

## Feasibility of Lung Ultrasonography in Management of Patients with COVID-19

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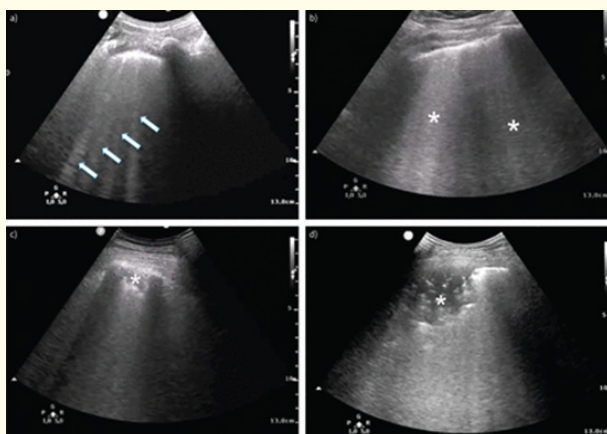
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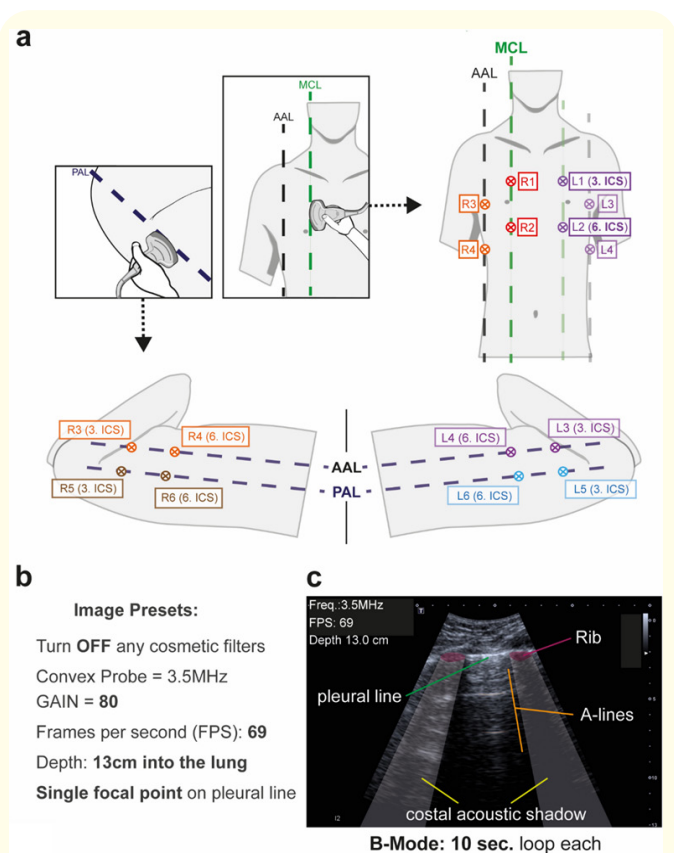
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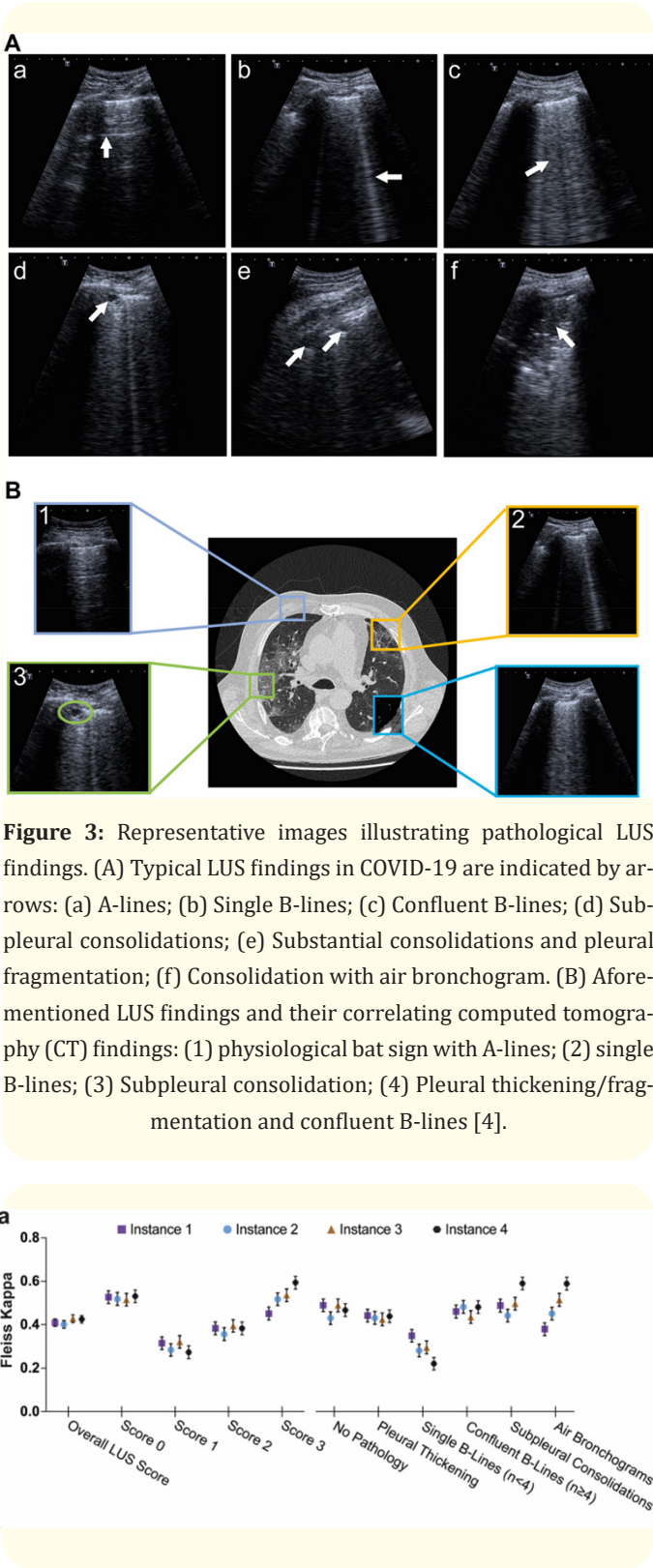
The use of lung ultrasonography (LUS) has gradually and importantly increased in the past few decades, particularly in patients with varieties of acute respiratory conditions [1]. Clinical-condition-suggestive-of COVID-19 could be early decision of hospital supported by relatively simple procedure of lung ultrasonography (Figures 1-5) [1-4]. Desirable bed-side imaging modality for disease-progression monitoring is essentially needed, whereas non-enhanced computed tomography (CT) can primarily detect the COVID-19-lung involvement [5-7]. Lung lesion detection and follow-up of COVID-19 patients with lung lesions is particularly appropriate due to typically and peripherally lung involvement of COVID-19 providing the patients' conditions information, immediately and limitation of the disease transmission [8-10]. This method is an assumed-operator-dependent modality with interobserver variabilities [11]. Worldwide, LUS publications and the specific applications of the LUS are demonstrated in the Figure 6 and 7 [1].



**Figure 1:** Demonstrating characteristic lung ultrasound findings in patients with COVID-19 pneumonia. a) Interstitial involvement with separated B-lines (arrows) and irregular pleural line; b) confluent B-lines (asterisks); c, d) consolidations (asterisks); d) air bronchograms [1].

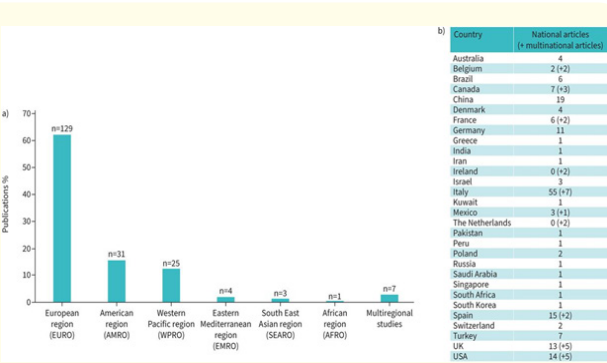
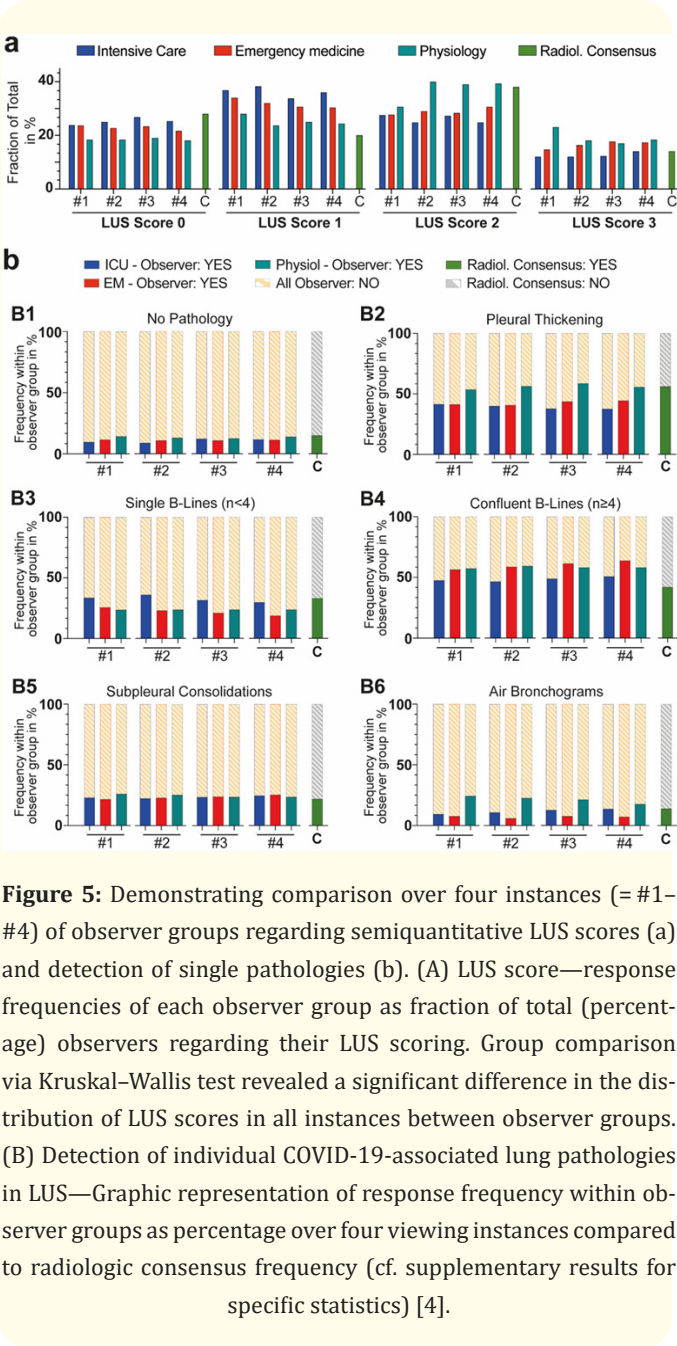


**Figure 2:** Demonstrating standard operating procedure (SOP) for image acquisition. (A) Lung ultrasound (LUS) regions of interest for standardization of image acquisition; Points L1-L6 and R1-R6 located in the midclavicular (MCL), anterior axillary (AAL) and posterior axillary line (PAL) in the 3rd & 6th intercostal spaces (ICS) (B) Lung ultrasound imaging presets defined by SOP. Cine-loops were recorded as B-mode images for 10 s each. (C) Physiological LUS acoustic window confined by ribs and their corresponding shadows [4].

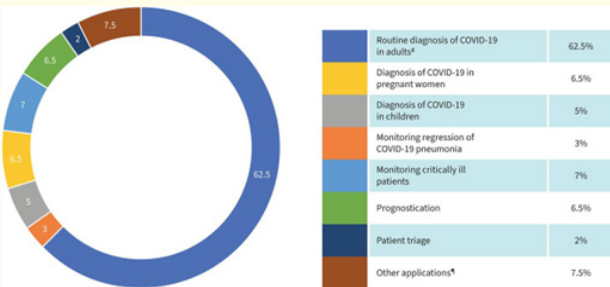


**Figure 3:** Representative images illustrating pathological LUS findings. (A) Typical LUS findings in COVID-19 are indicated by arrows: (a) A-lines; (b) Single B-lines; (c) Confluent B-lines; (d) Subpleural consolidations; (e) Substantial consolidations and pleural fragmentation; (f) Consolidation with air bronchogram. (B) Aforementioned LUS findings and their correlating computed tomography (CT) findings: (1) physiological bat sign with A-lines; (2) single B-lines; (3) Subpleural consolidation; (4) Pleural thickening/fragmentation and confluent B-lines [4].

**Figure 4:** Demonstrating interobserver (a) and intraobserver (b) agreement measured by Fleiss-Kappa between observers. For interobserver (A) last assessment of the quadrupled cine-loops (= instance 4) resulted in median  $\kappa = 0.41$  (95% CI 0.39–0.43) for overall LUS score,  $\kappa = 0.53$  (95% CI 0.50–0.56) for LUS score 0,  $\kappa = 0.27$  (95% CI 0.24–0.30) for LUS score 1,  $\kappa = 0.38$  (95% CI 0.35–0.41) for LUS score 2,  $\kappa = 0.59$  (95% CI 0.56–0.62) for LUS score 3,  $\kappa = 0.47$  (95% CI 0.44–0.50) for no pathology,  $\kappa = 0.44$  (95% CI 0.41–0.47) for pleural thickening/fragmentation,  $\kappa = 0.22$  (95% CI 0.19–0.25) for single B-lines ( $n < 4$ ),  $\kappa = 0.48$  (95% CI 0.45–0.51) for confluent B-lines ( $n \geq 4$ ),  $\kappa = 0.59$  (95% CI 0.56–0.62) for subpleural consolidations, and  $\kappa = 0.59$  (95% CI 0.56–0.62) for air bronchogram respectively. For intraobserver (B) over all four assessments with median  $\kappa = 0.63$  (IQR 0.54–0.69) for total LUS score, median  $\kappa = 0.71$  (IQR 0.6–0.76) for LUS Score 0, median  $\kappa = 0.52$  (IQR 0.46–0.58) for LUS Score 1, median  $\kappa = 0.65$  (IQR 0.53–0.7) for LUS Score 2 and median  $\kappa = 0.79$  (IQR 0.74–0.83) for LUS Score 3. In terms of single pathologies, intraobserver agreement showed median  $\kappa$ -values of 0.65 (IQR 0.5–0.78) for no pathology, 0.66 (IQR 0.59–0.69) for pleural thickening; 0.49 (IQR 0.44–0.53) for single B-lines; 0.55 (IQR 0.49–0.64) for confluent B-lines; 0.67 (IQR 0.63–0.76) for pleural consolidations and 0.72 (IQR 0.56–0.76) for air bronchograms ( $p < 0.005$  for all, cf. supplementary results for specific Fleiss Kappa values). All variabilities are color- and symbol-coded for the respective observer as well as observer group [4].



**Figure 6:** Demonstrating geographical distribution of publications on use of lung ultrasound in coronavirus disease 2019 (COVID-19) based on the results of the literature review. a) Distribution of the publications according to the six World Health Organization regional offices for a total of 200 publications on use of lung ultrasound in COVID-19, including 187 national articles and 13 multinational papers. Data presented as “EURO” comprise papers published by one single country in Europe as well as six articles jointly published by more than one European country. The literature review identified seven inter-regional articles (i.e. papers jointly published by authors from countries in different parts of the world) which were not included in any specific region and are therefore presented separately in this figure. b) The 31 countries involved in the literature review are listed together with the number of national articles submitted by each country. The numbers provided between brackets indicate, when appropriate, the number of multinational studies to which a given country has contributed [1].



**Figure 7:** Demonstrating specific application of lung ultrasound in the different studies. COVID-19: coronavirus disease 2019; including evaluation of the diagnostic accuracy of lung ultrasound in comparison with lung computed tomography and chest radiography; screening, contrast-enhanced ultrasound, application of lung ultrasound in nursing homes, “self-ultrasound”, guiding therapy, deciding on intubation, wireless ultrasound, assisting in patient resuscitation, application of lung ultrasound with artificial intelligence and with robotics [1].

In conclusion, a high number of observers with fair to moderate interobserver agreement and moderate to much intraobserver agreement led to highest agreement (Figure 4, 5) [4] for more severe LUS scores (Table 1) [4], subpleural consolidations and air bronchograms.

LUS score	Corresponding US pattern
0	Normal aeration (= A-lines and up to 2 B-lines/ICS)
1	Moderate loss of aeration (= multiple single B-lines/ICS)
2	Severe loss of aeration (= multiple coalescent B-lines/ICS)
3	Complete loss of aeration (= tissue-like pattern, consolidation, air bronchograms)

**Table 1:** Demonstrating semiquantitative LUS scoring based on four different grades with regard to aeration of the lung [4].

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