

August 27, 2013

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 4126-review.doc).

Title: CONTRAST-ENHANCED ULTRASONOGRAPHY IN PERIPHERAL LUNG CONSOLIDATIONS. WHAT'S ITS ACTUAL ROLE?

Author: Sergio Sartori, Simona Postorivo, Francesca Di Vece, Francesca Ermili, Davide Tassinari, Paola Tombesi

Name of Journal: *World Journal of Radiology*

ESPS Manuscript NO: 4126

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 00225358

1. The Methods and Results sections have been structured according to the Reviewer's suggestion.
2. The filled STARD check-list has been enclosed and table 4 has been modified to add 95% Confidence Intervals. However, some points of the check-list were not applicable to this manuscript

Reviewer 00053451

1. The US contrast agent has been specified in the Abstract
2. The sentence in Page 2, lines 12-14, has been modified and made better understandable
3. NYHA has been defined and a reference (#15) has been added
4. Low- and high-frequency convex and linear transducers (indicatively, from 3.5 to 7.5 and even 10 MHz) are commonly - and from a long time - used to investigate the pleura and lung, according to the target to be evaluated and the patient's body size. Our US technique of examining the lung did not differ from that widely reported in literature. We have briefly explained this point, and have added three references (#16, 17, 18)
5. PT (not PA) and SP are the initials of the two authors who performed the examinations. In this revised version, we have moved the initials from the end of the sentence to "one of two physicians", to make this indication more understandable. However, if you think it is pleonastic, we can remove the initials from the text
6. The arterial phase was defined as the twenty seconds following the appearance of the first microbubbles in the lesion or the surrounding parenchyma (or the chest wall, liver, or spleen), according to the definition of the arterial phase in the abdominal organs. This explanation has briefly been added to the text
7. The section Results has been organized using subheadings, according to also the suggestion of the Reviewer 00225358
8. Median follow-up and range have been added
- 9-10. No difference in contrast effect between the two kinds of transducer was observed, and the same acoustic power was used for both transducers. These informations have been added in the sections Results and Material and methods, respectively
11. The paragraph has been modified. Of course, our opinion on CEUS is quite positive...

12. Table 1 has been reorganized

Reviewer 0070200

Sorry, but I don't agree with the Reviewer's remarks about the methodology of the study:

1. He states that the section Material and Methods is too long and confusing. This is not a methodological problem, but, in case, a drafting problem. It is true that the section is very long, but the study design was complicated, and we described it in detail to make it better understandable. However, we have tried to improve and shorten the section, according to the constructive criticisms of the other two Reviewers.
2. Of course, the parameters were obtained via visual assessment. Likewise, CEUS examinations of abdominal organs are worldwide performed via visual assessment of the enhancement and wash-out (if any). For instance, the visual assessment of a marked enhancement in the arterial phase, followed by slight wash-out in the portal venous phase, is considered diagnostic of hepatocellular carcinoma by the guidelines of several Scientific Societies in both western and eastern countries dealing with the diagnostic work-up of focal liver lesions in cirrhotic patients. Are these guidelines methodologically wrong, in the Reviewer's opinion?
The quantitative assessment of the wash-in and wash-out curves (the so-called D-CEUS) is a quite interesting issue and we believe it will become a very useful tool in the diagnostic work-up of many focal lesions in the next future, but to date it is still under evaluation and no definitive data on both technique and reliability are available in literature. Our pilot study aimed at evaluating if CEUS could play some role in the differential diagnosis of peripheral pulmonary lesions, it would be fairly excessive to perform also a quantitative analysis of CEUS parameters...
3. The analysis of the interobserver variance was done, and was reported in the lines 2-5 of the section Results of the original version of the manuscript.

3 References and typesetting were corrected

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

Sincerely yours,

A handwritten signature in black ink, appearing to read 'Sergio Sartori'.

Sergio Sartori, MD

Section of Interventional Ultrasound, Department of Medicine

St Anna Hospital

I-44100 Ferrara, Italy

Phone: +39-0532-236551

Fax: +39-0532-239613

e-mail: srs@unife.it