

## **A Technical Overview of Technegas as a Lung Ventilation Agent**

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Key words: lung imaging, ventilation, Technegas

Footline: Technegas ventilation

## **Abstract**

Technegas is a carbon-based nanoparticle developed in Australia in 1984 and in widespread clinical use, including SPECT imaging, since 1986. While  $^{81m}\text{Kr}$  offers the ideal ventilation properties of a true gas, Technegas is considered preferred in more than 60 countries for ventilation imaging, yet has limited adoption in the United States of America (USA/US). In March 2020, a new food and drug authority (FDA) application was lodged for Technegas and the impending approval warrants a detailed discussion of the technical aspects of the technology for those for whom the technology is new.

Technegas is a simple yet versatile system for producing high quality  $^{99m}\text{Tc}$  based ventilation studies. The design affords safety to patients and staff including consideration of radiation and biological risks. Technegas is the gold standard for ventilation studies for performing SPECT based V/Q studies in pulmonary embolism and a number of respiratory pathologies. When approved by the US FDA, Technegas will extend advantage to workflow, safety and study quality for departments who adopt the technology.

## Introduction

Ventilation and perfusion (V/Q) lung scintigraphy has been used in the evaluation of patients with suspected pulmonary embolism for more than half a century. While the underlying principles have not changed during this period, there have been significant advances in technology. Imaging equipment has emerged with superior resolution and sensitivity, single photon emission computed tomography (SPECT) techniques added advantages over planar imaging alone, hybrid systems allow SPECT and computed tomography (CT) to produce physiological information co-registered with morphology, and positron emission tomography (PET) and PET/CT have become more widely available. Concurrently, developments in radiotracers have seen improved microspheres for perfusion in macro aggregated albumin (MAA) and replacement of 133-xenon ventilation with 99m-technetium ( $^{99m}\text{Tc}$ ) aerosols, 81m-krypton ( $^{81m}\text{Kr}$ ) and Technegas, although 133-xenon is still used at some sites. Technegas is a carbon-based nanoparticle which has a strongly bound  $^{99m}\text{Tc}$  atom trapped in a cage-like structure. It was developed in Australia in 1984 (1) and began widespread clinical use, including SPECT imaging, in Australia from 1986 (2). While  $^{81m}\text{Kr}$  offers the ideal ventilation properties of a true gas, Technegas is considered preferred in more than 60 countries for ventilation imaging, yet has limited adoption in the United States of America (USA/US). Indeed, in 1991 a Newsline article in the *Journal of Nuclear Medicine* (3) posed the question “when, if ever, will the device that has won near ubiquitous use in Australia gain approval for lung ventilation studies in the USA?”. In March 2020, a new food and drug authority (FDA) application was lodged for Technegas and early in 2021 both the SNMMI and SNMMI-TS, concerned about the decline in ventilation studies in response to COVID19 risk, requested fast tracking of FDA approval of Technegas. Since Technegas does not produce aerosolised particles nor is it a gas, it allows imaging of the ventilation to the lungs to optimize patient outcomes while maintaining staff safety. The impending approval of Technegas by the US FDA warrants a detailed discussion of the technical aspects of the technology for those for whom the technology is new. This discussion will not examine the broader debate on the role and application of V/Q imaging, clinical applications or the advances in imaging technology (SPECT, SPECT/CT and PET/CT) and the associated image interpretation. It is, however, important to note that using Technegas for ventilation imaging allows the entire V/Q protocol to move to 3-dimensional SPECT imaging with the

associated improved sensitivity and specificity (4-6). SPECT performance is further enhanced with the addition of a co-acquired low-dose CT (4-6).

### **Lung Ventilation**

A number of approaches to lung ventilation studies are available in nuclear medicine with the predominant approaches being  $^{81\text{m}}\text{Kr}$  as an inert gas,  $^{99\text{m}}\text{Tc}$  diethylenetriaminepentaacetate acid (DTPA) aerosol and the ultrafine  $^{99\text{m}}\text{Tc}$  carbon dispersion of Technegas.  $^{81\text{m}}\text{Kr}$  use is limited by availability, cost, the short half-life and less practical SPECT. [ $^{99\text{m}}\text{Tc}$ ]DTPA as aerosolized droplets with varying sizes (0.5-2  $\mu\text{m}$ ) with distribution dependent on the aerodynamics of gas flow. As a result, aerosol ventilation studies can be confounded by deposition in large airways and this is exacerbated in patients with respiratory symptoms. The ultrafine Technegas particles (< 0.1  $\mu\text{m}$ ) by contrast have a gas-like distribution, particle-like retention and the attractive properties of  $^{99\text{m}}\text{Tc}$  to allow high quality imaging, including SPECT. Internationally, Technegas is considered the best alternative for the ventilation portion of the V/Q scan (7,8).

### **Technegas Production**

Technegas is hexagonal shaped graphite capsule enclosing  $^{99\text{m}}\text{Tc}$  (1). These graphite particles are small (< 0.1 micron) and hydrophobic which not only allows penetration deep into the airways but resists attachment to the airways which makes it ideal for evaluation of deposition in the lungs (9). Technegas is distributed in the lung airways by diffusion and becomes fixed in the lumen of the airway sufficiently long to allow SPECT (10).

The commercially available Technegas® Generator (Cyclomedica Pty Ltd., Sydney, Australia) operates with  $^{99\text{m}}\text{Tc}$  sodium pertechnetate eluted from the  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator. The graphite crucible accommodates 0.17 mL and this should not be exceeded. Once the  $^{99\text{m}}\text{Tc}$  has been added to the crucible, the liquid is evaporated (“simmer”) at 70°C for 6 minutes in an ultrapure argon environment. On completion of the simmer cycle, the combustion cycle is initiated (“burn”) where an alternating current arc is produced between the terminals holding the crucible to ablate the graphite and  $^{99\text{m}}\text{Tc}$  (11). This produces temperatures of 2750°C for 15 seconds in an ultrapure argon environment to produce the carbon nanoparticles (11). Operation of the Technegas generator is simple when following the stepwise process. Specific steps in the

process are detailed in the user guide so will not be repeated here but outlined below are general comments associated with each step for consideration when using the Technegas generator (figure 1).

### **Operation of the Technegas Generator**

The first step is to ensure the Technegas generator is in good working order, is connected to an adequate supply of argon supply (or change argon gas bottles), is connected to mains power, and the system is powered on (figure 2). The delivery to the patient can occur at the patient's bedside using battery power. This is a very useful option because it allows the Technegas generator to be prepared in a radiation safe location remote from patient, staff and scanning areas (e.g. in or adjacent to the radiopharmacy) and delivered under battery power to patients in an inpatient trolley bay, an outpatient consultation room, on the gamma camera, or in a remote ward. The burn must be performed connected to mains power after which there is a 7-10 minute window to complete patient ventilation and thus remote delivery requires careful planning.

The second step is the simmer phase where the  $^{99m}\text{Tc}$  sodium pertechnetate is evaporated in the crucible well. This is usually undertaken 10-30 minutes in advance of the patient arriving. Prior to loading the new crucible, it is important to ensure the previous crucible has fractured and dropped into the collection tray. If the collection tray needs to be emptied, this should also be done before loading a new crucible and usually prior to the first lung scan patient for the day to ensure there is minimal radioactivity remaining. A visual inspection of the condition of the contacts and checking for any debris in the chamber that might interfere with chamber closure is also a useful exercise in preventative maintenance. The operator should avoid touching the ends of the crucible where it will connect to the contacts because oil from the skin will reduce connection efficiency and Technegas yield. Loading the new crucible requires a degree of dexterity to manipulate using forceps (figure 3). It is important to note that anything inside the chamber is potentially radioactive, so this also requires gloves and standard radiation safety practices to be applied. The crucible void (well) needs to be wet with ethanol on its surfaces at the time of adding the  $^{99m}\text{Tc}$  or the  $^{99m}\text{Tc}$  volume may be displaced from the well during the heating (simmer) phase. The ethanol is generally applied before loading the crucible but if at the time of adding  $^{99m}\text{Tc}$  the well is dry, the process can be repeated with the crucible *in situ*. The

operator gently rotates the crucible back and forward between the contacts before adding the  $^{99m}\text{Tc}$  to ensure good connection is made to optimize Technegas yield. This rotation motion should not be a twisting motion to avoid fracturing the fairly fragile crucible. The operator then adds 0.14-0.17mL of  $^{99m}\text{Tc}$  sodium pertechnetate containing 400-900 MBq. The meniscus should be flat or concave and not overflow the well (figure 4; top) as this simply results in  $^{99m}\text{Tc}$  being blown off the top of the crucible and produces a wet aerosol of free pertechnetate for inhalation that deteriorates image quality. If the total activity in 0.17 mL is lower than 400 MBq, multiple six-minute simmers can be performed as outlined below to increase activity and avoid overloading the crucible volume. Ensure the argon pressure is optimised in the green zone of the regulator, close the drawer and commence the simmer.

The third step is preparing the patient with a “practice run”. This is no doubt amongst the most important step in optimizing Technegas performance. The key to successful Technegas delivery is patient compliance, which is achieved through good patient education and practice, and should not be rushed. A detailed explanation of the ventilation process in language that the patient understands with ample opportunity for clarification and questions is essential. The process will be foreign to many patients while others will have been snorkelling and be very comfortable. This is compounded by different levels of respiratory distress which can produce a large variation in patient performance and thus impacts on ventilation image quality. The practice run should be done under the same conditions as the actual ventilation procedure, so the patient is not baulked by surprises. If practice is performed sitting and the ventilation performed lying, then one can expect a different performance. If the practice is done in a waiting area and the ventilation on the gamma camera, patients will respond differently, especially if the imaging device causes anxiety. A common error is practicing without the nose peg which creates a completely different environment and level of compliance when the ventilation itself is done with the nose blocked. The practicing improves timing, the ventilation process, patient compliance (especially with seals) and optimization of the appropriate mouthpiece for that patient (figure 5). Practicing the process is as much about preparing the patient as it is creating awareness for the administering staff about compliance and projected number of inspirations required.

The fourth step is initiate the burn phase which produces the combination of  $^{99m}\text{Tc}$  and carbon as nanoparticles under high temperatures in just 15 seconds. This should not be commenced until the patient is ready to be ventilated. As soon as the burn phase is completed, it should be used to deliver the Technegas to the patient. The message “burn complete” is displayed and this is followed by instruction to disconnect the mains. For delivery at the point of Technegas production, this is simply switching the power button to off (figure 2). If this is remote from the production location, mains power and the argon should be disconnected and the entire Technegas generator transported to the patient.

**Tip:** Performing the ventilation upright produces different distribution than when performed supine. Ensure the [ $^{99m}\text{Tc}$ ]MAA is administered for perfusion in the same position as the ventilation was performed.

The important fifth step is patient ventilation. The single most important inspiration is the first one and this requires careful timing. The first release of Technegas (delivery knob) occurs under a small amount of pressure. The best results occur when the release is timed during inspiration. If it is released during expiration or during the dead space at the end of inspiration or expiration, then the high concentration Technegas of the first release is directed to the filter and wasted. The release should be timed to occur in the second quarter of the inspiration and if practiced correctly, that will be a deep inspiration. The patient will have been instructed for that first inspiration to breath out and take in a deep breath, hold for a second and then breath out. The operator should be providing those instructions during the delivery and timing the release with the first inspiration. The patient should return to normal volume breaths after the initial inspiration but care should be taken not to offer the instruction “breath normally now” as patients have a tendency to do exactly that and break the seal or remove the apparatus from their mouth. Perhaps “*continue to breathe through the tube with normal size breaths*” is a better alternative. Once ventilation is completed, the patient should continue to breathe through the patient administration set to remove any remaining airborne Technegas residue for 4-5 breaths. If the delivery knob is not depressed, the system is diverted to breathing room air. After the ventilation has achieved the desired amount deposited the entire patient administration set is designed to be returned to the plastic bag (figure 5) it came in for storage as radioactive waste and disposed

of as biological waste after 10 half-lives. The biggest risk of contamination comes when patients try to breath in or out around rather than through the mouthpiece.

**Tip:** Gloves and gown should be worn when performing the ventilation stage as this is the biggest risk for contamination. This stage also requires face masks to be worn for COVID19 compliance.

The count rate from the lungs in a posterior orientation on the gamma camera should be about 1000-1500 counts per second which equates to between 20-50 MBq delivered to the lungs. This allows a standard [<sup>99m</sup>Tc]MAA administered dose to produce counts 4-7 times higher than the ventilation. Four times higher count rate for the perfusion is the accepted minimum value to provide sufficient contrast to identify perfusion defects without being “filled in” by ventilation counts, while seven times higher is optimal. Consequently, an over-efficient ventilation delivery could undermine diagnostic integrity. This might occur when a patient is highly compliant with excellent inspiration or because the <sup>99m</sup>Tc is in high specific concentration. For example, fresh eluate from a <sup>99</sup>Mo/<sup>99m</sup>Tc generator early in the generator life cycle can have substantially more than 900 MBq in 0.15 mL and, even in a less than optimal ventilation process, result in count rates in the lungs well in excess of 3000 counts per second with one or two breaths. The long residence time of Technegas in the lungs means that radioactive decay is the only option to manage the count differential. A level of 3000 counts per pixel would need to be delayed by a full half-life (6 hours) before the perfusion is performed, for example. If the ventilation process is performed away from the gamma camera and its instantaneous feedback on amount deposited, then a radiation detector can be used to monitor count rate in the lungs. In this case, the device should be “calibrated” against gamma camera count rate so specific readings on the radiation detector are known to equate to specific count rates on the gamma camera. While it is common for the ventilation process to occur on the gamma camera itself, non-compliance during ventilation can produce detector contamination (increased background) that impacts scanning for the remainder of the day.

**Tip:** For high eluate specific concentration days, dilute the eluate so no more than 900 MBq is contained in the 0.15 mL volume.



The final step is the system purge which takes a further 6 minutes and requires the Technegas generator to be reconnected to argon and mains power. Residual Technegas in the chamber is purged through the system filter and the system is ready for the next simmer cycle. The purge is the rate limiting step for a busy department although occurs well within the acquisition window of the ventilation scan let alone the entire V/Q. The patient administration sets are single use disposables and must be discarded after each patient however it is possible on busy days with multiple ventilation scans required to use a single simmer/burn phase to ventilate more than one patient. This requires careful planning and timing, with each patient having their own patient administration set. There is no biological contamination from the patient into the Technegas system itself so changing patient administration sets between patients eliminates risk of contamination between patients. The first patient ventilated should be the patient with the least compliance or greatest difficulties, to capitalize on the higher activity available for the first release and then the residual used for the second patient with more optimal breathing status.

**Tip:** When used as per instruction, Technegas produces minimal contamination risk to staff and no risk of cross contamination between patients. A very important advantage with COVID19 (12).

### **Low Specific Concentration of $^{99m}\text{Tc}$**

There are numerous situations in a clinical department when the  $^{99m}\text{Tc}$  eluate concentration produces less than 400 MBq in the 0.17 mL crucible well volume. Some clinical departments do not have an on-site  $^{99}\text{Mo}/^{99m}\text{Tc}$  generator and unit doses or bulk  $^{99m}\text{Tc}$  may have low specific concentration, especially at the end of the day. Clinical sites operating with smaller generators may not produce the concentration to add 400 MBq to the crucible in 0.17 mL. For example, a generator eluted with 40 GBq in 20 mL, even at the time of elution will only have 300 MBq in 0.15 mL which obviously decreases to 150 MBq in the afternoon at 6 hours after elution. Even departments with large generators can have low specific concentrations of  $^{99m}\text{Tc}$  towards the end of the weekly generator cycle. For example, a  $^{99}\text{Mo}/^{99m}\text{Tc}$  generator calibrated Monday with 120 GBq might only expect to yield in the order of 50 GBq (accommodating elution efficiency)

and if eluted in 20 mL would produce less than 400 MBq in 0.15 mL at elution time and less than 200 MBq at 6 hours after elution.

There are a number of solutions to this problem and the best approach will depend on specific circumstances. The first option is to simply perform multiple simmers with additional  $^{99m}\text{Tc}$  added to the crucible well between simmers. At the end of the simmer cycle, cancelling the process and opening the chamber drawer allows additional  $^{99m}\text{Tc}$  to be added as the volume has been reduced by evaporation, effectively doubling the total activity. This is perhaps the best approach for low volume departments where low specific concentration may only impact 1 or 2 patients per day, at the end of the day or towards the end of the generator week. It may also, on occasions, be necessary to do 3 or more simmer cycles (e.g., low yield days of  $^{99}\text{Mo}/^{99m}\text{Tc}$  generator at the end of the day or after hours). Where this impact most departments, particularly those receiving bulk  $^{99m}\text{Tc}$  or unit doses from centralised radiopharmacies, a more efficient approach would be to purchase the larger volume crucibles. The standard crucible has a 0.15 mL well volume that accommodates up to 0.17 mL while the larger well crucibles have a volume of 0.3 mL which accommodates enough  $^{99m}\text{Tc}$  to be equivalent to a double simmer cycle.

Some models of the Technegas generator have a built-in simmer oven for multiple crucibles (figure 4, bottom). This allows up to 5 crucibles to be mounted and loaded with  $^{99m}\text{Tc}$  and evaporated during each simmer cycle. The crucibles can be topped up between simmer cycles or between full cycles of patient delivery. As the crucibles are not in connection with the contacts, no arc is formed and no Technegas is produced during a burn cycle. An alternative approach that pre-dates the in-built crucible ovens were external crucible ovens. These were simple hot plates enclosed and shielded for radiation safety where up to 10 crucibles could be loaded with  $^{99m}\text{Tc}$  and evaporated multiple times. These are no longer commercially available but can be manufactured locally where a built-in oven is not available (the model for the USA market will not include the built-in crucible oven). In either case, the pre-loaded and pre-evaporated crucible is required to undergo a full simmer and burn cycle when placed between the contacts.

**Tip:** Any unused crucibles in the simmer over at the end of the day can be cleansed with ethanol the next day and re-loaded for simmer.

## Technegas Ventilation Imaging Protocol

Following Technegas inhalation to 1000-1500 counts per second count rate, imaging is commenced immediately. Planar protocols, which is not recommended today with SPECT/CT preferred, would involve 8 projections for 500000 to 1000000 counts, or 5 minutes per image (anterior/posterior, RAO45/LPO45, LAO45/RPO45 and left lateral/right lateral). SPECT approaches with a minimum of 120 projections at 10-12 seconds per projection with a 128x128 matrix using a high-resolution collimator is advised in spite of respiratory motion limits on spatial resolution. Following iterative reconstruction some sites 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) (4). A better approach is to reproject the SPECT data with an associated attenuation map (5). More commonly, however, the SPECT data provides the insights (figure 6) required and the planar extracted data is not required or produced. While the principal application of the V/Q is in the evaluation of known or suspect pulmonary embolism (13), Technegas ventilation studies are also useful in the evaluation of chronic obstructive pulmonary disease, chronic thrombo-embolic pulmonary hypertension, silicosis, cystic fibrosis, asthma, emphysema and pre-surgical evaluation of regional variability in lung function although a discussion of the clinical applications are beyond the scope of this manuscript but are detailed elsewhere (6).

**Tip:** Since Technegas does not clear through the kidneys, compared to [<sup>99m</sup>Tc]DTPA aerosol studies, radiation dose to the kidneys bladder and fetus are lower (14).

## Pertechnegas

If the ultra-pure argon (>99.99%) is adjusted with the addition of 2-3% oxygen during the burn phase, the resulting carbon bound <sup>99m</sup>Tc produces the same gas-like distribution in the lungs but with rapid clearance from the lungs (7-10 minute half clearance time) (1,15) referred to as "Pertechnegas". Standard Technegas has no effective clearance which means it cannot be used for lung clearance studies. The oxygen-containing variant Pertechnegas allows functional dynamic studies for lung clearance (15).

## Galligas

Gallium-68 ( $^{68}\text{Ga}$ ) chloride from a  $^{68}\text{Ge}/^{68}\text{Ga}$  can be added to the Technegas generator in the same way as  $^{99\text{m}}\text{Tc}$  is used (no modifications) for ventilation PET imaging. This is commonly referred to as “Galligas”. One very important consideration for Galligas is that the standard Technegas generator is designed for shielding the 140 keV gamma emissions of  $^{99\text{m}}\text{Tc}$  and is, therefore, inadequate for appropriate radiation safety from the 511 keV gamma emissions of  $^{68}\text{Ga}$  (16). [ $^{68}\text{Ga}$ ]-Galligas can be used in combination with  $^{68}\text{Ga}$ -labelled microspheres to perform PET based V/Q (17). This exploits the advantages of PET/CT in terms of superior resolution, sensitivity, respiratory gating, dynamic imaging and quantification, faster imaging time and potentially lower patient radiation absorbed dose to the V/Q (16) compared to SPECT imaging. Conversely,  $^{68}\text{Ga}$  is more expensive and less readily available, even for those sites with a  $^{68}\text{Ge}/^{68}\text{Ga}$  generator, PET/CT is not as widely available as SPECT/CT, and PET/CT generally has a demanding oncology case load. However, it is an excellent tool for studying regional ventilation in respiratory physiology and research.

An alternative to Galligas that emerged in conference abstracts in 2011 and 2012 was the potential for [ $^{18}\text{F}$ ]fluorogas ventilation in combination with [ $^{64}\text{Cu}$ ]MAA. Details are scarce in mainstream literature and clinical utilization has not emerged. The obvious barrier for both  $^{68}\text{Ga}$  and  $^{18}\text{F}$  PET imaging of the lungs is that the lungs are low density producing less attenuation of 511 keV photon emissions of PET combined with the high energy positron (especially for  $^{68}\text{Ga}$ ) which means the positron travels some distance before annihilation which reduces spatial resolution (16).

## Practical Protocol

Technegas is a very simple system to safely and effectively operate following a stepwise procedure (figure 7):

### 1. Check and load.

- Check mains power and argon are connected.
- Switch the power on and ensure the argon regulator is in the green zone.
- Open the chamber drawer (open button) and check for debris or whether ash tray needs emptying.

- Wet and drain the well of the crucible with ethanol and load between the contacts.
- Close the drawer by simultaneously holding down the interlock knob and the close drawer until the chamber is fully closed.

## 2. Simmer.

- Press the start button to initiate the 6-minute simmer cycle.
- Re-check the argon regulator to ensure the pressure stays in the green zone as the argon purge is initiated.

## 3. Prepare patient.

- Identify the correct patient, explain the procedure and obtain informed consent.
- Open a new patient administration set and perform practice breathing through the apparatus with specific attention to keeping an air-tight seal.
- Change mouth pieces of necessary. Identify and resolve any compliance issues.

## 4. Burn.

- Press the start button to initiate the 15 second burn.
- The patient should be positioned and prepared ready for Technegas delivery prior to initiating the burn.

## 5. Delivery.

- After the burn is verified, disconnect the mains (power and argon).
- Transport the entire Technegas generator to the patient and connect the patient administration set to the system.
- Ensure the patient has the appropriate seal and press the start button to commence Technegas delivery.
- Release of Technegas for patient ventilation requires depression of the delivery knob during patient inspiration.
- Monitor the activity delivered with a target of 1000-1500 counts per second on the gamma camera or equivalent using a radiation detector.

## 6a. Purge.

- After successful patient ventilation is confirmed, return the Technegas generator to mains power and argon supply and connect both.
- Adjust the argon regulator to the green zone.

- Turn on the power switch and the system will cycle through a 6 minute purge.
- At the end of the purge, the system is ready for the next patient cycle.

6b. Image.

- Upon successful patient ventilation, the ventilation phase of the lung scan should commence immediately.
- Dispose of the patient administration set.

### **Conclusion**

Technegas is a simple yet versatile system for producing high quality  $^{99m}\text{Tc}$  based ventilation studies. The design affords safety to patients and staff including consideration of radiation and biological risks. Technegas is the gold standard for ventilation studies for performing SPECT based V/Q studies in pulmonary embolism and a number of respiratory pathologies. When approved by the US FDA, Technegas will extend advantage to workflow, safety and study quality for departments who adopt the technology.

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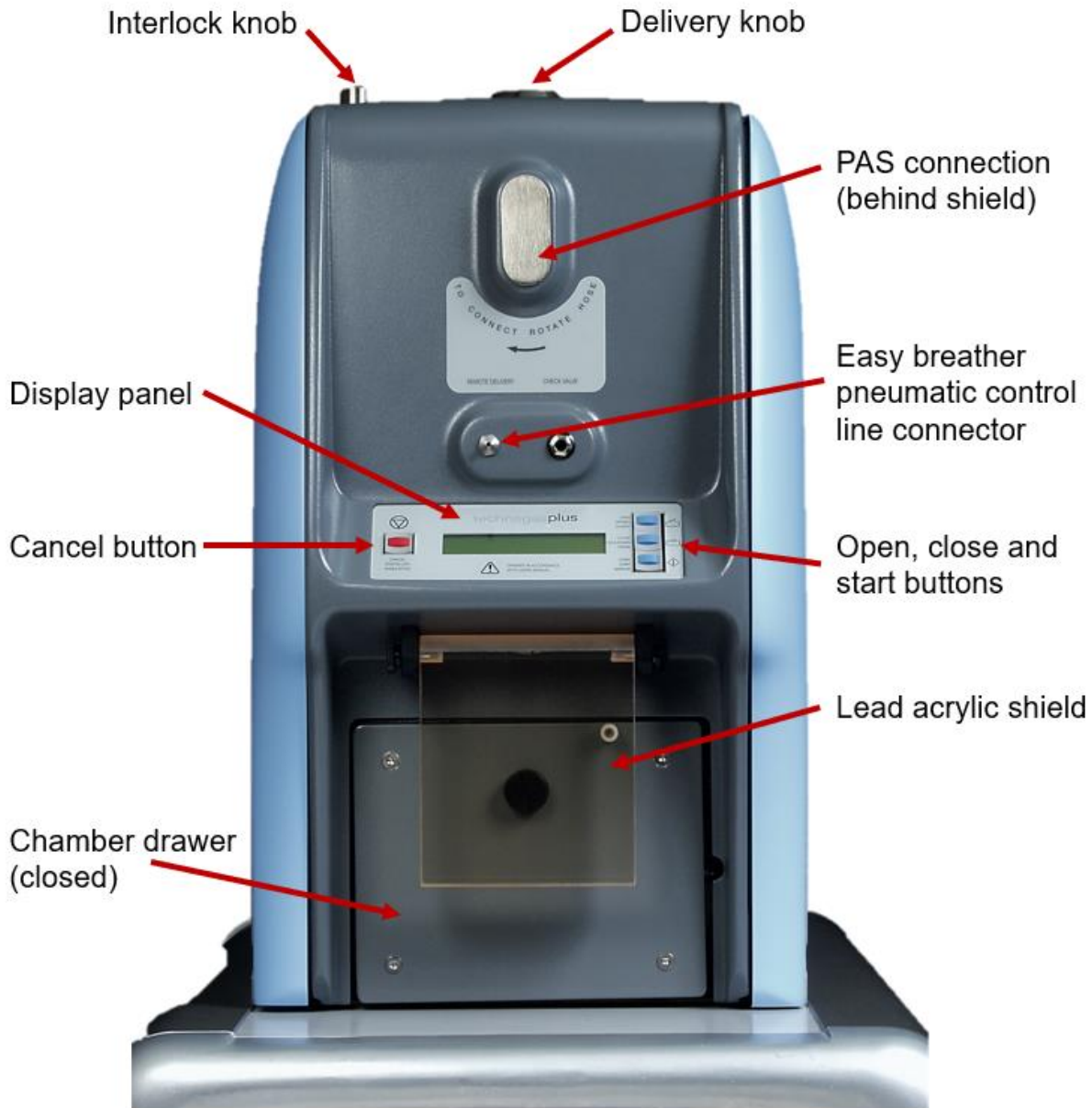


Figure 1: Annotated front view of the Technegas generator. The chamber drawer is in the closed position and the shield is closed down over the patient administration set (PAS) port. Not all models are fitted with an easy breather option (image courtesy of Cyclomedica).

Power indicator light

Push back argon connector to attach

Power switch

Release connector to lock argon line



Figure 2: Annotated rear view of the Technegas generator demonstrating connection of argon to the system (image courtesy of Cyclomedica).

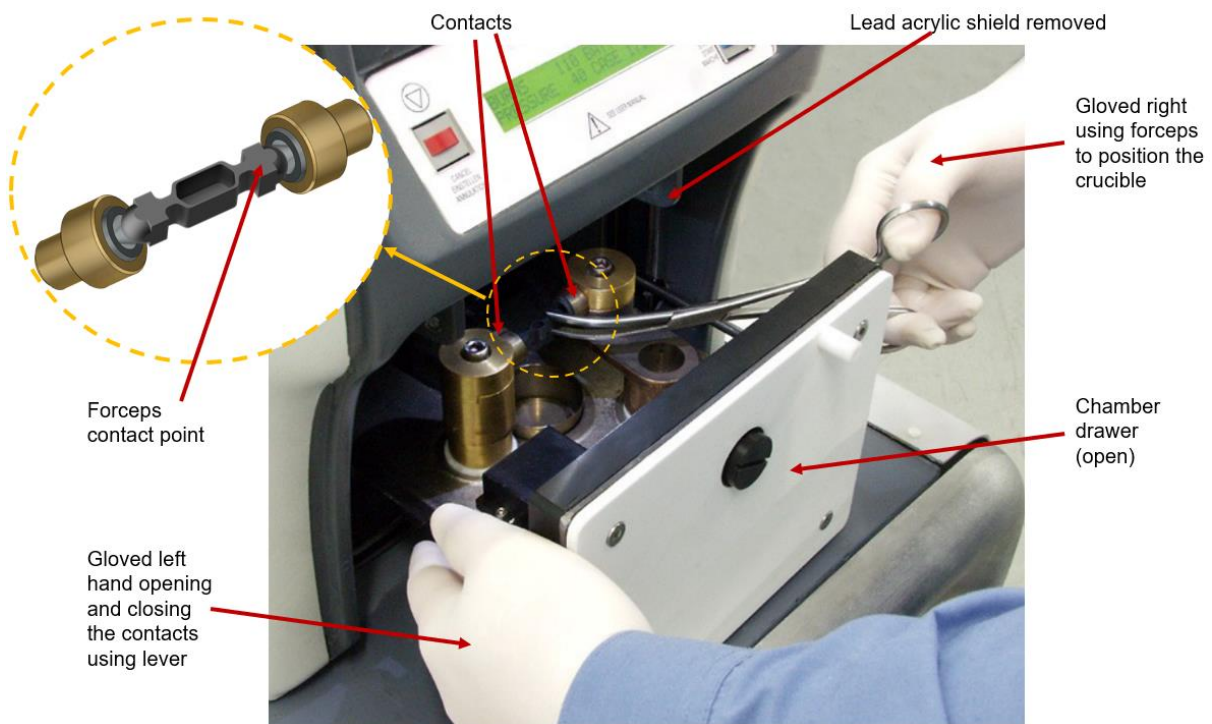


Figure 3: Use of gloves and good dexterity is required to place the crucible between the contacts, making good connection with fracturing the crucible. Note for photography purposes, the lead acrylic shield has been removed (image courtesy of Cyclomedica).

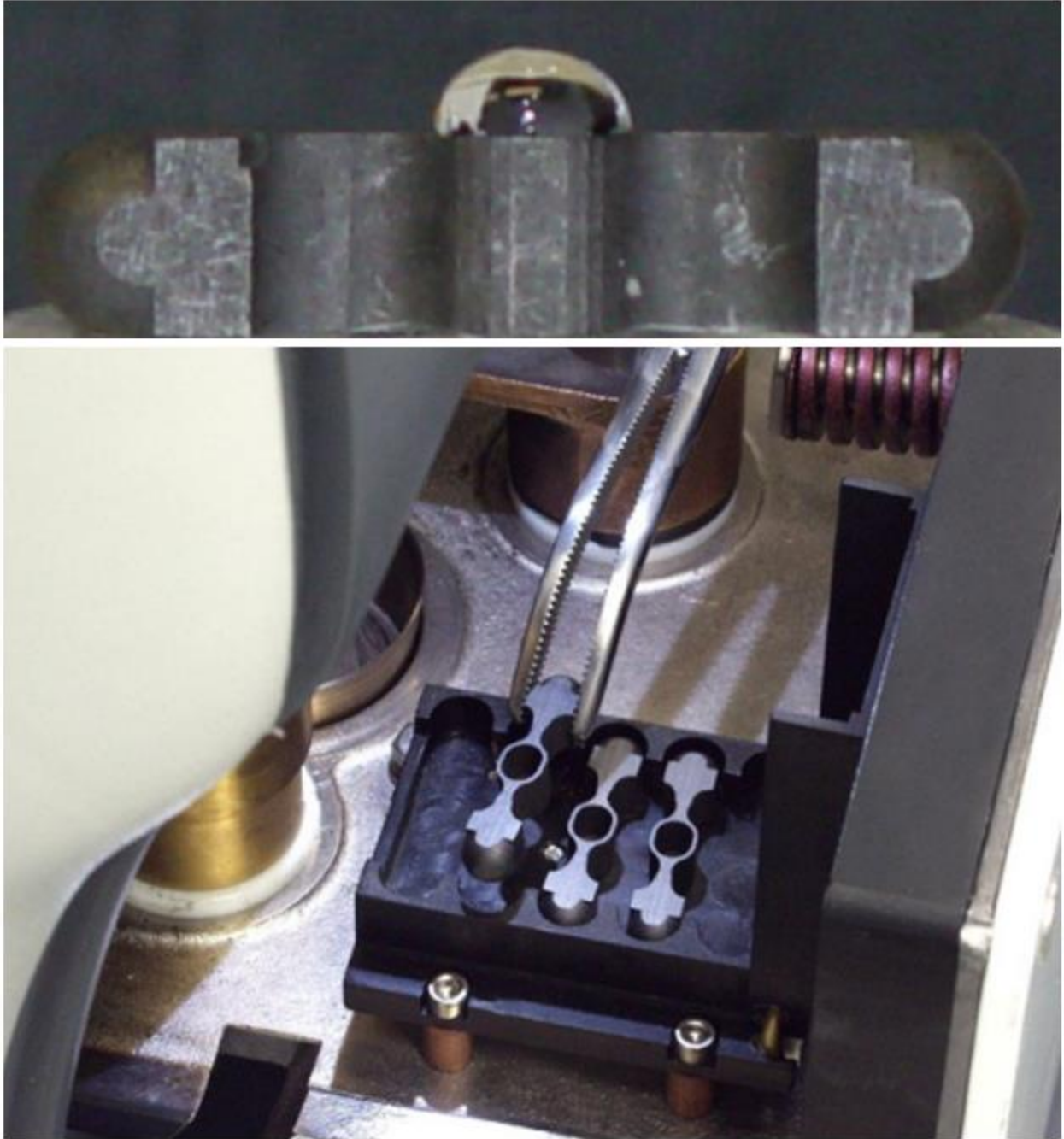


Figure 4: Top, excess  $^{99m}\text{Tc}$  added to the crucible well will be blown off during simmer and wasted (image courtesy of 18). Bottom, built-in simmer oven for crucibles in the chamber to allow multiple simmer cycles for low concentration  $^{99m}\text{Tc}$  (images courtesy of Cyclomedica).

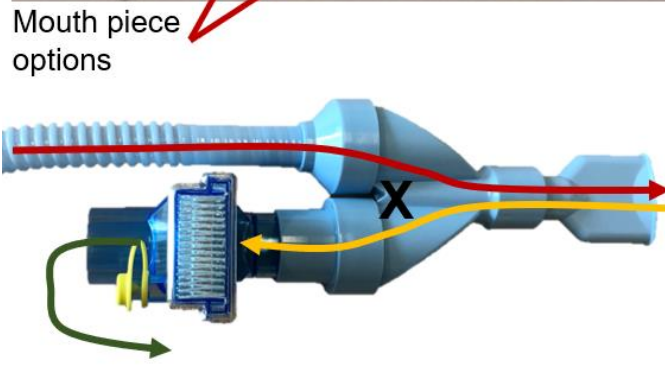
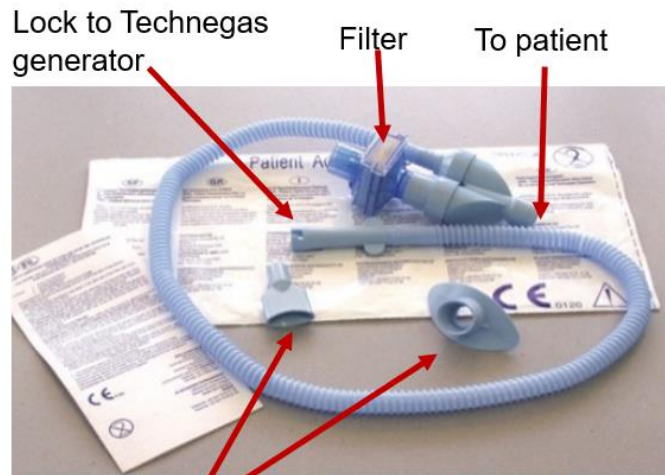


Figure 5: Top left, the disposable Patient Administration Set (PAS) with multiple mouthpiece options to suit the patient. Bottom left, the PAS delivers Technegas to the patient (red line) and returns the patient breath through the filter (yellow line) using a one way vale to prevent communication between the two airflows (black cross) and filtering both the radioactive and biological content of the patient expiration to produce uncontaminated output into room air (green line). Right, the PAS can be disposed of in whole using the PAS plastic bag it originated from (images courtesy of Cyclomedica).

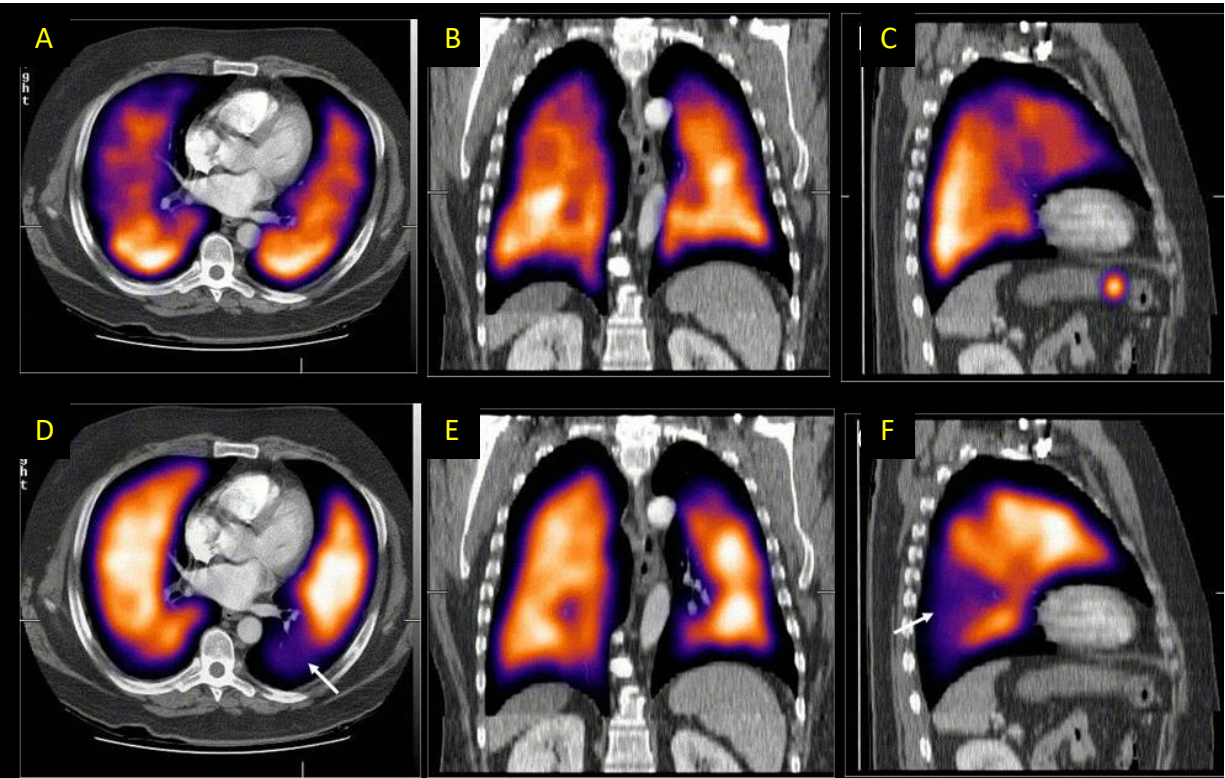


Figure 6: State of the art contemporary SPECT/CT imaging of lung ventilation (top row) and perfusion (bottom row) in three orthogonal planes. The fusion SPECT/CT images demonstrates a segmental perfusion defect (arrow in 7D and 7F) in the left lower lobe. This appears mismatched when compared with the corresponding ventilation images. The “notch” at the apex of the left lung seen in the sagittal views (7C and 7F) is matched on ventilation and perfusion and therefore is unlikely to be due to an embolus.

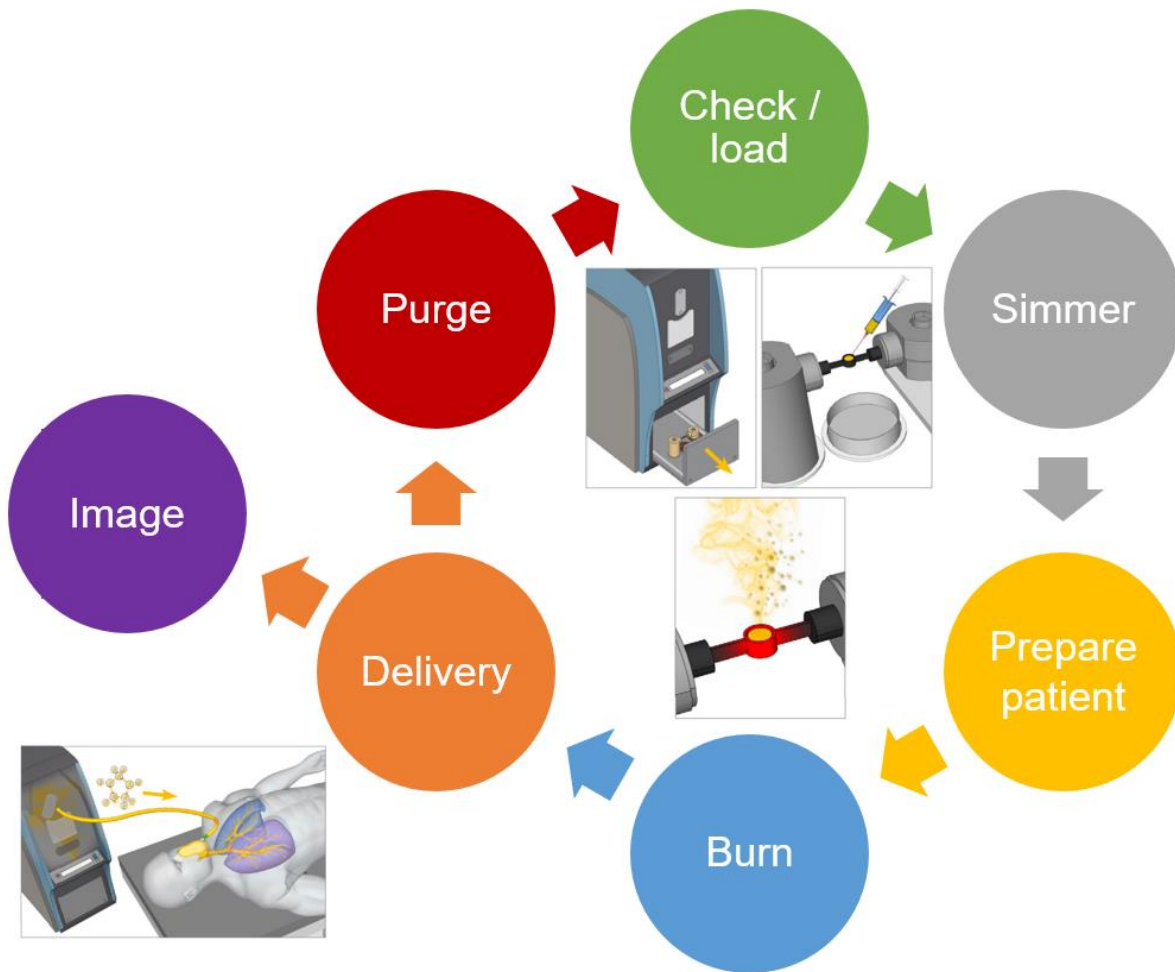


Figure 7: The Technegas production cycle beginning with checking and loading the chamber (green) (inset images courtesy of Cyclomedica).