CHEST MANIFESTATIONS OF COLLAGEN DISEASES, EVALUATION BY SPIRAL CT SCANNING

Thesis
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(Radio-Diagnosis)

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List of abbreviations

ACR = American College of Radiology
ARA = American Rheumatism Association
AS = Ankylosing spondylitis
ATS = American Thoracic Society
BAL = Bronchoalveolar lavage
BOOP = Bronchiolitis obliterans organizing pneumonia
CK = Creatine kinase
COPD = Chronic obstructive pulmonary disease
CTA = CT angiography
CTD = Connective tissue disease
CVD = Collagen vascular disease
CXR = Chest x-ray
DFOV = Display field of view
DIP = Desquamative interstitial pneumonia
DLCO = Single breath diffusing capacity for carbon monoxide.
FEF 25-75 = Forced expiratory flow between 25% and 75% of the vital capacity
FEV1 = Forced expiratory volume in 1 second
FRC = Functional residual capacity.
FVC = Forced vital capacity
FWHM = Full width at half maximum
FWTM = Full width at tenth maximum
HRCT = High resolution CT
HRCT-M = HRCT of the middle lung zone
HRCT-L = HRCT of the lower lung zone
HU = Hounsfield unit
ILD = Interstitial lung disease
IP = Interphalangeal
IPF = Idiopathic pulmonary fibrosis
IV = Intravenous
KVP = Kilovolt peak
LAM = Lymphangiolyomatosis
LDH = Lactic dehydrogenase
LI = Linear interpolation
mA = Milliampere
MCP = Metacarpophalangeal
MCTD = Mixed connective tissue disease
MIP = Maximum intensity projection
mIP = Minimum intensity projection
MRA = Magnetic resonance angiography
MRI = Magnetic resonance imaging
MTP = Metatarsophalangeal
Nominal thickness = the fixed or settled thickness
PAN = Polyarteritis nodosa
PFTs = Pulmonary function tests
PM/DM = Polymyositis/Dermatomyositis
PMF = Progressive massive fibrosis
PSS = SSC = Progressive systemic sclerosis
RA = Rheumatoid arthritis
ROI = Region of interest
SjS = Sjogren’s syndrome
SLE = Systemic lupus erythematosus
SSD = Shaded surface display
SSP = Section sensitivity profile
TLC = Total lung capacity
UIP = Usual interstitial pneumonia
WG = Wegener’s granulomatosis
WL = Window level
WW = Window width
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Aim of the Work
Aim of the work

The aim of this study is the demonstration of the value of the Spiral Volumetric CT scanning of the lung in patients with collagen vascular diseases.
Review of Literature
Fig. 1

Spiral CT data acquisition geometry translation of the patient in the direction shown is equivalent to translation of the scanner in the opposite direction. The apparent trajectory of the x-ray source is a spiral or helix surrounding the patient. The projection of the source as a function of time onto the scanner axis (z-axis) is a line segment that begins at the position from which the patient begins to move and whose end point travels at the same speed as the patient, but in the opposite direction. (After Napel, 1998).
THORACIC APPLICATION OF SPIRAL CT

Spiral CT has revolutionized the way in which chest disorders are evaluated. With spiral CT, continuous table feed and synchronous data acquisition generate a volumetric acquisition that can be performed during a single breath-hold (fig 1) (Vock et al, 1990; Kalender et al, 1990; Costello, 1994).

Limitations of conventional CT for chest imaging

The traditional stepwise technique with interscan delays of 3-10 sec between axial slices often results in slice misregistration because of variations in depth of inspiration from one CT slice acquisition to the next. Slice misregistration, patient motion, and partial volume averaging with conventional CT increase the likelihood of missing significant pathology in the lung (Costello, 1994).

Advantages of spiral CT for chest imaging

Spiral CT is essentially a gapless scanning technique. Volume acquisition eliminates discontinuities between slices. Spiral CT performed during a single breath-hold further limits respiratory motion (Vock et al, 1990; Kalender et al, 1990). The resulting data set allows the generation of superior multiplanar and 3-D images. An added benefit of spiral CT is that the faster scanning times eliminate delays during IV injection, allowing for superior vascular enhancement with smaller amounts of IV contrast (Kalender et al, 1990; Costello, 1994; Zeman et al, 1995).

Spiral technique

Spiral CT options of chest imaging

The optimal, single best spiral CT protocol for imaging the chest has yet to be determined. When performing spiral CT examination of the chest, the radiologist has a number of new parameters to manipulate compared to conventional CT scanning, including linear interpolation algorithm, reconstruction algorithms, slice
Fig. 2

Graph illustrates principle of linear interpolation, which refers to a mathematical technique of deriving data at a given point from two adjacent data points. Data at point c on an arbitrarily selected plane p is derived by linear interpolation between points a and b. Data points a and b are two points nearest to point c at same degree of rotation (for 360° linear interpolation). t = time required for one gantry rotation (360°), d = distance traveled by table in one gantry rotation (360°).

(After Paranjpe and Bergin, 1994).
Spiral CT of the lung with overlapping reconstruction which is not attainable by conventional CT.

Fig. 3

Illustration of intensity loss due to through-plane partial volume effect. The full width at half maximum of the SSP is given by the separation between solid lines. The lesion is only partly imaged by section K and K+1; thus its intensity will be decreased due to volume averaging with surrounding soft tissue. However, section K', which can be positioned and reconstructed from the acquired spiral projection data, images the lesion with less volume averaging with greater intensity. (After Napel, 1998).
acquisition thickness, slice reconstruction interval, table speed, duration of scan, and single versus variable mode of acquisition.

By optimizing each of these parameters, the CT radiologist can customize a spiral CT examination by taking into account patient and equipment factors as well as the particulars of the chest problem to be investigated (Janet, 1998).

1-Linear interpolation algorithms

Image generation in spiral CT is accomplished through a process of linear interpolation that reconstructs planar images from the raw spiral data (fig 2). The first generation of spiral CT scanners used a 360-degree linear interpolation algorithm. These older algorithms have now replaced by newer, improved 180-degree linear interpolation algorithms that result in less broadening of the section sensitivity profile and less blurring of the images (Polacin et al, 1992).

2-Reconstruction Algorithms

Depending on the manufacturer, a number of image display reconstruction algorithms are also available. A standard or soft tissue algorithm is usually chosen for display of soft tissue structures of the mediastinum and chest wall, where as a lung algorithm is preferable for displaying the lung parenchyma. Newer high-resolution lung algorithms available on some manufacturer’s scanners dramatically improve image quality for lung detail (Janet, 1998).

3-Reconstruction interval

The interval at which each planar CT image is reconstructed (the degree of overlap between reconstructed axial images and the reconstruction incrementation) is a new spiral CT parameter that must be designated by the operator. For example, each 10-mm thick slice may be reconstructed every 10-mm with no overlap or every 5 mm, giving an overlap of 5 mm. As a general rule when performing chest studies, reconstructing images at an interval that is one-half the slice thickness (two images per slice incrementation) increases the information gained from the spiral CT data set (fig 3). Little additional information is gained by reconstructing
at close intervals, unless one is performing CT angiography or multidimensional imaging (Janet, 1998).

Reconstructing images at closer intervals increases the number of images that must be filmed and reviewed, increasing both the dollar and time cost of the examination (Brink, et al 1994).

4-KVP, mA, Duration of spiral scan, Scanning mode
Specific spiral CT scanning parameters, such as Kilovolt peak (KVP) and milliampere (mA) settings, vary by manufacturer and should be adjusted for patient characteristics.

The maximum spiral imaging time for one spiral acquisition or the duration of the scan depends on the manufacturer’s available x-ray power and the patient’s ability to hold his or her breath (Brink et al, 1994). The option to perform only a single spiral CT acquisition versus multiple spiral acquisitions in rapid succession—so-called variable-mode spiral CT—also varies among manufacturers.

In variable-mode spiral CT, a series of shorter spiral CT acquisitions can be preprogrammed to be acquired sequentially with short breaks between the acquisitions to allow the patient to breathe (Brink et al, 1994; Tomiak et al, 1995; Foley & Oneson, 1994; Korobkin 1994). This mode of scanning is preferable for patients who cannot hold their breath for the extended 24-40 sec required for a single acquisition spiral scan. It is also ideal for combined chest and abdomen studies that use a single injection of IV contrast, as is often employed when scanning cancer patients for lung and liver metastases. Variable-mode spiral CT allows both the pulmonary hila and the liver to be imaged during their optimal phases of the contrast enhancement (Foley & Oneson, 1994; Korobkin, 1994).

5-Slice Acquisition Thickness and Table speed
Slice acquisition thickness or beam collimation can be varied from 1 to 10-mm in thickness in most spiral CT scanners. Table speed can also be varied from 1 to 10-mm/sec. Choice of slice thickness and table speed depends on the clinical question of concern and determines the pitch that is used.
Fig.4

Section sensitivity profiles for different spiral CT algorithms (5-mm collimation, pitch of 1). The profiles for the 180° interpolation nearly approximate that of the rectangularly shaped profile of conventional scanning. 360 LI = 360° linear interpolation, 180 LI = 180° linear interpolation, 180 HI = 180° higher-order (cubic spline) interpolation, d = table feed (mm/s), Z-position = longitudinal position (mm). (From Brink, 1995).
**Pitch**

Pitch is defined as the “table feed distance per 360-degree tube rotation divided by the nominal section thickness”. Because each 360-degree rotation occurs in 1 sec,

\[
\text{Pitch} = \frac{\text{Table speed}}{\text{Slice thickness}}.
\]

Using a pitch of 1 is generally a good compromise in the chest to achieve adequate area coverage with a minimum of z-axis blurring. A pitch of more than 1 is valuable if a larger volume needs to be covered in a single breath-hold acquisition (Brink et al, 1994). Increasing the pitch widens the section sensitivity profile, which in turn causes increased partial volume averaging and z-axis blurring. The impact of the image quality is lessened to certain extent in the chest, where there is high inherent contrast between structures. Widening of the section sensitivity profile has also been markedly decreased by the newer 180-degree interpolation algorithms on modern spiral scanners (Wright et al, 1996). In the chest, pitches of 1.5-1.7 can be used with little apparent degradation of image quality caused by z-axis blurring (fig 4).

By choosing a pitch of more than 1 and decreasing the slice collimation, the same volume of tissue can be scanned in the same time with higher spatial resolution (Rubin & Napel 1995). For example, by increasing the pitch to 1.7 and decreasing slice thickness from 10-mm to 6 mm, one can actually improve the spatial resolution within the axial plane but still cover the same territory in the chest in the same amount of time. However, decreasing slice collimation increases pixel noise (Brink et al, 1994; Rubin & Napel 1995).

Wright et al. studied the effect of increasing the pitch on pulmonary nodule detection and found a tendency to undercount lung nodules as pitch increased above 1.5. Spiral artifacts also become more noticeable at higher pitches. One such artifact consists of an area of an image dropout or low attenuation that occurs at branch points of vessels at pitches of more than 1.5 (Wright et al, 1996).

The trade-off in the chest can be summarized as follows: increasing pitch allows the use of thinner-slice collimation with resultant higher spatial resolution and
lower radiation dose, but at the expense of increased pixel noise and more noticeable spiral CT artifacts (Brink et al, 1994; Wright et al, 1996; Rubin & Napel 1995). Understanding these trade-offs allows one to choose the slice thickness and pitch that are most appropriate for the individual examination.

Optimizing spiral CT technique for the chest

Two protocols have been found practical for most chest imaging.

For studies of the chest requiring fine detail and high resolution but a limited area of coverage, the following parameters are preferred: 3-5 mm section acquisition thickness, table speed of 3-5 mm /sec, pitch 1, high resolution algorithm (lung algorithm on GE system), and reconstruction of overlapping slices every 1-2 mm. The distance covered can be increased by increasing the pitch from 1 to 1.5-1.7 (Janet, 1998).

The second protocol is used when the entire chest must be covered in a routine fashion (e.g., as a screening or follow up examination for pulmonary pathology). Using 10-mm slice acquisition thickness, 10-mm /sec table speed, pitch 1, lung algorithm, and reconstruction of overlapping slices every 5-mm. The use of a 50% overlap of reconstructed images is particularly useful when screening or following lung metastases.

Using a variable-mode acquisition, a series of 3 or 4 back-to-back, 7-10-sec helical scans is often chosen for patients who find it difficult to hold their breath for an extended period of time. If it is more desirable to scan the entire chest during a single breath-hold (e.g., to generate multiplanar or 3-D images of the airways or vessels), a single 30-32-sec spiral acquisition is chosen, pitch is increased from 1 to 1.5-1.7, and the narrowest slice collimation that will cover the distance required in the chest is chosen (usually 5-7 mm). The images can then be reconstructed at 2-3 mm intervals.

Also it is helpful to hyperventilate the patient by having him take 3 deep breaths just before the spiral scan. After taking the 3 breaths in and out, the patient is then
asked to take in a deep breath and hold it. With this type of preparation, many patients can successfully hold their breath for 24-32 sec (Janet, 1998).

**Peridiaphragmatic pathology**

Evaluation of peridiaphragmatic nodules and processes is particularly difficult with conventional CT because of the degree of excursion of the lung bases and diaphragm from one breath to the next tends to be great (estimated to be up to 8 cm) and quite variable (Costello, 1994; Brink et al, 1994).

Spiral CT acquired during a single breath-hold maneuver eliminates problems with respiratory excursions and facilitates examination of nodules and abnormalities near the diaphragm. Additional information regarding the relationship of the lesion and the diaphragm can be gained from multiplanar images in the coronal and sagittal plane that are free of the respiratory artifacts (Costello, 1994).

**2 / 3D imaging of the thorax**

With the advent of spiral CT, high-quality multiplanar and 3D images of the lung are now possible.

The improved quality of the reconstructed images is due to the fact that spiral CT is volume acquisition obtained during a single breath-hold. This eliminates interslice variability and discontinuities between slices that degrade reformatted images.

A number of 3D techniques can be applied to spiral CT data sets, including thresholding and surface-rendering techniques, maximal- or minimal-intensity projections and volumetric rendering (Zeman et al, 1995). The advantage of 2 D and 3 D imaging of spiral CT data are numerous. It allows for multiplanar and 3 D display of the airways and pulmonary vasculature, enabling the bronchoscopist or surgeon to obtain a through understanding of the anatomy and pathology prior to procedures. In addition, the volume of a given region of interest can be measured in three dimensions.
Fig. 5
Slice thickness versus pitch for three different interpolation algorithms. A substantial improvement in slice thickness broadening is seen with 180° interpolation (180 LI, 180 HI) for pitch > 1 as compared to 360° interpolation (360 LI). Graph displays simulated slice thickness (defined here as the full width at tenth maximum of the section sensitivity profile) for spiral CT performed with 5-mm collimation. Pitch = 0 refers to conventional scanning, 360 LI = 360° linear interpolation, 180 LI = 180° linear interpolation, and 180 HI = 180° higher-order (cubic spline) interpolation. (From Brink, 1995)
Fig. 6

Illustration of perceived loss of in-plane spatial resolution with increasing section thickness. Each subfigure shows a coronal view of a cylinder (solid line) and a measure of the section thickness w for the axial view below (ellipse).

(a) Cylinder is aligned perpendicular to a thin-section plane. Axial image is a sharply defined circle.

(b, c) Axial image is unchanged when scanned with thicker sections.

(d) Cylinder is inclined with respect to the section plane. For the thin-section plane, the axial image is a sharply defined ellipse.

(e, f) As the section becomes thicker, the edges of the ellipse are less sharply resolved due to partial volume. The result is that the ellipse appears less sharp with increasing section thickness. (After Napel, 1998)
A future application of 2D/3D spiral CT may be in oncology, to generate sophisticated 3D tumor volumetrics for planning and assessing tumor response to chemotherapy and radiation therapy (Kuriyama et al, 1994).

Disadvantage and limitations
Because of heat build up in the x-ray tube, there are limits in the amount of milliamps that can be generated over an extended period of time during a spiral CT acquisition. Depending on the manufacturer, there are also some postprocessing delays that occur while the spiral CT images are being reconstructed. Computer and data storage capacities on many scanners do not allow for unreconstructed data to be stored indefinitely.

The nature of the spiral CT data acquisition process and reconstruction algorithm creates certain unique problems (Kalender, 1995). When compared with conventional CT, spiral CT shows broadening of the section sensitivity profile, demonstrating a greater full width at half maximum (FWHM =1.8 for spiral CT using 360-degree-LI)(Kalender et al 1990). Broadening of the slice thickness is due to table transport during the spiral CT scan. This results in Z-axis blurring or blurring along the longitudinal table axis. Z-axis blur manifests itself on spiral CT images as lack of sharpness due to increased volume averaging (fig 5). It is particularly noticeable for structures oriented obliquely to the Z-axis or structures whose cross-sectional diameter changes rapidly along the table feed direction (fig 6)(Polacin et al, 1992; Kalender & Polacin 1991). Z-axis blur can be minimized by decreasing the speed of table feed with respect to the beam collimation (i.e., decreasing the pitch) and by narrowing the beam collimation with greater overlap of reconstructed images (Kalender, 1995; Kalender et al, 1994; Wang & Vannier 1994). Using a high-resolution or sharp algorithm also seems to help.

Newer 180-degree interpolation algorithms also significantly decrease the amount of Z-axis blur and demonstrate section-sensitivity profiles with FWHM as low as 1.1 (Polacin et al, 1992; Brink et al, 1994).
Trade-offs for spiral CT are between (a) increasing speed, greater distance covered, and lower radiation dose, and (b) increasing Z-axis blur and artifacts. For example, if a large area of interest needs to be scanned, one must choose a faster table speed and perhaps greater pitch, but at the cost of increased Z-axis blurring. Another trade-off is between increasing spiral scan time and maximum milliamps allowed. For longer scan times of 32-40 sec, only a lower maximum milliamperage is possible on many scanners. This will increase pixel noise and may be noticeable when examining large patients (Janet, 1998).

**HRCT versus Spiral CT**

Spiral CT has replaced conventional CT technique. If one compares a high-resolution CT with 1-mm thick collimation to a spiral CT, the differences in resolution are clearly visible.

Spatial resolution and linear edge detection are superior with HRCT techniques. Although linear structures are delineated better with HRCT, small nodules are better demonstrated with spiral CT (Zeman et al, 1995).

One approach that combines the advantages of both techniques is to start examination with a survey study of the chest using spiral CT technique and follow that with a few select HRCT images as needed (Janet, 1998).

**Radiation dose of the patient from a spiral CT**

Because spiral CT employs continuous scanning, the x-ray-tube power (i.e., the highest permissible milliampere-second setting) is currently limited to less than that used for standard CT scanning. This power limitation is greatest for long scans (e.g., 24 seconds or longer) and results in increased quantum noise. Given the same x-ray-tube power, the radiation dose to the patient for a spiral CT scan is equal to that for standard continuous-section CT, if a pitch is 1 is used (i.e., if table speed is matched to the collimation). Radiation dose for a spiral CT is decreased when the pitch is greater than 1, compared with standard continuous-section CT. Since the highest permissible milliampere-second setting for long-duration spiral scans is currently less than that used for standard CT, the radiation dose to the
patient is currently less for long duration spiral CT (Heiken et al, 1993). In addition, the need to rescan areas of interest is much less common with spiral CT than with conventional CT. This particularly true for chest examinations when evaluating a small, solitary pulmonary nodule. (Janet, 1998)

**Subsecond Spiral CT scanning**

Spiral CT continues to evolve with each new scanner introduced providing specific and unique features designed to either optimize classic scanning protocols or to develop newer study protocols or even completely new application. Total length of single spiral CT acquisitions has increased from 20-24 sec range in 1993 to 40-50 sec range in 1998. Similarly, initial scan parameters included values in the 140-210 mA range, where current systems provide values in the 280-320 mA range, making spiral protocols similar to standard dynamic CT protocol parameters. The most recent advance has been the introduction of subsecond spiral CT scanning. Classically, spiral CT scanners complete a single 360-degree scanner rotation in 1 sec, which means that the gantry rotates at a rate of 60 revolutions per minute (rpm). Introduction of advanced scanner technology permits the gantry to rotate at 80 rpm, so that 360-degrees are traversed in 0.75 sec. This means that 1.33 rotations/sec are achieved, with the rotation speed 33% faster. Thus when using subsecond spiral CT, a 33% larger volume can be acquired with identical resolution and pitch. For example, a pitch of 1 and 10-mm collimation set for 1-sec spiral CT scan will travel 10-mm/sec, where as at 0.75 sec with the same pitch and collimation setting will travel 13.33 mm/sec. With 0.75-sec scanner, a larger distance can be covered with similar collimation (Fishman, 1997).

**Spiral CT of parenchymal lung disease**

Over the past decade, thin-section CT has been widely performed to evaluate patients with diffuse infiltrative lung disease (DILD). By the direct visualization of fine details within the lung, such as septal and polygonal lines, honeycombing, and
traction bronchiectasis, thin-section CT enables assessment of parenchymal fibrosis. Also, thin-section CT may assist in the evaluation of disease activity by means of accurate depiction of ground glass attenuation (Terriff et al, 1992; Leung et al, 1993; Remy-Jardin et al, 1993c). Owing to the accuracy of thin-section CT, so, what is the diagnostic benefit of spiral CT in evaluating infiltrative and/or destructive lung changes. A few preliminary results suggest potential clinical applications of spiral CT of the lungs. Narrow collimation spiral CT and sliding thin-slab-maximum or-minimum intensity projection are the most promising developments.

_Narrow collimation spiral scanning_

Engeler et al. (1994) evaluated the accuracy of narrow collimation spiral scanning in the diagnosis of interstitial lung disease when four contiguous sections were acquired at three anatomical levels (the aortic arch, the carina, and 2 cm above the diaphragm). They concluded that the use of volumetric high-resolution CT increased the diagnostic accuracy, particularly in respect of bronchiectasis at lung base, without increasing the peak skin radiation exposure. With the availability of four contiguous scans per anatomical level, the subjective confidence in the interpretation and the number of motion-free studies are increased.

**Maximum intensity projection (MIP)**

Recent advances in CT have led to the introduction of volumetric scanning, which has the potential to combine the advantages of continuous data acquisition with the use of volume rendering techniques. At the level of a region of interest, a focal spiral CT acquisition is performed. From this data set, contiguous transverse CT scans are reconstructed then stacked to produce slabs of lung parenchyma. On each slab the maximum intensity projection algorithm is applied, enabling projection of the brightest voxels encountered along each ray, thus resulting in a MIP image (Remy-Jardin et al, 1996a).
Detection of micronodules

Although thin-section CT is the most accurate technique for evaluation of diffuse infiltrative lung diseases, a few limitations of this CT technique have been reported with regard the detection of micronodular infiltration (Remy-Jardin et al. 1990, 1991). On thin sections, micronodules may be difficult to distinguish from vessels seen on end (when equal in diameter to nearby vessels) and also from confluence of abnormal linear areas of attenuation.

In order to confirm or rule out radiographic suspicion of micronodular infiltration, Remy-Jardin et al (1996a) evaluated 81 patients suspected of having diffuse infiltrative lung disease. Each patient underwent both 8-mm and 1-mm conventional CT scans at the level of region of interest, completed by a focal spiral CT evaluation at the level of the region of interest. In this study group, the sensitivity of MIP was found to be significantly higher than that of conventional CT in detecting lung micronodules.

As the advantage of MIP over a single section is that vessels can be appreciated over a much longer segment of their course, the concurrent improvement in vessel and micronodule conspicuity accounted for the more frequent identification of centrilobular and perivascular changes on MIP images. However, care must be taken to differentiate actual perivascular micronodules from the beaded appearance of MIP artifacts due to partial volume averaging. These artifacts have been described as stair-step vessels and are expected to be found at the level of vessels that pass obliquely through the volume (Napel 1995).

These preliminary results suggest that a combination of conventional CT and MIP should be employed to achieve an adequate evaluation of mild forms of micronodular lung infiltration. Since patients cannot be imaged with multiple CT techniques because of the high radiation dosage and time constraints, a focal spiral CT acquisition over a region of interest could complement the conventional CT study performed over the entire thorax.

Detection of bronchiectasis and peripheral mucoid impactions
Diagnosis of mucoid impaction in the peripheral bronchioles on thin-section CT scans is usually based on the identification of short and non tapering tubular areas of attenuation, seen as either single or branched structures (Muller and Miller 1995). Two studies have evaluated the role of spiral CT in detecting peripheral bronchiectasis and mucoid impaction. Remy-Jardin et al (1996a) found that MIP enabled identification of a greater number of bronchiolar changes compared with 1-mm conventional CT scans. Also Engeler et al. (1994) observed that traction bronchiectasis could be accurately differentiated from vessels or small pulmonary nodules only by examination of four contiguous scans generated from volumetric CT acquisition.

**Minimum intensity projection**

The result of the minimum intensity projection (mIP) is to retain low-density structures at the expense of blood vessels. Consequently, this technique results in improved airway visibility along greater portions of their lengths and could detect mild forms of emphysema. Emphysema is a pathological diagnosis, which is diagnosed on the basis of combination of clinical, functional, and radiographic findings. Whereas radiographic assessment of emphysema requires moderate to severe destruction, it has been shown that CT is effective in the detection and quantification of emphysema (Muller et al, 1988; Klein et al, 1992). However, several authors have pointed out that mild emphysema may be missed on CT scans and the severity of emphysema may be underestimated (Miller et al, 1989).

Evaluating 29 patients with no chest x-ray evidence of emphysema with conventional thin-section CT and mIP immediately before surgery, Remy-Jardin et al. (1996b) found that volumetric CT could complement the visual inspection of CT images for the recognition of emphysema. The subjective superiority of mIP is directly related to the suppression of highly attenuated structures, i.e., vessels and fissures, with subsequent uniform appearance of lung parenchyma.
Fig. 7

(A) Components of the lung interstitium. The peribronchovascular interstitium and centrilobular interstitium constitutes the axial fiber system. The subpleural interstitium and interlobular septa constitutes the peripheral fiber system. The intralobular interstitium is equivalent to the septal fibers.

(B) Pulmonary lobules are supplied by small bronchiolar and pulmonary artery branches, which are central in location, and are variably margined by connective tissue interlobular septa that contain pulmonary vein and lymphatic branches. (After Webb et al, 1996)
NORMAL HRCT LUNG ANATOMY
The accurate interpretation of high-resolution CT (HRCT) images require a
detailed understanding of normal lung anatomy and the pathologic alterations in
normal lung anatomy that occur in the presence of diseases.

THE LUNG INTERSTITIUM
The lung is supported by a network of connective tissue fibers, called the lung
interstitium. Although the lung interstitium is not generally visible on HRCT in
normal subjects, interstitial thickening is often recognizable. The lung interstitium
has several components (Weibel, 1979) (fig 7a).
The peribronchovascular interstitium is a system of fibers that invests bronchi and
pulmonary arteries. In the parahilar regions the peribronchovascular interstitium
forms a strong connective tissue sheath that surrounds large bronchi and arteries.
The more peripheral continuum of this interstitial fiber system, associated with
small centrilobular bronchioles and arteries, is usually termed centrilobular
interstitium, although the term centrilobular peribronchovascular interstitium
would be appropriate. Taken together, the peribronchovascular interstitium and
centrilobular interstitium correspond to the “axial fiber system” described by
Weibel, which extends peripherally from pulmonary hila to the level of the
alveolar ducts and sacs (Weibel, 1979). The subpleural interstitium, is located
beneath the visceral pleura, and envelops the lung in a fibrous sac from which
connective tissue septa penetrate into the lung parenchyma. These septa include
the interlobular septa. The subpleural interstitium and interlobular septa are both
parts of the “peripheral fiber system” described by Weibel (1979).
The intralobular interstitium is a network of thin fibers that forms a fine
connective tissue mesh in the walls of alveoli, and thus bridges the gap between
the centrilobular interstitium in the center of the lobules, and the interlobular septa
and subpleural interstitium in the lobular periphery. Together, the intralobular
interstitium, peribronchovascular interstitium, centrilocular interstitium, subpleural interstitium, and interlobular septa form a continuous fiber skeleton for the lung. The intralobular interstitium corresponds to the septal fibers described by Weibel (1979).

**Large bronchi and arteries**

Within the lung parenchyma, the bronchi and pulmonary artery branches are closely associated and branch in parallel; they are encased by the peribronchovascular interstitium, which extends from the pulmonary hila into the peripheral lung. Since some lung diseases produce thickening of the peribronchovascular interstitium in the central or parahilar lung in relation to large bronchi and pulmonary vessels. When imaged at an angle to their longitudinal axis, central pulmonary arteries normally appear as rounded or elliptic opacities on HRCT, accompanied uniformly thin-walled bronchi of similar shape. When imaged along their axis, bronchi and vessels should appear roughly cylindrical, or show slight tapering as they branch, depending on the length of the segment that is visible; tapering of a vessel or bronchus is most easily seen when a long segment is visible.

The diameter of an artery and its neighboring bronchus should approximately equal, although vessels may appear slightly larger than their accompanying bronchus, particularly in dependent lung regions. Although the presence of bronchi larger than their adjacent arteries is often assumed to indicate bronchial dilatation, or bronchiectasis, bronchi may appear larger than adjacent arteries in a significant number of normal subject.

The outer walls of visible pulmonary artery branches form a smooth and sharply defined interface with the surrounding lung, whether they are seen in cross-section or along their length. The walls of large bronchi, outlined by lung on one side, and the air in the bronchial lumen on the other, should appear to be smooth and of uniform thickness. Thickening of the peribronchial and perivascula.
Fig. 8

(A) Relative size and relationships of "Miller's lobule" and "Reid's lobule"

(B) Anatomy of the secondary pulmonary lobule, as defined by Miller. Two adjacent lobules are shown in the diagram. Lobules are marginated by thin interlobular septa containing pulmonary vein branches. Bronchioles and pulmonary arteries are centrilobular. (After Webb et al, 1996).
can result in irregularity of the interface between arteries and bronchi and the adjacent lung (Zerhouni, 1989; Zerhouni et al, 1985).

The wall thickness of conducting bronchi and bronchioles is approximately proportional to their diameter, at least for bronchi distal to the segmental level. In general, the thickness of the wall of a bronchus or bronchiole less than 5-mm in diameter should measure from 1/6 to 1/10 of its diameter (Weibel & Taylor 1988). Because bronchi taper and become thinner walled as they branch, and thus become more difficult to see, as they become more peripheral. Bronchi less than 2 mm in diameter, and closer than 2 cm to the pleural surface are not normally visible on HRCT (Webb et al, 1988; Murata et al, 1986).

The secondary pulmonary lobule
The secondary pulmonary lobule, as defined by Miller, refers to the smallest unit of lung structure margined by connective tissue septa (Weibel & Taylor 1988; Miller 1947). Secondary lobules are easily visible on the surface of the lung because of these septa (Weibel & Taylor 1988; Heitzman et al, 1969)(fig 7b). The terms secondary pulmonary lobule, secondary lobule, and pulmonary lobule are often used interchangeably, and are used as synonymous. The term primary pulmonary lobule has also used by Miller to describe a much smaller lung unit associated with a single alveolar duct (Heitzman et al, 1969; Miller 1947).

Secondary pulmonary lobules are irregularly polyhedral in shape and somewhat variable in size, measuring approximately 1 to 2.5 cm in diameter in most locations (Weibel 1979, Weibel & Taylor 1988)(fig 8b). Each secondary lobule is supplied by a small bronchiole and pulmonary artery, and is variably margined by connective tissue interlobular septa that contain pulmonary vein and lymphatic branches (Heitzman et al, 1969). Secondary pulmonary lobules are made up of a limited number of pulmonary acini, usually a dozen or fewer (Weibel 1990). A pulmonary acinus is defined as the portion of the lung parenchyma distal to a terminal bronchiole and is supplied by a first order respiratory bronchiole (Reid
Since respiratory bronchioles are the largest airways that have alveoli in their walls, an acinus is the largest lung unit in which all airways participate in gas exchange. Acini are usually described ranging from 6 to 10 mm in diameter (Gamsu et al, 1971). Miller has defined the secondary lobule as the smallest lung unit margined by connective tissue septa. Reid has suggested an alternate definition of the secondary pulmonary lobule, based on the branching pattern of peripheral bronchioles, rather than the presence and location of connective tissue septa (Reid 1958)(fig 8a). On bronchograms, small bronchioles can be seen to arise at intervals of 5 to 10 mm from large airways, the so-called centimeter pattern of branching; these small bronchioles then show branching at approximately 2-mm intervals, the “millimeter pattern” (Reid & Simon 1958). Airways showing the millimeter pattern of branching are considered by Reid to be intralobular, with each branch corresponding to a terminal bronchiole (Reid 1958). Lobules are considered to be the lung units supplied by 3 to 5 “millimeter pattern” bronchioles. Although Reid's criteria delineate lung units of approximately equal size, about 1 cm in diameter and containing 3 to 5 acini, it should be noted, that this definition does not necessarily describe lung units equivalent to secondary lobules as defined by Miller and margined by interlobular septa (Itoh et al, 1993), although a small Miller's lobule can be the same as a Reid's lobule. Miller's definition is most applicable to the interpretation of HRCT, and is widely accepted by pathologists because interlobular septa are visible on histologic sections (Itoh et al, 1993). The term secondary pulmonary lobule to refer to a lobule as defined by Miller.

Anatomy of the secondary lobule and its components.

HRCT can show many features of the secondary pulmonary lobule in both normal and abnormal lungs, and many lung diseases particularly interstitial diseases, produce some characteristic changes in lobular structures (Webb, 1989). The visibility of normal lobular structures on HRCT is related to their size and orientation relative to the plane of scan, although size is most important. The
Fig. 9
Dimensions of secondary lobular structure (A), and their visibility on HRCT (B).
(After Webb et al, 1996)
smallest structures visible on HRCT range from 0.3 to 0.5 mm in thickness; thinner structures, measuring 0.1 to 0.2 mm, are occasionally seen (fig 9). For the purposes of the interpretation of HRCT, the secondary lobule is the most appropriately conceptualized as having three principal components: 1. The interlobular septa and contiguous subpleural interstitium, 2. The centrilobular or lobular core structures, and 3. The lobular parenchyma and acini.

1-Interlobular septa
Anatomically, secondary lobules are marginated by connective tissue interlobular septa, which extend inward from the pleural surface. These septa are part of the peripheral interstitial fiber system described by Weibel (1979), that extends over the surface of the lung beneath the visceral pleura. Pulmonary vein and lymphatics lie within the connective tissue interlobular septa that marginate the lobule. The interlobular septa are thickest and most numerous in the apical, anterior, and lateral aspects of the upper lobes, the anterior and lateral aspects of the middle lobe and lingula, the anterior and diaphragmatic surfaces of the lower lobes, and along the mediastinal pleural surfaces (Reid & Rubino 1959); thus, secondary lobules are best defined in these regions. Septa measure about 100 μm (0.1 mm) in thickness in a subpleural location (Webb 1989; Weibel 1979). Within the central lung, interlobular septa are thinner and less well defined than peripherally, and lobules are more difficult to identify in this location. Peripherally, interlobular septa measuring 100 μm or 0.1 mm in thickness are at the lower limit of HRCT resolution (Murata et al, 1986).

On clinical scans in normal patients, interlobular septa are less commonly seen. A few septa are often seen in the lung periphery in normal subjects, but they tend to be inconspicuous; normal septa are most often seen anteriorly and along the mediastinal pleural surfaces (Zerhouni 1989; Aberle et al, 1988). When visible, they are usually seen extending to the pleural surface. In the central lung, septa are thinner than they are peripherally and are infrequently seen in normal subjects;
often interlobular septa that are clearly defined in this region are abnormally thickened.

2- The centrlobular region and lobular core structures

The central portion of the lobule, referred to as the centrlobular region or lobular core (Heitzman et al, 1969), contains the pulmonary artery and bronchiolar branches that supply the lobule, as well as some supporting connective tissue (the centrlobular interstitium)(Webb et al, 1988; Murata et al, 1986). The branching of the lobular bronchiole and artery are irregularly dichotomous (Itoh et al, 1993). In other words, when they divide, they divide into two branches that are usually of different sizes; one branch is nearly the same size as the one it arose from, and the other is smaller. Thus, on bronchograms or arteriograms (or HRCT), there often appears to be a single dominant bronchiole and artery in the center of the lobule, which give off smaller branches at intervals along their length. The HRCT appearances and visibility of structures in the lobular core are determined by their size. Secondary lobules are supplied by arteries and bronchioles measuring 1 mm in diameter, while intralobular terminal bronchioles and arteries measure about 0.7 mm in diameter, and acinar bronchioles and arteries range from 0.3 mm to 0.5 mm in diameter. Arteries of this size can be easily resolved using HRCT technique (Webb et al, 1988; Murata et al, 1986)

On clinical scans, a linear, branching, or dot-like opacity seen within the center of a lobule, or within a centimeter of the pleural surface, represents the interlobular artery branch or its divisions (Webb 1989). The smallest arteries resolved extend to within 3 to 5 mm of the pleural surface or lobular margin and are as small as 0.2 mm in diameter (Webb et al, 1988).

Regarding the visibility of bronchioles in normals, it is necessary to consider bronchiolar wall thickness rather than bronchiolar diameter. For a 1-mm bronchiole supplying a secondary lobule, the thickness of its wall measures approximately 0.15 mm; this is at the lower limit of HRCT resolution. The wall of a terminal bronchiole measures only 0.1 mm in thickness, and that of an acinar
bronchiole only 0.05 mm, both of which are below the resolution of HRCT technique for tubular structure. In one in vitro study only bronchioles having a diameter of 2 mm or more or having a wall thickness of 0.1 mm were visible using HRCT (Murata et al, 1986); and resolution is certainly less than this on clinical scans. On clinical HRCT, intralobular bronchioles are not normally visible, and bronchi or bronchioles are not normally seen within 2 cm of the pleural surface.

3-The lobular parenchyma
The substance of the secondary lobule, surrounding the lobular core and contained within the interlobular septa, consists of functioning lung parenchyma, namely alveoli and the associated pulmonary capillary bed, supplied by small airways and branches of the pulmonary arteries and veins. This parenchyma is supported by a connective tissue stroma; a fine network of very thin fibers within the alveolar septa called the intralobular interstitium (Weibel 1979; Weibel & Taylor 1988), which are normally invisible. On HRCT, the lobular parenchyma should be of greater opacity than air, but this difference may vary with window settings. Some small intralobular vascular branches are often visible. All three interstitial fiber systems described by Weibel (axial, peripheral, and septal) are represented at the level of the pulmonary lobule, and abnormalities in any can produce recognizable lobular abnormalities on HRCT (Webb et al, 1988).

The pulmonary acinus
Pulmonary acini are not normally visible on HRCT (Itoh et al, 1993). As with lobules, acini vary in size. They are usually described as ranging from 6 to 10 mm in diameter (Gamsu et al, 1971). Secondary pulmonary lobules defined by the presence of connective tissue interlobular septa usually consist of a dozen or fewer pulmonary acini (Weibel, 1990). First order respiratory bronchioles and the acinar artery branch measure about 0.5 mm in diameter; thus, intralobular acinar arteries are large enough to be seen on HRCT in some normal subjects (Weibel & Taylor 1988). Murata et al (1986) have shown that pulmonary artery branches as small as 0.2 mm, associated with a respiratory bronchiole, and thus acinar in nature, are
visible on HRCT, and extend to within 3 to 5 mm of the lobular margins or pleural surface.

Lobular anatomy and the concept of “cortical” and “medullary” lung

Peripheral or cortical lung

Cortical lung can be conceived of as consisting of two or three rows of well-organized and well defined secondary pulmonary lobules, which together form a layer about 3 to 4 cm in thickness at the lung periphery and along lung surfaces adjacent to fissures (Heitzman et al, 1969). The pulmonary lobules in the lung cortex are relatively large in size, and are marginated by interlobular septa that are thicker and better defined than in other parts of the lung; thus cortical lobules tend to be better defined than those in the central or medullary lung. Bronchi and pulmonary vessels in the lung cortex are relatively small. Lobules in the lung cortex tend to be relatively uniform in appearance. They can appear cuboidal, or be shaped like a truncated cone or pyramid (Heitzman et al, 1969). However, the size, shape, and appearance of pulmonary lobules on HRCT are significantly affected by the orientation of the scan plane relative to the central and longitudinal axes of the lobules.

Central or “medullary” lung

Pulmonary lobules in the central or medullary lung are smaller and more irregular in shape than in the cortical lung, and are marginated by interlobular septa that are thinner and less well defined. When visible, medullary lobules may appear hexagonal or polygonal in shape. In contrast with the peripheral lung, parahilar vessels and bronchi in the lung medulla are large and easily seen on HRCT.

The subpleural interstitium and visceral pleura

The visceral pleura consists of a single layer of flattened mesothelial cells, subtended by layers of fibroelastic connective tissue; it measures 0.1 to 0.2 mm in thickness (Agostoni et al, 1969). The connective tissue component of the visceral pleura is generally referred to on HRCT as the subpleural interstitium, and is part of the “peripheral” interstitial fiber network described by Weibel (1979). The
Fig. 10

Anatomy of the pleural surface and chest wall (After Webb et al, 1996)
subpleural interstitium contains small vessels, which are involved in the formation of pleural fluid, and lymphatic branches. Interstitial lung diseases that affect the interlobular septa, or result in lung fibrosis, often result in abnormalities of the subpleural interstitium.

Abnormalities of the subpleural interstitium can be recognized over the costal surfaces of the lung, but are more easily seen in relation to the major fissures, where two layers of the visceral pleura and subpleural interstitium come in contact. In contrast to conventional CT, in which the obliquely oriented major fissures are usually seen as broad bands of increased or decreased opacity, these fissures are consistently visualized on HRCT as continuous, smooth, very thin, linear opacities. Normal fissures are less than 1-mm thick, smooth in contour, uniform in thickness, and sharply defined. The visceral pleura and subpleural interstitium along the costal surfaces of lung are not visible on HRCT in normal subjects.

The parietal pleura

The parietal pleura, as with the visceral pleura, consists of a mesothelial cell membrane in association with a thin layer of connective tissue. The parietal pleura is thinner than the visceral pleura, measuring about 0.1 mm (Agostoni et al, 1969). External to the parietal pleura is a thin layer of loose areolar connective tissue or extrapleural fat, which separates the pleura from the fibroelastie endothoracic fascia and lines the thoracic cavity. External to the endothoracic fascia are the innermost intercostal muscles pass between adjacent ribs, but do not extend into the paravertebral regions (fig 10).

A window level/width settings of 50/350 HU are best for evaluating the parietal pleura and adjacent chest wall. Images at level of -600, with an extended window width of 2000 are also useful in evaluating the relationship of peripheral parenchymal abnormalities to the pleural surfaces (Murata et al, 1989).

On HRCT in normal patients, the innermost intercostal muscles are often visible as 1- to 2-mm thick stripes (the intercostal stripes) of soft tissue opacity at the
Normal expiratory HRCT

The lung parenchyma normally increases in CT attenuation as lung volume is reduced during expiration. This change can generally be recognized on HRCT as an increase in lung opacity (Verschakelen et al, 1993). In a study (Webb et al, 1993) of ten normal subjects using dynamic expiratory HRCT, an increase in lung attenuation averaging 200 HU was consistently seen during expiration, but the increase was variable, and ranged from 84 to 372 HU. In some normal subjects, small areas of focal lucency are visible on expiratory scans; in these regions, lung does not increase normally in attenuation, probably as a result of focal air trapping. This appearance is most typical in the superior segments of the lower lobes, or in the anterior middle lobe or lingula (Webb et al, 1993).

Changes in lung attenuation during expiration can be related to changes in cross-sectional lung area as shown on HRCT. Simply stated, cross-sectional lung area decreases during expiration at the same time attenuation increases. Normal morphologic changes that can be seen on expiratory CT also include a decrease in tracheal diameter associated with the anterior bowing of the tracheal membrane (Stern et al, 1993), and a small decrease in the diameter of the bronchi. Pulmonary vessels may appear somewhat to increase in diameter on expiration. Following expiration, dependent lung regions increase more in attenuation than do nondependent lung regions. This results in an accentuation of the normal anterior to posterior lung attenuation gradient (Webb et al, 1993).
HRCT FINDINGS OF DIFFUSE LUNG DISEASE

Generally, HRCT findings of lung disease can be classified into four large categories based on their appearances. These are (i) increased lung opacity, (ii) linear and reticular opacities, (iii) decreased lung opacity, and (iv) nodules and nodular opacities (fig 11).

I-INCREASED LUNG OPACITY

Increased lung opacity, or parenchymal opacification, is a common finding on HRCT in patients with chronic lung disease. Increased lung opacity is generally described as being ground-glass opacity or consolidation (Webb et al, 1993a).

"Ground-Glass" opacity

Ground-glass opacity is a nonspecific term referring to the presence on HRCT of a hazy increase in lung opacity that is not associated with obscuration of underlying vessels; if vessels are obscured, the term consolidation is generally used (Webb et al, 1993a). This finding can reflect the presence of a number of diseases, and can be seen in patients with minimal air-space disease, interstitial thickening, or both (Leung et al, 1993).

Ground-glass opacity results from the volume averaging of morphologic abnormalities below the resolution of HRCT (Remy-Jardin et al, 1993d). It can reflect the presence of minimal thickening of the “septal” or alveolar interstitium, thickening of alveolar walls, or the presence of cells or fluid partially filling the alveolar spaces. Ground-glass opacity has been seen in patients with histologic findings of mild or early interstitial inflammation or infiltration (Leung et al, 1993). Also, when a small amount of fluid is present within the alveoli, as can occur in the early stages of an air-space filling disease, the fluid tends to layer against the alveolar walls, and is indistinguishable on HRCT from alveolar wall thickening (Naidich et al, 1985). In a study comparing the results of lung biopsy
with HRCT in 22 patients who showed ground-glass opacity, 14% had diseases primarily affecting air-spaces, 32% had a mixed interstitial and air-space abnormality, and 54% had a primarily interstitial abnormality (Leung et al, 1993). Ground-glass opacity is difficult to recognize if it is of minimal severity and is diffuse in distribution, involving all lung regions to an equal degree. However, this abnormality is usually patchy in distribution, affecting some lung regions while others appear spared; this “geographic” appearance of the lung parenchyma makes it easier to detect and diagnose with confidence. In some patients, entire lobules may appear abnormally dense, while adjacent lobules appear normal (Webb 1989; Naidich et al, 1985). Ground-glass opacity can involve individual segments, lobes, or can involve nonsegmental regions of the lung. The presence of air-filled bronchi that appear “too black” within an area of lung can also be clue as to the presence of ground-glass opacity; this “dark bronchus” appearance is essentially that of an air-bronchogram.

**Significance and Differential Diagnosis of Ground-Glass opacity**

Ground-glass opacity is a highly significant finding, as it often indicates the presence of an active and potentially treatable process. Of the 22 patients with ground-glass opacity studied by Leung et al. (1993), 18(82%) were considered to have active or potentially reversible disease on lung biopsy. Because of its association with active lung disease, the presence of ground-glass opacity often leads to further diagnostic evaluation, including lung biopsy, depending on the clinical status of the patient. Also, when a lung biopsy is performed, areas of ground-glass opacity can be targeted by the surgeon or bronchoscopist. Since such areas are most likely to be active, they are most likely to yield diagnostic material. Because ground-glass opacity can reflect the presence of either fibrosis or inflammation, one should be careful to diagnose an active process only when ground-glass opacity is unassociated with HRCT findings of fibrosis, or is the predominant finding. If ground-glass opacity is only seen in lung regions also showing significant HRCT findings of fibrosis, such as traction bronchiectasis or
honeycombing, it is most likely that fibrosis will be the predominant histologic abnormality. For example, in a study by Remy-Jardin et al. (1993c), patients showing traction bronchiectasis or bronchiolectasis on HRCT in regions of ground-glass opacity all had fibrosis on lung biopsy. On the other hand, in patients without traction bronchiectasis in areas of ground-glass opacity, 92% were found to have active inflammatory disease on lung biopsy.

A large number of diseases can be associated with ground-glass opacity on HRCT (Table 1). In many, this reflects the presence of similar histologic reactions in the early or active stages of disease, with inflammatory exudates involving the alveolar septa and alveolar spaces, although this pattern can be the result of a variety of pathologic processes. The most common causes of ground-glass opacity include usual interstitial pneumonia (UIP) or desquamative interstitial pneumonia (DIP) associated with idiopathic pulmonary fibrosis or scleroderma, bronchiolitis obliterans organizing pneumonia, sarcoidosis, and hypersensitivity pneumonitis. Other diseases associated with this finding include pneumonia particularly pneumocystis carinii pneumonia, alveolar proteinosis, acute interstitial pneumonia or other causes of diffuse alveolar damage or the adult respiratory distress syndrome (ARDS), pulmonary edema of various causes, pulmonary hemorrhage, respiratory bronchiolitis, and early radiation pneumonitis (Remy-Jardin et al., 1993c; Bessis et al., 1992; Godwin et al., 1988; Ikezoe et al., 1990).

In patients with UIP or DIP associated with idiopathic pulmonary fibrosis, scleroderma, or other collagen vascular diseases, a number of studies have correlated the presence of ground-glass opacity on HRCT with biopsy results, response to treatment, and patient survival (Remy-Jardin et al., 1993c; Lee et al., 1992). In histologic studies of patients with interstitial pneumonia, ground-glass opacity has been shown to be associated with the presence of alveolar wall or intra-alveolar inflammation. In patients with UIP, ground-glass opacity is associated with alveolar septal inflammation, varying numbers of intra-alveolar histiocytes, and varying degrees of fibrosis; ground-glass opacity in patients with
DIP largely reflects the presence of macrophages within the alveoli (Leung et al, 1993; Wells et al, 1992).

**Table (1): Differential diagnosis of ground-glass opacity (Webb et al, 1996)**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Usual interstitial pneumonia (UIP)</td>
<td>• Often present; patchy; usually dominant in peripheral, posterior, and basal regions; finding of fibrosis often present; consolidation less common</td>
</tr>
<tr>
<td>2. Desquamative interstitial pneumonia (DIP)</td>
<td>• Always present; diffuse or patchy; usually dominant in basal, peripheral regions; findings of fibrosis less common than in UIP; consolidation much less common</td>
</tr>
<tr>
<td>3. Lymphocytic interstitial pneumonia (LIP)</td>
<td>• Diffuse, patchy, or centrilobular</td>
</tr>
<tr>
<td>4. Bronchiolitis obliterans organizing pneumonia/cryptogenic organizing pneumonia (BOOP/COP)</td>
<td>• Common, consolidation may also present; can be dominant in peripheral regions; can be nodular</td>
</tr>
<tr>
<td>5. Sarcoidosis</td>
<td>• Present in about 25%; patchy; nodules usually predominate; consolidation less common</td>
</tr>
<tr>
<td>6. Hypersensitivity pneumonitis</td>
<td>• Very common; patchy or nodular; can be centrilobular; consolidation less common</td>
</tr>
<tr>
<td>7. Alveolar proteinosis</td>
<td>• Very common; patchy or diffuse; septal thickening common; fibrosis rare; consolidation much less common</td>
</tr>
<tr>
<td>8. Acute interstitial pneumonia</td>
<td>• Always present; consolidation common; patchy or diffuse</td>
</tr>
<tr>
<td>9. Pneumocystis carinii pneumonia, CMV pneumonia</td>
<td>• Common, diffuse or patchy; consolidation can be present; septal thickening in subacute stage</td>
</tr>
<tr>
<td>10. Eosinophilic pneumonia</td>
<td>• Sometimes seen; consolidation more common</td>
</tr>
<tr>
<td>11. Respiratory bronchiolitis</td>
<td>• Common, patchy or nodular; can be centrilobular; consolidation not reported</td>
</tr>
<tr>
<td>12. Pulmonary edema</td>
<td>• Diffuse or centrilobular; septal thickening</td>
</tr>
<tr>
<td>13. Pulmonary hemorrhage</td>
<td>• Patchy or focal</td>
</tr>
</tbody>
</table>
Technical Considerations and Pitfalls in the Diagnosis of Ground-Glass Opacity

First, it is important to recognize that since ground-glass opacity reflects the volume averaging of morphologic abnormalities below the resolution HRCT, the thicker the collimation used for scanning, the more likely volume averaging will occur, regardless of the nature of the anatomic abnormality. Thus, ground-glass opacity should be diagnosed only on scans obtained with thin collimation.

The diagnosis of ground-glass opacity is largely subjective and based on a qualitative assessment of lung attenuation. The use of lung attenuation measurements to determine the presence of increased lung density in patients with ground-glass opacity is difficult because of the variations in attenuation measurements that are known to be associated with gravitational density gradients in the lung, the level of inspiration, and fluctuations that occur as a result of patient size, position, chest wall thickness, and kVp. Using consistent window settings for the interpretation of HRCT is very important. Using too low a window mean in conjunction with a relatively narrow window width can give the appearance of a diffuse ground-glass abnormality (Remy-Jardin et al, 1993d). In assessing the attenuation of the lung parenchyma, it is often helpful to compare its appearance to that of air in the trachea or bronchi; if tracheal air appears gray instead of black, then increased attenuation or “grayness” of the lung parenchyma may not be significant.

Also, increased lung opacity is commonly seen in dependent lung on HRCT, largely as a result of volume loss in the dependent lung parenchyma; so-called dependent density (Aberle et al, 1988). This can result in a stripe of ground-glass opacity several centimeters thick in the posterior lung of supine patients; prone scans allow this transient finding to be distinguished from a true abnormality.

Similarly, on expiration, because of a reduction of the amount of air within alveoli, lung regions increase in attenuation and can mimic the appearance of ground-glass opacity resulting from lung disease.
Furthermore, in patients who have emphysema or other causes of lung hyperlucency such as airways obstruction and air trapping, normal lung regions can appear relatively dense, thus mimicking the appearance of ground-glass opacity. This pitfall can usually be avoided if consistent window settings are used for interpretation of scans. The use of expiratory HRCT can also be of value in distinguishing the presence of heterogeneous lung attenuation resulting from emphysema or air trapping from that representing ground-glass opacity (Webb et al, 1996).

Consolidation

Increased lung attenuation with obscuration of underlying pulmonary vessels; air-bronchograms may be present (Webb et al, 1993; Tuddenham 1984). HRCT has little to add to the diagnosis of patients with clear-cut evidence of consolidation visible on chest radiographs. However, HRCT can allow the detection of consolidation before it becomes diagnosable radiographically. By definition, diseases that produce consolidation, are characterized by a replacement of alveolar air by fluid, cells, tissue, or material (Naidich et al, 1985). Most are associated with air-space filling, but diseases that produce extensive, confluent interstitial abnormalities, such as UIP or sarcoidosis, can also result in this finding (Leung et al, 1993). Air-space nodules or focal areas of ground-glass opacity are often seen in association with areas of frank consolidation. The differential diagnosis of consolidation includes pneumonia of different causes including pneumocystis carinii pneumonia, bronchiolitis obliterans organizing pneumonia, hypersensitivity pneumonitis, Eosinophilic pneumonia, radiation pneumonitis, bronchioloalveolar carcinoma and lymphoma, UIP, alveolar proteinosis, acute interstitial pneumonia, sarcoidosis, drug reaction, pulmonary edema and ARDS (Naidich et al, 1985; Godwin et al, 1988; Leung et al, 1993; Ikezoe et al, 1990; Muller et al, 1990). Lobar consolidation is often due to infection, although consolidation due to alveolar proteinosis can also have a lobar predominance. Chronic lung diseases that result in consolidation often involve the
lung in a patchy fashion. Patchy consolidation can show a nonanatomic and
nonsegmental distribution, but can also be panlobular, involving individual
lobules, or can appear nodular and centrilobular on HRCT (Webb 1989; Naidich
et al, 1985).

11-LINEAR AND RETICULAR OPACITIES
Thickening of the interstitial fiber network of the lung by fluid, fibrous tissue or
because of interstitial infiltration by cells or other material, primarily results in an
increase in linear or reticular lung opacities as seen on HRCT. Linear or reticular
opacities can be manifested by the interface sign, peribronchovascular interstitial
thickening, interlobular septal thickening, intralobular interstitial thickening,
honeycombing, subpleural lines, centrilobular or lobular core abnormalities, and
airway abnormalities.

The interface sign
The presence of irregular interfaces between the aerated lung parenchyma and
bronchi, vessels, or the visceral pleural surfaces, has been termed the interface
sign by Zerhouni et al. (Zerhouni 1989; Zerhouni et al, 1985).

The interface sign is commonly seen in patients with an interstitial abnormality,
regardless of its cause. In the original description of the interface sign, this finding
was visible in 89% of patients with interstitial lung disease (Zerhouni et al,
1985). The interface sign is generally associated with an increase in lung
reticulation; the presence of thin linear opacities contacting the bronchi, vessels, or
pleural surfaces is responsible for their having an irregular or spiculated
appearance on HRCT. These linear opacities generally represent thickened
interlobular septa or thickened intralobular interstitial fibers.

Peribronchovascular Interstitial Thickening
Central bronchi and pulmonary arteries are surrounded by a strong connective
tissue sheath, termed the peribronchovascular interstitium, that extends from the
level of the pulmonary hila into the peripheral lung, in relation to alveolar ducts
and alveoli; this is termed the \textit{axial interstitium} by \textit{Weibel} (1979). Thickening of the parahilar peribronchovascular interstitium occurs in many diseases that cause a generalized interstitial abnormality (\textit{Webb} 1989). Peribronchovascular interstitial thickening is common in patients with lymphatic spread of carcinoma (\textit{Johkoh et al}, 1992) or interstitial pulmonary edema, and can be seen in many diseases that result in pulmonary fibrosis, particularly sarcoidosis, which has a propensity to involve the peribronchovascular interstitium. Peribronchovascular interstitial thickening has been also reported in as many as 19\% of patients with chronic hypersensitivity pneumonitis (\textit{Adler et al}, 1992).

Since the thickened peribronchovascular interstitium cannot be distinguished from the underlying opacity of the bronchial wall or pulmonary artery, this abnormality is usually perceived on HRCT as (i) an increase of the bronchial wall thickness and (ii) an increase in diameter of pulmonary artery branches (\textit{Munk et al}, 1988). Apparent bronchial wall thickening is the easiest of these two findings to recognize, and is exactly equivalent to "peribronchial cuffing" seen on plain chest radiographs in patients with an interstitial abnormality. Thickening of peribronchovascular interstitium can appear smooth, nodular, or irregular in different diseases.

Smooth peribronchovascular interstitial thickening is most typical of patients with lymphangitic spread of carcinoma and interstitial pulmonary edema (\textit{Bessis et al}, 1992), but can be seen in patients with fibrotic lung disease as well. Nodular thickening of the peribronchovascular interstitium is particularly common in sarcoidosis and lymphangitic spread of carcinoma. The presence of irregular peribronchovascular interstitial thickening, as an example of the interface sign, is most frequently seen in patients with peribronchovascular and adjacent lung fibrosis. Extensive peribronchovascular fibrosis can result in the presence of large conglomerate masses of fibrous tissue. This can occur in patients with sarcoidosis, silicosis, tuberculosis, and talcosis.
Peribronchovascular interstitial thickening is easy to diagnose if it is of a marked degree, and bronchial walls appear several millimeters in thickness, or bronchovascular structures show evidence of the interface sign or nodules. However, the diagnosis of minimal peribronchovascular thickening can be difficult and quite subjective, particularly if the abnormality is diffuse and symmetric. Although the thickness of the wall of a normal bronchus should measure from 1/6 to 1/10 of its diameter (Weibel & Taylor 1988), there are no reliable criteria as to what represents the upper limit of normal for the combined thickness of bronchial wall and the surrounding interstitium. Furthermore, these measurements vary depending on the lung window chosen, and too low a window mean can make normal bronchi or vessels appear abnormal. Fortunately, however, in many patients with peribronchovascular interstitial thickening, and particularly in patients with lymphangitic spread of carcinoma and sarcoidosis, this abnormality is unilateral or patchy, sparing some areas of the lung. In such patients, normal and abnormal lung regions can be easily contrasted. As a rule, bronchial walls in corresponding regions of one or both lungs should be quite similar in thickness.

In patients with lung fibrosis and peribronchovascular interstitial thickening, bronchial dilatation is commonly present, resulting from traction by fibrous tissue on the bronchial walls. This is termed *traction bronchiectasis*; it typically results in irregular bronchial dilatation that appears "varicose" (Webb et al., 1988). Traction bronchiectasis usually involves the segmental and subsegmental bronchi, and is most commonly visible in the parahilar regions in patients with significant lung fibrosis. It can also affect small peripheral bronchi or bronchioles; an occurrence termed *traction bronchiolectasis*.

Bronchial wall thickening, which occurs in patients with true bronchiectasis, produces an abnormality that closely mimics the HRCT appearance of peribronchovascular interstitial thickening. However, airway diseases and interstitial diseases can usually distinguished on the basis of symptoms or
pulmonary function abnormalities, and confusion between these two is not often a problem in clinical diagnosis. In addition, some HRCT findings also allow these two entities to be distinguished. First, peribronchovascular interstitial thickening is often associated with other findings of interstitial disease, such as septal thickening, honeycombing, or the interface sign, while bronchiectasis usually is not. Second, in patients with bronchiectasis, the abnormal thick-walled and dilated bronchi often appear much larger than the adjacent pulmonary artery branches. This results in the appearance of large ring shadows, each associated with a small, rounded opacity, a finding that has been termed the **signet-ring sign**, and is considered to be diagnostic of bronchiectasis (**Naidich et al, 1982; Grenier et al, 1986; Grenier et al, 1990**). In patients with peribronchovascular interstitial thickening, on the other hand, the size relationship between the bronchus and artery is maintained, and they appear of approximately equal size.

**Interlobular Septal Thickening**

Thickening of the interlobular septa is commonly seen in patients with interstitial lung disease. On HRCT, numerous clearly visible interlobular septa almost always indicate the presence of an interstitial abnormality; only a few septa are visible in normal patients. Septal thickening can be seen in the presence of interstitial fluid, cellular infiltration, or fibrosis.

Within the peripheral lung, thickened septa 1 to 2 cm in length may outline part of, or an entire lobule, are usually seen extending to the pleural surface, being roughly perpendicular to the pleura (**Webb 1989; Aberle et al, 1988a**). Lobules at the pleural surface may have a variety of appearances, but are often longer than they are wide, resembling a cone or truncated cone. Within the central lung, thickened septa outline lobules that are 1 to 2.5 cm in diameter, and appear polygonal, or sometimes hexagonal, in shape. Lobules delineated by thickened septa commonly contain a visible dot-like or branching centrilobular pulmonary artery.

Thickened interlobular septa also have been described using the terms “septal lines”, “peripheral lines”, “short lines”, and “interlobular lines” (**Aberle et al, 1988**)
1988; Akira et al, 1990). Thickened septa outlining one or more pulmonary lobules have been described as producing a "large reticular pattern" (Zerhouni 1989) or "polygons", and, if they can be seen contacting the pleural surface, as "peripheral arcades" or "polygonal arcades" (Stein et al, 1987). Septal thickening can be smooth, nodular, or irregular in contour in different pathologic processes.

Smooth septal thickening is seen in patients with pulmonary edema (Cassart et al, 1993), lymphangitic spread of carcinoma or lymphoma (Munk et al, 1988), alveolar proteinosis (Godwin et al, 1988), interstitial infiltration associated with amyloidosis (Graham et al, 1992), in some patients with pneumonia, and in a small percentage of patients with pulmonary fibrosis. Nodular or beaded septal thickening occurs in lymphangitic spread of carcinoma or lymphoma (Stein et al, 1987), sarcoidosis, silicosis or coal worker's pneumoconiosis (Remy-Jardin et al, 1990a) and amyloidosis (Graham et al, 1992). In patients who have interstitial fibrosis, septal thickening visible on HRCT is often irregular in appearance (Webb et al, 1988).

Although interlobular septal thickening can be seen on HRCT in association with fibrosis and honeycombing, is not usually a predominant feature (Nishimura et al, 1992). Generally speaking, in the presence of significant fibrosis and honeycombing, distortion of lung architecture make the recognition of thickened septa difficult. Among patients with pulmonary fibrosis and end-stage lung disease, the presence of interlobular septal thickening on HRCT is most frequent in patients with sarcoidosis (present in 56% of patients), and is relatively uncommon in those with usual interstitial pneumonia (UIP) of various causes, asbestosis, and hypersensitivity pneumonitis (Primack et al, 1993).

The frequency of septal thickening and fibrosis in patients with sarcoidosis reflects the tendency of active sarcoid granulomas to involve the interlobular septa. In patients with idiopathic pulmonary fibrosis or UIP of other cause, the appearance of irregular septal thickening correlates with the presence of fibrosis.
predominately affecting the periphery of the secondary lobule (Nishimura et al, 1992).

Parenchymal Bands
The term *parenchymal bands* has been used to describe non-tapering, reticular opacities, from 2 to 5 cm in length, that can be seen in patients with pulmonary fibrosis or other causes of interstitial thickening (Aberle et al, 1988). They are often peripheral and generally contact the pleural surface. In some patients, these bands represent contiguous thickened interlobular septa, have the same significance and differential diagnosis as septal thickening (Akira et al, 1990). Parenchymal bands visible on HRCT can also represent areas of peribronchovascular fibrosis, coarse scars, or atelectasis associated with lung or pleural fibrosis (Akira et al, 1990). These non-septal bands are often several millimeters thick, irregular in contour, and associated with significant distortion of the adjacent lung parenchyma and bronchovascular structures (Im et al, 1993). Parenchymal bands have been reported as most common in patients with asbestos-related lung and pleural disease, sarcoidosis with interstitial fibrosis, silicosis associated with progressive massive fibrosis and conglomerate masses, and tuberculosis. In patients with asbestos exposure, multiple parenchymal bands are common; in one study (Aberle et al, 1988) multiple parenchymal bands were seen in 66% of asbestos-exposed patients. These bands can reflect thickened interlobular septa, indicating pulmonary fibrosis, or areas of atelectasis and focal scarring occurring in association with pleural plaques (Aberle et al, 1988).

Subpleural Interstitial Thickening
Usually, thickening of the interlobular septa within the peripheral lung is associated with thickening of the “subpleural interstitium” (Webb 1989); both the septa and the subpleural interstitium are part of the “peripheral” interstitial fiber system described by Weibel (1979). Subpleural interstitial thickening can be difficult to recognize in locations where the lung contacts the chest wall or
mediastinum, but is easy to see adjacent to the major fissures. Since two layers of
the subpleural interstitium are seen adjacent to each other in this location, any
subpleural abnormality appears twice as “abnormal” as it does elsewhere. Thus
“thickening of the fissure” can represent subpleural interstitial thickening. If the
thickening is smooth, it may be difficult to distinguish from fissural fluid. If the
interface sign is present, and the thickening is irregular (Zerhouni 1989), or if the
thickening is nodular, an interstitial abnormality is more easily diagnosed.
Subpleural interstitial thickening is more common than septal thickening in
patients with idiopathic pulmonary fibrosis (IPF) or usual interstitial pneumonia of
any cause. The presence of subpleural interstitial fibrosis with irregular or
“rugged” pleural surfaces has been reported by Nishimura et al. (1992) as a
common finding in IPF, correlating with the presence of fibrosis predominately
affecting the lobular periphery; this finding was present in 94% of cases of IPF he
studied. A subpleural predominance of fibrosis can also be seen in patients with
collagen vascular diseases and drug reactions (Colby 1993).
Remy-Jardin et al. (1990) have reported the appearance of subpleural
micronodules, defined as less than 7 mm in diameter, on HRCT in patients with
sarcoidosis, coal worker's pneumoconiosis, lymphangitic spread of carcinoma, and
in a small percentage of normal subjects.

**Intralobular Interstitial Thickening**

Thickening of the intralobular interstitium results in a fine reticular pattern as seen
on HRCT, with the lines of opacity separated by a few millimeters. Lung regions
showing this finding characteristically have a fine mesh or net-like appearance.
Intralobular bronchioles are often visible on HRCT in patients with intralobular
interstitial thickening and fibrosis because of a combination of their dilatation
“traction bronchiolectasis” and thickening of peribronchiolar interstitium which
surrounds them. Interlobular septal thickening may or may not be present in
patients with intralobular interstitial thickening; when thickened septa are visible,
they appear irregular. The pleural surface also appears irregular in the presence of
intralobular interstitial thickening. Intralobular interstitial thickening can also be described using the term *intralobular lines* (Webb et al, 1988). This finding has also been called the *small reticular pattern* (Zerhouni et al, 1985).

Intralobular interstitial thickening as perceived on HRCT reflects thickening of the distal peribronchovascular interstitial tissues, in relation to small arteries and bronchioles, or thickening of the intralobular interstitium. It is most commonly seen in patients with pulmonary fibrosis. In patients with idiopathic pulmonary fibrosis (IPF) or other causes of usual interstitial pneumonia (UIP), such as rheumatoid arthritis, scleroderma, or other collagen vascular diseases, fibrosis tends to predominately involve alveoli in the periphery of acini, resulting in a "peripheral acinar distribution" of interstitial fibrosis (Colby 1993); this histologic finding correlates with the presence of intralobular lines on HRCT. In addition, the HRCT pattern of intralobular interstitial thickening can reflect the presence of very small honeycomb cysts or dilated bronchioles associated with surrounding lung fibrosis.

Intralobular interstitial thickening can also be seen in the absence of significant fibrosis, in patients with lymphangitic spread of carcinoma, pulmonary edema, and alveolar proteinosis (Munk et al, 1988).

**Subpleural lines**

A curvilinear opacity a few millimeters thick, less than 1 cm from the pleural surface, and paralleling the pleura, was first described in patients with asbestosis (Yoshimura et al, 1986). It has been reported that a subpleural curvilinear shadow, or subpleural line, is much more common in patients with asbestosis than those with idiopathic pulmonary fibrosis of other causes of UIP. Indeed, the presence of a subpleural line in nondependent lung has been reported in 41% of patients with clinical findings of asbestosis (Aberle et al, 1988). The presence of subpleural line also has been reported as common in patients with scleroderma who have interstitial disease (Swensen et al, 1992).
It was originally suggested that a subpleural line reflects the presence of fibrosis associated with honeycombing (Yosimura et al, 1986), and in some patients, a confluence of honeycomb cysts can result in somewhat irregular subpleural line. However, the appearance of a subpleural line has been reported to occur as a result of the confluence of peribronchiolar interstitial abnormalities in patients with asbestosis, representing early fibrosis with associated alveolar flattening and collapse (Akira et al, 1990). In these patients honeycombing was not present. A subpleural line can be seen in normal patients as a result of atelectasis within the dependent lung (e.g., the posterior lung when the patient is positioned supine) (Morimoto et al, 1989). Also, a thicker, less well-defined subpleural opacity, a so-called dependent density (Aberle et al, 1988), can be seen in normal subjects as a result of volume loss. Such normal posterior lines and opacities are transient, and disappear in the prone position.

**Centrilobular (Lobular core) Abnormalities**

Centrilobular linear or reticular abnormalities can reflect interstitial thickening or bronchiolar abnormalities such as bronchiolar dilatation and the finding of “tree-in-bud.”

**Interstitial thickening**

Diseases that cause interstitial thickening often result in prominence of the centrilobular vessel, which normally appears as a dot, Y-shaped, or X-shaped branching opacity. This finding represents an abnormality of the intralobular component of the peribronchovascular interstitium, termed the *centrilobular interstitium*. It is exactly analogous to the peribronchovascular interstitial thickening in the parahilar lung (Aberle et al, 1988). On HRCT, a linear, branching, or dot-like abnormality may be seen. Thickening of the intralobular bronchovascular interstitium is usually associated with interlobular septal thickening or intralobular interstitial thickening, but sometimes occurs as an isolated abnormality. Centrilobular interstitial thickening is common in patients
with lymphangitic spread of carcinoma or lymphoma (Munk et al, 1988), and interstitial pulmonary edema (Todo & Herman, 1986). In patients with lung fibrosis, centrlobular interstitial thickening is common but almost always associated with honeycombing or intralobular lines.

**Bronchiolar Dilatation and “Tree-in-Bud”**

The intralobular bronchiole, which is not seen in normal subjects, is sometimes visible on HRCT in patients with centrlobular interstitial thickening because of a combination of (i) increased attenuation of surrounding lung, (ii) Thickening of the peribronchiolar interstitium, and (iii) dilatation of the bronchiole, which occurs as a result of fibrosis.

Diseases that involve small airways can result in increased prominence of centrlobular branching structures recognizable as an increase in reticulation on HRCT (Akira et al, 1988). Visibility of the centrlobular bronchiole in the absence of other findings of interstitial thickening should suggest airways disease; this finding can indicate dilatation of the bronchiole and bronchiolar wall thickening, or peribronchiolar fibrosis or inflammation. In some patients, small airways that are dilated and/or filled with pus, mucus, or inflammatory exudate appear as small, well-defined, centrlobular nodular, linear, or branching structures of soft-tissue opacity (Gruden et al, 1994). This appearance on HRCT has been likened to a *tree-in-bud* (Im et al, 1993).

Abnormal bronchioles producing a tree-in-bud appearance can be usually distinguished from normal centrlobular vessels by their more irregular appearance, a lack of tapering, or bulbous appearance at the tips of small branches. This latter appearance reflects the presence of bronchiolar dilatation or peribronchiolar inflammation. Centrlobular bronchiolar abnormalities characterized by dilatation and tree-in-bud are seen in patients with Asian panbronchiolitis (Akira et al, 1988), endobronchial spread of TB (Im et al, 1993) or nontuberculous mycobacteria, cystic fibrosis, and bronchopneumonia, bronchiectasis of any cause. In patients with Asian panbronchiolitis, prominent
branching centrilobular opacities represent dilated bronchioles with inflammatory bronchiolar wall thickening and abundant intraluminal secretions (Akira et al, 1993). Similarly, in patients with active TB, a tree-in-bud appearance was visible in 72% of patients in one study (Im et al, 1993), correlating with the presence of solid caseous material within terminal and respiratory bronchioles.

III-DECREASED LUNG OPACITY AND CYSTIC ABNORMALITIES
A variety of abnormalities result in decreased lung attenuation or air-filled cystic lesions on HRCT. These include honeycombing, bronchiectasis, emphysema, lung cysts, cavitary nodules, mosaic perfusion, and air trapping due to airways disease. In most of cases these can be readily distinguished on the basis of HRCT findings (Hogg 1991).

Honeycombing
Extensive interstitial and alveolar fibrosis that results in alveolar disruption and bronchiolectasis produces the classic and characteristic appearance of honeycombing or honeycomb lung. Pathologically, honeycombing is defined by the presence of small air-containing cystic spaces, generally lined by bronchiolar epithelium, having thickened walls composed of dense fibrous tissue. Honeycombing indicates the presence of end-stage lung and can be seen in almost any process leading to end-stage pulmonary fibrosis (Primack et al, 1993). These cysts have fibrous walls and are lined by bronchiolar epithelium. On HRCT, honeycombing is characterized by the presence of air-filled, cystic spaces several millimeters to several centimeters in diameter, which often predominate in a peripheral and subpleural location, occur in several layers, and are characterized by clearly definable walls, 1 to 3 mm in thickness (Webb et al, 1988). In contradistinction to the lung cysts seen in patients with lymphangiomyomatosis and histiocytosis X, and the luencies seen in patients with centrilobular
emphysema, honeycomb cysts tend to share walls. The presence of honeycombing on HRCT indicates the presence of severe fibrosis.

Large subpleural cystic spaces, several centimeters in diameter, can be associated with honeycombing, mimicking the appearance of bullae. These large cysts tend to predominate in the upper lobes. These large honeycomb cysts decrease in size on expiratory scans (Aquino et al, 1994); this change would not be expected of bullae. Subpleural honeycomb cysts typically occur in several contiguous layers; this finding can allow honeycombing to be distinguished from subpleural emphysema (paraseptal emphysema) since subpleural cysts usually occur in a single layer (Webb et al, 1996).

Lung Cysts

On HRCT, the term lung cyst is used to refer to a thin-walled (usually >3 mm), well-defined and circumscribed, air-containing lesion (Naidich 1991). Lung cysts are also defined as having a wall composed of one of a variety of cellular elements, usually fibrous or epithelial in nature (Tuddenham 1984). For example, in patients with end-stage pulmonary fibrosis, honeycomb cysts are lined by bronchiolar epithelium; on the other hand, in patients with lymphangiomyomatosis the cysts are lined by abnormal spindle cells resembling smooth muscle.

Lymphangiomyomatosis (LAM) and histiocytosis X often produce multiple lung cysts, whose appearance on HRCT is usually quite distinct from that of honeycombing (Moore et al, 1989; Muller et al, 1990b). The cysts have a thin wall, ranging up to a few millimeters in thickness, associated findings of fibrosis are usually absent or much less conspicuous than they are in patients with honeycombing and end-stage lung disease. In LAM and histiocytosis X, the cysts are usually interspersed within areas of normal-appearing lung.

In patients with histiocytosis X, the cysts can have bizarre shapes because of the fusion of several cysts or perhaps because they represent ectatic and thick-walled bronchi. Although confluent cysts can also be seen with LAM, they are less
common; in patients with LAM, cysts generally appear rounder, and more uniform in size, than those seen with histiocytes X.

Lung cysts should be distinguished from air-containing spaces such as emphysematous bullae, blebs, and pneumatoceles (Webb et al, 1996).

**Emphysema**

Emphysema is defined as a permanent, abnormal enlargement of airspaces distal to the terminal bronchiole, accompanied by destruction of the walls of the involved airspaces (Naidich 1991). Emphysema can be accurately diagnosed using HRCT, and results in focal areas of very low attenuation that can be easily contrasted with surrounding, higher attenuation, normal lung parenchyma if sufficiently low window means (-600 HU to -800 HU) are used. Although some types of emphysema can have walls visible on HRCT, these are usually inconspicuous (Muller et al, 1988, Miller et al, 1989).

In many patients it is possible to classify the type of emphysema on the basis of HRCT appearance (Webb et al, 1988). *Centrilobular (centriacinlar) emphysema*, is characterized on HRCT by the presence of multiple small lucencies that predominate in the upper lobes. Even if the centrilobular location of these lucencies is not visible, a spotty distribution is typical of centrilobular emphysema. In most cases, the areas of low attenuation seen on HRCT in patients with centrilobular emphysema lack a visible wall, although very thin walls are occasionally visible. In severe cases, the areas of centrilobular emphysema become confluent. *Panlobular (paracinlar) emphysema* typically results in an overall decrease in lung attenuation, and a reduction in size of pulmonary vessels, without the focal areas of lucency typically seen in patients with centrilobular emphysema. Areas of panlobular emphysema typically lack visible walls. This form of emphysema has been described as a diffuse simplification of lung architecture. Severe centrilobular emphysema can mimic this appearance.

*Paraseptal (distal acinar) emphysema* results in the presence of subpleural
Lucencies, which often sharp very thin walls that are visible on HRCT, paraseptal emphysema can be seen as an isolated abnormality, but is often associated with centrilobular emphysema. *Irregular air-space enlargement*, previously known as irregular or cicatricial emphysema, can be seen in association with fibrosis, as in silicosis and progressive massive fibrosis (Kinsella et al, 1990). The appearance of panlobular emphysema and centrilobular emphysema can mimic the presence of honeycombing or lung cysts in some patients.

**Paraseptal emphysema vs. Honeycombing**

In patients with paraseptal emphysema, areas of lung destruction are typically margined by thin linear opacities, visible on HRCT, that extend to the pleural surface. These linear opacities often correspond to interlobular septa and sometimes are associated with minimal fibrosis. Because they are subpleural and margined by visible walls, areas of paraseptal emphysema can resemble the appearance of honeycombing. Honeycomb cysts are usually smaller, usually occur in several layers, tend to predominate at the lung bases, are associated with disruption of lobular architecture and other findings of fibrosis. On the other hand, areas of paraseptal emphysema are often larger and associated with bullae, usually occur in a single layer, predominate in the upper lobes, and may be associated with other findings of emphysema, but are typically unassociated with significant fibrosis (Webb et al, 1996).

**Cavitary Nodules**

Cavitary nodules have thicker and more irregular walls than do lung cysts, but there is some overlap between these appearances. Such nodules have been reported in histiocytosis X, tuberculosis, fungal infection, and sarcoidosis, but could also be seen in patients with rheumatoid lung disease, septic embolism, pneumonia, metastatic tumor, Wegener's granulomatosis, etc. Also some nodular opacities having central lucencies, may represent dilated bronchioles surrounded
by areas of consolidation or interstitial thickening (Moore et al., 1989; Im et al., 1993; Nishimura et al., 1993).

**Bronchiectasis**

Bronchiectasis is generally defined as localized, irregular bronchial dilatation (Grenier et al., 1993). While bronchiectasis usually results from chronic infection, airway obstruction by tumor, stricture, impacted material, or inherited abnormalities can also play a significant role. Bronchiectasis has also been classified into three types, depending on the morphology of the abnormal bronchi, although these distinctions are of little clinical value (Naidich 1991).

*Cylindrical bronchiectasis*, the mildest form of this disease, is characterized on HRCT by the presence of thick-walled bronchi, which extend into the lung periphery and fail to show normal tapering. On HRCT, bronchi are not normally visible in the peripheral 2 cm of lung, but in patients with bronchiectasis, bronchial wall thickening, peribronchial fibrosis, and dilatation of bronchial lumen, allow them to be seen in the lung periphery. Depending on their orientation relative to the scan plane they can simulate “tram tracks” or can show the “signet-ring sign,” in which dilated, thick-walled bronchus and its accompanying pulmonary artery branch are seen adjacent to each other (Naidich et al., 1982). Ectatic bronchi containing fluid or mucus appear as tubular opacities.

*Varicose bronchiectasis* is similar in appearance to cylindrical bronchiectasis; however, with varicose bronchiectasis the bronchial walls are more irregular, and can assume a beaded appearance. The term *string of pearls* has been used to describe varicose bronchiectasis. Traction bronchiectasis often appears varicose. *Cystic bronchiectasis* most often appears as a group or cluster of air-filled cysts, but cysts can also be fluid-filled, giving the appearance of a “cluster of grapes.” Cystic bronchiectasis is often patchy in distribution, allowing it to be distinguished from a cystic lung disease such as LAM. Also, air-fluid levels, which may be
present in the dependent portions of the cystic dilated bronchi, are a very specific sign of bronchiectasis, and are not usually seen in patients with lung cysts.

**Traction Bronchiectasis**

In patients with lung fibrosis and distortion of the lung architecture, traction bronchiectasis is commonly present. Traction by fibrous tissue on the walls of the bronchi results in irregular bronchial dilatation, or bronchiectasis, which is typically "varicose" in appearance (Webb et al, 1988).

Traction bronchiectasis usually involves the segmental and subsegmental bronchi, can also affect small peripheral bronchi or bronchioles. Dilatation of the intralobular bronchioles because of the surrounding fibrosis is termed *traction bronchiolectasis*. In patients with honeycombing, bronchial dilatation contributes to the cystic appearance seen on HRCT (Nishimura et al, 1992).

The increased transpulmonary pressure and elastic recoil associated with advanced pulmonary fibrosis, along with local distortion of airways by fibrotic tissue, all contribute to the varicose dilatation of airways seen in these condition. Traction bronchiectasis is usually most marked in areas of lung that show the most severe fibrosis. It is commonly seen in association with honeycombing (Webb et al 1996).

**Use of Expiratory CT to Differentiate Mosaic Perfusion from Ground-Glass Opacity**

Inhomogeneous lung attenuation visible on inspiratory scans can be the result of (i) ground-glass opacity, (ii) mosaic perfusion resulting from airways obstruction and reflex vasoconstriction, or (iii) mosaic perfusion resulting from vascular obstruction. In many patients with mosaic perfusion, HRCT findings of decreased vascular caliber in lucent lung regions, or airway abnormalities can be diagnostic; however, in others, HRCT findings are nonspecific.
Expiratory scans can usually allow the differentiation of patients with ground-glass opacity from those with mosaic perfusion resulting from airways obstruction. In patients with ground-glass opacity, expiratory HRCT typically shows a proportional increase in attenuation in areas of both increased and decreased opacity. In patients with mosaic perfusion resulting from airways disease, attenuation differences are accentuated on expiration; relatively dense areas increase in attenuation, while lower attenuation regions remains lucent. In patients with mosaic perfusion resulting from vascular disease, expiratory HRCT findings mimic those seen in patients with ground-glass opacity; both low-attenuation and high-attenuation regions increase in opacity (webb et al, 1996).

IV-NODULES AND NODULAR OPACITIES
An approach to the assessment and differential diagnosis of multiple nodular opacities is based on a consideration of their size (small or large), distribution, and appearance (well-defined or ill-defined).

Small Nodules
The term small nodule is defined as a rounded opacity less than 1 cm in diameter, whereas large nodule is 1 cm or greater in diameter. Some authors have used micronodule to describe nodules that are either less than 3 mm (Grenier et al, 1991) or less than 7 mm in diameter (Remy-Jardin et al, 1991), but it is not clear that this distinction is of value in differential diagnosis (Grenier et al, 1991). Differences in the appearances of nodules that are predominantly “interstitial” or predominantly “air-space” in origin have been emphasized by several authors. Nodules considered to be interstitial are usually well defined despite their small size. Nodules as small as 1 to 2 mm in diameter can be detected on HRCT in patients with interstitial diseases such as sarcoidosis (Murata et al, 1989), histiocytosis X (Moore et al, 1989), silicosis and coal worker's pneumoconiosis (Bergin et al, 1986), miliary TB (Lee et al, 1993), and metastatic tumor (Murata et al, 1992). Interstitial nodules usually appear to be of soft tissue attenuation and
obscure the edges of vessels or other structures in which they touch (Akira et al., 1991). Air-space nodules are more likely to be ill defined; they can be of homogeneous soft-tissue attenuation, thus obscuring vessels, or hazy and less dense than adjacent vessels (so-called ground-glass opacity). A cluster or rosette of small nodules can also be seen (Naidich et al., 1985). Air-space nodules have also been termed "acinar nodules," because they approximate the size of acini, but these nodules are not truly acinar histologically, but tend to be centrilobular and peribronchiolar (Itoh et al., 1978); ill-defined nodule or air-space nodule are preferable terms. Despite these differences in appearance, a distinction between interstitial and air-space nodules on the basis of HRCT findings can be quite difficult, because many nodular diseases affect both the interstitial and alveolar compartments histologically. The distribution or location of small nodules is more valuable in differential diagnosis than their appearance. In different conditions, small nodules can appear randomly distributed, perilymphatic in distribution, or predominantly centrilobular.

Random Distribution
Small nodules that appear randomly distributed in relation to structures of the secondary lobule are often seen in patients with miliary TB and miliary fungal infections (Lee et al., 1993). The nodules can be seen in relation to small vessels, interlobular septa, and the pleural surfaces, but do not appear to have a consistent or predominant relationship to any of these. In miliary TB or fungal infections, the nodules tend to be well defined and up to several millimeters in diameter. Hematogeneous metastases have a recognized tendency to predominate in the lung periphery and at the lung bases. As with miliary TB, the nodules can be seen in relation to small vessels in some locations, a fact, which likely reflects their mode of dissemination. In a study correlating HRCT and pathologic findings, nodules less than 3 mm in diameter had no consistent relationship to lobular structures. Nodules resulting from hematogeneous metastasis are characteristically well-defined (Murata et al., 1992).
Perilymphatic Distribution

Nodules that predominate in relation to the parahilar peribronchovascular interstitium, the centrilobular interstitium, interlobular septa, and in a subpleural location are typical of patients with sarcoidosis, silicosis and coal worker's pneumoconiosis, and lymphangitic spread of carcinoma (Colby, 1993). This pattern of abnormalities has been termed lymphatic or perilymphatic, in that it corresponds to the distribution of lymphatics in the lung (Remy-Jardin et al, 1990a).

In nearly all patients with sarcoidosis, HRCT shows nodules, ranging in size from several millimeters to 1 cm or more in diameter (Muller et al, 1989). The nodules often appear sharply defined despite their small size. Nodules are most frequently seen in relation to the parahilar peribronchovascular interstitium, the subpleural interstitium, and small vessels; histologically small clusters of granulomas are visible in these locations (Muller et al, 1989). An upper lobe predominance of nodules is common in sarcoidosis (Remy-Jardin et al, 1990). Nodules can cavitate in only 3% of cases (Grenier et al, 1991).

Silicosis and coal worker's pneumoconiosis are associated with the presence of small nodules, usually measuring from 2 to 5 mm in diameter, which predominantly appear centrilobular and subpleural in location on HRCT (Remy-Jardin et al, 1990). These correlate with areas of fibrosis surrounding centrilobular respiratory bronchioles and involving the subpleural interstitium, and are caused by the accumulation of particulate material in these regions. In patients with silicosis, the nodules can calcify.

A few small subpleural and centrilobular nodules can also be seen in smokers probably related to the presence of fibrosis and accumulated particulate material in the peribronchiolar regions and at the bases of interlobular septa, and probably related to pathways of lymphatic drainage. Lymphocytic interstitial pneumonia (LIP) can result in the presence of lymphocytic and plasma cell infiltrates in
relation to the peribronchovascular interstitium, interlobular septa and centrilobular regions. On HRCT, ill-defined centrilobular opacities can be seen. Subpleural nodules have been reported in about 80% of patients with silicosis or coal worker’s pneumoconiosis, 50% of patients with sarcoidosis, and are also common with lymphangitic spread of carcinoma (Remy-Jardin et al, 1990). Confluent subpleural nodules can result in the appearance of “psudoplaques”; linear areas of subpleural opacity several millimeters in thickness that mimic the appearance of asbestos-related parietopleural plaques (Remy-Jardin et al, 1990).

**Centrilobular Distribution**

Nodules limited to the centrilobular regions may be dense and of homogeneous opacity, or of ground-glass opacity, and range from a few millimeters to a centimeter in size. Either a single centrilobular nodule or a centrilobular rosette of nodules may be visible (Naidich et al, 1985). Because of similar size of the secondary lobules, centrilobular nodules often appear to be evenly spaced. Centrilobular nodules are usually separated from the interlobular septa and pleural surfaces by a distance of several millimeters; in the lung periphery the nodules are usually centered 5 to 10 mm from the pleural surface. They do not usually occur in relation to interlobular septa or the pleural surfaces, as do random or perilymphatic nodules, and the subpleural lung is typically spared.

It is typical for centrilobular nodules to appear perivascular on HRCT, surrounding or obscuring the smallest pulmonary arteries visible on HRCT. On occasional cases, the air-filled centrilobular bronchiole can be recognized as a rounded lucency within a centrilobular nodule.

Centrilobular nodules can be seen in patients with a variety of diseases that primarily affect centrilobular bronchioles or arteries and result in inflammation or fibrosis of the surrounding interstitium and alveoli (Colby 1993). Bronchiolar diseases most frequently result in this finding, sometimes in association with centrilobular airway dilatation or the appearance of a tree-in-bud. Well-defined,
small peribronchiolar nodules, representing interstitial granulomas, have been described in patients with histiocytosis X (Moore et al, 1989). Ill-defined centrilobular opacities can occur in patients with endobronchial spread of TB or nontuberculous mycobacteria, lobular or bronchopneumonia (Itoh et al, 1978), Asian panbronchiolitis (Akira et al, 1988), hypersensitivity pneumonitis (Lee et al, 1991), bronchiolitis obliterans with organizing pneumonia (BOOP) (Muller et al, 1990), and respiratory bronchiolitis in smokers. bronchiolitis obliterans, bronchiectasis with surrounding fibrosis in cigarette smokers, asbestosis, pulmonary edema, vasculitis, and talcosis. Bronchioalveolar carcinoma and endobronchial spread of tracheobronchial papillomatosis can also result in small centrilobular nodules (Gruden & Webb 1993; Leung et al, 1993).

Large nodules
The term large nodule is used to refer to rounded opacities that are 1 cm or more in diameter. The term mass is generally used to describe nodular lesions that are greater than 3 cm in diameter (Tuddenham 1984). Large nodules can be associated with a variety interstitial or air-space diseases, including those described above. In addition, in patients with diffuse or chronic lung disease, these can represent conglomerate masses of smaller nodules as are common in sarcoidosis or silicosis, infectious or inflammatory lesions, tumor nodules, infarctions, nodules of Wegener’s granulomatosis (Weir et al, 1992).

Conglomerate Nodules or Masses
In patients with disease characterized by small nodules, conglomeration or confluence of nodules can result in large nodular or mass-like opacities. Grenier et al. (1991) reported the presence of confluent nodules greater than 1 cm in 53% of patients with sarcoidosis. These masses were seen in upper lobes and peribronchovascular regions. These masses are often irregular in shape, surround the central bronchi and vessels, and can show small discrete nodules in their periphery.
Large masses of fibrous tissue may surround and encompass bronchi and vessels within the central or parahilar lung in patients with progressive fibrotic lung disease. The bronchi within these masses may be crowded together, reflecting the volume loss which is present, and are dilated as a result of fibrosis and traction bronchiectasis. Similar upper lobe masses associated with bronchiectasis have been reported in patients with TB, and are most frequent after treatment (Im et al, 1993).

Patients with silicosis and coal workers who have complicated pneumoconiosis or progressive massive fibrosis, also show conglomerate masses in the upper lobes, but these are more typically of homogeneous opacity, and tend to be unassociated with visible traction bronchiectasis as seen in sarcoidosis. Also, areas of emphysema peripheral to the conglomerate masses are common (Remy-Jardin et al, 1990a).

Focal fibrotic masses that are irregular in shape have been described as occurring in the peripheral lung, in relation to pleural abnormalities in patients with asbestos exposure. These represent focal areas of scarring or rounded atelectasis. It most always occurs in association with pleural disease, and typically contacts the pleural surface. Rounded atelectasis occurs most commonly in the posterior lung, in the paravertebral regions, and may bilateral. Bending or bowing of adjacent bronchi and arteries toward the area of atelectasis, because of volume loss or folding of lung is characteristic. This appearance has been likened to a “comet-tail.” Air bronchograms within the mass can sometimes be seen (Weir et al, 1992; Padley et al, 1993).
COLLAGEN VASCULAR DISEASES

The collagen vascular or connective tissue diseases (CTDs) are a group of immunologically mediated systemic diseases that involve connective tissue at various sites in the body. As a group, the CVDs share certain clinical characteristics and have a variable propensity for involving the tissues of the thorax. Their protean thoracic manifestations as seen on imaging studies reflect their ability selectively to involve, singly or in combination, different organs or structures that contain connective tissue. This group of diseases includes seven classic and several lesser CVDs. The classic CVDs are rheumatoid disease (RD), systemic lupus erythematosus (SLE), progressive systemic sclerosis (PSS), polymyositis-dermatomyositis (PM-DM), relapsing polychondritis (RP), mixed connective tissue disease (MCTD), and Sjogren's syndrome (SjS). The lesser CVDs are much less common and have a lower incidence of thoracic involvement. These include Behcet's disease and ankylosing spondylitis. Vasculitides are also included such as Wegener's granulomatosis, lymphomatoid granulomatosis, and allergic angitis with granulomatosis (Churg-Strauss syndrome) (Wiedemann and Matthay 1989).

Scleroderma (systemic sclerosis)

Scleroderma (systemic sclerosis) is a systemic collagen vascular disease of unknown cause characterized by vascular and connective tissue abnormalities. Scarring (fibrosis) and vascular obliteration in the skin, gastrointestinal tract, lungs, heart, and kidneys are typical findings. Hidebound skin is the clinical hallmark, and organ compromise is the major diagnostic marker (LeRoy et al 1988; Geppert 1990). Scleroderma is uncommon, the incidence being approximately 10 per million populations per year (Medsger & Masi 1971). Scleroderma is approximately one fourth as common as SLE and approximately one half as common as temporal arteritis. Scleroderma affects women three times
more commonly than men and is slightly more common in blacks than whites (Medsger & Masi, 1971).

The lungs rank behind only the skin, peripheral vasculature, and esophagus in frequency of organ involvement in scleroderma (Geppert, 1990; Silver & Miller, 1990; LeRoy, 1985).

**Limited versus diffuse scleroderma**

There are two broad categories of scleroderma based on clinical findings: (1) a limited form and (2) a diffuse form (LeRoy et al 1988; Geppert 1990). Approximately 60% of patients with scleroderma have limited disease usually manifested by the characteristic CREST syndrome of Calcinosis, Raynaud's phenomenon, esophageal involvement, sclerodactyly, and telangiectasias. These patients are generally older women who have Raynaud's phenomenon for 10 to 15 years, who have thickening of the skin over the digits and occasionally over the hands and forearms. And also have facial and digital telangiectasias (LeRoy et al 1988; Geppert 1990). These findings may be present for years before the appearance of systemic involvement. Anticentromere antibody (ACA) is detected in more than 50% of the patients with limited disease (LeRoy et al, 1988).

Patients with diffuse disease are usually young or middle-aged women. The disease begins abruptly with swelling of the hands, face, and feet, Raynaud's phenomenon, constitutional symptoms, and widespread skin involvement (LeRoy et al, 1988). The gastrointestinal tract (especially the esophagus), lungs, kidneys, and cardiovascular system may be involved.

**Circulating antibodies in scleroderma**

ACA and antitopoisomerase I (anti-scl 70) autoantibodies are found almost exclusively in patients with scleroderma. ACA is present in up to 82% of patients with limited disease but in only 3% of patients with diffuse disease. Only 33% of
patients with diffuse disease and 18% with limited disease, however, have anti-scl 70 antibodies (Steen et al, 1988).

Anti-scl 70 antibodies are associated with the presence of restrictive lung disease, even in patients with limited scleroderma. In contrast, ACA is not associated with the presence of pulmonary disease (Geppert 1990; Steen et al, 1988). Another study confirms that antinuclear antibodies (ANA) are detected in almost all patients with scleroderma (Kipnis et al, 1990).

**Pulmonary symptoms and signs**

Respiratory symptoms and signs in patients with scleroderma are similar to those seen in patients with idiopathic pulmonary fibrosis (IPF). Dyspnea is the most common pulmonary symptom in patients with scleroderma, occurring in 60% of patients (Owen & Follansbee 1987). Dyspnea is usually related to loss of lung compliance due to pulmonary fibrosis (Sackner et al, 1964). Severe dyspnea in the absence of opacities on chest radiographs suggests the presence of pulmonary vascular disease (Silver & Miller 1990). Nonproductive cough is a common complaint. Wheezing occurs in up to 19% of patient (McCarthy et al, 1988). Approximately 16% of patients with pulmonary scleroderma have pleuritic chest pain at some point in the course of the disease (Owens & Follansbee 1987).

**Physical examination**

The most common pulmonary abnormality in patients with scleroderma is the presence of "Velcro" crackles at the lung bases; these are heard in 50% of patients with a restrictive ventilatory defect and evidence of pulmonary fibrosis on chest radiographs (Steen et al, 1985). Approximately 9% of affected patients may develop a pleural rub (Steen et al, 1985).
As pulmonary fibrosis progresses, signs of cor pulmonale may develop; these include a right ventricular heave, a fixed split-second sound, murmurs of tricuspid or pulmonary valve insufficiency, leg edema, jugular venous distention, and cyanosis (Silver & Miller 1990).

Pulmonary function abnormalities

Restrictive and obstructive ventilatory defects

In a study by McCarthy et al (1988) one third of 34 patients had normal pulmonary function, one third had a restrictive ventilatory pattern, and one third had evidence of small airways disease. Other investigators have reported similar results (Silver & Miller 1990; McCarthy et al 1988). Guttaduria et al (1977) evaluated 45 patients who had had scleroderma for an average 4.25 years. Approximately one third were smokers. All patients had abnormal pulmonary function: 30% had a restrictive pattern and 70% had a reduced diffusing capacity for carbon monoxide (DLCO). The most common abnormality was an increased residual volume (92%) probably due to premature airway closure, suggesting the presence of small airway disease. Twelve of the patients (27%) had large airway disease defined by a forced expiratory volume in one second-to-forced vital capacity (FEV1/FVC) ratio less than 75% of predicted.

Diffusing capacity

The DLCO is commonly reduced in patients with scleroderma (Silver & Miller 1990). The degree of reduction usually parallels the severity of the restrictive ventilatory defect, but approximately 15% of patients with otherwise normal pulmonary function tests have a reduced DLCO (Silver & Miller 1990). This isolated abnormality is slightly more common in patients with limited scleroderma than in patients with diffuse disease (Steen 1990; Owens et al, 1983) and probably reflects pulmonary vascular disease, which is more prevalent in patients with limited disease (Young & Mark 1978). Some investigators have suggested
that a decreased DLCO is the earliest pulmonary function abnormality in scleroderma and the most sensitive index of pulmonary involvement in this disease (Steen 1990; Weaver et al, 1968).

Respiratory muscle abnormalities
Clements et al (1978) found that 23 of 24 consecutive, unselected patients with scleroderma had abnormalities of proximal skeletal muscle biopsy. The muscle disease in these patients progressed only slowly.
McCarthy et al (1988) measured maximum respiratory muscle power in 13 patients with scleroderma and 17 normal subjects. Maximum expiratory power (PE max) was measured at TLC and functional residual capacity (FRC) and maximum inspiratory power (PI max) were measured at RV and FRC. Maximum respiratory muscle power was significantly reduced (20 cm H2O or more) in 62% of patients with scleroderma, with PI max being more affected than PE max.

Plain chest radiographs
Lung parenchyma
Of the collagen vascular diseases, scleroderma has the highest incidence of pulmonary parenchymal involvement seen on plain chest radiographs and at autopsy, and postmortem examination has shown evidence of pulmonary involvement in 74% of patients (Weaver et al, 1968; D'Angelo et al, 1969). Changes in lung parenchyma are seen on plain chest radiographs in 25%-65% of patients with scleroderma (Steen 1990; Owens et al 1983).

Chest radiographic abnormalities are often subtle in patients with scleroderma. Diffuse interstitial lung disease and honeycombed lung are detected only in the more severe forms of the disease. Chest radiographs may be normal even in patients who are symptomatic and who have pulmonary function abnormalities, or fine interstitial opacities may be visible (Silver & Miller 1990). These changes occur most frequently at the lung bases and with time they may become denser may expand to involve the lower two thirds of the lung (Silver & Miller 1990). The apices are usually spared. The pattern of fibrosis is usually reticulonodular,
although reticular or nodular changes alone may occur (Steen 1990). Progression of the disease leads to a honeycombed pattern of fibrosis. Serial radiographs may show progressive loss of lung volume manifested by a serially diminished distance between the lung apex and the diaphragm.

Cardiovascular abnormalities include increased size of the cardiac silhouette (primarily due to right heart enlargement) and pulmonary artery enlargement usually caused by pulmonary vascular disease and associated PAH (Sacker et al 1964; Stupi et al, 1986; Angrier et al 1983; Slain et al 1977).

McCarthy et al (1988) reported that 6 of 36 patients (17%) with scleroderma had enlarged cardiac silhouettes and pulmonary arteries. The lung was normal on chest radiographs in 4 of 6 patients with cardiomegaly in this series. In addition to PAH, other causes of cardiomegaly in scleroderma are pericardial and myocardial disease.

Chest radiographs may also show rib notching commonly on the superior aspect of upper ribs. Owens et al (1983) reported this finding in 10 of 61 patients (61%) with diffuse scleroderma. These patients often have distal phalangeal tuft resorption (Steen et al, 1985). Owens et al (1983) also reported microcalcification of the lung parenchyma in 29 of 43 patients (67%) with limited disease and in only 6 of 43 patients (14%) with diffuse disease. Pulmonary calcification does not correlate with peripheral subcutaneous tissue calcification, which is often noted in patients with limited scleroderma.

**Pleural involvement**

Unlike patients with rheumatoid arthritis or SLE, patients with scleroderma rarely develop clinically significant pleural effusion, and pleural thickening on chest radiograph is seen only occasionally (Owens et al, 1983). These pleural effusions are exudative. McCarthy et al (1988) found pleural thickening on chest radiographs in only 8% of patients with scleroderma, whereas other investigators (Steen 1990) have reported pleural thickening or a pleural effusion on chest
radiographs in from 11% to 56% of patients. Pleural effusion may be to
scleroderma involving the pleura or may be secondary to congestive heart failure
from either myocardial fibrosis or renovascular hypertension.

**Pneumothorax**

Spontaneous pneumothorax in patients with scleroderma is rare. When it occurs,
the predominant cause is rupture of subpleural cystic air spaces that are found
mostly in the lower lung zones. These cysts apparently form secondary to
alveolitis and destruction of alveolar walls with subsequent deposition of abnormal
collagen. Because of decreased lung compliance, reexpansion is usually slow and
recurrence common. Treatment consists of prolonged chest tube suction and
chemical pleurodesis (Ng & Tan 1990).

**Chest CT scanning**

In scleroderma, the high prevalence of pulmonary involvement at autopsy
(Weaver et al, 1968) does not correlate well with abnormalities seen on plain
chest radiographs. Abnormalities are often present on lung biopsy or at autopsy in
patients who have normal chest radiographs. Plain chest radiographs may appear
normal in up to 10% of patients with biopsy proven diffuse infiltrative lung
disease of varying causes, including IPF (Eppler et al, 1978). The combination of
thin-section CT (1 to 2 mm collimation) and the use of high-frequency resolution
algorithm is referred to as "HRCT". HRCT provides optimal visualization of the
lung parenchyma in patients with diffuse lung disease (Muller & Miller 1990).

Schurawitzki et al (1990) reported that 21 of 23 patients (91%) with scleroderma
had evidence of interstitial lung disease on HRCT. 14 of the patients (61%) had
normal chest radiographs or equivocal signs of lung involvement suggesting that
HRCT is more sensitive than chest radiographs for detecting minimal parenchymal
interstitial lung disease. Harrison et al (1989) reported that HRCT showed that
lung parenchymal abnormalities in patients with diffuse disease were similar to those in patients with limited disease. The abnormalities most often detected by HRCT are subpleural lines, thickened septal lines, parenchymal bands, subpleural cysts, and honeycombing. These abnormalities often occur together (Schurawitzki et al, 1990; Harrison et al, 1989). Honeycombed lung indicating more severe involvement is less common in patients with normal chest radiographs (Harrison et al, 1989). The subpleural spaces are most frequently involved, predominantly dorsally (Schurawitzki et al, 1990; Harrison et al, 1989). Also, the lower-lung zones are most frequently involved, followed by mid-lung zones and, least frequently, the upper-lung zones. The interstitial changes observed on HRCT in scleroderma are not specific, have also been described in patients with IPF, rheumatoid lung, and mixed connective tissue disease (Schurawitzki et al, 1990; Harrison et al, 1989). All interstitial lesions persisted when the patients were scanned in the prone position, ruling out spurious causes such as hypostasis or hypoventilation. The duration of scleroderma did not correlate with the severity interstitial disease indicated by HRCT (Schurawitzki et al, 1990). Harrison et al (1989) found abnormal cell profiles in BAL fluid of patients who had normal chest radiographs and abnormal HRCT, suggesting that HRCT can detect subclinical pulmonary disease.

Imaging of esophageal abnormalities

The esophagus is reported to be involved in up to 87% of patients with systemic sclerosis (McCarthy et al, 1988; Akesson & Wollheim 1989). Patients with either limited disease or diffuse disease are equally affected by dysphagia, heartburn, and regurgitation; but the degree of disturbed motility measured by cineradiography was higher in patients with diffuse scleroderma (Akesson & Wollheim 1989). Mahrer et al (1954) reported that esophageal dilatation and decreased peristalsis were detected on esophagogram in 62% of patients.
Histologic examination of the esophagus showed muscle atrophy and fibrosis in 39 of 53 patients (74%) studied by D'Angelo et al (1969).

Some investigators suggest that pulmonary lesions are often due to aspiration secondary to esophageal involvement (Johnson et al, 1989). Because lung disease has been reported in scleroderma patients without esophageal abnormalities, however, most authorities agree that the pulmonary involvement is usually not caused by aspiration pneumonitis (McCarthy et al, 1988).

**Bronchoalveolar lavage (BAL)**

BAL, a safe technique used widely in various interstitial lung diseases, provides information on the number and types of cells in the lower respiratory tract. Single-site lavage accurately represents other areas of the lung in most cases.

In several studies, examination of BAL fluid has shown evidence of inflammation in patients with both limited and diffuse scleroderma, whether or not they had radiographic evidence of interstitial lung disease (Harrison et al, 1989; Wallaert et al, 1986). Studies showed an increase in BAL fluid cell count, an increase in the percentage of granulocytes (neutrophils and eosinophils), and, in some patients, a predominantly lymphocytic alveolitis. Some patients with lymphocytic alveolitis have sjogren's syndrome in association with scleroderma (Breit et al, 1989).

Additional support for an inflammatory component of scleroderma lung disease is provided by the significant elevation of IgG and immune complexes in BAL fluid and the increased release of fibronectin by alveolar macrophages isolated from BAL fluid (Silver et al, 1990; Kinsella et al, 1989). The presence of alveolitis and the associated increase of type III collagen synthesis in the lungs of patients with normal chest radiographs and normal PFT suggest that these findings may be early events in the pathogenesis of interstitial lung disease in patients with scleroderma (Harrison et al, 1989; Harrison et al, 1990; Silver et al, 1990).

Overall, 50% to 60% of patients with scleroderma have abnormal findings at BAL (Wallaert et al, 1986). Patients with evidence of alveolitis tend to have more severe dyspnea and more abnormalities on chest radiographs. Patients with
alveolitis also had a more severe restrictive ventilatory defect and lower DLCO (Silver et al, 1990). Serial studies of BAL fluid in patients with scleroderma have shown that alveolitis persists. Patients with a normal initial study tend to remain normal (Silver et al, 1990).

Pathology

On postmortem examination, approximately 70% of patients with scleroderma have interstitial lung disease, pulmonary vascular disease (D'Angelo et al, 1969; Owens et al, 1983). On gross examination, the lungs of patients with interstitial disease are stiff and may have a rubbery consistency. The surface of the lung is usually covered with air-filled cysts 1-2 cm in widest diameter, primarily located subpleurally. Small and large airways show changes consistent with bronchiolectasis and bronchiectasis (Silver & Miller 1990; D'Angelo et al, 1969). Distortion of the airways, replacement of smooth muscle in airways by fibrosis and alteration of the columnar to cuboidal epithelium have also been reported (D'Angelo et al, 1969).

On microscopic examination, findings in early-stage disease include interstitial edema, capillary congestion, hypercellularity of alveolar walls, increase fibrotic tissue within alveolar septa, and interstitial collections of mononuclear cells and neutrophils (Flint & Colby 1987). Findings in patients with progressive disease include a dense cellular and diffuse fibrotic replacement of the alveolar walls by connective tissue. This finding is similar to that observed in patients with usual interstitial pneumonitis and rheumatoid lung disease (Yousem 1990; Flint & Colby 1987). The fibrotic process is usually symmetric and is most pronounced in the lower lung zones (D'Angelo et al, 1969). With progressive disease, extensive parenchymal distortion can occur with coalescence of alveolar spaces to form cysts of various sizes surrounded by fibrous tissue (honeycombed lung). Vascular alterations in patients with progressive pulmonary disease and fibrosis include capillary obliteration, arteriolar intimal fibroelastosis, and thickening in areas of
parenchymal scars (Yousem 1990; D’Angelo et al, 1969). Pleural fibrosis and
adhesions have been described at autopsy in approximately 80% of cases
(D’Angelo et al, 1969).

**Limited versus diffuse scleroderma**

Isolated abnormalities of the pulmonary artery occur almost exclusively in patients
with limited disease. In a clinical study by Stupi et al. (1986), 20 of 331 patients
(6%) with limited scleroderma had isolated PAH diagnosed by cardiac
catheterization. None of the 342 patients with diffuse disease had PAH.

**Pathogenesis**

The pathogenesis of scleroderma lung disease is poorly understood. The
histopathologic and physiologic features resemble those of IPF (Harrison et al,
1989). Abnormalities have been described include pulmonary capillary endothelial
damage resulting in lung permeability (Harrison et al, 1989), alveolitis with an
increase in the number of neutrophils, lymphocytes, and macrophages (Harrison
et al, 1989; Sliver et al, 1990); and the presence in the lung of fibroblasts with a
stepped-up proliferative capacity. The alveolitis in patients with scleroderma is
characterized by infiltration of neutrophils, eosinophils and lymphocytes
(Harrison et al, 1989; Harrison et al 1990; Sliver et al, 1990). The presence of
neutrophils in BAL fluid has been suggested as an early event in the pathogenesis
of lung involvement, neutrophils may injure the lung parenchyma by the release of
elastase, collagenase, and oxygen radicles (Wallaert et al, 1986). Lymphocytes
can injure the lung both directly and indirectly through the production of
immunoglobulins and resultant immune complexes or by failure to release
cytokines (interferon-alpha, -beta, and -gamma) that can inhibit replication of
fibroblasts (Sliver et al, 1990).

Alveolar macrophages secrete various stimulatory and inhibitory cytokines that
affect the proliferation of fibroblasts and the formation of connective tissue matrix
substances (Silver & Miller 1990; Sliver et al, 1990). Alveolar macrophages in
BAL fluid of patients with scleroderma and IPF secrete higher amounts of
fibronectin than the alveolar macrophages of normal subjects (Kinsella et al,
1989). Fibronectin, a glycoprotein, may act both as a growth factor for fibroblasts
and as a chemoattractant for mononuclear and mesenchymal cells (Silver &
Miller 1990; Sliver et al, 1990). The pulmonary vascular damage is triggered by
unknown event that results in vascular leak, thereby facilitating an inflammatory
process with the release of many mediators. As a result of an imbalance between
stimulatory and inhibitory signals, fibroblasts with a higher proliferative capability
accumulate and presumably enhance type III collagen synthesis in the lung (Silver

Special complications of scleroderma

Pulmonary artery hypertension

PAH, a well-recognized complication of scleroderma can lead to cor pulmonale
The reported incidence of PAH varies from 6% to 60% depending on the method
used to detect it and the population studied (Sackner et al 1964; Stupi et al 1986;

PAH can occur secondary to severe interstitial fibrosis and restrictive disease, but
patients with limited scleroderma, present with isolated PAH independent of the
degree of interstitial fibrosis (Yousem, 1990; Young & Mark 1978). Stupi et al
(1986) identified isolated PAH at right heart catheterization in 20 of 331 patients
(6%) with limited scleroderma.

Cardiac examination, ECG, chest radiographic or echocardiographic
abnormalities, and a low DLCO (43% of predicted) and vital capacity (50% of
predicted) have all been relatively specific markers for detecting PAH (Ungerer et
al, 1983). The presence or absence of a combination of a low DLCO, an abnormal
chest radiograph (based on the size of the interlobar pulmonary artery), and abnormal echocardiogram have a sensitivity of 75% and specificity of 97% in patients with definite PAH (Ungerer et al, 1983).

Because patients with isolated PAH do not have significant pulmonary fibrosis, PFTs most often show either mild or no restrictive lung disease (Stupi et al, 1986; Salerni et al, 1977). The DLCO, however, is markedly decreased, and a DLCO <45% of predicted is probably the single most sensitive indicator of PAH (Stupi et al, 1986; Ungerer et al, 1983).

The natural history of PAH is almost always progressive deterioration and death (Salerni et al, 1977; Owens & Follansbee 1987), and isolated PAH has worse prognosis than PAH secondary to severe pulmonary fibrosis (Steen 1990).

**Lung cancer**

In 1980, Talbott and Barrocas reviewed the world literature and identified 41 cases of coexisting scleroderma and lung cancer; these cancers were predominantly alveolar cell carcinomas. Duncan and Winkelmann (1979) found an overall cancer rate of 4% and no increase in the incidence of lung cancer compared with the general population.

Roumm and Medsger (1985) suggested that there is a small but definite increase in the incidence of lung cancer, especially in affected men. They also reported predominantly adenocarcinomas and squamous carcinoma but no alveolar cell carcinomas.

The increase incidence of lung cancer appeared to be primarily in patients with diffuse scleroderma (Roumm & Medsger 1985). The increase incidence of lung cancer in scleroderma, especially in presence of pulmonary fibrosis, is attributed to a defect in immune surveillance, impaired clearance of carcinogens probably due to disordered lung architecture, and increased susceptibility to malignant transformation due to epithelial hyperplasia (Sela & Shoenfeld, 1988).
Course and prognosis

Patients with scleroderma have an overall 50% mortality rate of 7.2 years after diagnosis. Renal, cardiac, and pulmonary involvement correlate with decreased survival (Steen et al, 1985). Renal disease, formerly the leading cause of death from scleroderma, is more easily treated following the introduction of angiotensin-converting enzyme inhibitors. Pulmonary involvement is now considered the major cause of death in scleroderma patients (Steen et al, 1990).

Risk factors for progressive deterioration in lung function include male gender, a low DLCO, and cigarette smoking (Peter-Golden et al, 1984). Patients who have a restrictive ventilatory pattern and who smoke tend to have a lower vital capacity and a lower DLCO than patients who have a restrictive pattern but who do not smoke (Steen et al, 1985). Vasoconstriction caused by nicotine also may have an additive effect on the pulmonary vascular changes (Steen et al, 1990).

Rheumatoid arthritis (RA)

Rheumatoid arthritis (RA) is a common disease that manifests as inflammatory arthritis of multiple joints. The thorax is a common extra-articular site of involvement.

Noncardiac thoracic manifestations of RA
- Pleural disease
  1. pleurisy
  2. pleural effusion
  3. Pneumothorax
  4. empyema
  5. pyopneumothorax
- Necrobiotic nodules
- Interstitial disease
- Airway disease
- Vasculitis
Pleural disease
Pleural disease is the most common thoracic finding in patients with RA. In large autopsy series, 40% of patients with RA had pathologic evidence of pleural disease. Only 20% of patients with RA, however, have symptomatic pleural disease; the vast majority of these patients have mild pleurisy. Up to 5% of patients with RA have radiographic evidence of pleural effusion (Shannon & Gale 1992). Although RA typically affects women beginning in the third and fourth decades, pleural manifestations are more common in men in their fourth or fifth decades (Carr & Mayne 1962). Rheumatoid effusion typically occurs during periods of active arthritis in patients who have long-standing severe arthritis and subcutaneous nodules. 20% of patients who develop effusion, however, do so before the clinical onset of arthritis.

Many patients with pleural effusions are asymptomatic, the effusion being detected as an incidental radiographic finding. The effusions are typically small and unilateral at outset. They usually resolve over weeks to months, but may persist for more than a year or may recur. Effusions rarely become bilateral or large. Rheumatoid effusions may occur concurrently with pulmonary necrobiotic nodules or pulmonary fibrosis.

Pleural effusions in patients with RA result from necrobiotic nodule involvement of the pleura, subpleural space, or both. The visceral pleura is more commonly involved than the parietal pleura. The pleural fluid is typically turbid, yellowish-green, and nearly always an exudate by protein and lactate dehydrogenase criteria. Turbidity results from the high pleural fluid cholesterol concentration. The effusions are rarely grossly bloody (Shannon & Gale, 1992).

Rheumatoid pleural effusions are characterized by a markedly lower pleural fluid glucose level. A pleural fluid pH of less than 7.2 is common in rheumatoid effusion with low glucose. Pleural fluid leukocyte count may approach 15,000/mm³. Leukocyte differential count varies, with polymorphonuclear cells or lymphocytes predominating.
Rheumatoid factor in pleural fluid from patients with RA is nonspecific because rheumatoid factor is also found in pleural fluid from patients with SLE, pneumonia, tuberculosis, and malignancy.

Findings of RA cells (granulocytes containing rheumatoid factor complex) in pleural effusions is also nonspecific for RA, because these cells also can be found in the above-mentioned diseases (Shannon & Gale, 1992).

Biopsy specimens of the parietal pleura usually show nonspecific inflammation. Necrobiotic nodules, however, are sometimes found in the parietal pleura specimens.

Asymptomatic patients with effusions require no treatment. Because most effusions are associated with activity of the arthritic disease, the effusions usually resolve with treatment of active arthritis. If the effusions result in dyspnea, immediate relief can be obtained with thoracocentesis.

Pneumothorax and empyema are uncommon. Pneumothorax is thought to be due cavitation of the necrobiotic nodules and rupture into the pleural space. The mechanism of empyema development is unclear, but seeding of the pleural fluid by ruptured necrobiotic nodules has been postulated as a cause (Shannon & Gale, 1992).

Necrobiotic nodules
First described in 1954, radiographically detectable intraparenchymal necrobiotic rheumatoid nodules are rare (Maher 1954; Christie 1954). Several large series have provided a rough estimate of 2 cases of pulmonary necrobiotic nodules per 1000 patients. Like rheumatoid pleural effusions, necrobiotic rheumatoid nodules are common in men than women. The nodules may also be associated with cigarette smoking (Walker & Wright 1968).

Patients with rheumatoid nodules are usually asymptomatic, but cough, dyspnea, or hemoptysis may be presenting symptoms. The nodules vary in size from 0.5 cm to 7 cm on chest radiographs and are usually peripheral, with upper and midzone predominance. They may be single or multiple and they may resolve
spontaneously, recur, or develop at one site while resolving at another. Calcification has not been reported. About 50% of rheumatoid nodules cavitate. Cavitation of subpleural necrobiotic nodules can produce pneumothorax. Rheumatoid nodules most commonly occur in subcutaneous tissue overlying bone, but such nodules have been found in the lung. Necrobiotic nodules occur in 20% of patients with RA but are more commonly seen in patients with seropositive for rheumatoid factor with subcutaneous nodules. Pulmonary and subcutaneous necrobiotic nodules are histologically indistinguishable. Rheumatoid nodules consist of 3 concentric zones. The innermost zone is a fibrinoid area of connective tissue usually with a necrotic center. The middle zone is a layer of palisading mononuclear cells (mostly macrophages). The outermost zone consists of vascular granulation tissue and chronic inflammatory cells.

The pathogenesis of rheumatoid necrobiotic nodules is unknown. The two most cited mechanisms are vasculitis and immune complex deposition. Large amounts of proteinases and collagenases are present in these lesions and are thought to be instrumental in central necrosis (Kaye et al, 1984).

Pulmonary necrobiotic nodules have a similar radiographic appearance of that of carcinoma of the lung. Apart from spontaneous resolution of rheumatoid nodules, no radiographic features readily distinguish the two entities. This diagnostic dilemma is complicated by several reports of primary lung cancer in patients with RA being mistaken for rheumatoid nodules and controversy over a possibly increased risk of lung cancer in patients with RA. Such nodules should, therefore, be aggressively evaluated by flexible fiberoptic bronchoscopy, transthoracic core needle biopsy, or thoracotomy to obtain definitive tissue diagnosis (Jolles et al, 1989).

In 1953, Caplan described a characteristic radiographic pattern in coal miners with RA that was distinct from the typical progressive massive fibrosis pattern of coal
miner's pneumoconiosis. This less common presentation consisted of rounded
discrete nodules, 0.5 to 5 cm in diameter, distributed throughout the lungs but
predominating at the periphery. The onset of the nodules was typically sudden,
and their course varied, ranging from regression to progression. These findings
typically occurred in the setting of preexisting mild pneumoconiosis. These
nodules are histologically indistinguishable from rheumatoid nodules.
The prevalence of Caplan's syndrome in coal miners with pneumoconiosis ranges
from 2% to 6%. For unclear reasons, many more cases occur in Europe than in the
United States. The incidence of pulmonary rheumatoid nodules in patients with
pneumoconiosis and RA (25%) is much greater than the incidence in patients with
RA alone. The reasons for this phenomenon are unclear, but the nodules are
thought to be a manifestation of RA, and their development seems to be facilitated
by silica in the lung. The nodules in Caplan's syndrome may precede development
of clinical arthritis, but they follow exposure to dust with some degree of
pneumoconiosis (Shannon & Gale, 1992).

Pulmonary fibrosis
Elman and Ball in (1948) first described an association between RA and
pulmonary fibrosis. The reported prevalence of pulmonary fibrosis has varied
greatly because of the use of different diagnostic criteria. The chest radiograph,
which is insensitive for the diagnosis of early or minimal pulmonary fibrosis,
gives a prevalence of about 2% (Walker & Wright 1968). Pulmonary function
test abnormalities consistent with pulmonary fibrosis are present in 40% of
patients with RA, and most of these patients have normal chest radiographs.
Cervantes-Perez and colleagues (1980) studied 41 patients with RA and performed
open lung biopsy in 25 patients. Histologic evidence of interstitial disease was
found in 20 of these patients (80%), 11 of whom were asymptomatic and 3 of who
had normal chest radiographs.
The clinical manifestations of pulmonary fibrosis in RA are identical to those of
IPF. Dyspnea is the most common symptom, followed by cough and chest pain.
Physical findings include basilar rales, tachypnea, clubbing, and signs of pulmonary hypertension.

Clinical arthritis precedes development of pulmonary fibrosis in 90% of affected patients. Onset is usually in the fifth decade, and men are more affected than women. Subcutaneous nodules occur in up to 50% of patients with pulmonary fibrosis but are only seen in 20% of patients with RA without lung disease. Serum rheumatoid factor is found in more than 90% of patients with RA and pulmonary fibrosis; titers are usually higher than patients with RA and no lung disease. Rheumatoid pulmonary fibrosis is indistinguishable from pulmonary fibrosis caused by other diseases. Early disease may present with an acinar pattern, but the more common finding is basilar interstitial infiltrates that may be asymmetric. Upper lobe predominance is unusual. Progressive disease results in honeycombing typical of endstage fibrotic disease.

Histologic findings in pulmonary fibrosis caused by RA and other diseases are also indistinguishable. Early lesions show predominantly alveolar wall thickening, mononuclear cell infiltration of the interstitium, and desquamation of type 2 epithelial cells and inflammatory cells into alveolus. Advanced lesions show mature collagen deposition with little inflammatory infiltrate. Different areas of lung may show different stages of fibrotic process (Brannan et al, 1964).

The pathogenesis of pulmonary fibrosis in RA is incompletely understood. Deposits of immune complexes in the alveolar walls and throughout the interstitium are thought to activate alveolar macrophages. Activated macrophages elaborating superoxide anion, neutrophil chemotactic activating factor, and fibronectin have been found in BAL fluid of patients with pulmonary fibrosis and RA but not in patients with RA alone. BAL fluid leukocyte counts are also increased. With an elevated percentage of neutrophils. Elaboration of collagenase by the recruited neutrophils is thought to be important in the initiation of the fibrotic response. Macrophages also elaborate interleukin I, macrophage-derived growth factor, and interferon-alpha and interferon-gamma, all of which support
fibroblast growth and the fibrotic response. The natural history of the disease in patients with RA and pulmonary fibrosis is the same as that in patients with other causes of pulmonary fibrosis. The effect of therapy is difficult to ascertain because of the variable course of the disease. In general, patients with cellular inflammatory infiltrates respond better to corticosteroid therapy than patients with mature fibrosis. Methotrexate, cyclophosphamide, and cyclosporine have been found to be effective in isolated cases (Cervantes-Perez et al, 1980).

Drug-induced interstitial lung disease
Drug-induced interstitial lung disease, a common problem in patients with RA, complicates the diagnosis of interstitial opacities on chest radiograph. The agents most commonly causing interstitial disease in these patients are methotrexate and gold.

Low-dose methotrexate, 10mg/week, has been shown to be effective treatment for RA. At the higher doses used to treat malignancies, skin disorders, and polymyositis, methotrexate is a well-known cause of interstitial pneumonitis. Since the widespread use of low-dose methotrexate in RA, several reports have shown that even low-dose methotrexate therapy can cause interstitial pneumonitis (Shannon & Gale, 1992).

Carson and colleagues (1987) reviewed 168 patients receiving low-dose pulsed methotrexate (10 mg/week) for RA. Seven patients had probable methotrexate-induced pneumonitis and 2 patients had pneumonitis possibly induced by methotrexate, giving a prevalence of about 5%. Dyspnea, dry cough, fever, and rales were the predominant clinical features. All affected patients had abnormal chest radiograph, with diffuse acinar and interstitial opacities. Histologic examination showed either interstitial inflammatory cell infiltration with varying degrees of fibrosis or diffuse alveolar damage. These findings either a hypersensitivity reaction or a toxic drug reaction as the cause of methotrexate pneumonitis. Methotrexate-induced interstitial pneumonitis resolves when the drug is stopped.
Interstitial pneumonitis is also associated with gold therapy. Evans et al, (1987) compiled data from 60 case reports and found that interstitial pneumonitis developed from 4 weeks to 1.5 years after initiation of therapy. Dyspnea and cough were the most common symptoms, and basilar rales were heard on physical examination. About 33% of the patients had other, nonpulmonary evidence of adverse reaction to gold. Eosinophilia was present in less than one half of the patients. The chest radiograph typically showed a basilar predominance of interstitial or acinar opacities.

Histologic examination shows diffuse alveolar damage, interstitial and alveolar inflammation, and varying degrees of fibrosis, not specific for gold-induced diseases. Evidence in BAL fluid indicates that gold-induced pneumonitis reflects a hypersensitivity response. BAL fluid from patients with gold-induced pneumonitis contains increased percentages of lymphocytes, predominantly T-cells, with an inverse helper/ suppressor (CD4+/CD8+) ratio- a pattern characteristic of hypersensitivity pneumonitis. This finding may be helpful clinically in distinguishing gold-induced pneumonitis from interstitial fibrosis associated with RA.

Like methotrexate pneumonitis, gold-induced pneumonitis usually resolves when the drug is stopped, although corticosteroid therapy may hasten resolution.

A few cases of interstitial lung disease caused by D-penicillamine have been reported (Camus et al, 1982)

**Bronchiolitis obliterans**

In 1977, Geddes and colleagues described the development of highly fatal, rapidly progressive airway obstruction in 6 adult patients. The disease did not respond to therapy with antibiotic, inhaled bronchodilators, or corticosteroids. Histologic examination of 4 patients showed bronchiolitis obliterans. Five of the 6 patients had RA, and 3 were receiving penicillamine therapy.

There have since been sporadic reports of patients with RA developing bronchiolitis obliterans. In arthritis patients, bronchiolitis obliterans has been
associated with both penicillamine therapy and gold therapy, although patients not
taking either drug have also developed bronchiolitis obliterans. Affected patients
usually rapidly develop severe, irreversible airway obstruction. Chest radiographs
are normal except for hyperinflation. Therapy is uncertain because of the limited
experience, but corticosteroids are the mainstay, with cyclophosphamide in
refractory cases.
The cause of this disorder in patients with RA remains unknown. A study by
Geddes et al (1977) reported that PFTs revealed evidence of airway obstruction in
nearly 33% of patients with RA, suggesting some predisposition to airway
obstruction related to RA. An immune-mediated basis has been proposed by
Lahdensuo et al, (1984) who found IgM- and IgG-plasma cells in the bronchiolar
walls of a patient who developed bronchiolitis obliterans after receiving gold
therapy.
**Upper airway disease**
Cricoarytenoid arthritis is a relatively common upper airway manifestation of RA.
This disorder is a true inflammatory arthritis with synovial proliferation in the
cricoarytenoid joint. Using two series using symptoms referable to the larynx and
abnormalities seen on direct laryngoscopy suggest a prevalence as high as 38%. A
more recent series using CT scanning to detect laryngeal abnormalities found a
prevalence of 50%. The most common symptoms of cricoarytenoid arthritis are
difficulty with inspiration and intermittent sore throat. Other symptoms include
hoarseness, a persistent choking, fullness of throat, and dyspnea on exertion,
although these findings do not correlate with abnormal findings on indirect
laryngoscopy or CT scan (Lawry et al, 1984).
**Vasculitis**
Systemic vasculitis in patients with RA is rare. The classic findings are digital
vasculitis, mononeuritis multiplex, and purpuric skin lesions.
Rheumatoid nodules are thought by some investigators to result from vasculitis.
Pulmonary vascular involvement in rheumatoid vasculitis is uncommon. Pleuritis is often cited as the most common manifestations and it is difficult to separate from pleurisy in RA independent of vasculitis. The most common dramatic pulmonary presentation of rheumatoid vasculitis is alveolar hemorrhage and hemoptysis in the setting of a pulmonary-renal syndrome. Histologic examination shows necrotizing arteritis, thought to result from immune complex deposition and complement activation. The chest radiograph shows patchy, bilateral, acinar opacities. Therapy consists of systemic steroids and cyclophosphamide. Pulmonary arterial hypertension has also been reported as a manifestation of rheumatoid vasculitis. The clinical manifestations are similar to those of primary pulmonary hypertension. Treatment consists of corticosteroids and cyclophosphamide (Naschitz et al, 1989).

Lung infection
Lung infection is common in patients with RA. The incidence of bacterial lung infection has been estimated as high as 25%. Some authors have cited an increased incidence of bacterial pneumonia and bronchiectasis in patients before RA develops, raising the possibility of an infection predisposing to RA (Walker 1967).

Intrathoracic adenopathy
Peripheral adenopathy in patients with RA is common. Mediastinal adenopathy is frequently found at autopsy in these patients. Reactive lymphadenopathy has been detected antemortem by a CT scan (proved by mediastinoscopy and biopsy) in a patient with RA and pulmonary fibrosis, and this finding is likely to become more common with increased utilization of CT scanning (Martinez et al, 1990).

Neoplastic disease
Some evidence suggests an increased incidence of lymphoproliferative malignancies, including Hodgkin's and non-Hodgkin's lymphoma and myeloma. Patients with RA and pulmonary fibrosis, similar to patients with other fibrotic lung disease, have an increased incidence of lung cancer (Hakulinen et al, 1985). Cyclophosphamide therapy in patients with RA does not appear to increase the
incidence of primary lung cancer but does increase the incidence of bladder and skin cancers that can metastasize to the lung.

**Bone involvement**

There are two primary osseous manifestation of RA that can be seen on chest radiographs, these are (1) acromioclavicular joint erosions and (2) rib notching. The acromioclavicular joint may be involved with RA and appear to have an increased width due to erosions. Similar changes also are seen in the shoulder joint. Superior rib notching in a line with the medial clavicular border, also occurs in patients with RA (*Sargent et al, 1969*).

**Mixed connective tissue disease (MCTD)**

Clinicians have long recognized that some patients exhibit features of more than one rheumatologic disease and thus cannot be classified by traditional means. To describe the disease process in such patients who demonstrate clinical features of more than one rheumatologic disease, physicians have frequently used the terms, "overlap syndrome", "undifferentiated connective tissue disease", "sclerodermatomyositis", "RUPUS" (rheumatoid arthritis and SLE), "Lupoderma" (SLE and PSS), or "mixed collagenosis". Abnormal laboratory tests that aid in the diagnosis of RA, SLE, PSS, and PM-DM have been helpful but not pathognomonic. In fact, the diagnosis of these rheumatologic diseases depends more on the clinical features of the disease than on nonspecific serologic tests (*Prakash, 1992*).

The term, mixed connective tissue disease (MCTD), was used by Sharp et al, (1972) to identify patients with clinical features of SLE, PSS, and PM-DM and unusually high titers of anti-RNP antibody. Many studies have demonstrated that RNP is usually present in sera of patients with MCTD but uncommon in patients with SLE, PSS, PM-DM, RA, or other rheumatologic diseases (*Sharp & Singsen 1989*).
An international symposium on MCTD determined that, "on the basis of clinical, serologic, and immunologic data, MCTD seems to be a distinct entity (Alarcon-Segovia & Shiokawa 1987)."

The etiology and prevalence of MCTD is unknown, but it is believed to occur more commonly than PM-DM, less commonly than SLE, and as frequently as PSS. The majority patients are women, and the average age at time of diagnosis is 37 years. Renal disease occurs in from 10% to 20% of patients with MCTD. Common clinical features include Raynaud's phenomenon, polyarthritis, sclerodactyly, and inflammatory myositis. Certain clinical features may become more pronounced as the disease evolves (Prakash et al, 1985).

**Pleuropulmonary manifestations**

Overall, pulmonary involvement has been described in from 20% to 80% of patients with MCTD (Prakash et al, 1985). Most of the pleuropulmonary manifestations, both clinical and pathophysiologic, are similar to those observed in SLE, PSS, and PM-DM (Vitali et al, 1985).

**Pleural effusion:**

As in SLE, pleural processes may be the presenting manifestation of MCTD. Pleural effusions are usually small and resolve spontaneously. In retrospective report from the Mayo Clinic on 81 patients with MCTD, small pleural effusions were seen in 5(6%) patients, and 2 patients had pleural thickening (Prakash et al, 1985). On the other hand, the prospective study of 34 patients by Sullivan and associates (1984) observed pleuritic pain in 40%. This difference in the incidence of pleural processes can be explained by noting that pleural involvement is much more common in patients with SLE than in patients with PSS, and that patients who demonstrate predominantly PSS-like clinical features are less likely to exhibit pleural processes.

**Interstitial pulmonary processes**

Histologic analysis of the pulmonary parenchyma in patients with MCTD has shown abnormalities similar to those seen in IPF. The changes noted have
included alveolar septal infiltration by lymphocytes, plasma cells, and type III collagen; immunofluorescent stains for IgG, IgM, and IgA were negative (Wiener-Kronish et al, 1981). A prospective study by Sullivan et al (1984) discovered mild nonspecific interstitial fibrosis. Generally, the degree of fibrosis tends to be severe if the predominant clinical features are those of PSS.

Abnormal PFTs were seen in 69% of patients with MCTD studied by Harmon et al, (1976) even though the patients had no respiratory symptoms. It has been estimated that, even in the absence of pulmonary symptoms, about two-thirds of the patients with MCTD have significantly reduced diffusing capacity for carbon monoxide (DLCO), and that nearly half have a restrictive pattern. Patients with PSS, in spite of absence of respiratory symptoms, demonstrate evidence of subclinical alveolitis as judged by BAL. Chest radiographs in patients with MCTD show abnormalities typical of interstitial fibrosis. In a multicenter study of 100 patients with MCTD, diminished DLCO was noted in 67%, and restrictive lung volumes were observed in 50% (Sharp & Singsen 1989).

Pleuropulmonary involvement was noted in 25% of 81 patients with MCTD in the Mayo Clinic series. All the patients demonstrate features of SLE, PSS, and PM, but the predominant characteristics were those of PSS in 10, SLE in 7, and PM in 3. Similar to patients with PSS or IPF, patients with MCTD who exhibit interstitial lung parenchymal disease usually demonstrate a restrictive pattern manifested by reduced lung volume, relatively normal flow rates, and diminished DLCO. DLCO is the single most sensitive parameter for evaluating pulmonary dysfunction in MCTD.

The most common chest radiographic abnormality in MCTD is interstitial lung disease. It was observed in 21% of patients in the Mayo Clinic series (Prakash et al, 1985). The interstitial process appears first in the periphery of the lung bases and gradually extends superiorly with asymmetric distribution. The interstitial lung disease in MCTD mimics pulmonary fibrosis associated with PSS and IPF.
Pulmonary hypertension
PAH is a major cause of mortality and morbidity in patients with PSS. This is also true of MCTD, and fatal PAH has been reported in a number of patients with MCTD. PAH in MCTD may have 3 pathogenesis; (1) hypoxemia secondary to progressive massive fibrosis, (2) recurrent thromboemboli, and (3) plexogenic arteriopathy (Graziano et al, 1983). Progressive PAH in MCTD may be accompanied by severe vasculitic lesions in the lungs. A prospective study of 34 patients with MCTD documented that the most serious abnormality was the presence of PAH with increased vascular resistance in 10 of 15 patients studied (Sullivan et al, 1984). The increased vascular resistance was associated with diminished DLCO in 9 of 10 patients. Histologic analysis of lung tissue revealed marked intimal and medial thickening in small and medium sized pulmonary arteries, plexiform lesions, endarteritis obliterans and fibrous thickening of pulmonary veins in patients with MCTD (Wiener-Kronish et al, 1981).

Pulmonary vasculitis
Pulmonary vasculitis and PAH may occur simultaneously and may be independent of each other. Wiener-Kronish et al (1981) reported that pulmonary vascular involvement was responsible for the deaths of 4 of 5 patients with MCTD. One patient had intimal thickening, focal fibrinoid necrosis, and positive immunofluorescent stains for IgG, C3, and C1q in medium sized pulmonary arteries.

Pulmonary thromboembolism
The incidence of pulmonary thromboembolic disease is high in SLE in spite off a circulating anticoagulant. Therefore, patients with MCTD who demonstrate predominantly SLE-like clinical features can be expected to be at increased risk for developing pulmonary thromboembolism. Hainaut et al (1986) described a young woman with MCTD who had circulating lupus-type anticoagulant and PAH. Jones et al (1978) described young female with MCTD in whom fatal cor pulmonale developed due to recurrent thromboembolic PAH. Recurrent
thromboemboli play an important role in the pathogenesis of PAH in these patients.

**Aspiration pneumonia**
Esophageal dysmotility is extremely common in both PSS and PM-DM. Reflux esophagitis and recurrent aspiration are well recognized serious complication of PSS and PM-DM. Patients with MCTD with clinical manifestations mainly suggestive of PSS or PM-DM are more likely to develop aspiration pneumonia. In 81 patients with MCTD studies in Mayo Clinic, the barium examination of the esophagus and the esophageal manometry were abnormal in 53% and 69% of patients respectively. The hypotonicity of the lower esophageal sphincter is responsible for the reflux and resultant aspiration pneumonia. Aspiration pneumonia resulting in potentially lethal ARDS was responsible for the death of one patient in the Mayo Clinic series (Prakash et al, 1985).

**Pulmonary hemorrhage**
Pulmonary alveolar hemorrhage is one of the well-known complications of SLE. Patients with MCTD whose disease resembles SLE may develop pulmonary alveolar hemorrhage syndrome. A 37-year-old woman with long-standing MCTD, who had hemoptysis, bilateral pulmonary opacities, dyspnea, anemia, and acute renal failure has been reported. The renal failure was secondary to immunologically mediated tubulointerstitial disease that was documented by renal biopsy (Germain & Davidman 1984). Another patient with massive alveolar pulmonary hemorrhage resulting in death has been reported; the autopsy revealed renal necrotizing vasculitis and immune-complex deposit in the glomeruli. Pulmonary hemorrhage is a well-recognized complication of SLE, and the risk of hemorrhage increases with renal involvement (Sanchez-Guerrero et al, 1989).

**Respiratory failure**
Proximal myopathy is one of the common features of PM-DM, and the myopathic process may involve the respiratory muscles. Inflammatory myositis was observed in 79% of the 34 patients with MCTD studied by Sullivan et al (1984). Involvement of the respiratory muscles in the myopathic process may cause
hypoventilatory respiratory failure, a potential complication of MCTD. A case report described a 34-year-old woman who developed severe ventilatory muscle failure as a result of myositis associated with MCTD. Diaphragmatic weakness has also been described in patients with MCTD (Martyn et al, 1988).

**Systemic Lupus Erythematosus**

The lung and pleura are involved more frequently in SLE than in any other connective tissue disease, the prevalence ranging from 30% to 70% in different series.

**Etiology and pathogenesis:**

Genetic factors: The incidence of SLE in close relatives of patients with disease range from 5% to 10%(Decker et al, 1979). An association with DR2 and DR3 genes of the major histocompatibility complex has been described (Steinberg et al, 1984).

Environmental factors: Ultraviolet light is well known to induce a flare-up of SLE in susceptible individuals. Also viral infection may act in the same way (Rich 1981).

In addition, the SLE syndrome, including the presence of antinuclear antibodies (ANA) and a positive LE cell test, can be induced by certain drugs, such as hyralazine, isoniazid, phenytoin, quinidine, methyldopa, and propranolol. Affected patients are commonly found to be HLA-DR4 positive, in contrast to the predominance of DR3 or DR2 in idiopathic disease (Steinberg et al, 1984).

Endocrine factors: The susceptibility of females to SLE raises the possibility of an endocrine component in the pathogenesis of the disease (Steinberg et al, 1984).

Immune factors: T lymphocytes (particularly suppressor cells)(Decker et al, 1979) are reduced in number and B cells are hyper-reactive (Blaese et al, 1980). The result is the production of a variety of autoantibodies which are likely responsible for the majority of disease either directly by cytotoxicity or indirectly via the
formation of immune complexes. There is also evidence that defects in response to and in impaired production of interleukin-1 and interleukin-2 and disturbances in the activity of interferon may play pathogenetic role (Steinberg et al, 1984).

**Pathologic Characteristics**

Pathologic findings that have been proposed as being caused by SLE itself include pleuritis and pleural fibrosis (the most common abnormalities) (Miller et al, 1985), interstitial pneumonitis and fibrosis, vasculitis and changes indicative of pulmonary arterial hypertension. Diffuse interstitial lung disease similar to that of rheumatoid disease or progressive systemic sclerosis (PPS) is uncommon in SLE; for example, in one series of 120 patients, only five such cases were identified (Haupt et al, 1981).

The histologic findings have been those of fibrosing alveolitis. Immunopathological studies of biopsy specimens showed granular deposition of immunoglobulin G (Ig G), C3 and DNA in alveolar walls, and electron microscopy revealed electron dense deposits in a similar location, suggesting that immune complex deposition may be responsible (Inque et al, 1979).

Acute lupus pneumonitis refers to an uncommon manifestation of SLE characterized by fever, dyspnea, hypoxemia, and patchy diffuse lung opacities; the term should be restricted to patients with the clinical and radiographic features who respond to corticosteroids and azathioprine therapy but not to antibiotics (Hoffbrand & Beck 1965). Cases show diffuse alveolar damage (intra-alveolar proteinaceous exudate with hyaline membranes, interstitial edema, and an interstitial mononuclear inflammatory infiltrate) (Matthay et al, 1975), and others leukocytoblastic vasculitis (patchy but more or less diffuse alveolar septal infiltrate by polymorphnuclear leukocytes associated with intracapillary fibrin thrombi and airspace hemorrhage) (Churg et al, 1980; Myers & Katzenstein 1986).
Disease of large pulmonary vessels is also uncommon. Occasional cases of necrotizing vasculitis involving small pulmonary arteries have been reported, and some patients develop isolated pulmonary hypertension characterized by intimal fibrosis, medial hypertrophy (Gross et al, 1972).

**Radiographic manifestations:**

Pleural effusion, the most common manifestations, is frequently bilateral and usually small. Of 57 cases in one series (Winslow et al, 1958), it occurred in 42 cases. The importance of distinguishing pleural effusion due to direct involvement of the pleura by SLE from that associated with lupus nephritis have been emphasized (Levin, 1971); the former characteristically is accompanied by pain and splinting, whereas the serous effusions of nephritic patients are painless.

The lung changes are non specific consisting of poorly defined patchy opacities, usually in the lung bases and situated peripherally. These changes often are acute and may represent "lupus pneumonitis", edema or infection. Frequently, only the response to various therapeutic agents provides a definitive answer as to etiology, although diffuse pulmonary hemorrhage can be readily detected by MRI (Hsu et al, 1992).

Horizontal line shadows, usually in both bases and sometimes migratory, are probably attributable to discoid atelectasis. In some cases, sequential radiographic studies show progressive loss of lung volume (Hoffbrand & Beck 1965), "shrinkage" that may be associated with an elevated, sluggish diaphragm. Increase in size of cardiopericardial silhouette is generally the result of pericardial effusion, which usually is relatively small but may be massive. The radiographic manifestations of drug-induced SLE are no different from those of the idiopathic form.

**Clinical manifestation:**

The classic clinical picture is that of a young adult woman presenting with fever, arthralgias, facial rashes, nephritis, and pleural effusion. Symptoms referable to the respiratory tract includes cough and dyspnea (sometimes caused by interstitial
pneumonitis and fibrosis (Weinrib et al, 1990) and sometimes by diaphragmatic dysfunction) (Martens et al, 1983). Hemoptyis is rare (Myers & Katzenstein 1986) but may be massive. Pleuritis occurs in 35% to 40% of patients and may be associated with fever. Although clinically evident pulmonary hypertension is rare, there is evidence that mild hypertension may not be uncommon (Simonson et al, 1989). It presents as a rapidly progressive dyspnea and cardiac failure; death within 2 years is the rule. Raynaud's phenomenon is present in 75% of cases, and many patients have positive reaction to ribonucleoprotein (RNP), rheumatoid factor, and lupus anticoagulant.

Arthritis and arthralgia present in 95% of patients; they tend to be nonerosive and nondeforming (Kohler & Vaughan 1982) and may be associated with the periarticular subcutaneous nodules usually considered characteristic of rheumatoid disease. Cutaneous manifestations in the form of butterfly rash are seen in 50% of patients (Kohler & Vaughan 1982) and discoid lupus, alopecia, and photosensitivity.

Neuropsychiatric complaints, like seizures or psychotic episodes develop eventually in 50% to 70% (Hughes 1982). A similar percentage shows evidence of renal disease. Other less common manifestations include pericarditis, hepatosplenomegaly, and Raynaud's phenomenon.

Muscle weakness usually develops after institution of corticosteroid therapy and is most marked in proximal limb muscles. The clinical manifestations of drug induced lupus do not appear until months or years after initiation of therapy (Hughes 1982). Common findings include arthralgia, pleuritis, pericarditis, fever, and skin rash; renal, CNS, and pulmonary involvement are rare (Bass 1981). Clinical manifestations disappear within days to weeks of cessation of drug therapy, whereas serologic abnormalities may continue for months.

Laboratory findings:

The screening test most commonly used when SLE is suspected is a search for ANAs. Some of the 5% to 10% of patients with SLE who are ANA negative have
high titers of antibody to single stranded (denatured) DNA (anti-ssDNA Ab) (Hsu et al, 1992). These include the anti-Ro Ab and the anti-La Ab, both which are commonly found in patients with Sjögren's syndrome; in SLE, they are seen most often in the elderly and have been associated particularly with the presence of interstitial pneumonitis (Hedgpeth & Boulware 1988). Antibodies to native DNA (anti-nDNA Ab) are present in patients who are at greater risk for developing renal disease (Synkowski et al, 1980).

Patients with drug-induced SLE rarely have antibodies to native DNA but may show antibodies to denatured DNA; ANAs are common but hypocomplementemia is rare.

The majority of patients eventually have anemia, leukopenia, and elevated serum gammaglobulins. Thrombocytopenia, antiplatelet antibody. Antibodies against factor VIII, IX and XII can cause coagulation abnormalities (Kohler & Vaughan 1982). In most cases, pleural effusions are exudates that contain LE cells and a high ANA titer (1:160) and low complement component.

**Pulmonary function test (PFT)**

PFT typically reveal decreases in lung volume, diffusing capacity, and arterial oxygen saturation with low or normal Pco₂, compensated respiratory alkalosis, and reduced lung compliance (Huang & Lyons 1966). Evidence of airway obstruction is present in a minority of patients (Kinney & Angelillo 1982). In some, it is severe and of recent onset, resembling that described with obliterative bronchiolitis in patients with rheumatoid disease. A characteristic of the function values in SLE is impairment so profound that it is out of the proportion to the rather mild changes usually apparent clinically and radiologically (Jacobelli et al, 1985).

**Prognosis:**

SLE commonly has a chronic course with acute exacerbations. Death occurs after many years from renal failure, CNS involvement, or myocardial infarction.

Pleuropulmonary disease, although sometimes a cause of considerable morbidity,
rarely is fatal. However, patients receiving corticosteroids and immunosuppressive therapy are at risk for opportunistic infection, particularly of the lung.

**Sjögren's Syndrome**

Sjögren's syndrome (SjS) is a chronic autoimmune disorder characterized clinically by keratoconjunctivitis sicca, xerostomia, and recurrent swelling of the parotid gland. It can occur as an isolated disorder (primary SjS, Sicca syndrome), but more often is associated with other connective tissue diseases (secondary SjS). Rheumatoid disease is the most common of such associated disorders; it has also been documented in PSS, primary biliary cirrhosis, Hashimoto's thyroiditis, pernicious anemia, and primary hypothyroidism. The syndrome has also been identified in recipients of bone marrow transplants (Gratwhol *et al.*, 1977) and individuals infected with human immunodeficiency virus (HIV) (Itecsu *et al.*, 1990).

**Etiology and pathogenesis**
The etiology of SjS is unknown. In view of the occurrence of the disease in families, genetic factors have been implicated (*Reveille et al.*, 1984); expressed as depression of the immune surveillance, permitting increased antibody responses and the development of both benign and malignant lymphocyte proliferations. As in SLE, it is possible that antigenic alteration and resultant autoantibody production are related to viral infection. The human leukocyte antigens HLA-DW2 and DW3 are commonly present in patients with SjS, including both primary disease and the secondary form associated with SLE, whereas HLA-DW4 is characteristic of SjS associated with rheumatoid disease. HLA-B8 is found in 55% of cases of primary SjS but does not occur in secondary SjS associated with SLE or rheumatoid disease (*Manthorpe et al.*, 1981). Evidence of an autoimmune pathogenesis in SjS is as strong as in SLE. A variety of auto-antibodies can be detected. The presence of lymphocytes within salivary glands in association with
fibrosis and glandular atrophy, suggested a lymphocyte-mediated autoimmune process. Unexplained findings that suggest an immune-mediated or allergic component in SjS are blood eosinophilia (Bohan & Peter 1975).

Pathologic characteristics
Pulmonary disease in SjS can occur in the airways or the parenchymal interstitium. Atrophy of the tracheobronchial mucus glands associated with a lymphoplasmacytic cellular infiltrate is reported (Bucher & Reid 1959). These findings are analogous to salivary gland involvement and responsible for chronic cough observed clinically. Fibrosis and mononuclear cell infiltration of small airways have been reported in patients who manifest evidence of obstructive airway disease (Newball & Brahim 1977). Pulmonary parenchymal disease is a diffuse, usually bilateral, interstitial lymphoplasmacytic infiltrate (lymphocytic interstitial pneumonitis) (Liebow & Carrington 1973). This infiltrate is usually most dense in relation to bronchioles and their accompanying vessels but also extend into the alveolar interstitium itself, where fibrosis may develop. The pathologic differentiation from lymphoma can be difficult.

Radiographic manifestations
In one study of 42 patients with SjS (Silbiger & Peterson 1967), 14 (33%) showed a reticulonodular pattern similar to that of other connective tissue diseases. Pneumonitis and atelectasis are additional complications that are commonly seen (Silbiger & Peterson 1967).

Clinical manifestations
The chief symptoms of SjS are burning sensation of the eyes and dryness of the mouth, nose, and skin. Lachrymal or salivary gland enlargement occurs in 25% to 50% of patients (Shearn 1977). With the exception of parotid glands, such enlargement is usually bilateral. Involvement of the larynx and tracheobronchial mucous glands may result in hoarseness and a persistent cough productive of thick sputum. Interstitial cellular infiltration and fibrosis of the lungs may be associated with dyspnea. Approximately one half to two thirds of patients manifest symptoms and signs of an associated connective tissue disease. Patients with SjS, either
primary or secondary, are at increased risk for the development of non-Hodgkin's lymphoma, often with pulmonary involvement (Hansen et al, 1989). Those who develop this complication generally manifest a severe sicca syndrome associated with parotid swelling; there is often lymph node enlargement, splenomegaly, leukopenia, vasculitis, neuropathy, Raynaud's phenomenon, and/or hyperglobulinemia.

**Laboratory findings and pulmonary function tests**

Schirmer's test for the measurements of tear formation and slit lamp examination of the eyes for identification of superficial corneal scarring due to inadequate lachrymal gland secretion. Autoantibodies, including rheumatoid factor and ANAs may be found; Antibodies to ribonucleoproteins (termed SS-A and SS-B) are common in SjS (Isenberg et al, 1982). A high percentage of patients have circulating immune complexes, the complement being caused largely by IgG (Moutsopoulos et al, 1980). BAL specimens show a greater number of cells and an increased proportion of lymphocytes (Dalavanga et al, 1991). As the disease can involve the pulmonary interstitium or bronchial glands exclusively or both areas simultaneously, pulmonary function test results may be restrictive, obstructive, or mixed (Papathanasiou et al, 1986).

**Polymyositis-Dermatomyositis**

Polymyositis-dermatomyositis (PM-DM), one of the connective tissue diseases, is an idiopathic inflammatory myopathy that is mediated by autoimmune and cellular events and affects skeletal muscle resulting in proximal weakness. Systemic manifestations are responsible for significant additional morbidity and increased mortality. In United States, 5-10 new cases of PM-DM per million population are diagnosed each year. In this disease, as in other connective tissue diseases, women are more commonly affected. Two disease peaks occur: (1) one in the children and (2) the other in young to middle-aged adults (Schwarz, 1992).
Polymyositis and dermatomyositis are considered to be the same disease, the difference being the prominent rash in dermatomyositis. Occasionally, however, the muscle involvement can be minimal in DM. The onset of PM-DM in an older individual should alert the physician to the possibility of an underlying malignancy. Manchul et al (1985) found associated malignancy in 15 of 71 patients with PM-DM. The patients were usually over 50 years old of age, and the malignancies originated from the colon, breast, prostate, lung, and uterus. The neoplasm could predate, appear concurrently with, or become apparent after the diagnosis of PM-DM.

Clinical and pathologic features
Clinical classification of PM-DM (Pearson classification)
- Adult PM
- Adult DM
- Childhood PM-DM
- PM-DM with underlying malignancy
- PM-DM complicating an established connective tissue disease (Pearson, 1972).

The hallmark of PM-DM is the gradual onset of proximal muscle weakness over several weeks to several month periods. Typically, climbing stairs, brushing one's hair, and rising from a chair are activities that are impaired. With chronic disease and continued inflammation and fibrosis, atrophy of the affected muscles occurs and chronic disability results. In PM during the acute phase, lymphoplasmacytic cells infiltrate the muscle bundles and cause necrosis with subsequent regeneration of myofibrils. With progressive inflammation due to repeated exacerbation, atrophic muscle bundles appear. In DM, the inflammatory infiltrates are perivascular in location and are found in the septa between muscle bundles. In PM, the inflammatory round cell infiltrates directly involve the muscle fascicles (Plotz et al, 1989; Oddis & Medsger 1989).
Although proximal muscle weakness is the usual presentation, patients may present with dysphagia due to involvement of the pharyngeal and esophageal muscles, signs and symptoms of pneumonia due to aspiration or respiratory muscle dysfunction, dyspnea due to a primary pulmonary or cardiac complication. A concomitant rash indicates those patients in whom there is associated dermatomyositis. The classic heliotrope rash refers to a bluish discoloration over the anterior edge of the upper eyelids. Gottron's sign described an erythematous rash over the knuckles, and Gottron's rash is a raised scaly eruption over the skin in the same location. The intervening skin of the fingers is spared. Similar changes occur over bony prominences such as the elbows and knees (Oddis & Medsger 1989).

Systemic symptoms and signs include fever, weight loss, Raynaud's phenomenon, Sjogren's syndrome, and polyarthritis. Weight loss may be related to the mechanical swallowing difficulties. In one large series that included 38 patients with primary PM, fever was present in 18%, weight loss in 32%, Raynaud's phenomenon in 26%, Sjogren's syndrome in 39%, and polyarthritis in 45% (Schwarz, 1992).

Criteria for the diagnosis of PM-DM
1. Symmetric proximal muscle weakness with or without dysphagia or respiratory muscle weakness
2. Muscle enzyme elevations
3. Electromyographic abnormalities
4. Compatible muscle biopsy
5. Skin rash of dermatomyositis.

These criteria have been set forth by Bohan and Peter (1975). A definite diagnosis of polymyositis requires 4 criteria, probable diagnosis 3 criteria, and possible diagnosis 2 criteria. For a definite diagnosis of dermatomyositis, a rash and 3 criteria are necessary; and for a probable diagnosis 2 criteria and a rash are necessary.
The serum creatine kinase is the most specific test for skeletal muscle injury and is elevated in over 95% of patients with PM-DM at some time during the course of their illness. Normal levels may initially present, even in the face of an inflammatory muscle biopsy (Fudman & Schnitzer 1986). Creatine kinase elevation also precedes a clinical exacerbation, and a fall in the level of this enzyme indicates response to corticosteroids or other immunosuppressive treatment. Other serum enzymes including aldolase, transaminase, and lactic dehydrogenase may also be elevated. Electromyography reveals a constellation of findings that suggest the diagnosis. It is sensitive but not specific. A completely normal study, on the other hand, makes the diagnosis of PM-DM unlikely. A muscle biopsy demonstrating active inflammation as opposed to atrophy is the most specific test for establishing the diagnosis of PM-DM (Bohan et al 1977).

Cardiopulmonary disease
Cardiac complications
Cardiac abnormalities have been reported in 50% of patients with PM-DM. The cardiac complications of PM-DM include dilated cardiomyopathy with associated congestive heart failure, atrial and ventricular arrhythmias, atrioventricular conduction disturbances, the sick sinus syndrome, and cor pulmonale to either interstitial lung disease (ILD) or primary PAH. It has been claimed that the presence of an atrioventricular conduction disturbance in PM-DM is a poor prognostic finding and is usually associated with severe progressive muscle disease. In fact, it is reported that at least 20% of deaths in PM-DM are due to cardiac causes (Gottdiener et al, 1978).

Pulmonary Complications
Recurrent aspiration pneumonia is the most frequently encountered pulmonary complication in PM-DM and adds significantly to the morbidity and mortality of this disease because of the development of bacterial pneumonia, lung abscess, and ARDS. Aspiration pneumonia reportedly occurs in 15%-20% of patients, but 40%
to 45% of patients complain of dysphagia. Dysphagia results when the myopathy involves the striated muscle of the hypopharynx and upper esophagus (Dickey & Myers, 1984).

Hypercapnic respiratory failure is a life-threatening event resulting from myositis involvement of the muscles controlling respiration. The resultant reduction of the cough reflex and the inability to take a maximum inspiration lead to the development of hypostatic pneumonia or lobar atelectasis due to mucus plugging of the airways (Schwarz, 1992).

Physiologically, because of loss of respiratory muscle strength, restrictive lung disease results that are characterized by the reduction of the total lung capacity but preservation of the airway function. Respiratory muscle dysfunction can be detected by demonstrating reduction of the maximum inspiratory and expiratory pressures in addition to restrictive lung disease. The more severe the restrictive lung disease, the greater are the abnormalities of the blood gases, and eventually hypoxemia, carbon dioxide retention, and respiratory acidosis occur. In unusual situation, respiratory muscle involvement overshadows peripheral skeletal muscle dysfunction, and patients can present with hypercapnic respiratory failure (Blumberg et al, 1989).

Pulmonary hypertension in PM-DM follows congestive heart failure secondary to a cardiomyopathy, respiratory failure induced by respiratory muscle dysfunction, or the gas exchange abnormalities resulting from ILD. There is also a primary fibroproliferative process involving the walls of both arterioles and small muscular arteries of the lung. This leads to luminal obliteration of these vessels (plexogenic arteriopathy) and the development of severe irreversible pulmonary hypertension in PM-DM. The chest radiograph shows clear lungs and proximal enlargement of the pulmonary arteries. PFTs are often normal except for isolated reduction of the diffusing capacity for carbon monoxide. Arterial blood gases reveal hypoxemia and hyperventilation that is accentuated by exercise testing. These patients are dyspneic, and clinical signs of cor pulmonale will appear. Survival for longer than
2 years is unusual because this form of pulmonary hypertension is unresponsive to treatment (Bunch et al, 1981).

It is estimated that ILD occurs in 5% to 30% of patients with PM-DM depending on whether radiographic or physiologic methods are used for screening (Frazier & Miller 1974). HRCT can demonstrate early interstitial opacities, and BAL cell counts reveal alveolar inflammation in the face of normal chest radiographs and normal routine physiologic testing (Wallert et al, 1986).

Cough and dyspnea are the most commonly reported symptoms, and bibasilar crepitant rales are the most frequent physical finding. The chest radiograph early in the course of the disease may demonstrate alveolar and interstitial opacities with predilection for the lung bases, with time there is loss of lung volume, and changes of pulmonary arterial hypertension, and honeycombing appear. Alternatively, radiographic lung volumes may be reduced due to respiratory muscle weakness and diaphragmatic dysfunction (Schwarz et al, 1976).

In the typical case, PFTs reveals reduction of the vital capacity, residual volume, total lung capacity, thoracic gas volume, and diffusing capacity for the carbon monoxide. Arterial blood gases demonstrate hypoxemia and respiratory alkalosis. There are also PM-DM patients in whom ILD is present on chest radiographs, but routine PFTs are normal. It is only after the stress of exercise that gas-exchange problems are unmasked. Alternatively, patients with PM-DM may be symptomatic and have abnormal physiology in the face of a normal chest radiograph (Braun et al, 1983). In this instance, respiratory muscle dysfunction and primary PAH must also be considered. In this situation, HRCT of the lung and BAL are likely to have their greatest impact (Wallert et al, 1986).

There is a relatively acute form in which affected individuals experience coughs, dyspnea, and fever, with or without muscle, skin manifestations. This develops over a several week period. The chest radiograph reveals mixed alveolar and interstitial opacities. This presentation may mimic the rapidly progressive form of IPF (Hamman-Rich syndrome). In both patients with the accelerated form of
interstitial fibrosis (Hamman-Rich syndrome) and in those whose demonstrate diffuse alveolar damage, the prognosis is poor. Alternatively, there is a corticosteroid-responsive form of this acute pneumonitis; and in this case, the histology demonstrates either bronchiolitis obliterans/organizing pneumonia (BOOP) or a cellular nonfibrotic interstitial pneumonitis (Tazelaar et al, 1990).

BOOP occurs in most connective tissue diseases due to drug toxicity, or following infection, but most cases are idiopathic. In this lesion, inflammatory polyps project into the terminal bronchioles, and young connective tissue extends from the terminal bronchioles into the alveolar structures (organizing pneumonia)(Eppler et al, 1985).

In the more insidious presentation of ILD in PM-DM, the histology shows varying degrees of usual interstitial pneumonia. The more cellular forms reveal extensive alveolar wall lymphoplasmacytic infiltrates and intraalveolar macrophage collections. In the more advanced form, fibroblastic proliferation produces collagen and results in collagenous thickening of the alveolar walls. The end stage of this process is honeycombed lung in which there is total disarray of the distal lung architecture, and the lung is replaced by thick-walled cysts lined by metaplastic epithelium. This same sequence occurs in IPF (Schwarz, 1992).

Chest radiograph in this group of patients reveals progressive reticulonodular opacities. With progression of disease, there is reduction in lung volume, pulmonary hypertension becomes evident, and honeycombing is seen (Schwarz et al, 1976).

There is a significant correlation between the presence of ILD in PM-DM and the presence of a serum antibody, anti-J0-1. Anti-J0-1 is an autoantibody directed against the cellular enzyme histidyl-tRNA-synthetase; it is found in 25% of patients with PM-DM. In one study, 13 of 19 patients with ILD had this antibody; and in another study, a 50% incidence of ILD was seen in a group of PM-DM patients with anti-J0-1 antibody. On the other hand, in an anti-J0-1 negative group
of patients with PM-DM, the incidence of ILD was only 13%. Therefore, the presence of anti-JO-1 antibody in an individual with ILD and without systemic symptoms should prompt the clinician to intensify the search for polymyositis (Hochberg et al, 1984; Bernstein et al, 1984).

Patients with malignancy associated with PM-DM can also develop ILD (Holmes et al, 1980). One such case responds dramatically to treatment with corticosteroids. Those patients with the more cellular forms of ILD, that is, BOOP and cellular interstitial pneumonia, as opposed to those with advanced fibrosis, honeycomb lung, diffuse alveolar damage, and the Hamman-Rich syndrome, will respond to corticosteroids alone or in combination with another immunosuppressive agent. Open lung biopsy is recommended for those patients with a more acute clinical picture. There are isolated case reports supporting the use of cycloserine, cyclophosphamide, and azathioprine in corticosteroid-resistant cases (Maccioni & Colebatch, 1990)

Relapsing Polychondritis

Relapsing polychondritis is characterized by inflammation and destruction of cartilage at several sites, including the ribs, tracheobronchial tree, ear lobes, nose, and axial and peripheral joints. There is no sex predominance, and the disease occurs at all ages (peak incidence at age 40 to 60 years).

The etiology and pathogenesis are unknown. An associated autoimmune disorder has been found in 20% to 25% of cases (McAdam et al, 1976). In support of this hypothesis are studies documenting the presence of anticartilage antibodies in some patients (Homma et al, 1984). In addition, it has been shown that exposure of the peripheral blood lymphocytes to cartilage antigen in vitro results in increased blastogenesis (Herman & Dennis 1973) and the production of macrophage migration-inhibiting factor (Rajapakse & Bywaters 1974). Whatever the pathogenesis, damage to cartilage causes local areas of tracheomalacia or

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bronchomalacia, which in turn leads to expiratory airway obstruction and increased risk of pulmonary infection.

The gross appearance, there was severe narrowing of the trachea and major bronchi at autopsy (Kindblom et al, 1977), Microscopically, affected cartilage shows fragmentation and fibrosis. In clinically active disease, an inflammatory infiltrate of lymphocytes, plasma cells, and occasional neutrophils is often present at the fibrocartilaginous interface.

Radiographic manifestations include articular cartilage destruction, calcification of the earlobes, and narrowing of the trachea and major bronchial air columns (Dolan et al, 1966). CT of the airways or tracheobronchography at different lung volumes is necessary to identify the site of the obstruction. HRCT can reveal considerable deformity of peripheral as well as central airways. The disease is typically relapsing and remitting and usually has a prolonged course. The most common clinical manifestations are swelling, erythema, and pain of the ears and arthralgia (McAdam et al, 1976). Nasal chondritis may result in a saddle deformity. The larynx and trachea are involved in about 50% of cases, and in 15% are responsible for the presenting signs and symptoms (McAdam et al, 1976).

Tracheobronchial disease is manifested by dyspnea with a poor prognosis; in fact, respiratory complications are responsible for many of the reported deaths. In one series of 112 patients, the 5- and 10-year probabilities of survival after diagnosis were 74% and 55%, respectively (Michet et al, 1986). The predominant mechanism of expiratory airway obstruction in relapsing polychondritis is the airway abnormality itself and not a loss of elastic recoil forces of the lung (Krell et al, 1986). The site of airway obstruction is usually fixed, as assessed by maximal inspiratory and expiratory low-volume loops (Mohsenifar et al, 1982). If it is variable and intrathoracic (Gibson & Davis 1974), the expiratory flow-volume loop is markedly flattened.
Ankylosing Spondylitis

Extensive upper zonal pulmonary fibrosis may appear in patients with ankylosing spondylitis, usually 10 years or more after the onset of the disease (Gamsu 1992; Tanoue 1992). The precise frequency of pulmonary involvement is not known, and a range of 0% to 30% has been reported. The largest single series indicates a frequency of about 1% (Rosenow et al., 1977). Radiologically, the process begins as apical pleural involvement, and then an apical infiltrate develops and progresses to cyst formation. Generally, the disease begins unilaterally and becomes bilateral. The chest radiograph may mimic tuberculosis closely. Symptoms are usually absent, but the cavities become secondarily infected, most commonly by Aspergillus fumigatus, although a variety of other organisms may also infect the cavities. The histologic lesions consist of nonspecific inflammation and fibrosis. Bronchiolitis obliterans, together with distal lipid pneumonia, is commonly present.

Pulmonary vasculitis

Pulmonary vasculitis is conditions whose sole or predominant histologic feature is inflammation of pulmonary vessels. Clinical and radiographic manifestations of pulmonary vasculitis can be related to vascular inflammation itself or the pneumonitis that accompanies some of disorders. During the acute stages, the effects of vasculitis include alveolar hemorrhage and vascular thrombosis, with or without parenchymal necrosis. With more prolonged disease, weakening of the vessel wall can result aneurysm formation, and obliteration of the vessel lumina can cause pulmonary hypertension. Because of the frequent occurrence of concomitant extrapulmonary vasculitis and the occasional presence of glomerulonephritis, signs and symptoms of extrathoracic disease may overshadow the pulmonary manifestations (Leavitt & Fauci 1986).
Wegener’s Granulomatosis

In its classic form, Wegener's granulomatosis is a multisystem disease characterized by necrotizing granulomatous inflammation of the upper and lower respiratory tract, glomerulonephritis, and necrotizing vasculitis of the lungs and of a variety of systemic organs and tissues. Four diagnostic criteria have been proposed by the American College of Rheumatology (Leavitt et al, 1990); abnormal urinary sediment (red cell casts or more than 5 red cells per high power field); nodular cavities or fixed "infiltrate" (sic) on chest radiographs; oral ulcers or nasal discharge; and granulomatous inflammation on tissue biopsy. In one series of 807 patients with vasculitis, the presence of two or more of these criteria was associated with diagnostic sensitivity and specificity rates of 88% and 92%, respectively (Leavitt et al, 1990). The disease also may be manifested primarily or solely in the respiratory tract, in which case it is referred to as "limited" Wegener's granulomatosis (Carrington & Liebow 1966). The diagnosis of limited Wegener's granulomatosis, especially when the disease is manifested by a solitary pulmonary nodule or mass, should be made only after extensive investigations have excluded the possibility of an infectious etiology.

Etiology and pathogenesis
The prominent involvement of the upper and lower respiratory tract, as well as the occurrence of occasional cases predominantly limited to these sites, strongly suggests that the etiology of Wegener's granulomatosis is related to an inhaled substance; however lung and BAL cultures are typically sterile, and no organisms have been identified by light or electron microscopic examination (Hoffman et al, 1991). Although familial cases do occur (Hay et al, 1991), there is little evidence of a hereditary influence (Murty et al, 1991). Although the pathogenesis of Wegener's granulomatosis is also poorly understood, both the immunologic and pathologic manifestations implicate an autoimmune process (Fauci et al, 1976), a concept supported by the dramatic therapeutic response to immunosuppressive and cytotoxic drugs in many cases. Available evidence suggests a possible role for
both immune complex and cell-mediated immune reactions. Circulating immune complexes have been demonstrated in some patients with active disease and, in one case, (Howell & Epstein 1976) were found to disappear during remission induced by immunosuppressive therapy.

**Pathologic characteristics**

Grossly, pulmonary involvement is characterized by well-circumscribed nodules or masses ranging in diameter from 1 to 10 cm, often with central necrosis; occasionally, there is a more or less diffuse hemorrhagic consolidation (Yoshikawa & Watanabe 1986). Microscopically, the nodules are composed of variable amounts of inflammatory and necrotic tissue. In early lesions, the latter tend to be minute and multifocal; as the disease progresses, however, individual necrotic areas enlarge and coalesce, producing a rather characteristic serpiginous outline. The necrotic tissue is often bordered by large palisaded epitheloid histiocytes, which in turn, is surrounded by a polymorphic inflammatory infiltrate. The inflammation is most prominent in the parenchyma, but involvement of the tracheobronchial tree is also fairly common, either by direct extension from a parenchymal focus or independently. Pulmonary arteries and veins of small to medium size typically manifest one or more of three patterns of inflammation: (1) fibrinoid "necrosis" of the media, with or without a polymorphonuclear leukocyte infiltrate, (2) focal or diffuse infiltration of all vascular layers by a polymorphic infiltrate; or (3) well-defined granulomas or numerous multinucleated giant cells. In the presence of diffuse hemorrhagic consolidation, vasculitis predominates in arterioles, capillaries, and venules and is best described as leukocytoclastic vasculitis (Myers & Katzenstein 1987).

By definition, classic Wegener's granulomatosis is always associated with disease in extrapulmonary sites. In the upper respiratory tract, involvement of the mucous membranes of the paranasal sinuses result in thickening in the early stages and, in some cases, eventuates in destruction of bone and cartilage. The middle ear and orbital cavity may also be involved. The inflammatory and necrotic components
are similar to those seen in the lung parenchyma (Devaney et al, 1990). Characteristically, the kidneys show focal and segmental necrotizing glomerulonephritis. Vasculitis in systemic vessels is similar to that seen in polyarteritis nodosa; as in this disease, the bronchial arteries are occasionally affected.

Radiographic manifestations
The typical radiographic pattern in the lungs is that of rounded opacities, usually sharply defined, ranging from a few millimeters to 10 cm in diameter. They are commonly multiple, bilateral, and widely distributed, with no predilection for any zone (Gohel et al, 1973). Cavitation occurs eventually in one third to one half of the cases. These cavities are thick-walled and tend to have an irregular, rather shaggy inner lining; the thickness of the walls may diminish gradually until the cavities become thin-walled cystic spaces similar to those seen in coccidioidomycosis (Israel & Patchefsky 1971). After appropriate therapy— and even without treatment—cavities may disappear altogether. Distinct "feeding" vessels related to the nodules and abnormalities suggestive of infarcts may be seen with CT (Kuhlman et al, 1991).
Endotracheal and endobronchial masses can cause airway narrowing with resultant peripheral oligemia and sometimes lobar and total lung atelectasis (Maguire et al, 1978). Widespread airspace opacities can be caused by diffuse pulmonary hemorrhage (Travis et al, 1987). Pleural effusion has been reported in 50% of cases (Pinching et al 1983). With cytotoxic drug therapy, there is usually dramatic resolution of the pulmonary lesions. Despite this, intrathoracic relapse is common (Aberle et al, 1990). No distinctive radiologic features distinguish the "limited" from classic form of the disease.

Clinical manifestations
Wegener's granulomatosis typically affects adults in their fifth decade, men more than women (Littlejohn et al, 1985). The onset can be acute and its course fulminating, but it is more commonly insidious. The majority of patients present
with complaints referable to the nose, paranasal sinuses, or chest. Nasal disease is manifested by rhinitis, sinusitis, and epistaxis. Joint involvement is common and usually takes the form of arthralgia or nondeforming arthritis. Myalgia is also infrequent. Neurologic manifestations may be central or peripheral, the latter presenting as polyneuritis. Cardiac manifestations include conduction abnormalities and pericarditis. Thoracic symptoms consist of intractable cough, often with hemoptysis, dyspnea, and pleuritic pain. Hemoptysis is occasionally massive, the clinical presentation mimicking idiopathic pulmonary hemorrhage or Goodpasture's syndrome.

**Laboratory findings**
Laboratory findings include anemia, thrombocytosis, and leukocytosis, occasionally with eosinophilia. Rheumatoid factor may be detected in the serum in low titer, and some patients have elevated levels of IgE (Brandwein et al, 1983). Pulmonary function tests may show restrictive or obstructive disease, the latter generally resulting from involvement of the large airways. Antineutrophil cytoplasmic antibodies (ANCAs) can be detected in serum and BAL specimens (Hoffman et al, 1991) by indirect immunofluorescence or enzyme-linked immunosorbent assay (ELISA) techniques and appear to be related to several lysosomal enzymes (Tervaert et al, 1991). They are elevated in a large percentage of patients with Wegener's granulomatosis, although they also have been reported in individuals, with microscopic polyarteritis, idiopathic (crescentic) glomerulonephritis (Specks et al, 1989), and allergic granulomatosis (Tervaert et al, 1991).

**Takayasu's Arteritis**
Takayasu's arteritis (pulseless disease) is uncommon vasculitis that occurs predominantly in women in the second or third decade of life. It is worldwide in distribution; although most affected individuals have been Japanese. Although the
arteritis is often confined to the aorta and its branches, pulmonary artery involvement also is present in an appreciable number of cases; for example, in one autopsy review, the main pulmonary artery was found to be affected in 34 of 76 cases and the intrapulmonary arterial branches in 21 cases (Nasu, 1975). In fact the pulmonary artery can be the initial site of involvement (Hayashi et al, 1986). The etiology and pathogenesis are unknown. A majority of patients have evidence of active or remote TB (Lupi et al, 1967). The possibility that the condition represents an unusual form of hypersensitivity reaction to Mycobacterium organisms has been suggested (Lupi et al, 1967). A variety of serologic abnormalities and an association with connective tissue disease (Lupi-Herrera et al, 1977) also have been reported, raising the possibility of an immune mechanism.

Pathologically, most changes are limited to the larger, elastic vessels and consist of adventitial fibrosis and a mixed, largely mononuclear, inflammatory cellular infiltrate, intimal fibrosis, and, in active lesions, necrotizing or non-necrotizing granulomatous inflammation of the media. The vascular fibrosis is responsible for appreciable stenosis, resulting in pulmonary artery hypertension that is the principal manifestation of the disease in the lungs. In one study of the pulmonary circulation of 11 patients, pulmonary hypertension was found to be moderate in degree and to result from stenosis of the main pulmonary artery and its major branches down to subsegmental levels (Lupi et al, 1967).

The angiographic pattern was similar to that commonly observed in pulmonary thromboembolism. In addition to the changes anticipated in the lungs from pulmonary arterial hypertension, the chest radiograph may reveal abnormalities of the aorta, including prominence of the ascending arch, and intimal calcification (Berkmen & Lande 1975).

Clinical manifestations consist of both nonspecific constitutional symptoms and a variety of specific symptoms related to localized vascular insufficiency. These include angina, headaches, syncope, impaired vision and claudication in upper or
lower extremities. Localized pain over the affected arteries and arterial pulses may be absent. A midsystolic murmur in the pulmonic area may suggest pulmonary artery involvement (Lupi et al, 1967).

**Allergic Granulomatosis**

Allergic granulomatosis (Churg-Strauss Syndrome) is uncommon and somewhat controversial clinicopathologic abnormality. The American College of Rheumatology has proposed six criteria for its diagnosis (Masi et al, 1990); asthma, eosinophilia greater than 10% on differential white blood cell count, mononeuropathy or polynuropathy, paranasal sinus abnormalities, non-fixed pulmonary "infiltrate" (sic) on radiography, and biopsy containing a blood vessel showing vasculitis and extravascular eosinophils. In their investigation of 807 patients with vasculitis, the presence of four or more of these criteria was found to yield a sensitivity and specificity for diagnosis of 85% and 97%, respectively (Masi et al, 1990).

The etiology and pathogenesis of allergic granulomatosis are unknown. The association with asthma and rhinitis, the presence of elevated levels of serum IgE, the response to corticosteroids, and the pathologic findings all suggest a hypersensitivity reaction to unidentified antigen or antigens.

Allergic granulomatosis is a multisystem disease with predilection for involvement of lungs, skin, and nervous system; the lower urinary tract, spleen, gastrointestinal tract, and heart are less commonly affected (Leavitt & Fauci 1986; Chumbley et al, 1977). Although renal disease, manifested by necrotizing glomerulonephritis or vasculitis, was common in Churg and Strauss's initial series (Churg & Strauss 1951), other have found the kidneys to be infrequently affected (Chumbley et al, 1977). The characteristic microscopic findings are a combination of vasculitis and necrotizing, extravascular granulomatous inflammation (Koss et al, 1981). The former occurs in small to medium-sized
involvement of the bronchial arteries as a part of the systemic vasculitis can occur, the incidence of vasculitis in the pulmonary circulation is very low. Some cases possess clinicopathologic features common to both allergic granulomatosis and PAN, and the precise classification of these into one category or the other can be difficult. Pathologically, the lesions of PAN are patchy in distribution and are often located at arterial branch points of the systemic circulation; histologic features range from acute inflammation with necrosis of the vessel wall to healing and fully healed stages. Extravascular granulomatous inflammation and tissue eosinophilia is not found. Although radiographic abnormalities in the thorax may be present in classic PAN, it is probable that the majority is coincidental and not related to involvement of the lungs by the primary disease process. For example, in one review of the radiographic findings in 14 children with PAN, chest abnormalities were identified in eight, but all were consistent with the effects of chronic renal disease, hypertension, or cardiac decompensation (Fujioka et al., 1980). Despite the foregoing, occasional cases of parenchymal hemorrhage may be caused by bronchial arteritis. The predominant symptoms in PAN are related to the gastrointestinal tract, the kidneys, and the nervous system. Renal involvement is said to occur in 80% of cases (Hinshaw & Garland 1969), and systemic hypertension is a common clinical manifestation. Symptoms of pleuropulmonary disease are probably caused in most cases by complicating infection or by renal or cardiac failure; they include cough, wheezing, pleuritic pain, and occasionally hemoptysis.

**Necrotizing Sarcoid Granulomatosis**

Necrotizing Sarcoid Granulomatosis (NSG) is a rare disorder characterized pathologically by confluent granulomas associated with a variable amount of necrosis and prominent, focally destructive vasculitis (Koss et al., 1980). The etiology and pathogenesis are unknown. The vascular involvement, granulomatous
inflammation, and apparently good response to corticosteroid therapy have suggested a hypersensitivity reaction. Non-necrotizing granulomatous inflammation of vessel walls is common in other classic sarcoidosis (Rosen et al, 1977), although it is usually less marked in extent and severity than NSG. This observation, in addition to the occasional presence of granulomatous disease in hilar lymph nodes and extrapulmonary sites (Churg et al, 1979), suggests that some cases of NSG might be variants of classic sarcoidosis.

Radiographically, the condition presents as multiple well-defined nodules or ill-defined opacities (Fisher et al, 1984), occasionally, a solitary mass resembling carcinoma may be present. Small or large nodules may cavitate, and pleural effusion may develop (Koss et al, 1980). The incidence of hilar lymph node enlargement is quite variable in different series, ranging from 8% to 50%. Most patients are middle-aged adults, and there is a distinct female predominance (Churg et al, 1979). Clinically, patients may be asymptomatic or have cough, fever, sweats, malaise, dyspnea, hemoptysis, or pleuritic pain. Extrapulmonary findings are usually absent. The course of NSG is typically benign. Radiographic evidence of disease diminishes with corticosteroid therapy or, occasionally, spontaneous; however, relapse has occurred after cessation of therapy (Koss et al, 1980).

**Behcet’s Disease**

Behcet’s disease is uncommon systemic disorder characterized principally by recurrent aphthous stomatitis, genital ulcers, skin lesions and uveitis. Pulmonary manifestations are considered to be rare: only 28 examples had been documented in world literature by 1986 (Efthimiou et al, 1986). However, in a more recent report of 72 patients, 7 (10%) were considered to have pulmonary vascular involvement (Raz et al, 1989).
The basic pathogenesis is vasculitis, probably on the basis of immune complex deposition. Focal glomerulonephritis are seen in some cases (Herreman et al, 1982) and have been associated with subendothelial electron-dense deposits and immunofluorescence evidence of IgG and C3 deposition. The etiology is unknown, but there has been speculation that it may be a virus (Slavin & De Groot 1981).

The principal pathologic abnormality is a transmural inflammatory lymphocytic infiltrate that can affect any or all pulmonary vessels from arteries to alveolar capillaries to large veins (Efthimiou et al, 1986; Slavin & De Groot 1981). The inflammatory process can be so marked as to result in aneurysmal dilatation and can extend into adjacent airways with bronchial artery erosion and resultant massive hemoptysis. Recent or organized thrombi and parenchymal infarcts may be present and may be related to either local vasculitis and thrombosis or thromboembolism secondary to systemic thrombophlebitis (Efthimiou et al, 1986).

Radiographic manifestations consist of focal or diffuse airspace opacities, reflecting infarction or hemorrhage. Proximal pulmonary arteries may be prominent; in one study, aneurysms were identified in 7 of 13 patients examined by angiography (Raz et al, 1989).

Clinically, Behcet's disease is a systemic abnormality characterized by recurrent exacerbations and remissions (Chajek & Fainaru 1975). Men are affected more than women, and patients are 20 to 30 years old at diagnosis. The incidence is highest in the Middle East and Japan. In addition to the characteristic triad of uveitis and oral and genital ulcers, systemic disease can result in an assortment of erythema nodosum, arthritis, thrombophlebitis and various neurologic syndromes. Pulmonary manifestations appear 3 to 4 years after the onset of systemic disease and are related to both thromboembolism and pulmonary vasculitis. Typically, they consist of recurrent episodes of hemoptysis, chest pain, dyspnea and cough (Raz et al, 1989).
Patients
& Methods
Patients
Our study included 91 patients with a clinical and laboratory diagnosis of interstitial lung disease, of which:

- 67 patients with a diagnosis of collagen vascular disease (32 patients with PSS, 19 with RA, 3 with MCTD, 5 with SLE, 4 with PM/DM, 3 with WG and 1 case of Takayasu’s arteritis).
- 24 patients with a diagnosis of ILD other than CVD (14 patients with idiopathic pulmonary fibrosis (IPF), 2 cases of amiodarone toxicity, and 8 others).

Sex: They were 26 males and 66 females.

17 cases were done in Egypt before July 1997 (16 females, one male) and 74 cases were done in USA during the period between July 1997 and June 1999 at UCLA Medical Plaza outpatient Clinic (50 females, 25 males).

Race: 46 patients were Caucasian, 2 black, 11 Hispanic, 25 white, 2 Persian, 4 oriental, and 2 Asian.

Age range: 20-94 years with a mean age of 51 years.

Smoking history: 49 non-smokers and 43 smokers.

Clinical presentation: 27 patients present with dyspnea and cough, 24 with dyspnea alone, 8 with cough alone. With a range from 1 month to 15 years.

Nineteen (19) cases of Rheumatoid arthritis (RA): fulfilled the Proposed 1987 revised Rheumatism Association criteria for rheumatoid arthritis.

Four or more criteria must be present to diagnose RA
1. Morning stiffness for at least 1 hour and present for at least for 6 weeks.
2. Swelling of 3 or more joints for at least 6 weeks.
3. Swelling of the wrist, MCP, or proximal IP joints for 6 or more weeks.
4. Symmetric joint swelling.
### Table 2: Chest X-ray scoring

<table>
<thead>
<tr>
<th>X-ray sign</th>
<th>Lung zone score</th>
<th>RT. lung</th>
<th>LT. lung</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Upper</td>
<td>Middle</td>
</tr>
<tr>
<td>1-Parenchymal</td>
<td>Linear</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormalities</td>
<td>opacities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2- pulmonary a. size (PAH)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-pleural effusion or thickening</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-Mediastinal or hilar LNs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-lung volume</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-others</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Score = mild, moderate, severe (or 1,2,3)
The upper zones (above the carinal bifurcation), the middle zones (carinal bifurcation to inferior pulmonary vein) and the lower zones (caudal to the inferior pulmonary vein).

**A combination of spiral CT and HRCT technique was used**: High resolution CT chest was performed on a GE HiSpeed CT/i (Milwaukee) Scanner. A volume acquisition with 10-mm collimation pitch 1 study was obtained from apex to base in the supine position at TLC. High-resolution images were then obtained using 1-mm collimation every 10-mm from apex to base also in the supine position at TLC. A high-resolution spiral using 1-mm collimation pitch 1 was performed commencing 3 cm below the carina and extending for 2 cm in the same position and breath hold position. An expiratory scan was then obtained 1-mm collimation every 20-mm from carina to base to detect areas of focal air trapping. No
intravenous or oral contrast was given. Additional high resolution images in the
prone position were obtained when necessary to evaluate the reversibility of
posterior lung abnormalities.

2. **Spiral (thick-section 10 mm pitch 1) was done in 84 cases and HRCT (1 or
1.5 mm/10 mm) was done in 91 cases.**

**Thoracic Spiral CT** was performed with the patient imaged in the supine position
with their arms above their head. Image data was acquired during suspended end
inspiration (TLC). Volumetric chest studies were performed using 140 KVP, 140
mA, a 1-second scan time, 10 mm collimation pitch 1 reconstructed contiguously
using bone algorithm.

Photography will be filmed 12-20 on 1 with width 1500, level -600 to -750. The
scans done in helical thick sections (10-mm collimation) were not interpreted
because these scans were not suitable for assessment of fine details of lung
parenchyma.

**Technical guidelines for thoracic HRCT image data acquisition will include:**
- Beam collimation of 1-1.5 mm
- Image acquisition at 10-mm intervals from the lung apex to the
costophrenic sulcus
- High spatial frequency (bone) reconstruction algorithm using a 512x512
matrix
- Scan time of 1-second
- 200 mAs exposure minimum (adjusted for body habitus), at 120-140 KVP
- Acquisition field of view as small as allowed by patient size
- Lung window (width =1600, level = -550 to -700 HU) and mediastinal
window (width =400 HU, level =40 HU) images were photographed (12 on
1 format) for interpretation. The display field of view (DFOV) of the
photographed images were coned down to include only the lungs.
Thoracic HRCT image interpretation protocols
HRCT analysis was performed independently by 2 radiologists and blinded to the patient clinical condition. Final determination was reached by consensus.
Analysis of the extent of pleuropulmonary disease on thoracic HRCT was based on a simplified and modified scleroderma severity scoring system adapted from Remy-Jardin (Remy-Jardin 1993d). The scoring systems used in other published studies have also been used in the development of this modified scoring system (Kazerooni et al, 1997; Wells et al, 1997).
For analysis, the thorax was divided into three zones: upper zone, middle zone, and lower zone. The right and left hemithorax was evaluated individually in each zone, resulting in six scored regions. In each region, the presence or absence of the each HRCT finding (Ground glass opacity, honeycomb....) was assessed.
LN enlargement, esophageal dilatation, pulmonary artery size, and other significant finding (e.g., pulmonary nodules or masses) were also recorded.
The severity of lung involvement was individually determined in each of the six zones for the following two features: ground glass opacification, and fibrosis (including linear opacities and micronodules). Scores were based on a visual estimate of the percentage of the lung tissue demonstrating the abnormality. The scores of the six zones were averaged to obtain severity score for each HRCT finding.
The radiologists determined the presence and distribution of the following CT signs:
Parenchymal micronodules (<7 mm in diameter), nodules (7-20 mm in diameter), and masses (>20 mm in diameter).
Linear opacities: septal lines (thickened interlobular septa and identified as fine linear opacities or as a pattern of multiple polygonal lines) and nonseptal lines.
Irregularity of the interfaces between the peripheral pleura and aerated lung parenchyma or small lines perpendicular to the pleura detected along the chest wall and the mediastinum but also along the central vessels and bronchi.
Increased lung attenuation:
(a) *Ground-glass opacities* were defined as hyperattenuated area, varying from minimal to marked attenuation, in which the bronchi and vessels remained visible.
(b) *Consolidation* was defined as increased attenuation with obscuration of the adjacent bronchial walls and vessels.

Honeycombing: areas of cystic spaces with thickened walls. Distinction was made between small (<1 cm diameter) and large (>1 cm diameter) cystic airspaces, respectively recorded as microcystic and macrocystic honeycomb pattern.

Traction bronchiectasis and bronchiolectasis: bronchiolectasis were recognized from the abnormal appearance of bronchi in peripheral location.

Emphysema (characterized by areas of decreased attenuation, disruption of the vascular pattern, and absence of well-defined wall. Bullae were defined as regions of emphysema with a well-defined wall 1-2 mm in maximum thickness.

Diffuse thickening of the pleural surface.
The size of the main pulmonary artery and the intrapericardial portion of the right pulmonary artery were measured with mediastinal window settings to detect the presence of pulmonary hypertension.

Lymph node enlargement was recorded by using criteria defined by Glazer et al (1985)

Esophageal dilatation was diagnosed if a single, nonloculated pocket of air below the aortic arch of the esophagus was evident on four consecutive axial images and if the luminal diameter of such an air-filled esophagus exceeded 10 mm in the coronal plane.
Table (4) Spiral HRCT Scoring

<table>
<thead>
<tr>
<th>CT Sign</th>
<th>Right lung</th>
<th>left lung</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ground glass opacification</td>
<td>lower (3 cm below carina)</td>
<td>lower (3 cm below carina)</td>
</tr>
<tr>
<td>Linear opacities (septal &amp; nonseptal lines, irregular interface, reticulation)</td>
<td>(1-5)</td>
<td></td>
</tr>
<tr>
<td>Honeycombing</td>
<td>(1-5)</td>
<td></td>
</tr>
<tr>
<td>1. Pulmonary micronodules, nodules or masses</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td>2. Airspace consolidation</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td>3. Traction bronchiectasis</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td>4. Emphysema (hyperinflation)</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td>5. Associated malignancy</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td>6. Enlarged mediastinal or hilar LNs or masses</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td>7. Enlarged pulmonary artery (PAH)</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td>8. Pleural thickening or effusion</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td>9. Esophageal dilation</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td>10. Others</td>
<td>(1)</td>
<td></td>
</tr>
</tbody>
</table>

The HRCT Spiral scan was done 3 cm below the carina (taking part of middle and lower lung zones), 1 mm slice thickness pitch 1, and extending for 2 cm downwards.

4. Intravenous contrast media was given in (17) cases as a part of evaluation of pulmonary embolism (Chest CTA) or characterization of pulmonary nodules. IV contrast was given in 4 cases of RA, 4 PSS, 3 PM/DM, 2 SLE, 1 WG, 2 IPF, and one case of sarcoidosis.
### Table 3: HRCT Scoring

<table>
<thead>
<tr>
<th>HRCT signs</th>
<th>RT.lung</th>
<th>LT.lung</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Upper</td>
<td>Middle</td>
</tr>
<tr>
<td>Ground glass opacification</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linear opacities (septal &amp; nonseptal lines, irregular interface, reticulation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Honeycombing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary micronodules, nodule mass</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Airspace consolidation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchiectasis (traction)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>±bronchiolitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emphysema</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Associated malignancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enlarged mediastinal or hilar LN's</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enlarged pulmonary artery</td>
<td>(PAH)</td>
<td></td>
</tr>
<tr>
<td>Pleural thickening or effusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophageal dilation</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>(1)</td>
<td></td>
</tr>
</tbody>
</table>

- Upper zone = lung apex to the top of the aortic arch
- Middle zone = aortic arch to the right inferior pulmonary vein.
- Lower zone = right inferior pulmonary vein to the most caudal extent of the lungs (level)

0=Normal (none), 1=Minimal (1-5%), 2=Mild (6-25%), 3=Moderate (26-50%), 4=Marked (51-75%), 5=Severe (>75%).

3. **Spiral CT (thin-section 1mm pitch 1 for 2 cm distance 3 cm below the level of the carina) was done in 54 cases**
5. Follow up chest CT was done in 8 patients: 4 PSS, 2 SLE, 1 RA, and one IPF
6. 83 cases were done using GE, HiSpeed CT/i Scanner, 7 cases using picker PQ
6000 CT scanner and 1 case only by Elscint-Twin Scanner.

B-Pulmonary Function Tests (PFTs)
PFTs were done in 62 cases: 44 cases of CVD (27 PSS, 9 RA, 2 SLE, 2 MCTD, 1
WG, 3 PM/DM) and 18 cases of others (9 IPF, 2 amiodarone toxicity, 1
sarcoidosis, 1 occupational exposure, 1 ground glass opacity after liver transplant,
1 chronic cough, 1 asthma, 1 emphysema, 1 heart failure).
Technicians used equipment and procedures that meet all 1994 American Thoracic
Society criteria or standardization of spirometry (ATS, 1995).
Pulmonary function was interpreted into the following groups according to the
Normal: FVC ≥80% predicted; FEV1/FVC ≥ 70%; FEF 25-75 ≥60% predicted;
DLCO ≥ 80% predicted.
Restrictive: FVC < 80% predicted; FEV1/FVC ≥70%.
Obstructive: FEV1 / FVC <70%.
Isolated DLCO reduction: FVC ≥80% predicted; FEV1 / FVC ≥ 70%; FEF 25-75
≥60% predicted; and DLCO < 80% predicted.
Isolated FEF 25-75 reduction: FVC ≥80% predicted; FEV1 / FVC ≥70%; and FEF
25-75 < 60% predicted.
Where, FVC = forced vital capacity; FEV1 = forced expiratory volume in 1
second; FEF 25-75 = forced expiratory flow between 25% and 75% of the vital
capacity; DLCO = single breath diffusing capacity for carbon monoxide.

C-Bronchoalveolar Lavage (BAL)
BAL study was done in 24 cases: 20 cases of CVD (16 scleroderma, 1 Wegener’s,
1 SLE, 1 Takayasu’s arteritis, 1 PM) and 4 cases of others (3 IPF, and 1
sarcoidosis).
The patient is placed on supplemental oxygen and monitored by pulse oximetry, EKG telemetry, and intermittent blood pressure determination. The oropharynx is anesthetized with 4% lidocaine by hand-held nebulizer and also by 20% benzocaine spray to the posterior pharynx. The patient is then sedated with a total of 2 mg of Versed and 75 mg of Demerol given intravenously in small increments throughout the procedure. The patient is then placed in the supine position and a bite block is inserted.

Bronchoscope is advanced to the level of vocal cords and additional anesthesia with 2% lidocaine is administered topically as needed to control the coughing reflex. Bronchoscope is then introduced into the trachea and a complete examination of the right and left tracheobronchial tree is carried out.

Bronchoscope is then wedged in the left lingula or the right middle lobe and bronchoalveolar lavage carried out by steriley instilling 250 cc aliquots of sterile saline followed by manual syringe suction. Upon completing this, the bronchoscope is removed and the patient is placed in the sitting position. Bronchoalveolar lavage fluids is sent for cytology and cell differential counting. The presence of > 3% neutrophils & / or > 2% eosinophils in BAL fluid is indicative of active alveolitis. BAL can also rule out infection, malignancy or hemorrhage.

D-Histological evaluation
The diagnosis was pathologically proved in 23 cases: 15 cases of CVD (3 WG, 4 PM/DM, 3 PSS, 2 MCTD, 1 RA, 1 SLE, 1 Takayasu’s arteritis) and 8 cases of others (7 IPF and 1 Sarcoidosis).

27 biopsies were done as follows:
1. Transbronchial biopsy (TBB) in 5 cases: 2 WG, 1 Sarcoidosis, and 2 IPF
2. Direct lung biopsy in 5 cases: 3 IPF, 1 Takayasu’s arteritis, and 1 SLE
3. Pleural biopsy in 2 cases: 1WG, and 1 PSS.
4. Renal biopsy was done in 4 cases: 3 WG, and 1MCTD.
5. Muscle biopsy was done in 5 cases: Left deltoid muscle biopsy in PM, Left biceps muscle biopsy in PM, Left deltoid muscle biopsy in two cases of PSS, and Left quadriceps muscle biopsy in MCTD.
6. Skin biopsy: 1 PM/DM, and 1 IPF
7. Esophageal biopsy in a case of RA.
8. Liver biopsy in a case of IPF.
9. Endomyocardial biopsy in a case of DM.
10. Left common carotid artery biopsy in Takayasu’s arteritis.

E-Statistical Analysis
Statistical analysis was performed with SAS system software (SAS Institute Inc., SAS Campus Drive, Cary, NC 27513). Statistical Package: SAS Version. 6.12
By using Tables of Chest x-ray, HRCT, Spiral HRCT and HRCT-UML score data, the following parameters were statistically analyzed:
- Variable Means of Each Group.
- Frequency Table of Each Group (Frequency, Percent, Cumulative Frequency, Cumulative Percent)
- Means of each group
- Frequency table of subgroups (Group1 = normal HRCT scan, Group2 = without honeycombing on HRCT and Group 3 = with honeycombing on HRCT scan).
- Nonparametric Test of Spiral & HRCT-M(middle), Nonparametric Test of Spiral & HRCT-L(lower), Comparing the variable means using Wilcoxon 2-Sample Test (Normal Approximation) (with Continuity Correction of 0.5) and Kruskal-Wallis Test (chi-square Approximation). Average scores were used for ties
- Paired T-test for Spiral and HRCT-M Group.
- Paired T-test for Spiral and HRCT-L Group.
Results
Table (1) clinical findings (smoking history)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number</th>
<th>Smoker</th>
<th>Non-smoker</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS</td>
<td>30</td>
<td>19(60%)</td>
<td>11(36.7%)</td>
</tr>
<tr>
<td>RA</td>
<td>7</td>
<td>6(85.7%)</td>
<td>1(14.3%)</td>
</tr>
<tr>
<td>SLE</td>
<td>2</td>
<td>1(50%)</td>
<td>1(50%)</td>
</tr>
<tr>
<td>MCTD</td>
<td>3</td>
<td>0</td>
<td>3(100%)</td>
</tr>
<tr>
<td>WG</td>
<td>3</td>
<td>2(66.7%)</td>
<td>1(33.3%)</td>
</tr>
<tr>
<td>PM/DM</td>
<td>4</td>
<td>1(25%)</td>
<td>4(100%)</td>
</tr>
<tr>
<td>Takay</td>
<td>1</td>
<td>1(100%)</td>
<td>0</td>
</tr>
<tr>
<td>IPF</td>
<td>14</td>
<td>7(50%)</td>
<td>7(50%)</td>
</tr>
<tr>
<td>Amiodr</td>
<td>2</td>
<td>0</td>
<td>2(100%)</td>
</tr>
<tr>
<td>Others</td>
<td>8</td>
<td>6(75%)</td>
<td>2(25%)</td>
</tr>
<tr>
<td>Total</td>
<td>74(100%)</td>
<td>43(58%)</td>
<td>32(43%)</td>
</tr>
</tbody>
</table>

Table (2): Clinical findings (symptoms).

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number</th>
<th>Dyspnea</th>
<th>Cough</th>
<th>Both</th>
<th>Dyspne alone</th>
<th>Cough alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS</td>
<td>30</td>
<td>22(73.3%)</td>
<td>8(26%)</td>
<td>8(26%)</td>
<td>13(43.3%)</td>
<td>0</td>
</tr>
<tr>
<td>RA</td>
<td>7</td>
<td>4(57.1%)</td>
<td>5(71.4%)</td>
<td>3(42.9%)</td>
<td>1(14.3%)</td>
<td>2(28.6%)</td>
</tr>
<tr>
<td>SLE</td>
<td>2</td>
<td>2(100%)</td>
<td>1(50%)</td>
<td>1(50%)</td>
<td>1(50%)</td>
<td>0</td>
</tr>
<tr>
<td>MCTD</td>
<td>3</td>
<td>2(66.7%)</td>
<td>2(66.7%)</td>
<td>1(33.3%)</td>
<td>1(33.3%)</td>
<td>1(33.3%)</td>
</tr>
<tr>
<td>WG</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1(33.3%)</td>
<td>0</td>
</tr>
<tr>
<td>PM/DM</td>
<td>4</td>
<td>3(75%)</td>
<td>3(75%)</td>
<td>2(50%)</td>
<td>1(25%)</td>
<td>1(25%)</td>
</tr>
<tr>
<td>Takay</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1(100%)</td>
<td>0</td>
</tr>
<tr>
<td>IPF</td>
<td>14</td>
<td>10(71%)</td>
<td>8(57.1%)</td>
<td>7(50%)</td>
<td>3(21.4%)</td>
<td>1(7.1%)</td>
</tr>
<tr>
<td>Amiodr</td>
<td>2</td>
<td>1(50%)</td>
<td>2(100%)</td>
<td>1(50%)</td>
<td>0</td>
<td>1(50%)</td>
</tr>
<tr>
<td>Others</td>
<td>8</td>
<td>4(50%)</td>
<td>4(50%)</td>
<td>3(37.5%)</td>
<td>1(12.5%)</td>
<td>2(25%)</td>
</tr>
<tr>
<td>Total</td>
<td>74(100%)</td>
<td>48(65%)</td>
<td>33(45%)</td>
<td>26(35%)</td>
<td>23(31%)</td>
<td>8(10.8%)</td>
</tr>
</tbody>
</table>

32 patients were non-smoker (42.7%) and 43 smoker (57.3%). 48 (64%) patients had dyspnea, 33(44%) patients had cough.

In 30 patients with PSS: 11 non-smoker, 19 smoker, 22 had dyspnea, 8 had cough.

7 patients with RA, 1 non-smoker, 6 smoker, 4 had dyspnea, and 5 had cough.

3 patients with MCTD: 3 non-smoker, 2 had dyspnea, and 2 had cough.
2 patients with SLE: 1 non-smoker, 1 smoker, 2 had dyspnea, and one had cough.

3 patients with WG: 1 non-smoker, 2 smoker, one had dyspnea.

5 patients with PM/DM: 4 non-smoker, 1 smoker, 3 had dyspnea, 3 had cough.

1 patient with Takayasu’s A. he was smoker and had dyspnea.

14 patients with IPF: 7 non-smokers, 7 smoker, 10 had dyspnea, and 8 had cough.

2 patients with Amiodarone toxicity: 2 non-smokers, 1 had dyspnea, and 2 had cough.

8 patients with Miscellaneous ILD: 2 non-smoker, 6 smoker, 4 had dyspnea, and 4 had cough.

The (17) Egyptian patients were not included in the clinical findings but all the 17 patients were non-smokers.

Table (3): Classification of patients according to absence or presence of honeycomb on HRCT (91 patients)

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Without H/C</th>
<th>With H/C</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS(n=32)</td>
<td>7(21.9%)</td>
<td>13(40.6)</td>
<td>12(37.5)</td>
</tr>
<tr>
<td>RA(n=19)</td>
<td>10(52.6%)</td>
<td>8(42.1)</td>
<td>1(5.3)</td>
</tr>
<tr>
<td>MCTD(n=3)</td>
<td>0</td>
<td>1(33.3)</td>
<td>2(66.7)</td>
</tr>
<tr>
<td>IPF(n=14)</td>
<td>0</td>
<td>3(21.4)</td>
<td>11(78.6)</td>
</tr>
<tr>
<td>SLE(n=5)</td>
<td>1(20%)</td>
<td>3(60)</td>
<td>1(20)</td>
</tr>
<tr>
<td>WG(n=3)</td>
<td>0</td>
<td>3(100)</td>
<td>0</td>
</tr>
<tr>
<td>PM(n=4)</td>
<td>0</td>
<td>1(25)</td>
<td>3(75)</td>
</tr>
<tr>
<td>Takayasu(n=1)</td>
<td>0</td>
<td>1(100)</td>
<td>0</td>
</tr>
<tr>
<td>Amiodarone(n=2)</td>
<td>0</td>
<td>2(100)</td>
<td>0</td>
</tr>
<tr>
<td>Others(n=6)</td>
<td>4(50%)</td>
<td>4(50)</td>
<td>0</td>
</tr>
<tr>
<td>CVD(n=67)</td>
<td>18(26.9%)</td>
<td>30(44.8)</td>
<td>19(28.4)</td>
</tr>
</tbody>
</table>

Table (4): Classification of patients according to absence or presence of honeycomb on Spiral CT lower zones (54 patients)

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Without H/C</th>
<th>With H/C</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS(n=26)</td>
<td>4(15.5%)</td>
<td>12(46.1%)</td>
<td>10(38.5%)</td>
</tr>
<tr>
<td>RA(n=5)</td>
<td>0</td>
<td>5(100%)</td>
<td>0</td>
</tr>
<tr>
<td>MCTD(n=2)</td>
<td>0</td>
<td>1(50%)</td>
<td>1(50%)</td>
</tr>
<tr>
<td>IPF(n=9)</td>
<td>0</td>
<td>2(22.2%)</td>
<td>7(77.8%)</td>
</tr>
<tr>
<td>SLE(n=1)</td>
<td>0</td>
<td>1(100%)</td>
<td>0</td>
</tr>
<tr>
<td>PM/DM(n=4)</td>
<td>0</td>
<td>1(25%)</td>
<td>3(75%)</td>
</tr>
<tr>
<td>Takayasu(n=1)</td>
<td>0</td>
<td>1(100%)</td>
<td>0</td>
</tr>
<tr>
<td>Amiodarone(n=2)</td>
<td>0</td>
<td>0</td>
<td>2(100%)</td>
</tr>
<tr>
<td>Others(n=4)</td>
<td>2(50%)</td>
<td>2(50%)</td>
<td>0</td>
</tr>
<tr>
<td>CVD(n=39)</td>
<td>4(10.3%)</td>
<td>21(53.8%)</td>
<td>14(35.9%)</td>
</tr>
</tbody>
</table>
Table (5): Classification of patients according to absence or presence of honeycomb on chest x-ray (72 patients)

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Without H/C</th>
<th>With H/C</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS(n=18)</td>
<td>2(11.1%)</td>
<td>11(61.1%)</td>
<td>5(27.8%)</td>
</tr>
<tr>
<td>RA(n=18)</td>
<td>8(44.4%)</td>
<td>9(50%)</td>
<td>1(5.6%)</td>
</tr>
<tr>
<td>IPF(n=13)</td>
<td>0</td>
<td>6(46.1%)</td>
<td>7(53.8%)</td>
</tr>
<tr>
<td>SLE(n=5)</td>
<td>3(60%)</td>
<td>2(40%)</td>
<td>0</td>
</tr>
<tr>
<td>WG(n=3)</td>
<td>0</td>
<td>3(100%)</td>
<td>0</td>
</tr>
<tr>
<td>PM(n=4)</td>
<td>0</td>
<td>2(50%)</td>
<td>2(50%)</td>
</tr>
<tr>
<td>Takayasu(n=1)</td>
<td>0</td>
<td>1(100%)</td>
<td>0</td>
</tr>
<tr>
<td>Amiod (n=2)</td>
<td>1(50%)</td>
<td>1(50%)</td>
<td>0</td>
</tr>
<tr>
<td>Others(n=8)</td>
<td>2(25%)</td>
<td>6(75%)</td>
<td>0</td>
</tr>
<tr>
<td>CVD=(49)</td>
<td>13(26.5%)</td>
<td>28(57.1%)</td>
<td>8(16.3%)</td>
</tr>
</tbody>
</table>

In these tables (3,4&5), we classify patients into 3 groups: (1) Normal in which there was no signs of ILD seen on CT or chest radiographs, (2) Without honeycomb (without H/C) in which there was signs of interstitial lung disease such as ground-glass opacities, linear opacities but there was no honeycombing, (3) Patients with honeycombing (with H/C), in which chest radiographs or CT (whether spiral or HRCT) showed honeycombing in addition to other signs of interstitial lung disease.

On HRCT study, there was 91 patients, 22 (24.2%) patients had normal HRCT study, 39(42.9%) patients without honeycombing, and 30(33%) patients with honeycombing. There were 12/32 patients with scleroderma had honeycombing and 11/14 patients with idiopathic pulmonary fibrosis had honeycombing. While 10/19(52.6%) with rheumatoid arthritis were normal.

On Spiral CT, 54 patients underwent spiral high resolution CT, there were 6(11.1) patients had normal study, 25(46.3%) patients with ILD without honeycombing, and 23(42.6%) patients with honeycombing. While 10 patients of scleroderma and 7 patients with IPF had honeycombing.

On chest radiograph, 72 patients had chest x-ray, 16(22.2%) patients had normal chest X-ray, 41(56.9%) patients had abnormal chest x-ray without honeycombing, and 15(20.8) patients had honeycombing. While 8/18 with RA was normal, 5/18 of scleroderma and 7/13 of IPF had honeycombing.
Table (6): Prevalence of chest x-ray signs in CVD and IPF patients

<table>
<thead>
<tr>
<th>Disease</th>
<th>G/G opacity</th>
<th>Linear opacity</th>
<th>Air space consolidation</th>
<th>Honeycomb</th>
<th>Bronchiectasis</th>
<th>↑ PA size</th>
<th>Pleural effusion-thickening</th>
<th>Lymph nodes</th>
<th>↓ Lung volume</th>
<th>CM</th>
<th>Nodules</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS(18)</td>
<td>11</td>
<td>14</td>
<td>2</td>
<td>5</td>
<td>4</td>
<td>8</td>
<td>7</td>
<td>2</td>
<td>6</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>%</td>
<td>61.1</td>
<td>77.8</td>
<td>11.1</td>
<td>25.8</td>
<td>22.2</td>
<td>44.4</td>
<td>38.9</td>
<td>11.1</td>
<td>33.3</td>
<td>5.6</td>
<td></td>
</tr>
<tr>
<td>RA(18)</td>
<td>7</td>
<td>10</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>%</td>
<td>38.9</td>
<td>55.6</td>
<td>16.7</td>
<td>5.6</td>
<td>11.1</td>
<td>5.6</td>
<td>22.2</td>
<td>5.6</td>
<td>11.1</td>
<td>0</td>
<td>11.1</td>
</tr>
<tr>
<td>SLE(5)</td>
<td>1</td>
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<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>%</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>20</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>WG(3)</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>%</td>
<td>66.6</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>33.3</td>
<td>33.3</td>
<td>33.3</td>
<td>33.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM(4)</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>%</td>
<td>50</td>
<td>100</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>75</td>
<td>75</td>
<td>25</td>
<td>25</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Takay(1)</td>
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<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Alio(2)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPF(13)</td>
<td>10</td>
<td>11</td>
<td>2</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>5</td>
<td>3</td>
<td>6</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>%</td>
<td>76.9</td>
<td>84.6</td>
<td>15.4</td>
<td>53.8</td>
<td>46.2</td>
<td>53.8</td>
<td>38.5</td>
<td>23.1</td>
<td>46.2</td>
<td>15.4</td>
<td></td>
</tr>
<tr>
<td>CV(49)</td>
<td>23</td>
<td>34</td>
<td>8</td>
<td>7</td>
<td>7</td>
<td>13</td>
<td>17</td>
<td>5</td>
<td>12</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>%</td>
<td>46.9</td>
<td>69.4</td>
<td>16.3</td>
<td>14.3</td>
<td>14.3</td>
<td>26.5</td>
<td>34.7</td>
<td>10.2</td>
<td>24.5</td>
<td>8.2</td>
<td>8.2</td>
</tr>
</tbody>
</table>

CM = cardiomegaly, G/G = ground-glass, PA = pulmonary artery

On chest radiograph also, the prevalence of ground-glass opacities, linear opacities, honeycombing and bronchiectasis was higher among IPF patients than that for CVDs. Air space consolidation, had slight higher incidence in CVD patients than that for PM/DM. Cardiomegaly also had higher incidence among CVD patients than for IPF. The Collagen vascular disease that had an incidence of pulmonary fibrosis (honeycombing) that followed the incidence of IPF was scleroderma patients. Honeycombing incidence was 53.8% for IPF, 25.8% for PSS, 25% for PM/DM, and 5.6% for RA.
### Table (7): prevalence of HRCT signs in patients with different CVD and IPF

<table>
<thead>
<tr>
<th>Disease</th>
<th>G/G</th>
<th>Linear</th>
<th>H/C</th>
<th>Nodules</th>
<th>A/S</th>
<th>B/sis</th>
<th>Emphysema</th>
<th>Malign</th>
<th>LNs</th>
<th>PA</th>
<th>Pleural</th>
<th>Esophagus</th>
<th>CM+ thick</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS(32)%</td>
<td>23</td>
<td>71 9</td>
<td>24</td>
<td>37.5</td>
<td>12</td>
<td>18</td>
<td>3</td>
<td>21</td>
<td>1</td>
<td>1</td>
<td>16</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>RA(19)%</td>
<td>7</td>
<td>36.8</td>
<td>8</td>
<td>42.1</td>
<td>1</td>
<td>8</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Mix(3)%</td>
<td>2</td>
<td>66.6</td>
<td>3</td>
<td>100</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>SLE(5)%</td>
<td>4</td>
<td>80</td>
<td>4</td>
<td>100</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>WG(3)%</td>
<td>2</td>
<td>66.6</td>
<td>3</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>PM/DM(4)%</td>
<td>4</td>
<td>100</td>
<td>4</td>
<td>100</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Takay(1)%</td>
<td>1</td>
<td>100</td>
<td>1</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Amio(2)%</td>
<td>2</td>
<td>100</td>
<td>2</td>
<td>100</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>IPF(14)%</td>
<td>13</td>
<td>92.9</td>
<td>13</td>
<td>92.9</td>
<td>11</td>
<td>9</td>
<td>0</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>CVD(67)%</td>
<td>43</td>
<td>64.2</td>
<td>47</td>
<td>70.1</td>
<td>19</td>
<td>33</td>
<td>6</td>
<td>32</td>
<td>3</td>
<td>2</td>
<td>30</td>
<td>19</td>
<td>18</td>
</tr>
</tbody>
</table>

(GG = ground glass opacity, H/C = honeycomb, A/S = air-space consolidation, B/sis = bronchiectasis, Nod= nodules, LNs = lymph nodes, PA = pulmonary artery, CM = Cardiomegaly).

On HRCT, all the HRCT signs used for assessment of ILD and pulmonary fibrosis had a higher incidence in patients with IPF than in patients with a collagen vascular disease. The diseases that followed IPF in incidence of pulmonary fibrosis (e.g. honey combing) was in descending order: IPF (78.6%), PM/DM (75%), MCTD (66.6%), PSS (37.5%), SLE (20%), then RA (5.3%).

CVD patients compared to IPF patients had a higher incidence of air-space consolidation (9.1% compared to 0%), pericardial thickening &/or effusion (18.2%
compared to 7.1%), lung cancer (3% compared to 0%), and emphysema (4.5% compared to 0%).

Table (8): Nature and distribution of pulmonary abnormalities in CVD patients on HRCT-UML

<table>
<thead>
<tr>
<th></th>
<th>Ground glass</th>
<th>Linear opacity</th>
<th>Honeycomb</th>
<th>Nodules</th>
<th>Bronchiectasis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>U</td>
<td>M</td>
<td>L</td>
<td>U</td>
<td>M</td>
</tr>
<tr>
<td>PSS(32)%</td>
<td>37.5</td>
<td>17</td>
<td>23</td>
<td>13</td>
<td>20</td>
</tr>
<tr>
<td>RA(19)%</td>
<td>4</td>
<td>4</td>
<td>7</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Mixed(3)%</td>
<td>33.3</td>
<td>33.3</td>
<td>66.6</td>
<td>33.3</td>
<td>66.6</td>
</tr>
<tr>
<td>PM(4)%</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>SLE(5)%</td>
<td>20</td>
<td>40</td>
<td>80</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>W.G(3)%</td>
<td>33.3</td>
<td>33.3</td>
<td>66.6</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Takay(1)%</td>
<td>33.3</td>
<td>33.3</td>
<td>66.6</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Amiodrone(2)%</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>CVD=67%</td>
<td>23</td>
<td>43</td>
<td>43</td>
<td>23</td>
<td>43</td>
</tr>
<tr>
<td>IPF(14)%</td>
<td>64.3</td>
<td>78.6</td>
<td>92.8</td>
<td>64.3</td>
<td>78.6</td>
</tr>
</tbody>
</table>

(U = upper, M = middle, L = lower, the lower value in the same row is % value).

In IPF, the prevalence of all radiological signs in the three lung zones were higher than that for CVDs except for the pulmonary nodules which had higher prevalence in upper lung zones in CVDs (26.9%) compared to 7.1% in IPF. The incidence of honeycombing in the 3 lung zones was much higher in IPF than that for CVDs. Also the incidence of other signs in upper and middle lung zones was much higher in IPF than that for CVDs. This means that the prevalence ILD and pulmonary fibrosis is much common in upper and middle lung zones in IPF.
Table (9): Prevalence of CT signs on Spiral HRCT of the lower part of middle lung zones

<table>
<thead>
<tr>
<th>DIS</th>
<th>G/G</th>
<th>Linear</th>
<th>H/C</th>
<th>Nod</th>
<th>A/S</th>
<th>B/sis</th>
<th>Emphy</th>
<th>Malign</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS(28)</td>
<td>23(82.1)</td>
<td>21(75)</td>
<td>11(39.3)</td>
<td>12(42.9)</td>
<td>2(7.1)</td>
<td>1(53.6)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>RA(5)</td>
<td>4(80)</td>
<td>5(100)</td>
<td>0</td>
<td>1(20)</td>
<td>0</td>
<td>1(20)</td>
<td>1(20)</td>
<td>0</td>
</tr>
<tr>
<td>PM(4)</td>
<td>4(100)</td>
<td>4(100)</td>
<td>3(75)</td>
<td>1(25)</td>
<td>0</td>
<td>3(75)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SLE(1)</td>
<td>1(100)</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Taka(1)</td>
<td>1(100)</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Amio(2)</td>
<td>2(100)</td>
<td>2(100)</td>
<td>2(100)</td>
<td>2(100)</td>
<td>0</td>
<td>1(50)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other(3)</td>
<td>0</td>
<td>1(33.3)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1(33.3)</td>
<td>0</td>
</tr>
<tr>
<td>CVD(39)</td>
<td>33(84.6)</td>
<td>32(82.1)</td>
<td>14(35.9)</td>
<td>16(41.0)</td>
<td>2(5.1)</td>
<td>21(53.8)</td>
<td>1(2.6)</td>
<td>0</td>
</tr>
<tr>
<td>IPF(9)</td>
<td>8(88.9)</td>
<td>8(88.9)</td>
<td>7(77.8)</td>
<td>7(77.8)</td>
<td>0</td>
<td>7(77.8)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

(The value in parenthesis is a % value)

On Spiral HRCT, 9 patients with IPF underwent the same spiral thin sections that 39 patients with CVD go. All CT signs had a higher incidence among patients with IPF than patients with CVD except for air-space consolidation and emphysema which had a higher incidence in CVD patients than that for IPF patients. The incidence of ground glass and linear opacities were very close in CVD and IPF patients.

Table (10): Comparison of prevalence of radiological signs in CVD patients using different imaging techniques

<table>
<thead>
<tr>
<th>Technique</th>
<th>G/G</th>
<th>Linear</th>
<th>Honeycomb</th>
<th>Nodules</th>
<th>Bronchiectasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest x-ray(48)</td>
<td>23(47.9)</td>
<td>33(68.8)</td>
<td>7(14.6)</td>
<td>4(8.3)</td>
<td>7(14.6)</td>
</tr>
<tr>
<td>HRCT(66)</td>
<td>42(63.6)</td>
<td>46(69.7)</td>
<td>19(28.8)</td>
<td>33(50)</td>
<td>31(47)</td>
</tr>
<tr>
<td>HRCT-L(66)</td>
<td>43(65.2)</td>
<td>46(69.7)</td>
<td>18(27.3)</td>
<td>30(45.5)</td>
<td>21(31.8)</td>
</tr>
<tr>
<td>HRCT-M(66)</td>
<td>29(43.9)</td>
<td>31(47.0)</td>
<td>9(13.6)</td>
<td>16(24.2)</td>
<td>13(19.7)</td>
</tr>
<tr>
<td>Spiral(39)</td>
<td>33(84.6)</td>
<td>32(82.1)</td>
<td>14(35.9)</td>
<td>16(41.0)</td>
<td>21(53.8)</td>
</tr>
</tbody>
</table>

(The value in parenthesis is a % value)
Table (11): Comparison of Prevalence of radiological signs in IPF patients using different imaging techniques

<table>
<thead>
<tr>
<th>Technique</th>
<th>G/G</th>
<th>Linear</th>
<th>Honeycomb</th>
<th>Nodules</th>
<th>Bronchiectasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest x-ray (13)</td>
<td>10(76.9)</td>
<td>11(84.6)</td>
<td>7(53.8)</td>
<td>2(15.4)</td>
<td>6(46.2)</td>
</tr>
<tr>
<td>HRCT (14)</td>
<td>13(92.9)</td>
<td>13(92.9)</td>
<td>11(78.6)</td>
<td>9(64.3)</td>
<td>12(85.6)</td>
</tr>
<tr>
<td>HRCT-L (14)</td>
<td>13(92.9)</td>
<td>13(92.9)</td>
<td>11(78.6)</td>
<td>9(64.3)</td>
<td>12(85.7)</td>
</tr>
<tr>
<td>HRCT-M (14)</td>
<td>11(78.6)</td>
<td>13(92.9)</td>
<td>10(71.4)</td>
<td>4(28.6)</td>
<td>9(64.3)</td>
</tr>
<tr>
<td>Spiral (9)</td>
<td>8(88.9)</td>
<td>8(88.9)</td>
<td>7(77.8)</td>
<td>7(77.8)</td>
<td>7(77.8)</td>
</tr>
</tbody>
</table>

(The value in parenthesis is a % value)

The highest incidence of ground glass opacity was seen on spiral CT more than HRCT and Chest radiographs. Also, the highest incidence of linear opacities was seen on spiral HRCT. The same thing is applied for honeycombing and bronchiectasis. But pulmonary nodules were having a higher incidence on HRCT for the whole lungs simply because the score include the whole lung in HRCT not a small section of the middle zones as in spiral HRCT. So, it is clear that spiral HRCT is an excellent technique for detection of lung abnormalities in CVD.

Table (12): Mean score of Chest x-ray signs in different CVD and IPF patients (% value)

<table>
<thead>
<tr>
<th></th>
<th>Linear</th>
<th>G/G</th>
<th>H/C</th>
<th>A/S</th>
<th>B/sis</th>
<th>PA</th>
<th>Pleura</th>
<th>LN</th>
<th>↓Lung volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS(18)</td>
<td>15</td>
<td>14</td>
<td>5</td>
<td>6</td>
<td>15</td>
<td>7</td>
<td>6</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>RA(18)</td>
<td>8</td>
<td>4</td>
<td>2</td>
<td>6</td>
<td>5</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>SLE(5)</td>
<td>8</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>WG(3)</td>
<td>11</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>PM(4)</td>
<td>19</td>
<td>8</td>
<td>3</td>
<td>13</td>
<td>8</td>
<td>13</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Amio(2)</td>
<td>17</td>
<td>3</td>
<td>0</td>
<td>8</td>
<td>0</td>
<td>8</td>
<td>8</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>IPF(13)</td>
<td>24</td>
<td>17</td>
<td>9</td>
<td>17</td>
<td>22</td>
<td>9</td>
<td>6</td>
<td>1</td>
<td>8</td>
</tr>
</tbody>
</table>
Table (13): Mean score of HRCT signs found in CVD and IPF (% value)

<table>
<thead>
<tr>
<th></th>
<th>GG</th>
<th>Linear</th>
<th>H/C</th>
<th>Nodul</th>
<th>A/S</th>
<th>B/sis</th>
<th>Emp</th>
<th>Malig</th>
<th>LN</th>
<th>PA</th>
<th>Pleura</th>
<th>eso</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS(32)</td>
<td>27</td>
<td>20</td>
<td>6</td>
<td>28</td>
<td>2</td>
<td>36</td>
<td>2</td>
<td>1</td>
<td>44</td>
<td>34</td>
<td>25</td>
<td>56</td>
</tr>
<tr>
<td>RA(19)</td>
<td>8</td>
<td>7</td>
<td>2</td>
<td>26</td>
<td>4</td>
<td>12</td>
<td>5</td>
<td>1</td>
<td>16</td>
<td>21</td>
<td>16</td>
<td>5</td>
</tr>
<tr>
<td>MCTD(3)</td>
<td>27</td>
<td>27</td>
<td>17</td>
<td>17</td>
<td>0</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>67</td>
<td>33</td>
<td>67</td>
</tr>
<tr>
<td>SLE(5)</td>
<td>19</td>
<td>20</td>
<td>7</td>
<td>17</td>
<td>13</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>40</td>
<td>20</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>WG(3)</td>
<td>27</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>33</td>
<td>33</td>
<td>33</td>
<td>0</td>
</tr>
<tr>
<td>PM/DM(4)</td>
<td>30</td>
<td>28</td>
<td>8</td>
<td>33</td>
<td>0</td>
<td>38</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>75</td>
<td>0</td>
</tr>
<tr>
<td>Other(8)</td>
<td>9</td>
<td>5</td>
<td>0</td>
<td>19</td>
<td>0</td>
<td>31</td>
<td>6</td>
<td>0</td>
<td>38</td>
<td>25</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Amiod(2)</td>
<td>58</td>
<td>30</td>
<td>0</td>
<td>17</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>50</td>
<td>100</td>
<td>50</td>
</tr>
<tr>
<td>IPF(14)</td>
<td>36</td>
<td>41</td>
<td>24</td>
<td>33</td>
<td>0</td>
<td>63</td>
<td>0</td>
<td>0</td>
<td>53</td>
<td>47</td>
<td>53</td>
<td>33</td>
</tr>
</tbody>
</table>

The mean score for ground glass opacities in different CVD and IPF was in descending order: 58% for amiodarone toxicity, 36% for IPF, 30% for PM/DM, 27% for (PSS, MCTD, & WG), 19% for SLE, and 8% for RA. The mean score for honeycombing was: 24% for IPF, 17% for MCTD, 8% for PM/DM, 7% for SLE, 6% for PSS and 2% for RA.

Table (14): Mean score of HRCT signs on HRCT–UML (% value)

<table>
<thead>
<tr>
<th></th>
<th>GG</th>
<th>Linear</th>
<th>H/C</th>
<th>Nod</th>
<th>B/sis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>U</td>
<td>M</td>
<td>L</td>
<td>U</td>
<td>M</td>
</tr>
<tr>
<td>PSS(32)</td>
<td>13</td>
<td>26</td>
<td>41</td>
<td>8</td>
<td>20</td>
</tr>
<tr>
<td>RA(19)</td>
<td>6</td>
<td>7</td>
<td>12</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>SLE(5)</td>
<td>4</td>
<td>12</td>
<td>40</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>WG(3)</td>
<td>13</td>
<td>20</td>
<td>47</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>PM/DM(4)</td>
<td>15</td>
<td>30</td>
<td>45</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>IPF(14)</td>
<td>24</td>
<td>35</td>
<td>50</td>
<td>28</td>
<td>41</td>
</tr>
</tbody>
</table>

U= upper, M= middle, L= lower

As we can see here, the mean score of CT signs in all diseases including IPF had a higher mean score in lower lung zones more than the score for the middle zones and that for the middle zones was higher than that for upper lung zones except for bronchiectasis score in RA was higher in the upper lung zones (11%) than that for
middle lung zones (8%). It means that bronchiectasis in RA can occur alone not secondary to lung fibrosis. Also, the mean score of pulmonary nodules was higher in upper zones more than the middle zones in RA and SLE patients.

<table>
<thead>
<tr>
<th></th>
<th>GG</th>
<th>Linear</th>
<th>H/C</th>
<th>Nodul</th>
<th>A/S</th>
<th>B/sis</th>
<th>Emphysema</th>
<th>Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS(28)</td>
<td>38</td>
<td>29</td>
<td>0</td>
<td>20</td>
<td>0</td>
<td>48</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>RA(5)</td>
<td>18</td>
<td>24</td>
<td>0</td>
<td>20</td>
<td>0</td>
<td>20</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>SLE(1)</td>
<td>60</td>
<td>60</td>
<td>0</td>
<td>50</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PM/DM(4)</td>
<td>40</td>
<td>45</td>
<td>13</td>
<td>13</td>
<td>0</td>
<td>75</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Others (3)</td>
<td>0</td>
<td>7</td>
<td>13</td>
<td>13</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>33</td>
</tr>
<tr>
<td>Amiod(2)</td>
<td>70</td>
<td>50</td>
<td>10</td>
<td>75</td>
<td>0</td>
<td>50</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IPF(9)</td>
<td>42</td>
<td>51</td>
<td>27</td>
<td>67</td>
<td>0</td>
<td>67</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table (15): Mean score of HRCT signs seen by spiral HRCT (% value)

We will compare mean score of the 4 major groups by spiral CT

Ground glass mean score was: 42% for IPF, 40% for PM/DM, 38% for PSS, and 18% for RA.

Linear opacities mean score was 51% for IPF, 45% for PM/DM, 29% for PSS, and 24% for RA.

Honeycomb mean score was 27% for IPF, 13% for PM/DM, 7% for PSS, and 0% for RA.

Pulmonary nodules mean score was 67% for IPF, 30% for PSS, 20% for RA, and 13% for PM/DM.

Bronchiectasis mean score was 67% for IPF, 75% for PM/DM, 48% for PSS, and 20% for RA.
Table (16): Cephalocaudal distribution of ground-glass opacity on HRCT for different CVD patients (incidence)

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Right Lung</th>
<th></th>
<th></th>
<th></th>
<th>Left Lung</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Upper</td>
<td>Middle</td>
<td>Lower</td>
<td>Upper</td>
<td>Middle</td>
<td>Lower</td>
<td>Upper</td>
<td>Middle</td>
</tr>
<tr>
<td>PSS (n=32)</td>
<td>12 (37.5)</td>
<td>17 (53.1)</td>
<td>23 (71.9)</td>
<td>12 (37.5)</td>
<td>17 (53.1)</td>
<td>23 (71.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA (n=19)</td>
<td>4 (21.1)</td>
<td>4 (21.1)</td>
<td>7 (36.8)</td>
<td>4 (21.1)</td>
<td>4 (21.1)</td>
<td>7 (36.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCTD (n=3)</td>
<td>1 (33.3)</td>
<td>1 (33.3)</td>
<td>2 (66.6)</td>
<td>1 (33.3)</td>
<td>1 (33.3)</td>
<td>2 (66.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE (n=5)</td>
<td>1 (20)</td>
<td>1 (20)</td>
<td>3 (60)</td>
<td>1 (20)</td>
<td>1 (20)</td>
<td>4 (80)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>W.G (n=3)</td>
<td>1 (33.3)</td>
<td>1 (33.3)</td>
<td>2 (66.6)</td>
<td>1 (33.3)</td>
<td>1 (33.3)</td>
<td>2 (66.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM/DM (n=4)</td>
<td>3 (75)</td>
<td>3 (75)</td>
<td>4 (100)</td>
<td>3 (75)</td>
<td>3 (75)</td>
<td>4 (100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Takay (n=1)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiod (n=2)</td>
<td>2 (100)</td>
<td>2 (100)</td>
<td>2 (100)</td>
<td>2 (100)</td>
<td>2 (100)</td>
<td>2 (100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVD (n=67)</td>
<td>23 (34.3)</td>
<td>28 (41.8)</td>
<td>42 (62.7)</td>
<td>23 (34.3)</td>
<td>28 (41.8)</td>
<td>43 (64.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPF (n=14)</td>
<td>9 (64.3)</td>
<td>11 (78.6)</td>
<td>13 (92.9)</td>
<td>8 (57.1)</td>
<td>11 (78.6)</td>
<td>13 (92.9)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(The value in parenthesis is a % value)

Table (17): Cephalocaudal distribution of honeycombing on HRCT for CVD and IPF patients (incidence)

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Right Lung</th>
<th></th>
<th></th>
<th></th>
<th>Left Lung</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Upper</td>
<td>Middle</td>
<td>Lower</td>
<td>Upper</td>
<td>Middle</td>
<td>Lower</td>
<td>Upper</td>
<td>Middle</td>
</tr>
<tr>
<td>PSS (n=32)</td>
<td>1 (3.1)</td>
<td>5 (15.6)</td>
<td>12 (37.5)</td>
<td>0</td>
<td>5 (15.6)</td>
<td>12 (37.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA (n=19)</td>
<td>1 (5.2)</td>
<td>1 (5.2)</td>
<td>1 (5.2)</td>
<td>1 (5.2)</td>
<td>1 (5.2)</td>
<td>1 (5.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCTD (n=3)</td>
<td>2 (66.6)</td>
<td>1 (33.3)</td>
<td>1 (33.3)</td>
<td>1 (33.3)</td>
<td>1 (33.3)</td>
<td>1 (33.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE (n=5)</td>
<td>1 (20)</td>
<td>1 (20)</td>
<td>1 (20)</td>
<td>1 (20)</td>
<td>1 (20)</td>
<td>1 (20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>W.G (n=3)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM/DM (n=4)</td>
<td>0</td>
<td>1 (25)</td>
<td>3 (75)</td>
<td>0</td>
<td>0</td>
<td>3 (75)</td>
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<td></td>
</tr>
<tr>
<td>Takay (n=1)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiod (n=2)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVD (n=67)</td>
<td>5 (7.5)</td>
<td>9 (13.4)</td>
<td>18 (26.9)</td>
<td>3 (4.5)</td>
<td>9 (11.9)</td>
<td>18 (26.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPF (n=14)</td>
<td>9 (64.3)</td>
<td>10 (71.4)</td>
<td>11 (78.6)</td>
<td>8 (57.1)</td>
<td>11 (78.6)</td>
<td>11 (78.6)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(The value in parenthesis is a % value)

Table (18): Cephalocaudal distribution of air space consolidation in each disease on HRCT (incidence)

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Right Lung</th>
<th></th>
<th></th>
<th></th>
<th>Left Lung</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Upper</td>
<td>Middle</td>
<td>Lower</td>
<td>Upper</td>
<td>Middle</td>
<td>Lower</td>
<td>Upper</td>
<td>Middle</td>
</tr>
<tr>
<td>PSS (n=32)</td>
<td>0</td>
<td>0</td>
<td>3 (9.4)</td>
<td>0</td>
<td>0</td>
<td>2 (6.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA (n=19)</td>
<td>0</td>
<td>1 (5.3)</td>
<td>1 (5.3)</td>
<td>0</td>
<td>1 (5.3)</td>
<td>2 (10.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCTD (n=3)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE (n=5)</td>
<td>1 (20)</td>
<td>2 (40)</td>
<td>1 (20)</td>
<td>1 (20)</td>
<td>2 (40)</td>
<td>1 (20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>W.G (n=3)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM/DM (n=4)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Takay (n=1)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiod (n=2)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVD (n=67)</td>
<td>1 (1.5)</td>
<td>3 (4.5)</td>
<td>5 (7.5)</td>
<td>1 (1.5)</td>
<td>3 (4.5)</td>
<td>5 (7.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPF (n=14)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
As we see here the variable means of CT score of ground-glass opacities (G/G), linear opacities (linear), honeycombing (H/C), pulmonary nodules, and traction bronchiectasis in 48 patients with collagen vascular disease are higher on spiral CT than on HRCT in middle lung zones (HRCT-M) but these values are slightly higher on HRCT taken in lower lung zones (HRCT-L), this is because our spiral section was 3 cm below the carina.

Table (23): Paired T-test for Spiral and HRCT-M Group

| Variable            | Label        | N  | Mean     | Std Error | T           | Prob>|T| |
|---------------------|--------------|----|----------|-----------|-------------|---------------|
| Ground glass opacity| 48           | 0.1041667 | 0.2495995 | -4.4892211 | 0.0001      |
| Linear opacities    | 48           | -1.1458333 | 0.2325269 | -4.9277444 | 0.0001      |
| Honeycomb           | 48           | -0.4791667 | 0.1427615 | -3.3564146 | 0.0016      |
| Pulmonary nodules   | 48           | -0.2708333 | 0.1143110 | -2.3692673 | 0.0220      |
| Bronchiectasis      | 48           | -0.3958333 | 0.1419831 | -2.7878902 | 0.0076      |

When comparing variable mean of spiral and HRCT-M, it was found $P<0.05$, that means it is statistically significant.

Table (24): Paired T-test for Spiral and HRCT-L Group

| Variable            | Label        | N  | Mean     | Std Error | T           | Prob>|T| |
|---------------------|--------------|----|----------|-----------|-------------|---------------|
| Ground glass opacity| 48           | 0.5833333 | 0.2415841 | 2.4146179  | 0.0197      |
| Linear opacities    | 48           | 0.5833333 | 0.2015748 | 2.8938807  | 0.0058      |
| Honeycomb           | 48           | 0.3541667 | 0.2217947 | 1.5968220  | 0.1170      |
| Pulmonary nodules   | 48           | 0.1041667 | 0.1236257 | 0.8425970  | 0.4037      |
| Bronchiectasis      | 48           | 0.1666667 | 0.1407091 | 1.1844767  | 0.2422      |

On the other hand, on comparing spiral means for CT parameters with that of HRCT-L, it was found in most parameters it is not statistically significant ($p>0.05$).
### Table (25): PFTs (Restrictive ventilation and obstructive defects) in CVD and IPF patients

<table>
<thead>
<tr>
<th># of Cases</th>
<th>Restrictive ventilation</th>
<th></th>
<th>Obstructive defect</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild</td>
<td>Moderate</td>
<td>severe</td>
<td>Mild</td>
</tr>
<tr>
<td>PSS</td>
<td>27</td>
<td>10</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>37.04%</td>
<td>37.04%</td>
<td>3.70%</td>
<td>22.22%</td>
</tr>
<tr>
<td>RA</td>
<td>9</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>33.33%</td>
<td>11.11%</td>
<td>0.00%</td>
<td>33.33%</td>
</tr>
<tr>
<td>SLE</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>50.00%</td>
<td>0.00%</td>
<td>50.00%</td>
<td>0.00%</td>
</tr>
<tr>
<td>MCTD</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>0.00%</td>
<td>0.00%</td>
<td>50.00%</td>
<td>0.00%</td>
</tr>
<tr>
<td>PM/DM</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>0.00%</td>
<td>33.33%</td>
<td>33.33%</td>
<td>0.00%</td>
</tr>
<tr>
<td>WG</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Amio</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>IPF</td>
<td>9</td>
<td>2</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>22.22%</td>
<td>55.56%</td>
<td>33.33%</td>
<td>0.00%</td>
</tr>
<tr>
<td>CVD</td>
<td>44</td>
<td>31.82%</td>
<td>29.55%</td>
<td>9.09%</td>
</tr>
</tbody>
</table>
Table (26): PFTs (Diffusion impairment and % DLCO) in CVD and IPF patients

<table>
<thead>
<tr>
<th></th>
<th># of Cases</th>
<th>Diffusion Impairment</th>
<th>%DLCO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>PSS</td>
<td>27</td>
<td>9  33.3%</td>
<td>6  22.2%</td>
</tr>
<tr>
<td>RA</td>
<td>9</td>
<td>1  11.1%</td>
<td>2  22.2%</td>
</tr>
<tr>
<td>SLE</td>
<td>2</td>
<td>0  0%</td>
<td>0  0%</td>
</tr>
<tr>
<td>MCTD</td>
<td>2</td>
<td>0  0%</td>
<td>0  0%</td>
</tr>
<tr>
<td>PM/DM</td>
<td>3</td>
<td>0  0%</td>
<td>1  33.3%</td>
</tr>
<tr>
<td>WG</td>
<td>1</td>
<td>0  0%</td>
<td>1  33.3%</td>
</tr>
<tr>
<td>Amio</td>
<td>2</td>
<td>0  0%</td>
<td>1  100%</td>
</tr>
<tr>
<td>IPF</td>
<td>9</td>
<td>1  0.1%</td>
<td>3  33.3%</td>
</tr>
<tr>
<td>CVD</td>
<td>44</td>
<td>22.73%</td>
<td>22.73%</td>
</tr>
</tbody>
</table>

Table (27): Total number and percentage of patients regarding PFTs

<table>
<thead>
<tr>
<th>Disease</th>
<th>Restrictive impairment</th>
<th>Obstructive defect</th>
<th>Diffusion impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSS(27)</td>
<td>21 (77.7%)</td>
<td>7 (25.9%)</td>
<td>26 (96.3%)</td>
</tr>
<tr>
<td>RA(9)</td>
<td>4 (44.4%)</td>
<td>4 (44.4%)</td>
<td>4 (44.4%)</td>
</tr>
<tr>
<td>SLE(2)</td>
<td>2 (100%)</td>
<td>0</td>
<td>2 (100%)</td>
</tr>
<tr>
<td>PM/DM(3)</td>
<td>3 (100%)</td>
<td>0</td>
<td>3 (100%)</td>
</tr>
<tr>
<td>MCTD(2)</td>
<td>2 (100%)</td>
<td>0</td>
<td>2 (100%)</td>
</tr>
<tr>
<td>IPF(9)</td>
<td>9 (100%)</td>
<td>0</td>
<td>9 (100%)</td>
</tr>
<tr>
<td>Amiodarone(2)</td>
<td>2 (100%)</td>
<td>0</td>
<td>2 (100%)</td>
</tr>
</tbody>
</table>
Table (28): %DLCO in group 1 HRCT (no signs of ILD)

<table>
<thead>
<tr>
<th>#</th>
<th>Diagnosis</th>
<th>%DLCO</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>PSS</td>
<td>41%</td>
</tr>
<tr>
<td>52</td>
<td>PSS</td>
<td>66%</td>
</tr>
<tr>
<td>93</td>
<td>PSS</td>
<td>51%</td>
</tr>
<tr>
<td>94</td>
<td>PSS</td>
<td>63%</td>
</tr>
<tr>
<td>68</td>
<td>RA</td>
<td>92%</td>
</tr>
<tr>
<td>83</td>
<td>Occ. Exposure</td>
<td>90%</td>
</tr>
<tr>
<td>64</td>
<td>Asthma</td>
<td>125%</td>
</tr>
</tbody>
</table>

In this group, 7 patients underwent pulmonary function tests with the mean DLCO was 75.4%. HRCT scans of these patients were interpreted free from signs of interstitial lung disease.
Table (29): % DLCO in group 2 HRCT patients.

<table>
<thead>
<tr>
<th>#</th>
<th>Diagnosis</th>
<th>%DLCO</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>PSS</td>
<td>45%</td>
</tr>
<tr>
<td>35</td>
<td>PSS</td>
<td>63%</td>
</tr>
<tr>
<td>41</td>
<td>PSS</td>
<td>29%</td>
</tr>
<tr>
<td>54</td>
<td>PSS</td>
<td>41%</td>
</tr>
<tr>
<td>58</td>
<td>PSS</td>
<td>30%</td>
</tr>
<tr>
<td>67</td>
<td>PSS</td>
<td>54%</td>
</tr>
<tr>
<td>70</td>
<td>PSS</td>
<td>40%</td>
</tr>
<tr>
<td>73</td>
<td>PSS</td>
<td>44%</td>
</tr>
<tr>
<td>81</td>
<td>PSS</td>
<td>41%</td>
</tr>
<tr>
<td>89</td>
<td>PSS</td>
<td>35%</td>
</tr>
<tr>
<td>91</td>
<td>PSS</td>
<td>57%</td>
</tr>
<tr>
<td>92</td>
<td>PSS</td>
<td>42%</td>
</tr>
<tr>
<td>13</td>
<td>RA</td>
<td>44%</td>
</tr>
<tr>
<td>14</td>
<td>RA</td>
<td>43%</td>
</tr>
<tr>
<td>15</td>
<td>RA</td>
<td>44%</td>
</tr>
<tr>
<td>37</td>
<td>RA</td>
<td>43%</td>
</tr>
<tr>
<td>42</td>
<td>RA</td>
<td>56%</td>
</tr>
<tr>
<td>53</td>
<td>RA</td>
<td>26%</td>
</tr>
<tr>
<td>60</td>
<td>RA</td>
<td>46%</td>
</tr>
<tr>
<td>12</td>
<td>SLE</td>
<td>43%</td>
</tr>
<tr>
<td>85</td>
<td>SLE</td>
<td>18%</td>
</tr>
<tr>
<td>71</td>
<td>MCTD</td>
<td>38%</td>
</tr>
<tr>
<td>29</td>
<td>DM</td>
<td>39%</td>
</tr>
<tr>
<td>24</td>
<td>W G</td>
<td>44%</td>
</tr>
<tr>
<td>69</td>
<td>Amiodarone</td>
<td>43%</td>
</tr>
<tr>
<td>86</td>
<td>Amiodarone</td>
<td>25%</td>
</tr>
<tr>
<td>59</td>
<td>IPF</td>
<td>54%</td>
</tr>
<tr>
<td>65</td>
<td>IPF</td>
<td>37%</td>
</tr>
<tr>
<td>76</td>
<td>Ground glass</td>
<td>57%</td>
</tr>
<tr>
<td>66</td>
<td>Bronchiectasis</td>
<td>44%</td>
</tr>
<tr>
<td>63</td>
<td>Emphysema</td>
<td>39%</td>
</tr>
<tr>
<td>44</td>
<td>Sarcoid</td>
<td>83%</td>
</tr>
<tr>
<td>38</td>
<td>Heat Failure</td>
<td>55%</td>
</tr>
</tbody>
</table>

Group 2 patients whose HRCT scans were abnormal and contain HRCT signs of ILD but without honeycomb, 33 patients underwent PFTs with the mean DLCO = 43.7%
Table (30): % DLCO in group 3 HRCT patients.

<table>
<thead>
<tr>
<th>#</th>
<th>Diagnosis</th>
<th>%DLCO</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>PSS</td>
<td>5%</td>
</tr>
<tr>
<td>34</td>
<td>Crest</td>
<td>62%</td>
</tr>
<tr>
<td>47</td>
<td>Crest</td>
<td>41%</td>
</tr>
<tr>
<td>72</td>
<td>PSS</td>
<td>67%</td>
</tr>
<tr>
<td>74</td>
<td>PSS</td>
<td>27%</td>
</tr>
<tr>
<td>77</td>
<td>PSS</td>
<td>39%</td>
</tr>
<tr>
<td>78</td>
<td>PSS</td>
<td>57%</td>
</tr>
<tr>
<td>80</td>
<td>PSS</td>
<td>30%</td>
</tr>
<tr>
<td>87</td>
<td>PSS</td>
<td>33%</td>
</tr>
<tr>
<td>88</td>
<td>PSS</td>
<td>30%</td>
</tr>
<tr>
<td>90</td>
<td>Crest</td>
<td>23%</td>
</tr>
<tr>
<td>20</td>
<td>RA</td>
<td>33%</td>
</tr>
<tr>
<td>31</td>
<td>MCT</td>
<td>15%</td>
</tr>
<tr>
<td>28</td>
<td>PM</td>
<td>22%</td>
</tr>
<tr>
<td>62</td>
<td>DM</td>
<td>58%</td>
</tr>
<tr>
<td>36</td>
<td>IPF</td>
<td>44%</td>
</tr>
<tr>
<td>39</td>
<td>IPF</td>
<td>35%</td>
</tr>
<tr>
<td>43</td>
<td>IPF</td>
<td>62%</td>
</tr>
<tr>
<td>46</td>
<td>IPF</td>
<td>23%</td>
</tr>
<tr>
<td>48</td>
<td>IPF</td>
<td>36%</td>
</tr>
<tr>
<td>50</td>
<td>IPF</td>
<td>21%</td>
</tr>
<tr>
<td>55</td>
<td>IPF</td>
<td>36%</td>
</tr>
</tbody>
</table>

In Group 3 patients in which HRCT scans were abnormal with honeycomb change, 22 underwent PFTs with the mean DLCO was 36.3% 
62 patients underwent pulmonary function tests in the 3 groups. 
PFTs also suggest airway obstruction, small airway obstruction as in smoking, or the defect due to obesity, or there is occult asthma or if there is respiratory muscle weakness.
### Table (31): BAL Findings in patients with Group 2 HRCT (without honeycomb)

<table>
<thead>
<tr>
<th>#</th>
<th>Diag</th>
<th>BAL</th>
<th>Mac</th>
<th>Lym</th>
<th>Neut</th>
<th>Eosin</th>
<th>Hist</th>
<th>Squa</th>
<th>Colu</th>
<th>Lym</th>
<th>RBCs</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>PSS</td>
<td>RML</td>
<td>7</td>
<td>5</td>
<td>2</td>
<td></td>
<td>+</td>
<td>Few</td>
<td>+</td>
<td>Few</td>
<td>+</td>
<td>Inflammation.acute.mild</td>
</tr>
<tr>
<td>30</td>
<td>PSS</td>
<td>RML</td>
<td>20</td>
<td>4</td>
<td>3</td>
<td>+</td>
<td>Few</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Inflammation.acute</td>
</tr>
<tr>
<td>35</td>
<td>PSS</td>
<td>LLL</td>
<td>67</td>
<td>28</td>
<td>3</td>
<td>1.2</td>
<td>+</td>
<td>Few</td>
<td>+</td>
<td></td>
<td></td>
<td>Lymphocytosis.reactive changes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LLL</td>
<td>79</td>
<td>17</td>
<td>2.5</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Inflammation.chronic.mixed</td>
</tr>
<tr>
<td>41</td>
<td>PSS</td>
<td>RML</td>
<td>14</td>
<td>3</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Inflammation.acute</td>
<td></td>
</tr>
<tr>
<td>67</td>
<td>PSS</td>
<td>RLL</td>
<td>71.2</td>
<td>3.75</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Ve for malignant cells</td>
</tr>
<tr>
<td>70</td>
<td>PSS</td>
<td>LLL</td>
<td>59.2</td>
<td>13.2</td>
<td>12.75</td>
<td>14.75</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lymphocytosis</td>
</tr>
<tr>
<td>73</td>
<td>PSS</td>
<td>RML</td>
<td>95</td>
<td>4</td>
<td>1</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Inflammation.chronic.mixed</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>BAL</td>
<td>90</td>
<td>8</td>
<td>2</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Ve for malignant cells</td>
<td></td>
</tr>
<tr>
<td>92</td>
<td>PSS</td>
<td>LLL</td>
<td>81</td>
<td>18</td>
<td>1</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Histiocytosis.colm.cells</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>LLL</td>
<td>61</td>
<td>37</td>
<td>2</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Lymphocytes &amp; monocytes</td>
<td></td>
</tr>
<tr>
<td>93</td>
<td>PSS</td>
<td>BAL</td>
<td>87</td>
<td>13</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Colm,Histiocytosis,lymphocytes</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RML</td>
<td>87</td>
<td>12</td>
<td>0</td>
<td>1</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Colm,Histiocytosis,lymphocytes</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>WG</td>
<td>BAL</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>Histiocyte-multinucleated</td>
<td></td>
</tr>
<tr>
<td>57</td>
<td>Taka</td>
<td>Ling</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td>Scant cellularity</td>
<td></td>
</tr>
<tr>
<td>44</td>
<td>Sarc</td>
<td>RML</td>
<td>44</td>
<td>5</td>
<td>51</td>
<td>0</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Inflammation.acute</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>IPF</td>
<td>RML</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td>Bronchial epithelium- reactive</td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>IPF</td>
<td>RLL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
<td>Many lymphocytes, eosinophil</td>
<td></td>
</tr>
</tbody>
</table>

(Mac = macrophages, Lym = lymphocytes, neut = neutrophils, Hist = histiocytes, squa = squamous cells, col = columnar cells)

**BAL examination was done in 24 cases:**

16 scleroderma, 1 Wegener's, 1 SLE, 1 Takayasu's, 1 PM, (20 CVD), 3 IPF, 1 Sarcoidosis.

In group 2 HRCT, 14 cases (with a total of 21 lung Segments) underwent BAL examinations. As shown above, acute inflammation (alveolitis) was seen in Group 2 HRCT patients. Of note in our patients, we found that no patient with normal HRCT chest (Group 1) underwent BAL examination in our study, so subclinical alveolitis is not demonstrated in our study because most of our patients are either symptomatic or the patient who had normal HRCT study does not have BAL examination.
Table (32): BAL Findings in patients with Group 3 HRCT (with H/C)

<table>
<thead>
<tr>
<th>#</th>
<th>Diag</th>
<th>BAL</th>
<th>Cytological exam</th>
<th>Smear Characteristics</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>(cell count)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mac</td>
<td>Lym</td>
<td>Neutr</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>32</td>
<td>PSS</td>
<td>LLL</td>
<td>20</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>47</td>
<td>Cres</td>
<td>RML</td>
<td>74</td>
<td>25</td>
<td>1</td>
</tr>
<tr>
<td>72</td>
<td>PSS</td>
<td>RUL</td>
<td>79</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>74</td>
<td>PSS</td>
<td>RLL</td>
<td>54.5</td>
<td>40.2</td>
<td>2.5</td>
</tr>
<tr>
<td>80</td>
<td>PSS</td>
<td>LLL</td>
<td>65</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>88</td>
<td>PSS</td>
<td>RLL</td>
<td>70.7</td>
<td>6.7</td>
<td>8</td>
</tr>
<tr>
<td>90</td>
<td>Cres</td>
<td>RML</td>
<td>53</td>
<td>32</td>
<td>15</td>
</tr>
<tr>
<td>84</td>
<td>SLE</td>
<td>RLL</td>
<td>86</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>28</td>
<td>PM</td>
<td>RLL</td>
<td>29</td>
<td>3</td>
<td>67</td>
</tr>
<tr>
<td>59</td>
<td>IPF</td>
<td>LLL</td>
<td>75</td>
<td>4.5</td>
<td>17.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RLL</td>
<td>67</td>
<td>2.5</td>
<td>23.7</td>
</tr>
</tbody>
</table>

10 patients of this group (17 lung segments) underwent BAL examinations, as we see from the table, also alveolitis can be seen even in the presence of honeycomb change.

And this alveolitis does not mean that the condition is reversible but it means that there are different stages of disease activity and non-activity in the same lung segment.

The presence of >3% Neutrophil &/or >2% eosinophils in BAL fluid is indicative of active alveolitis. There are 14 cases consistent with these criteria in our study.

BAL can rule out infection, malignancy or hemorrhage.

In Scleroderma patients:

9 patients from group II with 16 BAL examinations, alveolitis was demonstrated in 4 examinations (25%).

7 patients from group III with total 11 BAL examinations, alveolitis was demonstrated in 8 examinations (72.7%). This means that alveolitis was higher among group III (with honeycombing on HRCT).

The total percentage of alveolitis in 27 (16+11) BAL examinations in scleroderma was 12/27= 44.4%.
case demonstration
**Technique**

(a) Summary of our CT protocol for examination of the lungs.

(b) Helical HRCT scan, 1 mm pitch 1 commencing 3 cm below the carina for 2 cm span.

(c) Helical CT, 10 mm pitch 1 from lung apex to diaphragm during inspiration.

Also HRCT scan, 1 mm/10mm from lung apex to diaphragm during inspiration.

(d) Expiratory HRCT scan, 1 mm/20 mm from carina down during expiration.
Case (1): PSS

A 55 year-old female with 6 month history of dyspnea, smoker 1 pack/day for 20 years.

PFTs showed mild reduction in vital capacity, moderate diffusion impairment, and DLCO was 42%.

A 1-mm HRCT scans showed the subpleural line in the right lung base (which is one the earliest findings of ILD on HRCT), mild ground glass and reticular opacities are also seen in the left lung base. Left pleural effusion is also seen.
Case (2): PSS

A 45 year-old female with LAM with scleroderma, non smoker with 2 years history of dyspnea and 1 year history of cough.

PFTs showed mild restrictive ventilation defect, severe diffusion impairment and DLCO was 41%.

Chest radiograph showed normal lung volumes and scattered rounded faintly lucent lung cysts.

A 5mm/ pitch 1, spiral CT scan of the lungs revealed scattered simple lung cysts on a background of normal lung a condition consistent with LAM in a patient with scleroderma. Left lung nodules are also seen.
Case (7): PSS

A 54 year-old female with history of dyspnea, cough and mild cigarette smoking. EMG showed scleroderma myopathy.

(a) A 1-mm collimation, pitch 3 spiral HRCT scan of lung window of lower lung zones showing a pulmonary nodule (arrow) which was not seen in HRCT scans. A subpleural line is seen in the posterior right lung with fine linear opacities in the peripheral lungs.

(b) A mediastinal window scan at the level of tracheal bifurcation of a 10-mm, pitch 1 spiral CT showing enlarged precarinal lymph nodes.

(c) Another 1-mm HRCT scan of lower lungs showing a small nodule seen in the left lung with mild reticular opacities in the posterior lungs.
Case (8): PSS

A 42 year-old Hispanic male with PSS with 6 month history of dyspnea, smoker for 25 years with 5 cigarettes/day.

PFTs showed mild restrictive ventilation defect, moderate diffusion impairment with DLCO = 39%.

Mediastinal window of 10-mm, pitch 1 spiral CT scan demonstrating enlargement of the right main pulmonary artery due to PAH.

A 1-mm, pitch 3 spiral HRCT scan showed basal, posterior, and peripheral ground glass opacity of early changes of scleroderma.
Case (9): PSS

A 43 year-old male with a diagnosis of PSS who had 9 years history of dyspnea, smoker for 20 years with 2 packs/day.

There was inflammatory myositis in muscle biopsy. In PFTs, there was no restrictive ventilation, mild obstructive defect due to obstruction of small airways which is smoking related, severely reduced diffusion capacity, with DLCO =30%.

A mediastinal window scan of 10-mm, pitch 1 spiral CT scan showed esophageal dilation and calcified mediastinal LNs.

A 1-mm, pitch 3 spiral HRCT scan of the lower lung zones showed panacinar emphysema with apparent ground glass opacity in the peripheral and posterior lung regions with crowding of vessels representing normal lung areas not affected by emphysematous changes.

An expiratory HRCT scan of the same region showed non symmetrical increase lung opacity of posterior lungs, and more airtrapping in the anterior 2/3rds of the lungs. The big caliber of vessels in the area of increased density than that in the rest of the lung favors that this is due to redistribution of blood to the normal areas which is seen in emphysema.
Case (10): PSS
A 38 year-old male with no dyspnea but smoker for 16 years with one pack/day.
PFTs showed no restrictive ventilation defect, mild obstructive ventilation defect
principally small airways, smoking related, mild diffusion impairment with
DLCO =63%. Chest radiograph in this patient revealed no abnormality. A 1-mm
HRCT scan of the lower lungs showed centrilobular fine nodular opacities
consistent with respiratory bronchiolitis related to cigarette smoking. No detected
chest abnormality related to scleroderma was found.

Case (11): Crest
A 77 year old white female with crest syndrome with one year smoking history
with 3 cigarette /day. PFTs showed moderate restrictive ventilation defect,
respiratory muscle weakness and severe diffusion impairment. A 1-mm HRCT
scan at the level of tracheal bifurcation (mediastinal window) showed mediastinal
lymphadenopathy.

Case (12): PSS
An 80 year-old white female, no dyspnea. PFTs showed normal ventilation, mild
diffusion impairment with DLCO = 63%. A 10-mm, pitch 1 spiral CT scan at the
level of aortic arch showed calcified mediastinal lymphnodes.
Case (13): PSS

A 68 year-old female with dyspnea, non-smoker.
PFTs showed FVC 62% (mildly reduced), mild diffusion impairment, with DLCO at 67%.
BAL showed neutrophils >10% (neutrophil alveolitis).
Chest radiograph showed linear and ground glass opacities, traction bronchiectasis (red arrow) with extensive honeycombing in the lung bases which is best demonstrated in the lateral film.

A 1-mm pitch 3, spiral HRCT scan at middle lung zones showed traction bronchiectasis in the right middle lobe and lingula. Subpleural nodules, patchy ground glass opacities and linear bands are also seen.
Case (14): PSS

A 44-year-old black female with PSS who had history of dyspnea for years.
PFTs showed severe restrictive ventilatory defect, respiratory muscle weakness, severe diffusion impairment, DLCO = 5%
BAL: showed chronic mixed inflammation of left lower lobe.
In chest radiograph, cardiomegaly, ground glass opacity with air-bronchogram in the lower lobes. Also reduced lung volume is seen.
A 3-mm, pitch 1 spiral CT scan at the level of left atrium with IV contrast in the evaluation of pulmonary embolism (CTA) showed extensive ground glass opacification with reticulation, extensive traction bronchiectasis, and pleural thickening.

Case (15): PSS

A non-smoker 74 year-old female.
PFTs showed a borderline restrictive ventilation defect, mild obstructive defect of small airway and mild diffusion impairment.
BAL: acute inflammation.
A 5-mm pitch 1.5 spiral CT scan of the lower lungs showed airspace consolidation in right lower lobe with air bronchogram which was proved to be malignant mass, another nodule is seen in right lower lobe, pleural effusion, with ground glass and reticular opacification
Case (16): RA

A 45 year-old Egyptian female with RA with restrictive ventilation defect with no airway obstruction on PFTs.

Chest radiograph revealed ground-glass and linear opacities in lower lung zones but no pulmonary nodules could be seen.

A 10-mm spiral CT scan with reconstruction every 3 mm showed ground glass opacity with scattered multiple pulmonary nodules.
Case (17): RA

A 30 year-old Egyptian male with RA.

Chest radiograph revealed left pleural effusion with no evidence of interstitial lung disease.

Spiral CT scan with 10-mm collimation reconstructed every 3-mm showed no evidence of interstitial lung disease but there is left pleural effusion.
Case (18): RA

A 75 year-old female with RA. She had 3 years history of dyspnea, 8 years history of cough and was smoking for 48 years with one pack a day. She had mild restrictive ventilation defect, moderate to severe diffusion impairment with DLCO = 33%, there was no airway obstruction.

Chest radiograph of this patient showed volume loss of the left lung, left pleural effusion, scattered linear opacities, honeycombing, traction bronchiectasis. In addition to enlarged pulmonary artery and mediastinal lymph nodes.

A 1mm-HRCT revealed focal consolidation with volume loss of the left lung with left pleural effusion, which was proved to be squamous cell carcinoma with metastasis in the liver. Linear opacities, pleural thickening and pulmonary nodules were also seen.
Case (19): RA

A 51 year-old female with RA. She had 15 years history of dyspnea, one-year history of cough, and smoking for one month. In PFTs, there was no restrictive ventilation defect but there was mild obstructive defect and mild diffusion impairment and DLCO was at 56%.
Chest radiograph showed few linear opacities in lower lung zones.
A1-mm, HRCT of the lungs revealed small centrilobular nodular opacities in this patient with RA consistent with bronchiolitis obliterans in addition to central bronchiectasis.
Case (20): RA

A 69 year-old male with RA, he had history of cough and smoking for 10 years with 2 packs a day. PFTs showed moderate restrictive ventilation defect, obstructive defect due to smoking related small airway obstruction, moderate diffusion impairment with DLCO at 46%.

(a) Chest radiograph showed ground glass opacities and few linear opacities. Bilateral pneumothorax.

(b) A 1-mm, pitch 3 spiral CT taken at the level of the inferior pulmonary veins revealed few ground glass opacities, scattered peripheral linear opacities, bronchiectasis without honeycomb changes in the left lung and multiple peripheral necrobiotic pulmonary nodules.

(c) A 1.5 mm/10mm, HRCT taken 6-month later at the same level showed cavitation in pulmonary nodules.

(d) Mediastinal windows of 10-mm spiral CT scans demonstrated mediastinal lymphadenopathy and pleural thickening.
Case (21): SLE

A 28 year-old Asian female with SLE, she had history dyspnea and cough. She was smoking for 2 years with 2 cigarettes a day. She had left lower lobe lung biopsy showed end stage fibrosis. BAL fluid from right and left lower lobes showed neutrophil alveolitis (neutrophil was at 67% in RLL and at 6% in LLL).

(a) Chest radiograph revealed only minimal linear opacities in lower lung zones.

(b) A 1.5 mm HRCT lung scan showed ground-glass and linear opacities involving the posterior lung regions.

(c) A 1-mm/10-mm HRCT prone scan of the lung bases showed the same findings as above in addition to traction bronchiectasis and peripheral honeycombing.

(d) A 1.5 mm HRCT of the same patient of the upper lobes showed honeycombing involving the peripheral parts of the anterior segments in addition to scattered centrilobular opacities, this upper lobe involvement was unusual for SLE.
Case (22): DM

A 66 year-old white female with a diagnosis of DM had a low-grade cough. She had also systemic hypertension and cardiac failure. Endomyocardial biopsy showed no inflammation, necrosis or fibrosis.

(a) chest radiograph revealed cardiomegaly, linear opacities in lung bases, enlarged pulmonary artery and pleural thickening.

(b) A 1.5mm/10mm HRCT lung scan showed bilateral pleural effusions and right fissural thickening. Scattered ground glass and linear opacities were also seen.

(c) A mediastinal window scan revealed pericardial effusion and thickening in addition to pleural effusion.
Case (23): WG

A 50 year-old female with Wegener’s granulomatosis. Its renal biopsy showed pauci-immune crescentic glomerulonephritis. Its transbronchial biopsy (TBB) showed changes of Wegener’s granulomatosis. BAL fluid examination showed mild acute inflammation.

Chest radiograph revealed few linear and ground-glass lower lung opacities.

A 10-mm pitch 1, spiral CT lung scan showed mosaic distribution of ground-glass opacities in both lungs.

Case (24): WG

A 62 year-old male with a diagnosis of WG, had history of dyspnea. He had also smoking history for 30 years with 3 packs a day. Renal biopsy revealed immune-complex mediated glomerulonephritis with crescents 90% and arteriolar nephrosclerosis. The right pleural material showed inflammation with no malignancy. PFTs showed moderate restrictive ventilation defect, obstructive defect possibly small airway obstruction that is smoking related and moderate diffusion impairment for DLCO.

Chest radiograph revealed few linear opacities in the right lower lung zone, in addition to right pleural effusion.

A 3-mm pitch 2, spiral CT lung scan showed few linear opacities in right lung, right pleural effusion, fissural thickening and right lung collapse.
Case (25): MCTD

A 31 year-old oriental female with a diagnosis of MCTD (clinically had features of both PSS and SLE), had dyspnea for 2 years and cough for 4 years. On PFTs, she had severe restrictive ventilation defect, respiratory muscle weakness, and severe diffusion impairment for DLCO (DLCO =15%). Renal biopsy revealed membranous glomerulonephritis, Ig A nephropathy.

(a) Chest radiograph revealed ground glass opacities, few linear opacities, honeycombing and bronchiectasis in lower lung zones.

(b) A 10-mm, pitch 1 spiral CT lung scan showed ground-glass, linear opacities and honeycombing. In addition to pericardial effusion.

(c) 1 year later, a 1.5 mm/10-mm HRCT lung scan of the same patient and nearly at the same level showed extensive honeycombing indicative of disease progression. Left pleural fluid is seen but pericardial effusion was resolved.

Case (26): MCTD

A 36 year-old female with a diagnosis of MCTD (she had clinical manifestations of PSS, SLE and DM), had dyspnea for 3 years. On PFTs, there was normal ventilation but there was severe diffusion impairment for DLCO (DLCO was 38%). Left quadriceps muscle biopsy revealed muscle changes of polymyositis.

A 1-mm HRCT mediastinal window scan revealed enlarged right main pulmonary artery indicative of PAH.
**Case (27): IPF**

A 79 year-old male who had a history of dyspnea for 5 years, 5 months history of cough and was smoking for 10 years. On PFTs, there was moderate restrictive ventilation defect and severe diffusion impairment for DLCO.

Chest X-ray revealed low lung volumes, tracheal shift to the right, right midzonal peripheral consolidation, basal reticulonodular shadows and cardiomegaly.

Spiral CT, 3mm pitch 1.4:1 at the level of tracheal bifurcation showed ground glass opacity of the right middle lung zone, interlobular and intralobular septal thickening and traction bronchiectasis of the middle lobe and lingula, no honeycomb could be seen.

**Case (28): IPF**

A 60 year-old female had a 3 months history of dyspnea and 3 years history of cough. She had severe restrictive ventilatory defect on pulmonary function tests. On echocardiography, there was left ventricular hypertrophy.

HRCT, 1-mm/10mm of the upper lung zones showed ground glass opacification of most of the right upper lobe and to less extent the left upper lobe. Increased lung reticulation especially thickened intralobular septa of the right lung. Such upper zonal involvement is rarely seen in CVD patients.
Discussion
Use of spiral CT in diffuse lung disease
The use of spiral or helical technique is not recommended for HRCT in patients
with suspected diffuse lung disease. In most instances, HRCT obtained with a
scanner capable of spiral or helical imaging should be performed without table
motion, using thin (1-mm) collimation, a 1-sec scan time, and a high-resolution
reconstruction algorithm. Obtaining scans with a spiral technique results in an
increase in effective slice thickness, as compared to scans obtained without table
motion, thus resulting in some loss of spatial resolution (Kalender et al, 1990;
Vock & Soucek 1993), although this effect may be minimal with proper technique
(Paranjpe & Bergin 1994). The ability to obtain contiguous slices during a single
breath hold, as is possible using spiral CT, is not a major advantage in assessing
most patients with diffuse lung disease; HRCT in patients with suspected diffuse
lung disease involves a sampling of the lung anatomy in different lung regions,
and obtaining contiguous scans in a single lung region is not usually of diagnostic
value (Webb et al, 1996).
The use of spiral HRCT is likely to be of more value in assessing patients with
focal lung disease or lung nodules than it is in patients with diffuse lung disease
(Vock & Soucek 1993).
Obtaining a volumetric HRCT, with 1 or 2 cm being scanned using 1-mm
collimation and a pitch of 1, would be of potential value in demonstrating the
secondary lobular distribution of abnormalities in patients with diffuse lung
disease, but this would seem to be of limited clinical utility (Vock & Soucek
1993).
Engeler et al, (1994) assessed the utility of volumetric HRCT, obtained without
helical technique. In this study, four contiguous HRCT scans were obtained at
each of 3 locations (the aortic arch, carina, and 2-cm above the right
hemidiaphragm) in 50 patients with interstitial lung disease or bronchiectasis.
Scans are analyzed for the presence of motion-induced artifacts or blurring, and
the diagnostic information obtained from each set of four scans was compared to that obtainable from the first scan in the set of four. The sensitivity of the first scan as compared to the set of 4 was 84% for the detection of bronchiectasis, 97% for ground glass opacity, 88% for honeycombing, 88% for septal thickening, and 86% for nodular opacities. They concluded that the use of volumetric high-resolution CT increased the diagnostic accuracy, particularly in respect of bronchiectasis at lung base, without increasing the peak skin radiation exposure. With the availability of four contiguous scans per anatomical level, the subjective confidence in the interpretation and the number of motion-free studies also increased. Although more findings of disease were identified when the contiguous scans were used (Engeler et al, 1994), it is likely that this improvement in sensitivity more likely reflects the number of scans viewed than the fact that they were obtained in contiguity.

Limited attention has been paid to the role of spiral CT for evaluating parenchymal lung disease. HRCT is pre-eminent in this area, but has limitation related to its use of thin slices and the presence of inter-slice gaps. Limitation of HRCT includes suboptimal detection of micronodular infiltration and the distinction of the nodules from vessels seen end on may be difficult. HRCT also underestimates the degree of emphysema. Spiral HRCT is a new technique that combines HRCT acquisition with post processing techniques for the examination of parenchymal lung disease. CT slices (1-mm thick) are acquired using a spiral technique for 10 sec at a pitch of one. Images are reconstructed using 180-degree linear interpolation and edge enhancing algorithm. The images are processed using sliding-thin-slab maximum or minimum intensity projections. Windowing is important: the optimal windows for MIPs are from WW 1000 to 1300 HU and WL -650 to -800 HU. For minimal intensity projections, from WW 350 to 500 HU and WL -750 to -800 HU are optimal (Padhani, 1998).
Remy-Jardin et al, using sliding-thin-slab MIPs in patients with diffuse infiltrative disease (Remy-Jardin et al, 1996a) found an improvement in the detection of micronodules of low profusion from 73% on conventional 1-mm thick slices to 92-100%

Similarly, Bhalla et al (1996), who used both maximum and minimum intensity projections in patients with diffuse lung diseases found that MIPs were better at identifying and characterizing nodule location as peribronchovascular or centrilobular. However, airways are not detected and there are poor visualization of interlobular septa and fissures using MIPs. Minimum intensity projections allow improved visualization of parenchymal changes, i.e., ground glass opacity, bullae and airtrapping, with improved visualization of airways in the absence of the walls.

Remy-Jardin et al (1996b), have found that minimum intensity projections allow improved detection of minimal degree of emphysema. However, the loss of vascular landmarks is a disadvantage as is the loss of luminal walls, i.e. of cysts and bronchial walls (Rubin et al, 1996).

In our study, a volume acquisition of 10-mm collimation pitch 1 study was obtained form apex to base in the supine position at TLC. A high-resolution spiral using 1-mm collimation pitch 1 was performed commencing 3 cm below the carina and extending for 2 cm in the same position and breath hold position. In addition, we did 10mm and or 30 mm thick slab maximum and minimum intensity projection sections reconstructed from the high resolution helical data set in the lower lung zones in 12 patients of CVD and IPF. On these images there was excellent details for depiction of traction bronchiectasis, honeycombing, ground glass opacities and pulmonary nodules especially if mild changes were seen on the traditional HRCT study or Spiral study, which helped us to confirm the radiological signs seen on the traditional CT scans because it displays the data contiguously in the examined region of interest. We applied this type of reconstruction for maximum and minimum intensity projection when there was a
need to clarify or confirm the signs seen on the traditional helical or HRCT studies. This was true and comes with a study introduced by Remy-Jardin et al (1996a) for detection of more subpleural micronodules using MIP and Bhalla et al (1996), stating that MIP was useful for detection of airway changes and better visualization of ground-glass opacities.

As the volumetric (helical) HRCT section was taken 3 cm below the carina extending downwards for 2 or sometimes for 3 cm, it is considered in lower part of middle lung zones (i.e. the section was slightly higher to be considered in lower lung zones). So, for actual comparison with HRCT scans, we compared the results of Spiral HRCT with both the middle and lower zone scores of HRCT. We got the following results:

Regarding the prevalence of the HRCT signs in both helical, HRCT-middle, and lower lung zones. In CVD (n=66), the nodular opacities was 41% on spiral CT, 24.2% on HRCT-M, and 45.5% on HRCT-L. So the incidence of nodules was higher on spiral CT than HRCT-M. If we compare the mean profusion scores for pulmonary nodules between the two using the paired T-test in 48 patients having CVD, it was found that it is statistically significant (P>0.0220) when comparing spiral CT with HRCT-M but not statistically significant on comparing spiral CT with HRCT-L (P>0.4037). The mean score of nodular profusion in scleroderma was 30% on spiral CT, and it was 22% on HRCT-M for scleroderma patients. This means that there were more nodules discovered on spiral CT, this coincided with the results of Remy-Jardin et al, (1996a), although she used MIPs reconstruction images to get these results. But in our study, we depended upon the film reading not image reconstruction at scoring.

Regarding the incidence of honeycombing in CVD patients, it was 35.9% on spiral CT, 13.6% on HRCT-M and 27.3% on HRCT-L. This means that Spiral CT detected more patients having honeycombing more than HRCT-M and HRCT-L. Also the mean score for Honeycombing in scleroderma (as an example) was 7% on spiral CT, 5% on HRCT-M and 14% on HRCT-L. and on comparing the mean
honeycomb profusion score for CVD, we found that it is statistically significant on comparing spiral CT with HRCT-M (P>0.0016), and not significant when comparing on spiral CT and HRCT-L (P>0.1170).

If we come to traction bronchiectasis, its incidence in CVD patients was 53.8% on spiral CT, 19.7% on HRCT-M, and 31.8% on HRCT-L. That means spiral CT detected more patients with bronchiectasis than HRCT.

Regarding the mean profusion score of bronchiectasis in scleroderma patients, it was 48% on spiral CT, 31% on HRCT-M, and 64% on HRCT-L.

If we compared the mean profusion score for bronchiectasis of 48 patients with CVD using paired-T test, it was found that it is statistically significant (P>0.0076) on comparing spiral CT with HRCT-M, but not statistically significant (P>0.2422) on comparing spiral CT with HRCT-L. This means that spiral CT depicts bronchiectasis better than HRCT. This result is in agreement with Engeler et al. (1994).

**Collagen vascular disease (CVD)**

In collagen vascular disease, many pathologic entities (e.g. UIP, DIP, BOOP, cellular interstitial pneumonia, lymphocytic interstitial pneumonia, and lymphoid hyperplasia) are often found in the lung. With the exception of PSS, two or more of these anomalies may be found. In PSS, the pathologic feature is UIP, which is indistinguishable from that in IPF (Colby & Carrington 1988). On the other hand, the pathologic findings of IPF are almost always UIP. With a few exceptions, desquamative interstitial pneumonia is found. Corticosteroid treatment is not always effective in UIP (Carrington et al, 1978). However, corticosteroid treatment is considered effective for BOOP and DIP (Colby & Carrington, 1988). If UIP can be differentiated from other pathological conditions in CVD
using imaging modalities, disease severity, prognosis and the effectiveness of corticosteroid therapy can be evaluated.

HRCT findings of UIP have proven to be honeycomb lesions, bronchiectatic changes, curvilinear shadow in the lung periphery, ground-glass opacity, and irregular small nodules (Muller et al, 1987a). Pathologically, UIP shows many abnormalities, often ranging from interstitial and intra-alveolar cellular infiltration to fibrotic end-stage lesions (Carrington et al, 1978). Increase of interstitial and intra-alveolar cellularity corresponds with ground-glass opacity or air-space consolidation at HRCT. Fibrotic end-stage lung corresponds with honeycombing at HRCT (Nishimura et al, 1992). In contrast, HRCT findings of DIP and BOOP have been proven to be ground-glass opacity and alveolar consolidation (Muller et al, 1990; Muller et al, 1987). Johko et al. (1994) in a study of 55 patients with various types of CVD: 10 with SLE; 14 with PM/DM; 14 with PSS; 9 with RA; and 8 with SjS as well as 9 patients with IPF, evaluated the HRCT findings of patients with various kinds of known CVD, and with pathologically or clinically diagnosed IPF. With special attention to honeycomb lesions and high attenuation areas in the analysis.

They found that honeycombing in various CVD (except for PSS) were significantly less frequently observed than in IPF on HRCT; and high attenuation areas were equally seen in patients with CVD or IPF.

These results suggested that honeycombing is the key HRCT finding to differentiate UIP from other pathological conditions. Some patients with CVD (except for PSS), who had ground-glass shadow and alveolar consolidation, had no or very low honeycomb score. However, even in early stages, UIP is considered to show honeycomb lesions, as well as other HRCT findings (Westcott & Cole 1986).

In our study, on HRCT honeycombing was of higher incidence among patients with IPF (78.6%) than for CVD (28.8%). Also in our study, honeycombing had a high incidence in PM/DM (75%) and MCTD (66.6%). But the incidence was
higher in scleroderma (37.5%) than for RA (5.3%), SLE (20%), or WG (0%). So, these results are in agreement with the above study except for MCTD and PM because these two groups were small.

Regarding the high attenuation areas, ground glass opacities in our study were 92.9% for IPF and 63.6% for CVD. So, the incidence is close to each other but not equal as in the above study. Also the incidence of air-space consolidation was not equal in our study, it was 0% incidence in IPF and 9.1% in CVD.

Also our study showed that on spiral CT, honeycomb score was higher in IPF (78.6%) than for CVD (28.8%). The ground-glass opacity incidence was nearly equal in IPF (88.9%) and CVD (84.6%). This result is in agreement with the above study. But the air-space consolidation was not equal; it was 0% for IPF and 5.1% for CVD.

The morphological changes seen at HRCT correlate well with the PFTs in diffuse infiltrative lung disease. In UIP, the disease extent seen at CT (total score) is reported to significantly correlate with impairment in gas exchange assessed by carbon monoxide diffusing capacity (%DLCO) (Staples et al, 1987).

Johkoh et al. (1994) also found that, the disease extent (total score) seen on HRCT significantly correlated with the degree of % DLCO in various kinds of CVD and IPF.

The importance in focusing on specific HRCT findings for predicting pulmonary function status has been reported in silicosis. The emphysema score on HRCT, rather than total score, is important in silicosis (Schurawitzki et al, 1990).

Regarding the individual HRCT findings, honeycomb score significantly correlated with %DLCO in PSS. The score of ground-glass shadow correlated well with %DLCO in SLE, SjS, and RA. The score of air-space consolidation correlated well with %DLCO in PM/DM. In IPF, the total score significantly correlated with %DLCO, but each of the honeycomb scores, the score of ground-
glass shadow, and the score of air-space consolidation did not (Johkoh et al., 1994).

In our study, the honeycomb score correlated well with DLCO %, as seen group III HRCT, the mean DLCO% in this group was 36.3%. Also the ground glass score and linear opacity score correlated well with DLCO% in our study group of CVD and IPF and it was 43.3% in group II patients in whom HRCT contains ground glass and linear opacities. Compared to group I in which HRCT does not contain ground glass opacity or honeycomb with mean DLCO% was 75.4%. This result correlated with that reported by Johkoh et al. (1994) and Staples et al. (1987).

**Scleroderma (PSS)**

Dyspnea is the most common pulmonary symptom in patients with scleroderma, occurring in 60% of patients, with a range of from 21% to 88% (Owen & Follansbee 1987). In our study, dyspnea was found in 22/30 patients (73.3%), cough in 8/30(26%).

Some investigators have suggested that a decreased DLCO is the earliest pulmonary function abnormality in scleroderma and the most sensitive index of pulmonary involvement in this disease (Steen 1990; Weaver et al, 1968).

**Restrictive and obstructive ventilatory defects**

In a study by McCarthy et al (1988) one third of 34 patients had normal pulmonary function, one third had a restrictive ventilatory pattern, and one third had evidence of small airways disease. Other investigators have reported similar results (Silver & Miller 1990; McCarthy et al 1988).

Guttadauria et al (1977) evaluated 45 patients who had had scleroderma for an average 4.25 years. Approximately one third were smokers. All patients had abnormal pulmonary function: 30% had a restrictive pattern and 70% had a
reduced diffusing capacity for carbon monoxide (DLCO). The most common abnormality was an increased residual volume (92%) probably due to premature airway closure, suggesting the presence of small airway disease. Twelve of the patients (27%) had large airway disease defined by a forced expiratory volume in one second-to-forced vital capacity (FEV1/FVC) ratio less than 75% of predicted. The most extensive evaluation of pulmonary function in patients with scleroderma was done by Owens et al (1983). The study group comprised 165 nonsmokers who had limited or diffuse disease. Pulmonary function abnormalities were found in 109 patients (66%); a restrictive ventilatory defect was present in 28% and airflow obstruction in 12% of these patients. An obstructive pattern was found in 6 of 77 patients (8%) with diffuse disease and in 14 of 88 patients (16%) with limited disease. The most common isolated finding was a reduction in the single breath DLCO; this was noted in 37 patients (22%).

In our study, 27 scleroderma patients underwent pulmonary function tests, 21 (77.7%) patients showed a restrictive ventilation defect, 2 (9.5%) patients were from group I (Normal HRCT study), 10 (47.6%) patients from group II (abnormal HRCT study without honeycombing) and 9 (42.9%) patients from group III (honeycombing on HRCT).

An obstructive pattern was seen in 7 (25.9%) patients; 1 from group I, 4 patients from group II, and 2 patients from group III.

26 patients (96.6%) had reduced diffusing capacity for carbon monoxide; 3 (11.5%) patients from group I, 12 (46.2%) from group II, and 11 (42.3%) patients from group III.

Our results are higher than that reported by previous studies.

Also our study showed that pulmonary function tests correlated well with the severity of ILD on HRCT study in scleroderma patients, the mean %DLCO was 73% in group I (normal HRCT study), 43.7% in group II (abnormal HRCT without honeycombing), and 37.3% in group III (with honeycombing). PFTs was found more sensitive in detecting early abnormalities in patients with scleroderma.
than HRCT did. In group 1 patients (normal HRCT), a restrictive ventilation defect was found in 2 patients, an obstructive pattern in one patient, and reduced diffusing capacity for CO in 3 patients. These 6 patients had a normal HRCT study.

Chest radiography

Chest radiographs may be normal in up to 10% of patients with documented diffuse interstitial disease (Eppler, 1978).

Of the collagen vascular diseases, scleroderma has the highest incidence of pulmonary parenchymal involvement seen on plain chest radiographs and at autopsy, and postmortem examination has shown evidence of pulmonary involvement in 74% of patients (Weaver et al, 1968; D'Angelo et al, 1969).

Changes in lung parenchyma are seen on plain chest radiographs in 25%-65% of patients with scleroderma (Steen 1990; Owens et al 1983).

Chest radiographic evidence of interstitial pulmonary parenchymal disease may be seen in up to 65% of patients with PSS (Arrolliga, 1992).

Chest radiographs may be normal even in patients who are symptomatic and who have pulmonary function abnormalities or fine interstitial opacities may be visible (Silver & Miller 1990).

In our study, Chest radiographic evidence of interstitial pulmonary parenchymal disease was seen in 16/18 (88%) of patients with PSS.

Pleural involvement

Unlike patients with rheumatoid arthritis or SLE, patients with scleroderma rarely develop clinically significant pleural effusion (Owens et al, 1983). McCarthy et al (1988) found pleural thickening on chest radiographs in only 3 of 36 patients (8%) with scleroderma, whereas other investigators (Steen 1990) have reported pleural thickening or a pleural effusion on chest radiographs in from 11% to 56%
of patients. Remy-Jardin et al (1993b) found diffuse pleural thickening in patients
with PSS in one-third of cases using HRCT.

In our study, the pleural thickening or effusion was found in 8 patients (25%) on
HRCT and in 7 patients of 18 (38.9%) on chest radiographs.

Chest CT scanning

Thoracic HRCT has documented utility as non-invasive means of detecting and
characterizing interstitial pulmonary parenchymal abnormalities in PSS lung
disease (Remy-Jardin 1993b; Meziane, 1992). In addition, HRCT is more
sensitive to the detection of pulmonary parenchymal changes of interstitial lung
disease than projectional chest radiography. HRCT evidence of interstitial lung
disease is present in up to 91% of PSS patients (Schurawitzki 1990; Remy-
Jardin 1993b), a percentage similar to the percentage of patients with PSS who
have pulmonary fibrosis on post-mortem examination (Scully et al, 1989).
Morphologic abnormalities of the pulmonary parenchyma in PSS as depicted at
HRCT are similar to those described in cryptogenic fibrosing alveolitis and other
collagen vascular diseases.

In the absence of associated airway changes (such as traction bronchiectasis,
bronchiolectasis), ground glass opacification of the lung identified on HRCT
corresponds to histologic evidence of alveolar inflammation in patients with
chronic diffuse infiltrative lung disease (Remy-Jardin 1993c). In this setting,
ground glass opacification seems to precede the HRCT appearance of
honeycombing, supporting the idea that alveolitis precedes irreversible fibrosis
(Remy-Jardin 1993c).

In patients with PSS, ground glass opacification may be present in combination
with varying degrees of interstitial pulmonary fibrosis. In these patients, the
implications of ground glass opacification are less well understood. More
extensive ground glass opacification on HRCT is significantly associated with a
lower DLCO (Remy-Jardin 1993b), similar to the association between BAL
and 37.5% in the lower zone. While the mean score of honeycombing was 0% in the upper zone, 5% in the middle zone and 14% in the lower zone. There was no difference between the right and left lung and the abnormalities were seen the peripheral and posterior lung regions. These finding are consistent with the findings reported by Schurawitzki et al, 1990 and Harrison et al, 1989.

The esophagus is reported to be involved in up to 87% of patients with systemic sclerosis (McCarthy et al, 1988; Akesson & Wollheim 1989). Mahrer et al (1954) reported that esophageal dilatation and decreased peristalsis were detected on esophagogram in 62% of patients. Asymptomatic esophageal dilatation present in 40% to 80% of cases, and enlarged mediastinal nodes seen in 60% of cases (Bhalla et al, 1993). The presence of esophageal dilatation may be helpful in the differential diagnosis of PSS from other diffuse interstitial lung diseases. The coronal luminal diameter of the esophagus in patients with PSS, as shown on CT, has been reported to range from 12 to 40 mm (mean 23 mm), a finding that was not seen in any of a control group of 13 patients with a variety of other parenchymal and airway abnormalities (Bhalla et al, 1993).

In our study, esophageal dilatation was found in 18/32 patients (56.3%) and mediastinal lymphadenopathy was found in 16/32 patients (50%).

**BAL in patients with connective tissue disease**

BAL is a sensitive method for the detection of inflammatory disease in the lower respiratory tract (wallaert et al, 1986). Alveolitis is characterized by increased number of alveolar macrophages and/or eosinophils, and a neutrophilic alveolitis is associated with symptoms of dyspnea and objective abnormalities of pulmonary function tests, as well as ground glass opacification on HRCT (Remy-Jardin 1993c, 1993h; sliver 1990; Moore et al, 1997). Alveolitis is defined on the basis of a BAL cell differential count (≥3% neutrophils and or≥ 2% eosinophils) (BAL Cooperative Group Steering Committee 1990).
There was an increase in the numbers of neutrophils and eosinophils recovered from both CTD and IPF patients compared to normals. These appears to be a relationship between the number of cells recovered and the activity of the disease (Klech & Hutter, 1990). The total protein, IgG, IgA, and IgM levels were elevated in the BAL fluid of patients with CTD and IPF compared to normals. BAL cellular patterns mirror alveolitis and to some extent correlate with disease activity and predict the likelihood of clinical deterioration (Haslam et al, 1980; Watters et al, 1987). Also BAL may be valuable for the diagnosis of other lung diseases frequently encountered in patients with CTD such as drug-induced pulmonary dysfunction, infection, pulmonary hemorrhage, alveolar proteinosis, and malignancy. Most BAL studies have been performed on patients with established ILD, usually at the middle to late stages of their disease. These patients tend to have significant pulmonary fibrosis and honeycombing. The striking BAL findings in these cases (both in isolated IPF and in CTD-associated pulmonary fibrosis) are the increase in the numbers of macrophages and neutrophils / eosinophils (Haslam et al, 1980). There is tendency for the level of BAL neutrophilia and eosinophilia to correlate with fibrosis and honeycombing (Watters et al, 1987). Furthermore, these patients do not appear to be responsive to therapy.

In contrast, many subjects with CTDs who undergo BAL before the onset of overt clinical signs of respiratory dysfunction will have an increased number of lymphocytes in BAL fluid (Fishler et al, 1986). On lung biopsy these patients tend to have extensive alveolar and interstitial inflammation and a relative absence of fibrosis and honeycombing. In addition, the patients with BAL lymphocytosis frequently respond to therapy; even patients with an associated neutrophilia or eosinophilia appear to improve or remain stable in response to treatment (Watters et al, 1987).

In several studies, examination of BAL fluid has shown evidence of inflammation in patients with both limited and diffuse scleroderma, whether or not they had
radiographic evidence of interstitial lung disease (Harrison et al, 1989; Wallaert et al, 1986). Studies showed an increase in BAL fluid cell count, an increase in the percentage of granulocytes (neutrophils and eosinophils), and, in some patients, a predominantly lymphocytic alveolitis. Some patients with lymphocytic alveolitis have sjoegren's syndrome in association with scleroderma, because lymphocytic pneumonitis is associated with sjoegren's syndrome (Breit et al, 1989). Overall, 50% to 60% of patients with scleroderma have abnormal findings at BAL (Wallaert et al, 1986).

Remy-Jardin et al (1993b) found that 47% of scleroderma patients with normal CT findings had abnormal BAL cell counts, demonstrating a lymphocyte or neutrophil alveolitis in similar proportions. Harrison et al (1991) confirmed that thin-section CT scans could be normal despite histologic evidence of fibrosing alveolitis and abnormal BAL cell profiles.

The interstitial changes observed on HRCT in scleroderma are not specific, have also been described in patients with IPF, rheumatoid lung, and mixed connective tissue disease (Schurawitzki et al, 1990; Harrison et al, 1989). Harrison et al (1989) found abnormal cell profiles in BAL fluid of patients who had normal chest radiographs and abnormal HRCT, suggesting that HRCT can detect subclinical pulmonary disease.

In our study, 16 patients of scleroderma underwent BAL examination, 9 patients were found among group II, and 7 patients among group III. No one patient from group I (normal HRCT study) underwent BAL examination, so subclinical alveolitis (alveolitis can be demonstrated in BAL fluid examination while HRCT study is normal as reported by Remy-Jardin et al, 1993b) is not demonstrated in our study. But alveolitis was seen group II and III because the patients had different stages of disease processes at the same time, in the same lung and in the same segment.
9 patients from group II with 16 BAL examinations, alveolitis was seen in 4 examination (25%).

7 patients from group III with total 11 BAL examinations, alveolitis was demonstrated in 8 examination (72.7%). This means that alveolitis was higher among group III (with honeycombing).

So BAL examination was abnormal in 12/27(44.4%) of scleroderma patients. This result is very near to that reported by Wallaert et al. (1986) and Remy-Jardin et al (1993b).

**Small airway disease**

Obstructive airway disease is clinically described in 16% of patients with limited scleroderma and in 8% of diffuse disease (Owens & Follansbee 1987; Owens et al, 1983). In our study, obstructive airway disease was found in 7/27 (25.9%) of scleroderma patients. Emphysema was found in 3.1%.

**Limited versus diffuse scleroderma**

Isolated abnormalities of the pulmonary artery occur almost exclusively in patients with limited disease. Young and Mark (1978) found changes of the pulmonary arteries in 3 of 6 patients with limited disease, and only 2 of 24 patients with diffuse disease. In a clinical study by Stupi et al (1986), 20 of 331 patients (6%) with limited scleroderma had isolated PAH diagnosed by cardiac catheterization. None of the 342 patients with diffuse disease had PAH.

PAH, a well-recognized complication of scleroderma can lead to cor pulmonale and death (Owens & Follansbee, 1987; Owens et al, 1983; Salerni et al, 1977). The reported incidence of PAH varies from 6% to 60% depending on the method used to detect it and the population studied (Sackner et al 1964; Stupi et al 1986; Ungerer et al, 1983, Salerni et al, 1977).

PAH can occur secondary to severe interstitial fibrosis and restrictive disease, but patients with limited scleroderma, present with isolated PAH independent of the degree of interstitial fibrosis (Yousem, 1990; Young & Mark 1978; Salerni et al,
1977). Salerni et al (1977) described the syndrome in 10 patients with long-standing limited scleroderma with no chest radiographic or pathologic evidence of pulmonary interstitial fibrosis. Stupi et al (1986) identified isolated PAH at right heart catheterization in 20 of 331 patients (6%) with limited scleroderma.

McCarthy et al (1988) reported that 6 of 36 patients (17%) with scleroderma had enlarged cardiac silhouettes and pulmonary arteries. The lung was normal on chest radiographs in 4 of 6 patients with cardiomegaly in this series. Owens et al (1983) reported pulmonary artery enlargement in 4 of 61 patients (6%) with limited scleroderma but in none of 43 patients with diffuse scleroderma. In addition to PAH, other causes of cardiomegaly in scleroderma are pericardial and myocardial disease.

In our study, the incidence of PAH was 11/32 (34.4%) on HRCT and in 44.4% on chest radiographs in patients with diffuse sclerosis. This incidence in agreement with that of Ungerer et al (1983). Cardiomegaly was found in 6 patients of PSS (18.3%) in our work on HRCT and 5.6% on chest radiographs in diffuse scleroderma. This is in agreement with that of MaCarthy et al (1988). There were 3 cases of limited disease (crest) with one case with PAH secondary to interstitial fibrosis not isolated.

Lung cancer

In 1980, Talbott and Barrocas reviewed the world literature and identified 41 cases of coexisting scleroderma and lung cancer; these cancers were predominantly alveolar cell carcinomas. Duncan and Winkelmann (1979) found an overall cancer rate of 4% and no increase in the incidence of lung cancer compared with the general population.

The increase incidence of lung cancer appeared to be primarily in patients with diffuse scleroderma (Roumm & Medsger 1985). The increase incidence of lung cancer in scleroderma, especially in presence of pulmonary fibrosis, is attributed
to a defect in immune surveillance, impaired clearance of carcinogens probably due to disordered lung architecture, and increased susceptibility to malignant transformation due to epithelial hyperplasia (Sela & Shoenfeld, 1988).

In our study, the cancer incidence in patients with PSS was 3.1% (1/32).

**Rheumatoid Arthritis**

**Pulmonary fibrosis**

Elman and Ball in (1948) first described an association between RA and pulmonary fibrosis. The chest radiograph, which is insensitive for the diagnosis of early or minimal pulmonary fibrosis, gives a prevalence of about 2% (Walker & Wright 1968). Pulmonary function test abnormalities consistent with pulmonary fibrosis are present in 40% of patients with RA, and most of these patients have normal chest radiographs (Frank et al, 1973). Cervantes-Perez and colleagues (1980) studied 41 patients with RA and performed open lung biopsy in 25 patients. Histologic evidence of interstitial disease was found in 20 of these patients (80%), 11 of whom were asymptomatic and 3 of who had normal chest radiographs. The prevalence of radiologically detectable interstitial disease in patients with RA is probably 10% (Laitinen et al, 1975; Frank et al, 1973). Histologically, radiologically, and on HRCT, the appearance of RA with interstitial fibrosis is usually indistinguishable from that of IPF (Bergin & Muller 1985; Bergin & Muller 1985; Steinberg & Webb 1984).

In our study, the prevalence of pulmonary fibrosis is found in 5.6% on chest radiograph, and 5.2% on HRCT, but evidence of interstitial lung disease in rheumatoid arthritis is found in 47.3% of patients on HRCT.

In our study, 9 with RA underwent PFTs. One patient in group 1, its PFTs was normal.
7 patients in group II with 3 patients had restrictive ventilation defect, 4 obstructive pattern, and 3 had diffusion impairment. Only one patient in group III had restrictive and diffusion impairment with no obstructive pattern. So the incidence of restrictive defect in patient with RA was 4/9 (44.4%), obstructive pattern was found in 44.4%. Also the diffusion impairment was in 4/9 patients (44.4%). This result was consistent with the above authors (Laitinen et al, 1975; Frank et al, 1973).

HRCT findings reported in patients with RA include nodules 3 mm to 3 cm in diameter that are predominantly subpleural in location (22%), bronchial abnormalities and bronchiectasis in the absence of fibrosis (21%), ground-glass opacity (14%), pulmonary fibrosis with or without honeycombing (10%), consolidation (6%), enlarged lymph nodes (9%), and pleural abnormalities (12%). Findings which were more frequent in symptomatic patients included honeycombing, Bronchiectasis, nodules, and ground-glass opacity. In patients with RA, the presence of ground-glass opacity, consolidation, and fibrosis likely reflect the presence of interstitial pneumonia, while the small and large nodules probably represent necrobiotic (rheumatoid) nodules. Bronchiectasis in RA can be associated with chronic infection, which has an increased incidence in rheumatoid patients, or bronchiolitis obliterans (Remy-Jardin et al, 1994).

Of the 19 patients with RA in our study, the incidence of HRCT findings in patients with RA was pulmonary nodules in 42.1%, bronchiectasis and bronchiolectasis in 21%, ground-glass opacity in 36.8%, honeycombing in 5.3%, airspace consolidation in 10.5%, enlarged mediastinal lymph nodes in 15.8%, pleural thickening or effusion in 15.8%, PAH in 21%, esophageal dilatation in 5.3% and lung cancer in 5.3%.

Pleural disease, either pleural effusion or pleural thickening is common in patients with RA, being seen in up to 40% of patients at autopsy. However, symptomatic
pleural disease is less common, and radiographic evidence of pleural thickening or pleural effusion is present in only 5% to 20% of patients (Gamsu 1992). In the study by Fujii et al. (1993), pleural thickening was visible on HRCT in 33% of the 91 patients studied and in 44% of the patients who had HRCT findings of interstitial pneumonia.

In our study, pleural thickening or effusion was found in 15.8% of patients with RA.

Pulmonary necrobiotic nodules have a similar radiographic appearance of that of carcinoma of the lung. Apart from spontaneous resolution of rheumatoid nodules, no radiographic features readily distinguish the two entities. This diagnostic dilemma is complicated by several reports of primary lung cancer in patients with RA being mistaken for rheumatoid nodules and controversy over a possibly increased risk of lung cancer in patients with RA. Such nodules should, therefore, be aggressively evaluated by flexible fiberoptic bronchoscopy, transthoracic core needle biopsy, or thoracotomy to obtain definitive tissue diagnosis (Jolles et al, 1989).

There are two case reports of primary carcinoma developing in areas adjacent to necrobiotic nodules (Blodgett et al, 1972).

In our study, there was one case of lung cancer in a patient of RA with an incidence of 5.3%. There was also one case with necrobiotic pulmonary nodules, which showed cavitation on follow up scans.

Bronchiolitis obliterans

In 1977, Geddes and colleagues described the development of highly fatal, rapidly progressive airway obstruction in 6 adult patients. The disease did not respond to therapy with antibiotic, inhaled bronchodilators, or corticosteroids. Histologic examination of 4 patients showed bronchiolitis obliterans. Five of the 6 patients had RA, and 3 were receiving penicillamine therapy.
Affected patients usually rapidly develop severe, irreversible airway obstruction. Chest radiographs are normal except for hyperinflation. Therapy is uncertain because of the limited experience, but corticosteroids are the mainstay, with cyclophosphamide in refractory cases.

The cause of this disorder in patients with RA remains unknown. A study by Geddes et al (1977) reported that PFTs revealed evidence of airway obstruction in nearly 33% of patients with RA, suggesting some predisposition to airway obstruction related to RA. An immune-mediated basis has been proposed by Lahdensuo et al, (1984) who found IgM- and IgG-plasma cells in the bronchiolar walls of a patient who developed bronchiolitis obliterans after receiving gold therapy.

In our study, there was one case of bronchiolitis obliterans complicating a patient with RA with no evidence of ILD detected.

**Mixed Connective Tissue Disease**

MCTD is commonly associated with radiologic and functional evidence of interstitial lung disease and/ or pleural effusion. Pulmonary vasculitis with pulmonary hypertension and pulmonary hemorrhage are also associated with MCTD (Prakash 1992; Gamsu 1992).

Overall, pulmonary involvement has been described in from 20% to 80% of patients with MCTD (Prakash et al, 1985). Most of the pleuropulmonary manifestations, both clinical and pathophysiologic, are similar to those observed in SLE, PSS, and PM-DM (Vitali et al, 1985).

A prospective study by Sullivan et al (1984) discovered mild nonspecific interstitial fibrosis. Generally, the degree of fibrosis tends to be severe if the predominant clinical features are those of PSS. Abnormal PFTs were seen in 69% of patients with MCTD studied by Harmon et al, (1976) even though the patients had no respiratory symptoms. It has been estimated that, even in the absence of pulmonary symptoms, about two-thirds of the patients with MCTD have
significantly reduced diffusing capacity for carbon monoxide (DLCO), and that nearly half have a restrictive pattern. Chest radiographs in patients with MCTD show abnormalities typical of interstitial fibrosis. In a multicenter study of 100 patients with MCTD, diminished DLCO was noted in 67%, and restrictive lung volumes were observed in 50% (Sharp & Singsen 1989).

Pleuropulmonary involvement was noted in 25% of 81 patients with MCTD in the Mayo Clinic series. 22 All the patients demonstrate features of SLE, PSS, and PM, but the predominant characteristics were those of PSS in 10, SLE in 7, and PM in 3. Similar to patients with PSS or IPF, patients with MCTD who exhibit interstitial lung parenchymal disease usually demonstrate a restrictive pattern manifested by reduced lung volume, relatively normal flow rates, and diminished DLCO. DLCO is the single most sensitive parameter for evaluating pulmonary dysfunction in MCTD.

The most common chest radiographic abnormality in MCTD is interstitial lung disease. It was observed in 21% of patients in the Mayo Clinic series (Prakash et al., 1985). The interstitial process appears first in the periphery of the lung bases and gradually extends superiorly with asymmetric distribution. CT usually corroborates chest radiographic findings. The interstitial lung disease in MCTD mimics pulmonary fibrosis associated with PSS and IPF.

In retrospective report from the Mayo Clinic on 81 patients with MCTD, small pleural effusions were seen in 5(6%) patients, and 2 patients had pleural thickening (Prakash et al., 1985). Pleural effusion or pleural thickening is present in less than 10% of cases of MCTD. More than two-thirds of patients with MCTD have abnormal pulmonary function tests, but chest radiographic abnormalities are less frequenting, visible in about 20%. The interstitial lung disease of MCTD appears identical to that of UIP or IPF on histologic examination, radiographs, and in the few cases in which HRCT findings have been reported (Prakash 1992).
We studied 3 cases of MCTD, on HRCT we found all 3 cases had linear opacities and mediastinal lymphadenopathy. 2/3 of cases had ground-glass opacities, honeycombing, PAH, and esophageal dilations. 1/3 of cases had pulmonary nodules and pleural involvement. None of the cases had airspace consolidation or malignancy. This incidence is near that of scleroderma indicating that PSS is predominant component of these cases.

There were 2 cases that had PFTs; both showed a restrictive ventilation defect and diffusion impairment i.e. 2/2(100%)

Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE) is commonly associated with pleural and pulmonary abnormalities. Pleuritis or pleural fibrosis is present in up to 85% of cases at autopsy, and pleural effusion is often visible on chest radiographs in patients with SLE (Wiedemann & Matthay 1992). Pleural effusion, the most common manifestations, is frequently bilateral and usually small. Of 57 cases in one series (Winslow et al, 1958), it occurred in 42 cases. The importance of distinguishing pleural effusion due to direct involvement of the pleura by SLE from that associated with lupus nephritis have been emphasized (Levin 1971); the former characteristically is accompanied by pain and splinting, whereas the serous effusions of nephritic patients are painless.

More than 50% of patients with SLE have lung disease at sometime (Gamsu 1992), but interstitial pneumonia and fibrosis similar to that seen in other connective tissue diseases is relatively rare in SLE, with a prevalence of only a few percent. More common pulmonary abnormalities include pneumonia, lupus pneumonitis, and pulmonary hemorrhage. Each of these can be associated with HRCT findings of ground-glass opacity (Wiedemann & Matthay 1992).

In our study of 5 cases of SLE, we found ground glass opacities and linear opacities in 80% of cases, nodular opacities in 60%, honeycombing and
bronchiectasis in 20%, pleural effusion or thickening was seen in 40%. The higher incidence of ILD (80%) and the lower incidence of pleural effusion (40%) in SLE here were because it is not a large study group.

Polymyositis-Dermatomyositis

Polymyositis-dermatomyositis (PM-DM) is less commonly associated with pulmonary involvement than other connective tissue diseases. The reported incidence of pulmonary function abnormalities is about 30%, while approximately 5% of patients show chest radiographic abnormalities (Schwarz 1992). The pattern of involvement is typically that of UIP or BOOP/COP (Tazelaar et al, 1990).

ILD occurring in PM-DM was first described by Mills and Mathews in 1956. Since then, over 138 cases have been reported in the literature. It is estimated that ILD occurs in 5% to 30% of patients with PM-DM depending on whether radiographic or physiologic methods are used for screening (Frazier & Miller 1974). Reports from Japan quote an extraordinarily high incidence of this complication ranging from 40% to 80% (Takizawa et al, 1987). It is likely that the reported incidence of this complication will increase as new methods for early detection such as thin section, HRCT of the lungs and BAL come into general use for screening of PM-DM patients. HRCT can demonstrate early interstitial opacities, and BAL cell counts reveal alveolar inflammation in the face of normal chest radiographs and normal routine physiologic testing (Wallert et al, 1986).

ILD is more common in women with PM-DM. Approximately 60% of ILD cases in PM-DM complicate PM and 40% complicate DM. Only the polyarthritis is thought to be associated with ILD in patients with PM-DM. It has been well established that ILD can appear concomitantly with, follow, or precede the onset of the skin or muscle manifestations.

In our study, all 4 cases (100%) showed radiological evidence of ILD on HRCT and chest radiographs. With honeycombing and traction bronchiectasis was seen
in 50% on chest radiographs and 75% on HRCT, ground-glass opacities was seen in 50% on chest radiographs and in 100% of cases on HRCT. The linear opacities was seen in 100% on both HRCT and chest radiographs. Mediastinal lymphadenopathy was seen in all cases, the pleura is affected in 3 cases, and pericardial thickening and cardiomegaly in 2 cases on HRCT study. Because of limited number of cases studied, our results do not coincide with the above studies.

*Wegener's Granulomatosis*

The typical radiographic pattern in the lungs is that of rounded opacities, usually sharply defined, ranging from a few millimeters to 10 cm in diameter. They are commonly multiple, bilateral, and widely distributed, with no predilection for any zone (Gohel et al, 1973). Cavitation occurs eventually in one third to one half of the cases. These cavities are thick-walled and tend to have an irregular, rather shaggy inner lining; the thickness of the walls may diminish gradually until the cavities become thin-walled cystic spaces similar to those seen in coccidiodomycosis (Israel & Patchefsky 1971). After appropriate therapy- and even without treatment- cavities may disappear altogether. Distinct "feeding" vessels related to the nodules and abnormalities suggestive of infarcts may be seen with CT (Kuhlman et al, 1991).

Endotracheal and endobronchial masses can cause airway narrowing with resultant peripheral oligemia and sometimes lobar and total lung atelectasis (Maguire et al, 1978). Widespread airspace opacities can be caused by diffuse pulmonary hemorrhage (Travis et al, 1987). Pleural effusion has been reported in 50% of cases (Pinching et al 1983). With cytotoxic drug therapy, there is usually dramatic resolution of the pulmonary lesions. Despite this, intrathoracic relapse is common (Aberle et al, 1990).

In our study, we found ground-glass opacities of 2 cases of 3, the 3 cases had linear opacities, mediastinal lymphadenopathy in one case, PAH in one case,
pleural effusion in one case, and non-of the cases had honeycombing, pulmonary nodules, airspace consolidation or bronchiectasis.

Takayasu's arteritis (pulseless disease) is uncommon vasculitis that occurs predominantly in women. Although the arteritis is often confined to the aorta and its branches, pulmonary artery involvement also is present in an appreciable number of cases; for example, in one autopsy review, the main pulmonary artery was found to be affected in 34 of 76 cases and the intrapulmonary arterial branches in 21 cases (Nasu, 1975). In fact the pulmonary artery can be the initial site of involvement (Hayashi et al, 1986).

The angiographic pattern was similar to that commonly observed in pulmonary thromboembolism. In addition to the changes anticipated in the lungs from pulmonary arterial hypertension, the chest radiograph may reveal abnormalities of the aorta, including prominence of the ascending arch, and intimal calcification (Berkmen & Lande 1975).

In our study, there was one case (45 old white female) of Takayasu'a arteritis with ground-glass opacities and linear opacities in the lung parenchyma, also there was bronchiectasis and emphysematous changes. Also there was mediastinal LNs enlargement. Regarding the pulmonary artery, it was normal; there was a stent in one of the carotid arteries seen in the chest radiograph. She had bilateral carotid reconstruction and bilateral carotid-subclavian by-pass.

Idiopathic pulmonary fibrosis (IPF)

Ground-glass attenuation is often visible on HRCT in patients with IPF. It usually indicates the presence of disease activity and potentially treatable disease (Leung et al, 1993), but also can be seen in the presence of fibrosis or honeycombing below the resolution of HRCT. Ground-glass attenuation should be considered to represent an active process only when there are no associated HRCT findings of fibrosis. Findings of fibrosis in association with ground-glass attenuation, thus
suggesting an inactive process, include intralobular interstitial thickening, honeycombing, and traction bronchiectasis and bronchiolectasis (Remy-Jardin et al, 1993c).

Another hallmark of IPF on HRCT is its patchy distribution. Areas of mild and severe fibrosis, mild and marked inflammatory activity, and normal lung are often present in the same patient, in the same lung, and in the same lobe. Also, and most important diagnostically, is that findings of IPF often predominate in the peripheral, subpleural regions and in the lung bases (Muller et al, 1986). Several studies have shown that CT and HRCT are superior to plain chest radiographs in the assessment of patients with IPF. For example, honeycombing is seen in up to 90% of CT studies as compared to 30% of cases on plain radiographs (Staples et al, 1987).

In our study, honeycombing was seen in 78.6% on HRCT as compared to 53.8% on plain radiographs in patients with IPF.

HRCT findings have been shown to correlate with symptoms and pulmonary function abnormalities in patients with IPF. Staples et al. (1987) compared CT with clinical, functional, and radiologic findings in 23 patients with IPF. The CT scans provided a better estimate of the pattern, distribution, and extent of pulmonary fibrosis and showed more extensive honeycombing than did radiographs. In this study, there was a good correlation between the extent of disease, assessed by the percentage of lung showing evidence of fibrosis on CT, and the severity of dyspnea (r=0.64, p<0.001). A significant correlation between the extent of ground-glass opacities seen on HRCT and the severity of dyspnea, and reduction in total lung capacity and carbon monoxide diffusing capacity (p<0.01) has been found (Terriff et al, 1992).

In our study, there was 2 patients with IPF in group II HRCT (no honeycombing) with mean %DLCO was 45.5% while there were 7 patients with IPF in group III HRCT (with honeycombing) with mean %DLCO for this group was 36.7%. So
patients with honeycombing showed more decrease in the diffusion capacity for carbon monoxide.

Several investigators now routinely use HRCT to assess disease activity in patient with IPF. In some patients with IPF, definite diagnoses of end-stage lung (honeycombing without ground-glass opacity) or active alveolitis (ground-glass opacity) can be made on the basis of HRCT findings.

In our study, the incidence of ground-glass opacities and linear opacities was seen 92.9% of cases of IPF on HRCT, honeycombing in 78.6%, nodules in 64.3% and bronchiectasis in 85.6%. On chest radiographs, the incidence of ground-glass opacities was 76.9%, linear opacities 84.6%, honeycomb was 53.8%, nodules was 15.4 and bronchiectasis was 46.2. So, chest radiograph is inferior to HRCT in the assessment of pulmonary nodules, honeycombing and bronchiectasis.

Amiodarone Pulmonary Toxicity

Diffuse, increased lung attenuation in the absence of calcification can be seen as a result of amiodarone lung toxicity (Graham et al, 1992; Padley et al, 1993). CT in patients with amiodarone can show high-attenuation areas of consolidation or high attenuation nodules or masses, sometimes in association with abnormal reticulation or ground-glass opacity (Kuhlman, 1991). High attenuation consolidation correlated with the presence of numerous foamy macrophages in the interstitium and alveolar spaces. Unconsolidated lung parenchyma does not appear abnormally dense. Because the drug also accumulated in the liver and spleen, these also appear dense.

In our study, there were 2 cases of amiodarone toxicity. On HRCT and Spiral CT, both showed ground glass opacities, linear opacities, and pulmonary nodules. On spiral CT, honeycombing was found in both and bronchiectasis in one case, these findings was not seen on HRCT. There was mediastinal lymphadenopathy and
pleural thickening in both cases but only one case showed PAH. In one case, there was dense liver and single focal liver lesion. There was moderate to severe restrictive ventilation defect in one case. Diffusion impairment in both cases, there was no obstructive pattern on PFTs. %DLCO for one case was 25%.
summary
&
conclusion
Summary and Conclusion

The collagen vascular diseases are a group of immunologically mediated systemic diseases that involve connective tissue at various sites in the body. In collagen vascular disease, many pathologic entities (e.g. UIP, DIP, BOOP, ...) are often found in the lung. With the exception of PSS, two or more of these anomalies may be found. In PSS, the pathologic feature is UIP, which is indistinguishable from that in IPF.

It was found that Chest radiographs may be normal in up to 10% of patients with documented diffuse interstitial disease. HRCT scans provided a better estimate of the pattern, distribution, and extent of pulmonary fibrosis and showed more extensive honeycombing than did radiographs. Limitation of HRCT includes the presence of inter-slice gaps, suboptimal detection of micronodular infiltration and the distinction of the nodules from vessels seen end on may be difficult.

Spiral CT has revolutionized the way in which chest disorders are evaluated. With spiral CT, continuous table feed and synchronous data acquisition generate a volumetric acquisition that can be performed during a single breath-hold. Spiral HRCT is a new technique that combines HRCT acquisition with post processing techniques for the examination of parenchymal lung disease.

We found that HRCT is much better than chest radiograph for the assessment of ILD in CVD (HRCT detect honeycomb changes in 28.4% of patients with CVDs while chest x-ray detect it in 16.3% of cases only). Spiral HRCT gives an early detection and an excellent depiction bronchiectasis, Nodules, and honeycombing in patients with CVD than HRCT (Spiral HRCT detect honeycomb changes in 35.9% of patients with CVDs, while HRCT detect these changes in 28.4% of
patients with CVDs). Thick section spiral CT (10-mm collimation) is not useful for the assessment of CVDs. The pulmonary function tests correlated well with the HRCT findings in patients with CVD, with %DLCO correlated well with severity of pulmonary fibrosis. BAL examination was abnormal in 44.4% of scleroderma patients.

In conclusion, we approached 3 new diagnostic points:

1. The incidence of traction bronchiectasis and bronchiolectasis (65.6%) was higher than that of honeycombing (37.5%) in scleroderma patients. So traction bronchiectasis is much sensitive indirect indicator of early lung fibrosis than honeycombing.

2. The pattern of pulmonary fibrosis in patients with scleroderma is of much less severity in upper and middle lung zones than that of IPF (honeycombing was seen in 3.1% of cases in upper zone in scleroderma patients while it was seen in 67% of cases in IPF).

3. We reached a new CT technique for examination of the lung parenchyma in patients with ILD and this technique is now applied at big centers in America. We recommend the use of focal spiral HRCT scan to be done in the lower lung zone combined with post-processing maximum and minimum intensity projection slab images for early detection of presymptomatic parenchyma changes in patients with CVDs which is reversible with steroids. In addition, pulmonary function tests and BAL examination should be done as baseline initial evaluation of those patients.
References
References


Abstract.


References


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Arabic summary
(الملخص العربي)

إن أمراض النسيج الضام هي مجموعة الأمراض المناعية التي تؤثر على مختلف الأنسجة المعمرة في الجسم، وفيها تجاربان بانولوجية مختلفة في الرئتين.

وقد تنبأ/آبة/صدر المزاجية (Chest x-ray) (لتينين شبة) 10% من حالات أمراض نسيج الرئة، وأي الأشعة المقطعية ذات الرئة (HRCT) هي.

أوصب الوسائل لتوجيه أمراض نسيج الرئة.

وإن الأشعة المقطعية الحزازية (Spiral CT) قد أظهرت تطوراً هائلاً في توجيه الأمراض الصدرية، وذلك لأنها تعطينا معلومات فائقة الجودة عن كل جزء في الرئتين.

وقد وجدت الأشعة المقطعية الحزازية إذا أخذت بالطريقة ذات الرئة (HRCT) فإنها تعطينا معلومات أكثر وصورة وأوضاعية أوهاق المعلومات التي نحصل عليها من الأشعة المقطعية.

لذلك نستخدمنا هذه الطريقة في ردالتغيرات التي تحدث في الرئتين نتيجة لاصباتها بأمراض النسيج الضام.

وقد وجدنا خلال فحصنا 91 مريضاً مصابين بأمراض نسيج الرئة منهم 67 مريضاً (Chest x-ray) (HRCT) يتفق

مصابين بأمراض النسيج الضام.

هذه الأمراض، وإن الأشعة (Spiral HRCT) قد تبين التغيرات التي تحدث في الرئتين بصورة أوضح ونفسية حدد على الأشعة (HRCT) مثل حلبات الرئة؛ موصلات الرئة؛ أو تمدد الشعب الهوائية نتيجة تليف نسيج الرئة، لذلك نوصي بعمل هذه الأشعة للمرضى الذين يعانون من أمراض في النسيج الضام.

وذلك لمناقشة الإبلات الأولية التي تحدث في الرئتين (Alveolitis) قبل حدوث تليف الرئتين الذي لا يرجع فيه ولا يمكن علاجه، وذلك بمصاحبة اختبارات الوظائف الرئوية واختبار غسيل الشعب الحوائي.
تقييم الظواهر الصردية لأمراض الأنسجة الضامة
عن طريق المسح الصردي بالأشعة المقطعية
الخزوية بالكمبيوتر
رسالة
مقدمة
من الطبيب/ محسن كامل جمعة عريض
(ماجستير الأشعة التشخيصية)
توظف للحصول على درجة الدكتوراه في
الأشعة التشخيصية

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