Spiral computed tomographic scanning and magnetic resonance angiography for the diagnosis of pulmonary embolism

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Introductory articles

Pulmonary embolism: prospective comparison of spiral CT with ventilation-perfusion scintigraphy

JR Mayo, M Remy-Jardin, NL Muller, J Remy, DF Worsley, C Hossein-Foucher, JS Kwong, MJ Brown

Purpose. To compare prospectively the accuracy of spiral computed tomography (CT) with that of ventilation-perfusion scintigraphy for diagnosing pulmonary embolism. Materials and methods. Within 48 hours of presentation, 142 patients suspected of having pulmonary embolism underwent spiral CT, scintigraphy, and (when indicated) pulmonary angiography. Pulmonary angiography was attempted if interpretations of spiral CT scans and of scintigrams were discordant or indeterminate and intermediate-probability, respectively. Results. In the 139 patients who completed the study, interpretations of spiral CT scans and of scintigrams were concordant in 103 patients (29 with embolism, 74 without). In 20 patients, intermediate-probability scintigrams were interpreted (six with embolism at angiography, 14 without); diagnosis with spiral CT was correct in 16. Interpretations of spiral CT scans and those of scintigrams were discordant in 12 cases; diagnosis with spiral CT was correct in 11 cases and that with scintigraphy was correct in one. Spiral CT and scintigraphic scans of four patients with embolism did not show embolism. Sensitivities, specificities, and \( \phi \) values with spiral CT and scintigraphy were 87%, 95%, and 0.85 and 65%, 94%, and 0.61, respectively. Conclusion. In cases of pulmonary embolism, sensitivity of spiral CT is greater than that of scintigraphy. Interobserver agreement is better with spiral CT. (Radiology 1997;205:447-452)

Diagnosis of pulmonary embolism with magnetic resonance angiography

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Background. Diagnosing pulmonary embolism may be difficult, because there is no reliable noninvasive imaging method. We compared a new noninvasive method, gadolinium-enhanced pulmonary magnetic resonance angiography, with standard pulmonary angiography for diagnosing pulmonary embolism. Methods. A total of 30 consecutive patients with suspected pulmonary embolism underwent both standard pulmonary angiography and magnetic resonance angiography during the pulmonary arterial phase at the time of an intravenous bolus of gadolinium. All magnetic resonance images were reviewed for the presence or absence of pulmonary emboli by three independent reviewers who were unaware of the findings on standard angiograms. Results. Pulmonary embolism was detected by standard pulmonary angiography in 8 of the 30 patients in whom pulmonary embolism was suspected. All 5 lobar emboli and 16 of 17 segmental emboli identified on standard angiograms were also identified on magnetic resonance images. Two of the three reviewers reported one false positive magnetic resonance angiogram each. As compared with standard pulmonary angiography, the three sets of readings had sensitivities of 100, 87, and 75 percent and specificities of 95, 100, and 95 percent, respectively. The interobserver correlation was good (\( \phi = 0.57 \) to \( 0.83 \) for all vessels, 0.49 to 1.0 for main and lobar vessels and 0.40 to 0.81 for segmental vessels). Conclusions. In this preliminary study, gadolinium-enhanced magnetic resonance angiography of the pulmonary arteries, as compared with
conventional pulmonary angiography, had high sensitivity and specificity for the diagnosis of pulmonary embolism. This new technique shows promise as a noninvasive method of diagnosing pulmonary embolism without the need for ionizing radiation or iodinated contrast material. (N Engl J Med 1997; 336:1422–7)

The introductory articles are timely in focusing a burgeoning interest in spiral (helical) computed tomographic (CT) scanning and magnetic resonance (MR) angiography for the diagnosis of pulmonary embolism (PE). Such interest is not surprising given the unsatisfactory accuracy of current diagnostic techniques. In spite of current limitations, spiral CT scanning is gaining broad acceptance among physicians and may soon be considered as the primary investigatory technique in the diagnostic strategy for PE. Gadolinium enhanced MR angiography of the pulmonary arteries shows promise as a useful alternative method for the detection and exclusion of PE, and obviates the need for ionising radiation or iodinated contrast material.

In this review diagnostic performances and technical limitations of these new imaging techniques in the diagnosis of PE are highlighted, and the questions raised by their potential inclusion in the diagnostic strategy are discussed.

Spiral CT angiography of pulmonary arteries

TECHNICAL CONSIDERATIONS

The CT technique consists of a volumetric spiral acquisition of radiographic data during breath holding and bolus intravenous injection of iodinated contrast agent. As spiral CT angiography is currently unable to identify reliably emboli within pulmonary arteries below the fourth generation, the region to be scanned may be confined to the volume between the aortic arch and the dome of the diaphragm. Using 3 mm collimation at a 5 mm/s table feed, a height of 12 cm may be covered during a 24 second breath hold. For patients who are unable to hold their breath, scanning is performed during quiet respiration.1 Contrast enhanced electron beam CT scanning based on a rotating source of x-rays produced by magnetically steering an electron beam round a 210° stationary tungsten target may also be used. The latter reduces acquisition time dramatically from one second to 50 ms. The rapid scanning time of this technique makes breath holding unnecessary and artifacts from respiratory and cardiac motion are minimised.2,3

Contrast medium, 100–140 ml, with a 24% or 30% concentration of iodine is injected through an antecubital vein catheter at a rate of 3–4 ml/s controlled by an automated injector with 15–20 s scan delay.4 Opacification of pulmonary arteries is assessed on mediastinal window settings. Accurate identification of segmental arteries on CT images requires a meticulous analysis of both mediastinal and lung window settings to identify the arteries according to their relationships with the bronchi. This CT scanning technique enables imaging of all main, lobar, segmental, and some subsegmental arteries in every patient. Reducing the collimation to 2 mm thickness will improve the ability to detect subsegmental emboli.5

As most of the pulmonary arteries are obliquely orientated to the scan plane, the cross sectional areas of the arteries are visually assessed by analysing successive images. A rapid display of images (cine mode) on the work station using a track ball may greatly facilitate the understanding of the vascular anatomy.

INTERPRETATION

The cardinal sign of acute pulmonary embolism on CT scans is a filling defect within the lumen of the pulmonary arteries (fig 1). When contrast medium can flow around a central clot, the appearance is either of a “railway track” if the artery lies parallel and within the scan plane, or a “polo mint” if the artery runs perpendicular to the scan plane. Mural defects are seen as peripheral areas of low attenuation within an arterial section.6 A complete occlusion is seen as an area of low attenuation which is not surrounded by contrast material and which occupies the entire arterial section. Ancillary signs of thromboembolic disease, such as small pleural effusion or pulmonary infarcts in subpleural lung, provide important additional evidence of pulmonary embolism. CT scanning may also reveal other abnormalities which provide an alternative explanation for the patient’s symptoms.6

Figure 1 Bilateral filling defects in the opacified lower lobe pulmonary arteries, central on the right (straight arrow) and peripheral on the left (curved arrow).
CAUSES OF MISTAKES
The most obvious patient-related factors that may cause suboptimal opacification of the pulmonary arteries include obstruction of the superior vena cava, a substantial left to right shunt, or a patent foramen ovale. Motion artifacts from rapid and deep breathing may cause severe image degradation, and this may generate pseudo filling defects in segmental arteries. The range of failed spiral CT examination for PE, including inconclusive examinations or technical failures, is reported to be between 2% and 10%.
False positive results may be due to streak artifacts at the level of the superior vena cava due to highly concentrated material contained within it. Hypodense and hyperdense radiating artifacts may generate pseudo filling defects in the anterior and superior branches of the right upper lobe and the right main pulmonary artery in particular.
Normal or slightly enlarged hilar lymph nodes and associated soft tissue seen as marginal areas of low attenuation, most often located between major bronchi and pulmonary arteries, may also be a potential cause of a false negative diagnosis of PE. Similarly, any peri-bronchovascular infiltration may result in areas of low attenuation and so simulate mural defects of PE. Although reformatted images that display the pulmonary artery in the longitudinal axis may be helpful, an intimate knowledge of the precise location of the hilar lymph nodes is desirable.
Parallel vessels running within the axial scanning plane may also create areas of low attenuation, and these too may be confused with PE. This artifact is mainly due to "partial volume averaging" between lung parenchyma and vessels—therefore, it is the attenuation of pulmonary vessels is averaged with the attenuation of lung parenchyma included within the thickness of the slice. (All structures within the unit volume of the slice, also known as a voxel, are averaged and represented by a single CT number for the surface of the image, also known as a pixel.) Thus, the attenuation values for each pixel represent the average of the attenuation values of all structures present within the voxel.) Such partial identification of vessels may create false positive or false negative results (fig 2). Tortuosity of vessels may also lead to misinterpretation of PE because this may give rise to linear or nodular low attenuation areas.

DIAGNOSTIC PERFORMANCE
In the landmark study six years ago by Remy-Jardin et al which included 45 patients, the sensitivity and specificity of spiral CT angiography for the detection of acute central PE (after exclusion of technically unsatisfactory examinations) were 100% and 96% respectively, as measured against conventional angiography. The sensitivity and specificity have since been re-evaluated by the prospective study by Mayo and colleagues (first introductory article) and by two other prospective series. The three investigations included 142, 75, and 149 patients, respectively, and compared spiral CT angiography with pulmonary angiography and ventilation-perfusion (V-P) scintigraphy. The reported sensitivity varied from 82% to 94%, and the specificity from 78% to 96% (table 1). The results of larger studies in progress—for example, the European Society of Thoracic Imaging multicentric prospective study—should define the accuracy with greater precision.

Inter-observer agreement in the diagnosis of PE with spiral CT was reported to be good (κ = 0.77, 0.85) providing the examination is restricted to within the central pulmonary artery and the main, lobar, and segmental arteries. Although clot within subsegmental arteries may be identified, many factors have contributed to limit the value of spiral CT scanning for vessels of this size.

Goodman et al were the first to emphasize the limitation of spiral CT scanning for the detection of subsegmental pulmonary embolism. In a study of 20 patients with an unresolved probability of having PE after V-P scintigraphy, pulmonary angiography identified emboli in 11 patients, in four of whom the embolus was limited to subsegmental vessels. Spiral CT scanning was positive in only one of the four patients, giving a sensitivity for spiral CT scanning of only 63% overall compared with 86% when only proximal pulmonary arteries are examined for analysis. These limitations raise two important questions: (1) What is the incidence of PE present as clot confined to subsegmental vessels, and (2) What is the clinical importance of such subsegmental emboli?

Pulmonary angiography allows detection of subsegmental clots but inter-observer variation at this anatomical level is high. Agreement between two experienced angiographers in the interpretation of angiograms from the PIOPED study of 1110 patients was 98% with lobar PE, 90% with segmental PE, and only 66% with subsegmental PE. The proportion of patients having PE located exclusively beyond the segmental arteries on pulmonary angiography varies according to the reported study from 6% to 30%. Of these, the PIOPED study included prospectively the broadest sample of patients, and so the reported prevalence of 6% is likely to be more representative of the entire population of patients suspected of having PE.

The clinical relevance of these smaller emboli remains controversial since the long term implications of such emboli have never been properly addressed, to our knowledge. The haemodynamic effects of a subsegmental embolus should be negligible in normal individuals but could be catastrophic in patients with pre-existing severe cardiopulmonary disease, and continued embolus confined to subsegmental vessels can be expected to exert an increasing cumulative adverse effect.

PLACE IN DIAGNOSTIC STRATEGY
V-P scintigraphy is currently the most commonly used first line examination in cases of clinically suspected PE. In approximately 70% of patients, however, results at V-P scintigraphy are non-diagnostic. Such results necessitate further investigation to exclude or confirm the diagnosis. Non-invasive colour Doppler ultrasound examination detects deep venous thrombosis in the legs in about 50% of patients with proved PE. Such detection would justify anticoagulant therapy and therefore obviate any further search for suspected additional pulmonary artery clot. However, negative findings of a leg study do not preclude the presence of PE. In patients with non-diagnostic results of V-P scintigraphy and normal findings at ultrasound examination of the leg veins, pulmonary angiography is classically the next imaging method recommended for the diagnosis of PE. Clinicians are reluctant to use it, however, because it is invasive with a 6% morbidity and a 0.5% mortality and is not always readily available.

Thus, most patients with intermediate probability of PE at V-P scintigraphy are treated without a definite imaging diagnosis. This may result in the overtreatment of patients who do not have acute PE or, more importantly, in the undertreatment of patients.
who do have acute PE. In their recent study Ferretti et al showed that spiral CT scanning allows an accurate diagnosis of acute PE in patients with intermediate probability at V-P scintigraphy and without deep venous thrombosis as shown by duplex sonography of the limbs.\textsuperscript{29} Spiral CT angiography was positive for PE in 39 of the 164 patients with intermediate probability at V-P scintigraphy and negative ultrasound examination, and provided an alternative diagnosis in 18 patients. In a three month follow up study PE occurred in six (5.4\%) of the 112 patients with a negative spiral CT scan who had remained untreated with anticoagulants.\textsuperscript{25}
of five diagnostic modalities (spiral CT scanning, lower limb ultrasonography, V-P scintigraphy, pulmonary angiography, and D-dimer plasma levels) van Erkel et al rated and the lowest cost per life saved included spiral CT scanning. In an analysis of 15 combinations of five diagnostic modalities (spiral CT scanning, lower limb ultrasonography, V-P scintigraphy, pulmonary angiography, and D-dimer plasma levels) van Erkel et al constructed a cost effectiveness decision model. They found that the five strategies with the lowest mortality rate and the lowest cost per life saved included spiral CT scanning, often in combination with lower limb ultrasonography. Such theoretical analysis, however, requires confirmation in large prospective studies.

Interestingly, Mayo et al in the introductory article compared V-P scintigraphy and spiral CT scanning prospectively in 142 patients and found that the sensitivity of spiral CT scanning was greater than that of scintigraphy (87% versus 65%) and that interobserver agreement was better with spiral CT scanning (κ = 0.85 versus 0.61). These findings consequently support the replacement of V-P scintigraphy by spiral CT scanning as the first line investigation in cases of suspected PE. There remains a reasonable argument, however, for using V-P scintigraphy first in young outpatients with no pre-existing lung disease when the clinical probability of PE is low.

Pulmonary MR angiography

MR imaging is also evolving as a valuable non-invasive means of detecting pulmonary artery clots directly. Major technical advances which have made pulmonary MR angiography practical include breath-hold three-dimensional gradient echo sequences, methods to shorten the echo time to enhance the vascular signal intensity, newer phased array surface coils, and intravenous injection of gadolinium used in conjunction with 3D or 2D gradient echo sequences. Several studies using different techniques on small numbers of patients have reported a sensitivity of 85–100% and specificity of 62–77%. The detectability of small clots in vessels at and beyond segmental branches and in vessels with in-plane orientation was limited.

The use of faster magnetic resonance hardware has made it possible to perform high resolution angiography during a single breath hold and in the second introductory article Meaney et al report a prospective comparison of gadolinium enhanced MR angiography with pulmonary angiography in 30 patients with suspected PE. In the eight patients with emboli demonstrated by pulmonary angiography, all five lobar and 16 of 17 segmental emboli were identified by the MR technique. The sensitivity of the readings from three independent radiologists were 100%, 87%, and 75%, respectively, with a specificity of 95%, 100%, and 95%. The authors emphasise that the technique is rapid, accurate, and more acceptable to patients than pulmonary angiography. The potential disadvantages include a lack of sensitivity in detecting subsegmental emboli and the fact that some patients may have a contraindication to MR imaging. There are three notable advantages of MR imaging over CT scanning: (1) MR imaging does not involve the use of nephrotoxic iodinated contrast agents; (2) pulmonary vascular imaging for PE may be combined with MR venography of the legs and pelvis for the evaluation of deep venous thrombosis; and (3) there is no radiation hazard. Recent studies have shown that gradient echo MR imaging is highly accurate for the diagnosis of lower limb deep venous thrombosis, the sensitivity and specificity being comparable to those of conventional venography. No venous access or injection of contrast agents is required.

Table 1

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<thead>
<tr>
<th>Symptoms suggestive of PE</th>
<th>Spiral CT angiography</th>
<th>Treatment</th>
<th>Ultrasoundography of lower limbs</th>
<th>Treatment</th>
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Table 1: Diagnostic performances of spiral CT angiography for diagnosing PE compared with pulmonary angiography and/or V-P scintigraphy

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<th>No. of patients</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
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<td>75</td>
<td>95</td>
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<td>139</td>
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Figure 3: Proposed decision tree for patients with suspected pulmonary embolism (modified from Goodman et al). Note that, in the presence of symptoms suggestive of both pulmonary embolism and deep venous thrombosis, the legs should be studied first.

Because the results of V-P scintigraphy are indeterminate in most cases and hence non-diagnostic/inconclusive, Goodman and Lipchik proposed in a recent editorial a new diagnostic algorithm where routine V-P scintigraphy is totally replaced by spiral CT angiography. The basic imaging methods for this decision tree are spiral CT scanning and ultrasonography of the lower limbs (fig 3). If a patient presents with symptoms and/or signs suggestive of PE but not deep venous thrombosis, CT scanning should be performed first. If PE is confirmed no further examination is necessary. If the CT findings are negative ultrasonography of the legs is performed. If the findings are positive the condition is treated. If the findings are negative there are three management options, depending on the degree of clinical suspicion of PE: no further action, pulmonary angiography, or repeat lower limb ultrasonography after about five days. If the symptoms suggest both PE and deep venous thrombosis, the legs should be studied first. If the findings are positive treatment is given without any need for CT scanning but, if the findings are negative, CT scanning is performed as above.

The authors pointed out that pulmonary angiography should be reserved for those patients in whom the CT scan and lower limb findings are non-diagnostic but in whom the clinical suspicion remains high or there is limited cardiorespiratory reserve. This strategy is relatively quick and decisive and is becoming widely available. In addition, the algorithm should be cost effective. The single published study that attempted to address the issue of cost effectiveness in PE argues in favour of spiral CT scanning.29 In an analysis of 15 combinations of five diagnostic modalities (spiral CT scanning, lower limb ultrasonography, V-P scintigraphy, pulmonary angiography, and D-dimer plasma levels) van Erkel et al constructed a cost effectiveness decision model. They found that the five strategies with the lowest mortality rate and the lowest cost per life saved included spiral CT scanning, often in combination with lower limb ultrasonography. Such theoretical analysis, however, requires confirmation in large prospective studies.

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**LEARNING POINTS**

- Spiral CT scanning is an accurate method for the detection and exclusion of PE with the exception of isolated subsegmental emboli.
- At the same level of specificity spiral CT angiography offers better sensitivity and inter-observer agreement than V-P scintigraphy for diagnosing PE.
- Spiral CT scanning can be considered as a complementary or an alternative imaging method to V-P scintigraphy for inpatients suspected of having PE.
- A diagnostic strategy for PE which includes spiral CT scanning and lower limb ultrasonography seems to be cost effective.
- MR angiography is a promising alternative for the non-invasive diagnosis of PE.
- MR has the potential advantage to combine angiography of pulmonary arteries, functional displays of lung ventilation and perfusion, and peripheral venography for the diagnosis of deep venous thrombosis, thereby providing a complete diagnostic evaluation of thromboembolic disease.

Preliminary data indicate that the sensitivity of MR venography exceeds that of ultrasound but has comparable specificity. This is because MR can accurately image the pelvis, common femoral vein, and superficial femoral vein in the adductor canal, areas which can be difficult to image with ultrasound. Thus combined pulmonary MR angiography and MR venography of the lower extremity and pelvis could provide a very attractive diagnostic approach if further technical developments improve the accuracy for the detection of smaller arterial clots.

On the other hand, CT scanning currently has advantages over MR of shorter examination times, greater ease of patient monitoring, and the detailed depiction of the lung parenchyma and mediastinum. It allows alternative diagnoses to be determined more readily in cases without embolism.

By modifying MR sequences Hatib et al recently proposed the evaluation of lung perfusion and the pulmonary arteries simultaneously. The data obtained before the contrast material was administered were used as a mask for subsequent image subtraction. This technique allows detection of perfusion defects in PE and offers much better spatial and temporal resolution than do radionuclide techniques. Ventilation scanning using MR imaging has also proved to be feasible. Inhalation of 100% molecular oxygen (O2) may be used as a contrast agent because of its two unpaired electrons. It is only weakly paramagnetic but produces substantial signal changes in the lungs because of their large surface area, and MR imaging may depict transfer of oxygen across the alveoli into the pulmonary vasculature.

Ventilation-perfusion mismatches may consequently be demonstrated in patients with PE. Thus, MR imaging may have the potential to combine functional displays of perfusion and ventilation with the angiographic images, thereby providing a comprehensive evaluation of the lungs.

In conclusion, spiral CT scanning and MR angiography will be used with increasing frequency for diagnosing thromboembolic disease. However, only well designed outcome trials will determine the most appropriate roles for these diagnostic techniques.

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Spiral CT scanning and MRI for the diagnosis of pulmonary embolism