domized, controlled trial. Ann Intern Med 1998;128:721–8.

21 Antonelli M, Conti G, Rocco M, Bufi M, et al. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. N Engl J Med 1998;339:429–35.

22 Leger P, Muir J. Selection of patients for long-term nasal intermittent positive pressure ventilation: practical aspects. Eur Respir Mon 1998;38(2):328–47.

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High-resolution computed tomography and diffuse lung disease

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High-resolution computed tomography (HRCT) dominates the recent literature about the imaging of diffuse lung diseases. The detailed images of the lungs available from HRCT occupy the middle ground between the sometimes vague impressions provided by chest radiography and the microscopic, but necessarily localised, information obtained from a lung biopsy. The evidence accumulated so far allows a reasonably objective view to be taken of the value and limitations of HRCT. The main uses of HRCT (Table 1) have changed little since its introduction 15 years ago, and reflect the increased confidence that this procedure is able to bring to the diagnosis of diffuse lung disease. More recently, the role of HRCT has been broadened to include the evaluation of disease reversibility and the identification of various forms of small airways disease.

Technical considerations

The key factors that define the HRCT technique are thin sections, widely spaced, with the data reconstructed without any ‘smoothing’ of the image. Despite this apparently simple definition, there may be striking differences in the appearances of images of the same patient obtained on two different CT scanners, even when the same technical factors are applied. Such discrepancies rarely cause diagnostic confusion (and are analogous to the sensation of playing tennis with an unfamiliar racquet). The two basic advantages of the HRCT technique are:

• the ability to identify fine parenchymal detail (Fig 1)
• a reduction in radiation dose at least sixfold compared with conventional CT protocols.

The effective radiation dose from a standard HRCT protocol is about 12 times that of a frontal and lateral chest radiograph.

HRCT should not be confused with spiral (also known as helical or continuous volume) CT scanning. Spiral CT involves the continuous acquisition of data by moving the patient table continuously into the CT scanner such that a ‘corkscrew’ or spiral of information is acquired. The data can be reconstructed in many ways, but are most usually presented as a series of conventional-looking (thick) transaxial sections. However, spiral CT is not necessary for the routine evaluation of diffuse lung disease.

Table 1. Roles of high-resolution computed tomography.

- to detect diffuse lung disease in patients with a normal or near normal chest radiograph and/or abnormal lung function tests
- to narrow the differential diagnosis or make a confident histospecific diagnosis in patients with obvious but non-specific radiographic abnormalities
- to investigate patients with suspected bronchiectasis or unexplained severe obstructive airways disease
- to guide the type and appropriate site of lung biopsy
- to assess disease reversibility, particularly in patients with fibrosing lung disease

Erratum

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German Berrios

New drug treatments in psychiatric disease

We regret the statement on page 310 that 'Olanzapine seems to cause less agranulocytosis and lowering of seizure threshold than risperidone or clozapine because it does not antagonise alpha2 adrenoreceptor function.' This should have read: 'Olanzapine is similar to clozapine in molecular structure and in having greater 5HT2 than D2 blockade, but does not antagonise alpha2 adrenoreceptor function, as do risperidone and clozapine; it has not been associated with agranulocytosis or lowering of seizure threshold.'
Basic high-resolution computed tomography anatomy and signs

There is close correspondence between the abnormalities seen on HRCT images and the macroscopic appearance of pathological specimens. Because of this correlation, precise anatomic terms can be used to describe many of the HRCT patterns of diffuse lung disease, rather than the sometimes whimsical terms used to describe its radiographic appearances. The smallest structures visible on HRCT images are less than 1 mm and may be less than 200 µm. Thus, the occasional interlobular septa, which are approximately 100 µm thick, will be visible in the lung periphery in healthy individuals (Fig 2). The interlobular septa border the secondary pulmonary lobule (which is regarded as the smallest anatomical unit of the lung surrounded by a connective tissue septum). Since many diffuse lung diseases have a characteristic distribution in relation to the secondary pulmonary lobule, it is useful to consider abnormalities seen on HRCT in terms of their relationship to the various components of the secondary pulmonary lobule.

The most frequently encountered HRCT signs of disease, namely a reticular or nodular pattern and ground glass opacification (GGO), can be briefly reviewed by considering the HRCT appearances of four of the commonest diffuse lung diseases: cryptogenic fibrosing alveolitis, lymphangitis carcinomatosa, sarcoidosis and extrinsic allergic alveolitis (subacute) (Fig 3(a)–(d)).

**Ground glass opacification**

The greatest number of problems in interpreting HRCT images is caused by GGO at its most subtle, it is an almost imperceptible and uniform increase in density of the lung parenchyma, such that the lungs appear slightly grey by contrast to the darker air within the bronchi (the ‘black bronchus’ sign). Such minor density differences are susceptible to many technical vagaries. Furthermore, an increase in lung density, indistinguishable from widespread GGO, occurs in normal individuals breath-holding at near residual volume. When GGO is patchy in distribution, it is readily recognisable.

At a histological level, the changes responsible for GGO may be complex, and include partial filling of the air spaces, considerable thickening of the interstitium or a combination of the two. It needs to be appreciated that this pattern is in itself diagnostically non-specific, but other HRCT features often help to refine the differential diagnosis (see Fig 3(d)). Diseases characterised by patchy or uniform GGO are listed in Table 2.

Importantly, GGO usually represents...
potentially reversible lung disease\textsuperscript{7}, but there are exceptions. Widespread fine intralobular fibrosis may also produce a pattern of GGO\textsuperscript{8}, but in this situation there is usually accompanying distortion and dilatation of the bronchi ('traction bronchiectasis') (Fig 4). It is erroneous simply to equate GGO on HRCT images with 'active alveolitis'.

Patchy density differences in the lung parenchyma (often referred to as a mosaic attenuation pattern) may be seen in patients with conditions that result in regions of underperfused lung. This situation occurs in patients with a primarily vascular disease, for example chronic thromboembolic disease. In patients with airways disease, areas of underventilated (and consequently underperfused) lung are of decreased attenuation relative to areas of over-perfused lung which appear as areas of GGO. In these situations, the vessels within the apparent areas of GGO will appear engorged (Fig 5).

One of the greatest challenges in HRCT interpretation is the recognition of GGO (most often in the face of a normal chest radiograph), and the assimilation of this basic sign with other HRCT features to determine whether the cause is infiltrative lung disease, vascular disease or small airways disease\textsuperscript{9}.

**Diagnostic accuracy of high-resolution computed tomography**

The improved sensitivity of HRCT over chest radiography and, in some instances, lung function testing, has been shown in a number of conditions.
For example, in one study of patients with extrinsic allergic alveolitis 11/14 (79%) of HRCTs showed GGO compared with only 5/14 (36%) on chest radiography\(^3\). In many of the connective tissue diseases, notably rheumatoid arthritis, systemic sclerosis and Sjögren's syndrome, HRCT reveals a variety of coexisting interstitial and airway abnormalities, often at a stage when patients are asymptomatic and have an apparently normal chest radiograph.

It is impossible to combine the evidence from many of the studies that have compared the sensitivity of HRCT to chest radiography because of differences in CT scanning technique, observer experience and patient selection. However, those studies that can be compared show that the average sensitivity of HRCT for the detection of diffuse interstitial lung disease is approximately 94%, compared with 80% for chest radiography. The superior sensitivity of HRCT reflects its ability both to detect extremely subtle density differences in the lung parenchyma,
example in cases showing emphysema or GGO, and also to show disease in radiographically inaccessible parts of the lung, for example early fibrosing alveolitis in the costophrenic recesses (Fig 6). Several rudimentary image processing techniques can be used to enhance the ability of HRCT to detect extremely subtle parenchymal abnormalities\textsuperscript{11,12}, but these are time-consuming and are not routinely applied.

The increased sensitivity of HRCT compared to chest radiography is not, as is often the case with diagnostic tests, achieved at the expense of reduced specificity: false-positive diagnoses of diffuse lung disease are relatively uncommon with HRCT, in contrast to the frequent difficulty of deciding whether or not a chest radiograph shows real diffuse lung disease.

Several diffuse lung conditions have a more or less diagnostic appearance on HRCT. Thus, the appearance of bizarre-shaped cavitating lesions concentrated in the upper lobes is virtually pathognomonic of Langerhans cell histiocytosis (Fig 7). By contrast, the relatively recently defined histopathological entity of non-specific interstitial pneumonitis has a wide variety of parenchymal patterns and distributions on HRCT – to the extent that there is some question as to whether a condition with such a heterogeneous appearance should be considered a single disease entity (Fig 8).

With increasing experience, several conditions are now regarded as having a diagnostic appearance on HRCT (Table 3), such that lung biopsy of any sort is rarely sought provided that the HRCT features and clinical picture are compatible. Nevertheless, it is easy to overlook the fact that several diffuse lung diseases have reasonably characteristic appearances on a plain chest radiograph. In this respect, the diagnostic gain of HRCT over chest radiography is sometimes overstated in, for example,
fibrosing alveolitis with its typical basal reticulonodular pattern. However, it is the added confidence that HRCT brings to the diagnosis of many diffuse lung diseases that is one of its most important assets. The greater degree of confidence, which is not easily quantified in clinical studies, was first highlighted by Mathieson et al\textsuperscript{13}, and has been subsequently reiterated\textsuperscript{14-17}.

The confidence with which an HRCT diagnosis of specific diffuse lung disease can be made depends heavily on experience. This is borne out in the sequence of published descriptions of the HRCT appearances of extrinsic allergic alveolitis. Early reports suggested that the findings of GGO and a faint nodular pattern were nonspecific\textsuperscript{18}, whereas more recent studies suggest that this constellation of signs is virtually diagnostic\textsuperscript{19}.

### Other uses of high-resolution computed tomography

The clinical use of HRCT is not confined to diagnosis. HRCT can be used both to delineate precisely the extent of disease and to gauge disease reversibility (more controversially termed 'disease activity'). The HRCT signs which denote reversible disease are largely applicable, irrespective of the histopathological diagnosis (listed in Table 4). These secondary uses of HRCT have been mainly applied to patients with fibrosing alveolitis\textsuperscript{20} in which the extent\textsuperscript{21} and pattern\textsuperscript{22} shown on HRCT are strongly predictive of response to treatment and prognosis. HRCT has elucidated the sometimes complex mixed obstructive and restrictive functional abnormalities found in some diffuse lung diseases such as extrinsic allergic alveolitis, sarcoidosis and fibrosing alveolitis admixed with emphysema. Specifically, patients with fibrosing alveolitis and coexisting centrilobular emphysema may have apparently normal lung volumes as measured by plethysmography (because of the opposing functional effects of the two diseases), and a strikingly low gas diffusing capacity. The coexistence of these two diseases, responsible for spuriously normal lung volumes, can be

### Table 3. Diffuse (interstitial and airways) lung diseases with 'diagnostic' high-resolution computed tomography appearances.

- cryptogenic fibrosing alveolitis (usual interstitial pneumonitis histological subtype)
- centrilobular emphysema
- sarcoidosis
- Langerhans cell histiocytosis
- extrinsic allergic alveolitis (subacute)
- lymphangioleiomyomatosis
- alveolar proteinosis
- bronchiectasis
- constrictive obliterator bronchiolitis
- diffuse panbronchiolitis

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**Key Points**

- High-resolution computed tomography (HRCT) lends precision to the detection of early diffuse infiltrative lung disease, particularly when interpreted in conjunction with lung function tests
- The degree of diagnostic advantage of HRCT over chest radiography is disease-specific and does not apply equally to all diffuse lung diseases
- Several diffuse lung diseases have sufficiently characteristic appearances on HRCT to obviate the need for biopsy confirmation of the diagnosis
- Estimation of disease reversibility and prognostic information can be extracted by careful interpretation of HRCT images, especially in fibrosing lung disease
readily recognised on HRCT images. Careful study of the morphological characteristics on HRCT of other diffuse lung diseases will doubtless yield further pathophysiologic insights.

References

1. Webb WR, Müller NL, Naidich DP. Technical aspects of HRCT. In: High-resolution CT of the lung, 2nd edn. Philadelphia: Lippincott-Raven, 1996: 1–21.
2. Colby TV, Swensen SJ. Anatomic distribution and histopathologic patterns in diffuse lung disease: correlation with HRCT. J Thorac Imag 1996;11:1–26.
3. Austin JHM, Müller NL, Friedman PJ, Hansell DM, et al. Glossary of terms for CT of the lungs: recommendations of the Nomenclature Committee of the Fleischner Society. Radiology 1996;200:327–31.
4. Webb WR, Müller NL, Naidich DP. An illustrated glossary of HRCT terms. In: High-resolution CT of the lung, 2nd edn. Philadelphia: Lippincott-Raven, 1996: 295–311.
5. Remy-Jardin M, Remy J, Giraud F, Watrinne L, Gosselin B. Computed tomography (CT) assessment of ground-glass opacity: semiotics and signifi-
cance. J Thorac Imag 1993;8:249–64.
6. Collins J, Stern EJ. Ground-glass opacity at CT: the ABCs. Am J Roentgenol 1997;169:355–67.
7. Leung AN, Miller RR, Müller NL. Parenchymal opacification in chronic infiltrative lung diseases: CT-pathologic correlation. Radiology 1993;188:209–14.
8. Remy-Jardin M, Giraud F, Remy J, Copin MC, et al. Importance of ground-glass attenuation in chronic diffuse infiltrative lung disease: pathologic-CT correlation. Radiology 1993;189:693–8.
9. Worthy SA, Müller NL, Hartman TE, Swensen SJ, et al. Mosaic attenuation pattern on thin-section CT scans of the lung: differentiation among infiltrative lung, airway, and vascular diseases as a cause. Radiology 1997;205:465–70.
10. Hansell DM, Moskovic E. High-resolution computed tomography in extrinsic allergic alveolitis. Clin Radiol 1991;43:8–12.
11. Remy-Jardin M, Remy J, Artaud D, Deschilfde F, Duhamel A. Diffuse infiltrative lung disease: clinical value of sliding-thin-slab maximum intensity projection CT scans in the detection of mild micronodular patterns. Radiology 1996;200:333–9.
12. Fotheringham T, Chabat F, Hansell DM, Wells AU, et al. A comparison of methods for enhancing the detection of areas of decreased attenuation on CT caused by airways disease. J Comput Assist Tomogr 1999;23:385–9.
13. Mathieson JR, Mayo JR, Staples CA, Müller NL. Chronic diffuse infiltrative lung disease: comparison of diagnostic accuracy of CT and chest radiography. Radiology 1989;171:111–6.
14. Nishimura K, Izumi T, Kitaichi M, Nagai S, Itoh H. The diagnostic accuracy of high-resolution computed tomography in diffuse infiltrative lung diseases. Chest 1993;104:1149–55.
15. Padley SPG, Hansell DM, Flower CDR, Jennings P. Comparative accuracy of high resolution computed tomography and chest radiography in the diagnosis of chronic diffuse infiltrative lung disease. Clin Radiol 1991;44:227–31.
16. Grenier P, Chevret S, Beigelman C, Brauner MW, et al. Chronic diffuse infiltrative lung disease: determination of the diagnostic value of clinical data, chest radiography, and CT and Bayesian analysis. Radiology 1994;191:383–90.
17. Bonelli FS, Hartman TE, Swensen SJ, Sherrick A. Accuracy of high-resolution CT in diagnosing lung diseases. Am J Radiol 1997;170:1507–12.
18. Silver SF, Müller NL, Miller RR, Lefcoe MS. Hypersensitivity pneumonitis: evaluation with CT. Radiology 1989;173:441–5.
19. Hansell DM, Wells AU. Clinical usefulness of high resolution computed tomography in cryptogenic fibrosing alveolitis. Thorax 1998;53:1080–7.
20. Wells AU, Hansell DM, Rubens MB, Cullinan P, et al. The predictive value of thin-section computed tomography in fibrosing alveolitis. Am Rev Respir Dis 1993;148:1076–82.

Table 4. Summary of reversible patterns on high-resolution computed tomography.

| Pattern of disease                        | Reversibility |
|-------------------------------------------|---------------|
| Ground glass opacification                | +++++/-       |
| Air space consolidation                   | ++/-          |
| Nodular pattern                           | ++/-          |
| Interlobular septal thickening            | +/-           |
| Reticular pattern with architectural distortion | - - -         |

+ = reliability of sign of reversible disease; - = reliability of sign of irreversible disease.