

HIGH-RESOLUTION CT OF THE LUNG PARENCHYMA: TECHNIQUES, SIGNS OF DISEASE, AND CLINICAL UTILITY

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To date, computed tomography has played a limited role in the investigation of diffuse lung disease. Plain radiography remains the standard for detection and characterization of diffuse pulmonary processes. One of the main limitations of plain radiography in the evaluation of diffuse pulmonary parenchymal disease is the superimposition of structures due to the projectional format of that imaging method. As computed tomography offers an unobstructed cross-sectional view of the thorax, its role is being investigated for early detection and characterization of diffuse parenchymal lung diseases. The advent of high-resolution CT (HRCT) has permitted detailed analyses of the lung parenchyma. A body of work now exists that establishes the basis for the interpretation and clinical application of HRCT. Although this is still an area of active research, its prospects appear exciting. This lecture will review the current state of the art.

WHAT IS HRCT ?

HRCT simply represents the use of a combination of 1-2 millimeters thick CT slices reconstructed with pixel sizes in the range of 200-300 microns. This technique can now be performed on any modern CT scanner. To achieve small pixel size, the circle of reconstruction or field of view is reduced so as to cover each lung field separately. To achieve maximum resolution, it is also important to use appropriate high-resolution reconstruction algorithms designed for visualizing small high-contrast structures. These algorithms are now standard on all current scanners. HRCT can therefore be implemented on a routine basis provided proper technique is used.

TECHNICAL CONSIDERATIONS

With thinly collimated sections, the signal-to-noise ratio of the image may be degraded because of the reduced number of photons reaching the detectors. Therefore, in HRCT it is necessary to increase radiation exposure levels to achieve optimal image quality. As a consequence it is not practical to study the entire lung with thin sections. The preferred method is to first scan the lungs with conventional 8-10 mm thick sections and then scan the areas of suspected abnormalities with a few thinner section scans.

Optimal studies of the lung parenchyma for diffuse pathology are best performed at full inspiration to promote uncrowding of vascular structures as well as to avoid gravity-dependent fluid accumulation and atelectasis. Such physiologic gravity-dependent densities can often be seen in the posterior aspect of the lower or upper lobes in the supine patient. Often, a repeat scan at full inspiration will demonstrate disappearance of these densities and is all that is necessary to clarify the nature of these densities. Alternatively, a prone scan of the same area can serve the same purpose. Contrast enhancement is rarely necessary to evaluate diffuse lung disease.

Proper window settings are critical for accurate display of diffuse pathology. The window level should be set at the CT value midway between that of the structure being examined and that of the surrounding tissue. For example, in a crated lung tissue measuring generally about -800 HU a small vessel measuring about 50 HU will be best displayed at a window level of -375 HU.

Using a lower window level makes structures appear larger than they truly are. The window width should be chosen so as to encompass the entire range of tissue densities present in the image. Generally, a window width of $1400-2000$ HU is appropriate in the lung parenchyma.

BASIC HRCT SIGNS

A good understanding of the basic HRCT signs of lung disease is essential to an appreciation of its potential clinical applications. Correlations with either inflated lung specimens or Gough sections indicate that the basic lobular anatomy of the lung can be recognized with HRCT. Resolution of structures in the order of $100-200$ microns has been reported. Secondary interlobular septa are readily visualized at the periphery of the lung. Differentiating

features of air-space versus interstitial disease have been defined keeping in mind that such a division is arbitrary in that most pathologic processes combine both.

Signs of Air-space Disease

Experiments with inflated lungs following intrabronchial injection of fluids and observation of autopsy or clinical cases in patients with air-space disease reveal characteristic appearances evolving into well-defined patterns. The earliest manifestation of an air-space process is the appearance of subtle poorly margined nodular densities corresponding to partially filled air-spaces within the primary lobule. Typically, these so-called air-space nodules may reach a size of up to 1 cm in diameter and rapidly coalesce with neighboring lesions to form larger opacities eventually assuming a segmental distribution with typical air-bronchograms. Interestingly, the distribution of these air-space processes is often shown by CT to be predominantly although not exclusively central with sparing of the subpleural zones, a fact not always appreciable on plain films.

More important is the ability of CT to detect air-space processes before they become apparent on plain films. The most significant impact of this capability relates to the monitoring of patients at high risk for infectious pulmonary complications such as bone marrow transplant recipients or other immunodeficient patients. CT can provide a lead time of several days over eventual detection by plain films and accurately pinpoint suspicious areas for eventual bronchoscopic sampling.

Signs of Interstitial Disease

Interface signs

The most common and earliest HRCT abnormality found in the presence of interstitial disease is a finely irregular and thickened appearance of the normally smooth interfaces of the parenchyma with vessels, bronchi and visceral pleura. Typically, interlobar fissures appear thick and irregular, vascular borders demonstrate a saw-toothed appearance and bronchial walls are also thickened and irregular thus becoming visible over a longer portion of their course than normal. These signs can be seen on HRCT in patients with normal radiography. A caveat is that with pulmonary emphysema the parenchymal interfaces may also appear irregular but only near areas of bullous destruction thus allowing differentiation.

Interstitial nodules

Unlike air-space nodules, interstitial nodules appear sharply marginated on HRCT and even when profuse do not coalesce into a single opacity. Nodules as small as 1 mm in diameter be detected, an important advantage over plain radiography.

Reticular patterns

Three patterns of interstitial reticulation distinguishable by the size of their lattice element can be recognized with HRCT. First and most characteristic is a large network of polyhedral reticular elements of 15-25 mm in diameter centered on a pulmonary artery characteristic of thickened secondary lobular architecture. This findings is typically seen in cases of interstitial pulmonary edema or lymphangitic carcinomatosis and has been observed in undocumented cases of presumed viral pneumonia. The HRCT appearance of lymphangitic carcinomatosis is very suggestive with a typical knotty-like appearance of the septa due to endo-lymphatic tumor nodules.

The second pattern of reticulation is characterized by smaller (then) 6-10 mm elements probably corresponding to primary lobules. This pattern is frequently associated with small cystic changes resulting in a honeycombed appearance. This pattern is found in cases of interstitial fibrosis as well as in diseases states involving diffuse thickening or infiltration of the interstitium as in lymphangioleiomyomatosis or diffuse amyloidosis. Furthermore, unlike air-space pathology, these changes are predominantly peripheral and concentrated in the subpleural zones of the lung.

An important pitfall is the frequent occurrence of pseudoreticulation in the gravity-dependent regions of the lungs due to accumulation of fluid and physiologic atelectasis. In such cases, prone views at full inspiration are mandatory to confirm presence of disease.

The last patterns of reticulation reported is that of a fine diffusely distributed network of 2-3 mm basic elements observed in a few cases of miliary TB and in cases of reactions to methotrexate therapy probably corresponding to a diffuse generalized involvement of the interstitium.

During the evolution of reticular patterns, focal thickening at the points of crossing of the reticular network leads to the formation of a reticulonodular pattern.

Ground glass opacities

The last category of signs described in interstitial disease is that of ill-defined patches of increased parenchymal density with a ground glass appearance which correlate pathologically with diffuse thickening of the interstitium with partial or complete obliteration of air-spaces. Early evidence indicates that

these patches may represent areas of more active disease thus offering a way of better guiding tissue biopsies and monitoring therapeutic response.

Various combinations of all these basic signs have been described in specific disease entities such as fibrosing alveolitis. Preliminary work suggestive of an enhanced diagnostic capability using HRCT have also been reported in differentiating entities such as bronchiolitis obliterans and usual interstitial pneumonia.

DISEASE-SPECIFIC APPLICATIONS

Pulmonary Emphysema

Pulmonary emphysema has been the subject of intensive CT studies. The destructive changes of emphysema can be exquisitely recognized with HRCT techniques. The most interesting prospect of such studies is the potential of more accurately quantifying the extent of pulmonary damage. A high correlation can be found between pathologic and HRCT-derived visual scores of centrilobular emphysema. Using image analysis techniques, the extent of destruction can be more precisely quantified. Such computational intensive methods now readily available offer the possibility of quantifying gas and tissue volumes and can serve as an adjunct to more conventional physiologic measurements. Positive correlations with volumetric parameters of pulmonary function tests (PFTs) have also been demonstrated, and ongoing studies are addressing the potential of using CT in further refining assessments of lung function. Clinically, CT has found some use in selecting patients for resection of bullous disease when PFTs are ambiguous.

Pneumoconioses

Very early, investigators realized that the clear visualization of pleural surfaces afforded by CT would lead to better detection of the pleural manifestations of asbestos exposure. More recently, the advent of high-resolution CT has opened the prospect of more accurate assessment of parenchymal asbestosis. Efforts to define and validate the basic signs of asbestosis are underway. These efforts are hampered by the understandable lack of a "gold standard" correlative data set and the known overlap between fibrotic changes due to asbestosis and those due to other etiologies. There is

great interest in further evaluating the ability of HRCT in more reliably detecting and classifying pneumoconioses as the current semiquantitative ILO classification suffers from methodological limitations related to frequent inter- and intra-observer interpretive errors. For example, the problem false negative as well as false positive plain film estimations of the presence and grading of pneumoconioses are well recognized. Attempts at correlating PFTs with CT findings in the assessment of asbestosis and silicosis have also been reported. Classification of silicosis using CT has also been suggested.

There is no doubt that HRCT, with its resolution on the order of 200 microns and its freedom from tissue super-imposition could offer significant advantages over plain radiology. For instance, unlike plain films, HRCT does not require summation of non-resolvable small lesions for effective detection. However, even at 200 micron the resolution of HRCT is still one to two orders of magnitude below what would be needed to match histologic resolution. Whether HRCT could provide more observer-independent and quantifiable data remains to be seen.

Assessment of Disease Extent, Activity, and Response

An exciting prospect for pulmonary CT would be a role in monitoring known disease to precisely quantify extent of damage, measure response to therapy and evaluate disease activity. The feasibility of quantifying damage secondary to bleomycin toxicity lung has already been demonstrated.

The CT changes in desquamative interstitial pneumonia can be monitored before and after corticosteroid therapy and used as an index of response. Ill-defined patches of increased CT density by CT have been correlated with regions of disease activity in idiopathic fibrosing alveolitis. Such a finding, if further confirmed, would indicate a potentially major role for HRCT monitoring of disease progression and guidance of pulmonary tissue sampling toward such areas and away from reticulated cystic regions of so-called honeycombed lung where end-stage non-diagnostic fibrosis is more likely to be found.

Similar findings can also be made in pulmonary sarcoidosis and usual interstitial pneumonia.

CONCLUSION

The chest radiograph is and should remain for the foreseeable future the primary method of imaging of the pulmonary parenchyma. CT is playing an increasingly important role in the characterization of focal pulmonary pathology using densitometric as well as specific morphologic information demonstrable only by CT. Although in its infancy, high resolution CT shows great promise in the investigation of diffuse parenchymal pathology. The richness of the HRCT semiology provides an opportunity to test whether this technique could offer:

1. More powerful classification of disease states
2. Possible quantification of disease extent
3. Less observer-dependent detection and characterization of pathology as in pneumoconioses
4. Means of monitoring disease activity and therapeutic response
5. More sensitive means than plain films to detect occult pulmonary disease in relevant clinical settings

As the real cost of CT has decreased and as this technology has become the mainstay of radiologic imaging, it is not unreasonable to expect a greater awareness of its potential in defined clinical contexts. This should lead, we believe, to more formal prospective studies and hopefully more definitive answers in the near future.

SUGGESTED READING

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