J Rheum Dis 2024;31(1):3-14
https://doi.org/10.4078/jrd.2023.0042
pISSN: 2093-940X, eISSN: 2233-4718

Review Article

Radiologic approach and progressive exploration of connective tissue disease-related interstitial lung disease: meeting the curiosity of rheumatologists

Hyeji Jeon, M.D.[1], Bo Da Nam, M.D.[2], Chong-Hyeon Yoon, M.D, Ph.D.[3], Hyun-Sook Kim, M.D, Ph.D.[1]

[1]Division of Rheumatology, Department of Internal Medicine, Soonchunhyang University Seoul Hospital, Soonchunhyang University College of Medicine, [2]Department of Radiology, Soonchunhyang University Seoul Hospital, Soonchunhyang University College of Medicine, [3]Division of Rheumatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea

Interstitial lung disease (ILD) is often observed in connective tissue diseases (CTDs), frequently in rheumatoid arthritis, systemic sclerosis, primary Sjögren's syndrome, and inflammatory myositis. Early detection of ILDs secondary to rheumatic diseases is important as timely initiation of proper management affects the prognosis. Among many imaging modalities, high-resuloution computed tomography (HRCT) serves the gold standard for finding early lung inflammatory and fibrotic changes as well as monitoring afterwards because of its superior spatial resolution. Additionally, lung ultrasound (LUS) and magnetic resonance imaging (MRI) are the rising free-radiation imaging tools that can get images of lungs of CTD-ILD. In this review article, we present the subtypes of ILD images found in each CTD acquired by HRCT as well as some images taken by LUS and MRI with comparative HRCT scans. It is expected that this discussion would be helpful in discussing recent advances in imaging modalities for CTD-ILD and raising critical points for diagnosis and tracing of the images from the perspective of rheumatologists.

Keywords: Interstitial lung disease, Connective tissue diseases, Pulmonary fibrosis, Rheumatology

INTRODUCTION

Connective tissue disease (CTD) encompasses a group of autoimmune disorders characterized by systemic involvement of various organs and tissues through complex and multifactorial mechanisms [1]. Among the manifestations of CTD, interstitial lung disease (ILD) stands out as a significant cause of morbidity and mortality [2]. ILD in the context of CTD, commonly referred to as CTD-ILD, represents a complex and challenging clinical entity with a broad spectrum of diseases, such as rheumatoid arthritis (RA), systemic sclerosis (SSc), primary Sjögren's syndrome (pSS), inflammatory myositis, and others. Clinical practice in CTDs presents a considerable number of patients with a heterogeneous spectrum of pulmonary manifestations, ranging from subtle interstitial inflammation to parenchymal lung disease causing fibrotic changes, ultimately leading to impaired lung function and respiratory compromise [2].

It is crucial to distinguish between ILDs, specifically idiopathic pulmonary fibrosis (IPF), and ILDs secondary to rheumatic diseases (i.e., CTD-ILDs), as their treatments and prognosis

Received July 28, 2023; **Revised** September 10, 2023; **Accepted** September 11, 2023, **Published online** October 18, 2023

Corresponding author: Hyun-Sook Kim, https://orcid.org/0000-0001-9213-7140
Division of Rheumatology, Department of Internal Medicine, Soonchunhyang University Seoul Hospital, 59 Daesagwan-ro, Yongsan-gu, Seoul 04401, Korea. **E-mail:** healthyra@schmc.ac.kr
Chong-Hyeon Yoon, https://orcid.org/0000-0003-2305-4637
Division of Rheumatology, Department of Internal Medicine, The Catholic University of Korea, Eunpyeong St. Mary's Hospital, 1021 Tongil-ro, Eunpyeong-gu, Seoul 03312, Korea. **E-mail:** chyoon@catholic.ac.kr

differ [3]. Patients with CTD-ILD are more likely to be treated with anti-inflammatory or immunosuppressive agents, and they generally have a more favorable prognosis than those with IPF of comparable severity [2]. Therefore, to provide the best chance of survival for patients with CTD-ILD, rheumatologists should focus on screening, early diagnosis, and appropriate follow-up to measure treatment progress.

The current diagnosis of CTD-ILD involves the use of imaging techniques, analysis of autoantibody profiles, and examination of pathology subtypes [4]. High-resolution computed tomography (HRCT) is the primary radiological tool for early diagnosis of ILD [5]. While chest X-ray is useful for the initial evaluation of the thoracic cavity, HRCT is preferred for detecting early lung inflammatory and fibrotic changes. In recent years, new insights on CTD-ILD have emerged, shaping perspectives and approaches to patient care. Techniques such as quantitative HRCT, lung ultrasound (LUS), and magnetic resonance imaging (MRI) have provided valuable tools for early detection, accurate assessment of disease extent and severity, and monitoring treatment response. These modalities allow us to identify subtle interstitial lung abnormalities, track disease progression, and guide therapeutic interventions. As rheumatologists specializing in CTD-ILD, we adopt a comprehensive and multidisciplinary approach to care for the heterogeneous systemic nature of these diseases, integrating emerging tools and therapies. Consequently, there is a growing demand to delve deeper into new perspectives on imaging to reflect early diagnosis, clinical activity, and specific situations in CTD-ILD.

This report evaluates and presents the existing imaging tools for CTD-ILD and discusses their current use and future potential in advancing our understanding and management of this condition.

MAIN SUBJECTS

Lessons from the era of idiopathic pulmonary fibrosis and progressive pulmonary fibrosis

ILDs often have no identifiable causes and are classified as idiopathic. Among them, IPF represents the most common form of idiopathic interstitial pneumonia (IIP), accounting for approximately 17% to 37% of ILD diagnoses [6]. Clinicians employ various techniques for screening, detection, tracking, and prognostication of ILD, including IPF. Diagnostic imaging and testing modalities have been well-established for IPF. The incidence of IPF diagnosis has been increasing along with the identification of CTD-ILDs, with approximately 25% of ILD patients being diagnosed as CTD-ILD cases [7]. Irrespective of the etiology, ILD is characterized by diverse patterns of inflammation and fibrosis, often exhibiting a fatal and progressive nature [8].

In the past, treatment options for IPF were limited; however, the development of antifibrotic agents such as nintedanib and pirfenidone has provided potential treatment avenues [9]. Consequently, there is an increasing demand for timely diagnosis, accurate monitoring of disease progression, and assessment of treatment response. These needs have been addressed by the concept of progressive fibrotic ILDs (PF-ILDs), characterized by radiological progression, worsening respiratory function, and symptoms [10-12]. The 2022 Official ATS/ERS/JRS/ALAT Clinical Practice Guideline introduced the term progressive pulmonary fibrosis (PPF) as a representative term for PF-ILD [13].

PPF refers to a subset of ILD characterized by a progressive and irreversible decline in lung function and aggressive fibrosis [9]. IPF, as the most common form of ILD, is characterized by progressive decline in pulmonary function and a short life expectancy. In addition to IPF, there are other ILDs that exhibit a similar clinical course, such as IIP, autoimmune-related ILD including CTD-ILD, sarcoidosis, hypersensitivity pneumonitis, and occupational pneumonias. These ILDs are considered PPF, as they manifest progressive fibrosis, worsening respiratory symptoms, decline in pulmonary function tests (PFTs), and high mortality [9,14].

In clinical settings, PPF can be highlighted through assessments with HRCT and PFTs. A decline of greater than 10% in forced vital capacity (FVC) and diffusing capacity of the lung for carbon monoxide (DLCO) is considered indicative of lung fibrosis progression. However, predicting changes in patient status and assessing variability based on PFT results can be challenging. Therefore, regular HRCT scans and comparison of the progression of honeycombing or reticular opacities are crucial for monitoring fibrotic changes. When it comes to prognostication, tracking the state of PPF can provide valuable insights [13]. PPF refers to patients with ILD who exhibit radiological evidence of lung fibrosis other than IPF. In addition, they should meet at least two of the following criteria within the past year: worsening of respiratory symptoms, physiological evidence of disease progression, and radiological evidence of disease progression using HRCT.

These diagnostic criteria for PPF are crucial, as they necessitate regular monitoring of individual symptoms, physiological parameters, and radiological evidence. Clinicians should consider not only patients' subjective perception of symptoms but also objective tools such as functional evaluation of declining FVC or decreasing DLCO, as well as precise radiological assessment using HRCT. These lessons can also be applied to CTD-ILD, a narrower and less common concept of pulmonary involvement in rheumatologic diseases, to effectively track patients with thoracic diseases.

High-resolution computed tomography

HRCT of the chest serves as the gold standard for assessing and monitoring CTD-ILD, similar to IPF. Despite its cost and radiation exposure, HRCT has proven to be superior to other conventional radiological imaging modalities such as chest X-ray or ultrasound [15]. In the early stages of lung involvement in CTD-ILD, HRCT typically reveals ground glass opacities (GGOs), which can indicate alveolitis as well as irreversible fibrosis, serving as a primary sign of ILD. However, it is important to note that HRCT imaging can be misleading based on the patient's position. In the supine position, lower parts of the lungs may exhibit increased opacity due to gravitational forces, which makes it difficult to differentiate GGOs caused by alveolitis in CTD-ILD. To prevent such confusion, acquiring images in the prone position is recommended (Figure 1).

CTD-ILD accounts for approximately 25% of PPF cases, and 33%~57% of patients with CTD have comorbid ILD [7]. HRCT imaging of CTD-ILD demonstrates similar characteristics to IPF, including GGO, honeycombing, traction bronchiectasis, and consolidation. The radiographic evidence of disease progression in PPF using HRCT is defined through visual assessment, with details described in Table 1 [13]. Fibrosis progression is typically assessed by the percentage of fibrotic lung volume in the upper, middle, and lower portions. Subsequent comparisons are made between HRCT sections of previous and follow-up images. Increasing fibrotic portions, along with features such as traction bronchiectasis, bronchiolectasis, newly appearing

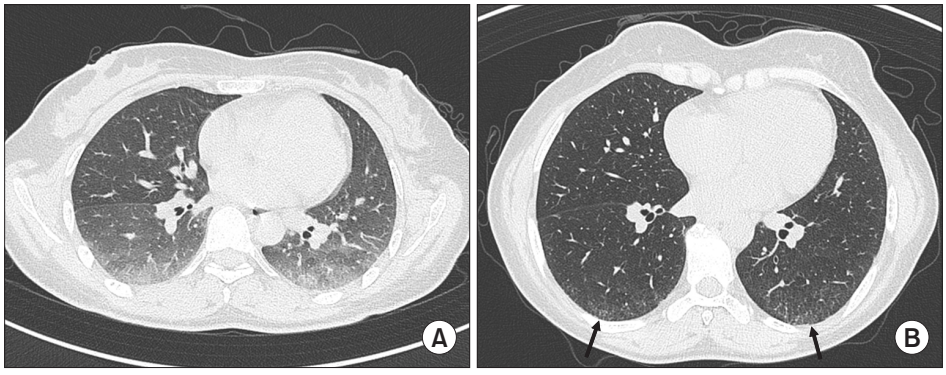

Figure 1. Effect of being in the supine position on high-resuloution computed tomography imaging. In the supine position, the effect of gravity on lung aeration and distribution of pulmonary abnormalities can lead to underestimation of lung abnormalities. (A) Supine expiratory scans may show increased opacity in dependent lung regions, limiting the assessment of interstitial abnormalities. (B) The prone scan demonstrates a recovery of aerated lung parenchyma in the lower lobes with a small area of residual consolidation. Subpleural reticulations are well delineated, suggesting early interstitial lung fibrosis (arrows).

Table 1. The definition of visual assessment within 12 months of progression in progressive pulmonary disease using HRCT [13]

	Definition
1. Increased traction bronchiectasis/bronchiolectasis	Irregular bronchial dilation by surrounding retractile pulmonary fibrosis
2. New GGO with traction bronchiectasis	Hazy opacity with dilated airways that may be seen as cysts or microcysts
3. New fine reticulation	Interlobular septal thickening, intralobular lines or honeycombing
4. Increased reticulation	Greater extent or coarseness of reticular abnormality
5. New or increased honeycombing	More clustered cystic air spaces, diameters of 3~10 mm, up to 2.5 cm
6. Increased lobar volume loss	Distorted lung anatomy due to pulmonary fibrosis accompanying lung volume loss

HRCT: high-resuloution computed tomography, GGO: ground glass opacity.

GGO or reticulation, and honeycombing, are all taken into consideration [13]. However, compared to IPF, CTD-ILD tends to exhibit more GGOs and less honeycombing [11,16]. HRCT can aid the identification of different pathologic classifications of ILDs, enabling the classification of various subtypes of CTD-ILDs and even the staging of the disease as early or progressive [10]. Dominant patterns of usual interstitial pneumonia (UIP) are observed in subpleural and basal regions, typically characterized by bilateral and peripherally dominant reticular opacities and honeycombing. UIP patterns may also present with features such as traction bronchiectasis, bronchiolectasis, structural distortion, or focal ground glass attenuation [10]. According to the Fleischner Society, honeycombing refers to clustered, thick-contoured cystic patterns with similar diameters and lengths of 3 to 5 mm, extending up to 25 mm [17]. Honeycombing often signifies advanced fibrosis and plays a significant role in diagnosing UIP (Figure 2). Characteristics of ILD in each CTD are organized in Table 2.

HRCT findings of RA-ILD commonly reveal GGOs and reticulation as the most frequent imaging patterns. Honeycombing, traction bronchiectasis, and architectural distortion are also common features observed in RA-ILD (Figure 3) [16]. In addition, non-cavitated nodules or peribronchial changes may be present [18]. Studies have reported that the dominant HRCT patterns in RA-ILD are UIP, nonspecific interstitial pneumonia (NSIP), and a combination of UIP and NSIP [19]. Apart from UIP and NSIP, bronchiolitis, and organizing pneumonia are also observed in RA-ILD [16].

Fibrosing ILD is a common presentation of SSc-ILD [11]. The characteristic feature of SSc-ILD is fibrosis predominantly affecting the basal portions of the lungs. The extent of fibrosis is often associated with an adverse prognosis [20]. The most frequent HRCT pattern seen in patients with SSc-ILD is NSIP, characterized by imaging findings of GGO, reticulation, and traction bronchiectasis primarily in the lower lobes of the lungs (Figure 4) [21]. UIP patterns are occasionally observed, and some patients may exhibit an unspecific pattern that does not fulfill the criteria of any defined classification [21].

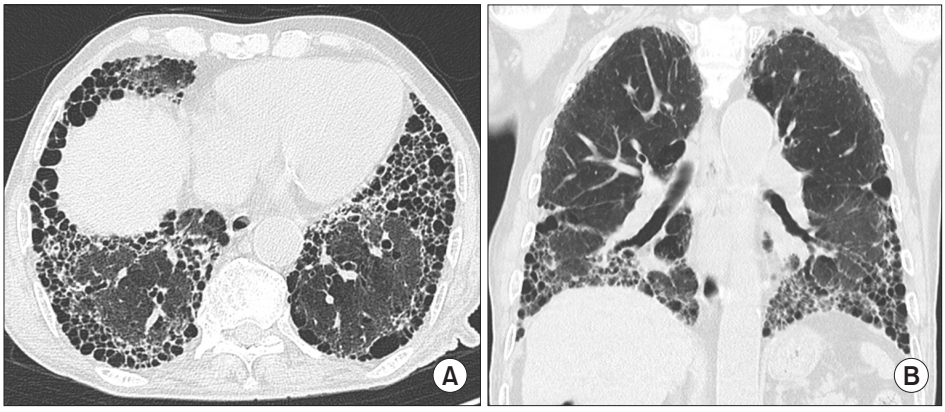

Figure 2. Honeycombing distribution showing the usual interstitial pneumonia (UIP) pattern. The image illustrates a predominant distribution of honeycombing with traction in the basal and subpleural regions. The presence of cystic spaces resembling honeycombs, primarily located in the lower regions of the lungs and adjacent to the pleural surfaces, indicates fibrotic changes characteristic of the UIP pattern. (A) Axial view, (B) coronal view.

Table 2. Characteristics of ILD in each CTD

CTD	Dominant characteristics (in order) HRCT patterns
1. Rheumatoid arthritis [16]	GGO, reticulation, honeycomb UIP, NSIP
2. Systemic sclerosis [21]	GGO, reticulation at basal portion NSIP, UIP
3. Sjögren's syndrome [23]	GGO, reticulation, consolidation, honeycomb NSIP, UIP, OP
4. Inflammatory myositis [27]	GGO, consolidation, reticulation NSIP, OP

ILD: interstitial lung disease, CTD: connective tissue diseases, HRCT: high-resuloution computed tomography, GGO: ground glass opacity, UIP: usual interstitial pneumonia, NSIP: nonspecific interstitial pneumonia, OP: organizing pneumonia.

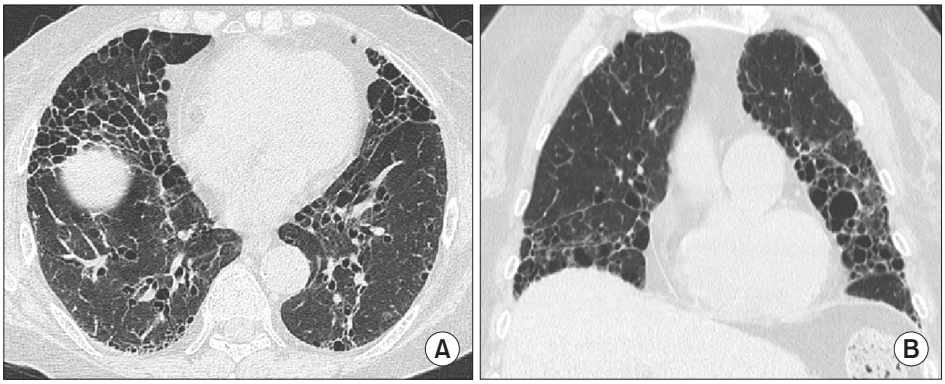

Figure 3. High-resuloution computed tomography (HRCT) in a rheumatoid arthritis (RA) patient. This image shows HRCT findings in a 60-year-old female patient with RA. The presence of honeycombing and traction bronchiectasis with upper to middle lung distribution is highly suggestive of connective tissue diseases-associated interstitial lung disease. (A) Axial view, (B) coronal view.

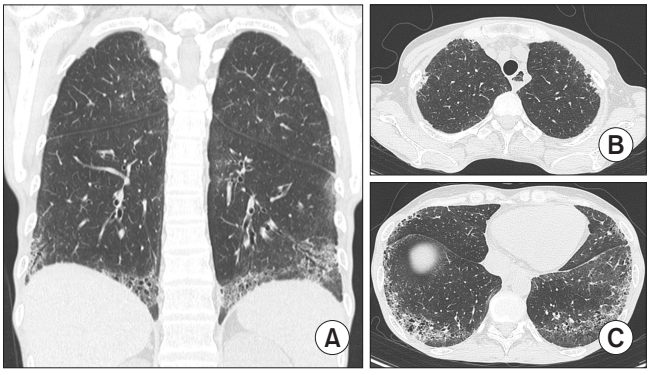

Figure 4. High-resuloution computed tomography (HRCT) of a systemic sclerosis patient. This image depicts HRCT findings in a 44-year-old female patient with systemic sclerosis. Peripheral and lower lung predominant reticulation, ground glass opacity, and traction bronchiolectasis with architectural distortion are observed. Immediate subpleural sparing is well visualized. A coronal reformatted scan highlights the presence of traction bronchiolectasis. In addition, esophageal dilation is noted in the upper thoracic esophagus. These findings are consistent with thoracic involvement in systemic sclerosis, with little evidence of honeycombing. (A) Coronal view, (B, C) axial view.

In pSS-ILD, patients manifest radiological patterns on HRCT that are similar to IIP [22]. Morphology consistent with NSIP, UIP, or lymphocytic interstitial pneumonia can all be observed in pSS-ILD (Figure 5). The common features include a combination of GGO, reticular patterns, consolidation, and honeycombing. Cysts, nodules, and bronchiectasis are often seen as well [23]. Bronchial involvement, both in small and large airways, can be observed, reflecting constrictive bronchiolitis with associated bronchiectasis [24]. HRCT images of pSS-ILD may sometimes reveal cylindrical-shaped isolated bronchiectasis in the lower lobes of the lungs [25].

The dominant HRCT patterns of inflammatory myositis-ILD are GGO, consolidation, and reticulation including intralobular reticular opacities, interlobular septal thickening, and nonseptal linear or plate-like opacities [26]. Inflammatory myositis is more commonly accompanied by NSIP and organizing pneumonia patterns than UIP patterns (Figure 6) [27]. In addition to those major features, HRCT scanning can demonstrate the parenchymal nodules, micronodules, interface irregularities, traction bronchiectasis and honeycombing [28].

When assessing disease severity and progression over time, HRCT and PFTs remain the most valuable tools for making treatment decisions for patients with CTD-ILD. Patients who have less than 10% pulmonary involvement as determined via HRCT, FVC greater than 75%, and DLCO above 65%, without respiratory symptoms, may not require immediate treatment. Instead, close observation with short-term follow-ups is recommended [27]. The recommended frequency of visits for CTD-ILD patients is typically every 3 to 6 months, with the same frequency for patients undergoing treatment. During each visit, PFTs and HRCT are suggested to assess any improvements or worsening in functional capacity and radiological changes. These evaluations help guide treatment decisions and monitor the response to therapy.

Lung ultrasound

Although HRCT is considered the gold standard imaging tool for ILD assessment, its high cost and risk of radiation exposure have prompted the search for more economical and safe methods of detecting ILD. In recent decades, LUS has gained increasing recognition in the clinical field [29]. Particularly af-

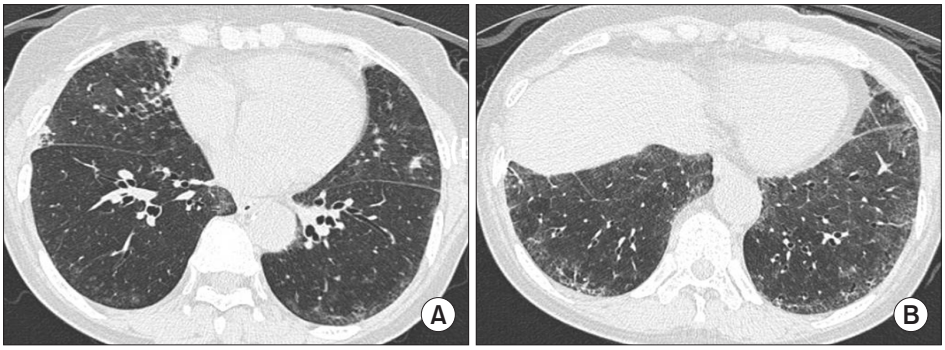

Figure 5. High-resuloution computed tomography (HRCT) of a patient with primary Sjögren's syndrome (pSS). HRCT findings in a 61-year-old female patient with pSS and biopsy-proven lymphocytic interstitial pneumonia. (A) The image reveals subpleural or peribronchial air space consolidation with ground glass opacity, along with multiple noncalcific nodules in both lungs. (B) Nodular or subpleural consolidations with septal thickening and traction bronchiolectasis are observed in the lower lobes.

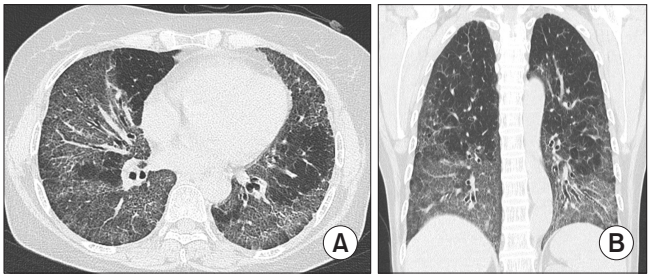

Figure 6. High-resuloution computed tomography (HRCT) of a patient with polymyositis (PM). HRCT findings in a 67-year-old male patient diagnosed with PM. The image shows areas of ground glass opacity and reticulations with peribronchovascular and lower lung predominance. The HRCT pattern suggests a differential diagnosis of nonspecific interstitial pneumonia and organizing pneumonia patterns. (A) Axial view, (B) coronal view.

ter the COVID-19 pandemic, attention has been drawn to the challenges faced by patients at risk for airborne infections who may have difficulties accessing shared examination spaces. LUS enables direct bedside examination of the lungs and pleural space, allowing patients to avoid prolonged stays in examination areas [30]. The scanning view of portable device enabling real-time examination is depicted in Figure 7 with its subdivision of truncal anterior and posterior area. While ultrasound beams have difficulty passing through air-filled lungs, lungs affected by CTD develop fluid or solid tissue, facilitating visualization using LUS [31]. Consequently, LUS has emerged as a cost-effective, noninvasive, radiation-free, and portable imaging tool that can complement traditional screening approaches [32].

When using LUS to assess ILD, three factors are considered crucial. B-lines, the main ultrasonographic sign originating from the pleural line, are synchronized with respiration and can be observed not only in CTD-ILD but also in other pulmonary conditions such as pneumonia and lung edema. B-lines are commonly seen in pulmonary fibrosis and appear as hyperechoic, laser-like vertical artifacts extending from the pleural line to the bottom of the ultrasound image. Multiple closely spaced and parallel B-lines indicate interstitial lung thickening and fibrosis. The pleural line, representing the lung surface, is an echogenic structure formed by the visceral and parietal pleura. Changes in the pleural line, such as thickening, fragmentation, or irregularity, can be associated with honeycombing in ILD, reflecting fibrotic changes and scarring in the lung tissue that affect the pleural surface. Subpleural changes, such as small hypoechogenic areas, are observed in conditions such as RA-ILD and sarcoidosis [33]. These markers play a role in evaluating CTD using LUS. LUS can detect subpleural lesions, appearing as hypoechoic areas or irregular nodules near the pleural line. These lesions may represent areas of fibrotic involvement or fibrotic lung masses in pulmonary fibrosis.

In addition to the three main factors mentioned earlier (B-lines, pleural line, and subpleural lesions), there are additional signs to consider when using LUS for examination. These include lung sliding, consolidations, and the shred sign. Lung sliding refers to the movement of the visceral and parietal pleura against each other during respiration. In pulmonary fibrosis, the loss of lung sliding can be observed due to the thickening and stiffness of the lung tissue [31]. Consolidations, which appear as hypoechoic regions with air bronchograms, may be present in areas of advanced fibrosis. Furthermore, the shred sign refers to the fragmented appearance of consolidated lung tissue, indicating fibrotic changes [34]. The presence of these signs in LUS

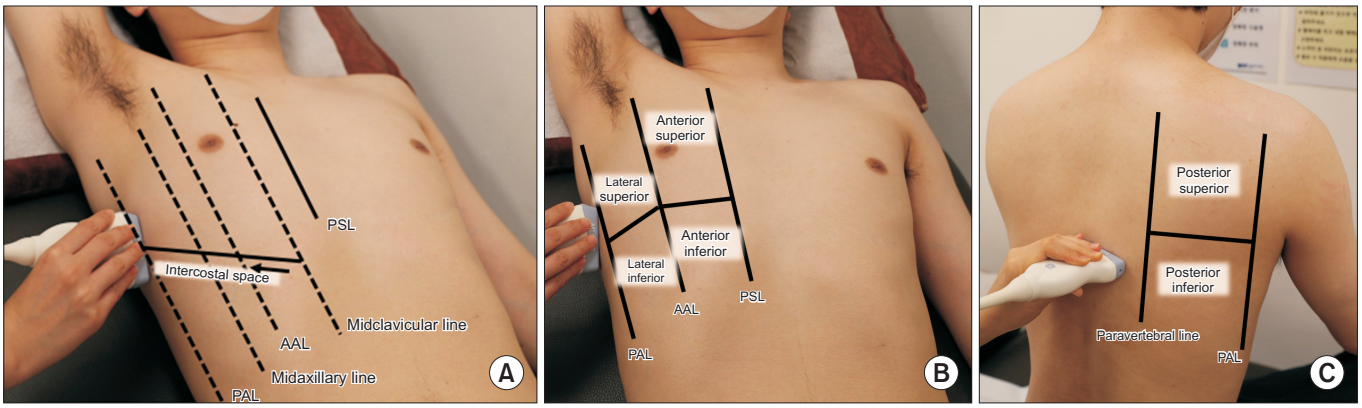

Figure 7. Subdivision of chest areas and scanning views in a lung ultrasound. (A) The image illustrates the subdivision of chest areas for basic scanning views in lung ultrasound. (B, C) A complete lung ultrasound examination includes transverse and longitudinal scans through the anterior, lateral, and posterior lungs. AAL: anterior axillary line, PAL: posterior axillary line, PSL: parasternal line [29,34,37].

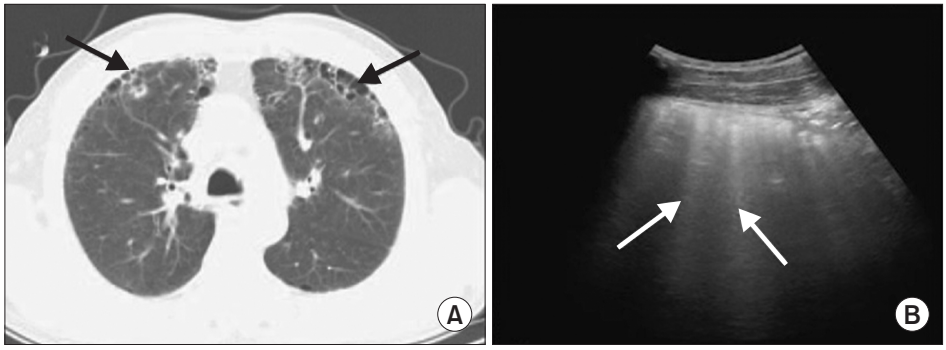

Figure 8. Characteristic findings in interstitial lung disease (ILD) detected by lung ultrasound. Lung ultrasound can reveal characteristic findings in ILD. However, the definitive diagnosis of ILD typically requires a combination of clinical assessment, imaging studies (such as high-resuloution computed tomography [HRCT]), and sometimes a lung biopsy. (A) Traction bronchiectasis and parenchymal changes of upper lung in HRCT (arrows). (B) Corresponding changes of lung ultrasound presented by B-lines (arrows).

may indicate abnormalities in the lungs.

One advantage of LUS is its ability to obtain dynamic images of the lungs without radiation, which makes it a safe examination method for pregnant women and children [35]. Using B-lines and the pleural line, LUS can evaluate lung parenchymal lesions and detect damage in the pleural or subpleural regions (Figure 8). The thickness of the pleural line can also be used to assess the severity of ILD, showing a good correlation with HRCT findings [36]. B-lines have been found to have a negative correlation with FVC and DLCO [37]. Despite its usefulness in detecting and tracking CTD-ILD, LUS imaging can be affected by the presence of air in the lungs, and its detection range is limited. While B-lines are valuable indicators, they are not specific markers of ILD and can be observed in other conditions such as aspiration, acute respiratory distress syndrome, or pneumonia [35]. In addition, the effectiveness of LUS depends on various factors, including scanning settings, probes, frequency, and most importantly, the operator's expertise. Therefore, while LUS can complement other imaging modalities, it has limitations when used as a standalone method for the diagnosis and follow-up of CTD-ILD.

Magnetic resonance imaging

MRI is an advanced radiological modality capable of acquiring detailed images of specific organs. While HRCT is critical in the initial and subsequent evaluations of CTD-ILD, the inherent exposure to radiation makes it less desirable. MRI, on the other hand, provides three-dimensional images of internal organ structures without radiation exposure. However, it is important to note that MRI is costly, time-consuming, and may pose challenges for patients with claustrophobia or those requiring close monitoring of vital signs. Because patients with rheumatologic

diseases are often diagnosed at a young age, the chronic nature of these conditions, including CTD-ILD, necessitates repeated radiological examinations to monitor disease progression and response to medication. This is particularly relevant for women of childbearing age and those who are pregnant, as they are more sensitive to radiation-related risks [38]. While LUS has been introduced as an alternative to avoid radiation, it has significant limitations such as a limited visual field and subjectivity in interpretation, as well as the absence of established quality control and licensing, which may lead to inappropriate assessments [38].

MRI presents a promising option for the diagnosis and monitoring of CTD-ILD. Unlike HRCT, MRI does not use ionizing radiation, addressing one of the main limitations of traditional imaging. Furthermore, MRI can provide both functional and structural information simultaneously [39]. Recent advancements in lung MRI techniques allow for the evaluation of lung structure, perfusion, ventilation, and inflammation. The ability to characterize tissues and differentiate between inflammatory and fibrotic changes could significantly advance the assessment of disease progression and treatment efficacy in ILD [40]. Some studies have shown that MRI is capable of detecting sensitive inflammatory changes by visualizing increased water content in affected tissues [41]. Consequently, MRI has demonstrated potential for superior detection of disease activity compared to HRCT [42]. These findings instill hope for the possibility of utilizing MRI for the detection and monitoring of CTD-ILD (Table 3) [43,44].

The primary protocol for lung MRI involves a non-contrast breath-holding technique lasting approximately 15 minutes [45]. This protocol utilizes two-dimensional balanced steady-state free-precession sequences and has shown that MRI has a sensitivity of 89% in identifying lung fibrosis, 75% in detecting GGOs, and 67% in visualizing traction bronchiectasis compared to CT [46]. When contrast-enhanced sequences are added to the standard protocol, they can further facilitate the evaluation of pulmonary fibrosis [47]. Currently, the most promising MRI sequences for assessing lung abnormalities are the ultra-short echo-time sequences (Figure 9) [48]. These sequences utilize extremely short echo times in the range of microseconds, limiting signal decay and providing high-resolution images.

However, patients with CTD-ILD, particularly those in the moderate to advanced stages of the disease, may encounter difficulties in maintaining breath-holding, which makes techniques that require prolonged breath-holding challenging. In addition, using high-field MRI systems can lead to motion artifacts and field inhomogeneities that complicate fat saturations. The lungs, in particular, pose a challenge due to their inherently poor signal-to-noise ratio [10]. Moreover, MRI is an expensive imaging modality, and patients often experience long waiting periods before undergoing the examination. The discomfort of remaining in a static position within the noisy MRI environment adds to the challenges associated with MRI. These limitations, along with the difficulties faced by patients with emergencies, metallic implants, or other monitoring accessories, hinder MRI from becoming the gold standard imaging modality for CTD-ILD.

It is important to emphasize that although MRI of the lung can provide valuable information about ILD, HRCT remains the imaging modality of choice for evaluating ILD due to its superior spatial resolution. HRCT allows for detailed visualization of lung parenchymal abnormalities, which makes it the preferred method for assessing ILD. MRI is typically reserved for specific

Table 3. Recent research comparing lung MRI and HRCT for detecting and tracing connective tissue diseases-related interstitial lung disease (CTD-ILD)

Author	Year of publication	Number of subjects	Result	Limitation
Lutterbey et al. [42]	2007	21	Lung MRI performed slightly better compared to CT	Enhanced motion artifacts, field inhomogeneities, fat saturation
Hekimoğlu et al. [43]	2010	20	Almost perfect agreement for lesion detection between MRI study groups and gold standard CT images	Breath-hold examination might be difficult for patients with progressive massive fibrosis
Pinal-Fernandez et al. [44]	2016	18	MRI showed good performance to detect ILD and was correlated with FVC, DLCO, and HRCT	MRI values were lower than HRCT values

MRI: magnetic resonance imaging, HRCT: high-resolution computed tomography, FVC: forced vital capacity, DLCO: diffusing capacity of the lung for carbon monoxide.

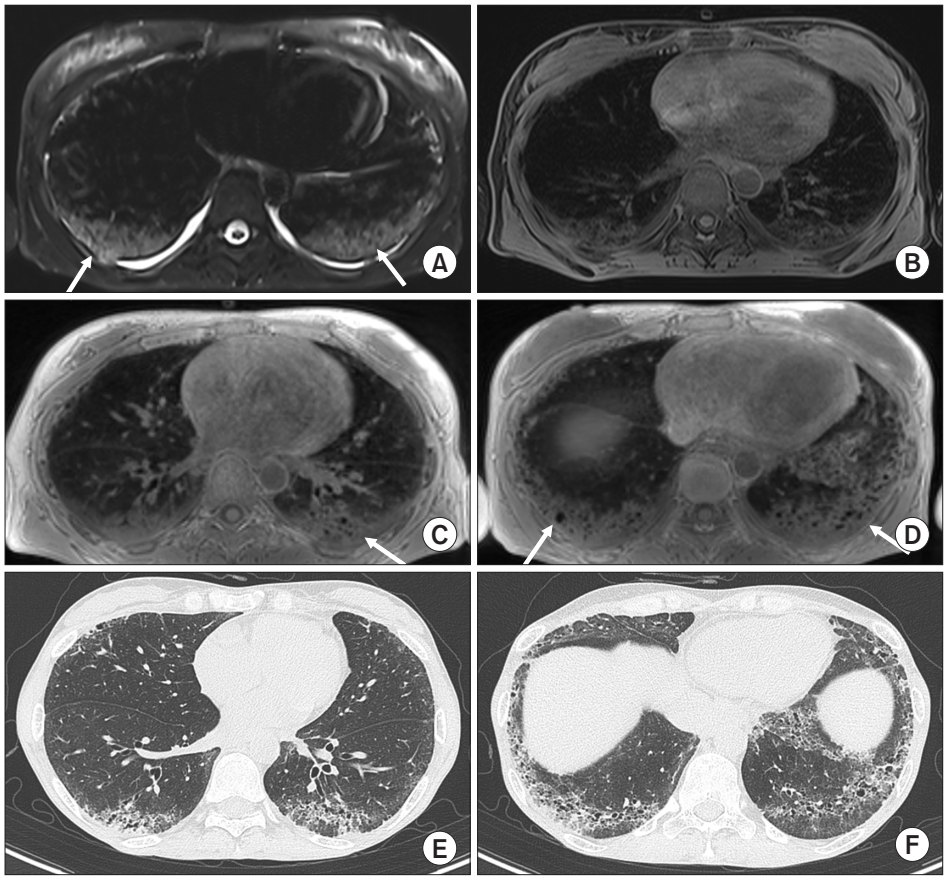

Figure 9. Characteristic findings in interstitial lung disease (ILD) detected by lung magnetic resonance imaging (MRI). In ILD, lung MRI can reveal several characteristic findings. (A) Single-shot fast spin echo T2-weighted MRI demonstrates high signal intensity in the area of lung fibrosis (arrows). (B) Fat-saturated nonenhanced T1-weighted MRI shows suspicious reticulations in both dorsal lungs. (C, D) Ultra-short echo-time sequence images provide more delineated reticulations and a microcystic appearance (traction bronchiolectasis and honeycombing cysts) in both lower lobes (arrows). (E, F) Comparative high-resuloution computed tomography scans corresponding to (C) and (D).

Table 4. Strengths and weakness of each imaging modality

	Strength	Weakness
HRCT	Spatial resolution enables detailed visualization of lung parenchymal abnormalities	Radiation exposure Moderate cost Immobility of the device Shared examination spaces
LUS	Portability Cost-effective Non-invasive Radiation-free Real-time dynamic images	Limited range of detection No specific markers of ILD Operator dependence
MRI	Radiation-free Non-invasive Differentiation between fibrotic and inflammatory changes in tissue	High cost Noise Lengthy examination time Immobility of the device Shared examination spaces Not possible for people with certain medical conditions (i.e. pacemaker or implantable cardiac defibrillator insertion, claustrophobia, inability of breath-holding etc.)

HRCT: high-resolution computed tomography, LUS: lung ultrasound, MRI: magnetic resonance imaging, ILD: interstitial lung disease.

indications or situations where HRCT is contraindicated, as it may have limitations in spatial resolution compared to HRCT. The strengths and weaknesses of each imaging modality are summarized in Table 4.

CONCLUSION

Timely diagnosis of CTD-ILD is crucial as it allows for the timely administration of appropriate medications, which can help prevent further disease progression and improve prognosis. Imaging modalities play a significant role in detecting adverse changes in the lungs. HRCT is widely recommended in established guidelines for the diagnosis and monitoring of PPF. It is considered the gold standard for assessing CTD-ILD and serves as a screening tool, particularly in SSc-ILD. The extent of pulmonary fibrosis observed via HRCT and the decline in PFTs at the time of diagnosis are important prognostic factors in SSc-ILD. Therefore, HRCT is essential for determining treatment strategies and predicting prognosis in CTD-ILD [7]. It is crucial for radiological examinations to not only provide accurate diagnostic information and disease monitoring but also prioritize patient safety. LUS and lung MRI have emerged as alternative imaging options that do not involve radiation exposure, but they each have their limitations.

Achieving appropriate detection of the clinical and radiological manifestations of CTD-ILD is essential for accurate diagnosis and effective treatment, ultimately leading to better patient outcomes. Advancing the clinical field of CTD-ILD research requires a collaborative multidisciplinary approach involving rheumatologists, pulmonologists, and radiologists. Their collective efforts are instrumental in improving the radiologic approach and advancing exploration in practical CTD-ILD practice, enhancing our understanding of the disease and developing effective strategies to manage it. Rheumatologists are dedicated to continuous improvement in this field, aiming to provide better care and outcomes for individuals with CTD-ILD.

FUNDING

None.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Conceptualization: H.S.K. Data curation or/and Analysis: B.D.N. Writing - original draft: H.J. Writing - Review & Editing: H.S.K., C.H.Y. All authors read and approved the final manuscript.

ORCID

Hyeji Jeon, https://orcid.org/0009-0002-8346-382X
Bo Da Nam, https://orcid.org/0000-0001-7822-6104
Chong-Hyeon Yoon, https://orcid.org/0000-0003-2305-4637
Hyun-Sook Kim, https://orcid.org/0000-0001-9213-7140

REFERENCES

1. Koo SM, Kim SY, Choi SM, Lee HK; Korean Interstitial Lung Diseases Study Group. Korean guidelines for diagnosis and management of interstitial lung diseases: part 5. Connective tissue disease associated interstitial lung disease. Tuberc Respir Dis (Seoul) 2019;82:285-97.
2. Fischer A, du Bois R. Interstitial lung disease in connective tissue disorders. Lancet 2012;380:689-98. Erratum in: Lancet 2012;380:1148.
3. Castelino FV, Goldberg H, Dellaripa PF. The impact of rheumatological evaluation in the management of patients with interstitial lung disease. Rheumatology (Oxford) 2011;50:489-93.
4. Shao T, Shi X, Yang S, Zhang W, Li X, Shu J, et al. Interstitial lung disease in connective tissue disease: a common lesion with heterogeneous mechanisms and treatment considerations. Front Immunol 2021;12:684699.
5. Hansell DM. Computed tomography of diffuse lung disease: functional correlates. Eur Radiol 2001;11:1666-80.
6. Sauleda J, Núñez B, Sala E, Soriano JB. Idiopathic pulmonary fibrosis: epidemiology, natural history, phenotypes. Med Sci (Basel) 2018;6:110.
7. Song JW. Interstitial lung disease in connective tissue disease. J Rheum Dis 2014;21:282-8.
8. Vij R, Strek ME. Diagnosis and treatment of connective tissue disease-associated interstitial lung disease. Chest 2013;143:814-24.
9. Duman D. Progressive pulmonary fibrosis (PPF). Tuberk Toraks 2022;70:375-81.
10. Walsh SLF, Devaraj A, Enghelmayer JI, Kishi K, Silva RS, Patel N, et al. Role of imaging in progressive-fibrosing interstitial lung diseases. Eur Respir Rev 2018;27:180073.
11. Cottin V, Hirani NA, Hotchkin DL, Nambiar AM, Ogura T, Otaola

M, et al. Presentation, diagnosis and clinical course of the spectrum of progressive-fibrosing interstitial lung diseases. Eur Respir Rev 2018;27:180076.
12. Torres PPTES, Rabahi MF, Moreira MADC, Escuissato DL, Meirelles GSP, Marchiori E. Importance of chest HRCT in the diagnostic evaluation of fibrosing interstitial lung diseases. J Bras Pneumol 2021;47:e20200096.
13. Raghu G, Remy-Jardin M, Richeldi L, Thomson CC, Inoue Y, Johkoh T, et al. Idiopathic pulmonary fibrosis (an update) and progressive pulmonary fibrosis in adults: an official ATS/ERS/JRS/ALAT clinical practice guideline. Am J Respir Crit Care Med 2022;205:e18-47.
14. Pugashetti JV, Adegunsoye A, Wu Z, Lee CT, Srikrishnan A, Ghodrati S, et al. Validation of proposed criteria for progressive pulmonary fibrosis. Am J Respir Crit Care Med 2023;207:69-76.
15. Emilsson ÖI, Dessle A, Johansson H, Adeli S, Malinovschi A, Eloranta ML, et al. Different chest HRCT scan protocols change the extent of ground glass opacities. BMC Pulm Med 2022;22:430.
16. Tanaka N, Kim JS, Newell JD, Brown KK, Cool CD, Meehan R, et al. Rheumatoid arthritis-related lung diseases: CT findings. Radiology 2004;232:81-91.
17. Lynch DA, Sverzellati N, Travis WD, Brown KK, Colby TV, Galvin JR, et al. Diagnostic criteria for idiopathic pulmonary fibrosis: a Fleischner Society White Paper. Lancet Respir Med 2018;6:138-53.
18. Balbir-Gurman A, Guralnik L, Yigla M, Braun-Moscovici Y, Hardak E. Imaging aspects of interstitial lung disease in patients with rheumatoid arthritis: literature review. Autoimmun Rev 2018;17:87-93.
19. Smith M, Dalurzo M, Panse P, Parish J, Leslie K. Usual interstitial pneumonia-pattern fibrosis in surgical lung biopsies. Clinical, radiological and histopathological clues to aetiology. J Clin Pathol 2013;66:896-903.
20. Hoffmann-Vold AM, Fretheim H, Halse AK, Seip M, Bitter H, Wallenius M, et al. Tracking impact of interstitial lung disease in systemic sclerosis in a complete nationwide cohort. Am J Respir Crit Care Med 2019;200:1258-66.
21. Khanna SA, Nance JW, Suliman SA. Detection and monitoring of interstitial lung disease in patients with systemic sclerosis. Curr Rheumatol Rep 2022;24:166-73. Erratum in: Curr Rheumatol Rep 2022;24:321.
22. Luppi F, Sebastiani M, Silva M, Sverzellati N, Cavazza A, Salvarani C, et al. Interstitial lung disease in Sjögren's syndrome: a clinical review. Clin Exp Rheumatol 2020;38 Suppl 126(4):291-300.
23. Lohrmann C, Uhl M, Warnatz K, Ghanem N, Kotter E, Schaefer O, et al. High-resolution CT imaging of the lung for patients with primary Sjogren's syndrome. Eur J Radiol 2004;52:137-43.
24. Nakanishi M, Fukuoka J, Tanaka T, Demura Y, Umeda Y, Ameshima S, et al. Small airway disease associated with Sjögren's syndrome: clinico-pathological correlations. Respir Med 2011;105:1931-8.
25. Soto-Cardenas MJ, Perez-De-Lis M, Bove A, Navarro C, Brito-Zeron P, Diaz-Lagares C, et al. Bronchiectasis in primary Sjögren's syndrome: prevalence and clinical significance. Clin Exp Rheumatol 2010;28:647-53.
26. Tanizawa K, Handa T, Nakashima R, Kubo T, Hosono Y, Aihara K, et al. The prognostic value of HRCT in myositis-associated interstitial lung disease. Respir Med 2013;107:745-52.
27. Gutsche M, Rosen GD, Swigris JJ. Connective tissue disease-associated interstitial lung disease: a review. Curr Respir Care Rep 2012;1:224-32.
28. Marie I, Hachulla E, Chérin P, Dominique S, Hatron PY, Hellot MF, et al. Interstitial lung disease in polymyositis and dermatomyositis. Arthritis Rheum 2002;47:614-22.
29. Vizioli L, Ciccarese F, Forti P, Chiesa AM, Giovagnoli M, Mughetti M, et al. Integrated use of lung ultrasound and chest X-ray in the detection of interstitial lung disease. Respiration 2017;93:15-22.
30. European Society of Radiology (ESR). The role of lung ultrasound in COVID-19 disease. Insights Imaging 2021;12:81.
31. Volpicelli G. Lung sonography. J Ultrasound Med 2013;32:165-71.
32. Tinti MG, Rea G, Mirijello A, Frongillo E, Sperandeo M. Is there any role for thoracic ultrasound for interstitial lung disease underlying rheumatologic conditions? Comment. Intern Emerg Med 2017;12:903-4.
33. Moazedi-Fuerst FC, Kielhauser SM, Scheidl S, Tripolt NJ, Lutfi A, Yazdani-Biuki B, et al. Ultrasound screening for interstitial lung disease in rheumatoid arthritis. Clin Exp Rheumatol 2014;32:199-203.
34. Marini TJ, Rubens DJ, Zhao YT, Weis J, O'Connor TP, Novak WH, et al. Lung ultrasound: the essentials. Radiol Cardiothorac Imaging 2021;3:e200564.
35. Huang Y, Liu T, Huang S, Qiu L, Luo F, Yin G, et al. Screening value of lung ultrasound in connective tissue disease related interstitial lung disease. Heart Lung 2023;57:110-6.
36. Sperandeo M, Varriale A, Sperandeo G, Filabozzi P, Piattelli ML, Carnevale V, et al. Transthoracic ultrasound in the evaluation of pulmonary fibrosis: our experience. Ultrasound Med Biol 2009;35:723-9.
37. Gargani L, Doveri M, D'Errico L, Frassi F, Bazzichi ML, Delle Sedie A, et al. Ultrasound lung comets in systemic sclerosis: a chest sonography hallmark of pulmonary interstitial fibrosis. Rheumatology (Oxford) 2009;48:1382-7.
38. Picano E, Matucci-Cerinic M. Unnecessary radiation exposure from medical imaging in the rheumatology patient. Rheumatology (Oxford) 2011;50:1537-9.
39. Barreto MM, Rafful PP, Rodrigues RS, Zanetti G, Hochhegger B, Souza AS Jr, et al. Correlation between computed tomographic and magnetic resonance imaging findings of parenchymal lung diseases. Eur J Radiol 2013;82:e492-501.
40. Tiddens HA, Stick SM, Wild JM, Ciet P, Parker GJ, Koch A, et al. Respiratory tract exacerbations revisited: ventilation, inflammation, perfusion, and structure (VIPS) monitoring to redefine treatment. Pediatr Pulmonol 2015;50 Suppl 40:S57-65.
41. Shioya S, Tsuji C, Kurita D, Katoh H, Tsuda M, Haida M, et al. Early damage to lung tissue after irradiation detected by the magnetic resonance T2 relaxation time. Radiat Res 1997;148:359-64.
42. Lutterbey G, Grohé C, Gieseke J, von Falkenhausen M, Morakkabati N, Wattjes MP, et al. Initial experience with lung-MRI at 3.0T: Comparison with CT and clinical data in the evaluation of interstitial lung disease activity. Eur J Radiol 2007;61:256-61.
43. Hekimoğlu K, Sancak T, Tor M, Beşir H, Kalaycioğlu B, Gündoğdu S. Fast MRI evaluation of pulmonary progressive massive fibrosis with VIBE and HASTE sequences: comparison with CT. Diagn Interv Radiol 2010;16:30-7.
44. Pinal-Fernandez I, Pineda-Sanchez V, Pallisa-Nuñez E, Simeon-Aznar CP, Selva-O'Callaghan A, Fonollosa-Pla V, et al. Fast 1.5 T

chest MRI for the assessment of interstitial lung disease extent secondary to systemic sclerosis. Clin Rheumatol 2016;35:2339-45.
45. Hochhegger B, de Souza VV, Marchiori E, Irion KL, Souza AS Jr, Elias Junior J, et al. Chest magnetic resonance imaging: a protocol suggestion. Radiol Bras 2015;48:373-80.
46. Rajaram S, Swift AJ, Capener D, Telfer A, Davies C, Hill C, et al. Lung morphology assessment with balanced steady-state free precession MR imaging compared with CT. Radiology 2012;263:569-77.
47. Lonzetti L, Zanon M, Pacini GS, Altmayer S, Martins de Oliveira D, Rubin AS, et al. Magnetic resonance imaging of interstitial lung diseases: a state-of-the-art review. Respir Med 2019;155:79-85.
48. Romei C, Turturici L, Tavanti L, Miedema J, Fiorini S, Marletta M, et al. The use of chest magnetic resonance imaging in interstitial lung disease: a systematic review. Eur Respir Rev 2018;27:180062.