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Superior Specimen and Diagnostic Accuracy with Endoscopic Ultrasound-Guided Liver Biopsies Using 19-Gauge versus 22-Gauge Core Needles

Rucha M. Shah¹, Jason Schmidt², Elizabeth John¹, Sheila Rastegari³, Priyanka Acharya⁴ and Prashant Kedia^{1,5}

¹Department of Gastroenterology, Methodist Dallas Medical Center, Dallas, TX, ²Department of Pathology, Methodist Dallas Medical Center, Dallas, TX, ³Department of Internal Medicine, Methodist Dallas Medical Center, Dallas, TX, ⁴Methodist Health System Clinical Research Institute, Methodist Dallas Medical Center, Dallas, TX, ⁵Digestive Health Associates of Texas, Dallas, TX, USA

Background/Aims: Endoscopic ultrasound-guided liver biopsy (EUS-LB) is an effective and safe method of procuring liver tissue. The aims of this study were to assess and compare the outcomes and tissue adequacy of a single-pass, single-actuation, wet suction technique between 19 G and 22 G needles in patients undergoing EUS-LB.

Methods: We performed a prospective case series study of 20 patients undergoing EUS-LB at a single center between September 2017 and April 2020. The primary objective was to evaluate differences in sample adequacy via a single actuation wet suction technique between a 19 G core needle and a 22 G core needle. Adequacy was gauged by cumulative core biopsy length and the number of portal tracts visualized.

Results: The 19 G needle provided a longer core length (2.5 cm vs. 1.2 cm, $p < 0.0001$), more complete portal tracts (5.8 vs. 1.7, $p < 0.0001$), more total tracts (8.8 vs. 3, $p < 0.0001$), and a longer, intact, fragment length (0.75 cm vs. 0.32 cm, $p < 0.0006$). The 19 G needle was superior in providing adequate (60% vs. 5%, $p < 0.001$) and diagnostic pathologic samples (85% vs. 10%, $p < 0.001$).

Conclusions: A single-pass, single-actuation, wet suction technique using a 19 G needle is superior to that using a 22 G needle for tissue acquisition and sample adequacy in EUS-LB. **Clin Endosc 2021;54:739-744**

Key Words: 19 G FNB; Endoscopic ultrasound-guided liver biopsy; Liver biopsy

INTRODUCTION

The use of noninvasive biomarkers and imaging studies such as transient elastography has increased; however, liver biopsy continues to be a cornerstone in the diagnosis, staging, and management of patients with hepatic disease.¹ Traditionally, liver biopsies have been performed via the transjugular or percutaneous routes.² While these methods have been shown

to be effective and safe, they have limitations. A percutaneous liver biopsy may be anxiety-provoking, painful, limited by a large body habitus, and cannot provide bilobar sampling. Transjugular liver biopsies expose the patient to radiation and potential complications such as hematomas and pneumothoraces from central venous access. In addition, neither route allows for real-time visualization of the liver parenchyma during needle insertion to avoid blood vessels and other major structures. Endoscopic ultrasound-guided liver biopsy (EUS-LB) sampling is emerging as an alternative to the aforementioned approaches, which offers several advantages without many of their limitations.¹⁻⁴ A recent meta-analysis showed EUS-LB provides a histological diagnosis in over 93% of cases with an adverse event rate of 2.3%.⁵ Despite the growing and encouraging literature on EUS-LB, standardized practice has not been achieved in terms of approach, needle type or gauge, acquisition techniques, and tissue handling. Multiple studies

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Correspondence: Prashant Kedia

Digestive Health Associates of Texas, Pav. II, 221 W Colorado Blvd Ste. 630, Dallas, TX 75208, USA

Tel: +1-214-941-6891, Fax: +1-214-943-5871, E-mail: Kediaps@gmail.com

ORCID: <https://orcid.org/0000-0001-6472-0902>

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have shown success with both 19 and 22 G needles; however, the number of needle actuations into the liver parenchyma was high, ranging from 9 to 20.⁶⁻⁸ Theoretically, the risk of complications increases with the number of needle actuations. Thus, limiting this number while still procuring an adequate specimen is ideal. Nieto et al. described success with a single-pass, single-actuation wet suction technique using a 19 G needle, where only two total needle actuations provided highly adequate specimens with a low adverse event rate of 1.8%.⁹ We chose to use the wet suction technique as presently it is the only technique in the literature published to date that requires only a single pass and single actuation of the EUS needle to procure an adequate liver biopsy specimen. The application of the single actuation wet suction technique has not been studied with different needle gauges. Therefore, the goal of this study was to assess the outcomes and tissue adequacy of performing a single pass, single actuation, and wet suction technique using specific 19 G and 22 G needles in patients, to help identify and standardize an EUS-LB technique that obtains adequate specimens and concurrently minimizes risk to the patient.

MATERIALS AND METHODS

This was a prospective case series of patients undergoing EUS-LB at a single center between September 2017 and April 2020. Patients were enrolled into the study if they were 18 years of age or older, with abnormal results for liver function tests of unclear etiology, with abnormal liver imaging, or needed staging for fibrosis, and were willing to undergo an EUS-LB for evaluation. They were excluded if they were younger than 18 years of age or did not want to undergo an EUS-LB. The study protocol was approved by the Institutional Review Board, protocol number 045.GID.2017.D.

Our primary objective was to evaluate differences in liver biopsy sample adequacy obtained via a single actuation wet suction technique using a 22 G core needle and a 19 G core needle from the transgastric position into the left lobe of the liver. All EUS procedures were performed by a single high-volume endosonographer (PK). The indication for liver biopsy in all patients was to investigate elevated liver function tests, abnormal liver imaging, evaluation of fibrosis, or evaluation for acute cellular rejection after orthotopic liver transplant, as noted in Table 1. Adequacy was gauged by the cumulative length of the core biopsy and the number of portal tracts visualized by a single gastrointestinal pathologist, JS. In accordance with the American Association for the Study of Liver Disease, our specimen adequacy was defined as a specimen containing ≥ 11 portal tracts or measuring ≥ 20 mm cumulative core

length.¹⁰ Secondary objectives included evaluating the difference in overall diagnostic yield, adverse events, number of tissue fragments, and maximum fragment length between the two needle specimens. A specimen was deemed diagnostic when the pathologist was able to establish a diagnosis with the tissue procured, whether or not 11 portal tracts were procured.

The electronic medical records were reviewed to identify case-based details including demographics such as age and sex, indication for liver biopsy, laboratory values including platelets and international normalized ratio (INR), comorbidities, American Society of Anesthesiologists (ASA) physical status class, and presence of ascites. Prospective procedure-related data, including needle gauge and adverse events, were recorded. A single, expert gastrointestinal pathologist reviewed all samples related to the study to prospectively record the cumulative core length, number of portal tracts, maximum fragment length, number of total fragments, sample adequacy, and diagnostic yield.

Procedure technique

All subjects were sedated under monitored anesthesia care and placed in the left lateral position for the procedure. A linear echoendoscope (EG-3870UTK; Pentax Medical, Montvale, NJ, USA) was advanced through the oropharynx to the gastric body, and the left lobe of the liver was identified. The scope was positioned to optimize the endosonographic visualization so that at least 7 cm of the liver parenchyma could be accessed by the needle without significant intervening vasculature using Doppler imaging. A 19 G core biopsy needle (SharkCore FNB; Medtronic, Minneapolis, MN, USA) was prepared by removing the stylet and flushing the entire needle catheter with sterile saline fluid. The needle was advanced through the echoendoscope and oriented at an angle to safely pass at a maximum length into the liver parenchyma. The actuation of the needle was a swift motion into the liver parenchyma. Once actuation was achieved, the syringe was set to maximum suction at the back end of the needle. The needle was kept in position until saline was seen rising into the syringe itself, at which point suction was turned off. The needle was slowly removed, and the tissue sample was extracted with a slow saline flush directly into formalin. The majority of superfluous samples of blood were removed from the specimen using the sifting method with additional formalin fluid (Fig. 1).

Subsequently, a second biopsy was obtained from the same lobe of the liver from the transgastric position but in a different tract through the liver using the 22 G core biopsy needle (SharkCore FNB; Medtronic). Any additional diagnostic endosonographic images required for completion of the EUS examination were obtained prior to termination of the procedure.

Table 1. Patient Baseline Characteristics

Subject	Sex	Age	ASA class	Indication for liver biopsy	Histology
Subject 1	M	54	3	Abnormal liver tests of unclear etiology	Mild steatosis without fibrosis
Subject 2	M	68	3	Assess for post liver transplant acute cellular rejection	No acute cellular rejection, mild fibrosis
Subject 3	F	48	2	Abnormal liver tests of unclear etiology	No steatosis or fibrosis Intrahepatocyte iron with Kupffer cells
Subject 4	M	54	3	Needed staging of fibrosis	PSC with steatohepatitis and fibrosis
Subject 5	F	74	3	Needed staging of fibrosis	Portal and lobular inflammation, no fibrosis
Subject 6	F	73	2	Abnormal liver imaging	Large duct obstruction, stage 1–2 fibrosis
Subject 7	F	55	3	Needed staging of fibrosis	Mild steatosis without fibrosis
Subject 8	F	40	3	Needed staging of fibrosis	Benign liver parenchyma without fibrosis
Subject 9	F	59	3	Needed staging of fibrosis	Mild steatosis, Stage 1 fibrosis
Subject 10	F	53	3	Needed staging of fibrosis	Mild macrovesicular steatosis without fibrosis
Subject 11	F	55	3	Abnormal liver imaging	Minimal steatosis, no fibrosis
Subject 12	M	45	2	Needed staging of fibrosis	Benign liver parenchyma with mild steatosis, no fibrosis
Subject 13	F	67	2	Abnormal liver imaging	Mild steatosis without fibrosis
Subject 14	F	40	2	Abnormal liver imaging	Mild steatosis without fibrosis
Subject 15	F	57	2	Needed staging of fibrosis	Benign liver parenchyma, no fibrosis
Subject 16	F	76	3	Needed staging of fibrosis	Moderate to severe bile duct inflammation, consistent with PBC
Subject 17	F	54	3	Needed staging of fibrosis	Moderate steatosis without fibrosis
Subject 18	F	58	2	Needed staging of fibrosis	Chronic hepatitis, plasma cell infiltration, consistent with autoimmune hepatitis, without fibrosis
Subject 19	M	55	3	Needed staging of fibrosis	Mild to moderate steatohepatitis, with cirrhosis
Subject 20	F	64	3	Needed staging of fibrosis	Chronic portal and lobular inflammation, stage 2 fibrosis, suggestive of drug induced liver injury or venous outflow obstruction

ASA, American Society of Anesthesiologists; PBC, primary biliary cholangitis; PSC, primary sclerosing cholangitis.



Fig. 1. Endoscopic ultrasound-guided liver biopsy core sampling, 19 gauge fine-needle aspiration needle.

Statistical analysis

Summary statistics for the two groups were calculated for specimen adequacy, cumulative length, cumulative number of tracts, number of fragments, maximum fragment length, and whether specimen was diagnostic. The Wilcoxon signed-rank test was used for analysis of continuous data and McNemar's test was used for the analysis of categorical variables to determine the difference between 19 G and 22 G needle biopsies for EUS-LB. All statistical tests were 2-tailed at a level of significance of .05. Statistical analyses were performed using Stata software version 16 (StataCorp LLC, College Station, TX, USA).

RESULTS

A total of 20 patients were prospectively included in this study. Fifteen (75%) of the subjects were women. The mean age of patients in this study was 57.4 years. The median pre-procedural platelet and INR values were 260 (interquartile range [IQR], 80) and 1.0 (IQR, 0), respectively. The median ASA class for patients was 3.

The overall results are shared in Table 2. The mean cumulative core length was significantly longer for the 19 G core sample vs. the 22 G core sample: 2.52 cm and 1.27 cm respectively ($p < 0.0001$). The 19 G needle also resulted in a significantly higher number of complete portal tracts (5.8 vs. 1.7, $p < 0.0001$), and total number of tracts (8.8 vs. 3, $p < 0.0001$) when compared to the 22 G needle. While there was no statistical difference between the number of fragments (11.55 vs. 9.6, $p = 0.179$), the 19 G needle yielded longer, intact fragments (0.75 cm vs. 0.32 cm, $p < 0.0006$). The 19 G needle was also superior in providing an adequate and diagnostic pathologic sample. A total of 17/20 (85%) of 19 G samples met the criteria for diagnostic specimens vs. 2/20 (10%) of the 22 G samples ($p < 0.0001$). A total of 12/20 (60%) of 19 G samples were adequate pathologic specimens vs. 1/20 (5%) of the 22 G samples ($p < 0.001$). There were no adverse events in either group.

DISCUSSION

Liver biopsies are the gold standard for diagnosing and staging parenchymal liver diseases, including, but not limited to, hepatitis C, autoimmune hepatitis, and nonalcoholic steatohepatitis. Traditional methods of liver biopsy, including percu-

taneous and transjugular biopsies, are effective, but not without limitations.

While percutaneous liver biopsy remains the most common alternative form of obtaining liver tissue, given the limited window of access to only the right lobe of the liver as well as a blind biopsy technique, percutaneous liver biopsy can miss and underestimate fibrosis staging.¹¹ Post procedural adverse event incidence has been quoted as high as 60% within two hours of the procedure.^{4,9,12} The limitations of percutaneous liver biopsies include pain, an uncooperative patient, inability to perform in cases of suspected hemangiomas or echinococcal cysts, and relative contraindications in those who have a higher risk of bleeding and large body habitus.⁹ Consequently, many providers choose not to perform percutaneous liver biopsy for fear of complications such as severe post-procedure pain, bile peritonitis, puncturing nearby organs, and intraperitoneal hemorrhage.¹³ Although transjugular liver biopsies can be safely performed in patients in whom percutaneous liver biopsy is contraindicated, the reported adverse event incidence range is between 1.3% and 20.2%, which includes neck hematoma and arteriovenous fistula formation.^{4,12}

EUS-LB has been shown to have fewer complications than percutaneous or transjugular liver biopsies, while procuring a comparable amount of tissue acquisition.¹⁴ In one comparative study, percutaneous and transjugular biopsies resulted in complications of pneumothorax, significant bleeding with hepatic artery pseudoaneurysm, and multiple cases of excruciating abdominal pain while EUS-LB had no adverse events. Diagnostic yields of percutaneous and transjugular liver biopsies are between 85%–99% and 80%–97% respectively.¹³ EUS-LB also has a similar yield of >90% with at least two needle passes.^{5,13,15,16} Additional benefits of EUS guided biopsy includes

Table 2. The Differences in Biopsy Characteristics between the 19 G and 22 G Needles

Characteristics of biopsy	19 G needle (n=20)	22 G needle (n=20)	p-value
Cumulative length, cm	2.52	1.27	<0.0001
Number of complete portal tracts	5.8	1.7	<0.0001
Total number of tracts	8.8	3	<0.0001
Number of fragments	11.55	9.6	0.1791
Maximum fragment length, cm	0.75	0.32	0.0006
Diagnostic specimen?			
No	3 (15%)	18 (80%)	0.0001
Yes	17 (85%)	2 (10%)	
Specimen adequacy?			
No	8 (40%)	19 (95%)	0.0010
Yes	12 (60%)	1 (5%)	
Adverse events (including early and late)	0	0	

high resolution imaging, ability to sample both lobes, visualization of vessels and bile ducts to prevent injury, staging and confirmation of malignancy, and ability to perform concurrent luminal upper gastrointestinal examination and intervention.¹

Early data on EUS-LB are encouraging enough to presume that it will be a useful technique for the management of patients with liver disease. Further studies will be required with regard to where it falls into the clinical algorithm for various tissue acquisition techniques. At present, it will be prudent for endoscopists to study the best methods for optimizing EUS-LB in terms of adequacy and safety. The primary advantage of EUS is that it may drive safer outcomes compared to other liver biopsy techniques in real-time liver parenchyma imaging during needle puncture. To further this benefit, it is necessary to reduce the number of necessary needle passes and the size of the needle gauge under direct visualization while still maintaining specimen adequacy.

Multiple studies have reported adequate EUS-LB specimens with various needle types and gauges, including 19 G and 22 G, but required a significant number of needle actuations in the liver, ranging from 9–20.^{6-9,13} One study showing very high specimen adequacy with only two total needle actuations was the single-pass, single-actuation, wet suction technique by Nieto et al.⁹ This study used a 19 G needle to obtain a specimen from the left and right lobes. Our study aimed to determine whether reducing the number of needle passes to a single actuation in the left lobe with various needle gauges, including both 19 G and 22 G, would still be adequate. From the small sample size in this study, it is clear that a 19 G needle provides more portal tracts and cumulative specimen length, which translate into higher specimen adequacy and diagnostic yield as compared to a 22 G needle. Given that we only performed one single actuation with each needle, the diagnostic yield reached 85% for 19 G, and 10% for the 22 G needle, while specimen adequacy was not optimal and only approached 60% for the 19 G needle and 10% for the 22 G needle. There were more diagnostic samples than adequate samples likely because in some cases the pathologist was able to make a diagnosis despite having fewer than 11 portal tracts in the tissue specimen. If we had performed 2 passes per needle, one into each lobe of the liver, and we assumed that the meaningful pathologic outcomes would double for each needle, then the 19 G needle would likely approach 100% adequacy and diagnostic yield while still remaining suboptimal to the 22 G needle. Thus, our conclusion is that for this specific needle design (Shark-Core FNB; Medtronic), a single-pass, single-actuation, wet suction technique, with two passes of a 19 G needle is likely the minimum number of passes and needle gauge that would result in a consistently adequate specimen. Gaining consistent

specimen adequacy with a 22 G needle would require multiple more passes/actuations. Other comparative studies have shown similar results in terms of higher diagnostic yield and specimen quality with a 19 G compared to a 22 G needle.^{11,12} That being said, other commercially available needles with different tip designs, including a tri-pronged beveled edge, may improve the quality of tissue acquisition and further reduce the number of passes required to obtain consistently adequate specimens.

The limitations of this study include the small sample size from a single center. In addition, there was likely a learning curve in the sampling technique that may have led to improved specimens as experience was gained. Despite these limitations, the difference in adequacy and yield between the two needle types was marked, and supports using a 19 G needle for this specific tissue acquisition technique. Larger prospective studies are needed to corroborate these findings and conclusions.

Conflicts of Interest

Prashant Kedia is a consultant Boston Scientific, Medtronic, and Olympus. The authors have no potential conflicts of interest.

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Author Contributions

Conceptualization: Rucha M. Shah, Prashant Kedia
 Data curation: RMS, Jason Schmidt, Elizabeth John, Sheila Rastegari, PK
 Formal analysis: RMS, EJ, SR, Priyanka Acharya, PK
 Investigation: JS, PK
 Methodology: PK
 Project administration: PK
 Resources: PA, PK
 Software: PA, PK
 Supervision: PK
 Validation: PA, PK
 Visualization: PK
 Writing-original draft: RMS, JS, EJ, SR, PK
 Writing-review&editing: RMS, JS, EJ, SR, PK

ORCID

Rucha M. Shah:	https://orcid.org/0000-0001-8538-8021
Jason Schmidt:	https://orcid.org/0000-0001-5470-7915
Elizabeth John:	https://orcid.org/0000-0002-1557-386X
Sheila Rastegari:	https://orcid.org/0000-0001-8847-9930
Priyanka Acharya:	https://orcid.org/0000-0003-3867-4492
Prashant Kedia:	https://orcid.org/0000-0001-6472-0902

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