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Enhancing Lung Scintigraphy With Single-Photon Emission Computed Tomography

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Although widely used for many years in the assessment of pulmonary embolism, planar ventilation-perfusion (V/Q) scintigraphy has well-recognized limitations. Single-photon emission computed tomography (SPECT) imaging, which can be readily performed in most modern nuclear medicine centers equipped with multihead gamma cameras, overcomes many of these limitations through its ability to generate 3-dimensional imaging data. V/Q SPECT has been shown to have a greater sensitivity and specificity than planar imaging and has a lower nondiagnostic rate. For reporting clinicians who may be reluctant to abandon conventional planar V/Q images, planar-like images can also be readily obtained from V/Q SPECT with the use of postacquisition techniques. The use of SPECT can also facilitate advances in V/Q imaging, including the generation of parametric V:Q ratio images, coregistration with computed tomography, respiratory gating, and more accurate quantification of regional lung function. Although direct comparisons in the literature are limited in number, V/Q SPECT appears to have comparable, or greater, sensitivity than multidetector computed tomography pulmonary angiography and is not associated with contrast-related complications such as allergy and nephropathy. It also involves significantly less radiation dose to breast tissue, an important consideration, particularly in young women. For the V/Q scan to remain relevant in the evaluation of patients with suspected pulmonary embolism, it is essential that image data are obtained so as to maximize their accuracy and diagnostic usefulness. V/Q SPECT can achieve this and, furthermore, may have a role in conditions other than pulmonary embolism, including both clinical and research fields.
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The accurate diagnosis of pulmonary embolism (PE) continues to be a challenge for both clinicians and imaging specialists. Misdiagnosis is problematic because untreated PE is reported to have a mortality rate of up to 30%, and unnecessary treatment with anticoagulation places the patient at risk of bleeding.[1-3] Historically, ventilation-perfusion (V/Q) lung scan and digital subtraction pulmonary angiography have been used as imaging investigations in the diagnosis of potential PE.[4] More recently, radiographic computed tomography pulmonary angiography (CTPA) has been increasingly used.[4] Although pulmonary angiography has previously been considered the gold standard investigation for PE, it is performed less frequently today because of its limited availability, requirement for operator expertise, and invasive nature.[4] To add to this, pulmonary angiography has recently been demonstrated to have less-than-optimal diagnostic accuracy.[5] Consequently, the V/Q scan and CTPA are the 2 most widely available and used investigations to image patients with suspected PE today.

Although V/Q scintigraphy has been used for more than 30 years in the assessment of patients with suspected PE, this technique is widely recognized as having limitations.[6-10] When the lungs are imaged in only two dimensions (2D), as occurs with planar imaging, there is significant overlap of anatomical segments, hence accurate assignment of defects to specific lung segments is difficult. Embolic defects may not be detected if there is "shine-through" occurring from underlying lung segments with normal perfusion.[9] The size and shape of each lung segment varies and accurately determining the extent of embolic involvement in each individual segment can be problematic.[9,11,12] In addition to these inherent technical limitations of planar lung scintigraphy, there

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are the problems posed by the widely used probabilistic PIOPED reporting schema.[13-17] PE is not a condition in which clinicians welcome "indeterminate" results and it is desirable to reduce such reports as much as possible.

SPECT is widely used in many areas of radionuclide imaging today because of its ability to image in three dimensions (3D). It has been shown to be superior to planar imaging in the evaluation of many conditions, such as assessing myocardial perfusion and brain and liver imaging.[18] In contrast to planar imaging, SPECT avoids the problems introduced by segmental overlap and "shine-through" of adjacent lung, making it better able to image all segments of the lungs and more accurately define the size and location of perfusion defects.[9] For these reasons, it would be expected that SPECT V/Q scintigraphy should be superior to planar imaging, and it is perhaps surprising that SPECT has not been more widely adopted for lung scanning. Furthermore, with the widespread availability today of multidetector gamma cameras and improved computing power allowing faster processing, lung scintigraphy is ideally suited to SPECT acquisition.

How to Optimally Perform V/Q SPECT

SPECT can be used to image both ventilation and perfusion, however, this requires the use of appropriate imaging agents.

Ventilation

For imaging ventilation, several alternatives exist. These include inert radioactive gases such as ^{81m}Kr and ^{133}Xe, radiolabeled aerosols such as ^{99m}Tc-diethylene triamine penta-acetic acid (^{99m}Tc-DTPA), and the ultrafine carbon suspension ^{99m}Tc-Technegas.[19] Although the gases are considered to most accurately represent regional ventilation, several problems exist with their use. The use of ^{81m}Kr requires a krypton generator that is expensive and needs to be replaced daily. As a result, ^{81m}Kr ventilation imaging can be problematic to perform, especially outside of routine working hours. In addition, ^{81m}Kr gas must be continuously administered during image acquisition due to its short half life.[20] Although ^{133}Xe gas has the advantage of a longer half life, errors result from its recirculation due to clearance into the pulmonary circulation.[21,22] Given that SPECT assumes a static distribution of tracer for the duration of the data acquisition, these in vivo dynamics impair ^{133}Xe's ability to be used for SPECT ventilation imaging. Further compounding these issues, the lower energy of ^{133}Xe results in poorer spatial resolution, making it less than ideal as an agent to image ventilation.[20]

Given these limitations, ^{99m}Tc-labeled particulate aerosols such as ^{99m}Tc-DTPA or the carbon labeled nanoparticle ^{99m}Tc-Technegas tend to be more widely used due to their greater availability, low cost and good image quality.[20] Although the choice of agent depends on factors such as local availability, both have been reported to produce SPECT ventilation scans of good diagnostic quality. The most widely available is ^{99m}Tc-DTPA, which can be used with doses of just 0.8 mCi (30 MBq).[23] However, because of the relatively larger mean particle mass, problems may arise from central airway deposition, particularly in patients with chronic obstructive pulmonary disease. Technegas, with a smaller particle size, generally has greater alveolar penetration than ^{99m}Tc-DTPA. This results in less impaction in the central airways, with Technegas being demonstrated to have a similar distribution to that of an inert gas.[24-28] Together with its lack of lung clearance during image acquisition, this would appear to make Technegas an ideal agent for ventilation SPECT.

Typically, the doses of ^{99m}Tc-based imaging agents administered are identical to those used in conventional planar imaging, however, some authors have proposed a slight increase to the administered dose in an attempt to improve image quality.[29,30] In our institution, 13.5mCi (500 MBq) of ^{99m}Tc is added to a Technegas generator, with the aim of delivering a dose of approximately 1.35 mCi (50 MBq) to the patient. This equates to a posterior count rate of approximately 2.0 to 2.5 kcps.

Perfusion

As with planar imaging, ^{99m}Tc-macro-aggregated albumin (^{99m}Tc-MAA) is generally used to assess perfusion.[19] The distribution of MAA, which is proportional to regional blood flow, will be reduced distal to vascular occlusions in the pulmonary arteries. Thus, it can be considered that perfusion imaging performed in this fashion has an inherent "amplification," as even a small embolus can cause a large section of lung to be underperfused.

The dose of ^{99m}Tc-MAA used is dependent on the ventilation agent used. In the case where a radioactive gas is used, the dose of perfusion agent is typically lower than if a technetium-based ventilation agent is used. This is because the signal from the radioactive gas can be separated from that of the perfusion agent based on the energy level of the emitted photons. Additionally, in the case of ^{81m}Kr, the short half-life results in negligible gas remaining in the lungs during perfusion imaging. If a technetium-based agent is used for both ventilation and perfusion imaging, the typical approach is to "drown out" the underlying ventilation signal by administering a substantially greater dose of perfusion agent. A perfusion-ventilation dose ratio of $\geq$4:1 is generally required.[19] At our institution, the standard administered activity of ^{99m}Tc-MAA is 6 mCi (220 MBq), resulting in an effective radiation dose for the combined ventilation and perfusion scan of $\leq$2.5 mSv. Other authors have proposed the use of lower activity.[23]

Another approach to perfusion imaging is to use MAA labeled with a different radionuclide. Sanchez-Crespo and coworkers have used ^{111}In-MAA for perfusion.[31] By combining this with ^{99m}Tc-Technegas for ventilation, the authors were able to simultaneously acquire both ventilation and perfusion data. Although the limited availability and high cost of ^{111}In make this approach more expensive than ^{99m}Tc-based perfusion imaging, this approach has the advantage of reducing overall imaging time and producing inherently registered ventilation and perfusion image data.