

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 64651

**Title:** New frontiers in liver ultrasound: from mono to multi parametricity

**Reviewer's code:** 02903429

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-02-21

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-02-24 14:59

**Reviewer performed review:** 2021-02-25 08:35

**Review time:** 17 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

I think the author should compare ultrasound with CT and MRI more specifically.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 64651

**Title:** New frontiers in liver ultrasound: from mono to multi parametricity

**Reviewer's code:** 05180942

**Position:** Editorial Board

**Academic degree:** MD, MSc

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** Turkey

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-02-21

**Reviewer chosen by:** Jin-Lei Wang

**Reviewer accepted review:** 2021-04-09 11:40

**Reviewer performed review:** 2021-04-10 19:58

**Review time:** 1 Day and 8 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

#### **SPECIFIC COMMENTS TO AUTHORS**

1. The expansion of FLL should be written (5th page, 3rd line). 2. The expansion of CEUS should be written (5th page, 4rd line). 3. It is sufficient to use only (HCC) on page 7, line 3 (abbreviation explained on page 4). 4. On page 10, at line 2, the (AC) abbreviation for attenuation coefficient should be made one sentence before.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 64651

**Title:** New frontiers in liver ultrasound: from mono to multi parametricity

**Reviewer's code:** 05418639

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Chief Doctor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-02-21

**Reviewer chosen by:** Jin-Lei Wang

**Reviewer accepted review:** 2021-04-07 06:37

**Reviewer performed review:** 2021-04-12 03:17

**Review time:** 4 Days and 20 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

1. The expansion of FLL(part of Doppler technique, last paragraph),CEUS(part of Contrast-enhanced US, 1st paragraph) and AC( part of Attenuation Imaging, 3rd paragraph) should be written. 2. Punctuation marks should be added in part of B-Mode, 2nd paragraph(when high-pressure US waves ( $>0.5$  MPa) travel through tissues, ...), part of Contrast-enhanced US, 2nd paragraph(In a multicenter study of 23,188 patients,...), part of Contrast-enhanced US, 4th paragraph from bottom(In cirrhotic patients,...).

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 64651

**Title:** New frontiers in liver ultrasound: from mono to multi parametricity

**Reviewer's code:** 03537453

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Chief Doctor, Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-02-21

**Reviewer chosen by:** Jin-Lei Wang

**Reviewer accepted review:** 2021-04-13 15:12

**Reviewer performed review:** 2021-04-17 13:30

**Review time:** 3 Days and 22 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

RE: New frontiers in liver ultrasound: from mono to multi parametricity. This is a well written review. Some concerns are listed as following: (1) Of title and content: "New frontiers in liver ultrasound: from mono to multi parametricity" aims to diagnostic ultrasonography and an integration of diagnosis and treatment based on diagnostic ultrasound system. Nevertheless, High-intensity-focused-ultrasound is different from diagnostic ultrasound and ultrasound mediates drug delivery (or genetic materials) by several aspects, so the reviewers suggested to cut the "High-intensity-focused-ultrasound" and related content off. (2) In the Abstract: Of "Such assessment is not only subjective, since quantitative data are also available." Rephrase this sentence to make it better. (3) In the Abstract: Of "High frequency ultrasound can also be deeply focused to liver tissue, targeting neoplasms and delivering enough energy to cause coagulative necrosis.". The "High frequency ultrasound" should be "High-intensity-focused-ultrasound". (4) Of "Page 4, down-to-up line 3-1: In this review we will focus on the main topics involving recents advances and modern applications in the field of liver ultrasound.", the word "recents" should be "recent". (5) Of "(kilopascal kPa) or wave speed (m/sec) can be calculated and usually displayed [57]. ", the wordf "(kilopascal kPa)" should be "(kilopascal, kPa)". (6) Of "Despite of being operator dependant,", the word "dependant" should be "dependent". (7) Of References "3 Bartolotta TV, Sidoti Pinto A, Cannella R, Porrello G, Taravella R, Randazzo A, Taibbi A. Focal liver lesions: interobserver and intraobserver agreement of three-dimensional contrast-enhanced ultrasound-assisted volume measurements. Ultrasonography. 2020. [PMID: 33080667 DOI: 10.14366/usg.20025]", it is not appropriate hear, and it had better be rplaced by other one. (8) Of "At CEUS, the main feature indicating a benign lesion is a sustained and prolonged contrast-enhancement in the portal-venous (i.e., 45-120 seconds after contrast injection) and late phases (i.e., 120



seconds up to 4-6 minutes after contrast injection) (Fig. 3) [25,26].” The starting of portal-venous has been addressed as “30-45s” in [Dietrich CF, Nolsøe CP, Barr RG, et al. Guidelines and Good Clinical Practice Recommendations for Contrast Enhanced Ultrasound (CEUS) in the Liver - Update 2020 - WFUMB in Cooperation with EFSUMB, AFSUMB, AIUM, and FLAUS. Aktualisierte Leitlinien und Empfehlungen für die gute klinische Praxis für CEUS der Leber. Ultraschall Med. 2020;41(5):562-585. doi:10.1055/a-11777-0530]. (9) Of “CEUS has also proved useful in the guidance, response assessment and detection of complications of interventional procedures [49-51].”. It seems that it should be “CEUS has also been proved useful...” (10) Of “US beam may be focused to directly ablate tumoral tissue or adequately modulated to deliver drugs and genetic material locally.”. the word “material” should be “materials”. (11) Of “Mastering this complex multiparametric technique is nowadays a cultural and practical challenge to be fully taken up in order to provide our patients the best care option in various liver diseases.”. This sentence had better be rewritten.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 64651

**Title:** New frontiers in liver ultrasound: from mono to multi parametricity

**Reviewer's code:** 05180942

**Position:** Editorial Board

**Academic degree:** MD, MSc

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** Turkey

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-02-21

**Reviewer chosen by:** Rajnish Kumar

**Reviewer accepted review:** 2021-05-30 13:21

**Reviewer performed review:** 2021-05-30 14:05

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

I think that the final version of the publication will contribute to the literature. Best



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regards.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 64651

**Title:** New frontiers in liver ultrasound: from mono to multi parametricity

**Reviewer's code:** 03537453

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Chief Doctor, Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-02-21

**Reviewer chosen by:** Rajnish Kumar

**Reviewer accepted review:** 2021-05-30 03:44

**Reviewer performed review:** 2021-05-30 14:22

**Review time:** 10 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

This is a well written review. Some concerns are listed as following: (1) In this review

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guidelines currently recommend CEUS as a useful imaging modality for the radiological work-up of HCC,>>>>” [31]” is not a best reference, and another guideline or recommendation should be added. To indicate Several. (7) The reviewer suggested that to add following into the article: >>>>>Compared with CT or MRI, CEUS is real-time dynamic enhancement, every second imaging can be read and tracted, so it’s able to avoid or markedly reduce imaging information losing. But it is not suitable for simultaneous evaluation of several liver focal lesions, and not suitable for large liver focal lesion of diameter > 10cm. (8) shearwave elastography (SWE)>>>>> shear wave elastography (SWE) (9) Liver stiffness £5 kPa (1.3 m/sec) has high probability>>>>??? (10) Recently, to overcome this issue, a consensus panel has proposed a manufacturer-neutral “rule of four” with values of 5, 9, 13, 17 kPa for ARFI assessment of liver fibrosis of viral etiologies and NAFLD. Liver stiffness £5 kPa (1.3 m/sec) has high probability of being normal; liver stiffness < 9 kPa (1.7 m/sec), without other known clinical signs, rules out compensated advanced chronic liver disease (cACLD); values between 9 kPa (1.7 m/sec) and 13 kPa (2.1 m/sec) are suggestive of cACLD (further test may be needed for confirmation); and values > 13 kPa (2.1 m/sec) are highly suggestive of cACLD. >>>>>>>Reference should be added. (11) The reviewer suggested to delete the following sentence: Another prospective study conducted on 104 patients Magnetic Resonance Elastography detected any fibrosis (stage 1 or more) with an area under the receiver operating characteristic curve (AUROC) of 0.82 (95% confidence interval [CI], 0.74-0.91), which was significantly higher than that of TE (AUROC, 0.67; 95%CI, 0.56-0.78) [44]. >>>>> It’s not suitable here. It’s not need to compare them for this parameter.