Porto Alegre, 22 february 2015.

**Title**: Non-invasive assessment of non-alcoholic fatty liver disease with imaging techniques: focus on liver scintigraphy

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**Name of Journal:** *World Journal of Gastroenterology* **(ID 00053580)**

Manuscript number 15257

Dear Editor of WJG

We thank you very much for the comments from the reviewers. All of them are of great importance and interest to us, and we tried to address them by answering or justifying all questions. The modifications are highlighted in the text in yellow. We hope we have met the reviewers' expectations in regards to the questions, and also that you appreciate to read the manuscript again.

**Reviewer 1 (2447023)**

In this paper, the authors review imaging techniques used in diagnosis of nonalcoholic fatty liver disease (NAFLD) with emphasis on liver scintigraphy. This topic is important because NAFLD is rapidly increasing worldwide, and imaging diagnosis is noninvasive. Furthermore, the manuscript is generally well written. However, the authors should consider the following points.

1. The quality of English is insufficient. The authors should seek assistance of a native English speaker.
   *Answer: The manuscript was submitted to a native English speaker recommended by the WJG (AMEditor)*

2. I advise the authors to make a Table that summarizes advantages and disadvantages of each imaging modality to make the manuscript more intelligible.

   *Answer: We agree this is a useful idea, and a Table was prepared (Table 1 on page 24 and cited on page 14 - highlighted in yellow).*

**Reviewer 2 (2098400)**

This manuscript was well written about the methods of non-invasive methods of NASH. But there are some problems in several parts.

1. In MRI explanation, MRS is the most famous measurement method of fat content. So more details about this method should be explained.

   *Answer: The modifications were done and can be seen in page 7 – highlighted in yellow.*

2. To quantify the fibrosis MRI were also widely used and MRE is the representative method but as you mention, it is much expensive and are used in restrict facilities. There are several papers that try to evaluate the fibrous stages by using EOB enhanced MRI which widely used in general Hospitals. The authors must introduce these methods (there are a lot of papers and a lot of methods which use several portions as a control (ex, muscle, spleen vertebral disk etc. but the paper that evaluate the utility between several controls were published, 2013 J gastroenterology and hepatology).

   *Answer: Although there are no studies evaluating NAFLD in humans with this method until now (the study of Nojiri et al - included as reference 33 - evaluated patients with hepatitis C), we agree it should be interesting to be mentioned in the text (page 7 – highlighted in yellow).*

3. About FDG-PET there are few scientific evidences because the data which the authors referred did not use certain NASH so the confidence is low. I think this part should be deleted.

*Answer: We agree with the reviewer that the confidence of the sole published study that evaluated this method is low. However, exactly because of this fact (only 1 study), with understand this is an important information, but the critical to the bias was made). So we intend to maintain this part, if the reviewer agree.*

4. About Technetium-99m colloid method the authors declared the usefulness of its method but all the papers that was referred had small data and there are no data which compare the methods and other previous one. So the authors should not say the usefulness so strongly. It seems to have some bias.
   *Answer: A comment about this problem was added in the text (page (page 13 – highlighted in yellow).*

5. There are a lot of paragraphs in the manuscripts. Please collect and combine some paragraphs
   *Answer: The study was reviewed and the number of paragraphs was reduced*

**Reviewer 3 (9221)**

The paper is complete and well conducted. However, it should be improved by adding explicative tables that compare the sensitivity-specificity of the various imaging results.

*Answer: This was also suggested by other reviewer and is covered in Table 1 (page 24 and cited on page 14 - highlighted in yellow).*

**Reviewer 4 (2541357)**

NAFLD has become one of the most prevalent chronic liver diseases nowadays. Its association with components of the metabolic syndrome and cardiovascular mortality has drawn attention of the scientific community. It has a broad spectrum ranging from simple steatosis to cirrhosis and hepatocellular carcinoma making mandatory the staging of the disease. Liver biopsy is the

reference standard, but it is an invasive method and may cause complications. The authors reviewed the contributions of imaging techniques in the diagnosis of NAFLD considering its applicability, efficiency and limitations. The approach is clear, objective and allows an interesting update on the issue.

*Answer: The authors thanks the comments of the reviewer.*

Porto Alegre, 13 march 2015.

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Dear Editor of WJG

The reviewer 2 (2098400) asked to delet the paragraph talking about the FDG-PET. This question was solved, and the paragraph was removed from page 12. Also, the references were reordered.

I hope this is suitable for publication. But if there is any disagreement, please contact me again

Best regards

Cristiane Tovo