### Proposal for international standardization of the use of lung ultrasound for COVID-19 patients; a simple, quantitative, reproducible method

#### Category: Technical Innovation

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Short running title: LUS acquisition protocol and scoring for Covid-19

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#### Summary

Growing evidences are showing the usefulness of lung ultrasound in patients with COVID-19. Sars-CoV-2 has now spread in almost every country in the world. In this study, we share our experience and propose a standardized approach in order to optimize the use of lung ultrasound in covid-19 patients. We focus on equipment, procedure, classification and data-sharing



#### Introduction

A decade of clinical (1-4) and physical studies (5-9) clearly showed that lung ultrasound (LUS) is able to detect interstitial lung disease, subpleural consolidations and acute respiratory distress syndrome from any etiological cause. New evidences from published studies (10-12), national and international organization statements, and informal case discussions with internationally recognized experts are showing the usefulness of LUS for the management of patients with COVID-19 pneumonia, from diagnosis monitoring follow-up. to and To date, available medical treatments for COVID-19 pneumonia include anti-HIV drugs, idrossicloroquine; ventilatory support, prone positioning and extracorporeal membrane therapy represent the supports for critical patients. However, recent findings suggest than anti interleukin-6 monoclonal antibodies can be useful in blocking the inflammatory cascade involved in lung inflammation during COVID-19 infection. Evidences also suggest that the earlier we treat the better patients improve with treatment (13). Therefore, LUS could be useful, being performed on several time points from clinical diagnosis, in determining early lung involvement during paucisymptomatic phase of the disease and potentially playing a role in treatment decisions. Funding organizations are starting to support clinical trials; in this regard, lung ultrasound can be used to monitor lung involvement during a specific treatment. Importantly, LUS can be used in every setting, including low to middle income countries, allowing the reduction of disparities in trials participation, since secondary level imaging studies (such as CT scan) are not everywhere easily accessible.

Therefore, this global emergency need a global unified approach, speaking all researchers the same language. For this reason, we propose a standardization for the international use of LUS for the management of COVID-19 patients.

Our LUS COVID-team is made by Italian experts in lung ultrasound currently involved in the clinical management of COVID-19 patients in different Italian areas, including the heavily involved cities of Northern Italy. Moreover, experts in ultrasound physics and image analysis are part of the team.

The team developed a standardized approach regarding equipment and acquisition protocol. Moreover, the team proposed a scoring system for severity classification. To this aim, clinicians shared 30 cases of confirmed COVID-19 on an anonymized virtual database, for a total of about 60000 frames up to date. All team members discussed their clinical cases through online meetings. Images were reviewed by all team members, blinded to the clinical background, and listed in classes of severity of lung involvement based on LUS images. At the end of this process, a

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biomedical engineer expert in lung ultrasound collected the data and suggested a lung ultrasound grading system for COVID-19 pneumonia. Again, the biomedical engineer re-submitted the images grouped in different classes of severity to the study members, blinded of clinical data, to review again the images and evaluated agreement regarding the LUS scores. The score was defined only when all team members agreed.

#### Methods

In the setting of COVID-19, wireless probe and tablets represent the most appropriate ultrasound equipment. These devices can easily be wrapped in single use plastic covers reducing the risk of contamination and making easy the sterilization procedures (14). Such devices are much less expensive than usual ultrasound machines including the portable ones.

In case of unavailability of these devices, portable machines dedicated to the exclusive use of COVID-19 patients can be used, although maximum care for sterilization is necessary. In these cases, probe and keyboard covers are anyway suggested, and sterilization procedures necessary following last recommendations (15).

Sharing our real world experience in performing LUS in COVID-19 patients, we propose two different ways of performing lung ultrasound with pocket devices aiming to reduce the exposition of health workers to cases (14).

One operator uses the probe performing the ultrasound; the other one keeps the tablet and freezes images/videos. The second operator can be either in the room being at safe distance from the patient (acout 2 meters), or even remain outside the door communicating by phone-call with the operator one in order to optimize the quality of images. Potentially, this last approach can reduce the operator-dependence of the ultrasound since the second operator blindly selects the images, being unaware of the clinical conditions of the patient. The two operators will follow an agreed, tested and standardized images acquisition protocol.

#### Acquisition protocol

Fourteen areas (three posterior, two lateral and two anterior) should be scanned per patient for 10 seconds along the lines here indicated. Scans need to be intercostal, as to cover the widest surface possible with one scan.

Standard sequence of evaluations is proposed using landmarks on chest anatomic lines. Echographic scans can be identified with a progressive numbering starting from right posterior basal regions. For patient able to maintain the sitting position:

- 1. Right basal on paravertebral line above the curtain sign
- 2. Right middle on paravertebral line at the inferior angle of shoulder blade
- 3. Right upper on paravertebral line at spine of shoulder blade
- 4. Left basal on paravertebral line above the curtain sign
- 5. Left middle on paravertebral line at the inferior angle of shoulder blade
- 6. Left upper on paravertebral line at spine of shoulder blade
- 7. Right basal on mid-axillary line below the internipple line
- 8. Right upper on mid axillary line above the internipple line
- 9. Left basal on mid-axillary line below the internipple line
- 10. Left upper on mid axillary line above the internipple line

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- 11. Right basal on mid-clavicular line below the internipple line
- 12. Right upper on mid-clavicular line above the internipple line
- 13. Left basal on mid-clavicular line below the internipple line
- 14. Left upper on mid-clavicular line above the internipple line

In case of performance of LUS in critical care settings (such as patients on invasive ventilation) and for patients that are not able to maintain sitting position, the posterior areas might be difficult to be evaluated. In these cases, the operator should try to have a partial view of the posterior basal areas, currently considered a "hot-area" for COVID-19, and however, start echographic assessment from landmark number 7.

se Convex or Linear probes, according to the patient's body size

• Use single focal point modality (no multifocusing), setting the focal point on the pleura line. Employing a single focal point, and setting it at the right location, has the benefit to optimize the beam shape for sensing the lung surface. At focus, the beam has the smallest width as is therefore set to best respond to the smallest details.

• Keep the mechanical index (MI) low (start from 0.7 and reduce it further if allowed by the visual findings). High MIs, employed for a long observation time, may result in damaging the lung [16].

• Avoid as much as possible saturation phenomena, control gain and diminish MI if needed (see example of lung ultrasound images in the figures). Saturation phenomena occurs, e.g., when the signal streight of the echo signals is too high for the receiving electronics to be converted into electrical signals conserving a linear relation with the pressure amplitude. This has the effect of distorting the signals, and produces images where the dynamics of the actual signal is lost. The

visual appearance of this phenomenon is the presence of areas which are completely white. In this case it is therefore not possible to appreciate local variations in the response to insonifications.

• Avoid the use of cosmetic filters and specific imaging modalities such as Harmonic Imaging, Contrast, Doppler, Compounding.

• Achieve the highest frame rate possible (e.g. no persistence, no multifocusing)

• Save the data in DICOM format. In case this is not possible, save the data directly as a video format. Visual findings, especially when related to very small alterations, do not appear on every frame. It is thus advantageous to acquire movies, where the lung surface below the landmark can be monitored for few seconds during breathing.

#### Scoring procedures (see figure 2 to 5)

- Score 0: The pleura line is continuous, regular. Horizontal artifacts (A-line) are present. These artifacts are generally referred as A-lines. They are due to the high-reflectivity of the normally aerated lung surface, and characterize the visual representation of the multiple reflections happening between the ultrasound probe and the lung surface itself [3,5,7].
- Score 1: The pleura line is indented. Below the indent, vertical areas of white are visible. These are due to local alterations in the acoustical properties of the lung, as for example the replacement of volumes previously occupied by air in favor of media which are acoustically much more similar to the intercostal tissue (water, blood, tissue). This phenomenon opens channels accessible to ultrasound, which can explain the appearance of the vertical artifacts [3, 5, 7].
- Score 2: The pleura line is broken. Below the breaking point, small to large consolidated areas (darker areas) appear with associated areas of white below the consolidated area (white lung).
  - The darkening of the consolidated areas signals the loss of aeration and the transition of these areas towards acoustic properties similar to soft tissue over the entire area represented by the consolidation itself. Beyond the consolidations, the appearance of areas of withe lung signals the presence of areas not yet fully deaerated, where air inclusions are still present but embedded in tissue like material. This highly scattering environment can explain this peculiar pattern [3, 5, 7].
- Score 3: The scanned area shows dense and largely extended white lung with or without larger consolidations

At the end of the procedure, the clinician will write for each area the highest score obtained (e.g quadrant 1, score 2; quadrant 10, score 1; and so on).

#### International database for data storage, image analyses, artificial intelligence studies

We strongly encourage to the scientific community the embrace the development of a protected, internationally available database that allow uploading images and videos of COVID-19 patients (X-ray, ultrasound and CT scan). This will speed the development of dedicated pattern recognition algorithms able to recognize COVID-19 related pathological findings, allow for the comparison between different centers, and foster the development of telemedicine programs (including remote evaluation of images, clinical advices and case discussions) and telematics teaching programs.

Here the link to our database (https://covid19.disi.unitn.it/iclusdb).

#### **Discussion and Conclusions**

COVID-19 is a worldwide health challenge, involving not only health, but also economics and social behaviors. For the first time in the era of modern medicine, the whole world is facing the same threat. This can give us the opportunity to change our research approach: time has probably come to share our knowledge and planning the best care all together. The aim of this paper is thus to share our experience and to propose a standardization with respect to the use of LUS in the menagement of COVID-19 patients. The paper introduces to the acquisition protocol, detailing landmarks and imaging settings, and presents the scoring mechanism developed within our group. We further emphasize on the need for a shared database, necessary to foster further developments and to disseminate the results achieved.

References

- Mojoli F, Bouhemad B, Mongodi S, Lichtenstein D. Lung Ultrasound for Critically Ill Patients. Am J Respir Crit Care Med. 2019 Mar 15;199(6):701-714.
- 2- Mayo PH, Copetti R, Feller-Kopman D, Mathis G, Maury E, Mongodi S, Mojoli F, Volpicelli G, Zanobetti M. Thoracic ultrasonography: a narrative review. Intensive Care Med. 2019 Sep;45(9):1200-1211

- 3- Soldati G, Demi M, Smargiassi A, Inchingolo R, Demi L. The role of ultrasound lung artifacts in the diagnosis of respiratory diseases. Expert Rev Respir Med. 2019 Feb;13:163-172.
- 4- Soldati G, Smargiassi A, Mariani AA, Inchingolo R. Novel aspects in diagnostic approach to respiratory patients: is it the time for a new semiotics? Multidiscip Respir Med. 2017 Jun 27;12:15
- 5- Demi M, Prediletto R, Soldati G, Demi L. Physical Mechanisms Providing Clinical Information From Ultrasound Lung Images: Hypotheses and Early Confirmations. IEEE Trans Ultrason Ferroelectr Freq Control. 2020 Mar;67(3):612-623
- 6- Demi L, van Hoeve W, van Sloun RJG, Soldati G, Demi M. Determination of a potential quantitative measure of the state of the lung using lung ultrasound spectroscopy. Sci Rep. 2017 Oct 6;7(1):12746.
- 7- Soldati G, Demi M, Inchingolo R, Smargiassi A, Demi L. On the Physical Basis of Pulmonary Sonographic Interstitial Syndrome. J Ultrasound Med. 2016 Oct;35(10):2075-86. doi: 10.7863/ultra.15.08023.
- 8- Soldati G, Smargiassi A, Inchingolo R, Sher S, Nenna R, Valente S, Inchingolo CD, Corbo GM. Lung Ultrasonography and Vertical Artifacts: The Shape of Air. Respiration. 2015;90(1):86.
- 9- Soldati G, Smargiassi A, Inchingolo R, Sher S, Nenna R, Valente S, Inchingolo CD, Corbo GM. Lung ultrasonography may provide an indirect estimation of lung porosity and airspace geometry. Respiration. 2014;88(6):458-68.
- 10-Peng QY, Wang XT, Zhang LN; Chinese Critical Care Ultrasound Study Group (CCUSG). Findings of lung ultrasonography of novel corona virus pneumonia during the 2019-2020 epidemic. Intensive Care Med. 2020 Mar 12. doi: 10.1007/s00134-020-05996-6. [Epub ahead of print]
- 11-Poggiali E, Dacrema A, Bastoni D, Tinelli V, Demichele E, Mateo Ramos P, Marcianò T, Silva M, Vercelli A, Magnacavallo A. Can Lung US Help Critical Care Clinicians in the Early Diagnosis of Novel Coronavirus (COVID-19) Pneumonia? Radiology. 2020 Mar 13:200847.
- 12-Soldati G, Smargiassi A, Inchingolo R, Buonsenso D, Perrone T, Federica D, Perlini S, Torri E, Mariani A, Mossolani EM, Demi L. Is there a role for lung ultrasound during the COVID-19 outbreak? J Ultrasound Med. 2020. In press

- 13-Chen J, Qi T, Liu L, Ling Y, Qian Z, Li T, Li F, Xu Q, Zhang Y, Xu S, Song Z, Zeng Y, Shen Y, Shi Y, Zhu T, Lu H. Clinical progression of patients with COVID-19 in Shanghai, China. J Infect. 2020 Mar 11
- 14-Buonsenso D, Less stethoscope more ultrasound, Correspondence, The Lancet Respiratory Medicine, 2020, In Press.
- 15-Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. J Hosp Infect. 2020 Mar;104(3):246-251. doi: 10.1016/j.jhin.2020.01.022. Epub 2020 Feb 6.
- 16-D. L. Miller, Z. Dong, C. Dou, and K. Raghavendran, "Pulmonary capillary hemorrhage induced by different imaging modes of diagnostic ultrasound," Ultrasound Med. Biol., vol. 44, no. 5, pp. 1012–1021, 2018.

Fig. 1: Schematic representation of the acquisition landmarks on chest anatomic lines.

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Fig. 2: Lung Ultrasound images obtained with linear (A-B) and convex (C-D) probe. The pleura line (indicated by red arrows) is continuous. Below, horizontal artifacts (indicated by blue arrows) may be visible. This pattern is classified as Score 0.

Fig. 3: Lung Ultrasound images obtained with linear (A) and convex (B) probe. The pleura line is not continuous. Below the point of discontinuity (indicated by red arrows), vertical areas of white are visible (indicated by blue arrows). This pattern is classified as Score 1.

**The**. 4: Lung Ultrasound images obtained with linear (A-B) and convex (C-D) probe. The pleura line is severely broken. Below the point of discontinuity (indicated by orange arrows), small consolidated areas (darker areas indicated by red arrows) appear with associated areas of white (indicated by blue arrows) in correspondence with the consolidations. This pattern is classified as Score 2.

Fig. 5: Lung Ultrasound images obtained with linear (A-B) and convex (C) probe. The pleura line is severely broken. Below the point of discontinuity, large consolidated areas (darker areas indicated by red arrows) appear with generalized white lung pattern (indicated by orange arrows). This pattern is classified as Score 2. In the box at the right bottom (D), a LUS image is shown where the edge between a Score 0 (green box) and Score 3 (purple box) patter is clearly visible.



## Landmarks

![](_page_10_Picture_0.jpeg)

А

В

# Score 0

Linear probe

### Convex probe

![](_page_10_Picture_3.jpeg)

![](_page_11_Picture_0.jpeg)

## Score 1

### Linear probe

![](_page_11_Picture_3.jpeg)

Convex probe

![](_page_11_Picture_5.jpeg)

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Δ

В

![](_page_12_Picture_1.jpeg)

### Score 2

Convex probe

![](_page_12_Picture_4.jpeg)

![](_page_13_Picture_0.jpeg)

![](_page_13_Picture_1.jpeg)

Score 3

![](_page_13_Picture_2.jpeg)

![](_page_13_Picture_3.jpeg)