

## Point by point responses to reviewers of Manuscript #74264 - by De Rosa et al.

We are grateful to the editors and reviewers for appreciating our work and for their constructive observations aimed to enhance the quality of the manuscript.

**Reviewer #1.** This work is interesting. Several aspects discussed are the research hotspots in the application of artificial intelligence in medical image.

1. It is recommended that charts and discussion paragraphs be placed together for easy reading and better understanding.

Answer: We agree with the reviewer's comment that a more appropriate position of charts in the final publication of the manuscript is required. In submitting the manuscript, we followed the guidelines of the journal on the position of appearance of charts and tables in the uploaded file (which we believe to be provisional in this evaluation phase).

2. The contents of the discussion chapter and the previous corresponding discussion points are mostly repeated, which makes the content redundant and reduces the compactness of the article.

Answer: According to the reviewer's suggestion, we extensively revised both the Results and Discussion sections, by shortening the text and removing redundant concepts. We hope that such revised sections are now more readable and the article is more compact.

3. Can you add to the discussion on the use of evaluation indicators in these related work? I think this is also a very meaningful work.

Answer: We totally agree with the reviewer that the use of evaluation indicators deserve a mention. The manuscripts selected in this paper used DL techniques for heterogeneous targets, ranging from diagnostic to prognostic purposes or evaluation of the severity of the pathology. This scatter in the intent makes any comparison or analysis very difficult.

However, we believe the reviewer raised an important point and, therefore, we added the following sentence into the discussion:

*"Finally, another important issue to mention is the use of the quantitative evaluation indicators and the analysis of the benchmarking techniques adopted to evaluate the effectiveness of the proposed methods. Unfortunately, the tools examined in the selected manuscripts had very heterogeneous targets (Table 1, Main results column), ranging from diagnostic to prognostic purposes or assessment of disease severity. This dispersion of intent and the few articles published in the literature at present make any comparison or analysis very difficult."*

**Reviewer #2.** I read the article with great interest. The material presented in the article has a high scientific level.

1. Ultrasound of the lungs allows detecting not pneumonia, but interstitial lesions in the lungs characteristic of COVID-19 (interstitial syndrome, consolidation). It should be remembered that these lesions are not a specific ultrasound sign of pneumonia in COVID-19. Many conditions (e.g. pneumonia, malignancy, pulmonary embolism, atelectasis, contusion, aspiration) may result in change of the lung tissue aeration.

Answer: We agree with the reviewer that ultrasound features found in COVID patients may also be present in other pathological conditions as outcome of changes in lung tissue aeration. This concept is in line with the low specificity of LUS in COVID patients recognized by the scientific community. Following the reviewer's comment, we found it appropriate to add the following sentences in the introduction to better specify this concept and make this limit for LUS more explicit.

*"On the other hand, the distinctive LUS features (B-lines, consolidations, pleural thickening and brokening) observed in patients with varying severity of COVID pneumonia are similar to the features seen in patients with pneumonia of different aetiologies. Indeed, a recent review<sup>[17]</sup> on ultrasound findings of LUS in COVID-19 demonstrated that LUS has high sensitivity and reliability in ruling out lung involvement, but at the expense of low specificity. Therefore, especially in the case of low prevalence of the disease, at present LUS cannot be considered a valid gold standard in clinical practice."*

2. The authors rightly point out that computed tomography has specificity limitations. However, ultrasound has the same specificity limitations.

Answer: This is a remarkable observation. In line with the reviewer's comment, we amended our sentence as follows:

*"In the last few years, lung ultrasound (LUS) technique has become increasingly popular and a good option for real-time point-of-care testing, with several advantages making it a valuable tool in the fight against COVID-19<sup>[13]</sup>, although it has specificity limits comparable to those of chest CT. "*

3. In the literature reference [16] I did not find information about high sensitivity in the differential diagnosis of various lung pathologies (viral versus bacterial).

Answer: We thank the reviewer for punctuating this point. It was our oversight to insert the wrong citation. The reference has been substituted with a new and more appropriate one.

## **Answers to the Editorial Office's comments**

**(1) Science editor:** Lung ultrasound (LUS) technology has been proved to be very valuable. The author discusses its role and limitations in the development of covid-19 pneumonia. The manuscript is well written and can be helpful for the readers to ameliorate the diagnostic and therapeutic approach for this scenario.

It is unacceptable to have more than 3 references from the same journal. To resolve this issue and move forward in the peer-review/publication process, please revise your reference list accordingly.

Answer: According to the Editor's advice, we have replaced three citations published in the same journal (i.e., #8, 9 and 10) with others (of equal appropriateness) published in different journals. In addition, we verified that in the revised version of the manuscript there were a maximum of 3 references from the same journal.

(2) *Company editor-in-chief*: I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the Artificial Intelligence in Medical Imaging, and the manuscript is conditionally accepted.

I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors...

Answer: According to the suggestions, we provided a decomposable Figure (reporting the copyright information) in a single PowerPoint file. Likewise, we provided standard three-line tables organized in a single Word file, following the described criteria.