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Surface area outcomes in EUS-guided liver biopsy: a comparative study of Franseen and Fork-tip needles

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Abstract

Background The practice of endoscopic ultrasound-guided liver biopsy (EUS-LB) is becoming more common due to its proven safety and effectiveness. For accurate diagnosis, it is vital to secure ample tissue specimens. However, gauging the volume of tissue specimens accurately poses a challenge with existing methods. Additionally, determining the most suitable fine-needle biopsy (FNB) needle requires further study. Our aim was to contrast the tissue surface areas obtained using Franseen and Fork-tip needles and to identify factors affecting tissue volume.

Methods This retrospective study analyzed liver tissue samples collected through EUS-LB using 19-gauge Franseen and Fork-tip needles from patients suffering from diffuse liver diseases, conducted in our hospital from April 2019 to April 2022. We primarily focused on measuring hepatic tissue surface area and portal tract count, alongside examining patient-related factors that could influence tissue surface area.

Results The study involved 20 cases for each type of needle. The comparison revealed no significant disparities in the total liver tissue surface area (22.0 mm^2 vs. 22.6 mm^2, $P=0.45$) or in the portal tract counts (30 vs. 20, $P=0.16$). No adverse incidents were noted in either group. Both univariate and multivariate analyses highlighted that fibrosis and metabolic dysfunction associated steatotic liver disease (MASLD) presence were significant determinants of the total hepatic tissue area ($P=0.04$, $P<0.05$; and $P=0.02$, $P=0.03$, respectively).

Conclusion The capabilities of both needles in acquiring liver tissue were comparably effective. The volume of tissue was affected by the severity of fibrosis and the occurrence of MASLD.

Keywords Endoscopic ultrasonography, Fine-needle biopsy, Liver biopsy, Diffuse liver disease, Tissue surface area

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Introduction

Endoscopic ultrasound-guided liver biopsy (EUS-LB) has emerged as a significant procedure in the diagnosis and management of chronic liver diseases. This technique offers a minimally invasive approach, providing an alternative to traditional methods like percutaneous and transvenous liver biopsies. Recent studies have highlighted the potential of EUS-LB in yielding accurate and reliable tissue samples for histopathological examination, marking it as a viable option for liver disease assessment [1–13]. Despite its growing acceptance, the EUS-LB procedure's effectiveness hinges significantly on the choice of biopsy needles, which remains a subject of ongoing research and debate.

The fine-needle biopsy (FNB) needles, specifically the Franseen-tip and Fork-tip needles, have been at the forefront of this technological advancement. The Franseen-tip needle, characterized by its unique three-tip and three-cutting face design, and the Fork-tip needle, with its six cutting faces and opposing bevel, have both shown promising results in procuring high-quality tissue specimens [14–16]. These needles have been engineered to maximize tissue acquisition, aiming to surpass the performance of conventional fine-needle aspiration (FNA) needles. However, while existing literature sheds light on the comparative efficiency of these needles in tissue retrieval, a consensus on the superior needle type for EUS-LB remains elusive.

A notable limitation in the current evaluation methods of liver tissue yield is the reliance on total specimen length (TSL). While TSL provides a straightforward metric, it does not fully capture the quality and volume of the tissue obtained, especially given the thinner and more fragmented nature of EUS-LB specimens compared to those from percutaneous liver biopsy (PLB). To address this gap, our study utilizes whole-slide imaging (WSI) for tissue assessment. While WSI has been widely used in previous research for evaluating various biopsy parameters, we applied this established technology to quantify tissue surface area in EUS-LB specimens. This standardized approach allows for precise measurement of tissue yield while accounting for the unique characteristics of EUS-LB specimens, including their increased tendency toward fragmentation compared to percutaneous biopsies.

In this study, we aim to address this area of uncertainty by comparing the tissue yield and safety of Franseen and Fork-tip needles in the evaluation of diffuse liver diseases. We employ WSI to accurately measure the tissue surface area, seeking to provide a clearer understanding of which needle type optimally supports the diagnostic process in EUS-LB.

Materials and methods

Patients

In this retrospective study, we assessed patients who underwent endoscopic ultrasound-guided liver biopsy (EUS-LB) at Teikyo University School of Medicine University Hospital, Mizonokuchi, during two consecutive periods: from April 2019 to December 2020 when the Franseen-tip needle was used, and from January 2021 to April 2022 when the Fork-tip needle was used. The study aimed to compare tissue acquisition outcomes between these two needle types.

Data were meticulously gathered from electronic medical records and the endoscope support system, securely stored in an encrypted database. As this was a retrospective exploratory study, no a priori sample size calculation was performed. Instead, the study aimed to provide preliminary data and effect size estimates for future prospective research. Participants were adults (18 years or older) who required liver biopsy for reasons like abnormal liver function tests, concerning imaging results, or fibrosis assessment. We excluded individuals below 18, those with thrombocytopenia (platelets < 50,000/μL), coagulopathy (INR > 1.5), pregnancy, liver mass lesions, biliary diseases, or inability to consent. Patients were under close observation for 1–2 h post-procedure to record any procedure-related events.

Techniques

Patients receiving EUS-LB were sedated with midazolam and pentazocine. All procedures were performed or supervised by experienced endoscopists (> 500 EUS procedures), with trainees (50–200 EUS procedures) participating under direct supervision. To maintain consistency, the supervising endoscopist guided critical aspects including needle selection, target site identification, and aspiration technique. The procedure used a linear-array echoendoscope (GF-UCT260; Olympus Medical Systems, Japan) and involved two needle types: the 19-gauge Franseen needle (Acquire™, Boston Scientific, United States) and the 19-gauge Fork-tip needle (SharkCore™, Covidien-Medtronic Inc., United States). The Franseen needle was used from April 2019 to December 2020, after which the Fork-tip needle was adopted until April 2022.

The EUS-LB targeted the left liver lobe, approached from the stomach, using 2–3 passes per procedure. Color Doppler imaging ensured a clear needle path, and the needle advanced 3–4 cm into the liver. The procedure involved multiple back-and-forth movements of the needle, under endosonographic guidance, to collect tissue (Fig. 1). A suction technique with a 20 mL vacuum syringe was the primary method for specimen retrieval. The slow-pull technique [17, 18] was utilized for the third biopsy in situations when there was inadequate tissue yield or significant blood contamination in the

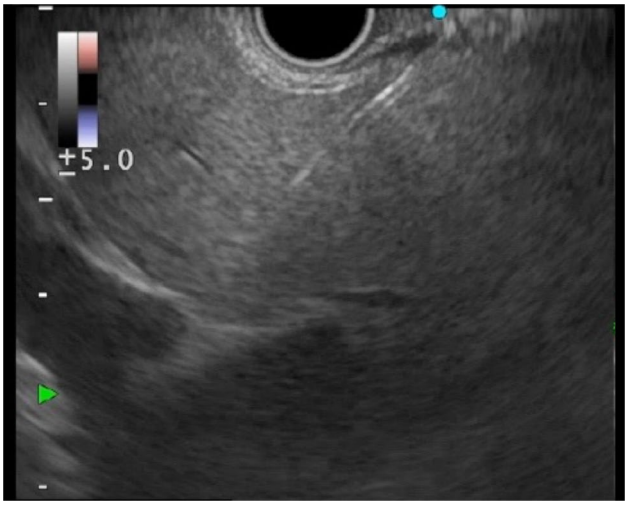

Fig. 1 Endoscopic ultrasound image showing fine-needle biopsy (FNB) of the left lobe of the liver. The image demonstrates the path of a 19-gauge FNB needle (Franseen-tip or Fork-tip) entering the liver parenchyma under ultrasound guidance

samples following two prior biopsies. Tissue adequacy was assessed using a macroscopic visual inspection approach, conceptually similar to macroscopic on-site evaluation (MOSE) [19], but specifically adapted for liver biopsy using fine-needle biopsy (FNB) devices. 'Inadequate tissue yield' was defined as specimens meeting any of the following criteria based on macroscopic evaluation: (1) insufficient visible tissue size cores, (2) excessive blood contamination obscuring tissue visualization, or (3) inability to clearly identify liver parenchyma. Although our approach shares conceptual similarities with MOSE, we deliberately did not apply a fixed threshold such as MVC ≥ 4 mm, as used in pancreatic FNA, because the tissue characteristics in liver biopsy and the performance of FNB needles differ substantially. During macroscopic evaluation, tissue color, size, and structural characteristics were used as indicators to determine whether adequate liver tissue had been obtained for pathological evaluation. When specimens were deemed inadequate based on these criteria, an additional pass using the slow-pull technique was performed. The specimens were transferred from the needle onto a slide using a stylet. Specimens from each pass were processed separately in individual formalin containers. Each specimen underwent a visual examination to verify the presence of sufficient tissue. For statistical analysis, these separately processed specimens were later aggregated to evaluate overall and per-pass outcomes.

Sample processing and quantification analysis

Specimens were immediately fixed in 10% formalin and processed by the Clinical Pathology Department following standard protocols. The liver biopsy (LB) samples were embedded in paraffin, sectioned at 4 μm, and stained with hematoxylin and eosin, trichrome, reticulin, and other necessary dyes. Digital imaging of the slides was done using a whole-slide scanner (Aperio CS2, Leica Biosystems), with Aperio ImageScope software for display and measurement (Fig. 2). For each patient, tissue samples from individual passes were processed and measured separately. The maximum tissue area per pass was defined as the largest surface area obtained from any single pass during the biopsy session, representing the optimal tissue acquisition capability of each needle type. This metric was chosen to evaluate the needles' ability to obtain adequate tissue in a single pass, which has clinical relevance for minimizing the number of passes required. The liver tissue surface area was defined as the portion of the biopsy specimen identifiable as liver parenchyma under microscopic observation. For accurate assessment, blood clots and adipose tissue were excluded from the measurement, whether present within or surrounding the tissue core. Measurements were performed manually by a hepatology specialist using digital slide images at low magnification, with careful attention to exclude non-parenchymal components. The area measurement tool in the Aperio ImageScope software was used to trace the boundaries of viable liver tissue, providing quantitative surface area measurements in square millimeters. Two pathologists independently validated the histological evaluation and quantification of portal tracts (PTs). The interobserver agreement was assessed using Cohen's kappa coefficient for categorical variables (inflammation grade, fibrosis stage) and intraclass correlation coefficient for continuous variables (portal tract counts). In cases of disagreement (defined as > 15% difference in portal tract counts or any difference in staging/grading), the two pathologists reviewed the slides together to reach a consensus. For cases where consensus could not be reached, a third pathologist was consulted for final determination. The interobserver agreement was excellent ($\kappa = 0.82$ for histological diagnosis, $\kappa = 0.78$ for fibrosis staging, and ICC = 0.85 for portal tract counts). Final diagnoses were established through a comprehensive evaluation combining histopathological findings, clinical laboratory data, and physical examination findings. For liver biopsy specimens, adequacy was assessed based on established criteria from the American Association for the Study of Liver Diseases (AASLD), which recommends at least 6–11 portal tracts for reliable pathological evaluation [20]. While complete portal tracts (containing bile duct, portal vein, and hepatic artery) are traditionally used as the standard metric in liver biopsy assessment, we defined PTs as structures containing at least two portal components. This modified definition was adopted because in some cases, particularly those with severe inflammation, bile duct degeneration or loss was observed as part of the

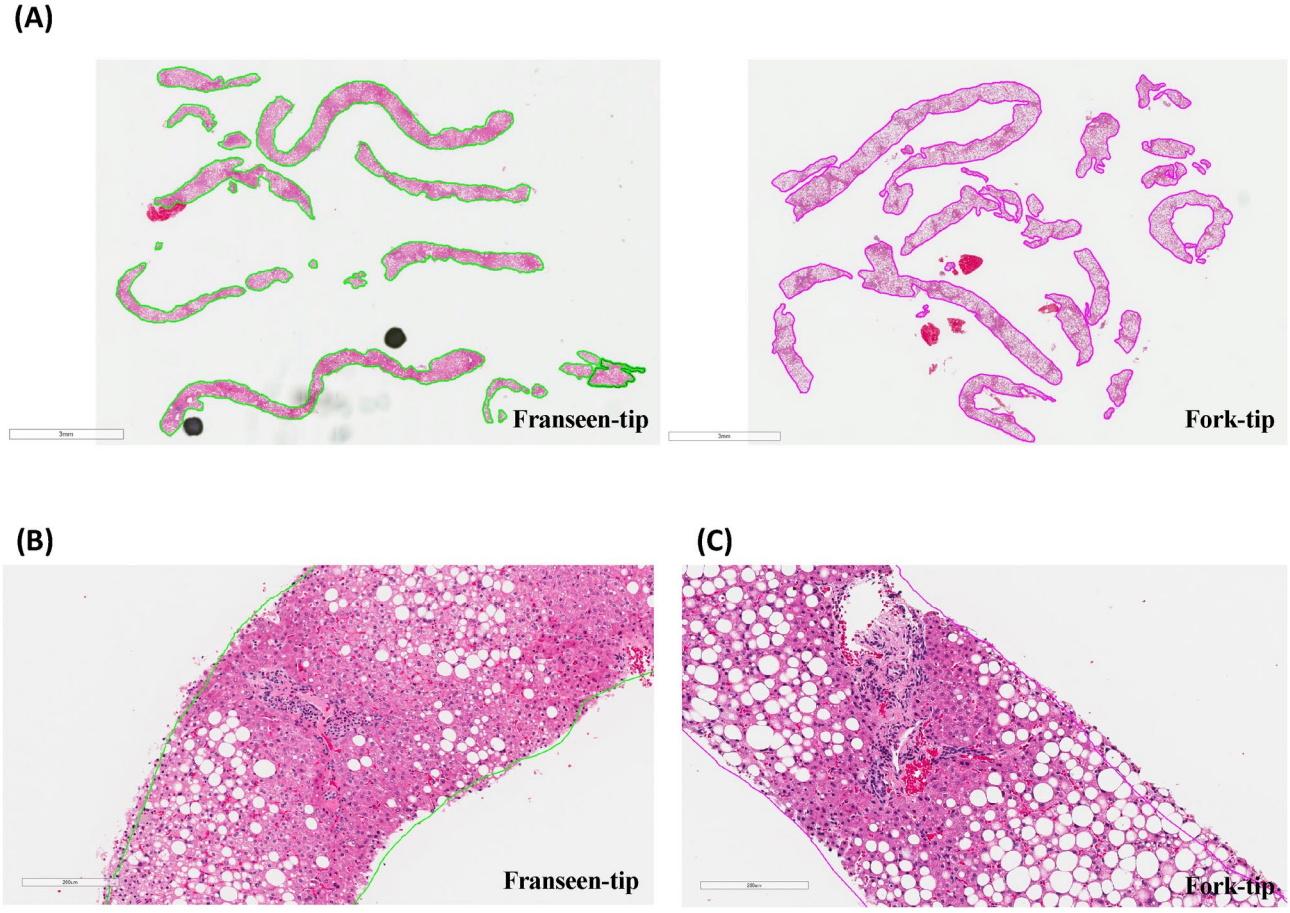

Fig. 2 Representative endoscopic ultrasound-guided liver biopsy samples obtained by Franseen-tip or Fork-tip. **A**. Whole slide imaging of liver biopsy specimens scanned at ×20 and measurement of tissue surface area (native resolution). **B**. Franseen-tip needle specimen showing liver parenchymal inflammation and steatosis (digitally magnified to ×15). **C**. Fork-tip needle specimen showing liver parenchymal inflammation and steatosis (digitally magnified to ×15)

disease process. We acknowledge that this definition differs from the complete portal tract standard used in previous studies.

Outcomes

The primary outcomes measured were the surface area of hepatic tissue and the number of PTs obtained from each needle type. Secondary outcomes focused on patient-related factors that could influence liver tissue surface area.

Statistical analysis

Descriptive statistics summarized the data, with frequencies and percentages for categorical variables and medians and interquartile ranges (IQR) for continuous variables. All statistical analyses were performed using JMP® Pro 17.0.0 (SAS Institute Inc., Cary, NC, USA). Fisher's exact test and the Student's t-test analyzed categorical and continuous data, respectively. To ensure robustness of our findings, we additionally verified our results using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) [21]. Both univariate and multivariate logistic regression analyses identified factors influencing hepatic tissue surface area. A P-value of less than 0.05 was indicative of statistical significance.

Results

In our study, we reviewed data from 40 patients who underwent endoscopic ultrasound-guided liver biopsy (EUS-LB) during two consecutive periods at our institution. During the first period (April 2019 to December 2020), the Franseen-tip needle was used (20 patients), while during the second period (January 2021 to April 2022), the Fork-tip needle was used (20 patients), reflecting a change in our institutional practice. Despite this sequential assignment, no significant differences in patient demographics or characteristics were observed between the two groups, allowing for a fair comparison (Table 1).

Table 1 Baseline characteristics and demographics of patients in the present study

Variables	Franseen-Tip($n=20$)	Fork-Tip($n=20$)	*P* value
Demographics			
Age, y, median (IQR)	57.5 (43.8–75.0)	69.0 (52.3–74.0)	0.27
Sex, male: female	7:13	10:10	0.52
Body mass index, median (IQR)	24.5 (19.9–28.3)	22.9 (21.0-26.5)	0.81
Indication for liver biopsy, n (%)			0.81
Investigation of acute liver disorder	1/20(5%)	2/20(10%)	
Suspected autoimmune liver disease	13/20(65%)	13/20(65%)	
Evaluation of suspected MASLD	6/20(30%)	5/20(25%)	
Coagulation			
Platelet counts (×10,000/μL), median (IQR)	19.8 (12.7–24.6)	21.9 (16.1–27.3)	0.30
PT-INR, median (IQR)	1 (0.96–1.36)	1 (0.92–1.04)	0.07

MASLD; Metabolic dysfunction associated steatotic liver disease, IQR; Interquartile range, PT-INR; Prothrombin time-international normalized ratio

Histological analysis focused on the hepatic tissue surface area and portal tract counts. The Franseen-tip group had a total hepatic tissue surface area with median 22.0 mm² (IQR: 14.7–32.9 mm²), while the Fork-tip group had a median of 22.6 mm² (IQR: 11.3–26.5 mm²). The maximum tissue sample obtained per pass was 14.8 mm² (IQR: 9.2–19.9 mm²) for the Franseen-tip and 11.1 mm² (IQR: 7.28–14.8 mm²) for the Fork-tip, representing each needle's optimal tissue acquisition capability in a single pass. The total portal tract (PT) counts were 30 (IQR: 19–32) for the Franseen-tip and 20 (IQR: 15–25) for the Fork-tip group, with the maximum number of PTs per pass being 16 (IQR: 14–23) for the Franseen-tip and 13 (IQR: 10–17) for the Fork-tip group. No significant differences were found in the total and maximum tissue surface areas ($P=0.45$, $P=0.23$) or in the PT counts ($P=0.16$, $P=0.15$) between the two groups (Fig. 3). While there was an apparent difference in the proportion of acute hepatitis cases between groups (0% vs. 25%), this difference did not reach statistical significance ($P=0.15$). Importantly, the diagnosis of acute hepatitis was based not only on histological findings but also on clinical

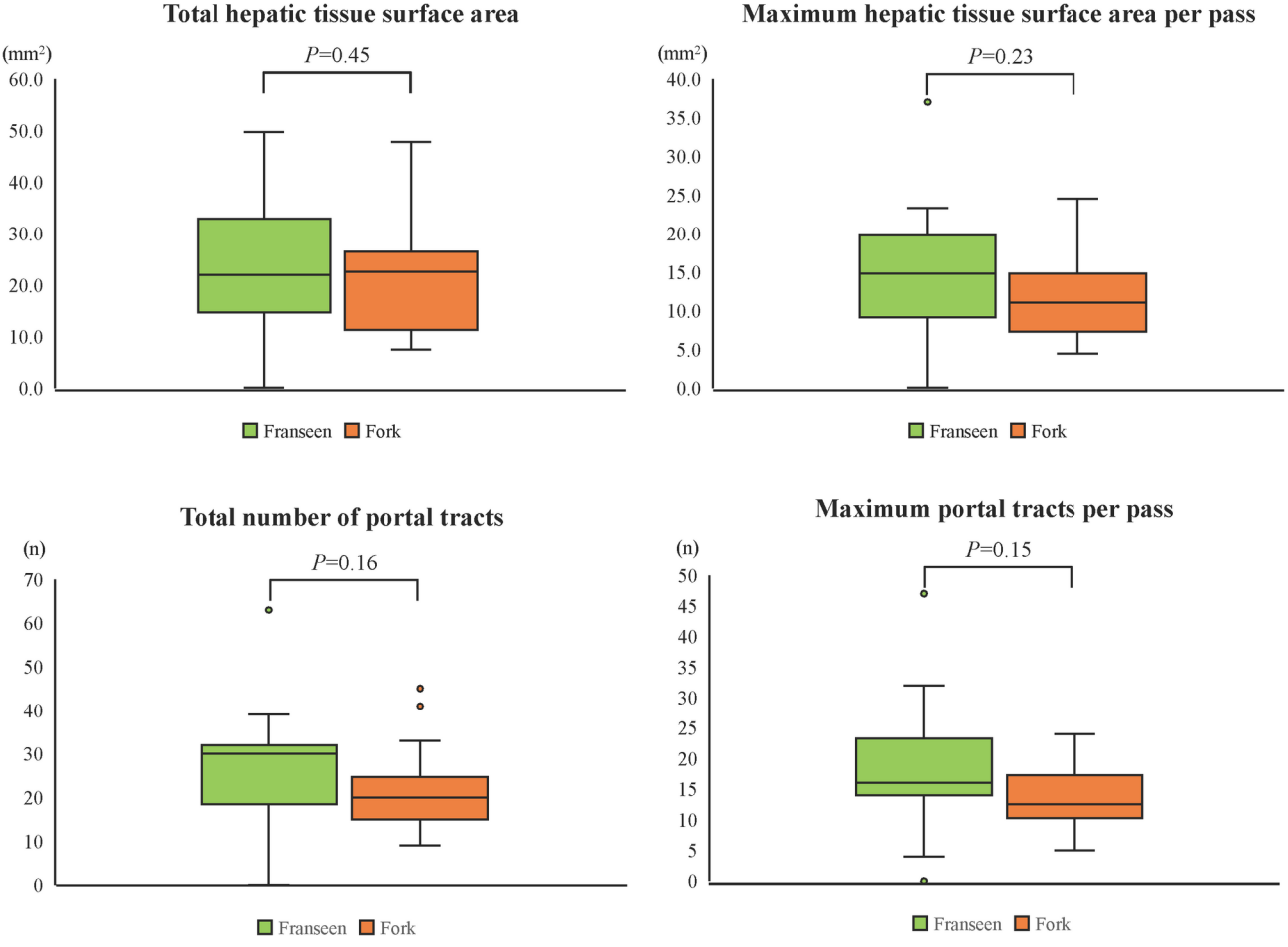

Fig. 3 Comparison of the hepatic tissue surface area and the number of portal tracts from Franseen-tip needle and Fork-tip needle

Table 2 Diagnoses obtained from Franseen-Tip and Fork-Tip

	Franseen-Tip($n=20$)	Fork-Tip($n=20$)	*P* value
Liver Histological findings, n (%)			0.15
MASH/MASLD	6(30%)	5(25%)	
Chronic hepatitis	9(45%)	9(45%)	
Acute hepatitis	0(0%)	5(25%)	
Non specific inflammatory change	3(15%)	1(5%)	
Others	1(5%)	0(0%)	
Inadequate specimen	1(5%)	0(0%)	

IQR; Interquartile range, MASH; Metabolic dysfunction associated steatohepatitis, MASLD; Metabolic dysfunction associated steatotic liver disease

Table 3 Liver biopsy properties between Franseen-Tip group (n=20) and Fork-Tip group (n=20)

Variables	Franseen-Tip($n=20$)	Fork-Tip($n=20$)	*P* value
Liver biopsy properties			
Total hepatic tissue area (mm2), median (IQR)	22.0 (14.7–32.9)	22.6 (11.3–26.5)	0.45
Maximum hepatic tissue area per pass (mm2), median (IQR)	14.8 (9.2–19.9)	11.1 (7.28–14.8)	0.23
Total number of portal tracts, n, median (IQR)	30 (19–32)	20 (15–25)	0.16
Maximum portal tracts per pass, n, median (IQR)	16 (14–23)	13 (10–17)	0.15
The number of fragmentations, n, median (IQR)	34 (14–45)	38 (31–56)	0.11
Inflammation grading(A0/A1/A2/A3), n	1/12/5/2	1/8/8/3	0.64
Fibrosis staging(F0/F1/F2/F3/F4), n	7/9/1/2/1	8/6/4/2/0	0.48
Histological diagnosis established, n (%)	19(95%)	20(100%)	1
Pass times, n, median (IQR)	2 (2–3)	2 (2–3)	0.50
Adverse event, n (%)	0(0%)	0(0%)	1

IQR; Interquartile range

presentation, timing of liver injury onset, and laboratory data.

While one patient in the Franseen-tip group did not yield sufficient tissue for histopathological analysis, the other 19 patients provided samples adequate for definitive diagnosis (Table 2). In the Fork-tip group, all patients offered specimens viable for pathological evaluation, marking no significant difference in diagnostic yield between the two needle types ($P=0.15$). Additionally, the analysis showed no significant variance in the number of tissue fragments, levels of inflammatory activity, fibrosis staging, or the number of passes needed to collect the biopsy samples in either group. No adverse events related to the procedures were reported for both groups (Table 3).

For patients with diffuse liver diseases, univariate and multivariate analyses were conducted to ascertain the factors influencing hepatic tissue surface area. Both analyses identified fibrosis staging and the presence of metabolic dysfunction associated steatotic liver disease (MASLD) as significant determinants of the total hepatic tissue area. Specifically, advanced fibrosis ($F\geq 2$) was associated with reduced tissue yield (OR 0.17, 95% CI 0.03–0.92, $P=0.04$ in univariate analysis; OR 0.15, 95% CI 0.02-1.00, $P<0.05$ in multivariate analysis), while the presence of MASLD was associated with increased tissue yield (OR 7.36, 95% CI 1.34–40.5, $P=0.02$ in univariate analysis; OR 8.24, 95% CI 1.27–53.3, $P=0.03$ in multivariate analysis). The median total hepatic tissue area was significantly lower in patients with $F\geq 2$ fibrosis (15.8 mm^2) compared to those with F0-1 fibrosis (24.3 mm^2), and higher in MASLD patients (28.4 mm^2) compared to non-MASLD patients (19.2 mm^2). Factors such as age, gender, body mass index (BMI), platelet count, prothrombin time-international normalized ratio (PT-INR), the device used, fibrosis staging, and the number of biopsy passes were not found to significantly influence the total hepatic tissue area. However, when considering the maximum hepatic tissue area per pass, univariate analysis showed that platelet count ($P=0.01$), portal inflammation grading ($P=0.01$), fibrosis staging ($P=0.04$), and the presence of MASLD ($P=0.02$) were significant. Multivariate analysis further refined these results, identifying platelet count ($P=0.04$) as the sole significant predictor (Table 4).

Discussion

Recent advancements in puncture needles for endoscopic ultrasound-guided biopsy have led to the development of FNB needles, which are superior to conventional FNA needles in terms of tissue sampling capacity. The commonly used FNB needles include EchoTip ProCore™ (Cook Medical, United States), Acquire™ (Boston Scientific, United States), and SharkCore™ (Covidien-Medtronic Inc, United States). The EchoTip ProCore™ features a reverse-bevel design, the Acquire™ needle is characterized by a Franseen-tip, and the SharkCore™ is designed with a Fork-tip. The optimal needle design for sampling is still under debate. However, a meta-analysis comparing the diagnostic performance of end-cutting fine-needle biopsy needles in EUS-guided sampling of solid pancreatic masses reported that both Franseen-tip and Fork-tip needles significantly outperformed reverse-bevel and FNA needles regarding diagnostic accuracy and sample adequacy [22].

In the context of EUS-LB, studies comparing FNA and FNB needles have demonstrated the superior tissue yield of FNB needles [14, 15], thereby highlighting the utility of FNB needles in liver disease diagnostics. Among the FNB needles, the Franseen-tip and Fork-tip needles are predominantly used in EUS-LB. Nieto et al. [23] and Aggarwal et al. [24] reported a significantly higher specimen length in the Franseen-tip group in their retrospective and prospective studies, respectively. Conversely,

Table 4 Factors affecting the hepatic tissue surface area of EUS-LB for diffuse liver diseases

Variables	Total hepatic tissue area				Maximum hepatic tissue area per pass			
	Univariate		Multivariate		Univariate		Multivariate	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value
Age(≧65)	0.55 (0.16–1.91)	0.34			0.82 (0.24–2.84)	0.75		
Sex(men)	2.85 (0.78–10.5)	0.11			2.85 (0.78–10.5)	0.11		
Body mass index(≧24)	3.45 (0.94–12.6)	0.06			3.45 (0.94–12.6)	0.06		
Plt (≧20 × 10,000)	3.50 (0.94-13.0)	0.06			5.57 (1.42–21.9)	0.01	5.96 (1.09–32.6)	0.04
PT-INR (≧1.00)	0.44 (0.12–1.57)	0.21			0.29 (0.08–1.06)	0.06		
Device (Fork-Tip)	1.00 (0.29–3.45)	1			0.44 (0.13–1.57)	0.21		
Grading(A≧2)	0.29 (0.08–1.06)	0.06			0.18 (0.05–0.70)	0.01	0.29 (0.05–1.68)	0.17
Staging(F≧2)	0.17 (0.03–0.92)	0.04	0.15 (0.02-1.00)	< 0.05	0.17 (0.03–0.92)	0.04	0.36 (0.04–3.50)	0.38
MASLD	7.36 (1.34–40.5)	0.02	8.24 (1.27–53.3)	0.03	7.36 (1.34–40.5)	0.02	6.29 (0.80–49.6)	0.08
Pass times (≧3)	1.62 (0.41–6.34)	0.49			-	-	-	-

Hashimoto et al. [25] found no significant differences in post-fix aggregate specimen length and post-fix longest specimen length between the two FNB needles in a repeated-measure crossover study with a prospectively maintained cohort of patients.

These discrepancies may be attributed to differences in tissue yield assessment, suction technique, and clinical context. First, Nieto et al. [23] used total and intact specimen length, which can overestimate viable tissue in fragmented samples. Our use of whole-slide imaging allowed direct measurement of hepatic parenchymal surface area, providing a more accurate reflection of diagnostic adequacy. Second, procedural differences—such as the use of wet suction (Nieto et al. [23]) versus dry suction and slow-pull (our study)—may have influenced tissue fragmentation and yield. Third, patient populations differed. While Nieto et al. [23] included patients undergoing EUS for pancreaticobiliary indications, our study focused on diffuse liver disease, where the liver biopsy was the primary target. Underlying hepatic conditions, including MASLD or fibrosis, may affect sampling characteristics. These methodological and clinical differences should be considered when interpreting comparative findings on needle performance in EUS-LB.

Our study is a single-center retrospective comparison of the Franseen-tip and Fork-tip needles, focusing on their efficacy and safety. A notable distinction from existing reports is our method of liver tissue yield assessment using tissue surface area rather than total specimen length (TSL) or length of longest piece (LLP). While surface area naturally correlates with specimen length, this approach offers several advantages: First, surface area measurement provides comprehensive quantification by considering both length and width of the tissue, more accurately reflecting the actual tissue volume available for histopathological analysis. Second, given that EUS-LB specimens tend to fragment more than percutaneous biopsy samples, surface area measurement helps minimize fragmentation bias by including all viable tissue fragments in the assessment. This is particularly important as length-based measurements become less reliable with increased fragmentation. The rationale behind this is the thinner nature of specimens obtained by EUS-LB compared to percutaneous liver biopsy (PLB), making length-based evaluation less reliable, especially considering the tendency of EUS-LB specimens to fragment. We previously reported that liver tissues obtained by both PLB and EUS-LB techniques with different gauge numbers, when evaluated in terms of surface area, yielded comparable tissue volume [10]. Therefore, we propose that surface area evaluation, facilitated by whole-slide imaging, represents a more accurate method for assessing EUS-LB tissue yield than TSL.

In this study, we performed univariate and multivariate analyses to explore the factors influencing liver tissue yield. Both analyses identified staging of F2 or greater and the presence of MASLD as significant factors impacting the total tissue surface area. Additionally, platelet counts emerged as a significant factor in determining the surface area of the most tissues sampled per pass in multivariate analysis. These findings demonstrate a clear relationship between pathological characteristics and tissue yield. Specifically, patients with advanced fibrosis (F ≥ 2) showed an 83% reduction in the odds of obtaining larger tissue samples (OR 0.17, $P = 0.04$), while MASLD patients had over 7-fold higher odds of yielding larger specimens (OR 7.36, $P = 0.02$). The reduced tissue yield in livers with advanced fibrosis (median 15.8 mm^2 vs. 24.3 mm^2 in F0-1) could be attributed to increased puncture resistance due to the needle's need to cut through dense collagen fibers, which hampers the needle's ability to encapsulate sufficient liver tissue. Conversely, the enhanced tissue yield in MASLD patients (median 28.4 mm^2 vs. 19.2 mm^2 in non-MASLD) suggests that steatotic changes might facilitate tissue acquisition, possibly due to altered liver tissue consistency.

Interestingly, our results indicate that EUS-FNB may procure more tissue in MASLD patients compared to

patients with other liver diseases. However, a bivariate analysis examining the relationship between fibrosis and MASLD, specifically assessing fibrosis staging and platelet count, did not reveal a statistically significant difference, indicating that MASLD cases did not exhibit significantly less fibrosis. This finding contrasts with Nieto et al. [23], who showed longer TSL associated with advanced fibrosis (F3-4) in both FNB needles. These disparate findings underscore the need for a standardized method of assessment, with our study suggesting that surface area evaluation through whole-slide imaging may provide a more accurate measure than TSL.

No studies to date have assessed liver tissue yield across different background liver diseases. In our cohort, most biopsy specimens met the histological adequacy criteria established by AASLD, enabling reliable pathological evaluation. While three patients in the Franseen-tip group were diagnosed with non-specific inflammatory changes, it's important to note that this diagnosis was reached after careful exclusion of other liver diseases and comprehensive evaluation of all available clinical data. While larger tissue samples might potentially provide additional diagnostic information in some cases, factors such as sampling location and disease heterogeneity also play important roles in diagnostic accuracy. The diagnosis of non-specific inflammatory changes in these cases reflects the complex nature of some liver pathologies rather than necessarily indicating inadequate sampling. The higher tissue yield observed in MASLD patients could be due to (1) the inherently easier collection of specimens from fatty livers, or (2) a relative increase in tissue yield in MASLD cases due to a higher prevalence of advanced fibrosis in other liver diseases. Moreover, this study noted a higher frequency of autoimmune liver diseases and cases with suspected diagnoses in pathological evaluation. Here, 'suspected diagnoses' refers to cases where histological findings suggested a specific liver disease but required correlation with clinical, serological, and imaging findings for definitive diagnosis. This diagnostic approach is particularly relevant in autoimmune liver diseases, where fibrosis tends to manifest after prolonged chronic active hepatitis, potentially leading to advanced fibrosis by the time of diagnosis. The need for comprehensive evaluation incorporating multiple diagnostic modalities highlights the complementary role of histological findings in establishing definitive diagnoses. Although not assessed in this study, disease duration may influence liver stiffness and consequently affect biopsy results, suggesting it as a factor worth considering in future studies.

Our study is not without limitations. The observed difference in the proportion of acute hepatitis cases between groups reflects the nature of our retrospective study design rather than any systematic selection bias. This variation did not significantly impact our primary endpoints of tissue acquisition and adequacy, as confirmed by our statistical analyses. The diagnosis of acute hepatitis, while partly based on histological findings, primarily relies on the comprehensive evaluation of clinical presentation, laboratory data, and disease course, making the histological findings one component of the overall diagnostic process. Being a single-center study with a relatively small sample size and retrospective in nature, it does not specify the disease of interest. Additionally, procedures were performed by both experienced endoscopists and trainees under supervision, which could have introduced variability in tissue acquisition. However, we attempted to minimize this potential bias through standardized procedures and direct supervision of all trainee-performed procedures by experienced endoscopists. The observed differences in demographic characteristics between groups, while not statistically significant, reflect the limitations of our retrospective design and small sample size. We verified our statistical findings using two different statistical software packages (JMP Pro and EZR) to ensure the robustness of our conclusions. Furthermore, as an exploratory study, no a priori power analysis was performed, which limits our ability to draw definitive conclusions about the comparative efficacy of the two needle types. The observed differences and effect sizes from our study, however, provide valuable information for sample size calculation in future prospective trials comparing these needle types. Additionally, our modified definition of portal tracts, which required only two portal components rather than the standard complete portal tract metric used in most studies, may limit direct comparability with existing literature. While this approach was adopted to account for cases with bile duct injury, future studies may benefit from reporting both complete and modified portal tract counts to facilitate better comparison across different research approaches. Furthermore, the study lacks a comparison with normal liver tissue, providing limited evidence to support the hypothesis that livers with less fibrosis yield more tissue. Additional studies focusing on specific diseases are warranted. The amount of tissue sampled in EUS-LB may vary with the operator's skill level; in our study, both a trainer and a trainee performed each procedure. Despite the retrospective nature of our study possibly limiting the capture of all adverse events, particularly minor symptoms such as post-procedural pain, we believe that no serious adverse events were missed, as all patients were followed up 1–2 weeks after discharge for test result collection. While major complications would have been documented in medical records, mild post-procedural symptoms may not have been systematically recorded due to the retrospective design of our study.

Conclusion

In conclusion, the findings of this study indicate no significant differences in the surface area of liver tissue and the number of portal vein areas obtained using two distinct puncture needles in a cohort predominantly composed of suspected autoimmune liver disease cases. Both needle types successfully provided sufficient liver tissue for histopathological analysis. While previous studies [23, 24] have suggested superior tissue yield with the Franseen-tip needle, the current data do not conclusively establish the superiority of either needle. Consequently, a multicenter randomized controlled trial is warranted to definitively ascertain the superior needle type for tissue yield. Additionally, technical advancements and standardization of the EUS-LB procedure are highly desirable. It is hoped that the outcomes of this study will contribute to the refinement and standardization of the EUS-LB technique, enhancing its efficacy and reliability in clinical practice.

Abbreviations

BMI	Body mass index
EUS-LB	Endoscopic ultrasound-guided liver biopsy
FNB	Fine-needle biopsy
FNA	Fine-needle aspiration
MASLD	Metabolic dysfunction associated steatotic liver disease
PLB	Percutaneous liver biopsy
PT	Portal tract
PT-INR	Prothrombin time-international normalized ratio
TSL	Total specimen length
WSI	Whole-slide imaging

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Author contributions

Study design, data analysis, and manuscript preparation: KM and SD; endoscopic procedures: KM, SD, TA, AW, NK, TT; pathological examination: KM, TA, MT; data collection: KM; manuscript supervisors: SD, KK. All authors have read and approved the submitted version of the paper.

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Data availability

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author on reasonable request.

Declarations

Ethical approval and consent to participate

The study design was reviewed and approved by the Teikyo University Ethical Review Board for Medical and Health Research involving Human Subjects (#21–158, approval dated 11/18/2021) and was conducted in accordance with the ethical principles related to the Declaration of Helsinki. Because of the retrospective nature of the study, the Teikyo University Ethical Review Board waived the need for written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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