Thoracic ultrasound in interstitial lung disease

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Shareable abstract (@ERSpublications)
B-lines and pleural line thickening on LUS are sensitive but nonspecific signs of ILD. LUS aids in early detection and monitoring, but HRCT and PFT remain the gold standards. Limitations include operator dependence and lack of standardised protocols. https://bit.ly/41vUQSn

Cite this article as: Shah DJ, Esposito A, Pitaktong A, *et al*. Thoracic ultrasound in interstitial lung disease. *Breathe* 2025; 21: 240170 [DOI: 10.1183/20734735.0170-2024].

Received: 11 Nov 2024
Accepted: 19 Feb 2025

A 62-year-old female presents to the pulmonary clinic with a 1-year history of progressively worsening shortness of breath. She also reports a persistent dry cough. She denies any associated symptoms such as fever, chest or joint pain. There is no history of recent infections or environmental exposures. She works at a convenience store and denies having pets. She has never smoked, vaped or used illicit drugs.

On physical examination, she appears without respiratory distress. Blood pressure is 125/80 mmHg, heart rate is 88 beats per min, respiratory rate is 22 breaths per min, oxygen saturation is 90% on room air and temperature is 37°C (98.6°F). Upon examination of her lungs, bilateral crackles are heard on auscultation, particularly prominent at the bases. There is no cyanosis or clubbing of the fingers, and her extremities show no signs of oedema.

A lung ultrasound (LUS) is performed in the office using a portable device with a 4 to 1 MHz phased array transducer and 12 to 4 MHz linear array transducer using the lung preset. Starting with the phased array probe, two intercostal spaces are examined over the anterior, lateral and posterior lung fields on both sides of the chest. B-lines, hyperechoic vertical lines originating from the lung surface, are observed in all lung fields, worse in the lower lung fields. A representative clip is shown in figure 1a and supplementary video S1a. Examination of the same lung fields with the linear probe shows a very irregular pleural line (figure 1b, supplementary video S1b).

LUS is a unique imaging modality, as it allows the clinician to obtain and interpret the images immediately as part of the routine patient examination. Because air causes soundwaves to be reflected and scattered, the lungs were thought not to be amenable to ultrasound examination until the groundbreaking work of Lichtenstein who first demonstrated its diagnostic potential [1]. His pioneering work uncovered an approach to interpreting ultrasound artefacts in the lung [2]. Normal lung on ultrasound appears as an echoed pattern of horizontal artefacts known as “A-lines” (figure 2, supplementary video S2). A-lines are separated by the distance between skin and pleura, and result from sound reverberation between the subpleural air and the ultrasound transducer [3]. By contrast, “B-lines” appear as vertical hyperechoic lines due to reverberations within lung tissue with abnormal interstitial thickening. B-line artefacts appear as laser-like vertical hyperechoic lines, arise from the pleura, and move synchronously with lung sliding [4]. The presence of multiple B-lines within one intercostal space corresponds with septal, reticular or ground-glass opacities on high-resolution computed tomography (HRCT) imaging.

B-lines are nonspecific and have a wide differential diagnosis, which can be narrowed by analysing their distribution and the appearance of the pleural line. Bilateral diffuse B-lines can be either due to pulmonary congestion or other diffuse interstitial pathologies, such as acute respiratory distress syndrome, viral pneumonia or lung fibrosis [4]. To differentiate these two groups, attention is paid to the appearance of the pleural line. Diffuse B-lines projecting from a smooth pleural surface support the presence of pulmonary

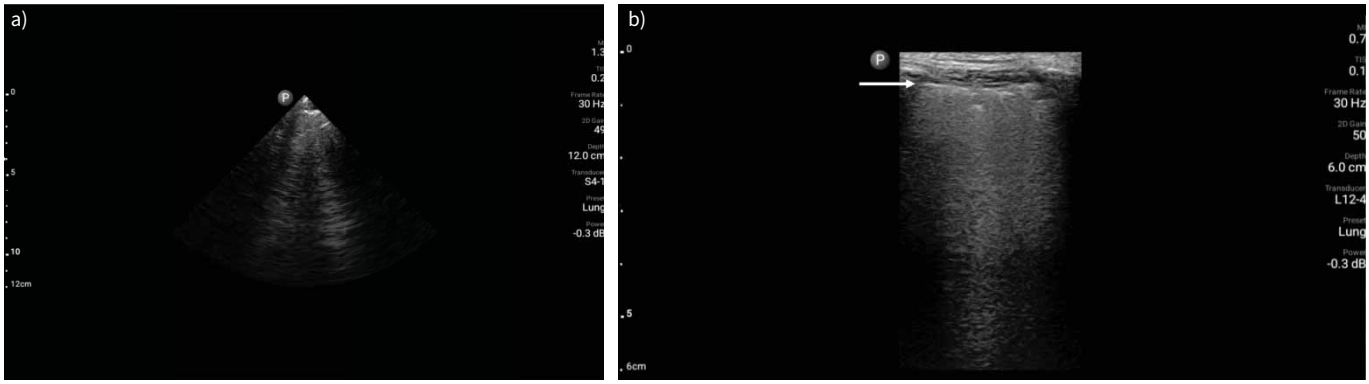

FIGURE 1 a) B-lines. b) Irregular pleural line.

oedema, whereas B-lines in the setting of an irregular pleural line point towards a noncardiogenic cause [5]. Hence, the ultrasound findings of bilateral diffuse B-lines with an irregular pleural line in the patient described earlier, with chronic progressive dyspnoea without infectious symptoms, suggest the presence of an interstitial lung disease (ILD) [6, 7].

The validity of LUS in patients with ILD has been confirmed by numerous studies comparing LUS with HRCT findings. Although the sensitivity is high, specificity (55–97.3%) is variable (table 1) [8, 9]. This variability may be explained by factors such as the study size, population and criteria used to define ILD, but also by operator and machine dependent factors. The level of training may vary widely, and there is no accepted protocol for LUS in general or specifically for ILD.

LUS is easy to learn, although beginners often acquire nondiagnostic images due to the probe not being positioned perpendicular to the lung surface. The previously described reverberation artefacts are only seen if the probe is applied strictly perpendicular to the lung surface. Examination for A- or B-lines can be undertaken with a phased-array or curvilinear transducer, whereas assessment of the pleura is best done with a high-frequency linear probe to optimise resolution of the superficial pleural surfaces. Numerous protocols for probe position have been published and the choice depends on the indication, patient

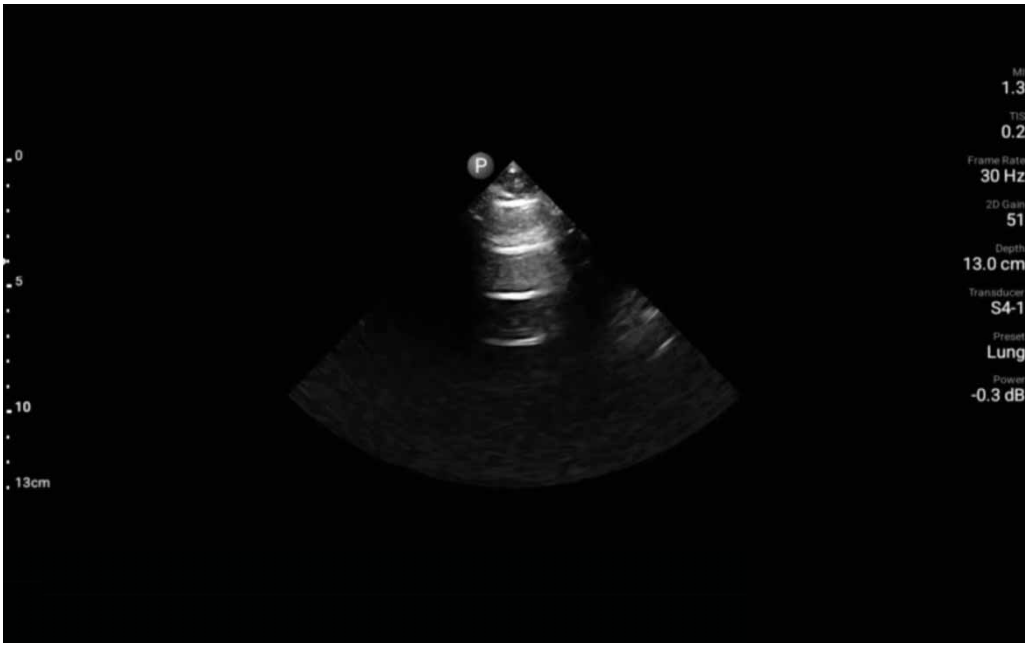

FIGURE 2 A-lines.

TABLE 1 Summary of selected studies comparing lung ultrasound with high-resolution computed tomography (HRCT) for interstitial lung disease

First author [ref.], year	Population	Protocol	Comparison with HRCT
Barskova [9], 2013	SSc (n=32)	ICS: 72 Probe: Phased array (2.5–3.5 MHz) Criteria: >3 B-lines in two adjacent ICS or >5 B-lines in total	Sensitivity: 100% Specificity: 55% AUROC: 0.94 (95% CI 0.89–0.99; p<0.0001)
Moazedi-Fuerst [18], 2014	RA (n=64) and healthy (n=40)	ICS: 18 Probe: Phased array (3.5 MHz) for parenchyma and linear for pleura Criteria: B-lines at two different locations, thickness >2.8 mm, pleural nodule	Sensitivity: 97.1% Specificity: 97.3%
Gasperini [19], 2020	SSc (n=41; 27 diffuse, 14 limited)	ICS: 50 Probe: Phased array (2.5–3.5 MHz) Criteria: >10 B-lines	Positive correlation (r=0.427; p<0.05)
Manolescu [21], 2020	IPF (n=31)	ICS: 12 Probe: Phased array (2–5 MHz) and linear (4–12 MHz) Criteria: Number of B-lines and pleural thickness	Positive correlation (r=0.871; p<0.001)
Fairchild [17], 2021	SSc (n=20; 9 diffuse, 11 limited)	ICS: 14 Probe: Linear (12 MHz) Criteria: Pleural irregularity, thickening and granularity	Sensitivity: 100% Specificity: 82%
Bruni [16], 2022	SSc (n=35; 14 diffuse, 21 limited)	ICS: 21 Probe: Not specified Criteria: Number of B-lines	AUROC 0.85 (95% CI 0.76–0.95; p<0.001)

AUROC: area under receiver operating characteristic curve; ICS: intercostal spaces; IPF: idiopathic pulmonary fibrosis; RA: rheumatoid arthritis; SSc: systemic sclerosis.

condition, time constraints and the environment. The most recent general guidelines state that LUS should be performed on the largest possible area of the chest that is available during the LUS examination [10]. As mentioned earlier, there is no generally accepted LUS protocol for the evaluation of ILD. Most protocols ask for the examination of several specified locations over the chest, and the summed total number of B-lines among the examined intercostal spaces is used to calculate a LUS score to quantify interstitial disease. Very extensive scoring protocols have been described, but the examination of 14 intercostal spaces resulted in similar sensitivity and specificity compared to more cumbersome protocols [11–15].

LUS is cost-effective, immediately available at the bedside or in the office setting, free of radiation and relatively easy to learn, but what is the evidence for its use in patients with ILD? LUS has shown high sensitivity in detecting ILD and may be useful for screening, particularly in patients with systemic sclerosis (SSc) [16]. In this patient population, it was demonstrated that a cut-off value of more than 10 B-lines on the whole chest or more than one B-line on the postero-basal chest has a sensitivity of 97% for detecting early ILD, which increased to 100% when pleural line alterations were included [16]. Another study showed 100% sensitivity and 82% specificity for detecting SSc-ILD, with perfect agreement between ultrasonographer and non-ultrasonographer readers [17]. In a prospective study involving 64 patients with rheumatoid arthritis, the authors reported a sensitivity of 97.1% and a specificity of 97.3% for the detection of pulmonary involvement by LUS with a positive predictive value of 94.3% and a negative predictive value of 98.6% [18].

The noninvasive, radiation-free nature and immediate availability during a patient visit makes LUS especially appealing for frequent monitoring of patients with ILD. This is supported by data showing correlation between traditional methods for monitoring of ILD (*e.g.* HRCT scanning and pulmonary function testing (PFT)) and LUS. In 41 patients with SSc, a moderate positive correlation between the number of B-lines and the HRCT score (r=0.51, p<0.05) was found. Conversely, there was a moderate negative correlation between the number of B-lines and diffusing capacity of the lung for carbon monoxide (D_{LCO}) (r= −0.49, p<0.05). At 12 months, a positive correlation between the number of B-lines and the change in D_{LCO} was observed, suggesting value in LUS to predict the worsening of the ILD [19]. A large multicentre Italian study further supports the diagnostic and prognostic value of LUS in patients with SSc. Gargani *et al*. [20] examined 396 outpatients with SSc using a comprehensive LUS protocol. During follow up, 16 patients developed new ILD, and ILD worsened in 34 patients. Having more than five

posterior B-lines at baseline significantly predicted new or worsening ILD (HR 3.378, 95% CI 1.137–9.994; p=0.028).

Although fewer studies have evaluated LUS in patients with idiopathic pulmonary fibrosis (IPF), the available data supports LUS use in this patient group. In 31 patients with IPF, B-lines and the average thickness of the pleural line were highly correlated with HRCT score, forced vital capacity and D_{LCO}, a finding that has been corroborated in other studies [21].

In summary, there is accumulating evidence supporting the use of LUS for the detection and monitoring of ILD in patients with connective tissue disease and IPF. The sensitivity of LUS findings as compared to HRCT appears to be excellent. However, B-lines and pleural line thickening are nonspecific findings, and the positive predictive value for ILD will depend on the prevalence in the studied population. HRCT and PFT remain the gold standard for the diagnosis of ILD, and further studies with larger sample sizes and improved methodological rigor are needed to better define the role of LUS within the available diagnostic armamentarium. Further research is also needed to define the best LUS protocol specifically for the evaluation of ILD.

The main limitation of LUS for ILD are operator dependence, lack of standardisation of protocols and subjectivity in measuring B-lines and pleural thickening. Application of artificial intelligence (AI) may alleviate these limitations, as AI-driven scoring systems are becoming available to standardise LUS findings and facilitate consistent measurements.

Key points

- B-lines and pleural line thickening are typical LUS findings in ILD.
- B-lines and pleural line thickening are not specific but show excellent sensitivity for ILD.
- Accumulating evidence supports the use of LUS for the early detection and monitoring of ILD.
- HRCT and PFT remain the gold standard diagnostic tests and the role of LUS within the diagnostic armamentarium needs to be further defined.
- Operator dependence, lack of standardised protocols and subjectivity in measuring B-lines and pleural thickening are the main limitations to LUS for ILD.

Self-evaluation questions

1. Which of the following statements about lung ultrasonography is accurate?
    a) B-lines are both sensitive and specific for ILD
    b) B-lines are sensitive, but not specific for ILD
    c) B-lines are specific, but not sensitive for ILD
    d) B-lines are neither sensitive nor specific for ILD
2. Which of the following statements regarding the typical LUS examination is correct?
    a) Evaluation of the pleura line is done with the phased array probe.
    b) Ideally, a standardised, widely accepted LUS protocol should be used for the evaluation of ILD.
    c) For convenience, evaluation of the posterior lung fields can be omitted when examining patients with LUS for ILD.
3. Normal lung on ultrasound appears as an echoed pattern of horizontal artefacts known as:
    a) A-lines
    b) B-lines
    c) Comet artefacts

Conflict of interest: The authors have nothing to disclose.

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Suggested answers

1. b.
2. b.
3. a.