Transthoracic ultrasound *versus* intraoperative ultrasound in patients with pulmonary fibrosis: Reappraisal of artifacts

Marco Sperandeo,[1] Giulia Gaudiuso,[2] Carla Maria Irene Quarato,[3] Anna Del Colle,[3] Michele Inglese,[4] Francesca Molinaro,[4] Salvatore De Cosmo,[4] Lucia Dimitri,[5] Marco Bizzarri,[6] Elisabettamaria Frongillo[6]

[1]Diagnostic and Interventional Ultrasound Unit, Department of Internal Medicine, Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo (FG); [2]Institute of Respiratory Disease, Aldo Moro University of Bari; [3]Institute of Respiratory Disease, Department of Medical and Surgical Sciences, University of Foggia; [4]Department of Internal Medicine, Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo (FG); [5]Unit of Pathology, Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo (FG); [6]Unit of Thoracic Surgery, Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo (FG), Italy

Abstract

In the last years, transthoracic ultrasound (TUS) has regained a growing interest from both clinicians and radiologists as a useful and non-invasive diagnostic tool for the study of many pleuro-pulmonary conditions, including interstitial lung diseases. Intraoperative lung ultrasound (ILU) is an ultrasound technique, developed for lung surface assessment during video-assisted thoracoscopic surgery procedures. It has been developed considering ultrasound basic physics principles for images generation and interpretation. Most of the TUS findings are due to the high difference in acoustic impedance between the chest-wall structures and the air in the lungs. In this brief communication, we compared ILU and TUS images in interstitial lung diseases. Most of the TUS artifacts-based diagnostic algorithms should be reappraised.

Correspondence: Marco Sperandeo, Diagnostic and Interventional Ultrasound Unit, Department of Internal Medicine, Casa Sollievo della Sofferenza Hospital, Viale Cappuccini 1, 71013 San Giovanni Rotondo (FG), Italy.
E-mail: sperandeom@libero.it

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Introduction

Transthoracic ultrasound (TUS) is a imaging technique, mainly used for detecting pleural thickening, pleural/subpleural nodules and other subpleural lung abnormalities diseases adherent to the 70% of pleural surface visible by ultrasound. TUS is the gold standard for studying pleural effusion and for echo-guided thoracentesis.[1] The TUS has been established[2-4] as a complementary diagnostic tool, as well as a valuable guide for both diagnostic and therapeutic interventional procedures (pleural drainage guidance and in ultrasound-guided pleural/subpleural lesions biopsies). Moreover, we previously demonstrated the good applicability of TUS in the detection of early and late-stage changes associated with pulmonary fibrosis. Indeed, for example, in systemic sclerosis TUS enable to detect ultrasonographic signs (*i.e.* pleural line thickness and subpleural nodes) of initial pulmonary fibrosis prior to the onset of respiratory symptoms and function test abnormalities, showing a good concordance with typical high-resolution computed tomography (HRCT) patterns of lung fibrosis and changes attributable to its progression.[5,6] In the last decade, many studies focused on the clinical usefulness of TUS in the management of patients with pulmonary fibrosis. In particular, at this regard, unlike several reports suggested the use of the *B lines* artifacts has not a high diagnostic accuracy in interstitial lung diseases; in fact *B lines* or *ring down* artefacts are an *error in image* and are not specific signs of lung injury being commonly detectable in many conditions, such as heart failure, acute pulmonary oedema, uniformly distributed pleural effusion, lymphangitis, hydropneumothorax, emphysema, parasectal bullae and exacerbations of chronic obstructive pulmonary diseases.[7] For these reasons, a basic understanding of the physical principles of ultrasound seems to be essential for an accurate and reliable interpretation of sonographic images of the chest cavity and its contents. *B lines* are an ultrasound artifact mostly generated when the ultrasound beam crosses areas of great difference in acoustic impedance (*i.e.*, chest wall *vs* air) that reduce the propagation speed of the ultrasound beam. The air can be considered the worst enemy of ultrasounds, implying a reduction of propagating sound waves in this physical medium at a speed of only 331 m/s. The lung is by its nature an organ full of air. Manufacturers' calibration of ultrasound devices is usually based solely on the speed of sound in tissues of the chest wall (~1500 m/s), whereas the propagation

speed is much lower in other structures within the chest (-440 m/s in the interstitium, bronchi, vessels and lymphatic tissue). Unfortunately to employ an ultrasound device calibrated on the speed of sound in lung parenchyma is not possible because the ultrasound wave could reach neither the pleural surface, being stopped by the chest wall. As a result, employing an ordinary ultrasound device, more than 96% of the ultrasound beam is reflected by the tissue/air interface. This produces a hyperechoic pleural line without a real anatomic match, and also generates vertical (*B lines* or *ring downs*) and horizontal artifacts (*A-lines* or simple reverberations).[8] In particular, *B-lines* are a type of reverberation artifact most commonly seen when sound waves interact with gas/air bubbles, exciting the fluid trapped between the bubbles and causing the fluid to resonate.[9] These artifacts (*B lines*) are detectable even also in the bowel loops (containing gas and film fluid) and in the residual cavity of the post-pneumonectomy space (containing residual air, liquid films and/or edema and scar tissue) (Figure 1A-D).[10,11] Beyond that, the number and intensity of the visible vertical artifacts (*B lines*) depend on the type and frequency of the probe used, as well as the degree of total gain compensation (TGC) electronic focus and tissue harmonics used.[12] The detection of B-lines remains largely subjective and at best semiquantitative and it is questionable whether a firm relationship between the number of *B lines* and a specific disease can be established.[13,14] Conversely, TUS is currently recognized as an indispensable tool to detect and characterize pleural effusions, guide thoracentesis and in detection of pleural and pulmonary nodule adherent to pleural surface.[15]

Intraoperative lung ultrasound (ILU) is a technique developed for a triportal video-assisted thoracoscopic surgery (VATS) approach according to Hansen *et al*.,[16] suitable also for uniportal VATS and robotic-assisted thoracoscopic surgery (RATS). Unlike TUS, the ILU approach is not limited by differences in acoustic impedance, as the probe is directly in contact with the lung. ILU is a completely novel technique; the scan is performed using a non-dedicated laparoscopic linear probe with a dedicated setting (7-12 MHz, gain less than 50%, electronic focus on the interface with the lung. This technique was developed for a triportal VATS approach according to Hansen *et al*., but it could be suitable also for uniportal VATS and RATS. The surgeon uses the two ports on the 8th and 7th intercostal space to scan the whole lung surface, checking on the screen the correct position of the probe. Starting from this assumption, we tried to describe the US semeiotic signs of interstitial lung diseases (ILDs) assessed during VATS comparing TUS and ILU findings and interpreting the images according the ultrasound physics principles.[17]

Materials and Methods

In our protocol we perform to all VATS patients both TUS and ILU.[17] Participants provided informed written consent for all procedures. We studied 13 patients, among which 10 patients were affected of undefined ILD (9 male and 1 female, mean age 53±7) (Figure 2A-D) and 3 patients were known to have pulmonary

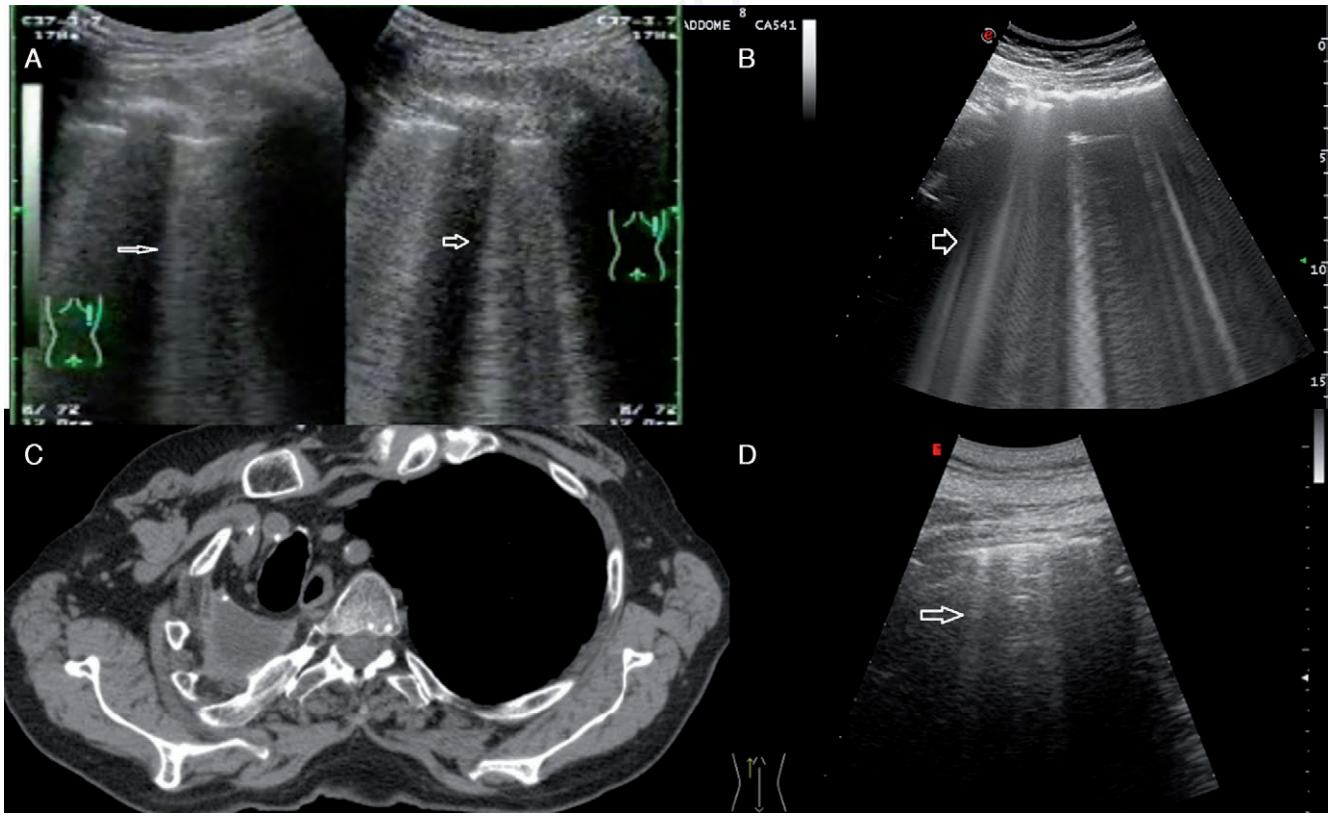

Figure 1. The *B line* in different contests. A) Transthoracic ultrasound (TUS) showed hyperechoic pleural line and *B line* below it (white arrows). B) Abdominal scan showed hyperechoic peritoneal line and *B line* below it (white arrows). C, D) Computed tomography corresponding and TUS in residual cavity post pneumonectomy a showed hyperechoic line and *B line* (white arrows).

fibrosis in systemic scelorosis (SSc) and also lesions suspected for carcinoma (3 female, mean age 53±3) (Figure 3A-D). The histologic diagnosis of fibrosis was: 8 usual interstitial pneumonia (UIP), 3 nonspecific interstitial pneumonia (NSIP) and 1 hypersensitivity pneumonitis (HP). The histologic diagnosis of nodule in patients with fibrosis in SSc was 1 adenocarcinoma and 2 squamous carcinomas.

The TUS investigation was carried out using an ultrasound scanner Esaote "Twice" (Genoa, Italy) with thoracic set up and with a convex probe (3.5-8 MHz) and a linear probe (8-12 MHz). A tissue harmonic, electronic focus on the pleural line and the TGC not exceed the 55% of the total gain were used in an effort to reduce the natural artifacts. We started the exploration of each hemithorax with the patient in a sitting position from the back, with paravertebral and hemiscapular scans, exploring from the base up to the ipsilateral posterior pulmonary apex, passing, then, to the examination of the lateral chest side along the posterior, middle and anterior axillary line. The anterior chest has been evaluated with parasternal and hemiclavear scans. Videoclips of transthoracic ultrasound scans were recorded and examined by two expert sonographers, in a double-blind way. All patients underwent thoracic HRCT and/or thoracic computed tomography (CT) scan before VATS and the imaging were checked by two expert radiologist, in a double-blind way.

VATS-Ultrasound examination was performed using an Esaote "My Lab 25 GOLD" set for superficial tissue with tissue harmonic gain <50% and electronic focusing at the interface level and a laparoscope probe with a flexible tip (LP 4-13, ± up/down 90°, right/left 90°) and linear array transducer at frequencies 8.0-12.0 MHz. The probe had a diameter of 10 mm and length of 38 cm. The sound wave was perpendicular to the pulmonary surface. Localization, size, and US pattern of the lesion(s) of interest were recorded by VATS-US, and comparison was made with the TUS data according to the final histological diagnosis.

VATS was performed under general anesthesia with single-lung ventilation through double-lumen endotracheal intubation in all patients. The operative time of VATS-US was 15-20 min longer compared to VATS.

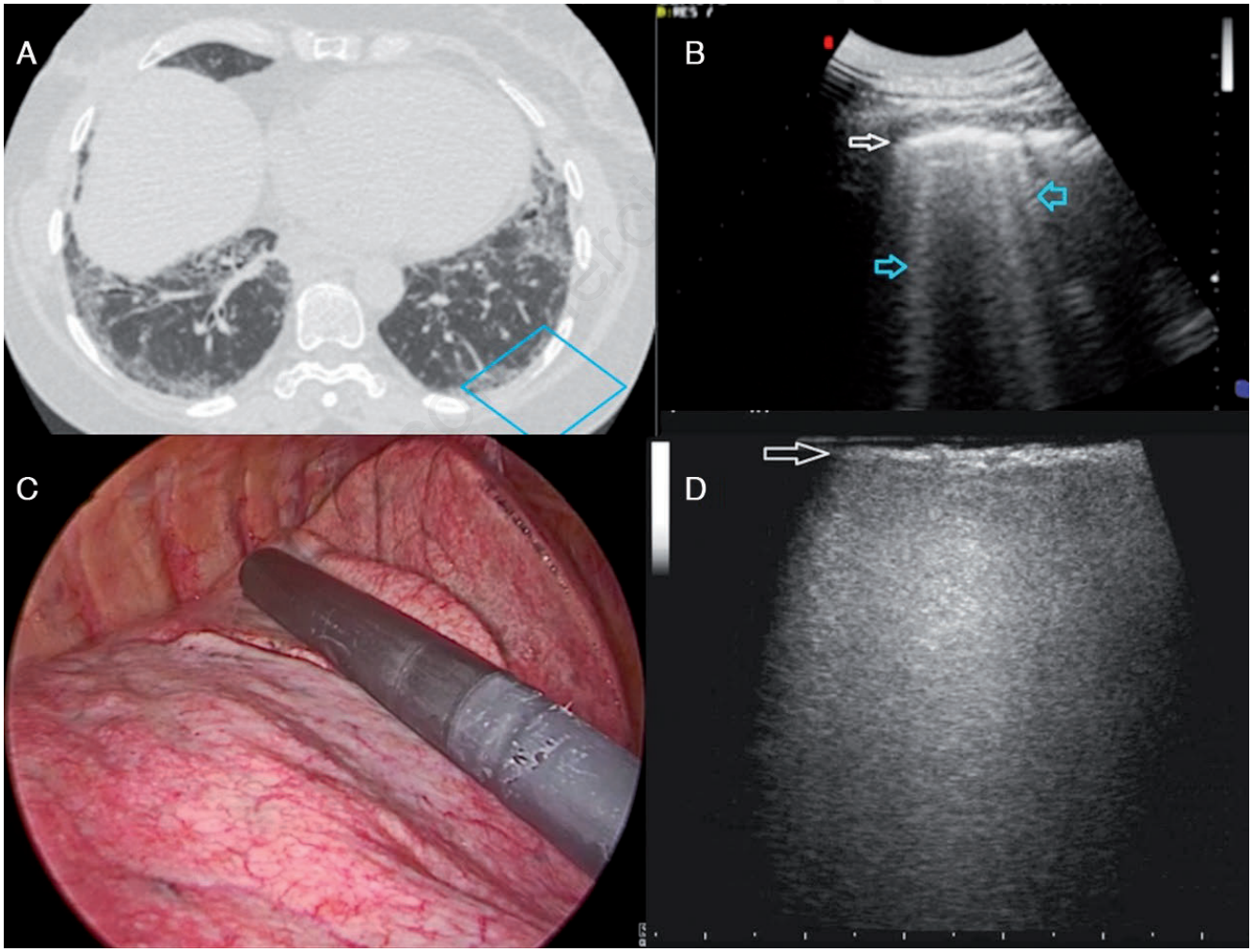

Figure 2. Usual interstitial pneumonia fibrosis (histologic diagnosis). A) Transthoracic ultrasound (TUS) (convex probe, 5 MHz) showing increased thickness of the hyperechoic pleural line (white arrow) and increased number of *B lines* below it (blue arrows). B) Corresponding high-resolution computed tomographic scan of the same TUS scan (blue box) showing undefined lung fibrosis. C) Image of the pulmonary parenchyma during video-assisted thoracoscopic surgery; D) Intraoperatory lung ultrasound (linear probe, 12 MHz) showing irregular increased thickness of the pleura line (white arrow) with no artifact below it.

Results and Discussion

Several authors studied a possible role of *B lines* in the early detection of ILDs, especially when associated with autoimmune disorders.[18-20] *B lines* and other artifacts may be present in association with lung or pleural modifications in many interstitial lung diseases and other diffuse parenchymal lung diseases, including idiopathic pulmonary fibrosis (IPF), systemic sclerosis, interstitial pneumonia, rheumatoid arthritis, nephrotic syndrome, ARDS, radiation fibrosis.[21-26] As *B lines* are a type of reverberation artifact mainly generating when sound waves excite the fluid trapped between air bubbles causing the fluid to resonate, the number of *B lines* will increase in all those pathological pleuro-pulmonary conditions where the proportion of air/liquid film changed. However, despite many recent attempts of counting artefacts for the diagnosis of pulmonary fibrosis, pulmonary oedema, or any extra-vascular lung water have been proposed, these artifacts lack any disease-specificity.[27]

The generation of ring-down artifacts is dependent on several factors, including the interaction between the chest wall, the air and the fluid film in the lung. In addition, the machine setting, the type of probe used (*i.e.*, convex, linear or phased-array) and the frequency strongly influence the generation and the number of ring down (or *B lines*) artifacts.[28] Moreover, it does not seem to be correct to *count* the *B line*, since it is more an overview, which is quite subjective, than a real unit of *measurement*. In our experience, indeed, intra- and inter-observer variability in *B lines* count in several sonographic assessments is high, probably beyond the possibility of using these measurements as an *objective* reference suitable to be used for educational purposes.[29] The nature itself of *B lines* artifacts also explains how some of them can be seen in normal lungs, especially at the bases, where the hydrostatic pressure creates a more fluid-rich interstitium, and in the residual cavity post-pneumonectomy (where there is residual air and effusion and/or fibrotic tissue).[10]

Generation of *B lines* artifacts did not occur in our intraoperative examination in VATS-Ultrasound in all the patients examined, despite the presence of *B lines* in TUS. Indeed, in this and other our experiences, in patients with pulmonary fibrosis only a thicker

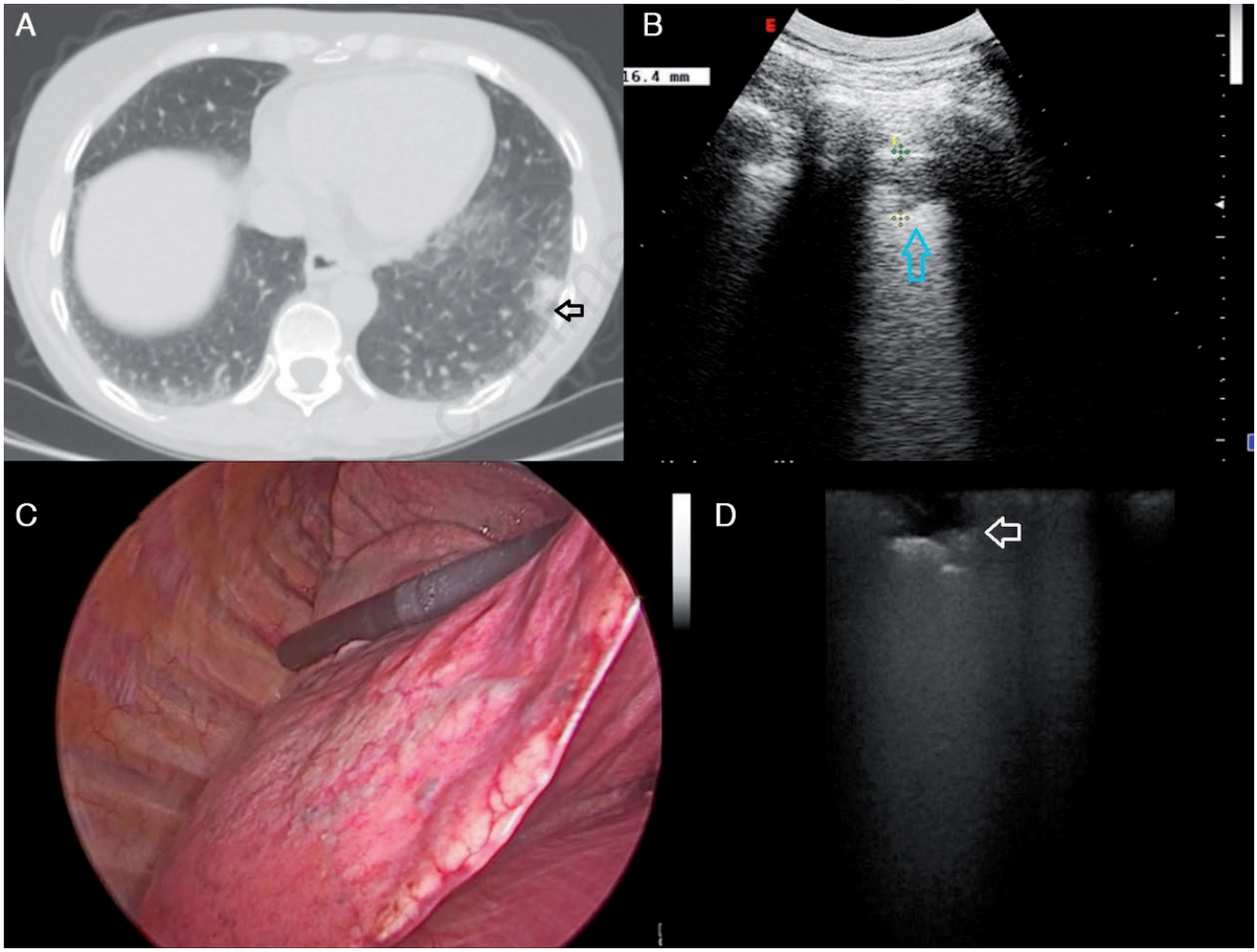

Figure 3. Systemic sclerosis patient with adenocarcinoma (histologic diagnosis) and pulmonary fibrosis. A) Thorax computed tomography: axial scan image showing the pulmonary nodule (white arrow) and the pattern of mild fibrosis. B) Transthoracic ultrasound, convex probe, % MHz) showing the subpleural nodule adhering to pleural surface (white arrow). C, D) Video-assisted thoracoscopic surgery and intraoperative lung ultrasound showing the pulmonary nodule (white arrow) with jagged margins.

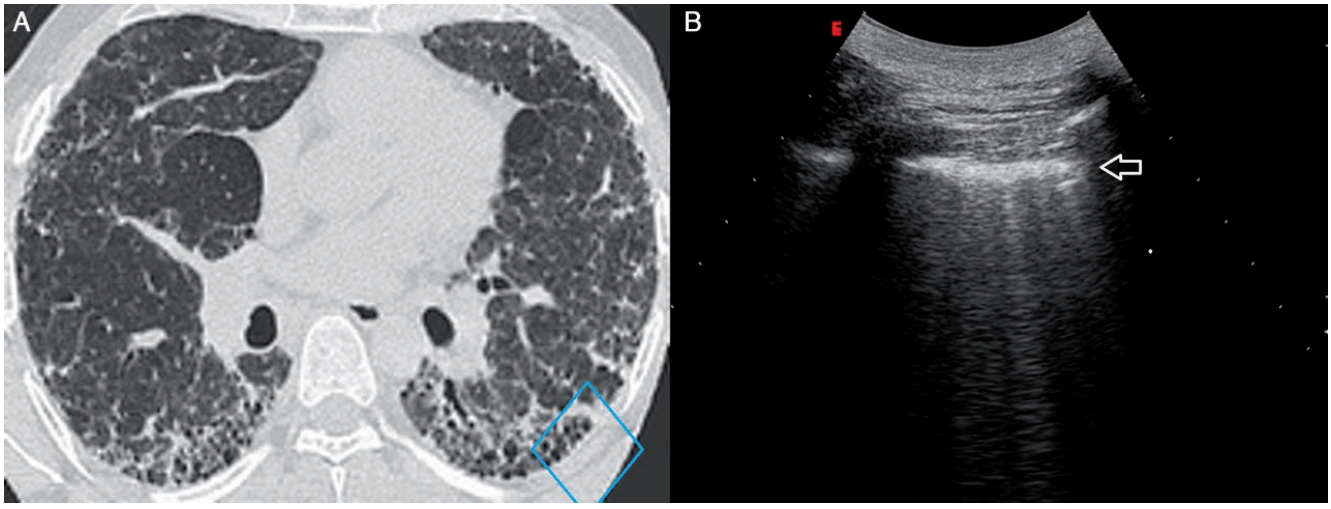

Figure 4. A) High-resolution computed tomography (HRCT) systemic sclerosis fibrosis pattern (peribronchiolar fibrosis, reticular-nodular and initial honeycombing). B) Transthoracic ultrasound scan, corresponding blue box in HRCT: thickness (5 mm) hyperechoic pleural line (white arrow) and *B line* below it.

hyperechoic line compared to the non-fibrotic lung was studied and no other artefact below it (*i.e.*, *B line* or *ring down*) (Figure 4A and B).[30] Our report, therefore, confirms how the high difference in acoustic impedance between chest wall and air influences the visualization of the pleurae and the lungs during TUS and, consequently, generate artifacts. This point is of utmost importance in US semeiotics, as TUS is routinely used in the diagnosis of various pleuro-pulmonary disorders and the assessment of *B line* artifacts is a crucial point in this context.[31]

We compared[32] the findings of chest US to those of HRCT scan in 175 consecutive patients with systemic sclerosis, diagnosed according to ACR/EULAR criteria. In all patients without HRCT signs of interstitial involvement, pleural line thickness was lower than 3.0 mm. Moreover, among the 95 asymptomatic patients with normal pulmonary function tests and single-breath diffusing capacity for carbon monoxide (DLCO), 26 patients had normal HRCT features and pleural line thickness ≤3 mm, while the 69 patients with pleural line thickening had reticular or reticular-nodular HRCT pattern limited to basal area. The sensitivity of pleural line thickness to identify HRCT-detected interstitial lesions ranged from 74.3% for reticular-nodular if the width was >3.5 mm, to 80.0% for reticular pattern with a width of >3.0 to ≤5 mm and to 90.1% for honeycombing, if width was higher than 5.0 mm.[5] In our experience, therefore, TUS is a useful diagnostic tool in the detection of early and late-stage changes associated with pulmonary fibrosis only in the revelation of thickness in the hyperechoic pleural line and, possibly, of morphological subpleural alterations, such as subpleural nodes.

Conclusions

In conclusion, the comparison between TUS and ILU highlights how a deep knowledge of ultrasound basic physics principles is crucial for images interpretation. To our knowledge, this is the first study that has systematically compared US findings during VATS procedures to TUS ones in the effort to avoid TUS images misinterpretation in the diagnosis of a condition of pulmonary fibrosis (PF). TUS signs presumably visible in ILD are not yet cited in the most important scientific societies guidelines.[33,34] In our experience *B lines* and A-lines artefacts are absent in intraoperatory ultrasound scans also in patients with pulmonary fibrosis, according with their nature of simple physical artifacts. As a result, these findings cannot be considered useful signs for the diagnosis of a pulmonary fibrosis. On the other hand, TUS enables detection of pleural abnormalities, notably pleural line thickening and morphological alteration (*i.e.*, subpleural nodes), even before the onset of respiratory symptoms and function test abnormalities. According to the Health Technology Assessment (HTA) statements, however, a gold standard technique is needed to validate any imaging technique. In all of this studies it is not possible a real comparison between TUS (imaging for the evaluation of 70% of the surface of the pleura) and the volumetric and multiparametric acquisition of the thoracic HRCT, that can elicit a confident diagnosis for appropriate management of interstitial pulmonary disease.[35] Therefore, TUS is a useful complementary tool to HRTC and conventional radiology for the study of pleural and interstitial lung diseases and appearing helpful for indicating timely HRCT assessment in early stage an in the follow-up of PF.

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