

Manuscript: Emerging Curative-Intent Minimally-Invasive Therapies for Hepatocellular Carcinoma

Reviewers' Comments to the Authors:

Reviewer 1

- **Comment 1:** *The review may be structured in a better way that technique, indication, contraindications and complications related to a particular therapy may be included under the sub heading only.*

Response: Thank you for this suggestion. We have reorganized the manuscript to incorporate these changes. The former section Introduction to Locoregional Therapies has been removed and relevant paragraphs from it have been incorporated into the corresponding subsections as suggested.

Comment 2: *Important studies LEGACY and DOSISPHERE trial may be explained in a tabular format.*

Response: Thank you for this suggestion. A table comparing the LEGACY study and DOSISPHERE trial has been added as Table 2.

- **Comment 3:** *Cryoablation should also be included in minimally invasive therapy as this is important for peripheral lesions near to liver capsule.*

Response: Thank you for this suggestion. We have expanded the description of cryoablation in the “Ablation” section.

- **Comment 4:** *The new BCLC 2021 update is now available. If feasible may be included.*

Response: Thank you for this highly relevant feedback. Multiple sections of the manuscript were edited to include the recent incorporation of TARE into the latest BCLC guidelines, resulting in a stronger and more relevant manuscript. A figure reflecting the most recent guidelines has been added.

Reviewer 2

- **Comment 1:** *The title is appropriate and reflects the main subject of the manuscript. The abstract summarizes and reflects the work described in the manuscript.*

Response: Thank you!

- **Comment 2:** *The key words reflect the focus of the manuscript.*

Response: Thank you!

- **Comment 3:** *The manuscript adequately describes the background, present status and significance of the study.*
Response: Thank you!
- **Comment 4:** *The manuscript describes the methods in adequate detail.*
Response: Thank you!
- **Comment 5:** *The manuscript interprets the findings adequately and appropriately, highlighting the key points concisely, clearly and logically.*
Response: Thank you!
- **Comment 6:** *The tables are sufficient and of good quality and appropriately illustrative of the paper contents.*
Response: Thank you!
- **Comment 7:** *The manuscript cites appropriately the latest, important and authoritative references in the introduction and discussion sections.*
Response: Thank you!

Science Editor

- **Comment 1:** *This review was well written and informative.*
Response: Thank you!
- **Comment 2:** *Tables showing summary of results with transarterial treatment may help readers to understand.*
Response: Thank you for this suggestion. A summary of results with transarterial radioembolization is included in Table 1- we focused on overall survival at 5 years and local tumor progression at 2 and 5 years for HCC tumors of both ≤ 3 and ≤ 5 cm. Disease-free survival was not included for TARE as not enough of this data is available in the literature. We chose these specific datapoints to compare the efficacy of TARE with established HCC treatments.

Company Editor-In-Chief

- **Comment 1:** *I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Hepatology, and the manuscript is conditionally accepted.*
Response: Thank you!
- **Comment 2:** *Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of*

the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response: Thank you for bringing this to our attention. This change has been made to Table 1 in the manuscript.