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Comparison of ventilation/perfusion scintigraphy and helical CT for diagnosis of pulmonary embolism; strategy using clinical data and ancillary findings

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Key words
lung embolism; lung scintigraphy; spiral CT

Abbreviations
CT; helical computed tomography; DVT, deep venous thrombosis at venography; MSPD, multiple segmental and subsegmental mismatched perfusion defects on SCINT; No, number of patients; PE, pulmonary embolism; SCINT, ventilation/perfusion scintigraphy.

Summary

Study objective: To address the question whether ventilation/perfusion scintigraphy (SCINT) or helical computed tomography (CT) should be the first hand method for diagnosis of pulmonary embolism (PE).
Setting: Departments of radiology, nuclear medicine and internal medicine of a large university hospital.
Patients: During 3 years all 128 patients examined for PE with both methods were analysed. The strategy of interpretation behind original clinical reports, i.e. clinical CT and clinical SCINT, was based upon basic criteria for PE, ancillary findings and information from the referring doctor and from previous examinations. Reviewed SCINT and CT reports were obtained from experts in each field blinded to clinical and laboratory data. The findings with respect to PE were classified as no PE, PE or non-diagnostic. Other pathology than PE was described. A final diagnosis serving as reference was based upon CT, SCINT and other information including clinical follow for 6–24 months.
Methods: Planar SCINT was made with ventilation always preceding perfusion. CT was made with contrast injection using 3 mm collimation and table feed of 3 mm s^{-1}.
Results: PE was diagnosed in 32 patients. For clinical and reviewed SCINT sensitivity was 91 and 97%, specificity 96 and 100% and rate of non-diagnostic findings 10 and 9%, respectively. For clinical and reviewed CT sensitivity was 81 and 78%, specificity 99 and 100% and non-diagnostic findings was observed in 8 and 1%, respectively. In patients with PE, concordant positive results were obtained with both modalities in 23 of 32 patients (72%).
Conclusion: SCINT remains the first hand method because its high sensitivity, general feasibility, low radiation burden and low rate of non-diagnostic findings in our setting. CT is indispensable when SCINT is not available or its result non-diagnostic.

Introduction

Ventilation/perfusion scintigraphy (SCINT) is a preferred diagnostic method for pulmonary embolism (PE) because of its non-invasive character, easiness to perform, high sensitivity, low radiation burden and low cost (ACCP, 1998; Burkill *et al.*, 1999; Maki *et al.*, 1999). However, a high incidence of non-diagnostic findings has led to disbelief of its value (Gottschalk *et al.*, 1993; Woodard, 1997) and stimulated the use and development of helical computed tomography (CT). It has been suggested that CT may complement and even replace SCINT (Goodman & Lipchik, 1996; Hansell, 1997; Cross *et al.*, 1998), although also CT has largely unnoticed shortcomings (Fennerty, 1997) in terms of non-diagnostic, false positive and negative results (Maki *et al.*, 1999; Rathbun *et al.*, 2000). Evaluation of non-invasive techniques is hampered by that even the 'golden standard' for diagnoses of PE, angiography, is not absolutely reliable (Baile *et al.*, 2000), and gives high radiation and contrast doses.

Our objective was to find an answer to the question whether SCINT or helical computer tomography (CT) should be the first hand method for diagnosis of (PE).

Material and methods

Among 4426 SCINTs and 422 CTs performed during 3 years, both methods were performed with respect to PE on clinical indication in 128 patients (33 inpatients and 95 outpatients,

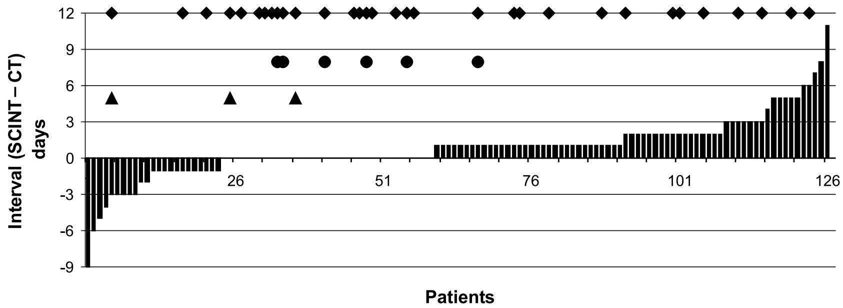

Figure 1 Time interval between SCINT and CT in 126 patients (negative numbers indicate that SCINT precedes CT). ◆ All patients with PE. ● Patients with PE and with negative or non-diagnostic CT. ▲ Patients with PE and non-diagnostic SCINT.

aged 15–90 years). Time interval between the methods is shown in Fig. 1. Approval was obtained from the ethical committee.

Lung scintigraphy

The method that allows ventilation and perfusion to be studied in 1 h was recently described (Tägil *et al.*, 2000). Supine patients inhaled 30 MBq of aerosolized ^{99m}Tc-DTPA (TechneScan DTPA, Mallinckrodt Medical, Petten, Holland). Planar images in posterior, anterior and posterior oblique projections were taken in sitting position. A second posterior image was taken to allow calculation of DTPA clearance from the lungs. Immediately thereafter, perfusion was studied after i.v. injection of 100 MBq ^{99}Tc^{m}-MAA (TechneScan LyoMAA, Mallinckrodt Medical) in the same projections.

Interpretation

CT and SCINT were read from computer displays. Clinical CT and clinical SCINT refer to original clinical reports based upon all available images and clinical information. To obtain reviewed CT and SCINT, a specialist in each discipline (UA and MB), blinded to all clinical data, re-interpreted the images.

Interpretation criteria for SCINT

The findings with respect to PE were described as (1) no embolism, (2) embolism and (3) non-diagnostic. Basic criteria were.

No embolism

- Absence of perfusion defects
- Perfusion defects matched by ventilation defects or caused by known pathology

Embolism

- More than one area of mismatch with a pattern suggesting segmental or subsegmental nature, which implies a peripheral location and usually a wedge-shaped form. One clearly delineated segmental perfusion mismatch in a lower lobe is also considered as PE.

Non-diagnostic

- Ventilation/perfusion abnormalities so severe that match and mismatch cannot be evaluated
- A single lobar or pulmonary perfusion defect with mismatch.

Ancillary findings like patterns of obstructive or parenchymal disease, heart failure or alveolar inflammation as well as clinical data were considered in the interpretation with respect to PE and reported. On the basis of a vast experience our tradition is to avoid intermediate reports and to give the clinician a clear answer as above.

CT method

With a Toshiba Express CT scanner (Toshiba Corporation, Medical System Division, Tokyo, Japan) a contrast-enhanced study was performed from 2 cm above the diaphragm to the upper aspect of the aortic arch, using 3-mm collimation and a table feed of 3 mm s^{-1}. The field of view (FOV) was 22–40 cm. A 200 ml of Omnipaque 240 mg I ml^{-1} (Amersham Health, Buckinghamshire, UK) was infused at 5 ml s^{-1} starting 15 s before scanning. Standard scan time was 50–60 s.

Interpretation criteria for CT

PE was diagnosed when central, eccentric or mural filling defects was observed in pulmonary arteries (Rathbun *et al.*, 2000).

Final diagnosis

The final diagnosis was based upon the results from both CT and SCINT, combined with available laboratory records, X-ray and clinical information. It was reached in consensus between the authors. Patients with PE were seen for follow-up for at least 6 months (CGO); or if treated with a thrombolytic drug for up to 24 months. Patients without PE were followed by their medical records.

Results

Both CT and SCINT were studied because of non-diagnostic results from initial test ($n = 19$), physician's opinion that CT ($n = 48$) or SCINT ($n = 5$) has low sensitivity, continuing symptoms after negative initial test or follow up of treatment ($n = 43$) or unclear ($n = 13$). A final diagnosis was established in 126 of 128 patients as one or both methods failed in two. Thirty-two had PE.

Clinical SCINT was true positive in 29 (sensitivity 91%) and non-diagnostic in three of 32 patients with PE. Accordingly, none was false negative in the sense that a case with PE was reported as ‘No embolism’. Three reports were false positive (specificity 96%). Clinical SCINT was non-diagnostic in 10% (Table 1). Figures 2 and 3 show patients with obstructive lung disease and PE to illustrate how far we go in order to avoid non-diagnostic reports.

Reviewed SCINT was true positive in 31 and non-diagnostic in one of 32 patients with PE (sensitivity 97%). None was false positive or false negative (specificity 100%). Rate of non-diagnostic reports was 9%. Clinical CT was true positive in 26 (sensitivity 81%) and non-diagnostic in three of 32 patients with PE. One was false positive (specificity, 99%). Rate of non-diagnostic reports was 8%.

Reviewed CT was true positive in 25 of 32 patients (sensitivity 78%) and non-diagnostic in one of 32 patients with PE. Specificity was 100%.

Clinical CT and clinical SCINT reports showed concordant positive results for PE in 23 of 32 patients with PE (72%). In Table 2 discordant results from the two methods are explained. All false negative or non-diagnostic clinical CT or SCINT reports in patients with PE were performed on the same day or earlier than the method giving the diagnosis. Both clinical SCINT and clinical CT negated PE in 75 of 94 patients without PE (80%).

Among 94 patients without PE, 52 showed ancillary findings of type obstructive or parenchymal disease, increased clearance as in alveolitis, perfusion redistribution as in heart incompensation or focal perturbation of ventilation and perfusion suspected for tumour. In the same group CT described parenchymal and interstitial changes, obstruction/emphysema, pleural effusion, atelectasis or tumour in 38 patients.

Clinical and reviewed SCINT differed with respect to PE in 14 of 126 patients (11%). In 13 of these, one of the reports was

Table 1 Diagnostic performance of clinical and reviewed SCINT and CT.

	True positive	False positive	True negative	False negative	Non diagnostic
Clinical SCINT	29	3	81	0	13 (3 PE)
Reviewed SCINT	31	0	84	0	11 (1 PE)
Clinical CT	26	1	86	3	10 (3 PE)
Reviewed CT	25	0	94	6	1 (1 PE)

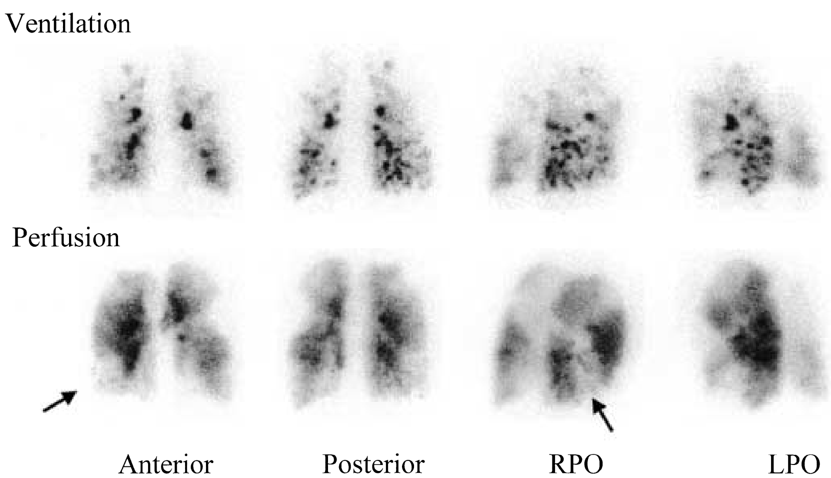

Figure 2 Patient with obstructive lung disease and final diagnosis of PE. Ventilation: uneven ventilation and hot spots because of the deposition of the aerosol. Perfusion: apart from matching defects, mismatch is observed in the lower right lobe (arrow). SCINT reported obstructive disease and suspicion of PE, i.e. a non-diagnostic finding.

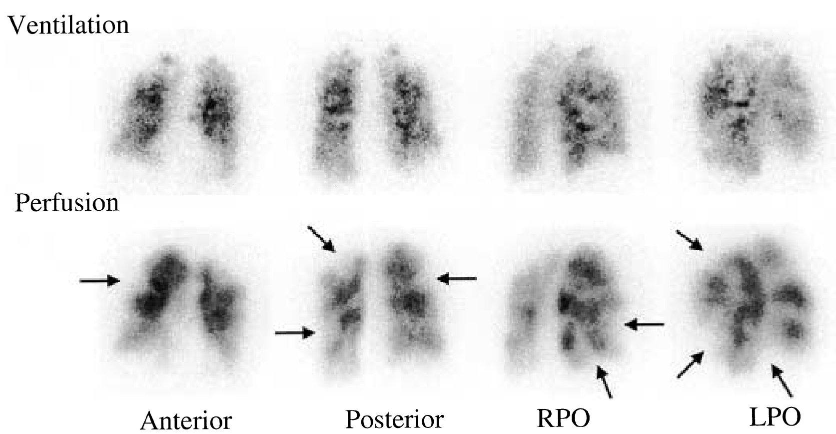

Figure 3 Patient with obstructive lung disease and final diagnosis of PE. Ventilation: uneven ventilation and hot spots because of the deposition of the aerosol. Perfusion is dominated by multiple mismatches typical for PE (arrows). SCINT reported PE and obstructive lung disease.

Table 2 Discordant findings in 13 patients in which PE was diagnosed with one of the methods.

Clinical SCINT	Clinical CT	No.	Comments
True positive	False negative	1	MSPD. Chronic PE.
		2	MSPD. DVT.
		3	Leg and chest pain.
True positive	Non diagnostic	4	MSPD, which were normalized at follow up. CT showed fibrosis
		5	MSPD. CT reported suspicion of subsegmental PE.
		6	MSPD and matched defects. DVT in leg and neck. CT showed pneumonia
Non diagnostic	True positive	7	SCINT reported suspicion of PE. Reviewed SCINT showed PE.
		8	SCINT reported obstructive lung disease and suspicion of PE, Fig. 2
		9	MSPD unchanged since previous episode. Obstructive lung disease.
True negative	False positive	10	Normal SCINT. Reviewed CT was normal.
False positive	True negative	11	MSPD and high DTPA clearance as in alveolitis. Clinical lung fibrosis.
		12	Known asthma; new perfusion defects compared to previous SCINT.
		13	Very high DTPA clearance as in alveolitis. Scleroderma.

Patient number; MSPD, multiple segmental and subsegmental mismatched perfusion defects on SCINT; DVT, deep venous thrombosis at venography.

non-diagnostic. In one, clinical SCINT was false positive and reviewed SCINT true negative. Clinical and reviewed CT differed with respect to PE in 10 patients (8%). In eight of these, one of the reports was non-diagnostic. One clinical and one reviewed CT were false positive.

During follow-up, PE was found postmortem in one patient in which CT and SCINT showed no embolism.

Discussion

The main finding is that SCINT performed and interpreted as described is diagnostic at higher rates than previously reported. Previous reports about high sensitivity of SCINT were confirmed, as was the usefulness of CT (Maki *et al.*, 1999). To define a diagnostic strategy other factors than the diagnostic performance of each method must be considered. The use of angiography golden standard is disputed (Fennerty, 1998). In embolized pig sensitivity was only 87%. Interobserver agreement at segmental and subsegmental levels is reported to be only 81 and 66%, respectively (Stein *et al.*, 1992). Angiography is invasive and associated with high radiation exposure and large amounts of contrast. Ethically, angiography can hardly be performed only for science. As an alternative an accepted principle for comparisons between methods was modified. To quote Bland & Altman (1986), ‘We do not know the true value, and the mean of the two measurements is the best estimate we have’. In this study ‘the mean’ is represented by the final diagnosis based upon both methods combined with clinical data and particularly follow-up. As scintigraphy is a recognized sensitive method (Maki *et al.*, 1999) and CT is known to have a high specificity (Rathbun *et al.*, 2000), the methods complement each other in the process to reach a final diagnosis. Our results confirmed the high sensitivity of SCINT and high specificity of CT. Among patients with a negative final diagnosis PE was observed during follow-up in only one, in whom at autopsy 6 weeks after the study, a small peripheral PE with lung infarct 1·5 cm wide was observed. Grave general arteriosclerosis, old and new myocardial infarction, heart incompensation and pneumonia were stated as main causes of death. Embolism is commonly observed in terminal disease. Both SCINT and CT were therefore not regarded as false negative in this case. However, it remains possible that pulmonary embolism was missed by both methods in some subject. Reported sensitivity should therefore be regarded with caution. However, this problem does not invalidate comparison between the methods, which was the objective of the study.

Among cases with PE observed with only one of the methods the negative study was never performed on a later day than the positive one. Accordingly, thrombolysis was not considered as a reason for the discrepancies.

The study includes a highly selected group of patients in which the second of the two methods CT and SCINT was performed on clinical indication as described. This is a limitation with respect to conclusions valid for the whole population. However, it also strengthens the results as the selection implies a bias towards difficult cases. The observed concordance between methods is from this aspect notable. Likewise, for both methods, clinical and reviewed reports showed good agreement. The low rate of non-diagnostic reports is, particularly for SCINT, in contrast to most previous reports (PIOPED, 1990; Fennerty, 1997). However, a recent study in which ventilation/perfusion scintigraphy was interpreted according to principles similar to ours, the rate of non-diagnostic findings was only marginally higher than the present (Bargouth *et al.*, 2000).

A prerequisite for the high diagnostic power of SCINT, which others and we report, is high quality ventilation and perfusion scintigraphy (Bargouth *et al.*, 2000; Tägil *et al.*, 2000). Ventilation is always studied for reasons discussed by Tägil *et al.* (2000). In the present selected material only 18 patients had normal perfusion. In two of these, alveolar inflammation was indicated by fast clearance of ^{99m}DTPA from the lungs. The diagnostic efficiency furthermore reflects daily co-operation and feedback between our departments and a holistic view in diagnostics of PE. Accordingly 'the assimilation and review of countless cases' based upon all available information is a prerequisite for optimal diagnostics of PE and alternative pathology as explained by Freeman *et al.* (2001). Figures 2 and 3 illustrate that optimal diagnostics cannot rely entirely on fixed diagnostic criteria.

CT had a high specificity with respect to PE while sensitivity was lower. This is in line with previous data (Rathbun *et al.*, 2000; Perrier *et al.*, 2001). Beside lower sensitivity, especially on subsegmental level, CT has other limitations. One is radiation exposure. In our setting it is 4·5–5·5 mSv for CT covering 12–15 cm length of field. It is 1·3 mSv for SCINT. (Five mSv corresponds to one year's natural radiation in Sweden). The importance of the radiation doses associated with CT has been emphasized particularly with respect to studies of women, whose breast receives 20–35 mSv at CT (Remy-Jarden & Remy, 1999). In a woman aged 35, 10 mSv increases the risk for breast cancer by 13·6%. The difference in radiation dose between CT and SCINT is particularly important when repeated studies are needed. Studies with large numbers of patients with low prevalence of PE imply that 'indiscriminate use of CT would have dire consequences in terms of radiation dose to the population as a whole' (Howling & Hansell, 2000).

Another obstacle is that large amounts of iodinated contrast medium restricts or prevents the use of CT at very high age, in patients with renal failure and, of course, in rare cases of known hypersensitivity. The requirement for breath holding is another problem although lessened with the last generation CT machines.

With respect to the limitation related to the selection of the material, this study renders support for SCINT as the first hand modality in circumstances like ours. Even in a material of 'difficult cases', SCINT has a superior sensitivity combined with adequate specificity and low rate of non-diagnostic tests. The low radiation dose, the possibility to quantify the degree of embolism and to use the test for follow-up of treatment and its feasibility in very sick patients contribute to the priority of SCINT over CT. The value of CT when SCINT was not available or non-diagnostic was confirmed. Recently, Perrier *et al.* (2001) considered that CT has too low sensitivity to be used as a single test, but suggests its use within a combined strategy. Important is that SCINT is expeditious and a complete examination is obtained within 1 h (Tägil *et al.*, 2000). However, a limitation in our setting is that SCINT is only available during working hours. In a longer perspective the fast development of CT techniques must be matched by further development of SCINT. Also, tomographic SCINT rendering three-dimensional images of ventilation, perfusion and ventilation/perfusion quotient is feasible in less than 1 h with the same low radiation exposure as our planar method (Palmer *et al.*, 2001). This technique yields even higher sensitivity and specificity with regards to subsegmental emboli than planar SCINT (Bajc *et al.*, 2002).

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References

ACCP Consensus Committee on Pulmonary Embolism. Opinions regarding the diagnosis and management of venous thromboembolic disease. *Chest* (1998); **113**: 499–504.

Baile EM, King GG, Muller NL *et al.* Spiral computed tomography is comparable to angiography for the diagnosis of pulmonary embolism. *Am J Respir Crit Care Med* (2000); **161**: 1010–1015.

Bajc M, Bitzén U, Olsson B, perez de Sa V, Palmer J, Jonson B. Lung ventilation/perfusion SPECT in the artificially embolized pig. *J Nucl Med* (2002); **43**: 640–647.

Bargouth G, Yersin B, Boubaker A *et al.* Combination of clinical and V/Q scan assessment for the diagnosis of pulmonary embolism: a 2-year outcome prospective study. *Eur J Nucl Med* (2000); **27**: 1280–1285.

Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* (1986); **i**: 307–310.

Burkill GJ, Bell JR, Padley SP. Survey on the use of pulmonary scintigraphy, spiral CT and conventional pulmonary angiography for suspected pulmonary embolism in the British Isles. *Clin Radiol* (1999); **54**: 807–810.

Cross JJL, Kemp PM, Walsh CG, Flower CDR, Dixon AK. A randomized trial of spiral CT and ventilation perfusion scintigraphy for the diagnoses of pulmonary lung emboli. *Clin Radiol* (1998); **53**: 177–182.

Fennerty T. Fortnightly review: the diagnoses of pulmonary embolism. *BMJ* (1997); **314**: 425–437.

Fennerty T. Pulmonary embolism. Editorials. *BMJ* (1998); **317**: 91–92.

Freeman LM, Krnyckyi B, Zuckier LS. Enhanced lung scan diagnosis of pulmonary embolism with the use of ancillary scintigraphic findings and clinical correlation. *Semin Nucl Med* (2001); **2**: 143–157.

Goodman LR, Lipchik RJ. Diagnosis of acute pulmonary embolism: time for a new approach. *Radiology* (1996); **199**: 25–27.

Gottschalk A, Sostman HD, Coleman RE *et al.* Ventilation-perfusion scintigraphy in the PIOPED study. Part 2. Evaluation of the scintigraphic criteria and interpretations. *J Nucl Med* (1993); **34**: 1119–1126.

Hansell DM. Spiral computed tomography and pulmonary embolism: current state. *Clin Radiol* (1997); **52**: 575–581.

Howling SJ, Hansell DM. Spiral computed tomography for pulmonary embolism. *Hosp Med* (2000); **61**: 41–45.

Maki DD, Gefter WB, Alavi A. Recent advances in pulmonary imaging. *Chest* (1999); **116**: 1388–1402.

Palmer J, Bitzén U, Jonson B, Bajc M. Comprehensive ventilation/perfusion SPECT. *J Nucl Med* (2001); **42**: 1288–1294.

Perrier A, Howarth N, Didier D *et al.* Performance of helical computed tomography in unselected outpatients with suspected pulmonary embolism. *Ann Intern Med* (2001); **135**: 88–97.

PIOPED. Value of the ventilation/perfusion scan in acute pulmonary embolism: results of the prospective investigation of pulmonary embolism diagnosis. *JAMA* (1990); **263**: 2753–2759.

Rathbun SW, Raskob GE, Whitsett TL. Sensitivity and specificity of helical computed tomography in the diagnosis of pulmonary embolism: a systematic review. *Ann Intern Med* (2000); **132**: 227–232.

Remy-Jarden M, Remy J. Spiral CT angiography of the pulmonary circulation. *Radiology* (1999); **212**: 615–636.

Stein PD, Athanasoulis C, Alavi A *et al*. Complications and validity of pulmonary angiography in acute pulmonary embolism. *Circulation* (1992); **85**: 462–468.

Tägil K, Evander E, Wollmer P, Palmer J, Jonson B. Efficient lung scintigraphy. *Clin Physiol* (2000); **20**: 95–100.

Woodard PK. Pulmonary arteries must be seen before they can be assessed [editorial; comment]. *Radiology* (1997); **204**: 11–12.