

Case Report -

Value of ventilation/perfusion SPECT detecting extensive pulmonary embolism in a patient with pneumonia

A woman, aged 25, with known cholelithiasis had used oestrogen contraception pills for six months, when she got dyspnoea and left-sided pain in chest and epigastrium. Due to suspicion of PE, she was examined with multislice CT angiography (mCT) the day after onset of symptoms. Small, basal parenchymal changes were bilaterally found on mCT (Fig 1A). No pulmonary embolism (PE) based upon presence of partial or a complete filling defect within pulmonary arteries was found.

Penicillin prescribed for pneumonia, was omitted on day 6 due to an allergic skin reaction. On day 24, subfebrility (37.8o C) and breathing correlated, right-sided chest pain appeared. The patient returned to the emergency department and erythromycin and diclofenac were given for 7 days. On day 29, she was hospitalized for increasing fever (39.4 °C), tachycardia (140/min) and tachypnoea. No hypotensive episode was noted at that point. ECG showed inverted T-waves in leads V1-V4. Echocardiography showed right heart dilatation and pulmonary artery pressure 42 mm Hg. D-dimer was 2.4 mg/l (normal < 0.25). A second mCT showed pneumonia but not PE. Symptoms worsened in spite of the antibiotics. On day 31 a third mCT (considered suboptimal) showed the same results. However, low molecular heparin was given due to continuing clinical suspicion for PE. The next morning, ventilation/perfusion single photon emission tomography (V/P SPECT) showed extensive bilateral PE and signs of pneumonia (Fig 1B). Before starting thrombolytic therapy (alteplase 100 mg was given on day 32 and 33), the patient had tachycardia (125/min), increased breathing rate (30/min) and normal systolic blood pressure (120 mmHg). The subsequent small improvement motivated angiography, which confirmed PE in the same areas as V/P SPECT (Fig 1B). A third thrombolytic dose was given and was followed by tinzaparin and warfarin. Leg compression ultrasonography was normal. The patient was discharged on day 41, largely improved with respect to symptoms, echocardiography (26 mm Hg) and V/P SPECT (Fig 1B). She returned to work on day 135.

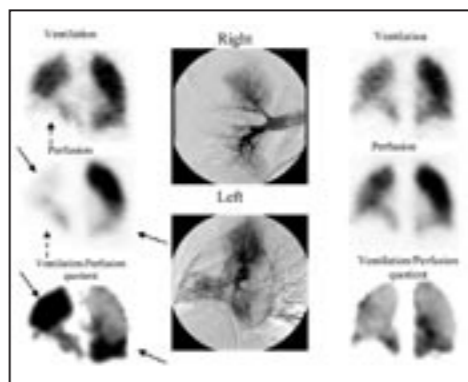
Early CT studies indicated high sensitivity and specificity for PE safely identifying major PE. However, as shown in a recent review sensitivity may vary between 53 and 100 % (1). An argument in favour of CT is that it may provide the clinician with an alternative diagnosis based upon lung parenchymal and pleural abnormalities. Coche at al. showed wedged shaped opacities in 62% among patients with PE, (2). Shah et al. found similar changes in 25% of patients with PE, 75% of which were found in the same regions as the vessels occluded by an embolus (3). They noted that a peripheral wedge-shaped opacity on CT is associated with PE, but that the finding is not specific. They may sometimes be attributed to pneumonia. In general, identification of such ancillary findings may be useful to instigate other examinations (2).

Different reasons for the repeatedly negative CT examination can be discussed in the light of a recent review by Worsley and Alavi (4). An anatomical one is particularly important in the right middle lobe and in the lingula, where arteries are running parallel rather than perpendicular to the scan plane. The severe shortness of breath may have reduced image quality, particularly in the 2nd and 3rd CTs. Too early or too late scanning is another recognised pitfall. In our case, the volume of the pulmonary vascular bed was limited by the combination of pneumonia and PE. A low volume will lead to a reduced mean transit time of contrast in the pulmonary arteries. We speculate that scanning time and passage of contrast were not adequately synchronized in our patient. Could PE have occurred after the 3rd mCT? Before that examination the patient was in a very poor clinical condition. The eminent signs of right heart strain indicated a severely compromised pulmonary vascular bed, with no vascular reserve. If the extensive PE observed on V/P SPECT should occur on the top of another disease, severe hemodynamic consequences would lead to clinical deterioration. This was not observed. Accordingly, PE occurring between the 3rd mCT and the 1st V/P SPECT remains a remote possibility.

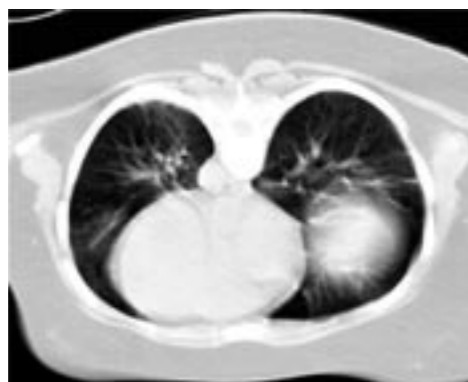
According to PLOPED criteria, lung scintigraphy has been considered non-diagnostic in the presence of ventilation disturbances or a pathological chest x-ray (5). Notably, the ventilation method predominantly used in PLOPED based on I33Xe is obsolete as are the interpretation criteria. As discussed by Reinertz et al., the PLOPED diagnostic criteria have severe shortcomings when applied

to either planar or tomographic scintigraphic technique (6). Freeman pointed out that description of ancillary findings would rather enhance the usefulness of lung scintigraphy (7). Using planar V/P scintigraphy and routine interpretation of ancillary findings, only 10% of our examinations were non-diagnostic for PE, while CT showed 8% (8). In comparison to planar scintigraphy, V/P SPECT further enhances diagnosis of PE by better delineation of defects (6), improved quantification, showing 53% more mismatches and less inter-observer variability (6, 9). In routine, the rate of non-diagnostic findings using V/P SPECT may be as low as 1- 4 % (10, 11). Furthermore, V/P SPECT clarifies PE even in the presence of other diseases as pneumonia, heart failure and COPD (9, 12). Obviously, a weakness is that V/P SPECT is still not in use in many centres and holistic criteria are not generally applied.

This case indicates the power of V/P SPECT in detecting life threatening PE in presence of extended pneumonia. Identifying ancillary findings by V/P SPECT is an important benefit shared by both mCT and V/P SPECT. Such findings do not necessarily exclude PE. The trend that mCT is regarded as golden standard radically replacing V/P scintigraphy is a point for discussion. The diagnostic options are always changing. However, V/P SPECT with up to date interpretation criteria offers excellent diagnostics.



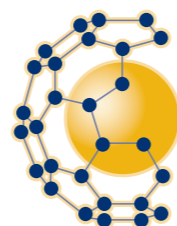
Coronal slices of ventilation/perfusion SPECT on day 32.



Transaxial mCT image on day 1, showing basal parenchymal changes in the lungs interpreted as pneumonia.

Vita Medical Limited wishes to thank Dr Bajc for allowing the reproduction of her article and the Journal of Thrombosis and Haemostasis for permission to reprint.

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Quality and Regulatory

Customer Feedback

Vita Medical collects and uses feedback from you, our customers, to help us continuously improve our products, systems and service.

Positive or negative, your comments are of value to us and by being pro-active in measuring Customer Satisfaction we are trying to respond to any potential problems before they happen.

Periodically we investigate any comments or complaints received and look at corrective or preventive action that we can take.

In a recent instance, we investigated what we thought was a customer complaint that was found to be caused by another piece of equipment at the customer's site and not their Technegas Generator. During our investigations, we did find that we could improve the performance of the Technegas machine in several areas and subsequently these improvements have now been included into newer machines. While the improvements were slight and found not to be necessary in light of the original complaint, Vita felt that the changes were worthwhile in enhancing the overall performance of the Technegas Generator.

While our representatives are in your department please take a few moments to let them know a bit of what you think of the product and the service you receive from us. From time to time we may also ask you to complete a short questionnaire to provide further specific information. Alternatively you can call our offices on (02) 9541 0411 or email to me at gsomerville@vitamedical.com.au.

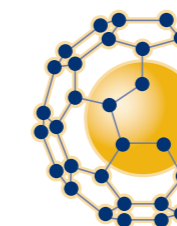
Gary Somerville – Quality Manager

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VITA Medical Newsletter

Issue 1 January 2006

In the early 1990's Technegas Topics was introduced as way of bringing interesting information on Technegas technology to the end users and I must say I remember the articles well as it was always a source of good reading while I waited invariably for that last minute lung scan patient to arrive that the ward upstairs had held up for the past half hour. When our newly appointed Sales & Marketing Manager, Charles Buttigieg came to me with the proposal to resurrect a newsletter I naturally encouraged him to pursue his idea as I firmly believe it is an excellent tool in communicating relevant Technegas information to all our loyal customers and it also brings our many friends within the wider Nuclear Medicine community just that little bit closer. I hope the articles in the proceeding pages you will find interesting and I encourage you to give us feedback and stories of interest that you would like to share with others.

The next few months are an exciting time for Vita Medical as the first update of the Technegas Generator since its release in 1986 will be made available. Technegas Plus was introduced to the market at the European Association Meeting in Istanbul, Turkey in October, and attracted huge interest. The new generator has been totally updated and re-designed around what you the customers have told us we need to change so we look forward to being able to demonstrate the many new features and benefits to you. We will be offering great deals to update your old generator to the new model and we look forward to your comments on the new look and what we are offering to upgrade.

As you are all aware Nuclear Medicine as part of the wider diagnostic imaging regime continues to evolve and during recent years PET has dominated and provided most of our interest in the future of our modality. The basic tests of Nuclear Medicine have been under siege during this time as MRI and CT technology have improved and have started to encroach on tests that Nuclear Medicine have traditionally performed.

This has directly impacted on Technegas as the growth of the VQ lung scan has been affected by the rise in multi slice CT scanners and their ability to image lung PE. This use of CT has been a global phenomena but I think it is compounded by the fact that Technegas is not represented in the USA and their usage of inferior ventilation agents such as Xenon and DTPA aerosol allow CTPA an easier road in shifting diagnostic regimes. However even allowing for this fact, during 2004 Vita Medical had a record sales year and sold 162,500 Patient Administration Sets against a global inventory of 993 generators operating in 43 countries which underlines the strength of Technegas even in an adverse market. Australia and France are our strongest markets where we have around 80-90% market share and these markets continue to grow albeit slowly even with the CT competition. Our quickest growing market has been Canada where there are now 27 generators installed since 2003 and PAS usage has grown 250% which bodes



well when we finally make it to the USA.

Our final NDA clinical trial for the FDA is currently due to start re-enrolling patients by the end of this year and it is envisaged that the trial will be completed, the dossier submitted to the FDA during 2006 and approval to use Technegas in the USA will be authorized during 2007. Entry in to the biggest Nuclear Market in the world will be challenging because of the timing but it is my belief that Technegas as the ventilation agent of choice for SPECT imaging will be positioned well to take advantage of the current push to hybrid SPECT/CT scanners. The excellent work of the team at Royal North Shore Hospital on SPECT Lung imaging underpins this belief as they have recently made the move to perform SPECT only on all their lung imaging after extensive evaluation of the image results and confidence in reporting. I believe their current work on fused SPECT/CT images will enhance the quality of the VQ study again as areas of abnormality on the VQ study can now be matched directly with the CT image and will allow patients with any lung pathology to be assessed. I look forward to seeing their latest results to encourage many other departments to adopt SPECT only imaging and ultimately SPECT/CT as hybrid scanners are purchased.

I am very cognizant that Vita Medical is a one product company so I am always looking for areas where we can grow our business. We are currently looking to expand our interest into PET products and have recently become agents for ROTEM products which include O18 water and consumables used in cyclotrons for production of FDG. I invite all potential customers to contact us for pricing and I am sure we will be able to help you.

I hope the following articles and information are of interest to you and I look forward to your positive response to the exciting release of the new Technegas Generator. I can assure it will be best investment in equipment you have made in a long time.

Best Regards,

David Rundell
Chief Executive Officer
Vita Medical Ltd

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Literature Review

Technegas: the optimal ventilation agent.

It's now 20 years since we began formal clinical trials with *Technegas*, at that time doing a direct comparison with the only internationally recognised agent Xenon-133. By then the results of the most comprehensive PE diagnostic assessment ever, the PIOPED trial, were long established, finally giving Clinicians some peer consensus criteria on which to base their interpretation of ventilation-perfusion (V/Q) images. Sadly, PIOPED is still being quoted as though it is relevant today, by proponents of x-ray tomographic (CTPA) technology, to denigrate V/Q. They conveniently ignore the technological advances of quantitative tomographic scintigraphy (SPECT or SPET) combined with the ideal ventilation agent *Technegas*. It is difficult to understand why anyone would contemplate using ¹³³Xe now with all its clearly identified limitations as a ventilation agent.

Technegas, being a dry hydrophobic aerosol, does not grow in size as it traverses the bronchial tree, finally being captured by the surfactant secretions as it diffuses to the walls of the alveoli. This is in marked contrast to the aqueous aerosols like ^{99m}Tc-DTPA commonly used for ventilation. No matter how small they are at the patient's mouth, the supersaturated milieu beyond the 3rd division of the bronchial tree guarantees these droplets will grow in milliseconds, by an order of magnitude at least. Remember that the evolving lung was specifically designed to eliminate atmospheric particles by, among other things, increasing the branching angle of the bronchi with each successive generation. Note too, that the particle diameter only needs to double for its momentum to increase 8 fold, thereby greatly enhancing impaction at those bronchial junctions. Thus aqueous aerosols simply cannot penetrate as far as *Technegas* and are also far more sensitive to impaction at inhomogeneities in the airways that are very common, particularly in an industrialised urban environment or where patients smoke.



Bill Burch had the honorary appointment as Visiting Fellow since 1976 at the John Curtin School of Medical Research at the ANU, Canberra. His background includes stints in Antarctica in geophysics, radiotherapy and nuclear medicine in Melbourne, the U.K. and Canberra where from 1976 to 1984 he began his quest to find a good ventilation agent. He "stumbled" upon *Technegas* and has been its champion ever since.

Many of your patients will exhibit pleuritic chest pain, and find any deep breathing difficult. Unlike other aerosols *Technegas* can be created with an extremely high specific activity, making it suitable for single breath inhalation to achieve a diagnostic dose. This feature is also very useful with frail, aged or infirm patients who cannot perform breathing manoeuvres on demand.

Well over 200 peer-reviewed reports have now been published about *Technegas* and it is particularly pleasing to note the clinical and experimental research appearing that extends applications for it well beyond diagnosing PE. Sweden especially has been prominent recently, with three reports. *Physiological evaluation of a new quantitative SPECT method measuring regional ventilation and perfusion*, by Petersson J et al (J Appl Physiol 96(3): 1127-36; 2004); *Regional ventilation and distribution of emphysema – a quantitative comparison*, by Johansson A et al (Clin Physiol Funct Imaging 24(1): 58-64; 2004); and *Positive end-expiratory pressure affects regional distribution of ventilation differently in prone and supine sheep*, by Johansson MJ et al (Crit Care Med 32(10): 2156-7; 2004). McLean RG et al *Comparison of new clinical and scintigraphic algorithms for the diagnosis of PE*, (Br J Radiol 77(917): 372-376; 2004) have demonstrated in a series of 238 patients that algorithms are not automatically transferable to new technology environments.

The great value of SPECT imaging is most effectively illustrated in a major oral paper presented at the European Nuclear Medicine Congress in Istanbul in October, *Ventilation-perfusion lung SPECT with co-registered CTPA: enhancing diagnostic accuracy*, by Bailey DL et al. This group's work represents 'state-of-the-art' in SPECT. It brings "unclear medicine" well beyond the need for the Specialist's exclusive interpretive skills, and allows the all-important sharing of the definitive images with the referring Clinician, of what can be a life threatening diagnosis.

Imaging with SPECT: New Possibilities for V/Q Scanning

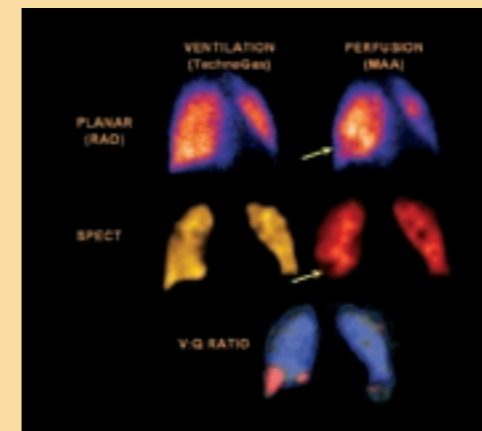
Anyone with an interest in ventilation/perfusion lung scanning will have noted the developments in V/Q SPECT scanning that are emerging in the published literature and being presented at various nuclear medicine scientific meetings.

In an overview session presented at the Australian & New Zealand Society of Nuclear Medicine's "Clinical Skills Symposium" in Melbourne, the Director of Nuclear Medicine at Royal North Shore Hospital in Sydney, Dr Paul Roach, noted that, while there was still relatively little published data in the medical literature, SPECT was likely to improve sensitivity, specificity, reproducibility and reporter confidence, and therefore yield a reduction in the number of intermediate results. Dr Roach noted that in a time when V/Q scanning is under threat from X-ray CT pulmonary angiography (CTPA) worldwide, it was imperative that lung scanning be optimised and lung scanning using SPECT was a key way to achieve this. Based on preliminary results released from the PIOPED 2 study, Dr Roach suggested there was a key opportunity for clinicians to revisit the strengths and weaknesses of both lung scanning and CTPA. He also noted that SPECT would allow new ways of displaying data, including image registration, separation of superimposed structures, ventilation-subtracted perfusion images, V:Q ratio parametric images and novel surface shaded displays. SPECT would also facilitate developments in areas such as respiratory gating and image fusion with CT.

The team at Royal North Shore Hospital, which includes physicians and scientists from the Nuclear Medicine and Respiratory departments, have, in particular, addressed the issue of how to make the transition from planar imaging to SPECT-only imaging. One approach that has been published previously is to acquire SPECT-only data and add a

number of the frames together from the adjacent angles to produce a planar image(1). However, this method can be count poor and also contains a degree of radial blurring due to the summing together of a number of frames acquired at different angles. The alternative developed by Assoc.Professor Dale Bailey and the RNSH group has been to reproject the reconstructed SPECT transverse sections through an appropriate attenuation map to produce high count, high quality planar images at the desired angle (anterior, obliques, etc) (2, 3). In addition, it is possible to remove either right or left lung and produce lateral and medial views of the single isolated low with no "shine through" from the contra-lateral lung. A novel aspect of this work reported by A/Prof Bailey was the ability to use "scattered" photons from the ventilation and perfusion SPECT scans to generate a realistic, synthetic attenuation map which makes the technique widely applicable and not restricted to SPECT cameras with either radionuclide or CT transmission sources.

Dr Geoff Schembri presented preliminary clinical data comparing planar and SPECT lung scanning. It was noted that the SPECT lung scans identified more mismatched defects (which are most likely to represent pulmonary emboli) than planar images. SPECT images were demonstrated to show better localisation and delineation of perfusion abnormalities improving reporter confidence. Subtracting the ventilation data from the perfusion allows for greater contrast, making perfusion defects more apparent. His work has shown that SPECT has the potential to improve detection of pulmonary emboli. The RNSH group are now exploring the application of V/Q SPECT in other areas of respiratory medicine, including non-embolic pulmonary vascular disease such as primary pulmonary hypertension.



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Dr Paul Roach *FRACP* is a senior staff specialist and Head of the Department of Nuclear Medicine, Royal North Shore Hospital. He has published a number of articles on lung scanning and been instrumental in implementing multi-modality "fusion" imaging into Australian nuclear medicine.

Associate Professor Dale Bailey *PhD* is principal physicist in Nuclear Medicine at Royal North Shore Hospital. His main interest is in quantitative emission tomography. He

has published extensively in the areas of lung and airways tomographic imaging, and has been at the forefront in developing combined emission/transmission scanning devices for SPECT and PET.

Dr Geoff Schembri *FRACP* is a senior staff specialist in Nuclear Medicine at Royal North Shore and Bankstown Hospitals. He is an strong advocate of the benefits of functional imaging as a complement to anatomic modalities and currently has been

investigating how ventilation/perfusion lung SPECT best fits into the diagnostic algorithm for the assessment of thrombo-embolic disease.

Into the 21st Century with Technegas Plus

Technegas Plus incorporates many new features designed to improve patient comfort and compliance, make the job easier and safer for the technologist and simplify service and maintenance.

It is envisaged that the older machines will be phased out as their finite life is reached and parts no longer available while the advantages of *Technegas Plus*, outlined here, are more widely appreciated.

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pertechnetate. A permanent purge filter reduces maintenance and technologist radiation exposure.

From a service perspective, Allen key activated contact clamping, improved drawer access and illumination, larger display screen, flash card programming and other engineering changes will make calibration, servicing and fault finding simpler, quicker and more accurate.

More on the advantages of *Technegas Plus* in future issues of *Vita News* along with helpful hints on how to improve your V/Q scans. Suffice it to say comments from users would be most welcome.

Richard F Gotch
Global Service Manager
Vita Medical Ltd



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