

## Original Research Article

# Evaluation of diffuse lung diseases by high resolution computed tomography of chest

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### ABSTRACT

**Background:** Diffuse lung diseases describe a heterogeneous group of disorders of the lower respiratory tract characterized by inflammation and derangement of the interstitium and loss of functional alveolar units. The disease is not restricted to the interstitium only, as it involves epithelial, endothelial and mesenchymal cells with the disease process extending into the alveoli, acini and bronchioles. Thus, the entire pulmonary parenchyma is involved. The objective of the study was to evaluate diffuse lung diseases by high resolution computed tomography of chest.

**Methods:** A cross-sectional observational study was done in 30 patients. Adult patients of either sex of age group 18 and above showing reticular opacities on chest X-ray and those patients who were incidentally diagnosed as cases of diffuse lung diseases on HRCT chest were included in present study.

**Results:** Reticular opacities were the most common roentgenographic finding followed by reticulonodular opacities. On HRCT, intra and interlobular septal thickening was the most common finding in Idiopathic interstitial pneumonia (usual interstitial pneumonia).

**Conclusions:** High resolution computed tomography (HRCT) is superior to the plain chest X-ray for early detection and confirmation of suspected diffuse lung diseases. In addition, HRCT allows better assessment of the extent and distribution of disease, and it is especially useful in the investigation of patients with a normal chest radiograph. Coexisting disease is often best recognized on HRCT scanning.

**Keywords:** Computed tomography, Diffuse lung diseases, High resolution

### INTRODUCTION

Diffuse lung diseases describe a heterogeneous group of disorders of the lower respiratory tract characterized by inflammation and derangement of the interstitium and loss of functional alveolar units. The disease is not restricted to the interstitium only, as it involves epithelial, endothelial and mesenchymal cells with the disease process extending into the alveoli, acini and bronchioles. Thus, the entire pulmonary parenchyma is involved.

The disorders in this heterogeneous group are classified together because of similar clinical, roentgenographic,

physiologic, or pathologic manifestations. These disorders often are associated with considerable rates of morbidity and mortality. Diffuse lung diseases comprise over 200 entities of known and unknown causes, with or without associated systemic diseases, of acute or chronic onset, of indolent or rapidly progressive course and wide variations in treatment response.

#### Classification

American Thoracic Society/European Respiratory Society classified these disorders into 4 broad categories:<sup>1</sup>

- Diffuse lung diseases of known causes
- Idiopathic interstitial pneumonia
- Granulomatous diseases
- Rare forms of diffuse lung disease

#### ***Diffuse lung diseases of known causes***

##### *Drugs*

- Chemotherapeutic- Bleomycin, Methotrexate
- Cardiovascular- Amiodarone
- Antibiotics- Nitrofurantoin, Sulphasalazine
- Anti-inflammatory- Gold, Penicillamine
- Illicit drugs- Heroin, Methadone
- Miscellaneous- Oxygen, Radiation

##### *Systemic diseases*

- a. Connective tissue disorders
  - Systemic Sclerosis
  - Sjogren's syndrome
  - Systemic Lupus Erythematosus
  - Ankylosing Spondylitis
  - Rheumatoid Arthritis
- b. Vasculitis
  - Wegener's granulomatosis
  - Good pasture's syndrome
  - Microscopic polyangitis
- c. Inherited disorders
  - Tuberous Sclerosis
  - Neurofibromatosis
  - Lipid storage disorders
  - Hermansky-Pudlak syndrome

##### *Occupational/ environmental exposure*

- a. Inorganic dusts
  - Fibrogenic- Asbestosis, Silicosis
  - Non-fibrogenic- Siderosis (Iron), Stannosis (Tan)
  - Granulomatous-Berylliosis
- b. Organic dusts
  - Bacteria- Farmer's lung (thermoactinomycetes in mouldy hay)
  - Bagassosis- (thermoactinomycetes in mouldy sugarcane)
  - Fungi- Suberosis (in cork workers), Cheese workers' lung (mouldy cheese)
  - Animal protein- Bird fanciers' lung (avian protein on feathers)

#### ***Idiopathic interstitial pneumonia***

- Usual interstitial pneumonia
- Non-specific interstitial pneumonia
- Desquamative interstitial pneumonia
- Acute interstitial pneumonia
- Respiratory bronchiolitis- interstitial lung disease
- Cryptogenic organizing pneumonia
- Lymphocytic interstitial pneumonia

#### ***Granulomatous diseases***

- Sarcoidosis
- Wegener's granulomatosis
- Churg Strauss syndrome
- Extrinsic allergic alveolitis

#### ***Rare forms of diffuse lung diseases***

- Lymphangiomyomatosis
- Langerhans cell histiocytosis
- Alveolar proteinosis
- Eosinophilic pneumonia

Though the etiology may vary vastly, yet the clinical signs and symptoms may differ little from one condition to another. The majority of patients present typically with progressive or unremitting dyspnoea and dry unproductive cough. Chest pain, wheezing and haemoptysis are unusual symptoms. Symptoms in diffuse lung diseases are usually chronic, ranging from few months to years. The physical examination may reveal bilateral basal or widespread inspiratory crept on auscultation. Resting tachypnea and tachycardia may be present. Digital clubbing and cyanosis usually indicates far advanced fibrotic disease.

The assessment of pulmonary function is an essential component of the evaluation of patients suspected of having diffuse lung disease. They typically show a reduction in the static lung volumes, decreased pulmonary compliance and a reduction in diffusing capacity.

Plain radiography remains the first and foremost imaging modality in patient with suspected diffuse lung diseases. In most cases this is abnormal. The radiographic appearances may be sufficiently characteristic to enable a specific diagnosis. However, in a small proportion (10-20%) of patients with open lung biopsy confirmation of diffuse lung disease, the chest radiograph may be normal.

Introduction of computed tomography (CT) revolutionized the radiologic diagnosis of chest diseases. The disadvantage of conventional CT was inability to resolve small structures in lung parenchyma. The use of CT, especially high resolution computed tomography for the precise anatomic definition of diffuse lung diseases

became possible with technical advancement in CT technology.

High Resolution CT is currently the most accurate non-invasive modality for evaluating the lung parenchyma. HRCT uses various technical factors which can increase the spatial resolution and they include narrow collimation, reconstruction using a high spatial frequency algorithm and targeting the image to a small field of view.

#### **Indications for the use of HRCT in diffuse lung diseases**

- Presence or confirmation of abnormality in patients with symptoms suggestive of diffuse lung disease with a normal or near normal chest radiograph
- Further assessment in patients with an abnormal but non-diagnostic chest radiograph.
- As a guide to the site and method of biopsy.
- As a guide to assessment of disease activity, especially in fibrosing alveolitis.
- To diagnose superimposed complications such as infection or tumor when they are clinically suspected but not visible on the chest radiograph.
- Histopathology is conventionally regarded as the gold standard in the definite diagnosis of diffuse lung disease. The suitable tissue for diagnosing intrathoracic disease may be obtained by medical techniques i.e. bronchoscopic and transcutaneous biopsy or by surgery i.e. mediastinal or open lung biopsy. However, the cost effectiveness and risks associated with it must be weighed against the potential benefits in an individual case.
- Though HRCT is an established technique for evaluating acute or chronic diffuse lung diseases, many potential pitfalls exist that may influence image analysis.

#### **METHODS**

This Cross-sectional Observational study was conducted in the department of Radiodiagnosis, Post Graduate Institute of Medical Education and Research, Dr. Ram Manohar Lohia Hospital, New Delhi, India from November 2014 to March 2016. Approval from hospital and Institutional Ethical Committee was obtained prior to initiation of the study.

Adult patients of either sex of age group 18 and above showing reticular opacities on chest X-ray and those patients who were incidentally diagnosed as cases of diffuse lung diseases on HRCT chest were included in our study. Patients who were referred to the Department of Radiodiagnosis, Dr R.M.L. Hospital and in whom chest X-ray findings matched the selection criteria were subjected to the HRCT chest. HRCT Chest was performed on Philips Brilliance 40 slice CT. A written informed consent was taken from all the patients.

After obtaining the scout film, area of scanning was defined which included the entire chest from apex to domes. The chest was scanned with 1mm thick sections at an interval of 10mm using HRCT techniques. HRCT was performed in supine position and at the end of suspended deep inspiration. No intravenous contrast was given. Scanning parameters included 1.9sec scan time, 105mA and 130kVp. The images thus generated were photographed at lung window i.e. ww 1650; wc 600. Additional window settings were adjusted manually at the time of imaging to enhance photography of subtle ground glass opacities that are best appreciated on wider window settings. The sections thus obtained were carefully studied for various HRCT characteristics of non-occupational diffuse lung diseases. The HRCT findings were correlated with forced vital capacity reports wherever possible.

#### **RESULTS**

We evaluated 30 patients of non-occupational diffuse lung diseases during the tenure of the study. 8 male and 22 female patients were evaluated with age range of 18-80 years.

- The mean age for the group was 44.2 years.
- The mean age for male patients was 52.3 years.
- The mean age for female patients was 44.1 years.
- Male to female ratio was 1:2.3.

The severity of dyspnea in these patients was graded from 0 to 4 as follows:<sup>2</sup>

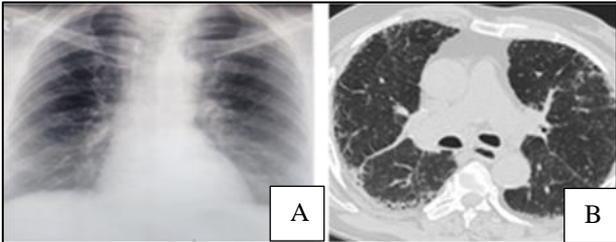
- Grade 0- No dyspnea
- Grade 1- Dyspnea following strenuous activity- doing heavy housework or climbing three flights of stairs.
- Grade 2- Dyspnea following moderate activity- with light housework or climbing one flight of stairs.
- Grade 3- Dyspnea with minimal activity
- Grade 4- Dyspnea at rest or with eating or talking

Dyspnea and dry cough were the most frequent associated symptoms. Chest pain and fever occurred together in a group of patients. Two patients have symptoms of joint pain. Six patients have a history of smoking. Inspiratory crackles on auscultation was the most common finding. Digital clubbing and cyanosis occurred in association with grade 3-4 dyspnea. Four patients showed no clinical finding.

Majority of the patients (46%) have reticular opacities on Chest X-ray. Reticulonodular opacities were noted in nearly 26% of the patients. No abnormality on chest X-ray was detected in 26% of incidentally diagnosed cases on HRCT Chest. Intra and interlobular septal thickening was noted in majority of the patients (90%). Ground glass opacities were present in 43% of patients and honeycombing in 40% of patients. Traction

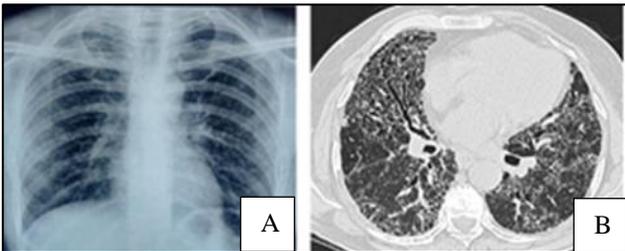
bronchiectasis was noted in association in nearly 23% of patients. Idiopathic Interstitial pneumonia was noted in majority of patients (~80%).

In IIPs, UIP pattern was noted in 46% of patients and NSIP pattern in 30% of patients. Diffuse lung disease was noted in connective tissue disorders such as rheumatoid arthritis and scleroderma in 16% of patients. History of Smoking associated diffuse lung disease, RB-ILD and Langerhans cell histiocytosis was noted in one patient each.



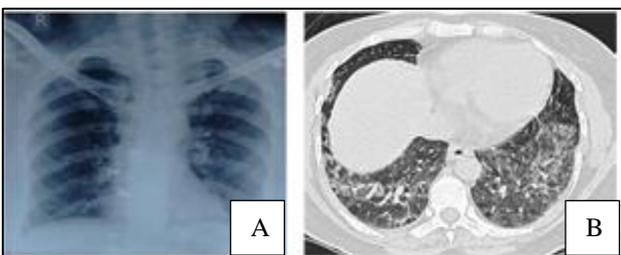
22-year-old female with dry cough. a) Chest x-ray reveals no abnormality. b) Axial HRCT image shows interstitial thickening and honeycombing predominantly in the sub pleural region suggestive idiopathic interstitial pneumonia likely usual interstitial pneumonia.

**Figure 1: Idiopathic interstitial pneumonia.**



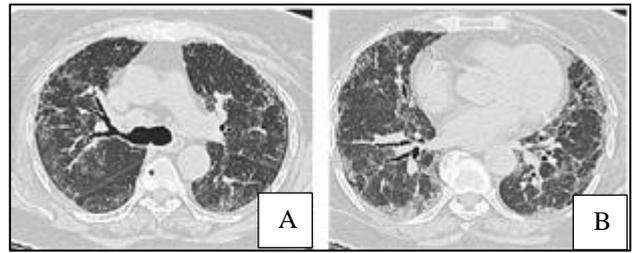
65-year-old male with dyspnoea and dry cough. a) Chest x-ray shows diffuse reticular opacities in b/l lung fields. b) Axial HRCT image shows diffuse interlobular septal thickening, honeycombing and traction bronchiectasis suggestive of idiopathic interstitial pneumonia likely usual interstitial pneumonia.

**Figure 2: Usual interstitial pneumonia.**



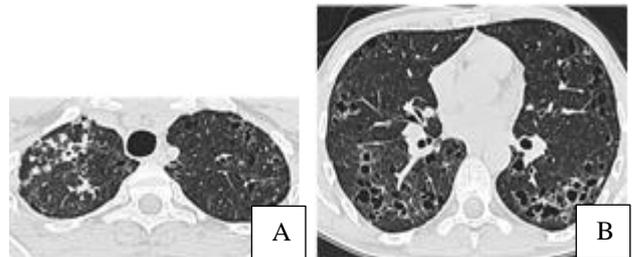
34-year-old female with dyspnoea. a) Chest x-ray shows reticular opacities in b/l lower lung zones. b) Axial HRCT image shows ground glass opacities in the basal segments of b/l lower lobes with areas of interstitial thickening suggestive of idiopathic interstitial pneumonia likely NSIP pattern.

**Figure 3: Idiopathic interstitial pneumonia NSIP pattern.**



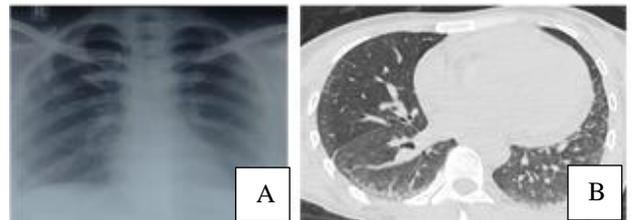
Axial HRCT image of a 65-year-old female shows interlobular septal thickening, ground glass opacities in bilateral lung parenchyma with peripheral sub pleural predominance and traction bronchiectasis suggestive of idiopathic interstitial pneumonia likely NSIP pattern.

**Figure 4: Idiopathic interstitial pneumonia.**



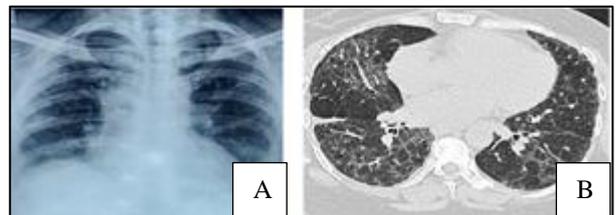
Axial HRCT image of a 38-year-old male with no history of smoking shows a) multiple centrilobular nodules in right upper lobe b) multiple cysts of bizarre shapes and variable sizes in bilateral lung parenchyma suggestive of pulmonary Langerhans cell histiocytosis.

**Figure 5: Langerhan's cell histiocytosis.**



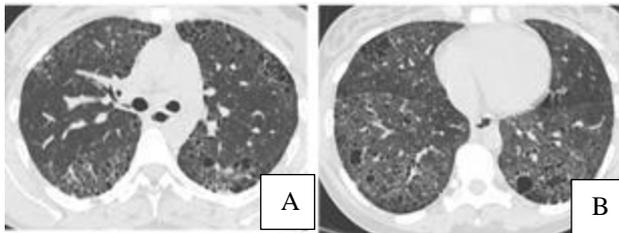
40-year-old female with known case of rheumatoid arthritis. a) Chest x-ray reveals no abnormality. b) Axial HRCT image shows interlobular septal thickening predominantly in b/l lower lobes in subpleural region with mild honeycombing suggestive of early UIP pattern.

**Figure 6: UIP pattern rheumatoid arthritis.**



31-year-old female with known case of scleroderma. a) Chest x-ray shows reticular opacities in b/l lower lung zones. b) Axial HRCT image shows diffuse interlobular septal thickening and ground glass opacities in bilateral lung fields. Fissural thickening noted in right lung fields F/S/O NSIP pattern.

**Figure 6: NSIP pattern scleroderma.**



53-year-old female with known case of scleroderma. Axial HRCT image shows diffuse interlobular and intralobular septal thickening with honeycombing predominantly involving the subpleural region of b/l lung fields suggestive of UIP pattern.

**Figure 8: UIP pattern scleroderma.**

## DISCUSSION

### *Clinical spectrum*

#### *Age and sex distribution*

The mean age of patients in our study was 44.2 years with the range of 21 to 72 years. There was a female preponderance in our study (~70% of the total cases). The previous reported series by Fulmer et al in 1979 also had a similar age distribution with the mean age of 47±15 years.<sup>3</sup> However, their series had no male to female preponderance. In the series reported by Murata et al, the mean age of their patients was around 53 years with slight female preponderance.

#### *Severity and duration of dyspnoea*

dyspnoea was the main presenting complaint in 60% of the patients in our study group. We graded the dyspnoea, according to the severity as suggested by Mawson et al.<sup>4</sup> 23% of the patients had grade 3 to 4 dyspnoea at the time of presentation. The dyspnoea was gradually progressive in the patients.

Only two patients had dyspnoea as an isolated symptom. In the rest, dry cough was the predominant associated symptom. The symptoms like fever, chest pain and joint pain were common in patients with connective tissue disorders (rheumatoid arthritis and scleroderma).

Various authors have tried to establish the relationship between a history of smoking and diffuse lung diseases. Ryu JH et al described four lung disorders linked to smoking- desquamative interstitial pneumonia, respiratory bronchiolitis- associated lung disease, pulmonary Langerhans cell histiocytosis and idiopathic pulmonary fibrosis.<sup>5</sup> 6 patients in our study gave a history of smoking and they all had diffuse lung disease as described by Ryu JH et al.

#### *Physical examination findings*

Inspiratory crackles on auscultation was the most frequent finding (53%) in our patients. Inspiratory crackles were heard in all patients of IIP (UIP) and

connective tissue disorders. They were present mostly in the basal lung fields. Epler et al reported that bilateral fine crackles were common in patients with idiopathic pulmonary fibrosis and connective tissue disorders, occurring in 60% of the patients, but generally reported in 90% of the patients with IPF.<sup>6</sup>

Digital clubbing (16%) and cyanosis (13%) were seen in patients with grade 3 or 4 dyspnoea, showing predominantly reticular opacities on chest radiography and on HRCT, most of these were IIP (UIP). Crystal et al found digital clubbing in 58% of cases of idiopathic pulmonary fibrosis.<sup>7</sup>

### *Forced vital capacity*

Forced vital capacity reports of all patients were evaluated in our study. All the values were expressed as percentage of predicted value, as per the standards laid down by American Thoracic Society.

Interstitial lung diseases show a typical restrictive pattern. Chinnet et al have described the restrictive lung pattern with FVC≤80%.<sup>8</sup>

In present series, mean value of FVC was 73.3% of the predicted value.

### *Radiological spectrum*

#### *Idiopathic interstitial pneumonias*

##### a. Usual Interstitial pneumonia

Present study included 14 patients with Idiopathic Interstitial pneumonia of UIP pattern, comprising 46% of total cases. The age of patients ranged from 24 to 72 years with most of the cases between 45-65 years. There was a preponderance of females in patients with UIP pattern.

On chest radiograph, a reticular pattern spread throughout the lung fields was the most commonly observed finding. The lower zones were involved more often (36%) as compared to upper and mid zones; and in cases of diffuse disease, the findings were more profuse in the lower zones. Staples et al reported similar findings in their study.

On HRCT scans, the predominant features observed were intra and interlobular septal thickening (92% cases) in a reticular pattern throughout the lung fields. Thickening of the interstitial network of the lung by fluid, fibrous tissue or cells primarily results in this appearance. Nishimura et al reported the incidence of septal thickening in 94% of cases.<sup>9</sup> Though a diffuse pattern of disease was observed in 55% of cases, the lower zones and the peripheral lung fields were more commonly involved. Muller et al reported the similar findings.

Honeycombing was present in 85% of cases, more commonly present in the sub pleural and peripheral location. Staples et al reported 90% incidence of honeycombing in cases of IPF identified on HRCT. Traction bronchiectasis and conglomerate fibrosis were associated with the presence of honeycombing.

Ground glass opacities were present in 60% of cases with UIP pattern. Similar findings were reported by Remy-Jardin et al.<sup>10</sup> Patchy ground glass opacities were seen in three cases, suggestive of early disease. It results from volume averaging of morphologic abnormalities below the resolution of HRCT. These findings suggest the presence of active reversible disease as suggested by Leung et al.<sup>11</sup>

#### b. Nonspecific interstitial pneumonia

Present study included 9 patients with Idiopathic NSIP comprising 30% of cases. Majority of the cases were in the range of 35-50 years. Plain radiography shows reticulonodular opacities in 55% cases and no abnormality was detected in the rest of the cases. On HRCT, the predominant feature observed was ground glass opacities in 88% cases. Patchy ground glass opacities were noted in three cases. Intra and interlobular septal thickening was present in 66% cases. Similar findings were reported by Cottin et al.<sup>12</sup> HRCT chest showed ground glass opacities in 81% cases, patchy areas of consolidation in 54% cases and thickening of interlobular septa in 45% cases

#### c. Respiratory bronchiolitis- interstitial lung disease

One case of respiratory bronchiolitis- interstitial lung disease was diagnosed in our study. Patient had a history of smoking of 15 pack years. On plain radiography reticulonodular opacities were noted in basal lung zones. On HRCT, ground glassing with interstitial thickening and bronchiolectasis were present. Similar findings were reported in patients with current or previous history of smoking by Ryu et al with ground glass opacities as the predominant finding in 100% of cases with RB-ILD.<sup>13</sup>

### **Connective tissue disorders**

#### *Rheumatoid arthritis*

Two cases of Rheumatoid arthritis had interstitial lung disease as an extraarticular manifestation. One case showed reticular opacities on plain radiography and diffuse septal thickening and honeycombing on HRCT suggestive of UIP pattern. The second case showed no abnormality on plain radiography, however on HRCT, intra and interlobular septal thickening was the only finding present suggestive of NSIP pattern. Akira et al reported similar HRCT findings for patients with RA-ILD.<sup>14</sup> 65% of cases had UIP pattern and the rest NSIP pattern. Tanaka et al demonstrated that 41% of a

retrospective RA-ILD cohort had UIP pattern seen on HRCT scans with 30% showing a NSIP pattern.<sup>15</sup>

#### *Scleroderma*

Three cases of scleroderma had interstitial lung disease as a pulmonary manifestation. Two cases showed no abnormality on plain radiography and on HRCT showed intra and interlobular septal thickening with ground glass opacities suggestive of NSIP pattern. One case showed reticular opacities on plain radiography and interlobular septal thickening and honeycombing on HRCT suggestive of UIP pattern. Schurawitzki et al studied patients with progressive systemic sclerosis in detecting interstitial lung involvement in these patients.<sup>16</sup> Chest radiographs showed definite interstitial opacification patterns in 39%, 26% had reticular areas of attenuation while 35% had normal chest radiographs. HRCT scans showed interstitial disease in 91% patients. The most frequent finding was sub pleural interstitial thickening demonstrated in 74% cases. Honeycombing was seen in 30% cases while parenchymal bands were seen in 26% cases.

#### ***Pulmonary langerhans cell histiocytosis***

One case of pulmonary Langerhans cell histiocytosis was diagnosed in our study. The patient had a history of smoking of 10 pack/day for 10 years. Plain radiography showed reticulonodular opacities and on HRCT scan, bizarre shaped cysts with multiple centrilobular nodules were present. Mogulkoc et al described similar findings in patients with pulmonary Langerhans cell histiocytosis. Chest radiography showed multiple focal nodules throughout both lungs with sparing of the costophrenic angles. HRCT confirmed the presence of multiple small nodules, many of which had central cavitation, forming cysts 1 to 5mm in diameter.

### **CONCLUSION**

HRCT has been proposed as a technique for determining the activity of IPF.<sup>17</sup> The CT finding of ground glass opacity refers to the presence of a diffuse homogenous increase in density of the lung. When this finding occurs in association with reticular lines and dilated bronchi or bronchioles (traction bronchiectasis or bronchiolectasis), it always indicates lung fibrosis. In conditions other than IPF, isolated ground glass density is usually associated with inflammatory cells in the alveolar septum or alveolar lumen (i.e. alveolitis).<sup>18</sup>

The ground glass opacity seen on HRCT in some patients with IPF can be associated with alveolar inflammation, but is predominantly associated with patchy fibrotic thickening of alveolar septa, and intraalveolar granulation tissue.<sup>19,20</sup> Ground glass opacity on HRCT often regresses on treatment but may not decrease as readily in patients with UIP. An area of ground glass opacity may progress to reticular opacity or honeycombing on follow-up

examination. Patients with predominant reticular opacity or honeycombing usually progress despite treatment. The extent of lung fibrosis on HRCT is an important predictor of survival.<sup>21</sup> HRCT is increasingly used for quantification of disease extent. Subjective, semi quantitative assessment of disease extent by HRCT shows moderate interobserver variability. This semi quantitative assessment correlates with evidence of physiologic impairment.<sup>22</sup> One study showed that the extent of overall lung involvement and the extent of ground glass pattern in the HRCT scans show a moderate correlation only with FVC and arterial PO<sub>2</sub> at peak exercise.

For detection of early or mild infiltrative lung disease, HRCT is clearly more sensitive than the chest radiograph. However, in the early stages of any lung disease, including IPF, the degree of parenchymal infiltration may be too slight to cause any CT abnormality.

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