Role of EUS-guided liver biopsy in benign parenchymal disease (with video)

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INTRODUCTION

Etiology of liver disease is often established on serology, metabolic profile, or less commonly genetic testing in conjunction with sound structural imaging. Staging of liver disease, however, is more complex and noninvasive methods such as transient elastography, shear wave elastography, or specialized magnetic resonance imaging can be helpful in this regard. However, the ultimate gold standard is a liver biopsy (LB) for both diagnosis (especially in seronegative disease) and staging of both acute and chronic liver disease. This can be performed via the percutaneous, transjugular, or surgical approach. EUS-guided LB (EUS-LB) is a promising new technique with some advantages over the traditional methods. This chapter will cover the merits of EUS-LB including technique, needle types, safety, and diagnostic yield.

EUS TECHNIQUE

The patient is positioned in the typical left lateral position under moderate sedation. A linear echoendoscope is used to study the liver parenchyma with Doppler imaging. Avoidance of ductal structures

is of paramount importance, and a 19G needle is used to procure liver cores via a transgastric and/or transduodenal approach to target the left or right lobe of liver [Figure 1a]. The optimal technique is yet to be established hence techniques vary among expert centers. This could range from a single pass to multiple passes, a variable number of to-and-fro needle movements and degree of suction is at the discretion of the proceduralist. Tissue acquisition technique has been evaluated recently in cadaveric tissue[1] found no difference between the degree of suction ranging from slow pull (capillary pressure) to 30 ml syringe suction. In general, however, higher suction (20 ml) with larger needles tend to generate greater negative pressures at the needle tip.[2] Priming the needle with a column of fluid may increase the volume of tissue acquisition[3] as demonstrated in a three-dimensional computational fluid dynamic model. Finally, cessation of Doppler signals [Figure 1b] within the needle tracts should be observed before needle withdrawal from the Glisson's capsule to theoretically reduce the risk of subcapsular hematoma. Our current technique includes high suction (20 ml) with a 19G needle primed with heparin-saline to decrease clotting of blood within the needle lumen.

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NEEDLE TYPES

Four-needle types have been used for EUS-LB in the clinical setting. The tru-cut biopsy (TCB) needle [Figure 2a] was first used for EUS-LB in 2007[4] on two patients demonstrating feasibility. Two further studies were then conducted by Gleeson and Levy[5] and Dewitt et al.[6] yielding somewhat suboptimal specimens but without adverse events. Subsequently, three studies used the straight standard needles [SSN, Figure 2b][7-9] with better results [Table 1]. A study utilizing the core histology needle [CHN, Figure 2c] with a built-in reverse bevel followed and a comparison between TCB and CHN revealed the CHN to be superior to the TCB needle.[11] The only study to involve SSN and CHN[12] showed the SSN procured almost double the number of CPT compared to the CHN (19.4 vs. 9.8). Most recently, a new shark core needle [SC, Figure 2d] had been shown

Figure 1. (a) FNA into the left lobe of liver, care is taken to avoid all ductal structures. (b) Doppler signal within the needle tract therefore the needle is yet to be withdrawn from the liver parenchyma
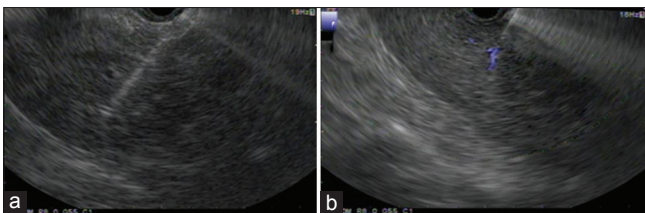
in a cadaveric study[13] to be superior to all preceding needle types; even better than the 18G percutaneous LB needles.[1] Clinical studies were subsequently carried out on 165 patients with excellent yield [Table 1]; although, this was not a comparative study.[10]
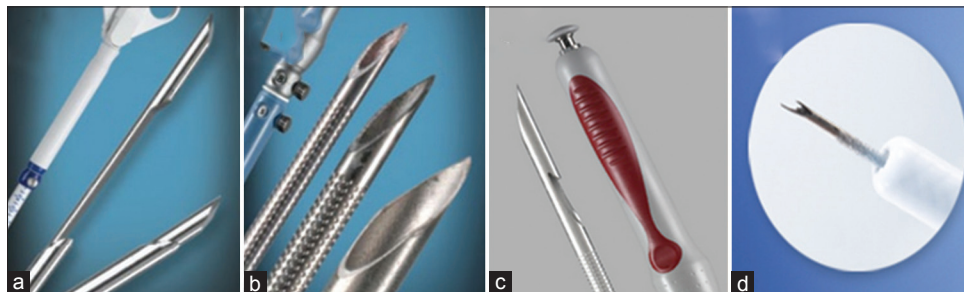
SPECIMEN HANDLING

Following withdrawn of the FNA needle from the linear echoendoscope, the liver cores are expressed from the FNA needle. This is the best accomplished by gentle, steady flushing of saline from the needle handle. If, however, the specimen does not deliver with saline flush, the stylet can be used to advance the specimen, followed again by saline flush. At this point, it is ideal to separate the liver cores from the blood clots carefully as these cores are extremely fragile. Blood should be removed as this is likely to hinder histological preparation and assessment. The cores can either be placed directly into a formalin bottle or placed on filter paper then enclosed by a cassette and submitted in formalin [Video 1].

TECHNICAL ADVANTAGE AND SUCCESS RATE

The key advantage of EUS-LB is in obese patients with liver disease (e.g., suspected nonalcoholic

Figure 2. (a) True-cut biopsy needle. (b) Standard straight needle. (c) Core histology needle with reverse bevel. (d) Shark core

Table 1. Summary of results in the literature

Study	Needle	No	CPT (mean)	Length (mm)	Passes (median)	Serious AE	Suspected cirrhosis, %
Gleeson and Levy[5]	19G TCB	9	7	12	2	0	22
DeWitt et al.[6]	19G TCB	21	2	9	3	0	19
Stavropoulos et al.[7]	19G SSN	22	9	36.9	2	0	23
Gor et al.[8]	19G SSN	10	9.2	14.4	3	0	20
Diehl et al.[9]	19G SSN	110	14	38	2-3	1	5
Nieto et al.[10]	19G SC	165	18**	60**	1	1	15.8
Sey et al.[11]	19G TCB	45	3	N/A	2	0	5
Nakanishi et al.[12]	19G CHN	33*	9.8	N/A	3	0	
	19G SSN	35	19.4	N/A	N/A	N/A	N/A

*Nakanishi et al. described 33 patients of which 30 of these patients were in the study conducted by Sey et al, **Median (not mean) was used in this study. TCB: Trucut biopsy, SSN: Straight standard needle, CHN: Core history needle, SC: Shark core, CPT: Complete portal, AE: Adverse event, N/A: Not available

steatohepatitis-NASH). This patient cohort may pose technical difficulties to the percutaneous or transjugular methodologies due to subcutaneous adiposity. There will also be an increasing need for LB in patients with NASH because these patients are at risk of progression to advanced fibrosis.[14-16] EUS-LB in a morbidly obese patient would not pose any additional technical challenges to the endoscopist, as internally, there is little anatomical variability with views obtained at EUS regardless of body weight.

TLB actually carries a 3.2% chance of procedural failure largely due to venous cannulation difficulties.[17] There had been no reports of technical failures related to EUS-LB to date.

PATIENT SAFETY AND SATISFACTION

The conventional algorithm for higher risk patients (obese, coagulopathic, and thrombocytopenic) are often deferred for TLB which carries a complication rate of up to 7.5%;[17-19] however, major complication rate between 0.5% and 1.8%,[17-19] which is very similar to image-guided PLB.[20] The collective patients who had undergone EUS-LB are 470 [Table 1], with only two reports of major complication (both involved bleeding managed conservatively). This early data would suggest EUS-LB is relatively safe; however, certainly larger studies are necessary.

Patients who have had both the percutaneous and EUS-LB preferred the EUS-LB[7] and were happy to have it again if necessary. Reports of EUS-LB-related pain are rare;[7-9,11] therefore, the recovery protocol is no different to that of a diagnostic endoscopy which translates into improved flow efficiency compared to PLB patients who would have to lie on their right side for a several hours to reduce risk of bleeding (and pain) as studies have shown 20% of PLB patients experience severe pain post-PLB,[21] 35% requiring analgesia[22] and 39% had ongoing pain at 24 h post-PLB.[23]

DIAGNOSTIC YIELD AND STAGING OF CHRONIC LIVER DISEASE

The EUS-LB technique is capable of a high diagnostic yield [Table 1]. The diagnostic yield is between 90% and 100%. Objective assessment of histologic yield revealed that studies using non (TCB) needles have produced a mean CPT yield of at least 9 CPTs from 2 to 3 passes (median) which is more than adequate by conventional standards.[24] Although the staging of viral hepatitis may require a higher quality specimen,[25] the need for liver biopsies in the management of viral hepatitis has declined significantly.[23]

EUS-LB would be particularly well suited for diseases with patchy distribution[26] (*e.g.*, Fatty liver disease) as multiple to and fro movements can sample liver parenchyma more widely as well as sampling both left and right lobes if required. There has been no significant difference in yield (CPTs) when targeting left or right lobe of the liver via the traditional percutaneous[27] or the new EUS[9] method.

EUS-LB is capable of obtaining very impressive length of specimen; however, there is a tendency toward excessive fragmentation which may hinder histological interpretation [Figure 3a]. Hence, emphasis on total length of specimen probably is of less importance as opposed to length of the longest intact core [Figure 3b].

The endoscopic approach facilitates concurrent assessment for the presence or complications of portal hypertension by conventional and novel means. A conventional endoscopic mucosal assessment for evidence of portal hypertension can be carried out (*e.g.* gastroscopy to look for varices and portal hypertensive gastropathy) before EUS-LB and the novel method of measuring portal pressure gradient can be performed simultaneously.[28] These two additional examinations can certainly be invaluable adjuncts to the liver histology in the staging of chronic liver disease.

SUMMARY

The inherent advantages of the endosonographic approach to LB are clear. From the patient's
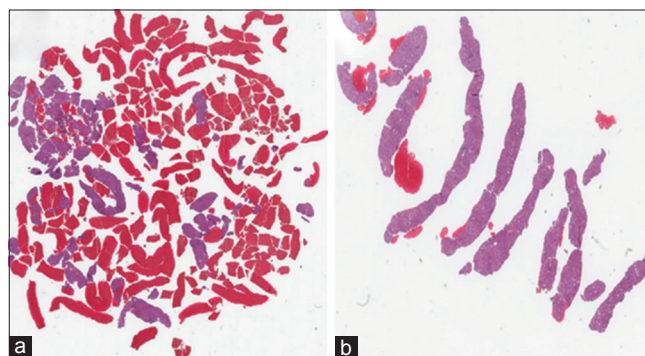
Figure 3. (a) Severe fragmentation of liver cores (purple) in a background of blood clots (red). (b) Intact cores with minimal fragmentation

perspective, it appears safe and largely painless. From a technical standpoint, it allows for sampling of a wider area of the liver and is not hindered by morbid obesity, therefore, highly successful in these patients. Finally, diagnostic yield is now well beyond conventional standards and further bolstered by information gathered from same session mucosal inspection for signs of portal hypertension and direct measurement of the portal pressure gradient. With ongoing refinement in needle type and suction techniques, further improvements in sample quality are only a matter of time. For some, adoption of this technique may be simply a mental barrier, as conventionally, liver biopsies have come from larger 16 or 18G needles, which may no longer be necessary.

Conflict of Interest

There are no conflicts of interest.

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