

ANSWERING REVIEWERS



December 9 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6057 TEXT R2).

Title: Contrast Enhanced Ultrasound (CEUS) with Quantitative Perfusion Analysis for Objective Characterization of Pancreatic Ductal Adenocarcinoma: feasibility study.

Author: D'Onofrio M, Canestrini S, Crosara S, De Robertis R, Pozzi Mucelli R

Name of Journal: *World Journal of Radiology*

ESPS Manuscript NO: 6057

I found all the comments useful adding the suggestions in the text.

- No patient was excluded from the study.
- Discussion: "CTP" - please write out this abbreviation. OK
- Please mention the figures within the text. OK
- Linguistic/stylistic problems. OK
- The patients were selected prospectively during a short period of time and only lesion location and size, together with final diagnosis, were considered to understand the feasibility of the quantification CEUS study of ductal adenocarcinoma. I have no answers to questions not on the object of the study like the following: how does CEUS quantitative perfusion analysis work for each of the ten patients? Is the result correlated with tumor location and sizes? Is there a minimum or maximum limit for the tumor size that can be studied with this method? For diagnosis purpose, is there data from normal people? How does the measurement variation affect the results?
- The two figures were labeled correctly. They are both Fig 1ab and the ROI is present in the color map.
- The software used analyzed the time-intensity curve just using logarithmically compressed data. This as a limit to be overcome is now discussed in the discussion section.

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

1 In The discussion part, we need more comparison of the study with perfusion ct scan and MRI.

Sentences dedicated to CT and MRI perfusion has been added moved to the discussion section (underlined at page 5).

2 However, I have some concern about the study design, as the authors do not specify the type of software used to analyze the time-intensity curve. It is not clear if linear raw data (or linearised log-compressed data) were analyzed, or just logarithmically compressed data were used to analyze the time-intensity curve.

The software used analyzed the time-intensity curve just using logarithmically compressed data. This as a limit to be overcome is now discussed in the discussion section (underlined at the end of page 5).

3 How were the patients selected for this study? Were tumor location and size the only consideration? The averaged results does not represent the results from each case. How does CEUS quantitative perfusion analysis work for each of the ten patients? This study has small amount of cases, so data from each of the 10 patients studied can provide more information. Is the result correlated with tumor location and sizes? Is there a minimum or maximum limit for the tumor size that can be studied with this method? For diagnosis purpose, is there data from normal people? Does the ROI location in parenchyma affect the conclusion? How does the measurement variation affect the results? Without the error study, I would doubt the validation of the proposed diagnosis method. Where in the manuscript you refer to the figure? The two figures were not labeled correctly. Are they both Fig 1? Where do I find "ROI in a" or "ROI in b"? Without the questions answered and data added, I would not be able to judge the validation of the study."

The patients were selected prospectively during a short period of time and only lesion location and size, together with final diagnosis, were considered to understand the feasibility of the quantification CEUS study of ductal adenocarcinoma. I have no answers for the other questions not on the object of the study like the following: how does CEUS quantitative perfusion analysis work for each of the ten patients? Is the result correlated with tumor location and sizes? Is there a minimum or maximum limit for the tumor size that can be studied with this method? For diagnosis purpose, is there data from normal people? How does the measurement variation affect the results? Regarding the two figures were labeled correctly. They are both Fig 1ab and the ROI is present in the color map.

4 Were any patients excluded from the study (e.g. patients with cardiac risk factors)?

No patient was excluded from the study.

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

Sincerely yours,

Mirko D'Onofrio

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