John R. Mathieson, MD • John R. Mayo, MD • Catherine A. Staples, MD • Nestor L. Müller, MD, PhD

Chronic Diffuse Infiltrative Lung Disease: Comparison of Diagnostic Accuracy of CT and Chest Radiography[1]

The accuracies of chest radiography and computed tomography (CT) in the prediction of specific diagnoses in 118 consecutive patients with chronic diffuse infiltrative lung disease (DILD) were compared. The radiographs and CT scans were independently assessed by three observers without knowledge of clinical or pathologic data. The observers listed the three most likely diagnoses in order of probability and recorded the degree of confidence they felt in their first-choice diagnosis on a three-point scale. Confidence level 1 (definite) was reached with 23% of radiographic and 49% of CT scan readings, and the correct diagnosis was made with 77% and 93% of those readings, respectively ($P <$ .001). The correct first-choice diagnosis regardless of the level of confidence was made with 57% of radiographic and 76% of CT scan readings ($P <$ .001). The CT scan interpretations were most accurate in silicosis (93%), usual interstitial pneumonia (89%), lymphangitic carcinomatosis (85%), and sarcoidosis (77%). Observers correctly predicted whether a transbronchial or open lung biopsy was indicated with 65% of radiographs and 87% of CT scans ($P <$ .001). It is recommended that CT be performed before lung biopsy in all patients with chronic DILD.

Index terms: Computed tomography (CT), comparative studies • Computed tomography (CT), clinical effectiveness • Lung, CT, 60.1211 • Lung, diseases, 60.213, 60.22, 60.331, 60.77 • Lung, fibrosis, 60.792 • Lung neoplasms secondary, 60.331 • Pneumoconiosis, 60.77 • Radiography, comparative studies • Sarcoidosis, 60.22

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A large number of chronic diseases may result in diffuse infiltration of the lungs. The clinical and functional features of most of these entities are similar (1). Radiologically, the differential diagnosis is based on the type and distribution of opacities. Traditionally, the radiographic appearance has been divided into interstitial and air-space patterns of disease. Felson showed, however, that the prediction of microscopic distribution from the radiographic pattern is unreliable (2). It is now recognized that it is better to assess the type and distribution of opacities, to determine the predominant pattern, and then to try to predict the clinical diagnosis without trying to label the pattern as air space or interstitial (2).

McLoud et al (3) devised a scheme for semiquantitative description of the radiographic appearances of diffuse infiltrative lung disease (DILD) that was based on the International Labour Office (ILO) classification of pneumoconioses. This scheme allows for standardization of the method of analysis. In a review of the chest radiographs of 365 patients, an experienced chest radiologist was able to include the correct histologic diagnosis in the first two radiologic diagnostic choices in 50% of cases and among the first three choices in 78% of cases. Although certain radiologic patterns may be suggestive of a particular disease process, a confident diagnosis is rarely possible (3). In most patients, lung biopsy is required for definitive diagnosis. The radiograph is also of limited value in determining whether transbronchial or open lung biopsy should be performed and which area of lung is most likely to yield a representative sample. Transbronchial biopsy is the less invasive of these procedures, but in chronic DILD it is limited almost exclusively to the diagnosis of sarcoidosis and lymphatic spread of tumor (4). Open lung biopsy is required in the diagnosis of most other chronic diseases; it is an invasive procedure, and its sensitivity and specificity are limited by the small sample of lung parenchyma being assessed, which may not be representative of the diffuse process involving the lungs (5).

A number of recent studies have described the computed tomographic (CT) appearances of various DILDs (6–18). It has been suggested that CT of the chest is superior to chest radiography because the decreased superimposition of structures on CT images allows a better assessment of the type, distribution, and severity of parenchymal abnormalities than is possible on the radiograph (8). However, to our knowledge the value of CT in the prediction of pathologic diagnosis has not been previously evaluated. The aim of the present study was to assess the accuracy of CT compared with that of chest radiography in the determination of specific diagnoses in patients with chronic DILD. We also compared the accuracy of both methods in the prediction of whether transbronchial biopsy was likely to yield a diagnostic-quality specimen.

PATIENTS AND METHODS

All patients with chronic DILD referred to our hospital for CT of the chest between September 1983 and October 1987 who had both undergone chest radiography and received a definitive diagnosis were included in the study. One hundred eighteen patients met these criteria,

[1] From the Department of Radiology, University of British Columbia and Vancouver General Hospital, 855 W 12th Ave, Vancouver, BC, Canada V5Z 1M9. From the 1988 RSNA annual meeting. Received August 3, 1988; revision requested October 17; revision received October 31; accepted November 3. **Address reprint requests to** N.L.M.

See also the editorial by Naidich (pp 22–24) in this issue.

Abbreviations: DILD = diffuse infiltrative lung disease, ILO = International Labour Office, UIP = usual interstitial pneumonia.

73 men and 45 women with a mean age of 56.8 years (range, 24–84 years). The CT scans were obtained on an 8800 (24 patients) or 9800 (94 patients) scanner (GE Medical Systems, Milwaukee). The median time interval between chest radiography and CT scanning was 2 days. The scanning routine initially consisted of 1-cm-collimation scans at 1-cm intervals. The scans were obtained at end-inspiratory lung volumes with the standard algorithm and photographed at window levels and widths appropriate for lung parenchyma (level = −600 to −700 HU, width = 1,000–2,000 HU) and mediastinum (level = 30–50 HU, width = 350–500 HU). After July 1986, additional 1.5-mm-collimation scans were routinely obtained at the level of the aortic arch, tracheal carina, and 1 cm above the right hemidiaphragm (66 patients). These high-resolution CT images were obtained with 120 kVp and 360–420 mAs. Retrospective targeting of the 1.5-mm-collimation scans was performed with a field of view of 20 or 25 cm and the high-spatial-resolution algorithm (bone algorithm). This field of view is best because it permits evaluation of an entire lung.

The chest radiographs and CT scans were separately reviewed in random order by three independent observers (J.R.Mathieson, J.R.Mayo, C.A.S.). The observers had no knowledge of clinical or pathologic data, other than the age and sex of the patient. The type and distribution of small opacities on the radiographs were analyzed according to the ILO classification for pneumoconioses, modified to include the descriptors of septal lines, honeycomb cysts, and air-space consolidation, as suggested by Felson (2).

The CT scans were analyzed for the type, size, and extent of small opacities, as well as for the presence or absence of honeycomb cysts, septal lines, and hilar and mediastinal adenopathy. The distribution of small opacities was classified as being either predominantly in the upper or lower lung zone; as being central, diffuse, posterior, or peripheral; and as having either predominantly peribronchovascular distribution or as being randomly scattered throughout the parenchyma. These findings were then interpreted on the basis of previously published data on the radiographic and CT appearances of DILD, as summarized in Table 1 (3,6–23). Each observer listed three diagnostic choices in decreasing order of probability for both the radiographic and CT findings for each patient. The observers recorded the degree of confidence they felt in their first-choice diagnosis on a three-point scale (1 = definite, 2 = probable, 3 = possible). The observers were not aware of the different disease entities included in the study and did not know the frequency with which any individual entity was included.

In 41 patients (silicosis, 20 of 20; asbestosis, two of two; usual interstitial pneumonia [UIP], 15 of 34; extrinsic allergic alveolitis, four of seven), the diagnosis had been made before the CT scan was obtained. In the remaining 77 patients the CT scans were part of the initial examination. In all but three of these patients the final diagnosis was made by means of either transbronchial or open lung biopsy. In three patients the diagnosis of sarcoidosis was made by means of mediastinal nodal biopsy. Seven of the patients with UIP had associated rheumatoid arthritis, and one had associated scleroderma. These were included with the other cases of UIP because their pathologic and radiologic findings are indistinguishable from those of idiopathic UIP (11,24).

A transbronchial biopsy was considered to have been appropriately suggested when the first-choice radiologic diagnosis was correctly limited to either sarcoidosis or lymphangitic carcinomatosis. An open lung biopsy was considered to have been correctly suggested when the first-choice diagnosis avoided the erroneous inclusion of either sarcoidosis or lymphangitic carcinomatosis.

Table 1
Summary of CT Appearances of Chronic Diffuse Infiltrative Lung Diseases (References 3,6–23).

Disease	CT Appearances
UIP	Reticular pattern predominantly subpleural; usually lower-zone predominance; may show areas of haziness or air-space opacification, but reticular changes predominate; may show honeycombing
Silicosis	Randomly distributed, well-defined nodules; upper-zone predominance; may show posterior predominance; may show confluence
Sarcoidosis	Nodules predominantly along bronchovascular bundles; middle- and upper-zone predominance; may show reticulation/haziness/consolidation; bilateral hilar and mediastinal adenopathy often present
Lymphangitic carcinomatosis	Peribronchovascular nodules, thickened bronchovascular bundles; often shows polygonal lines; may show lymphadenopathy; sometimes unilateral
Extrinsic allergic alveolitis	Small, randomly distributed nodules with poorly defined margins, often associated with patchy haziness or consolidation and reticulation
Bronchiolitis obliterans organizing pneumonia	Patchy peripheral consolidation, few reticular markings; dense consolidation versus haziness or mild air-space opacification of desquamative interstitial pneumonia and UIP; no lower-zone predominance; tends to be asymmetric
Asbestosis	Same as for UIP, plus bilateral pleural plaques
Desquamative interstitial pneumonia	Patchy subpleural haziness with mild or absent reticular changes
All other conditions	Specific CT appearances not yet described; well described in radiology and pathology literature (references 1–3,19,20,23,28)

Table 2
Percentage of Correct Diagnoses by Disease Entity

Disease	No. of Cases	First-Choice Diagnosis		Top Three Choices	
		Chest Radiography	CT	Chest Radiography	CT
UIP	34	75	89	85	98
Silicosis	20	63	93	78	97
Sarcoidosis	19	61	77	79	95
Lymphangitic carcinomatosis	18	56	85	80	96
Extrinsic allergic alveolitis	7	14	43	43	71
Bronchiolitis obliterans organizing pneumonia	3	33	11	56	44
Alveolar proteinosis	2	0	17	33	33
Asbestosis	2	33	50	83	83
Bronchoalveolar carcinoma	2	50	50	83	100
Eosinophilic granuloma	2	33	83	50	100
Lymphoma	2	50	67	50	83
Chronic eosinophilic pneumonia	1	0	33	33	67
Desquamative interstitial pneumonia	1	33	67	33	67
Lymphangioleiomyomatosis	1	33	100	67	100
Lymphoid hyperplasia	1	0	0	0	0
Lymphomatoid granulomatosis	1	0	0	0	0
Hemangiomatosis	1	0	0	0	0
Metastatic disease	1	33	33	67	33
Total	118	57	76	73	89

Statistical Analysis

The data were analyzed using the SPSSx (SPSS, Chicago) statistical package. The percentage of correct diagnoses with radiography versus that with CT was compared by means of the χ^2 test of significance. The degree of concordance

Table 3
Percentage of First-Choice Diagnoses Made with a High Level of Confidence (Level 1) That Were Correct

Disease	No. of Cases	Chest Radiography		CT	
		Confident Interpretations	Correct	Confident Interpretations	Correct
UIP	34	30	87	73	95
Silicosis	20	37	100	72	100
Sarcoidosis	19	9	60	28	88
Lymphangitic carcinomatosis	18	20	64	54	93
Extrinsic allergic alveolitis	7	10	0	10	50
Total	118	23	77	49	93

Table 4
Percentage of Selected CT Findings in Five Most Common DILDs

CT Finding	UIP	Silicosis	Sarcoidosis	Lymphangitic Carcinomatosis	Extrinsic Allergic Alveolitis*
Small opacity distribution					
Upper	1.0	**78.3**	**59.6**	9.4	5.3
Lower	**58.4**	1.7	10.5	45.2	47.4
All zones	39.6	20.0	26.3	41.5	47.4
Nodular densities	7.8	**100.0**	**89.5**	**84.9**	50.0
Reticular densities	**97.1**	43.3	**73.7**	**94.3**	65.0
Pleural fluid or thickening	8.8	5.1	7.0	**60.4**	20.0
Septal lines	15.0	1.7	7.0	**66.0**	15.0
Unilateral predominance of small opacities	3.0	1.7	8.8	38.5	5.3
Peripheral predominance	**94.0**	3.3	3.5	15.4	36.8
Peribronchovascular	4.0	6.7	**70.2**	**59.6**	5.3
Posterior predominance	2.0	**38.3**	3.5	1.9	21.1
Polygonal lines	1.0	1.7	3.5	**50.9**	5.0

Note.—The percentages for the most important diagnostic features are in bold type.
* In retrospect, the reticular densities, septal lines, and small pleural effusion seen on the radiograph and CT scan in one patient with extrinsic allergic alveolitis were probably due to concomitant mild congestive heart failure. Open lung biopsy showed that the patient did have mild interstitial disease consistent with the clinical diagnosis of extrinsic allergic alveolitis. However, clinical and radiologic follow-up suggested that most of the initial CT findings were due to congestive heart failure.

among observers was established with the Kendall test of concordance. The percentage of correct diagnoses with the two modalities represents the sum of the correct interpretations by the three observers divided by the totals of 354 radiographic and 354 CT readings.

RESULTS

The 118 cases in the study included 18 different pathologic entities. The correct first-choice diagnosis was made in 57% of radiographs and 76% of CT scans. The correct diagnosis was among the top three choices in 73% of radiographs and 89% of CT scans (Table 2). These differences were statistically significant ($P < .001$). A high confidence level (level 1) of diagnosis was reached in 23% of radiographic and 49% of CT scan interpretations (Table 3). With this level of confidence, the radiographic diagnosis was correct in 77% of cases as compared with 93% for CT diagnosis ($P < .001$).

Five conditions accounted for 83% of the cases (Table 2). These included UIP (29%), silicosis (17%), sarcoidosis (16%), lymphangitic carcinomatosis (15%), and extrinsic allergic alveolitis (6%). The characteristic CT findings for these conditions are summarized in Table 4. The number of patients within each of the other categories was too small to permit valid conclusions to be drawn with regard to characteristic findings. The presence of polygonal lines, pleural fluid or thickening, septal lines, and a unilateral predominance of small opacities all correlated highly with lymphangitic carcinomatosis. A predominantly peribronchovascular distribution of nodular densities was seen almost exclusively in lymphangitic carcinomatosis and sarcoidosis. Well-defined, randomly distributed upper lobe nodules correlated highly with silicosis. The presence of peripherally distributed lower-zone reticular areas of increased attenuation and honeycomb cysts was noted exclusively in UIP and in the two patients with asbestosis. CT scanning was most accurate in the diagnosis of silicosis, UIP, lymphangitic carcinomatosis, and sarcoidosis (Table 4). Both radiography and CT were of limited value in the diagnosis of extrinsic allergic alveolitis (Table 4). Typical examples of the CT appearances of these five diseases are shown in Figures 1–5.

A transbronchial biopsy was correctly suggested by the radiographic results in 65% of cases and by the CT results in 87% of cases ($P < .001$). An open lung biopsy was correctly suggested by the radiographic results in 89% of cases and by the CT results in 99% of cases ($P < .001$).

The concordance among the observers' first-choice diagnoses was good with the CT scans (Kendall $W = .089$, $P < .001$) and lower but still significant with the chest radiographs ($W = .029$, $P < .05$).

DISCUSSION

Accurate interpretation of chest radiographs with diffuse abnormalities has been called "one of the most difficult problems in diagnostic radiology" (23). The radiologic custom has been to divide the diseases causing diffuse pulmonary parenchymal abnormalities into two groups: those predominantly involving the interstitium and those predominantly involving the terminal air spaces. Felson (19) described the radiographic characteristics of each of these groups but later related his frustration at being unable to teach others to recognize these radiographic patterns (2). There are several fundamental problems with this approach. First, most disease processes involve both the air spaces and the interstitium (3). Second, the degree to which each compartment is involved varies not only from patient to patient but over time in a given patient. Third, it is not always possible to differentiate between the radiographic features of interstitial and air space abnormalities. The radiographic terminology has been called inconsistent (2), misleading (3), and equivocal (25). Many attempts have been made to improve the diagnostic value of the chest ra-

diograph in patients with diffuse pulmonary parenchymal disease. In 1930 the ILO established a classification system to analyze chest radiographs in patients with pneumoconiosis, mainly by quantifying nodular opacities and, later, reticular opacities (26,27). Gaensler et al (28) broadened this quantitative approach to include all chronic diffuse lung diseases. McLoud et al (3) suggested ignoring the distinction between airspace and interstitial locations for these chronic conditions and proposed use of the term "diffuse infiltrative lung disease." McLoud et al also modified the ILO scheme to include reticulonodular and ground-glass patterns. Although the chest radiograph is helpful in the assessment of DILD, it rarely allows a confident diagnosis. In our series, the observers were confident about the radiographic diagnosis in only 23% of readings and were correct in only 77% of those readings.

Recently, a number of investigators have suggested that CT may be useful in the assessment of chronic DILD (6–18). The advantages of CT include its superior contrast resolution and the decreased superimposition of shadows. In almost half of our patients, CT scans demonstrated findings that were characteristic enough to allow a confident interpretation (49%), and when a confident interpretation was given, it was usually correct (93%). This subset included most of the patients with UIP, silicosis, sarcoidosis, and lymphangitic carcinomatosis. A minority of cases (20%) were difficult to interpret, and, in these cases, CT was no more accurate than chest radiography.

Transbronchial biopsy is a diagnostic method that involves considerably less risk than open lung biopsy and is appropriate in diseases involving the peribronchovascular spaces, which primarily includes sarcoidosis and lymphangitic carcinomatosis. We found that CT was more helpful than chest radiography in predicting the appropriate biopsy method.

The high percentage of correct diagnoses of UIP, silicosis, and lymphangitic carcinomatosis is not surprising given the characteristic macroscopic appearance of these conditions (10,18). However, the high proportion of correct diagnoses of sarcoidosis was unexpected, considering the well-known radiologic variability of the related parenchymal changes. The majority of patients had nodular areas of attenuation along the bronchovascular bundles. Presumably, these nodules represent granulomas and therefore a relatively early stage of disease. It is conceivable that the CT appearance may not be as characteristic in patients with more advanced disease, although most patients in this series who had fibrosis still had a predominantly peribronchovascular distribution of the CT findings.

CT was of limited value in the diagnosis of extrinsic allergic alveolitis. This is at least in part due to the paucity of data in the literature. The CT appearance has been described in only a few patients (9), and the CT findings have not been correlated with pathologic specimens or with the clinical stage of disease. Whereas small, randomly distributed nodules with poorly defined margins associated with patchy areas of air-space opacification were seen in the CT scans of some patients, this pattern

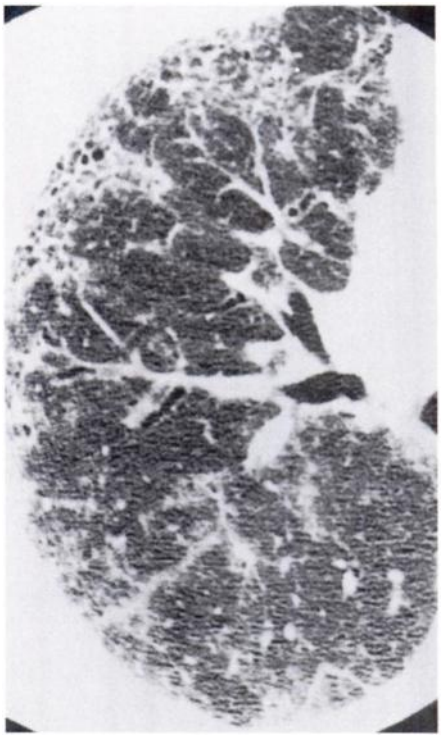
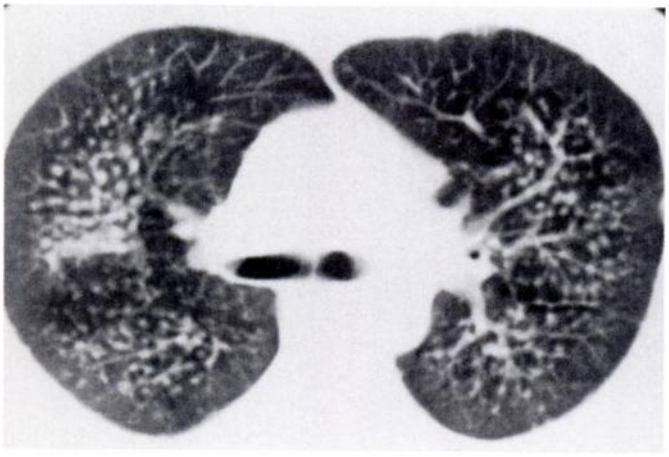


Figure 1. A 1.5-mm-collimation CT scan of the right lung in a patient with UIP shows reticular areas of increased attenuation and small honeycomb cysts in a predominantly subpleural distribution. Retrospective targeting was performed with the bone algorithm and a field of view of 25 cm. This leads to optimal depiction of the small honeycomb cysts but is associated with considerable noise due to quantum mottle. This noise could have been reduced by increasing the milliamperage.



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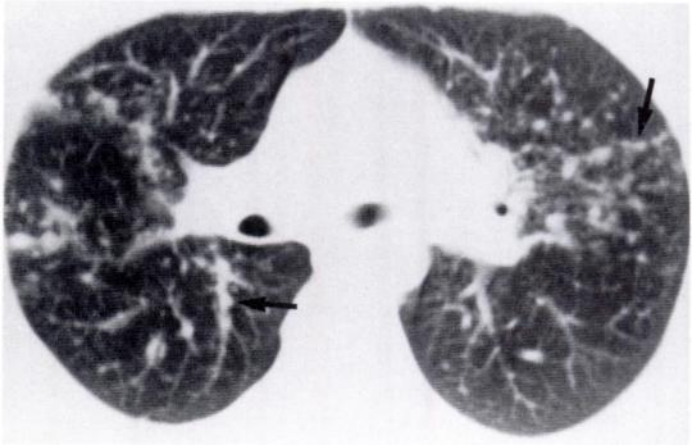

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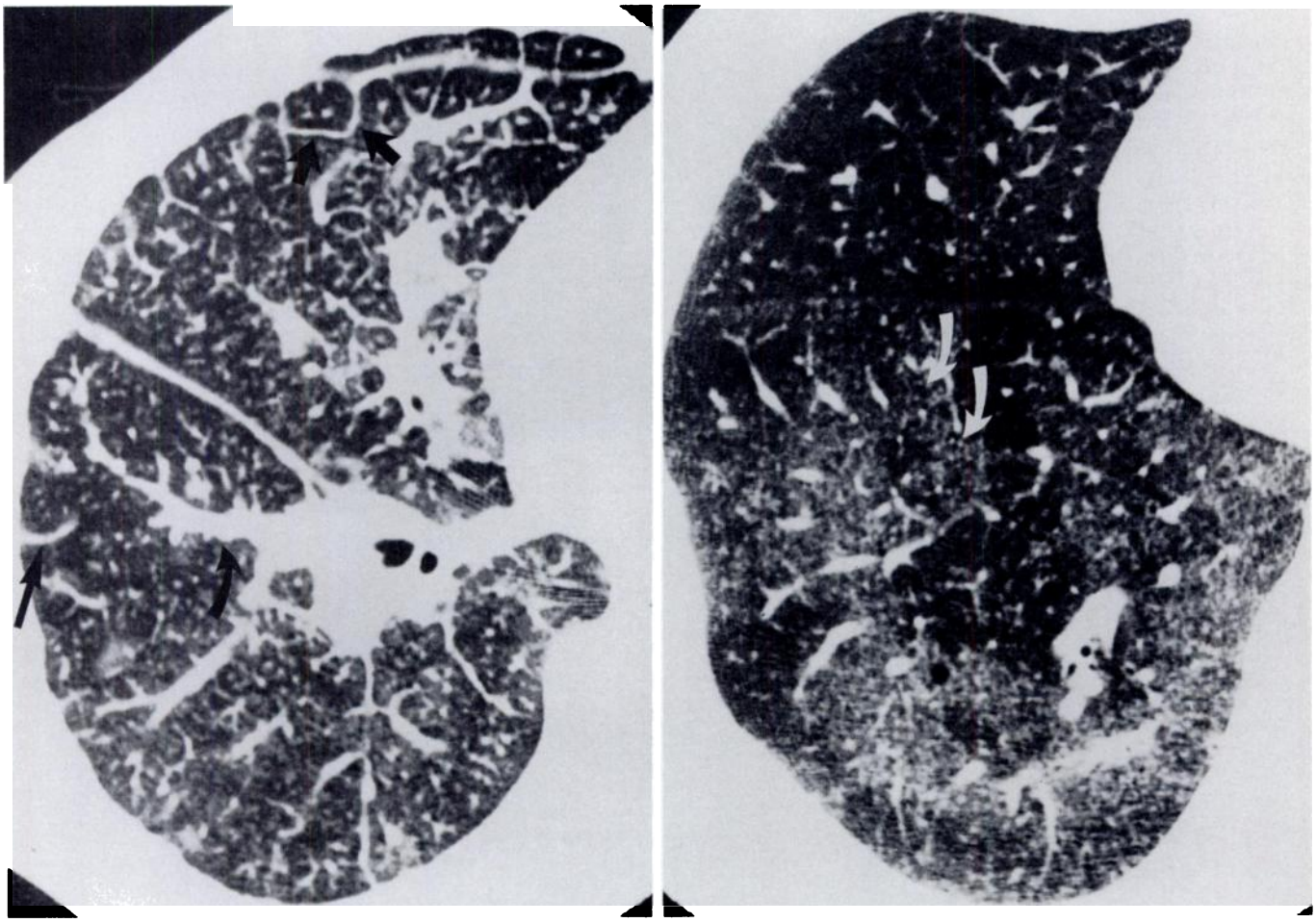
Figures 2, 3. **(2)** A 1-cm-collimation CT scan in a patient with silicosis shows multiple, small, well-defined nodular areas of attenuation that are randomly distributed in the upper lung zones. The 1-cm-collimation scan allows easy distinction of small nodules from blood vessels. **(3)** A 1-cm-collimation CT scan in a patient with sarcoidosis shows multiple, ill-defined, upper-zone nodular areas of attenuation, situated predominantly along the bronchovascular bundles (arrows). The beaded appearance of the bronchovascular bundles, which is clearly seen on 1-cm-collimation scans, is difficult to appreciate with high-resolution CT. Also notable is bilateral hilar lymphadenopathy.

may be present in only the acute or subacute stage.

Our study was limited by the relatively small number of cases of some diseases and by the relatively small number of diseases included. We did, however, include all consecutive cases of DILD studied over a 4-year period, reflecting a mixture of the prevalence and incidence of DILD in our community. The frequency and range of diseases in our study were similar to those in the study by McLoud et al (3), with the exception of a lower prevalence of desquamative interstitial pneumonia in our study. Our observers, being deprived of clinical information, were similarly at an unrealistic disadvantage compared with what would be the case in a real clinical situation. The accuracy of the radiographic diagnoses in our series was similar to that in the series of McLoud et al, supporting their conclusion that a systematic approach to the analysis of the chest radiograph greatly enhances its usefulness. Nevertheless, we have shown that the CT diagnosis is significantly more accurate.

We currently use CT in the initial examination of all patients with DILD. The methods and the advantages of the 1.5-mm collimation scans and retrospective targeting have been described by Mayo et al (29). Targeting increases spatial resolution and improves fine image detail despite an increase in visible noise (29). The three high-resolution CT images we obtained provide sections through each lobe of the lungs. These levels were selected after consultation with the two thoracic surgeons at our institution. They include virtually all open lung biopsy sites in patients with chronic DILD. Our routine is also dictated in part by time constraints and scanning practice at our hospital. Ideally, additional high-resolution CT sections should be obtained on the basis of the assessment of the chest radiograph or the scanogram.

High-resolution CT is superior to 1-cm-collimation CT in demonstrating small cystic areas of honeycombing (10). It is essential in the detection of the characteristic polygonal lines seen with lymphatic spread of tumor (18) and in the assessment of disease activity in idiopathic pulmonary fibrosis (13). However, the beaded appearance of the bronchovascular bundles seen in lymphatic spread of tumor and in sarcoidosis is much easier to assess with 1-cm-collimation scans. Small nodules can be easily missed between high-resolution CT sections and, when present, are difficult to distinguish from blood vessels. Because high-resolution CT is superior in the assessment of diseases with predominantly irregular linear opacities, whereas conventional CT is superior in the assessment of small nodular opacities, we believe that both should be used in the initial examination of patients with DILD. We do not routinely obtain supine and prone scans except in



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Figures 4, 5. **(4)** A 1.5-mm-collimation CT scan of the right lung in a patient with lymphangitic carcinomatosis shows irregular nodular thickening of the bronchovascular bundles (curved arrow), polygonal lines (short arrows), and septal lines (long arrow). **(5)** A 1.5-mm-collimation CT scan of the right lung in a patient with extrinsic allergic alveolitis shows areas of normal parenchyma; small, ill-defined, nodular areas of attenuation that are randomly distributed (arrows); and areas of air-space opacification.

patients with suspected asbestosis. In those patients we use a technique described by Aberle et al: high-resolution CT at five spaced intervals through the lower thorax with the patient in both supine and prone positions (30).

We conclude that CT is superior to chest radiography in the diagnosis of DILD. Even though chest radiography will undoubtedly remain the initial imaging modality in these patients, the CT diagnosis is more often correct. CT is highly accurate in the diagnosis of UIP, silicosis, sarcoidosis, and lymphangitic carcinomatosis. Our data suggest that CT is indicated when the clinical, functional, and radiographic findings do not allow a specific diagnosis. CT should be performed in all patients before lung biopsy. A confident diagnosis of silicosis or UIP may preclude the need for lung biopsy. A diagnosis of sarcoidosis or lymphangitic carcinomatosis will indicate transbronchial biopsy as the next step. In patients in whom CT does not provide diagnostic information, CT can help direct the surgeon to the optimal biopsy site (5). Finally, the relatively small biopsy specimen cannot reflect true extent of disease, especially since many chronic infiltrative lung diseases are nonuniform in distribution (5,10,13). Correlation of the pathologic specimen with CT studies gives the best overall estimate of disease pattern and distribution. ■

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