investigation. The needle was then advanced into the lesion after an endosonographic window was identified. Precision features a sharp stylet to facilitate crossing through the GI wall, which is then retracted once the needle is at the target lesion. A control button on the novel device allows the physician to begin rotational coring as previously described, creating a motorized rotational electromechanical cutting movement into the lesion, allowing for intact motorized tissue acquisition without crushing or pulverizing the sample.

RESULTS

Baseline patient characteristics

Nine patients, 6 men and 3 women with a mean age of 72 years, were enrolled in the study between May 2019 and February 2020. The average patient body mass index was 24 kg/m^2. The target lesions under endosonographic investigation were 9 solid pancreas masses. A transduodenal route for both types of EUS sampling was used for 2 pancreatic head masses, whereas a transgastric approach was used for the 6 pancreatic body masses and 1 pancreatic tail mass. No adverse events occurred for any patient using either means of sampling. The average lesion size was 30 mm in maximal diameter (Table 1).

Diagnostics and histologic scoring of the motorized needle compared with traditional sampling

The diagnostic yield was similar in both arms. All 9 target lesions had a final pathologic diagnosis of pancreatic

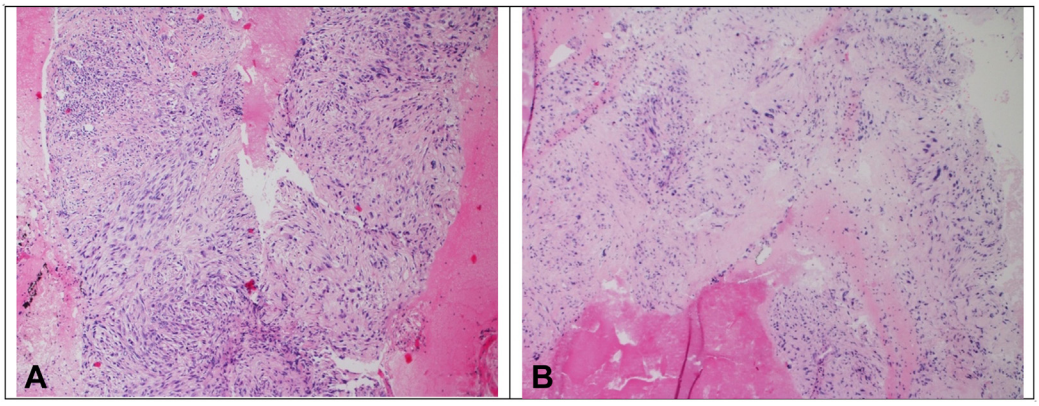

Figure 2. Histologic comparison of Precision versus manual needle. **A,** EUS-guided tissue acquisition with the Precision device. The core sample has preserved tissue architecture allowing for histopathology analysis. **B,** EUS-guided tissue acquisition with the SharkCore manual device. The core sample lacks preserved tissue architecture allowing only for cytopathologic analysis.

adenocarcinoma obtained by both the Precision motorized biopsy needle and the SharkCore manual biopsy needle. Four samplings (44%) required more than 1 pass with the manual needle compared with 1 (11%) with the motorized needle. The average number of throws with the Precision was 5 per patient compared with 55 per patient with SharkCore ($P = .00002$). The average time needed for tissue sampling using the motorized needle was 3.87 minutes compared with 5.64 minutes with the manual needle ($P = .001$). The average histologic score in the motorized arm was higher (4.6/5) compared with the manual needle arm (3.2/5, $P = .002$). Differences in the throws per patient, mean times required for tissue sampling, and histologic scores for the motorized versus manual needle were compared using a 2-tailed paired *t* test. It is notable that these superior results with Precision were achieved using just 5 throws per case on average versus 55 per case on average with the manual needle (Table 2).

DISCUSSION

EUS has been able to provide relatively noninvasive diagnostic sampling to aid in treatment decisions and clinical management of patients presenting with tumors of the GI tract or adjacent structures. Although FNA has been a standardized approach and has aided in the diagnostic accuracy of target lesions, the ability of EUS-FNB to provide core tissue samplings has broadened this technique's ability to provide more diagnostic data to include genomic and molecular profiling including the search for K-*ras* mutations. As cancer therapies continue to evolve to identify personalized molecular and immune checkpoint inhibitors using whole exome and whole genome sequencing, obtaining large, intact core tissue samples with high tumor content using EUS will become more important than ever.[7-9] Here we presented the interim results of the first human feasibility pilot study using a motorized needle during EUS.

In our study we found no difference in the diagnostic accuracy between the manual needle and motorized needle approaches. Traditional EUS-FNB core needles have provided diagnostic accuracy over FNA since their advent within the past decade. However, we showed that the manual approach compared with our novel motorized needle significantly increased overall procedural time by 150% and the number of average needle throws and passes per procedure, which implies more efficacy and efficiency for the motorized technique. In addition, we found that the histologic scoring for the motorized needle tissue samples was significantly higher than for the traditional manual needle, likely because of the ability to obtain standardized, unfragmented core samples with the Precision technique. The samples with higher histologic scoring not only provide more clinical information and better diagnostic confidence, but also are more likely to be amenable for comprehensive genomic sequencing and molecular marker analysis.

Although the initial results of this pilot study investigating a novel method of EUS-FNB tissue acquisition suggest that an automated motorized needle biopsy approach may offer superior means of EUS tissue sampling, there are several limitations to the current investigation. First, a 19-gauge motorized biopsy needle was compared with a 22-gauge manual needle as a result of supplies available to the investigator team at the time of the study. The difference in needle size biases the EUS sampling toward the motorized compared with the manual approach, and future studies controlling for differences in needle gauge are needed to validate the current findings. Second, the investigator was not blinded to needle type during the time of tissue acquisition, which may have biased the endosonographer toward increasing the numbers of passes and throws with the manual needle compared with the motorized needle. Finally, although the results are promising, the current investigation represents a pilot study, and a larger sample size is needed.

TABLE 1. Patient age, demographics, and target lesion data

Patient	Gender	Age (y)	Body mass index (kg/m^2)	Target lesion	Lesion size (mm)
1	Female	82	25.8	Pancreatic body	18
2	Female	73	22.9	Pancreatic head	30
3	Male	64	23.2	Pancreatic tail	25
4	Male	68	24.2	Pancreatic body	32
5	Male	75	24.9	Pancreatic body	30
6	Male	71	32.3	Pancreatic body	40
7	Male	62	22.5	Pancreatic body	40
8	Female	87	19.6	Pancreatic body	30
9	Male	62	21.0	Pancreatic head	25

TABLE 2. Procedure measures for Precision vs SharkCore needle

	SharkCore				Precision				
Patient	Passes	Throws	Time (min)	Histologic score	Passes	Throws	Time (min)	Histologic score	Diagnosis
1	1	25	3	5	1	4	1.5	5	Pancreatic adenocarcinoma
2	2	61	4.5	3	1	4	3.17	5	Pancreatic adenocarcinoma
3	2	62	10	3	2	8	7	4	Pancreatic adenocarcinoma
4	1	52	5	3	1	4	5	4	Pancreatic adenocarcinoma
5	2	80	9	3	1	6	6	3	Pancreatic adenocarcinoma
6	1	67	3.5	3	1	6	3	5	Pancreatic adenocarcinoma
7	1	45	5.17	3	1	6	3.67	5	Pancreatic adenocarcinoma
8	2	70	5.5	3	1	3	3	5	Pancreatic adenocarcinoma
9	1	35	5.17	3	1	3	2.5	5	Pancreatic adenocarcinoma
Average	1.5	55.2	5.64	3.2	1.1	4.9	3.87	4.6	Pancreatic adenocarcinoma

The interim results of this small human feasibility clinical trial suggest a novel motorized EUS-FNB method of tissue acquisition can provide more consistent histologic quality from the core tissue biopsy samples, along with allowing for molecular profiling of tumors with fewer throws and passes compared with currently commercially available manual EUS-FNB needle types. Future larger studies are needed to validate these findings.

DISCLOSURE

The following authors disclosed financial relationships: Iyad Khamaysi: Stock options with Limaca Medical. S. A. Gross: Consultant for Medtronic, Olympus, Cook, and Microtech. All other authors disclosed no financial relationships.

Abbreviations: EUS-FNA, EUS-guided FNA; EUS-FNB, EUS-guided fine-needle biopsy sampling.

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https://doi.org/10.1016/j.igie.2023.03.005

Received November 15, 2022. Accepted March 21, 2023.

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