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Advances in imaging

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ABSTRACT: In recent years there have been major advances in chest imaging. These include significant refinements in previously available techniques such as computed tomography (CT) and magnetic resonance (MR) imaging and the introduction of new techniques into the clinical armamentarium, particularly positron emission tomography (PET) imaging.

These advances have led to changes in the diagnostic approach to a number of conditions, particularly pulmonary embolism, lung cancer, diseases of the large and small airways, and diffuse lung disease. They have also brought new insights into the pathophysiology of lung disease.

State of the art CT and MR imaging now allow objective quantification of lung disease and assessment of regional changes in ventilation and perfusion caused by airway and parenchymal abnormalities.

The aim of this article is to summarize the most important clinical applications of the recent advances in imaging and to emphasize the topics of imaging research likely to attract particular attention from radiologists and clinicians in the near future.

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In recent months the *European Respiratory Journal* has published a series of articles on advances in imaging [1–8]. These articles have reviewed the current role of imaging in the diagnosis and management of various airway and pulmonary diseases and have highlighted potential areas of research. The present article will only consider what the author deems to be the most important clinical applications and the most pressing topics of imaging research. The article will focus on imaging in pulmonary embolism, lung cancer, airway diseases, and parenchymal lung disease. The discussion will be based on recent advances in computed tomography (CT) and magnetic resonance (MR) technology and the introduction of positron emission tomography (PET) imaging.

The main developments of CT in the chest have been the introduction of high-resolution CT (HRCT), spiral CT and, more recently, multislice CT.

HRCT is defined as thin-section CT (1–2-mm collimation scans) optimized by using a high spatial-resolution (edge enhancing) algorithm. Several studies

have shown that HRCT closely reflects the macroscopic (gross) pathological findings. HRCT presently has the best sensitivity and specificity of any imaging method for the assessment of focal and diffuse lung diseases.

Spiral (helical) CT provides continuous scanning while the patient is being moved continuously through the CT gantry. It allows true volumetric scanning of the entire lung during a single breath hold and has replaced the slice-by-slice acquisition of conventional CT. Spiral CT permits for reconstruction of images in any plane as well as three-dimensional (3D) display of structures. With the use of graphics based software programs, spiral CT allows depiction of the luminal surface of the airways with images that resemble those of bronchoscopy (CT bronchoscopy) or bronchography (CT bronchography). The combination of spiral CT with administration of intravenous contrast (CT angiography) allows visualization of pulmonary and systemic vessels with a detail that is comparable to that of conventional angiography. CT angiography

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is rapidly becoming the imaging modality of choice in the diagnosis of pulmonary embolism.

While conventional spiral CT scanners were limited to one detector, multislice CT utilizes more than one data acquisition system connected to multidetector arrays. Currently four and eight detector array multislice CT scanners are available. Multislice CT results in improved temporal resolution (faster scanning time, decreased cardiac and respiratory motion artifacts) and improved spatial resolution. The new scanners also have markedly increased image processing capabilities, which will almost certainly lead to enhancements in computer-aided diagnosis.

The main recent developments in MR imaging have been the introduction of MR angiography and functional MR ventilation imaging. MR angiography consists of 3D single breath-hold images obtained using gadolinium-based contrast agents. This technique holds great promise in the diagnosis of pulmonary embolism. Functional MR ventilation imaging allows assessment of regional ventilation as well as evaluation of regional oxygen partial pressure and ventilation/perfusion ratios (V'/Q').

PET imaging depicts differences in the metabolism of tissues. PET imaging with ^{18}F -fluoro-2-deoxyglucose (FDG) is rapidly becoming a major tool in oncology, particularly in the staging of lung cancer. Because cancer cells have a much higher rate of glycolysis than non-neoplastic cells, they have increased uptake of glucose and therefore high signal on FDG-PET imaging.

Pulmonary embolism

Until recently lung scintigraphy, lower-limb ultrasonography and pulmonary angiography were the main imaging techniques employed for the diagnosis of pulmonary embolism (PE). However, despite the development of a variety of diagnostic algorithms, in many cases a definitive diagnosis was not made due to limitations of these imaging techniques. The introduction of spiral CT angiography in the early 1990s was quickly followed by its application to the diagnosis of PE. Spiral CT for PE has rapidly evolved in conjunction with advances in single detector and more recently multislice spiral CT scanners and is increasingly employed in the diagnostic algorithm for acute PE.

The diagnostic accuracy of spiral CT is influenced by a number of technical parameters, including section thickness, reconstruction algorithms, quality of contrast enhancement, and use of single slice or multislice spiral CT. Using optimal technique on single-detector scanners the sensitivity and specificity of spiral CT in the diagnosis of acute PE is ~90% [1, 9]. Several studies have shown that spiral CT is clearly superior to scintigraphy but it does have limitations particularly in the diagnosis of subsegmental PE.

Because of the limitations of each of the various imaging modalities, there is considerable controversy about the optimal diagnostic algorithm for the assessment of patients who have clinically suspected PE. Based on recent reviews on the subject by

DONKERS-VAN ROSSUM [1] and other investigators [9, 10], it seems reasonable to make the following recommendations for imaging of patients with suspected PE. 1) Patients who have symptoms or signs of deep vein thrombosis (DVT) should first undergo ultrasound of the legs. 2) Patients who have no signs or symptoms of DVT and symptomatic patients with negative Doppler ultrasound examination and who have no chronic obstructive pulmonary disease (COPD) or parenchymal lung disease should undergo V'/Q' scintigraphy. 3) Patients with intermediate probability V'/Q' scans and patients with low probability scans but high clinical index of suspicion for acute PE should undergo spiral CT. 4) Spiral CT should replace scintigraphy as the initial imaging modality in patients who have severe COPD or extensive parenchymal lung disease.

It seems reasonable to conclude that in the vast majority of outpatients adequate assessment can be provided by various combinations of clinical evaluation, measurement of plasma D-dimer levels, lower-limb ultrasonography, and lung scintigraphy. It is likely that spiral CT will be used most often in inpatients with underlying pulmonary disease because D-dimer has a very low specificity in these patients and scintigraphy has a greater likelihood of intermediate probability scans [1, 11]. However, a large number of questions remain to be answered and will require careful evaluation in the near future. 1) What is the most cost-effective diagnostic algorithm for the evaluation of patients with clinically suspected PE? 2) What is the diagnostic accuracy of multislice spiral CT and what is the optimal technique for the evaluation of these patients on multislice CT? 3) How useful is pulmonary angiography in the evaluation of patients with negative spiral CT? 4) Can treatment be safely withheld in patients who have a negative spiral CT? 5) What is the natural history of acute PE? 6) How long do these patients need to be treated?

Proper evaluation of the first four questions will require prospective multicentre studies. These studies will need to include a sufficiently large number of patients to provide adequate statistical power and will need to employ multisection spiral CT technology. The reliability of the interpretation of all modalities will need to be assessed using blinded independent interpretations. Furthermore, clinical follow-up of negative patients must be performed to establish the safety of a negative spiral CT examination.

Proper evaluation of the natural history of acute PE and optimal treatment period may be difficult with CT because of the concerns about radiation dose with repeated scans and the need for iodinated intravenous contrast. Recent studies have shown a potential role of MR angiography in the diagnosis of acute PE [12, 13]. As with CT, MR angiography allows direct visualization of pulmonary emboli. MR has the advantage of not requiring radiation or the use of iodinated intravenous contrast. Because it is more expensive and less readily available it will probably play a less important role than CT in the near future. However, it is ideally suited for follow-up studies of patients being treated for PE to determine the natural history of the emboli and time required for complete

resolution of the emboli with different treatment strategies. Further research in MR imaging will also include evaluation of new intravascular contrast agents, faster MR gradients and more efficient MR techniques to allow better assessment of segmental and subsegmental pulmonary arteries. Of particular interest is the potential to develop MR contrast agents that will remain in the blood pool for long periods of time and therefore allow optimal imaging of the entire pulmonary vasculature.

Lung cancer

Imaging of lung cancer on chest radiography, CT, and MR imaging is based largely on morphological assessment and has well-known limitations. PET imaging permits assessment of metabolic function and therefore has a higher accuracy in distinguishing malignant from benign tissues. Currently the main substance utilized for the assessment of lung cancer with PET is FDG.

Several studies have shown that FDG-PET imaging is superior to CT in the diagnosis and staging of nonsmall cell lung cancer. As summarized by VANTEENKISTE and STROOBANTS [2] the sensitivity of PET imaging in distinguishing malignant from benign nodules is ~95%, the specificity 80% and the accuracy 90%. False-negative results occur mainly in nodules <1 cm in diameter and in bronchoalveolar carcinoma. False-positive results occur mainly in inflammatory lesions such as tuberculosis. PET imaging has a sensitivity, specificity and accuracy of 90% in the staging of mediastinal lymph nodes [2]. False-negative results are seen mainly in patients who have small tumour deposits within the lymph nodes.

Although the studies so far have included small numbers of patients the results are sufficiently convincing to suggest the following indications for FDG-PET imaging as a complementary tool to CT. 1) Assessment of indeterminate lung nodules ≥ 1 cm in diameter. 2) Staging of mediastinal lymph nodes. Patients with negative PET scan can proceed directly to thoracotomy. Because of the <100% specificity of PET imaging, however, patients with positive PET imaging need to have further evaluation by biopsy or mediastinoscopy.

The results of several preliminary studies indicate that whole body FDG-PET imaging is superior to CT, MR imaging and bone scintigraphy in the extrathoracic staging of lung cancer [2]. The only exception has been assessment of brain metastases, where PET imaging has been shown to have a lower sensitivity than CT and MR imaging. It needs to be emphasized, however, that the studies to date have included small numbers of patients and have included some false-positive results. Therefore, although PET imaging can complement conventional imaging in the assessment of the presence of extrathoracic metastases there is insufficient data to determine that it can replace conventional imaging [2].

The main areas of imaging and clinical research in the near future will need to focus on the validation of the results of the studies performed so far and

assessment of the cost-effectiveness of various diagnostic algorithms using PET imaging. Specific questions that need to be addressed include. 1) What is the optimal diagnostic algorithm for the assessment of patients with a solitary lung nodule? 2) In which patients should PET imaging replace CT? 3) What is the role of PET imaging in the evaluation of extrathoracic metastases? 4) What is the optimal imaging algorithm for the staging of lung cancer? 5) What is the cost-efficiency of the various imaging algorithms in the diagnosis and staging of lung cancer? 6) To what extent do these algorithms influence patient outcome and survival? 7) What is the role of PET imaging in patients with small cell lung cancer?

Sufficient answers to these questions will require large prospective randomized multicentre studies. Research will also need to focus on radiopharmaceuticals other than FDG that may provide greater accuracy in the diagnosis and staging of lung cancer.

Airway diseases

Spiral CT with the use of multiplanar reconstructions and 3D reformations is helpful in the assessment of focal airway stenoses and involvement of central airways by pulmonary carcinoma [3]. Because of the ability to provide simultaneous depiction of endoscopic images (CT bronchoscopy) and adjacent tumour or enlarged nodes, spiral CT with volume rendering can be a helpful guide to transbronchial biopsy. However, although the various types of reconstructions available on spiral CT allow better depiction of intraluminal and airway wall abnormalities, their diagnostic accuracy and role in the initial evaluation and follow-up of patients with large airway diseases remains to be established.

HRCT is the method of choice in the diagnosis of bronchiectasis and in the vast majority of centres it has completely replaced bronchography in the assessment of these patients. As reviewed by HANSELL [4], in the past few years HRCT has been increasingly used in the evaluation of patients with clinically suspected small airway disease. These include the evaluation of the various forms of bronchiolitis as well as other entities, such as extrinsic allergic alveolitis and asthma, in which bronchiolar obstruction may play an important role in the severity of airway obstruction. In many patients with bronchiolitis a specific diagnosis can be suggested based on the clinical history and the pattern and distribution of abnormalities on HRCT. HRCT allows not only assessment of the direct morphological changes related to bronchiolitis but also assessment of regional alterations in ventilation and perfusion. Bronchiolar obstruction results in decreased ventilation, which in turn results in reflex vasoconstriction. These changes are detected on HRCT by the presence of lobular or larger areas of decreased attenuation and vascularity and the presence of air trapping on expiratory CT images. These parameters on HRCT have been shown to correlate well with functional measurements of airway obstruction and air trapping [4].

Based on the data in the literature it seems reasonable to conclude that HRCT is indicated in the assessment of patients with unexplained obstructive lung disease or suspected infectious bronchiolitis. HRCT may also prove to be a useful research tool to characterize and quantify the morphological and functional abnormalities of the various diseases associated with small airway abnormalities. However, further studies are required to determine the exact role of HRCT in the evaluation of small airway diseases.

Functional imaging of pulmonary ventilation and perfusion can also be obtained using MR imaging [5]. MR allows assessment of global lung function, such as measurement of inspiratory and expiratory lung volumes, as well as regional lung function, such as ventilation per unit volume at the lobar, segmental, or subsegmental level. It also allows simultaneous measurement of lung perfusion. Although MR has a lower resolution than CT, it has the advantages of lack of radiation and ability to provide information about a broader range of functional parameters such as V'/Q' ratios and regional oxygen partial pressure [5]. MR imaging may provide higher sensitivity than CT, scintigraphy and pulmonary function tests in the diagnosis of ventilation defects in patients with airway diseases and emphysema [5]. Therefore, it may allow earlier recognition of obstructive airway disease.

The results using MR for the assessment of ventilation and perfusion are encouraging but are based on a small number of studies performed in a few centres and using different techniques. The research in the near future will need to focus on optimal MR techniques and comparisons of MR with other functional parameters to determine the role of functional MR imaging in the assessment of various airway and parenchymal abnormalities.

Lung parenchyma

A number of studies in the late 1980s and early 1990s showed that HRCT closely reflected the macroscopic pathological findings of focal and diffuse lung diseases [14–16]. Several groups of investigators have shown that HRCT allows better assessment of the pattern and distribution of parenchymal lung diseases than is possible on the chest radiograph, and that it is therefore superior to chest radiography in the differential diagnosis of chronic infiltrative lung diseases [17–19]. As reviewed by FRANQUET [7], more recent studies have shown that HRCT can also be a useful adjunct to conventional radiography in the assessment of acute lung disease, particularly in the immunocompromised host. Based on the data in the literature, it seems reasonable to recommend the use of HRCT in immunocompromised patients who have clinically suspected lung disease but who have normal or questionable radiographical findings and as a guide to the optimal site for bronchoalveolar lavage or lung biopsy [7].

Most of the studies using CT to evaluate the lung parenchyma have relied on subjective analysis of the CT images. Such analysis is inevitably associated with considerable inter- and intra-observer variability.

Because the CT data are digital there is great potential for objective analysis and quantification of the parenchymal abnormalities. Such quantification is particularly useful in evaluating progression of the disease over time and efficacy of medical or surgical treatment. Thus far objective evaluation of lung disease has been largely limited to the quantification of emphysema. These measurements are based on analysis of the frequency distribution of the attenuation values of the lung and have been shown to correlate closely with pathological severity of emphysema [6]. However further research is required to establish the optimal CT parameters for quantification of emphysema, the reproducibility of the CT measurements, and the accuracy of CT in distinguishing emphysema from other obstructive lung diseases.

Quantification of emphysema on computed tomography is based on a relatively straightforward evaluation of attenuation values. Quantification of infiltrative lung disease requires more sophisticated techniques such as texture analysis. One such technique is the adaptive multiple feature method which uses as many as 22 independent texture features to classify the normal lung and different types of parenchymal abnormality [20]. This kind of analysis may reveal abnormalities not readily identified on visual inspection and a greater reliability in evaluating lung changes on longitudinal studies. Computer-assisted diagnosis also has a great potential in the detection of pulmonary nodules. Research in the near future will need to focus on optimal computed tomography techniques and improved algorithms for the objective quantification of pulmonary parenchymal abnormalities.

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