Reviewer Suggestions:

Hepatocellular Carcinoma: State of the Art Diagnostic Imaging

Reviewer #1:

"I want to congratulate all authors for this outstanding paper. It was a privilege to read it. The English language is perfect. . The abstract and the whole structure are well-designed. Although there is no table with summarized data (these tables are somewhat "necessary" in review-type articles), the text is very well organized and exciting to read. All sections have sufficient and clear presenting data"

RESPONSE: Thank you for your time and your review.

"In Contrast-Enhanced Ultrasound section; (such as SonoVue®, Definity®, SonoVue®). Sonovue seems to be twice."

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RESPONSE: Thank you for your concise and accurate review of this work. We appreciate that you noticed this grammatical error, and it has been resolved within the manuscript.

" In the same section; "…the CEUS-LIRADS was released…." It should be "CEUS LI-RADS."

RESPONSE: Thank you, we have adjusted this error in the manuscript.

"I can not find any "figure X" in the T1 mapping section."

RESPONSE: Thank you, this was an error and there is no image for the T1 mapping section. We removed this figure reference in the manuscript.

Reviewer #2:

"Congratulations to the authors for well written review."

    RESPONSE: Thank you for your thorough review!

"1. Diagnosis of HCC at an early stage has a favorable impact on outcome. 2. Many previously published articles have suggested that the screening for HCC in patients with cirrhosis is awfully inadequate even in developed countries. The reasons are multifactorial but the major being lack of co-ordination between clinicians and radiology scheduling. 3. In developing countries and underdeveloped world cost, availability of radiology services and trained radiologists adds to dismal rates of HCC screening/detection. How can this be improved? The authors can share their thoughts about this pertinent issue. 4. Though the review is about the state of art diagnostic imaging I request the authors to kindly propose a flowchart/ algorithm for HCC screening that could be universally feasible and acceptable."

    RESPONSE: Surveillance is a crucial component to HCC and the multiple modalities that can be used for its diagnosis. While we also agree with the reviewer that surveillance methods are not necessarily within the scope of the main body of the manuscript, we agree that it is pertinent and should be mentioned. Therefore, within in the body of the section we provided some potential solutions to improving, at least in part, surveillance outcomes for HCC.

    "While the objective of this review is to elucidate the latest advancements in technological imaging for the screening and diagnosis of HCC, it is important to note the efficacy of detection can be limited due to multifactorial screening challenges. In fact, less than 1 in 5 patients with cirrhosis receive surveillance

screening for HCC.[20] Previous reviews have extensively examined the numerous challenges encountered during the screening process, including the inability to properly stratify high-risk patients, the presence of socio-economic and logistical impediments to accessing healthcare, as well as training and detection limitations using conventional imaging techniques, as previously discussed. One of the most common attributable factors to surveillance underuse includes lack of surveillance orders or unrecognized cirrhosis.[5] Therefore, strategies to improve education and integrating primary care providers in surveillance efforts can have a drastic and meaningful effect on rates of patients undergoing HCC screening.[21] The implementation of patient-centered outreach programs reminder protocols or embedding best-practice advisories within the electronic health record may be solutions to improve barriers of patients undergoing surveillance. [5,21]The decision to determine which patients should be screened has also been discussed and the development have scoring system that refine and improve risk stratification have been proposed.[22] Other methods have also focused on improving surveillance outcomes and detection rates, such as utilizing serological biomarkers (e.g. AFP) either as a single screening modality or in concert with imaging to improve sensitivity, at the potential cost of increase in rates of false positivity. The use of biomarkers may also be especially helpful for smaller HCCs, not easily visible with ultrasound.[22]"