Ventilation Agents Compared

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As the physical characteristics, radioactive intensity and half-life, mode of administration and the physiological behaviour of the various agents used for the ventilation (V) component of the V/Q test are so different, it is critical to relate all the factors back to a final image representation of true lung ventilation. For this purpose, the discussion of each agent that follows will be summarised in a form of "league table" to put everything into perspective.

Xenon-133

This is an inert gas, a by-product of nuclear fission, with a gamma energy of 81KeV, a beta spectrum from 350KeV, and a half-life of 5.24 days. It is supplied in a lead shielded plastic bag from which individual aliquots can be withdrawn by syringe for insertion into the circuit of the patient breathing apparatus. This is a closed circuit using a CO2 absorber requiring the patient to re-breathe continually during imaging. The idea is that it creates a uniform distribution of Xenon in the functioning airways. In some centres it was normal procedure for the circuit to be switched to waste after the main image acquisition so that a second image could be acquired a few minutes after clearing the gas from the airways. The purpose was to identify regions of delayed 'wash-out' which would represent possible PE as there would be no blood/gas transpiration and the gas would tend to pool more at those sites.

Although the clear positive aspect of ^{133}Xe imaging is that it can represent very precisely the physiological ventilation of the airways, two major drawbacks were (1) the low energy of the gamma photons, and (2) the high lung dose delivered by the ß emission. Gamma cameras are very specifically designed to be optimum for the 140KeV energy of the ^{99m}Tc radionuclide. At that energy, there is the best trade-off between ultimate image resolution and self-absorption in tissue. When combined with the significantly increased absorption at the much lower, 81KeV of the ^{133}Xe gamma, both spatial resolution and count density are severely compromised. Thus the chances of detecting ventilation integrity at even the segmental level, in an image cluttered with non PE defects were very remote. One of the severe limitations from the high dose drawback, is that imaging is generally restricted to a single planar posterior view. Although some centres have ignored this limitation even to performing SPECT studies with ^{133}Xe, this is not to be encouraged and goes against the ALARA principle of radiation dose containment when other more suitable agents are available.

Finally, the action of having to breathe continuously through an apparatus, naturally encourages much more lung movement during imaging compared with totally passive, rested breathing by a supine person. This degrades further the image quality already compromised.

Krypton-81m

This is an inert gas, derived directly as the daughter product from a Rubidium "generator" containing cyclotron-produced ^{81}Rb. The parent ^{81}Rb, is a positron emitter with a half-life of 4.57h, and the ^{81m}Kr is simply obtained by passing air over the ^{81}Rb matrix contained in a shielded pot, leading directly to inhalation by the patient. As the ^{81m}Kr only has a 13.1s half-life, inhalation and imaging has to be simultaneous. Indeed there is no need to trap the exhaled gas as it decays so fast. Needless to say, the radiation burden for the patient is negligible. The 190KeV gamma emission is ideal for imaging. Also, it is far enough above the ^{99m}Tc value at 140KeV, for energy discrimination settings on the camera to allow for ventilation imaging after perfusion with MAA - if a perfusion defect is discovered.

^{81m}Kr gas as a ventilation agent has not become widely used primarily because of the high production cost for the generator and that it only has a useful lifetime of one day. In practice hospitals would order one generator a week. Thus ventilation studies had to wait for the day it was available. This flies in the face of the concept of PE as an urgent diagnosis. Also, for the same reasons as ^{133}Xe, the lung motion artefacts caused by the patient needing to breathe continuously during imaging mitigated against what would otherwise be high resolution images.

An unreported consequence of the 13s half-life of ^{81m}Kr is the tendency for penetration to the lung bases to generate much lower activity. The time taken for the gas to get to the bases via inter-breath mixing would leave insufficient signal there for good image quality. This first showed up in a comparison in the UK between Technegas and ^{81m}Kr using a software analysis tool devised by John Agnew at the Royal Free Hospital London, a tool he named the "Penetration Index" or PI.

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PI looked at the central and the peripheral lung regions on the posterior view, expressing relative count density as a ratio. It was originally devised to demonstrate how well different aerosol systems performed compared with ^{81m}Kr. When it came to comparisons with Technegas in some patients with healthy lungs, the PI for Technegas was better than that for ^{81m}Kr. This anomaly came about from a combination of the central conducting airways having a high concentration of ^{81m}Kr, a lower activity by the time it reached the periphery of the lung bases, and the fact that Technegas, once inhaled, deposited uniformly in the periphery, but did not deposit in the conducting airways leaving them largely free of activity. The lung bases are routinely sites for multiple small emboli, thus good count density there can be crucial for an accurate diagnosis.

Aqueous Aerosols

Although several different molecules, all labelled with ^{99m}Tc, were tried over the years, for all intents and purposes the single remaining agent is ^{99m}Tc- labelled diethylenetriamine penta-acetate (DTPA). This large molecule was originally produced as an injectable renal function imaging agent, but was found to clear from the lungs directly into the circulation, following inhalation as an aerosol, with a half-time of about 20min. By contrast, straight generator eluent, ^{99m}TcO4-, washed out in less then 10 minutes.

An aerosol of DTPA is generated by one of two standard physical techniques; either some form of air-driven nebuliser, using the Collison impaction atomiser principle, or an ultrasonic-based aerosol generator. The latter has the advantage of being more efficient in terms of aerosol generation, but suffers from the major drawback of the tendency for the DTPA molecule to become unlabelled in the intense ultrasonic fields, effectively producing a simple pertechnetate aerosol for inhalation. Nebuliser systems have the advantage of being cheap, but they demand a relatively large volume and activity of DTPA in the container (~ 2GBq), and that on its own presents a significant radiation hazard for the Technologists in the course of preparation, administration to a patient and ultimately waste disposal. Add to that the inefficient aerosol creation, leading to 2-5minutes of inhalation manoeuvre for the patient. Note too, that nebulising absorbs energy by evaporation of the smallest droplets, so that the solution cools under prolonged nebulisation, increasing the viscosity and reducing the particle forming efficiency.

What is not readily appreciated is that as both these types of generators create aqueous aerosols, these aerosols are also, by definition, hydrophilic. In practice, what this means is, despite all measures taken to ensure the particle size is small at the patient's mouth, such as a settling chamber, there is growth in a matter of milliseconds by orders of magnitude once the particles reach the supersaturated region only a matter of 3 divisions into the 23 that make up the bronchial tree. A doubling in particle diameter, creates an 8-fold increase in momentum and hence inertia, so the tendency for a particle to leave the guidance of the laminar flow lines in the conducting airways, and impact on walls at junctions, rises rapidly with penetration depth. Add to this, the increase in bronchiolar branching angle with depth into the lung, an evolutionary development to filter out particles from reaching the alveoli, and combine some turbulence from airways disease in many patients, and its not surprising that aqueous aerosols often lead to unsatisfactory images.

A false sense of security, in terms of an over diagnosis of PE could be built up from the lack of penetration depth of aqueous aerosols in apparently smooth images. The combination of organ movement, particularly in an anxious patient, coupled with the intrinsic resolution limits of a camera and planar views, could readily mask peripheral sub-segmental ventilation defects visible on a congruent MAA perfusion image.

Technegas

Technically, it is a micro-aerosol of graphitic platelets containing pure ^{99m}Tc metal. Only a carbon surface is presented to the outside world. Thus the particles remain intact up to about 500^{o}C. They are also hydrophobic thus do not grow in size as they penetrate deeper into the lung. Technegas will transit the bronchial tree all the way to the alveoli, or respiring airways, except where there is a high degree of turbulence or curtain of obstruction in severe airways disease. Even so, it is clear that where patients have been studied with both conventional aerosols, however produced, or Technegas, the penetration beyond obstructions is always much better with Technegas.

Importantly too for imaging, once Technegas has reached the alveoli, and there is a slight breath-hold, (3-5s), particles rapidly diffuse to the alveolar walls where they are captured by the surfactant. Thus once the count-rate in the chest is sufficient for imaging, a few breaths of air exhaled through the filter trap on the apparatus is sufficient to leave Technegas only deposited in the respiring airways, effectively for the lifetime of the ^{99m}Tc.

Again, unlike conventional aerosols, Technegas can be

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made at as high a specific activity as is desired. Thus it is not uncommon in some centres to find patients only needing to inhale one or two breaths for a full imaging study. This is of a particular advantage when testing frail-aged, the very young, comatose or otherwise poorly compliant patients.

V agent	133Xe	81mKr	DTPA	Technegas
Ease of admin	Moderate	Moderate	Low/mod	Very easy
Pt comfort	Moderate	Moderate	Low	High
Cost	Moderate	V high	Moderate	Moderate
Availability	Variable	1 day p/w	24/7	24/7
Dose to pt	High	V low	Moderate	Moderate
Dose to staff	Medium	Negligible	Mod/high	Low
Image quality	Poor	Good	Variable	Good