



# The Role of EUS in Liver Biopsy

Shaffer R. S. Mok<sup>1</sup> · David L. Diehl<sup>2</sup>

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## Abstract

**Purpose of Review** EUS-guided liver biopsy (EUS-LB) is being used with increased frequency to perform parenchymal liver biopsy. Evolution of the technique can now achieve excellent liver tissue cores. This review covers important developments in this procedure.

**Recent Findings** Clinical studies have recently demonstrated that the 19G EUS core biopsy needle is superior to non-core needles for liver tissue acquisition. In addition, wet suction provides more robust tissue samples than dry suction. Heparin priming of the needle (instead of saline) can prevent blood clogging within the needle lumen. A 1-hour recovery time after the EUS-LB is sufficient in almost all cases. The EUS-LB can deliver bilobar biopsies, which can decrease sampling error. Patients who need a liver biopsy in addition to an endoscopy or EUS are best served by the EUS-LB, as the combination procedure saves time and cost.

**Summary** The EUS-LB is a safe and effective means for procuring good liver core biopsies. Incremental improvements in technique have increased quality of the resulting specimen. Future directions of this technique are discussed.

**Keywords** Liver biopsy · Endoscopic ultrasound · Fine needle biopsy · Non-alcoholic steatohepatitis

## Abbreviations

EUS	Endoscopic ultrasound
EUS-LB	Endoscopic ultrasound-guided liver biopsy
FNA	Fine needle aspiration
FNB	Fine needle biopsy
G	Gauge
LB	Liver biopsy
NAFLD	Non-alcoholic fatty liver disease
U/S	Ultrasound

## Introduction

This is a rapidly changing time in the field of hepatology. While development of effective therapies for hepatitis C has

allowed for control and cure of that disease, the rising incidence of non-alcoholic fatty liver disease (NAFLD) has led to the need for new diagnostic and therapeutic approaches to deal with this potential serious condition. As pharmacologic treatments emerge for management of NASH, the need for accurate diagnosis and staging will continue to grow. Newer non-invasive diagnostic modalities have supplanted the need for liver biopsy (LB) in some cases. However, there remains a large number of clinical situations where non-invasive diagnostic tests are inconclusive, and therefore, histopathology still remains important [1].

Initially, liver biopsy was done by localizing a site on the right flank with manual percussion of the liver span. With the advent of portable ultrasound probes, the U/S was used instead of percussion to mark a site for the needle puncture. In the last several years, fewer and fewer hepatologists and gastroenterologists have been trained in percutaneous liver biopsy, and this workload has been transferred to the interventional radiology department. The transjugular (transvenous) route is used in patients with coagulopathy, or when portal pressures are required.

Since the first published description in 2007, EUS-guided liver biopsy (EUS-LB) has emerged as an attractive alternative means for parenchymal liver biopsy in the diagnosis and staging of chronic liver diseases [2]. Multiple case series and more

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✉ David L. Diehl  
dldiehl@geisinger.edu

<sup>1</sup> Case Western Reserve University—School of Medicine, Cleveland, OH, USA

<sup>2</sup> Department of Gastroenterology and Nutrition, Geisinger Medical Center, 100 N. Academy Ave, 21-11, Danville, PA 17822, USA

recently prospective randomized trials have shown that specimen yields of the EUS-LB are excellent, being at least equal to transjugular and percutaneous routes [3••]. Importantly, the adverse effect profile of this technique is low (Table 1).

## Traditional Approaches to Liver Biopsy

Liver biopsy was first described in 1883 by the renowned microbiologist and immunologist Dr. Paul Ehrlich. Initial techniques for acquiring liver tissue involved the use of percussion to delineate liver span. This was then followed by puncture of the liver through the skin at the mid-axillary line with large bore (14 to 16-gauge, G) needles. In the last 10 years, “image-guided” biopsy has become the standard approach, with use of a transcutaneous ultrasound probe replacing percussion to localize a suitable biopsy site. Interventional radiologists can choose between ultrasound, CT, or fluoroscopic imaging to accomplish the biopsy. It is important to note that even with image guidance, the biopsy is

not controlled with “real-time” U/S, and some risks of the procedure remain.

Bleeding is the most common adverse effect of liver biopsy and occurs in about 0.6% of cases (approximately 1 in 200) [4•]. Bleeding as a complication of LB does not seem to be decreased by image guidance. Other concerns include pneumothorax and gallbladder puncture, both of which are decreased using image guidance. Death is very rare following LB, with an incidence of approximately 1 in 10,000 biopsies [5].

To lessen the biopsy-associated bleeding risk coagulopathic patients, the transjugular (transvenous) route of biopsy was developed and first reported in 1973 [6]. This transjugular method also allows for portal pressure gradient measurements, if required. However, transjugular biopsy also carries additional risks including local hematoma at the site of puncture, intraperitoneal bleeding, arrhythmia, and inadvertent carotid arterial puncture. Use of the transjugular approach for LB is not necessary in the absence of coagulopathy or the need for portal pressure measurement, although may still be done in cases of ascites or obesity.

**Table 1** Summary of published data on the EUS-guided liver biopsy

Author	Year	N	Design	Device	Adequacy (%)	Median ASL (mm)	Median PT	Adverse events
Gleeson	2008	9	Retrospective case series	19G Tru-cut	100	16.9	7	0
DeWitt	2009	21	Prospective case series	19G Tru-cut	90	9	5	0
Stavropoulos	2012	22	Prospective case series	19G FNA	91	36.9	9	0
Gor	2014	10	Prospective case series	19G Tru-cut	100	14.4	9.2	0
Diehl	2015	110	Multicenter retrospective cohort	19G FNA	98	38	14	0
Pineda	2016	110	Retrospective cohort	19G FNA	98	40	17	NA
Sey	2016	75	Retrospective cross-sectional	19G ProCore 19G Tru-Cut	97 73	20 versus 9	5 versus 2	2 <sup>a</sup>
Schulman	2017	48	Prospective ex-vivo	18G1 18G2 19G FNA 19G FNB ProCore 19G FNB SharkCore 22G FNB	83.3 81.3 46 <sup>b</sup> 19 <sup>b</sup> 85.4 85.4	NA	2.5 3.5 1.9 1.7 6.2 3.8	NA
Mok	2017	20	Prospective cross-over	19G FNA 22G SharkCore	97.5 97.5	76.5 66.9	7.4 6.1	1 <sup>c</sup>
Ching Campanioni	2018	20	Prospective randomized	19G FNA 19G Acquire	100 100	11.8 16.3	29 54	1 <sup>c</sup>
Nieto	2018	165	Prospective observational	19G SharkCore	100	60	18	36 <sup>d</sup>
Mok	2018	40	Prospective cross-over	19G FNA 19G FNA dry heparin 19G FNA wet heparin	80 93 98	23.9 29.7 49.2	4 4 7	1 <sup>c</sup>

ASL aggregate specimen length, PT portal tracts, FNA fine needle aspiration, FNB fine needle biopsy

<sup>a</sup> Pain in 2 patients

<sup>b</sup> Approximations given figure interpretation and text

<sup>c</sup> Pain in 1 patient, seeking emergency care and discharged

<sup>d</sup> All with post-procedure pain, 2 emergency visit, 1 admitted to hospital, remaining discharged. One patient with hematoma

## What Defines an “Adequate” Liver Biopsy?

There are a variety of recommendations from professional societies as how to determine “adequacy” of liver biopsies. A range of quantitative standards have been given. For example, a frequently cited publication [7] states that 6–8 portal tracts and length of 1.5 cm is adequate, although a source for this recommendation is not given. A systematic review and meta-analysis of over 10,000 percutaneous biopsies demonstrated that a mean of 7.5 portal tracts and aggregate specimen length of 17.7 mm determined adequacy [8]. By comparison, a meta-analysis performed of transjugular means, demonstrating adequacy of 6.5 portal tracts and a 12-mm aggregate specimen length [9]. The present guidelines of the American Academy for the Study of Liver Diseases (AASLD) recommend 11 or more portal tracts to determine “adequacy.” The AASLD guideline document also defines specimen length above 15 mm to obtain adequacy, but an “ideal size is 30 mm” [10••]. In general, smaller needles are being used than in years past, and it appears that pathologists are becoming comfortable “doing more with less.”

## Development of the Endoscopic Ultrasound–Guided Liver Biopsy

The first published cases of the EUS-guided liver biopsy (EUS-LB) were described in 2007 using a novel Tru-Cut core biopsy needle [11] (QuickCore, Cook Medical, Winston Salem, NC). After this initial report, other case series were undertaken to validate this technique [2, 12]. One group with extensive experience with the Tru-Cut needle did a 7-year retrospective study comparing the QuickCore to a non-Tru-Cut needle (ProCore needle, Cook Medical). They found that the ProCore needle required fewer passes to gain more aggregate tissue versus the Tru-Cut needle [13]. Due to technical difficulty in using this needle technology, liver tissue yields were inconstant, and the device was discontinued by the manufacturer.

In 2012, Stavropoulos et al. described the EUS-guided parenchymal liver biopsy using a standard 19G EUS FNA needle [14•]. This study demonstrated a mean portal tract count of 9 (range 1–73), aggregate specimen length of 36.9 mm (2–185 mm), and adequate tissue in 20 of 22 subjects. This landmark study provided “proof of concept” that the EUS-LB could be successfully performed with a regular 19G EUS-FNA needle. Following this positive result, we organized a large multicenter trial of 8 centers and 110 patients using the 19G FNA needle for the EUS-LB. This study demonstrated high tissue adequacy, portal tract counts, and aggregate specimen lengths using the 19G FNA needle [15]. Following this publication, future studies set out to optimize the EUS-LB technique.

Our group conducted a tissue adequacy comparison of the EUS-LB compared with percutaneous and transjugular approaches. Patients with cirrhosis were excluded from the transjugular group, since it is known that cirrhosis contributes to specimen fragmentation and, therefore, could artifactually decrease tissue yields. We found that the EUS-LB compared to the transjugular or percutaneous route provided comparable or even superior tissue yields in terms of CPTs, length of the longest piece of tissue, and aggregate length [3••]. This study validated the ability for the EUS-LB to deliver adequate histologic material compared to existing biopsy techniques.

## Fine Tuning the EUS-LB Procedure

An ex vivo comparative trial of 2 explanted human livers set out to compare six different needle types and FNA technique [16]. In this study of 288 liver biopsy samples, two 18G percutaneous biopsy needles (QuickCore, Cook Medical) were compared to a 22G core needle (SharkCore, Medtronic), two 19G core needles (SharkCore and ProCore Echo Tip, Cook Medical, Inc.), and a 19G FNA needle (Expect, Boston Scientific). The results of this study concluded that tissue from the 22G core needle was adequate and that the 19G core needle was superior in terms of tissue yield to that of 19G FNA and 18G percutaneous needles. It should be noted that measurements of biopsy length were made on tissue pieces prior to histologic processing.

Regarding tissue fragmentation with smaller needle size, our group conducted a prospective pilot study comparing a 19G FNA needle with a 22G core needle (SharkCore) [17]. In this prospective study of 80 biopsies in 40 patients, we found that 22G specimens had significantly higher tissue fragmentation as compared to the 19G cores. The tissue fragmentation appears to take place during the histological processing and tissue embedding process. This easier fragmentation of the delicate 22G core samples led to lower tissue adequacy. In fact, specimens adequate for pathological interpretation could be obtained in only 60% of cases versus 90% with the 19G needle. There does not seem to be a safety advantage in using the smaller needle, while there is an unacceptable fall in specimen adequacy, so use of the 22G core needle for EUS-LB cannot be recommended.

As a means of further improving specimen yields, our group next looked at use of “wet suction” [18] versus “dry suction” to see if this variable would increase yields. To accomplish this, the needle is primed, usually with saline, and then full suction is applied to the vacuum syringe. Using three study groups with a prospective cross-over design, we evaluated the EUS-LB using a 19G needle and three preparations; standard needle from the package (“dry suction”), needle primed with heparin and then flushed with air (“dry heparin”), needle flushed with heparin, and wet suction attached (“wet

heparin”). In a prospective cross-over design, we performed a left-sided EUS-LB and evaluated objective metrics of the biopsies for 40 patients [19]. There was a 98% specimen adequacy for wet heparin compared to 80% for the dry suction technique. Wet suction gave longer aggregate specimen length, length of the longest piece, more portal tracts, and less fragmentation compared to dry suction. This study indicated that using wet suction is preferred to dry suction. There is no deleterious effect of heparin on tissue cytology, histology, or immunohistochemistry [20], so heparin is reasonable to use instead of saline.

Next, we wanted to compare 19G FNA versus 19G FNB needles to see if this conferred an advantage. We conducted a prospective trial evaluating a 19G core biopsy needle (Acquire, Boston Scientific) with a 19G FNA (Expect Flexible, Boston Scientific) [21]. This trial demonstrated increased better performance of the core needle for all standard metrics for core liver biopsy. Specimen yields, portal tracts, and length of the largest piece are metrics vital to disease staging. This study demonstrated that a 19G core needle, with wet suction, is the best approach to the EUS-LB technique.

Most studies of the EUS-LB have used from 1 to 10 needle actuations (i.e., “to-and-fro” movements). We recently completed a prospective randomized study of 1 versus 3 needle actuations for the EUS-LB, utilizing the Acquire 19G core needle biopsy device [22]. As could be predicted, three actuations provided more tissue than a single actuation, but robustly long specimens could be obtained with a single pass. Based on this experience, we recommend 3 to-and-fro actuations. At present, it is our practice to use only 1–3 needle actuations for the delivery of adequate tissue. A recent study did highlight the potential for only one pass required for the delivery of liver core tissue. This study yielded high length of the longest piece and aggregate specimen length, with portal tract counts equivalent to prior studies [23]. It should be noted that the actuation technique described in this study involved a very long trajectory of 7 cm, and that more expertise is required to accomplish this safely.

## Technique of the EUS-Liver Biopsy

The EUS-LB is performed with the linear echoendoscope. After passing the EUS scope down to the proximal stomach, the scope is gently torqued counterclockwise to localize the left liver lobe. Care must be taken to identify the left liver lobe and distinguish this structure from the spleen, which can appear similar to the liver in some cases of hepatic steatosis. Misidentification of the left hepatic lobe can lead to inadvertent splenic puncture with potentially catastrophic consequences.

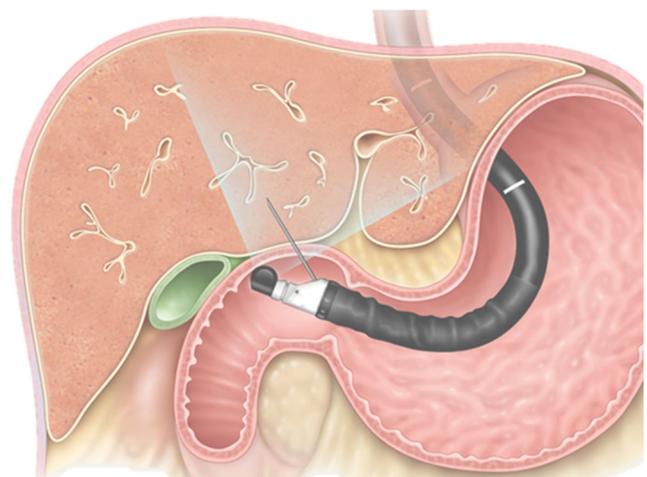
To identify the right hepatic lobe, the scope is advanced to the pyloric channel and into the duodenal bulb (Fig. 1). Again,

the echoendoscope is torqued counterclockwise to localize the right lobe. Next, assisted by Doppler imaging, the endosonographer identifies a vessel-free needle trajectory measuring 3–4 cm, and possibly more. In the absence of significant biliary obstruction, inadvertent biliary puncture is very unlikely as the intrahepatic bile ducts are typically not seen. Next, the needle is introduced into the liver parenchyma with a quick stroke. The suction syringe is turned “on” prior to actuation of the needle. The needle is actuated with three deliberate to-and-fro movements with slight “fanning” (i.e., slight change in the trajectory of the needle with each pass). Before removing the needle from the liver, the suction is turned off.

It is good technique in the EUS to watch the needle tip during the entire needle biopsy procedure. We have found that in very hyperechoic (“white”) livers, the echogenic needle tip is hard to visualize clearly during needle actuation. However, subtle movement of liver tissue near the tip of the needle can be seen, and this should be looked for if clear visualization of the tip is not possible.

As a means to prevent blood in the sample from clotting and “contaminating” the specimen, we are now applying the heparin priming approach to the EUS-LB [19]. Stylet handling is greatly improved, and there is no increased bloodiness of the specimen. Also, importantly, there is no adverse effect of the heparin on cytology, histology, or interference with immunohistochemical staining [20].

Bilobar sampling can reduce sampling error [24–26], and this is much more easily accomplished with the EUS-LB than the percutaneous approach. In patients who have had altered surgical anatomy such as Roux-en-Y gastric bypass, only left hepatic lobe biopsy is possible.



**Fig. 1** Diagram of visualization and biopsy of the right lobe of the liver through the duodenal bulb during EUS-LB. Used with permission from Boston Scientific Corporation

## Specimen Handling

Upon completion of liver biopsy, the delicate tissue cores should not be handled excessively. We recommend expressing the tissue directly into formalin rather than onto a Telfa pad or gauze, as the latter can lead to “iatrogenic” fragmentation. The sample should be left to fix in formalin for at least 1 h. Care must be taken on the receiving end by the histopathology technician to avoid rough handling, which can lead to additional tissue fragmentation. It is worth discussing tissue handling with the histopathology technicians and pathologists at your institution before starting an EUS-LB program. However, we think that they will find, like ours did, that the tissue cores that are obtained are typically superior to those obtained by either percutaneous or transjugular approaches.

As discussed above, we have found that the use of wet-heparinized suction and use of a 19G core needle provide the best specimens with the least amount of fragmentation [19]. However, it can be difficult to make an “on-site” evaluation of adequacy, because blood admixed with tissue in the formalin jar hinders. As a solution for this problem, we have adopted the use of a microsieve for the EUS-LB. With the microsieve technique, the specimen is collected into the sieve, allowing the non-clotting blood to drip through. The blood tissue is gently “washed” from the tissue with 5–10 mL of saline using a 10 cc syringe. This separates the tissue from the blood, and adequacy can be immediately assessed. Finally, the tissue on the sieve is gently floated off into formalin.

## Post-Procedure Adverse Events

It is estimated that as many as 80% of patients undergoing percutaneous liver biopsy may experience pain after the procedure. Traditionally after liver biopsy, patients are placed in a right lateral decubitus position for 2–4 h after liver biopsy to allow for tamponade of the puncture site at the liver capsule. However, such “tamponade” is not possible after the EUS-LB because the site of puncture is not on the lateral margin of the liver.

Our group reviewed data on 124 patients undergoing EUS-LB, with recovery for up to 2 h. Overall, 30% of patients experienced pain after the procedure and was controlled in 92% within 1 h with a single dose of intravenous analgesia. The remaining 8% were pain-free within 2 h. These results indicated that 1 h of recovery is sufficient in the vast majority of patients undergoing the EUS-LB. In our prospective comparison of FNB versus FNA needles for EUS-LB, we found slightly more occurrences of severe pain (25%) when using the core needle compared to the regular needle (5%).

Data from other EUS-LB studies show a low incidence of prolonged post-procedure pain. An early study using a Tru-Cut needle for biopsy described 2 patients that sought

emergency medical care for abdominal pain following the procedure [2, 11–13, 20]. Both subjects underwent diagnostic imaging which excluded bleeding and perforation, with discharge home. Another trial of 20 patients reported 1 patient with post-procedure pain. Imaging in the emergency department demonstrated no significant pathology, and the patient was discharged home [17].

Hemorrhage after the EUS-LB remains a concern, but appears rare. In a multi-center trial of 110 patients, only 1 incident of bleeding was described in a person with evolving disseminated intravascular coagulopathy [15]. One patient with bleeding was identified in a different prospective trial of 40 patients undergoing the EUS-LB [17]. This patient was observed overnight and required no intervention or transfusions of blood products. It is our hypothesis that the low rate of bleeding is due to the ability to directly identify and avoid intervening vascular and biliary structures for the EUS-LB, as compared with non-real-time imaging modalities.

Though not yet reported in the medical literature, our group has become aware of reports of inadvertent splenic puncture during the EUS-LB [27]. This can result in severe bleeding requiring splenic artery embolization by interventional radiology, or potentially even death. The echotexture of a fatty liver can be very similar to the spleen, which can lead to misidentification of these organs. Care must be taken by the endosonographer to confirm the identity of the left hepatic lobe and, positively, distinguish it from spleen.

## Future Directions

There are nuances to performing the EUS-guided liver biopsy. Although we have not formally assessed the learning curve, we have found that at least 10–15 procedures are necessary for basic competence in organ identification, and effective needle biopsy technique that results in adequate liver cores. Further study would be beneficial to assess competency for obtaining liver tissue by the EUS-LB. Advances in needle technology, specifically, the availability of a “core” needle, seem to shorten the learning curve. There likely still remains a need for a purpose-made needle for the EUS-LB, utilizing the Tru-Cut-type technology.

Exciting research is ongoing involving techniques to safely measure portal pressure gradients (PPG) via the EUS. Using a 25G needle and a novel pressure-measuring device with a compact manometer and non-compressible tubing, the EUS-guided pressure measurements of the hepatic vein and portal vein have been done. These measurements allow calculation of the PPG, which is a valuable measurement in the management of some liver diseases and early cirrhosis. Several pilot studies have been done in animals and humans and have demonstrated the feasibility of this technique [28, 29, 30, 31]. In animal studies, the PPG as measured by the EUS-guided

approach correlates very nicely with transjugular PPG measurements (wedged balloon technique). This approach to portal pressure measurement appears safe, even in the presence of portal hypertension. Prospective multicenter study would be beneficial to further use of this approach, with the goal being to see if it could replace the transjugular approach in some cases.

## Conclusions

The EUS-guided liver biopsy is a safe and straightforward procedure, which has significant advantages over traditional methods for liver biopsy. Though newer non-invasive staging technologies play a role in the diagnosis and management of liver disease, the gold standard remains delivery of liver histology. The importance of delivering hepatic tissue in a safe and effective manner will allow the EUS-LB to continue gathering a clinical presence backed with continued perfection in technique.

Present data have objectively shown comparable or superior specimen adequacy of the EUS-LB to percutaneous or transjugular approaches to biopsy. After determining that the EUS-LB is at least equal to other means for procuring hepatic tissue, future trials focused on improving procedural technique. Advancement in needle technology has led to dramatic improvements in the EUS-LB specimens.

There are several advantages to the EUS-guided liver biopsy including:

- Established procedural safety
- Effectiveness at delivering excellent liver biopsy cores
- Improved patient experience (sedated procedure)
- Bilobar biopsy easily achievable
- Cost and time saving when endoscopic procedure also needed in addition to liver biopsy
- Procedure is kept within the sphere of gastroenterology/hepatology rather than being “farmed out” to interventional radiology

With increasing interest in this technique among hepatologists and endosonographers, as well as ongoing clinical reports of favorable results, the EUS-LB has a bright future. Future clinical studies will continue to define when the EUS-guided approach to liver biopsy is most appropriate.

## Compliance with Ethical Standards

**Conflict of Interest** David Diehl reports working as a consultant for Boston Scientific, Medtronic, Olympus America, and Cook Medical. Shaffer Mok reports working as a consultant for Medtronic and grants from Pentax/C2 Therapeutics, outside the submitted work.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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## References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Caldwell S. Liver biopsy: the reports of its demise are greatly exaggerated. *Clin Transl Gastroenterol*. 2016;7(5):e171. <https://doi.org/10.1038/ctg.2016.30>.
2. Dewitt J, McGreevy K, Cummings O, et al. Initial experience with EUS-guided Tru-cut biopsy of benign liver disease. *Gastrointest Endosc*. 2009;69(3 Pt 1):535–42. <https://doi.org/10.1016/j.gie.2008.09.056>.
3. Pineda JJ, Diehl DL, Miao CL, et al. EUS-guided liver biopsy provides diagnostic samples comparable with those via the percutaneous or transjugular route. *Gastrointest Endosc*. 2016;83(2):360–5. <https://doi.org/10.1016/j.gie.2015.08.025> **Comparison of EUS-LB to other methods of LB (transvenous and percutaneous), demonstrating equivalence.**
4. Tapper EB, Lok ASF. Use of liver imaging and biopsy in clinical practice. *N Engl J Med*. 2017;377:756–68. <https://doi.org/10.1056/NEJMr1610570> **Recent review of use of liver biopsy as well as non-invasive imaging in clinical practice.**
5. Garcia-Tsao G, Boyer JL. Outpatient liver biopsy: how safe is it? *Ann Intern Med*. 1993;118(2):150–3. <https://doi.org/10.7326/0003-4819-118-2-199301150-00013>.
6. Rösch J, Hanafee WN, Snow H. Transjugular portal venography and radiologic portacaval shunt: an experimental study. *Radiology*. 1969;92:1112–4. <https://doi.org/10.1148/92.5.1112>.
7. Bravo AA, Sheth SG, Chopra S. Liver biopsy. *N Engl J Med*. 2004;344:495–500.
8. Cholongitas E, Senzolo M, Standish R, Marelli L, Quaglia A, Patch D, et al. A systematic review of the quality of liver biopsy specimens. *Am J Clin Pathol*. 2006;125(5):710–21. <https://doi.org/10.1309/W3XC-NT4H-KFBN-2G0B>.
9. Kalambokis G, Manousou P, Vibhakorn S, Marelli L, Cholongitas E, Senzolo M, et al. Transjugular liver biopsy - indications, adequacy, quality of specimens, and complications - a systematic review. *J Hepatol*. 2007;47(2):284–94. <https://doi.org/10.1016/j.jhep.2007.05.001>.
10. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD. AASLD position paper liver biopsy. *Hepatology*. 2009. <https://doi.org/10.1002/hep.22742> **Comprehensive review of liver biopsy including indication, technical aspects, and histology analysis.**
11. Mathew A. EUS-guided routine liver biopsy in selected patients [7]. *Am J Gastroenterol*. 2007;102(10):2354–5. [https://doi.org/10.1111/j.1572-0241.2007.01353\\_7.x](https://doi.org/10.1111/j.1572-0241.2007.01353_7.x).
12. Gleeson FC, Clayton AC, Zhang L, Clain JE, Gores GJ, Rajan E, et al. Adequacy of endoscopic ultrasound core needle biopsy specimen of nonmalignant hepatic parenchymal disease. *Clin Gastroenterol Hepatol*. 2008;6(12):1437–40. <https://doi.org/10.1016/j.cgh.2008.07.015>.
13. Sey MSL, Al-Haddad M, Imperiale TF, McGreevy K, Lin J, Dewitt JM. EUS-guided liver biopsy for parenchymal disease: a

- comparison of diagnostic yield between two core biopsy needles. *Gastrointest Endosc.* 2016;83(2):347–52. <https://doi.org/10.1016/j.gie.2015.08.012>.
14. Stavropoulos SN, Im GY, Jlayer Z, et al. High yield of same-session EUS-guided liver biopsy by 19-gauge FNA needle in patients undergoing EUS to exclude biliary obstruction. *Gastrointest Endosc.* 2012;75(2):310–8. <https://doi.org/10.1016/j.gie.2011.09.043> **Seminal paper demonstrating that a regular 19G EUS needle could be used to procure adequate liver biopsy.**
  15. Diehl D, Johal A, Khara H, Stavropoulos S, al-Haddad M, Ramesh J, et al. Endoscopic ultrasound-guided liver biopsy: a multicenter experience. *Endosc Int Open.* 2015;3(03):E210–5. <https://doi.org/10.1055/s-0034-1391412>.
  16. Schulman AR, Thompson CC, Odze R, Chan WW, Ryou M. Optimizing EUS-guided liver biopsy sampling: comprehensive assessment of needle types and tissue acquisition techniques. *Gastrointest Endosc.* 2017;85(2):419–26. <https://doi.org/10.1016/j.gie.2016.07.065>.
  17. Mok SR, Diehl DL, Johal AS, Khara HS, Diehl M, Mudireddy PR, et al. Mo1245 19 versus 22 gauge fine needle biopsy for endoscopic ultrasound guided liver biopsy (EUS-LB): a prospective randomized trial. *Gastrointest Endosc.* 2017;85(5):AB473–4. <https://doi.org/10.1016/j.gie.2017.03.1553>.
  18. Attam R, Arain MA, Bloechl SJ, Trikudanathan G, Munigala S, Bakman Y, et al. “Wet suction technique (WEST)”: a novel way to enhance the quality of EUS-FNA aspirate. Results of a prospective, single-blind, randomized, controlled trial using a 22-gauge needle for EUS-FNA of solid lesions. *Gastrointest Endosc.* 2015;81(6):1401–7. <https://doi.org/10.1016/j.gie.2014.11.023>.
  19. Mok SRS, Diehl DL, Johal AS, et al. A prospective pilot comparison of wet and dry heparinized suction for EUS-guided liver biopsy (with videos). *Gastrointest Endosc.* 2018. <https://doi.org/10.1016/j.gie.2018.07.036> **Study demonstrating significant advantage of wet suction for EUS-LB.**
  20. Diehl D, Mok S, Khara H, Johal A, Kirchner H, Lin F. Heparin priming of EUS-FNA needles does not adversely affect tissue cytology or immunohistochemical staining. *Endosc Int Open.* 2018;06(03):E356–62. <https://doi.org/10.1055/s-0043-121880.15>.
  21. Ching Companioni RA, Johal AS, Confer B, Khara HS, Diehl DL. Mo1349 a prospective randomized trial of 19-gauge (G) aspiration needle versus 19G core biopsy needle for endoscopic ultrasound-guided liver biopsy. *Gastrointest Endosc.* 2018;87(6):AB457–8. <https://doi.org/10.1016/j.gie.2018.04.1999>.
  22. Ching Companioni R, Johal AS, Confer B, Khara HS, Diehl DL. Modified 1 pass, 1 versus 3 actuation wet suction technique for endoscopic ultrasound guided liver biopsy (EUS-LB): a randomized prospective trial. *GIE.* 2018;87(6):AB457-AB458.
  23. Nieto J, Khaleel H, Challita Y, et al. EUS-guided fine-needle core liver biopsy sampling using a novel 19-gauge needle with modified 1-pass, 1 actuation wet suction technique. *Gastrointest Endosc.* 2017;85:AB494–5.
  24. Baunsgaard P, Sanchez GC, Lundborg CJ. The variation of pathological changes in the liver evaluated by double biopsies. *Acta Pathol Microbiol Scand Sect A Pathol.* 2009;87A(1–6):51–7. <https://doi.org/10.1111/j.1699-0463.1979.tb00023.x>.
  25. Abdi W, Millan JC, Mezey E. Sampling variability on percutaneous liver biopsy. *Arch Intern Med.* 1979;139:667–9. <https://doi.org/10.1001/archinte.1979.03630430043014>.
  26. Maharaj B, Leary WP, Naran AD, Maharaj RJ, Cooppan RM, Pirie D, et al. Sampling variability and its influence on the diagnostic yield of percutaneous needle biopsy of the liver. *Lancet.* 1986;327:523–5. [https://doi.org/10.1016/S0140-6736\(86\)90883-4](https://doi.org/10.1016/S0140-6736(86)90883-4).
  27. Diehl DL. Endoscopic ultrasound-guided liver biopsy. In: Adler DG, editor. *Interventional Endoscopic Ultrasound.* New York, NY USA, Springer; 2019. <https://doi.org/10.1007/978-3-319-97376-0>.
  28. Huang JY, Samarasena JB, Tsujino T, et al. EUS-guided portal pressure gradient measurement with a simple novel device: a human pilot study. *Gastrointest Endosc.* 2017;85(5):996–1001. <https://doi.org/10.1016/j.gie.2016.09.026> **EUS-guided portal pressure gradient measurement is likely to be adopted after more clinical data is accumulated.**
  29. Huang JY, Samarasena JB, Tsujino T, Chang KJ. EUS-guided portal pressure gradient measurement with a novel 25-gauge needle device versus standard transjugular approach: a comparison animal study. *Gastrointest Endosc.* 2016;84(2):358–62. <https://doi.org/10.1016/j.gie.2016.02.032>.
  30. Schulman AR, Ryou M, Aihara H, Abidi W, Chiang A, Jirapinyo P, et al. EUS-guided intrahepatic portosystemic shunt with direct portal pressure measurements: a novel alternative to transjugular intrahepatic portosystemic shunting. *Gastrointest Endosc.* 2017;85:243–7. <https://doi.org/10.1016/j.gie.2016.07.041>.
  31. Schulman AR, Thompson CC, Ryou M. Endoscopic ultrasound-guided direct portal pressure measurement using a digital pressure wire with real-time remote display: a survival study. *J Laparoendosc Adv Surg Tech.* 2017;27:1051–4. <https://doi.org/10.1089/lap.2017.0032>.