

V/Q SPECT and SPECT/CT in Pulmonary Embolism

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Abstract

Ventilation and perfusion (V/Q) lung scintigraphy has been used in the assessment of patients with suspected pulmonary embolism for more than 50 years. Advances in imaging technology make SPECT and SPECT/CT feasible. This article will examine the application and technical considerations associated with performing 3-dimensional V/Q SPECT and the contribution of a co-acquired CT. The literature tends to be mixed and contradictory in terms of appropriate investigation algorithms for pulmonary embolism. V/Q SPECT and SPECT/CT offer significant advantages over planar V/Q, with or without the advantages of Technegas ventilation, and if available should be the preferred option in the evaluation of patients with suspected pulmonary embolism.

Introduction

While ventilation and perfusion (V/Q) lung scintigraphy has been used in the assessment of patients with suspected pulmonary embolism for more than 50 years, there have been advances in imaging technology to provide superior resolution and sensitivity, SPECT techniques, and SPECT/CT hybrid imaging. Advances in ventilation agents, Technegas (Cyclomedica, Sydney Australia) in particular, have contributed to assimilation to SPECT and SPECT/CT protocols. Technegas was developed in Australia in 1984 (1) and Chris McLaren, an Australian pioneer nuclear medicine technologist, was part of the team evaluating its original clinical application. Unlike radioaerosols, Technegas does not redistribute after administration, a requirement for any prolonged tomographic acquisition (such as SPECT). McLaren appears to be the first to recognise not only the potential for performing SPECT V/Q lung scanning but also the potential for computerized subtraction of SPECT data to map and quantify potential perfusion defects in 1986 (2). His approach highlighted the major issue associated with both phases using ^{99m}Tc in a single day protocol and provided a solution:

“A useful spin-off from the subtraction technique is that ‘true’ perfusion images are obtainable”
(2).

This discussion will not examine the broader debate on the role and application of V/Q imaging nor the merits of Technegas; these have been detailed widely elsewhere. The discussion will explore the application and technical considerations associated with the entire V/Q protocol being performed as 3-dimensional SPECT imaging and the addition of a co-acquired CT.

This article aims to both challenge and inform readers in relation to the role of single photon emission computed tomography (SPECT) and SPECT/computed tomography (SPECT/CT). The original perspective for the article focussed on the value-add of technological innovation that not only makes planar imaging redundant, but makes SPECT a requisite. Drawing a comparison to omitting SPECT from the armamentaria of myocardial perfusion, skeletal or cerebral perfusion imaging was thought to highlight the importance of SPECT in lung scanning. Challenging readers to consider appropriateness of a clinical department that performed planar cerebral perfusion, myocardial perfusion or spine imaging was initially thought analogous to a department only performing planar lung scanning. While provocative, the challenge was not intended to be critical or insulting. Nonetheless, the optics changed with the realization that there are additional

factors that might influence the decision to use SPECT or SPECT/CT in lung scanning. Not the least of these factors is the excellent positive and negative predictive value for planar V/Q. This feature of V/Q is challenged when single-day, ^{99m}Tc -based ventilation and perfusion is undertaken, especially where the ratio of count rate differences is not met. To further clarify, an informal poll was posted for 24 hours on two separate nuclear medicine technologists groups; one predominantly comprised members from the United States of America (USA) and another predominantly Australian members (table 1). While not expected to be quantitatively representative of either population, the insights did provide a snapshot with generalizability of findings. The stark contrast in results, with 67% of respondents from the USA indicating they performed planar only studies compared to just 3% of Australian sites is thought to reflect, in part, the greater suitability of Technegas for SPECT compared to ^{81m}Kr , ^{133}Xe or ^{99m}Tc aerosol ventilation studies. As previously outlined (3), Technegas is considered the preferred ventilation method in more than 60 countries, including Australia, yet has limited adoption in the USA. Indeed, a number of additional comments were provided in the USA respondents that indicated that poor ventilation SPECT was a barrier while omission of the ventilation scan in favour of CT in COVID patients was a driver for SPECT/CT. Conversely, the principal discussion among the Australian respondents related to advanced techniques of SPECT/CT using breath-hold approaches and justification of base-apex against radiographer apex-base preferred protocols. The impending approval of Technegas by the Food and Drug Authority (FDA) in the USA may change that landscape and, therefore, demands a detailed discussion of the advances that allow the entire V/Q protocol to move to 3-dimensional SPECT or SPECT/CT imaging.

The V/Q Test

While pulmonary embolism is the principal pathology of interest in V/Q lung scanning, it is not the only application investigated with the V/Q scan. The basic premise in pulmonary embolism is the mismatch scan where a perfusion deficit is accompanied by normal ventilation. The V/Q mismatch, however, can be caused by pathology other than pulmonary embolism and not all pulmonary emboli produce a mismatch (4). Acute pulmonary embolism may partially resolve (diminishing the perfusion defect) or could progress to infarction which produces a matching ventilation and perfusion defect (4). Traditionally, the chest x-ray was used to improve the accuracy of the V/Q scan and to identify those patients more suited to CT pulmonary

angiography (CTPA). The use of SPECT V/Q independently improves V/Q accuracy and when combined with CT produces co-registration with anatomical detail superior to the chest x-ray. The possibility of combining the SPECT with CTPA creates an additional layer of insight that demands attention. Redundancy of the chest x-ray and the ventilation scan warrant consideration with the emergence of lung V/Q SPECT/CT and V/Q SPECT/CTPA.

Planar V/Q has a number of challenges. Firstly, perfusion defects are segmental or sub-segmental often with overlap of segments using 2-dimensional planar imaging. As a result, identification of specific defect localization or segments is difficult (5). Secondly, the overlap of tissues using 2-dimensional images means a perfusion defect may have events superimposed from over- or under-lying normally perfused lung tissue. This “shine-through” can confound perfusion defect detection and interpretation (5). For example, a small sub-segmental defect may have sufficient superimposed counts to go undetected while a larger defect may have the perfusion deficit underestimated. Thirdly, the “shine-through” of ventilation data in the perfusion data can also confound perfusion defect detection and interpretation. The count rate difference between ^{99m}Tc based ventilation and the subsequent ^{99m}Tc based perfusion study is ideally a minimum of 7 times higher perfusion counts with 4 times being an absolute minimum. This is seldom actually confirmed prior to imaging or reporting and has the same implications as anatomical “shine-through” either globally or, particularly for aerosol studies that can produce airways deposition at the branching of the airways, focally. Next, there are variable approaches to ventilation that directly impact interpretability of the studies and the proportion of indeterminate studies. Availability of Technegas as the preferred method is not universal which also influences lack of universality of interpretation criteria. Adoption of Technegas in a same day ventilation followed by perfusion protocol that comes with the “shine-through” (figure 1) issues discussed above, or a two-day protocol of perfusion first with the ventilation only performed on abnormal studies. The latter approach has been revisited during the COVID-19 pandemic due to concerns about aerosols and disease transmission. It may also reduce radiation dose for some patients (normal perfusion) and eliminate ventilation “shine-through” on the perfusion study but delays confirmatory diagnosis by 24 hours in an emergency. Finally, the interpretation criteria generally used are not fit for purpose and have largely migrated from probabilistic approaches to categorical classification.

Despite significant advances in the technology associated with nuclear medicine imaging, planar V/Q imaging has not evolved since the mid-1980s despite the application of advanced technology and associated protocol modifications to most other long-standing procedures. The arguments against SPECT V/Q adoption are largely the same confronting the transition to SPECT and gated SPECT myocardial perfusion. Transitioning to Technegas might be analogous to displacement of ^{201}Tl by $^{99\text{m}}\text{Tc}$ -based agent for myocardial perfusion. The additional time required for acquisition of both planar and SPECT acquisitions during the “learning phase” of SPECT adoption are shared between V/Q and myocardial perfusion, although a number of authors have shown how to produce adequate “pseudo-planar” images from the SPECT data. The invested experience in planar interpretation and associated new learning for SPECT interpretation are also common. While transition to Technegas confronts regulatory hurdles in the USA, perhaps the only barrier elsewhere to the adoption of SPECT V/Q is the net benefit given planar V/Q has high accuracy and the incremental benefit of SPECT is much smaller than for myocardial perfusion imaging.

Regardless of the $^{99\text{m}}\text{Tc}$ ventilation method adopted (radioaerosol or Technegas) or the imaging approach used (planar or SPECT), both the ventilation of the patient and the administration of the perfusion radiopharmaceutical should be performed supine to minimise the effects of gravitational gradients. Ventilation count rate should not exceed 1000-1500 counts per second otherwise the residual ventilation counts could reduce detectability of perfusion defects. The Rose model associated with image contrast and object detection defines mathematically that human perception requires a signal to noise ratio of at least 5-7 (6). This conflicts with advice from the SNMMI guidelines (7) suggesting the count rate of 3-4 times is adequate and decreased contrast may lead to increased false negative studies. With 100 MBq of $^{99\text{m}}\text{Tc}$ -MAA producing count rates of 2.3-5.0 counts per second (decreasing with increasing BMI), a patient dose of 200-250 MBq of $^{99\text{m}}\text{Tc}$ -MAA is generally required. Where ventilation has been efficient and produces higher count rates, a delay before the perfusion administration and acquisition should be used until count rates reduce to 1000-1500 counts per second. Increasing the administered dose beyond 250 MBq not only imposes a higher radiation dose to the patient but also poses a greater risk due to increased capillary blockade.

SPECT V/Q

SPECT and the associated 3-dimensional imaging overcomes many of the challenges of planar imaging. Firstly, SPECT allows more accurate localization of segmental and sub-segmental perfusion defects. Secondly, SPECT eliminates over- and under-lying tissues and the associated “shine-through” which enhances defect detection and interpretation. Thirdly, the ventilation study “shine-through” can be normalized and subtracted, and parametric approaches can be used (e.g., the V:Q ratio). All three of these factors enhance V/Q contrast and the ability to detect perfusion defects. Importantly, SPECT can improve sensitivity, specificity, accuracy, and reproducibility of the V/Q study compared to planar and reduce the proportion of indeterminate studies (table 2) (5). SPECT has been reported to increase detection of segmental perfusion defects by >10% and sub-segmental perfusion defects by as much as 80% (8) (figure 2). Indeed, the advantages of SPECT V/Q over planar V/Q are so well established in the literature nowadays that it is standard practice in many European and Latin American countries, Canada and Australia. SPECT V/Q is also the preferred approach of the EANM (9) while the SNMMI guidelines indicate that, outside the patient with complex comorbidities, planar V/Q remains preferred in the USA (10). This reflects lack of access to a suitable ventilation agent at present and may change in the future. One should keep in mind, however, simultaneous V/Q imaging with continuous tidal breathing using $^{81\text{m}}\text{Kr}$ for ventilation has been widely reported as providing high quality V/Q SPECT studies.

SPECT acquisition protocols should include 120-128 projections using a dual detector gamma camera over 360 degrees with a 128 x 128 matrix and high-resolution collimation. The ventilation study is typically 10-12 seconds per projection (but could be 15-20 seconds) while the higher count perfusion study is typically 8-10 seconds per projection (but could be 12-15 seconds). For a single day, V/Q scan the patient should be positioned supine with arms hyperextended above the head and an injection line in place in either arm. On completion of the ventilation SPECT, without the patient moving, the $^{99\text{m}}\text{Tc}$ -MAA should be administered and perfusion SPECT commenced. For convenience, protocols can be established to perform dual SPECT studies using the same orbit parameters with the ventilation rotating clockwise and then the perfusion simply rotating back counter-clockwise. The SPECT images should be reconstructed using an iterative reconstruction algorithm, typically the ordered-subset expectation maximization

(OSEM) algorithm. The images produced can be used to produce planar equivalent images from the data set. One approach is to sum a number of projections either side of the required view (anterior for example would be projection 1 summed with projections 2, 3, 119 and 120) (11). A better approach is to reproject the SPECT data with an associated attenuation map (12). More commonly, however, the SPECT data provides the insights required and the planar extracted data are not required or produced. The OSEM parameters depend on the acquisition parameters and total counts per pixel, however, 8 subsets and 4 iterations with a low-pass filter are typical and 3-4mm slice thickness. SPECT V/Q data should be displayed after simultaneous reconstruction as ventilation and perfusion pairs sequentially for each projection (figure 3). Representative slices can be extracted to correlate with parametric images (figure 4).

SPECT/CT V/Q

The low dose CT acquired with SPECT reduces the radiation dose to the patient compared to a diagnostic CT scan. When used in conjunction with V/Q SPECT provides attenuation correction, localization and additional insight into vascular, parenchymal and pleural abnormalities (4). For example, low dose CT provides richer detail than chest x-ray in identifying hypoperfused lung (Westermarck sign), pulmonary artery enlargement (Palla sign and Fleishner sign) or pulmonary artery tapering (knuckle sign) that may support a diagnosis of pulmonary embolism (figure 5). Conversely, opacities more consistent with pathologies that cause a matched V/Q defect (figure 6) and, thus, less likely to represent pulmonary embolism can also be identified on low dose CT (e.g., consolidation, bullae, atelectasis, interstitial disease or space occupying lesions). The combination of SPECT/CT in the evaluation of pulmonary emboli may reduce the false positive rate, improving specificity (4). While it seems intuitive that CT may make the ventilation study redundant, evidence suggests that the ventilation study substantially improves test specificity over perfusion SPECT/CT alone (13).

For simple attenuation correction, low dose CT parameters might include 120 kV_p, 10 mAs per slice, and a pitch of 1.0-1.5 to produce an additional radiation dose of less than 1 mSv. More typically and of greater value is a low dose CT for co-registration and mapping of anatomical information. This low dose CT produces a higher dose of 2-3 mSv using 80-120 kV_p, 20 mAs per slice, 512 x 512 matrix and a pitch of 0.8 (14). Specific parameters and doses will vary

depending on the CT system used. The V/Q SPECT alone is typically 2 mSv (4). A full diagnostic CT without contrast could also be performed using 100-140 kV_p, 130-200 mAs per slice, 512 x 512 matrix and a pitch of 0.9 producing a dose of 3-8 mSv (15). While not feasible for the SPECT phases, a mid-inspiration breath-hold should be used for the CT with imaging adjusted to base to apex rather than the traditional apex to base to minimize co-registration artefact. In the absence of a mid-inspiration breath-hold for the CT shallow, continuous breathing can be used (4).

SPECT/CT V/Q and CTPA

It is possible to combine SPECT and CTPA studies using software fusion and while this adds additional insight, it also adds additional radiation exposure and confronts registration errors. Hybrid technology allows SPECT/CT and SPECT/CTPA to be performed with hardware fusion that overcomes registration errors of software fusion (figure 7). The value of SPECT/CTPA is the combination of the highly sensitive perfusion map with the highly specific angiographic map to enhance diagnostic efficacy. In the majority of patients, despite the feasibility of SPECT/CTPA in a single session, both procedures are usually neither required nor justified.

A CTPA could be performed using 80-120 kV_p, 150-200 mAs per slice, 512 x 512 matrix and a pitch of 0.9 with 80 mL of iodine contrast using bolus tracking and a deep-inspiration breath hold producing a dose upwards of 8-20 mSv (14,16). A key concern for CTPA is the contrast adverse effects, risk of nephropathy and the high radiation dose. These factors preclude justified use of CTPA in pre-menopausal women, pregnancy, renal dysfunction, diabetes and for some medications. Breast radiation dose during CTPA is a significant issue that perhaps does not get enough attention. The breast dose from CTPA ranges from 10-70 mSv which is the equivalent of as many as 25 mammograms or 400 chest x-rays which substantially increases the lifetime risk of developing breast cancer (16).

While adverse reactions to iodinated contrast media have been reduced with the introduction of non-ionic, low osmolality contrast media, there remains a 3% adverse reaction rate with a 1 in 170000 fatality rate (17). Acute kidney injury and contrast-induced nephropathy are of particular concern with as many of 3% of contrast administrations resulting in contrast induced

nephropathy (16). Generally, contrast-induced nephropathy is evidenced with increased serum creatinine, however, these effects may not be noted until 2 days post contrast, peaking at 4 days after the scan and returning to baseline after 1-3 weeks later (18). It is likely that many patients with contrast induced nephropathy go undetected and consequently the incidence is probably underestimated. While risk factors for contrast induced nephrotoxicity are well documented (e.g., renal dysfunction, diabetes and congestive heart failure), there is a paucity of literature outlining the longer-term effects of contrast on renal function or on the confounding effects of contrast on medications that increase the risk of renal toxicity (e.g., the “triple whammy” of a concurrent diuretic, angiotensin converting enzyme inhibitor or angiotensin receptor blocker and a non-steroidal anti-inflammatory drug added to contrast risks). As a general rule, an effective glomerular filtration rate (eGFR) estimated from serum creatinine levels below 30 mL/min/1.73 m² is a relative contraindication for contrast media (17,19). Contrast induced nephropathy increases in incidence from 3% in normal renal function (greater than 60 mL/min/1.73 m²) to 12-27% in renal dysfunction to 50% in diabetic nephropathy (17). Indeed, concurrent use of metformin with chronic renal insufficiency and intravenous iodinated contrast is associated with 50% mortality (17,19).

Conclusion

The literature tends to be mixed and contradictory in terms of appropriate investigation algorithms for pulmonary embolism. This may reflect political, health, economic or professional preference based factors. The EANM provides an evidence based diagnostic algorithm that provides an excellent resource (9). The SNMMI guidelines (7) requires updating to reflect the advances discussed. For the patient presenting with suspected acute pulmonary embolism, if V/Q SPECT is available, that is the preferred approach. A positive scan should direct treatment for pulmonary embolism, a negative scan excludes pulmonary embolism and a non-diagnostic SPECT should be followed up with CTPA. Where V/Q SPECT is not available, CTPA or planar V/Q should be used (9). V/Q SPECT and SPECT/CT offer significant advantages over planar V/Q with or without the advantages of Technegas ventilation.

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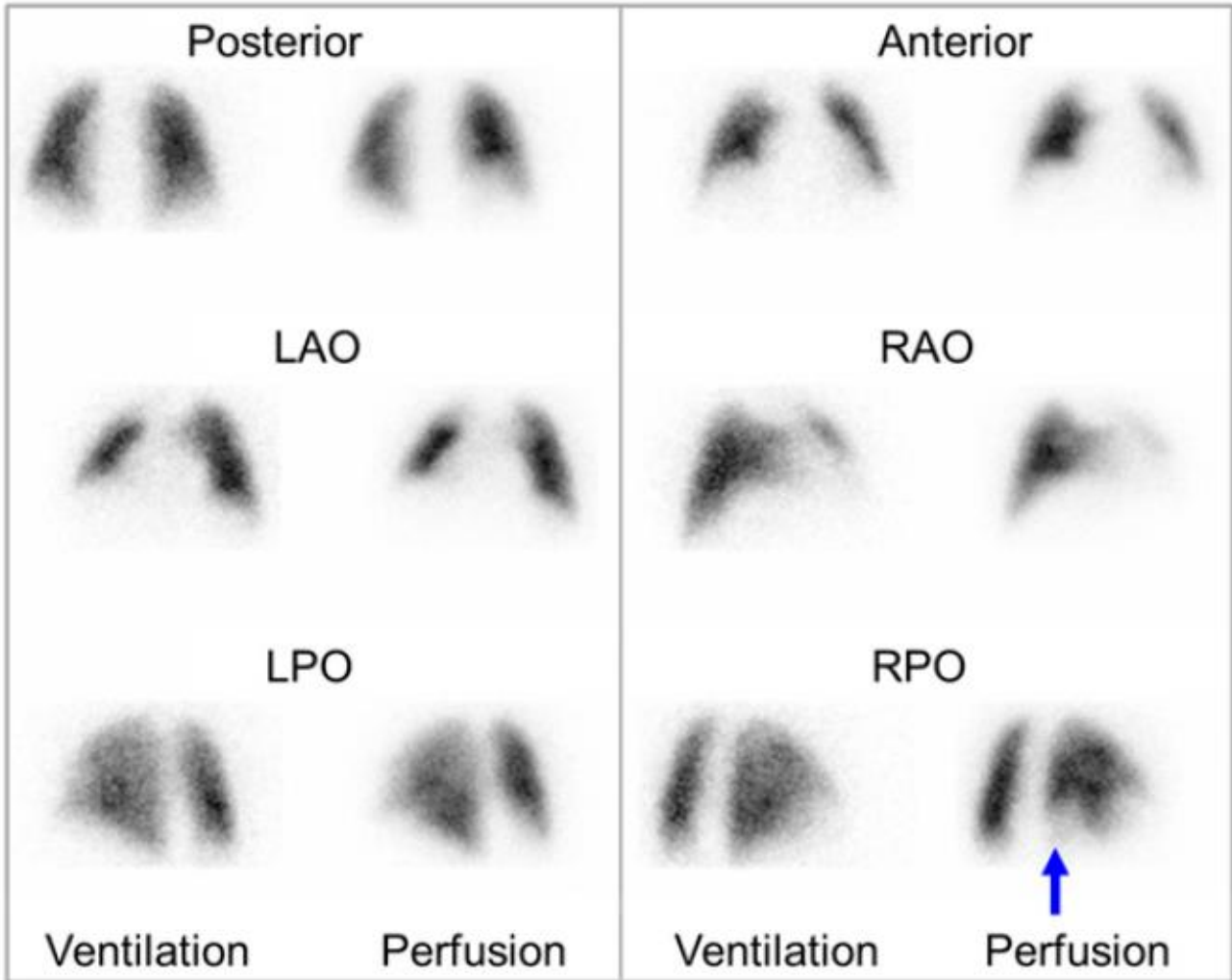


Figure 1: Planar V/Q scan with a single mismatched perfusion defect (arrow) suggestive of an intermediate probability of pulmonary embolism. Image from (5) and used with permission.

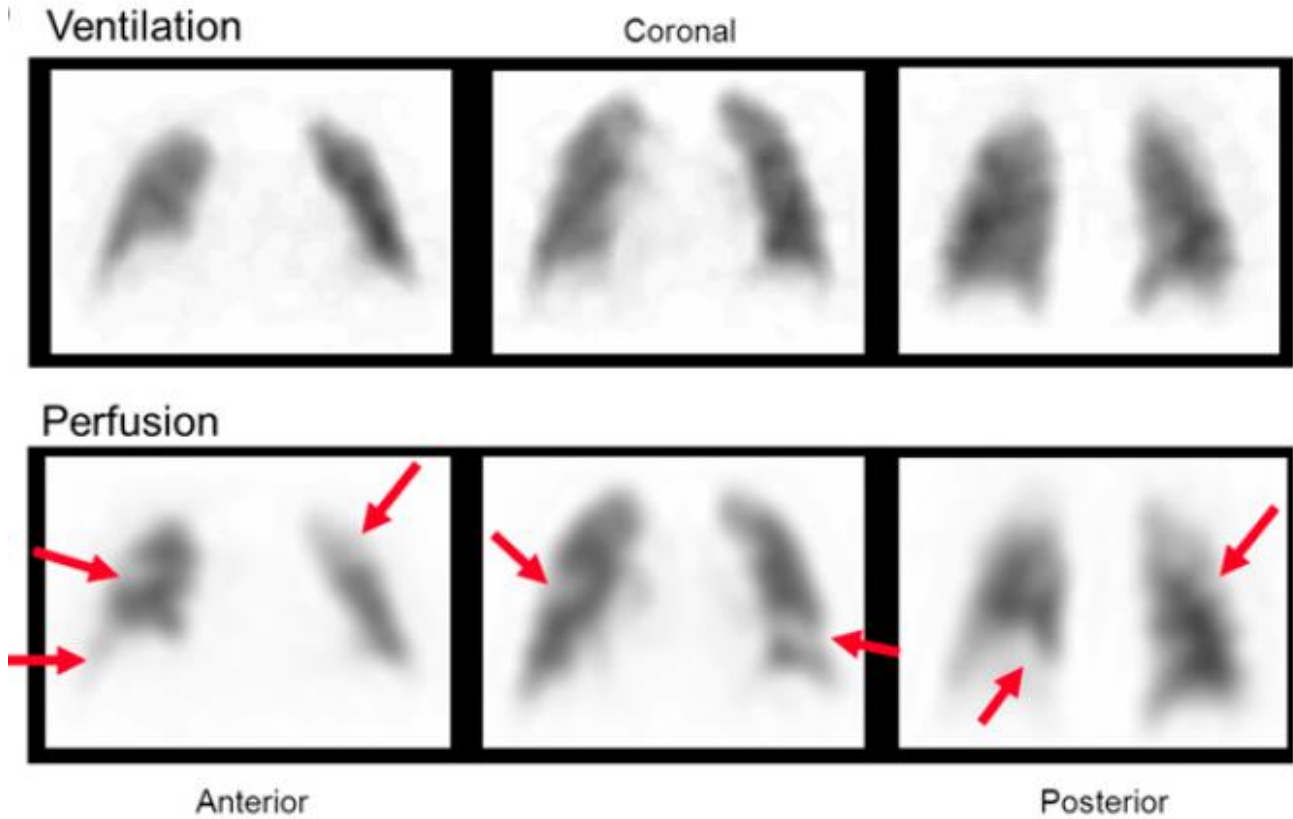


Figure 2: The same patient study as outlined in figure 1 planar V/Q scan following SPECT with representative slices demonstrating multiple defects (arrows) indicating more widespread pulmonary emboli. Image from (5) and used with permission.



Figure 3: Slice by slice ventilation and perfusion pairs for SPECT data with arrows highlighting a mismatch defect typical of pulmonary embolism. Image with permission 26.

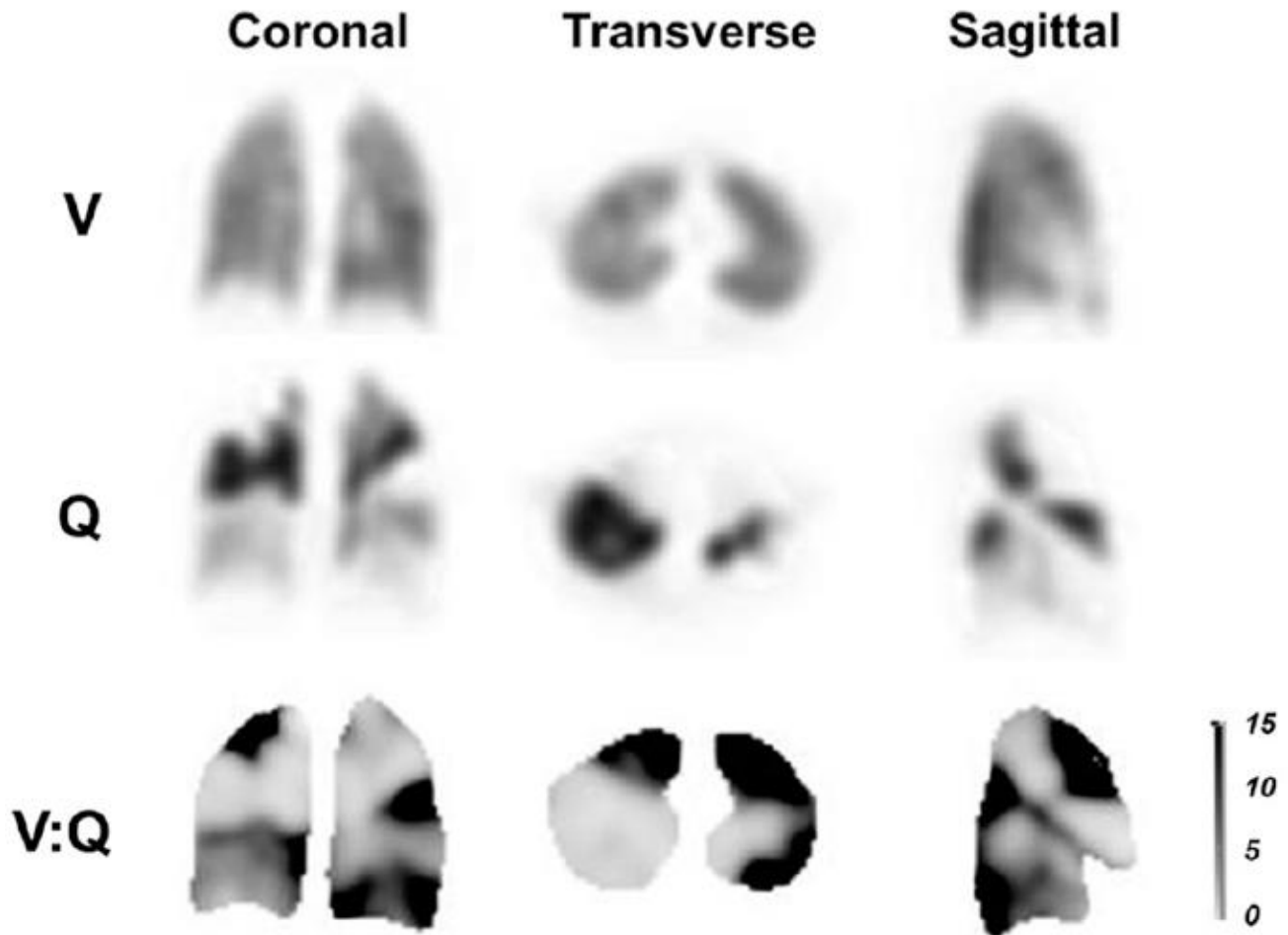


Figure 4: Representative slices for ventilation (top), perfusion (middle) and parametric V:Q ratio images (bottom) with positive segments for pulmonary embolism denoted by darker shading on the parametric images. Image with permission 27.

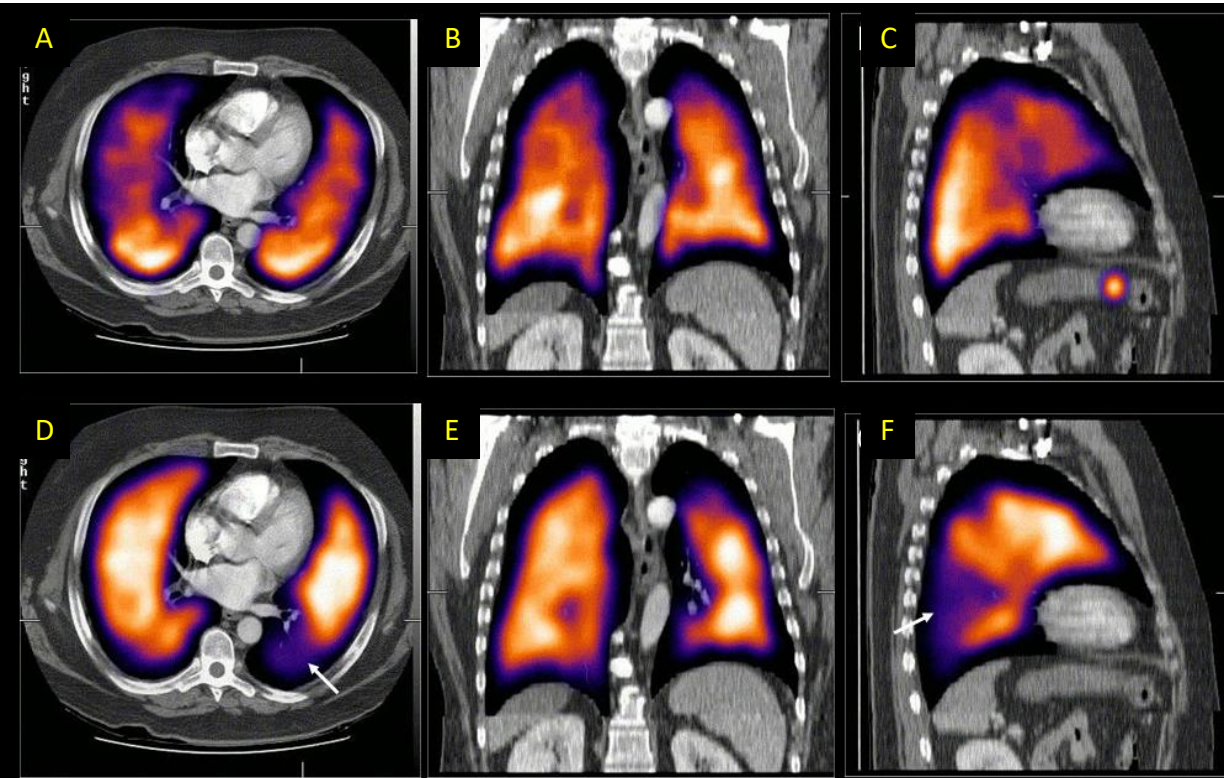


Figure 5: Representative slices of a SPECT/CT fused imaging of lung ventilation (top row) and perfusion (bottom row). The fusion SPECT/CT images demonstrates a segmental perfusion defect (arrow in 7D and 7F) in the left lower lobe with no CT opacity or matched ventilation defect consistent with pulmonary embolism. Image from (3) and used with permission.

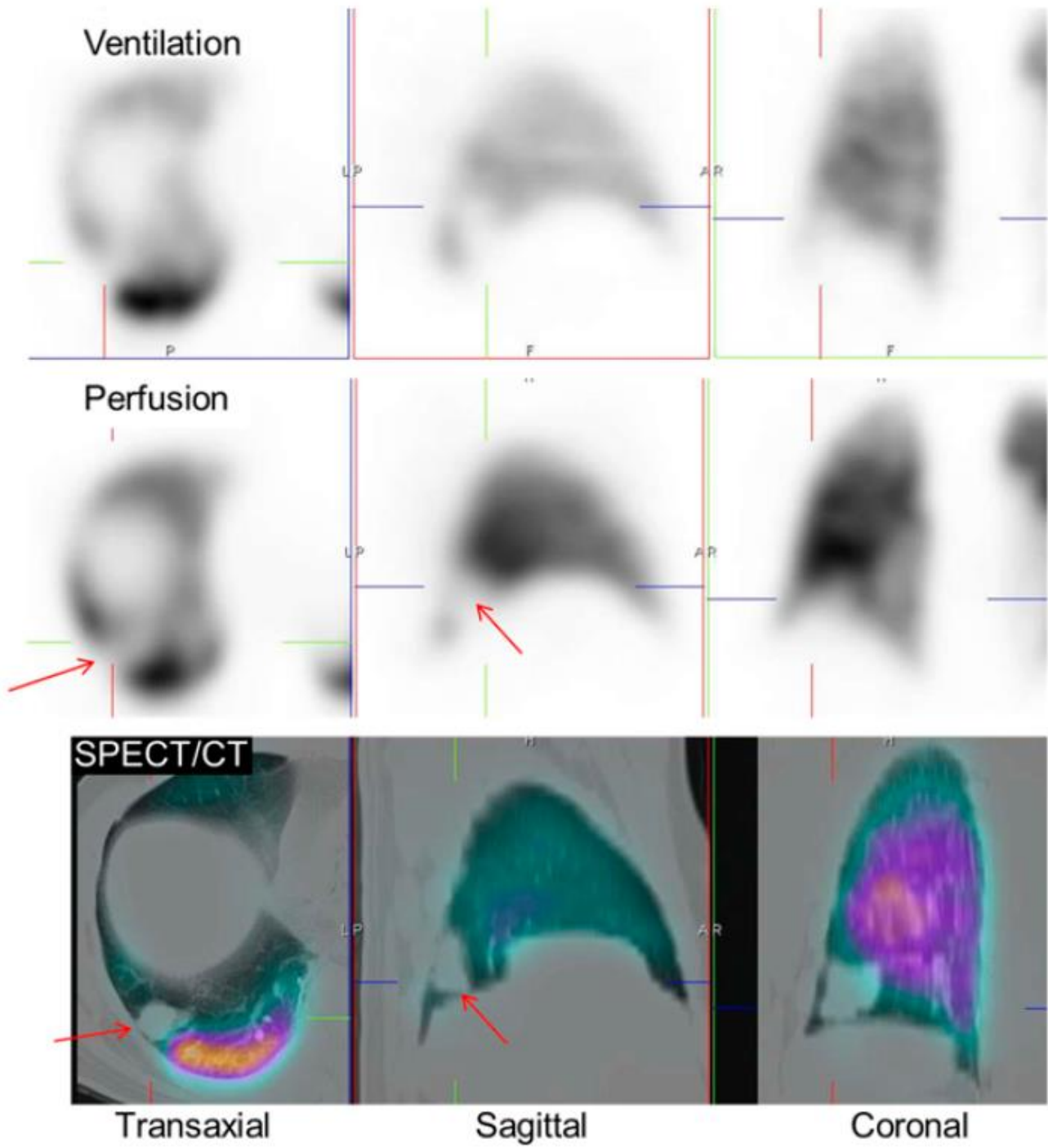


Figure 6: Fusion of SPECT and low dose CT showing an opacity (arrows) on the CT corresponding to the perfusion defect producing a matching defect consistent with lung metastases. Image with permission 5.

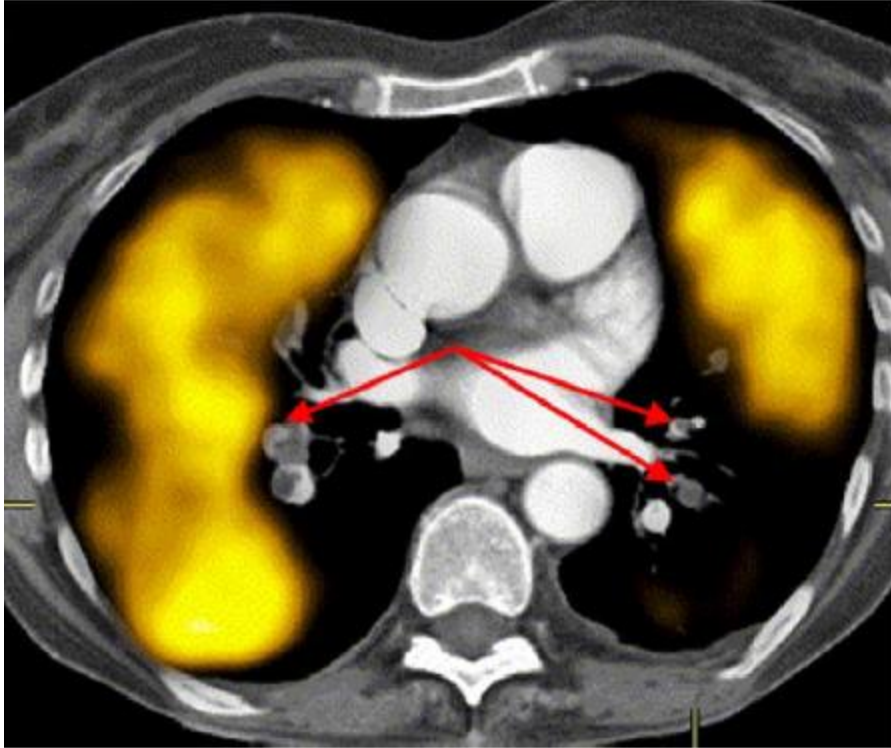


Figure 7: Fused perfusion SPECT and CTPA showing pulmonary emboli in bilateral arteries with the associated perfusion defects on SPECT. Image with permission 4.

Table 1: Summary of results of 24-hour social media poll conducted 22 August 2022.

	USA (%) N = 222	Australia (%) N = 154
Planar only	66.7	3.2
Planar and SPECT	2.7	1.9
SPECT only with planar generated from SPECT	11.3	27.3
Planar and SPECT/CT	12.6	3.9
SPECT/CT only with planar generated from SPECT	5.4	61.1
SPECT/CT only	1.4	2.6

Table 2: Characteristics enhanced by SPECT over planar imaging for the V/Q scan.

	Planar	V/Q SPECT	V/Q SPECT/CT	CTPA	Q/CT	Source
Sensitivity	85%	100%	-	-	-	20
	76%	97%	-	-	-	8
	-	97%	97%	68%	93%	21
	-	97%	-	86%	-	22
	-	-	-	83%	-	23
	87%	91%	100%	-	100%	13
	high	very high	high	moderate	very high	5,24
Specificity	100%	95%	-	-	-	20
	78%	96%	-	-	-	25
	85%	91%	-	-	-	8
	-	88%	100%	100%	51%	21
	-	91%	-	98%	-	22
	-	-	-	96%	-	23
	40%	56%	98%	-	52%	13
moderate	high	very high	very high	low	5,24	
Other findings	uncommon	uncommon	often	often	often	5,24
Radiation dose	low	low	high	very high	high	5,24
Technical issues	rare	rare	uncommon	often	uncommon	5,24
Availability	in hours*	in hours*	in hours*	in and out of hours	-	5,24
Adverse effects	no	no	no	yes	no	5,24

* Availability after hours is available in some nuclear medicine departments.