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**An Update on Endoscopic Ultrasound-Guided Liver Biopsy
Responses to Reviewers**

Name of Journal: *World Journal of Gastroenterology*

Manuscript Type: MINIREVIEWS

Number ID: 02954022

An Update on Endoscopic Ultrasound-Guided Liver Biopsy

Shiva Rangwani, Devarshi R. Ardeshta, Khalid Mumtaz, Sean Kelly, Samuel Han, Somashekar
G Krishna

Reviewer #1:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: It was a pleasure to read the minireview titled: "An Update on Endoscopic Ultrasound-Guided Liver Biopsy". The manuscript is well-written and very informative. It compared the 3 main techniques for obtaining a liver biopsy from many aspects.

- General considerations: Some punctuations are missing, e.g. commas after "however" and "Similarly".
- Thank you for pointing out these grammatical / punctuation errors. The aforementioned errors have been corrected and the paper has been proof-read by a native English speaker for grammar and punctuation prior to sending the edits.
- Introduction Page 4: Wilsons disease, change to Wilson disease or Wilson's disease Alfa-1 Anti-trypsin Deficiency, Hemochromatosis: remove capital letters
- Thank you for the correction of both of these items, they have been changed per your correction.
- Methods of Liver Biopsy Page 6: Endoscopic ultrasound-guided fine-needle aspiration was first done in 1993 and EUS-LB was first described by in 2007.12,13 Mention the authors in references 12 and 13: described by-----in 2007.



- We have cited Mathew's 2007 study where EUS-LB was first described in the manuscript. There is no specific attribution for a practitioner who performed endoscopic ultrasound-guided FNA, however, therefore item 12's author name (a review paper) was not stated.
- **Needle Pass / Actuation: Page 9: Needle pass refers to the amount of times a needle is introduced into the liver parenchyma through puncture of the liver capsule, Change to: Needle pass refers to the number of times a needle is introduced into the liver parenchyma through puncture of the liver capsule, while actuation refers to the amount of back-and-forth motions are made in a specified needle pass. Change to: while actuation refers to the number of back-and-forth motions made in a specified needle pass.**
- Thank you for this grammatical correction. The reflected change has been made on page 9.
- **Needle Selection: Size Page 9: As time progressed, so did a proclivity for smaller gauge needles in EUS-LB. After the aforementioned statement the authors included several reports where gauge 19 was better than gauge 22. Do they mean that these 19 G are smaller than the sizes 14G- 16G mentioned at the beginning of the paragraph? These statements need more clarification.**
- Thank you for bringing up this point, as the initial manuscript was not clear. The 19 and 22 gauge needles provided better yield than the 14-16 gauge counterparts. The above-mentioned sentence has been changed to: "As time progressed, researchers found that smaller-gauge needles provided better results than their 14G - 16G counterparts." This change is reflected on page 9 of the manuscript.
- **Although there is a mention of pediatric patients at the end of the manuscript, but the authors did not elaborate on any studies using EUS-LB in pediatric age group.**
- We had only found anecdotal mention of the potential use of EUS-LB in pediatric patients; however, no formal studies have been done to our knowledge. I have clarified this in the manuscript by adding " - although to our knowledge, formal studies in pediatric populations are yet to be done." We believe that this consideration is worth mentioning in the paper as it may spark future interest upon reading.
- **The table is very informative and the comparison is crystal clear.**
- We thank you for the time taken for the review and your comments that made the paper more informative and precise.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)



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Specific Comments to Authors: This is a minireview of updates in EUS-guided liver biopsy, a technique that has been gaining increasing popularity and acceptance among the gastroenterology community. This review provides a quick summary of the latest literature in terms of the safety and efficacy and EUS-guided liver biopsy in comparison to traditional techniques of liver biopsy, namely percutaneous- and transjugular guided liver biopsy. This review is well-written and includes the most important publications in the area of EUS-guided liver biopsy. The overall conclusion based on the most recent published studies is this technique is more effective than traditional techniques providing higher specimen length and more CPT while keeping an excellent safety profile. The review also discusses a number of technical aspects in performing EUS-guided liver biopsy highlighting some deficiencies such as the use of suction and needle type. This review does not have any major limitations. It is well-written, includes the most important data in the field summarized in an-easy to read fashion. The only grammatical correction needed is on page 9, line 12 in the sentence " A 2021 study found showed that EUS-LB using" should be corrected to "A 2021 study showed that EUS-LB using ..." This review should be accepted as it is.

- We thank you for your diligent review of our manuscript and your words that highlight the strength of the review. We have made the grammatical correction on page 9 and have highlighted it in the returned manuscript.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors: This paper is short of innovation and creativity. These articles also discuss the advantages of this technology and the existing liver puncture technology, the selection of puncture needle, etc. (PMID: 30846147, 32218838, 3482658). At the same time, there are relatively few charts in this paper, which can not make readers understand the principle and operation of this technology. It is suggested to improve the new progress in other aspects of this technology

- We thank you for your commentary and time taken to review our proposed publication. While there are multiple publications that discuss the advancements made in EUS-LB separately, we do believe that a holistic review outlining the current state of literature would be valuable to your readership. We do agree that, since this paper does hinge on the technique of EUS-LB, that it is important to incorporate a figure that clearly depicts the notion of EUS-LB to your readership. Therefore, we have added Figure 1 to the paper as well as a reference to the Figure in the "General Technique" section on page 8. These changes are reflected in the edited manuscript.



Reviewer #4:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Jan 21, 2022 Dear Authors submitting to WJG Manuscript ID – WJG75127 Manuscript Title: An Update on Endoscopic Ultrasound-Guided Liver Biopsy All Author List: Shiva Rangwani, et al. Manuscript Type: MINIREVIEWS The endoscopic ultrasound-guided liver biopsy (EUS-LB) was an effective alternative to percutaneous and trans-jugular liver biopsy (PC and TJ-LB). (1) EUS-LB demonstrated equivalent diagnostic yield, provided adequate specimen and facilitated liver biopsy for lesions in the left lobe of the liver, obese patients or patients with ascites. (2, 3) Compared to conventional procedures, EUS-LB had less post-procedural pain and recovery time. (2, 3) This study compared the benefit and drawbacks of three methods of liver biopsy and highlighted evidence-based data of the technique and devices of EUS-LB.

Comments 1. The use of EUS-LB for the tissue diagnosis of liver mass or focal lesion was promising. (4, 5, 6) and it will be better if you can add data of EUS-LB in cases of liver mass or focal lesion.

- Thank you for these citations and information. We do agree that it is important to frame the reader's notion that EUS-LB has a powerful diagnostic capacity as shown by these studies. Therefore, we have added the below citations #4-6 (cited as 14-16 in manuscript) in our paper and have incorporated them into the EUS-LB portion of the "Methods of Liver Biopsy" section with the below addition. This is reflected in the edited manuscript.
 - "Further, the use of EUS in close proximity to the liver allows for better visualization of liver lesions for targeted liver biopsies.¹⁰ In fact, multiple studies have shown a diagnostic accuracy between 85-90% for solid liver masses using EUS-guided FNB.¹⁴⁻¹⁶
2. Please provide references for the first paragraph of the general technique section.
- Thank you for this comment, the technique section was prepared using generalized methodology at our center, which is derived from literature / training published on EUS-LB. We have added several citations to this section to bolster the section and for reviewers to refer to when reading the manuscript. The citations can be found in the first paragraph of the section entitled "General Technique" and are reflected in the edited manuscript.



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3. The slow-pull technique was mentioned in previous systematic review and meta-analysis. (7) Please provide a comparison advantage and disadvantage between the suction and slow-pull techniques.

- Thank you for bringing this important item to our attention. We have cited the below paper and included this information in the section entitled "Suction." The below text has been added to the manuscript and is reflected in the edited document:
- "In contrast, specimens can be obtained without applying suction via stylet, in a "slow-pull" technique. A 2020 metanalysis showed that FNB with a slow-pull technique provided similar total specimen length (44.3 mm vs 53.9 mm, $p = 0.40$) when compared to suction application; however, the slow-pull technique provided improved CPT than suction (30 vs. 14.6 ($p < 0.001$)).²⁵ Authors hypothesize that this stems from reduced fragmentation of the tissue specimen as it is subjected to an environment of less negative pressure with the slow-pull technique."

4. "Through our literature review, it appears the 1-pass 1 actuation technique is the most common mode of the EUS-LB acquisition". Please provide references for this sentence in the needle Pass/ Actuation section.

- Thank you for pointing this omission of citation out. We have provided the appropriate citation as below and outlined / referenced in the edited manuscript.
- "Through our literature review, it appears the 1-pass 1-actuation technique is the most common mode of EUS-LB acquisition."^{22,26}

5. In the Needle Selection: Tip and Design section, the comparison of EUS-LB with FNB and FNA should be separated from the design of needle tips. Please rewrite this section for a better understanding of the readers.

- Thank you for this commentary, we do elucidate that a Franseen needle tip does provide better sampling than its FNA counterparts; however most recent literature has compared Franseen vs Fork-tip needle designs as both of these have performed better than their FNA counterparts as above. Due to this, we do not believe that a specified section comparing FNA vs FNB needles would be appropriate in our review.

6. In the previous review, the EUS-guided portal pressure measurement and intervention had details such as the technique of venous catheterization, the instrument and the interpretation of the result. (8) Please add more information on the EUS-guided portal pressure measurement or remove this part from the review article.

- Thank you for the reference and commentary regarding the portal pressure gradient. While this paper does focus on EUS-LB, we agree that it is important that readers have an understanding of the general procedure that is done to



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obtain PPG via EUS. Therefore, we have added the following excerpt to the section entitled "Portal Pressure Gradient." We have also incorporated your suggested reference.

- "To obtain EUS-guided measurement of portal pressure, endoscopists first puncture the hepatic vein via a transgastric transhepatic approach, with the needle hooked up to a digital manometer via non-compressible tubing.³⁸ Once obtaining hepatic vein pressure averages, endoscopists then turn their attention to the portal vein, which is accessed in a transgastric transhepatic approach usually at the umbilical portion of the portal vein. Once the portal vein pressure is obtained, the portal pressure gradient is calculated by subtracting the mean portal vein pressure from the mean hepatic vein pressure.³⁸ These readings are usually obtained with a small-gauge (25G) FNA needle.^{37,38}

References

1. Dawod E, Nieto J, Saab SJOjotACoG, ACG. Endoscopic Ultrasound-Guided Liver Biopsy: Where Do We Stand? 2021;10.14309.
2. McCarty TR, Bazarbashi AN, Njei B, Ryou M, Aslanian HR, Muniraj TJCe. Endoscopic Ultrasound-Guided, Percutaneous, and Transjugular Liver Biopsy: A Comparative Systematic Review and Meta-Analysis. 2020;53(5):583.
3. Johnson KD, Laoveeravat P, Yee EU, Perisetti A, Thandassery RB, Tharian BJWjoge. Endoscopic ultrasound guided liver biopsy: Recent evidence. 2020;12(3):83.
4. Lee YN, Moon JH, Kim HK, Choi HJ, Choi MH, Kim DC, et al. Usefulness of endoscopic ultrasound-guided sampling using core biopsy needle as a percutaneous biopsy rescue for diagnosis of solid liver mass: Combined histological-cytological analysis. 2015;30(7):1161-6.
5. Chon HK, Yang HC, Choi KH, Kim THJCe. Endoscopic ultrasound-guided liver biopsy using a core needle for hepatic solid mass. 2019;52(4):340.
6. Kongkam P, Nalinthassanai N, Prueksapanich P, Sanpavat A, Cañones AR, Luangsukrerk T, et al. A comparison of the antegrade core trap and reverse bevel needles for EUS-guided fine-needle biopsy sampling of liver mass: a prospective randomized cross over study. 2021.
7. Baran B, Kale S, Patil P, Kannadath B, Ramireddy S, Badillo R, et al. Endoscopic ultrasound-guided parenchymal liver biopsy: A systematic review and meta-analysis. 2021;35(10):5546-57.
8. Samarasena JB, Chang KJJCe. Endoscopic ultrasound-guided portal pressure measurement and interventions. 2018;51(3):222.

Science Editor



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This is a minireview of updates in EUS-guided liver biopsy, a technique that has been gaining increasing popularity and acceptance among the gastroenterology community. This review provides a quick summary of the latest literature in terms of the safety and efficacy and EUS-guided liver biopsy in comparison to traditional techniques of liver biopsy, namely percutaneous- and transjugular guided liver biopsy. This review is well-written and includes the most important publications in the area of EUS-guided liver biopsy. In general, the reviewers positively commented on the value of this manuscript. However, a few minor issues need to be addressed as below.

1. The only grammatical correction needed is on page 9, line 12 in the sentence " A 2021 study found showed that EUS-LB using" should be corrected to "A 2021 study showed that EUS-LB using ..." This review should be accepted as it is. CDS is "Centers," not "Center."

- Thank you for your diligent review and time on this paper. The aforementioned grammatical errors have been corrected

2. Some punctuations are missing, e.g. commas after "however" and "Similarly".

- These corrections have been made, please refer to Reviewer 1 response. Thank you.

Introduction Page 4: Wilsons disease, change to Wilson disease or Wilson's disease 3.

- The diction has been changed to Wilson disease, please refer to reviewer 1 comments. Thank you.

Page 6: Endoscopic ultrasound-guided fine-needle aspiration was first done in 1993 and EUS-LB was first described by in 2007. Please either delete "by" or add the authors.

- Mathew was the first to perform EUSLB and publish in 2007, which has been added to the manuscript as above (refer to bulleted point in Reviewer 1's comments). Thank you.

4. Needle Pass / Actuation: Page 9: Needle pass refers to the amount of times a needle is introduced into the liver parenchyma through puncture of the liver capsule, Change to: "Needle pass refers to the number of times a needle is introduced into the liver parenchyma through puncture of the liver capsule". 5. while actuation refers to the amount of back-and-forth motions are made in a specified needle pass. Change to: while



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actuation refers to the number of back-and-forth motions made in a specified needle pass.

- Thank you for this grammatical correction. The reflected change has been made on page 9.

6. Although there is a mention of pediatric patients at the end of the manuscript, but the authors did not elaborate on any studies using EUS-LB in the pediatric age group. References need to be added.

- We had only found anecdotal mention of the potential use of EUS-LB in pediatric patients; however, no formal studies have been done to our knowledge. I have clarified this in the manuscript by adding “ – although to our knowledge, formal studies in pediatric populations are yet to be done.” We believe that this consideration is worth mentioning in the paper as it may spark future interest upon reading.

7. The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement.

- Thank you for your time and for reviewing our proposed publication. COI / Disclosure forms have been attached.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

Company Editor in Chief

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office’s comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, the author(s) must add a figure (medical imaging) to the manuscript. There are no restrictions on the figures (color, B/W)

- Thank you for your time and diligence in reviewing our proposed manuscript. We thank each of the Reviewers for their comments in improving the manuscript



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from an informational and stylistic standpoint. Each of the changes have been incorporated as above. Further, Figure 1 has been added to the manuscript, which depicts the echoendoscopic image of a biopsy needle passing into the left hepatic lobe. We believe that this will aid readership in understanding the technique of EUS-LB.



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Re-Reviewer's code: 02445721

SPECIFIC COMMENTS TO AUTHORS

The authors address all of the suggestions and questions.

Answer-Thank you!



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Re-Reviewer's code: 03476715

SPECIFIC COMMENTS TO AUTHORS

This minireview article is well-written and informative, which discusses the advance of endoscopic ultrasound-guided (EUS) liver biopsy in comparison to the traditional techniques, percutaneous (PC) or transjugular (TJ) liver biopsy. Since EUS-LB is safer and multi-functional, it has been popularly accepted in recent years. This review can help to introduce this technology to clinical practitioners. The authors have carefully revised the manuscript according to the peer-reviewers' comments. However, several parts of the edited manuscript still need to be revised and clarified as below:

1. In the "Methods of Liver Biopsy" section, page 7, "...EUS-LB was first described by in Mathew 2007" should be changed to "...EUS-LB was first described by Mathew in 2007".

Answer - Edited per reviewer comments

2. In the "Methods of Liver Biopsy -- Comparisons" section, page 10, the author cited a 2021 study by Patel HK et al., showing that EUS-LB liver biopsy was similar to TJ-LB in CPTs acquisition (EUS-LB vs. TJ-LB, $P = 1$). The abstract of this latest publication only provided this $P > 0.05$. Since I can not access the full text of this citation, the author should confirm this P-value.

Answer-Confirmed

3. In the "Technique of EUS-guided liver biopsy" section, page 10, the sentence "Since the inception of EUS-LB in 2007 with a Tru-Cut core biopsy needle (QuickCore, Cook Medical, Winston Salem, NC) multiple studies have aimed at optimizing EUS-LB technique." It should add a comma.

Answer - Comma added before multiple studies



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4. In the "Technique of EUS-guided liver biopsy" section, page 12, "A 2020 metanalysis" should change to "A 2020 meta-analysis".

Answer - Edited per reviewer comments

5. The style of the P-value should be uniform as "P" or "p" in the whole article.

Answer - Changed to "P" in whole article

6. In the "Future Research and Practice" section, page 18, the full name of the acronym LFTs should be provided.

Answer - Added full name