

July 04, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 3729-edited.docx).

**Title:** Imaging appearance of treated Hepatocellular Carcinoma

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**Name of Journal:** *World Journal of Hepatology*

**ESPS Manuscript NO:** 3729

We updated format, added author contributions, modified abstract results and added core tip; moreover we reformat all the reference numbers as indicated. As requested by Editor and reviewers, the manuscript has been revised by a native English speaker with extensive experience in medical and scientific editing, and English style and orthography were further checked.

We modified text according to reviewer comments, and we wish to thank the editor and two referees for the helpful comments on the earlier version of this paper.

Below you find the changes we have done, as point-by-point reply. In the letter, all sentences added to the revised version are underlined.

We hope that the study is now acceptable for publication, and look forward to hearing from you soon.

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewers:

## **Reviewer 1**

#1

*In the Radiofrequency ablation section, the author mentions that if the arterially enhancing zone is small and nodular, a correct characterization may be difficult and a 3 to 6 months follow-up is recommended. Does the evident base support the duration of 3 to 6 months? Or may give it a reference should be better.*

As requested, we added a reference to support this sentence (ref. 16)

Park Y, Choi D, Lim HK, Rhim H, Kim YS, Kim SH, Lee WJ. Growth rate of new hepatocellular carcinoma after percutaneous radiofrequency ablation: evaluation with multiphase CT. AJR Am J Roentgenol. 2008 Jul;191(1):215-20. doi: 10.2214/AJR.07.3297. PubMed PMID: 18562748.

*#2 In the Percutaneous ethanol injection section, there is unsatisfied description of the percutaneous ethanol injection such as the tumor located at the pericholecistic, subphrenic, and closely contact the main vessel, in which RFA is not suitable to perform.*

As requested, we better clarified PEI indications as follows:” It is a well-tolerated, inexpensive procedure with few adverse effects. This alternative procedure may be performed in patients with small HCCs, in those which RFA is not suitable to perform by tumor location<sup>[18]</sup>. In fact, some tumors are located at risky sites (defined as less than 5 mm from a large vessel or an extrahepatic organ, near gallbladder, or in subphrenic locations) and RFA treatment can incur severe complications. In addition, in tumors larger than 2 cm in size, initial RF may leave a tiny nest of viable tissue that will easily be ablated by ethanol with a relevant saving of resources.”

*#3 The followed-up image appearance of this kind of lesions need descript more detail.*

As requested we added details for Figure 8 legend, as follows: “Incomplete HCC necrosis after PEI. (a and b) Arterial and portal venous CT obtained 1 month after treatment shows that approximately 10-20% of the tumor, located in the dorsal and lateral portion, is still viable as demonstated by the presence of enhancement in arterial phase (white

arrow) and hypoattenuation ("wash-out") on portal venous phase. The majority of tumor does not show enhancement (black arrow) as a result of the treatment. "

*#4 The image appearance of TACE with drug eluting beads (DEB) is a hot topic recently. Tumors shrinkage without enhancement of the contracted CT should be difficult to confirm the viable part of the treated hepatocellular carcinoma need more descript.*

As requested, we better clarified this relevant issue, as follows: "In addition, absence of iodized oil does not mask arterial enhancement<sup>[32]</sup>, allowing easier assessment of residual, viable tumor in comparison to traditional TACE performed with iodized oil (Fig. 10)."

*#5 Many space typing error found in the text and the legends.*

As requested by Editor and reviewers, the manuscript has been revised by a native English speaker with extensive experience in medical and scientific editing, and English style and orthography were further checked.

*#5 Finally, there are 34.9% (14/39) references more than 5 years recently should be update if possible.*

As requested, many references have been updated.

## **Reviewer 2**

*#1 The language needs polishing.*

As requested by Editor and reviewers, the manuscript has been revised by a native English speaker with extensive experience in medical and scientific editing, and English style and orthography were further checked.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

Sincerely yours,

A handwritten signature in purple ink, appearing to read 'G. Cabibbo'.

**Giuseppe Cabibbo, MD, PhD**

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