

Cyclopharm

Financial Year 2019
Results Presentation

James McBrayer, CEO & Managing Director



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All references to dollars unless otherwise specified are to Australian dollars.

Company Overview

Cyclopharm Limited (CYC) is a leading diagnostic lung imaging company

- A world leader in functional lung ventilation imaging technology
- Recurring consumables and capital equipment revenue streams
- A profitable and growing company with a history of dividend payments
- Lead nuclear medicine product Technegas® is currently available in 59 countries with significant opportunity to expand into the USA with sales targeted for early 2021 following completion of USFDA New Drug Application review
- Opportunity to broaden Technegas applications beyond pulmonary embolism diagnosis into large addressable markets such as COPD and Asthma



Our Strategic Priorities

CYC has clear strategy to leverage our position as a leading player in the global nuclear medicine imaging market and **lung health** space to expand the use of our proprietary products and introduce new innovative technology.

We will do this by:

1. Attaining approval to **distribute Technegas in the USA**
2. **Expanding the use of Technegas** beyond the traditional diagnosis of Pulmonary Embolism into significantly larger applications such as **COPD¹ and Asthma**, Lung Cancer and Pulmonary Hypertension for both diagnosis and patient management.
3. Identifying, developing and commercialising complementary innovative technology such as **Ultralute™**
4. Leveraging our core global regulatory strengths, fiscal discipline, strong balance sheet and well developed expertise in nuclear medicine and pulmonary healthcare to seek out **complementary technologies** and businesses

Technegas

World's Best Functional Lung Ventilation Imaging Agent



Patient inhales extremely small carbon particles labeled with ^{99m}Tc Technetium¹



The small size and hydrophobic properties demonstrates gas like-behavior and alveoli deposition into the lungs²⁻³



Clinicians can visualise functional ventilation using Technegas



1. Senden TJ, et al. J Nucl Med 1997; 38: 1327-1333

2. Fawdry RM, et al. Australas Radiol 1988; 32(2): 232-238

3. Leblanc M, et al. CANM guidelines; Nov 2018: www.canm-acmn.ca/guidelines

Pulmonary Embolism



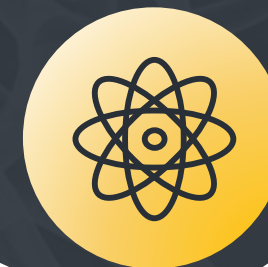
~3 million cases of PE p.a.
but could be much higher



30%
of pulmonary embolisms are fatal if left untreated



Symptoms
are varied with diagnosis confirmed either through CTPA or a nuclear medicine ventilation-perfusion study



Nuclear Medicine using 3-D imaging is the most accurate method of diagnosis

FY2019 Results Highlights

Group Sales Revenue

\$14.08 million - an increase of 5%

Gross Margin

\$11.62 million – an increase of 7%

Gross Margin %

82.5%

Net Loss After Tax

(\$2.91) million including USFDA investment

Dividends

1.0 cents per share

Underlying Technegas PBT¹

\$0.89 million

FDA Trial expenses

(\$3.84) million

Strong balance sheet

\$12.66 million of cash reserves as @ 31 December 2019

Guidance

The Board expects continuing modest growth in underlying Technegas revenues from existing markets for FY2020

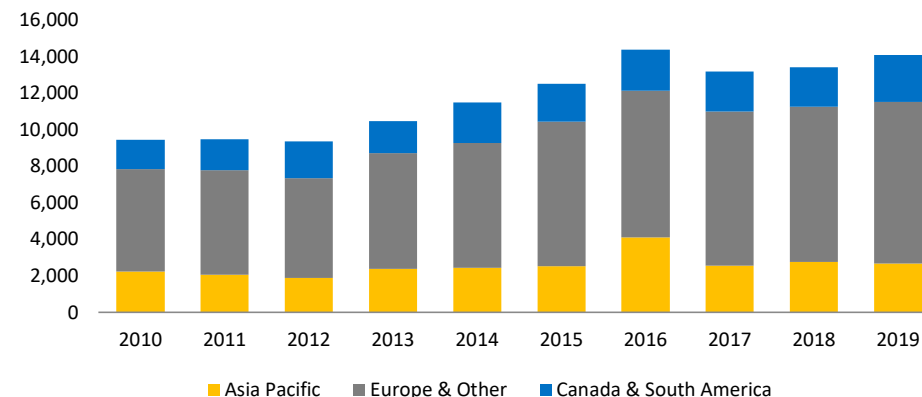
1. Profit Before Tax

Building for Growth – Company Development

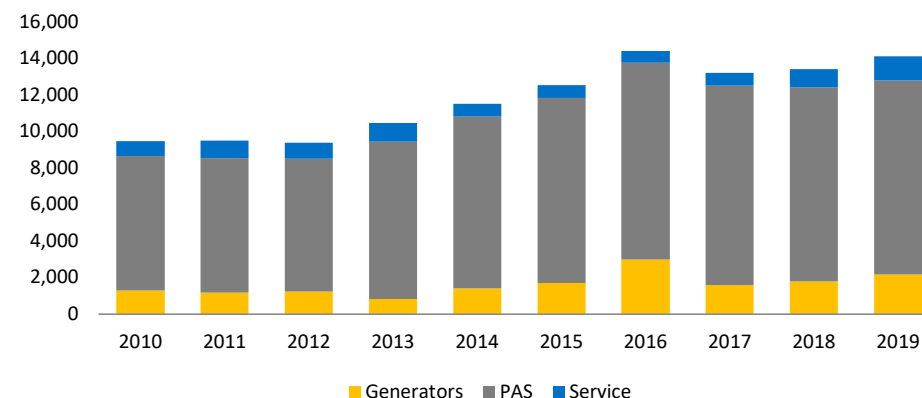
Technegas is a substantially de-risked commercial proposition with significant upside in the USA market

- Total global sales of \$118 m from 2010
- Technegas currently available in **59 countries**
- **Over 4,200,000 patient procedures** performed since first approved
- **1,600 Technegas generators** sold globally since first approved
- Approximately **182,100** patient procedures in 2019
- **Europe** represents **62%** of global revenue in 2019
- **Canada** was the **largest single country** market by volume (45,400 patients) followed closely by **France** (42,500 patients) in 2019
- CYC is growing, the underlying business is **profitable** and the company has a history of paying **dividends**
- **Stable gross margins** of greater than **80%** - (**82% in 2019**)
- Around **80%** of historical revenue is recurring consumable sales - (**75% in 2019**)

Technegas Revenue by Region (\$ 000's)



Technegas Regional Revenue by Category (\$ 000's)



Technegas® is not commercially available in the USA



FY2019 Operational Highlights

Technegas

USFDA

USA Commercialisation

Indication Expansion

R&D Tax Incentive

Strategic Partnerships

Building a Team for the Future

Guideline Development

Capital Raising

Record revenues recorded in the key markets of Canada and France

All internal documentation completed with a Q1 2020 USFDA submission

USA entity established

HMRI completes recruitment – New initiatives commence in Canada and Australia

\$2.93 received November 2019

Leveraging our infrastructure through Distribution partnerships – Draximage, Tema and Rotop

Key resources in place for growth – Sales, Quality, Regulatory and Service

CANM and European Guidelines naming TG as the nuclear med ventilation imaging agent of choice for diagnosing PE

\$9.2m net of costs received in December following a strategic share placement

Group Underlying Performance

Solid Underlying Financial Results

YEAR ENDED 31 DECEMBER	2019 \$'000	2018 \$'000	INC/(DEC) \$'000	CHANGE %
SALES REVENUE	14,079	13,404	675	5%
GROSS MARGIN	11,619	10,855	764	7%
GROSS MARGIN % SALES	82.5%	81.0%	1.5%	
UNDERLYING PROFIT BEFORE TAX TECHNEGAS®	887	1,406	(519)	(37%)
ADD BACK NON-OPERATING ACTIVITIES :				
INCOME				
CYCLOPET DIVISION	746*	(335)	1,081	323%
R&D TAX INCENTIVE GRANT	2,934	2,122	812	38%
REVERSAL OF CONTINGENT CONSIDERATION ON ACQUISITION OF SUBSIDIARY	-	314	(314)	(100%)
UNREALISED GAIN ON FORWARD EXCHANGE CONTRACT	-	275	(275)	(100%)
RECOVERY FROM GERMAN LITIGATION	339	-	339	100%
EXPENSES				
FDA EXPENSES	(3,842)	(2,965)	(877)	(30%)
BEYOND PE CLINICAL TRIALS	(351)	(251)	(100)	(40%)
RETIREMENT/SEVERANCE PAYMENTS	(322)	-	(322)	(100%)
QUALITY AND REGULATORY DEPARTMENT EXPANSION	(238)	-	(238)	(100%)
CYC QUALITY SYSTEM INVESTMENT	(827)	-	(827)	(100%)
LITIGATION EXPENSES	(1,064)	(410)	(654)	(160%)
COST OF TERMINATING PUT OPTION	(309)	-	(309)	(100%)
COST OF LTIP PROGRAM	(378)	(38)	(340)	(895%)
REPORTED (LOSS) / PBT	(2,425)	118	(2,543)	(2,155%)

*INCLUDES ONE-OFF RENT ABATEMENT OF \$1,043K

During the year, CYC continued to implement its strategic priorities, which are to:

- 1 Accelerate the path to regulatory approval to sell Technegas into the world's largest and new highly prospective USA market;
- 2 Pursue sales of Technegas in new applications: Chronic Obstructive Pulmonary Disease ("COPD") and Asthma which are significantly larger markets than the Pulmonary Embolism market where CYC traditionally operates;
- 3 Identifying, developing and commercialising complementary innovative technology such as Ultralute™; and
- 4 Leveraging our core global regulatory strengths, fiscal discipline, strong balance sheet and well-developed expertise in nuclear medicine and pulmonary healthcare to seek out complementary technologies and businesses.

Group Balance Sheet

Financial Foundation to Leverage Growth Strategy

Year ended 31 December (\$000's)	2019	2018	2017
Cash	12,660	5,855	8,690
Other current assets	6,950	9,600	8,139
Non-current Assets	12,918	8,082	6,548
Total Assets	32,528	23,537	23,377
Current Liabilities	3,480	5,219	5,212
Non-current Liabilities	5,844	1,302	916
Total Liabilities	9,324	6,521	6,128
Net Assets	23,204	17,016	17,249

1

Low debt & cash on hand – provides balance sheet and funding flexibility

2

Funding used toward USFDA clinical trial enrolment and New Drug Application submission

3

Strong financial position supports ongoing investment in R&D and expansion into new markets and indications

Group Cash Position

Cash Position Funding Growth

Year ended 31 December (\$000's)	2019	2018	2017
Operating Activities	(489)	(1,107)	(682)
Investing Activities	(821)	(1,403)	(1,136)
Financing Activities	8,091	(353)	5,828
Net Increase / (Decrease) in Cash	6,781	(2,863)	4,010
Opening Cash	5,885	8,690	4,591
Foreign Exchange	24	28	89
Closing Cash @ 31 December (\$000's)	12,660	5,855	8,690

- 1 Institutional share placement of 8.5 million shares in December 2018 resulting in \$9.78m at an 11.7% premium
- 2 Benefited from expanded R&D tax Incentive Program resulting in Other Income of \$2.93 million

TECANE GAS™



Benefits of using Technegas



Easy
to prepare and
administer



Only need
3 to 4 breaths



3D images
provide functional
imaging through to
the alveolus



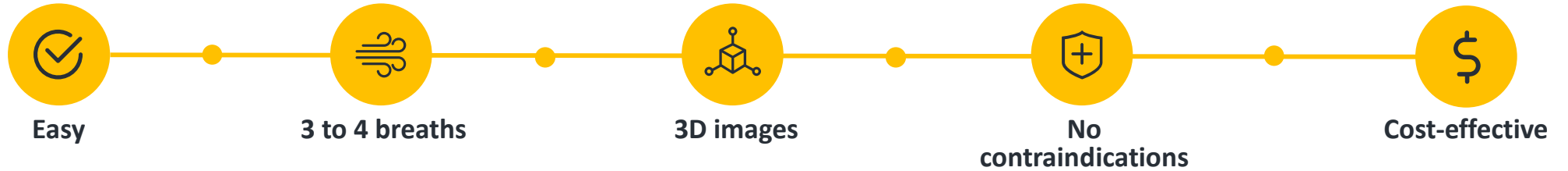
No
contraindications



Cost
effective

Superior to competitive nuclear medicine products

Technegas



Xenon - 133



True radioactive gas
inhaled with full face mask



Constant inhale-exhale breathing
for 15 mins



No 3D images
limited to planar imaging resulting in inferior clinical outcomes



Requires special rooms
to contain radioactive gas in the event of a release

DTPA Tc99m



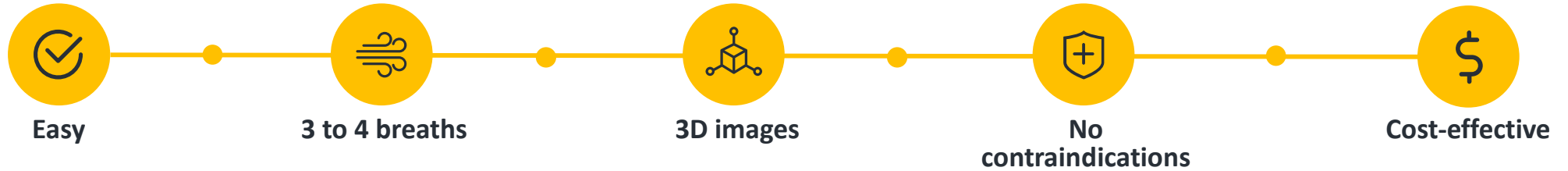
Wet Aerosol
impacts efficacy and clinician interpretations



Creates hotspots
in presence of small airways lung diseases, which is a frequent comorbidity in PE

Superior to competitive imaging modalities

Technegas



CTPA



High radiation burden

CTPA delivers at least 27 times more radiation to the breast as compared to V/Q SPECT¹

1. Isidoro J, et al. Phys Med 2017; 41: 93-96
2. Bajc M, et al. Eur J Nucl Mol Imaging 2015; 42: 1325-1330
3. Miles S, et al. Chest 2009; 136: 1546-1553

Contraindications

CTPA should not be performed with pregnancy¹⁻², renal impairment³, contrast media allergy³, diabetes⁴

Acute kidney injury (AKI)

AKI occurs in up to 13% of CTPA cases⁵

4. Roach PJ, et al. J Nucl Med 2013; 54: 1588-1596
5. Doganay S, et al. Renal Failure 2015; 37(7): 1138-1144

Lower clinical sensitivity

V/Q planar⁶ = 76%
CTPA⁷ = 82%
V/Q SPECT⁷ = 93%

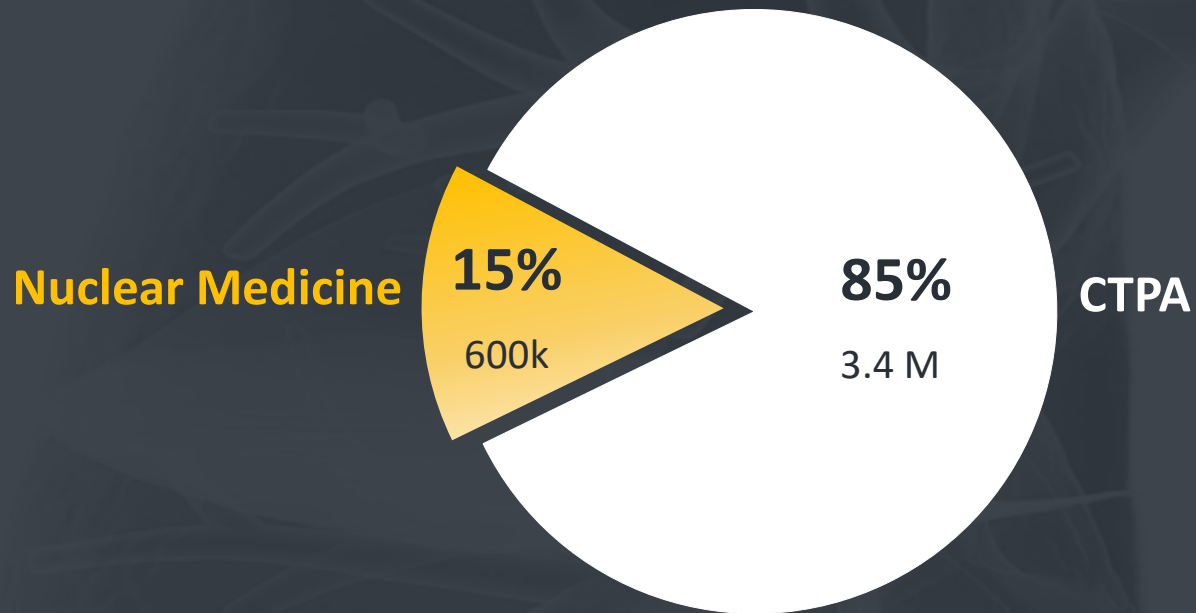
6. Reinartz P, et al. J Nucl Med 2004; 45: 1501-1508
7. Hess S, et al. Semin Thromb Hemost 2016; 42(8): 833-845

Availability

Radiology ED services are generally provided 24/7 vs. nuclear medicine after hours on call service

Technegas – USA Market Opportunity

600K Nuclear Medicine Ventilation
Procedures p.a. = \$90m USD



- 4,000,000 patient procedures conducted in the USA per annum to diagnose pulmonary embolism (15% Nuclear Medicine – 85% CTPA)
- 600,000 Nuclear Medicine Ventilation procedures equals \$90m USD
- Target market for Technegas in the USA equates to ~480,000 patient procedures of the total 600,000 procedures.
- The USA represents the single largest market for Technegas with half of the world's nuclear medicine departments
- Subject to a successful FDA approval, the Company is targeting US commercialisation in 2021
- First priority following USFDA approval is to repeat our Canadian experience by displacing Xe133 as the standard of care diagnostic product
- 3D SPECT imaging using Technegas is proven to be clinically superior and safer than CTPA. Once commercialised Cyclopharm will target to double the existing nuclear medicine PE market dominated by CTPA from 15% to 30%.
- Once established in the USA market, the company will seek to expand the use of Technegas into disease states exponentially larger than the existing PE market

Technegas FDA Clinical Trial Process and Design

Approval Pathway

USFDA Clinical trial¹ registered at: <https://clinicaltrials.gov/ct2/show/NCT03054870?term=technegas&rank=1>

Non-inferiority structural ventilation study comparing Xe133 vs. Technegas¹

Planned 240 patient study at 9 clinical sites

200 Patients enrolled as at 25 February 2020

Currently compiling a 505(b)2 New Drug Application for submission

The 505(b)2 New Drug Application is expected to be sufficient for USFDA approval

Six-month Priority Review application will be submitted with the 505(b)2 New Drug Application

Clinical Trial enrollment will continue whilst the 505(b)2 submission is being reviewed



Timeline

1H 2018

Finalised Trial Site Recruitment

1H 2018

Submitted Preliminary Trial Results for FDA Review

1Q 2020

Planned NDA Submission

2H 2019

Commence USA Generator Inventory Build

Q4 2020 – Q1 2021

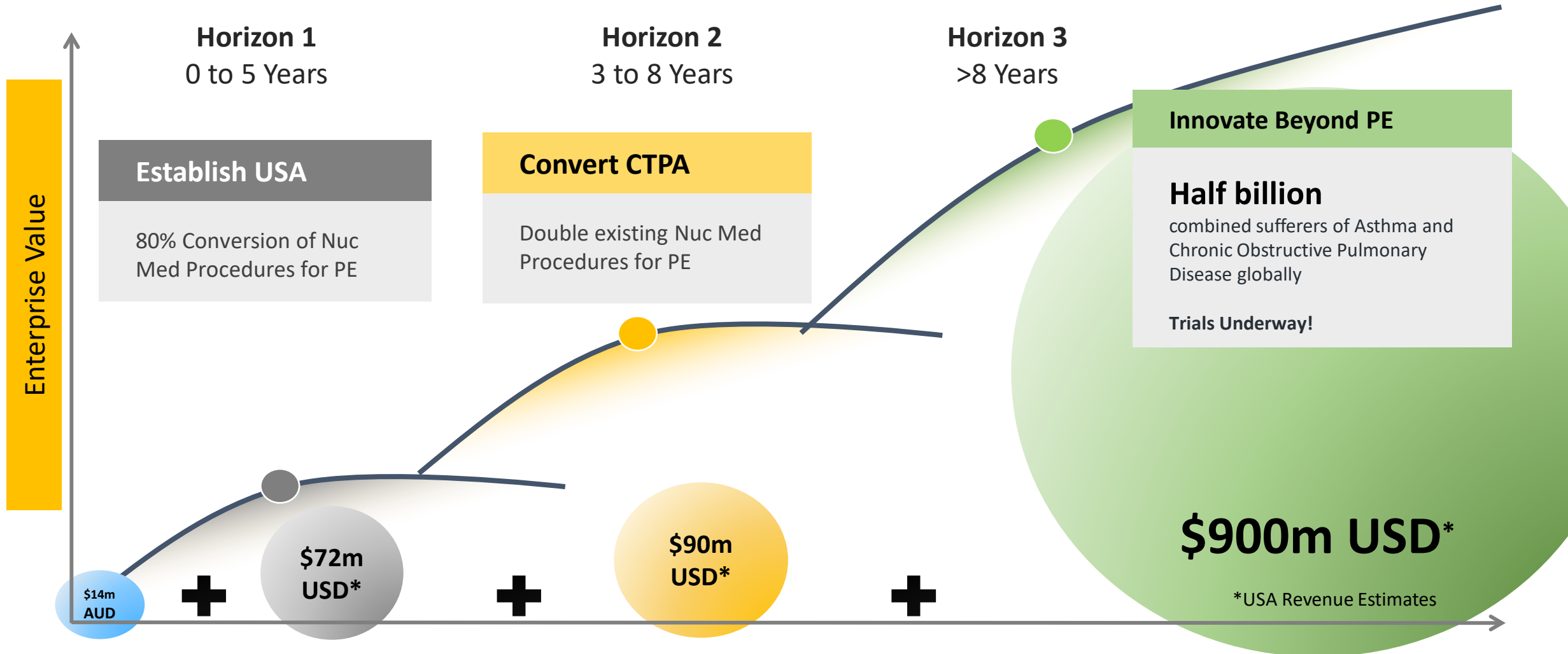
Anticipated USA Launch provided successful USFDA approval

1. ClinicalTrials.Gov – A comparison of Technegas and Xenon-133 Planar Lung Imaging in Subjects referred for Ventilation Scintigraphy. <https://clinicaltrials.gov/ct2/show/NCT03054870?term=technegas&rank=1>

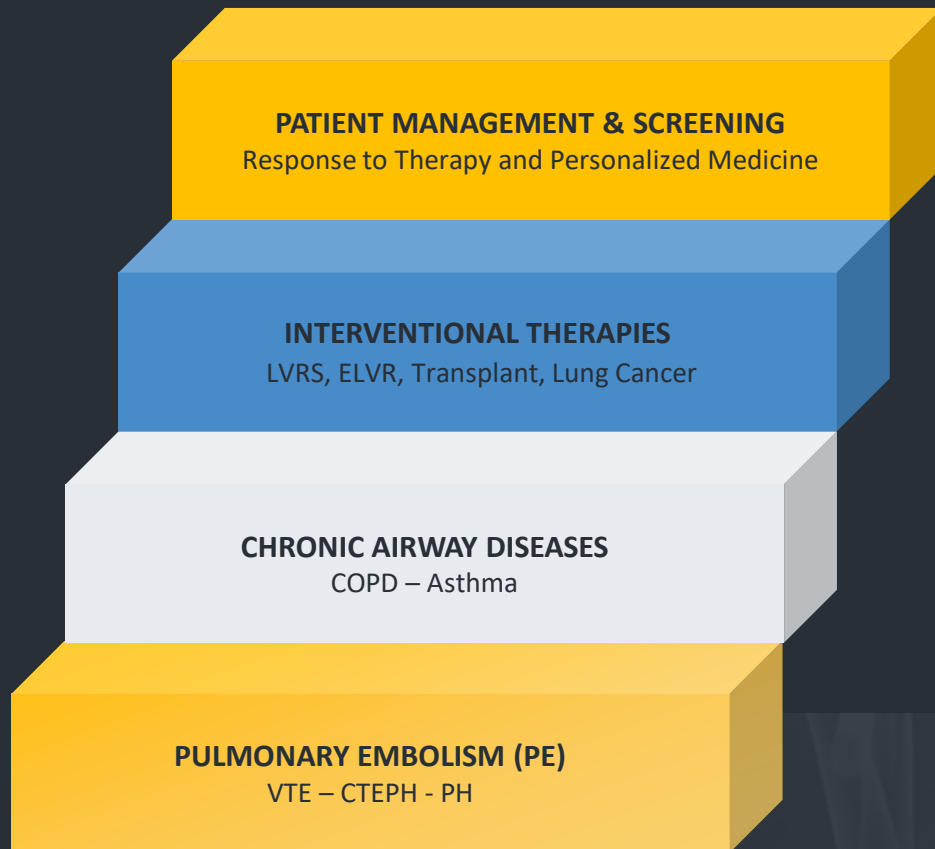
USA 2020 Commercialisation Plan



Three Value Horizons



Beyond PE : clinical initiatives



Clinical Trials Sponsored by Cyclomedica

- **Hunter Medical Research Institute (Newcastle, AU):** Diagnosis and response to therapy in severe asthma and COPD¹
- **Woolcock Institute (Sydney, AU):** Diagnosis and response therapy in mild to moderate COPD³
- **CHUM (Montreal, CA):** Early detection of COPD in asymptomatic smokers⁴
- **Dalhousie (Halifax, CA):** Post-lung transplant patients
- **Firestone Institute (St. Joseph's Healthcare Hamilton, CA):** Prevalence and clinical relevance of ventilation heterogeneity and luminal cellular inflammation in lung cancer patients pre and post lung resection ²



Other Non-Sponsored Clinical Initiatives

- **Macquarie University (Sydney, AU):** ELVR with endobronchial valves in severe COPD patients
- **Macquarie University (Sydney, AU):** Bronchial Thermoplasty procedure in asthma patients

1. ACTRN12617001275358 - Can functional lung ventilation imaging identify treatable traits in obstructive airway disease?

2. <https://clinicaltrials.gov/ct2/show/NCT04191174?term=technegas&draw=2&rank=3>

3. http://investor.cyclopharm.com/site/PDF/1561_0/BetterDefiningAirwaysDiseaseWithTechnegas

4. <https://ichgcp.net/clinical-trials-registry/NCT03728712>

CYCLOPHARM INVESTMENT CASE TECONEGAS™



Profitable & Growing MedTech

underlying business is cash positive and issuing dividends



First in class

proprietary product sales to 59 countries with over 4.2 million studies to date



Recurring revenue

from consumables similar to an annuity model



USFDA approval

set to quadruple the size of the existing PE business and further leverage penetration into the CTPA market



Optionality

into indications beyond PE into chronic respiratory disease management could deliver exponential growth

Building from a strong & well-established foundation

Near term opportunities providing significant growth potential beyond PE toward patient management



USA Market

nuclear medicine
ventilation imaging
market to diagnose PE
equal to \$90m USD with
reimbursement already
in place



Targeting USA CTPA PE market

opportunity to convert
CTPA to nuclear medicine
imaging by shifting market
to SPECT imaging



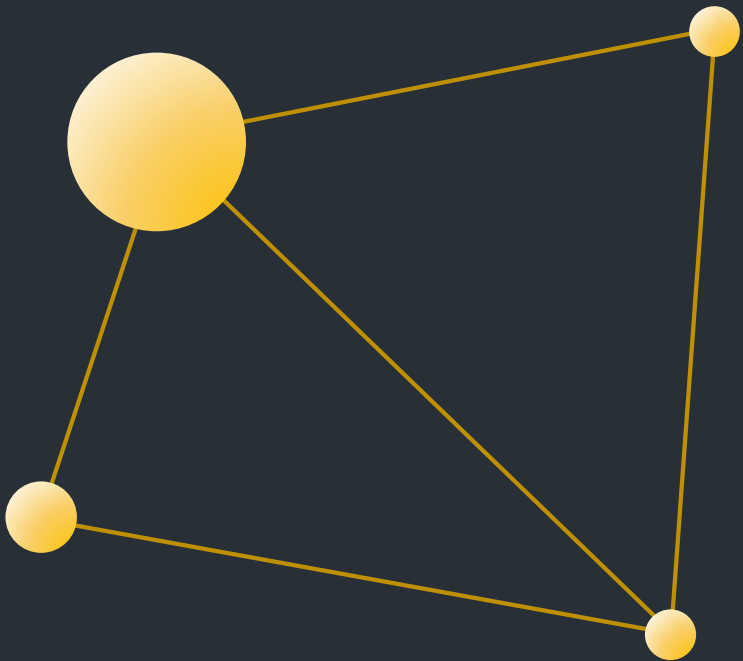
Half billion

combined sufferers of
Asthma and Chronic
Obstructive Pulmonary
Disease globally.

Trials underway

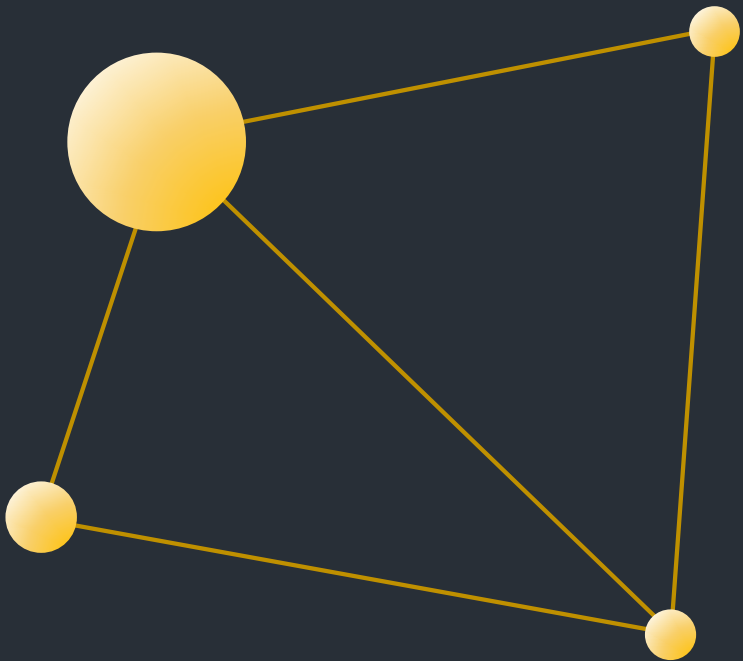
Cyclopharm

Thank You



Cyclopharm

Appendix Section



What is Technegas?

Particle characteristics

Technegas is composed of Tc-99m cores encapsulated within layers of graphite to form individual hexagonal plate-like particles.¹

These particles agglomerate to reach a dynamic equilibrium with regard to particle size distribution best described as a bell-shaped curve with an average size of 100nm.²



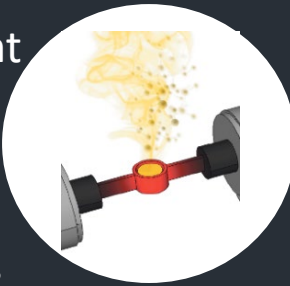
Manufacture and Distribution

Technegas is produced on site at the point of patient administration.

Technegas is manufactured by heating Technetium-99m in a carbon crucible within an argon environment for a few seconds at 2,750 degrees Celsius.³

Because of the very small particle size, Technegas is distributed in the lungs almost like a gas and deposited in alveoli by diffusion, providing for SPECT³ ventilation imaging

Particles remain in the lung until they are cleared by ciliary action or phagocytosis⁴.



1. Wiebe LI, et al. Current Radiopharmaceuticals 2010; 3(1): 49-59
2. Lemb M, et al. Eur J Nucl Med 1993; 20(576-579)

3. Leblanc M, et al. CANM guidelines; Nov 2018: www.canm-acmn.ca/guidelines
4. Möller W, et al. Am J Respir Crit Care Med 2008; 177: 426-432

Technegas Product Overview

Cyclopharm's leading product is the Technegas technology system

- The Technegas proprietary technology provides high quality diagnostic functional lung imaging.
- Predominantly used to diagnose the presence of blood clots in the lung otherwise known as Pulmonary Embolisms (PE). With advances in complementary technology, the potential for use in other indications is rapidly evolving.
- In a clinical setting, the patient inhales, in only a few breaths, an ultrafine dispersion of Technegas particles. Once inhaled and deposited in the lungs, Technegas images are then captured by using conventional nuclear medicine scanning equipment.
- The Technegas images provide the clinician an understanding of how well the patient's lungs are functioning across a range of disease states.
- CYC sells the Technegas Generator to hospitals as a one-off capital item. Consumable components are inserted into the Technegas Generator which then produce the gas like particles that are inhaled by the patient. The consumables which deliver Technegas are single patient use items.



Technegas around the world



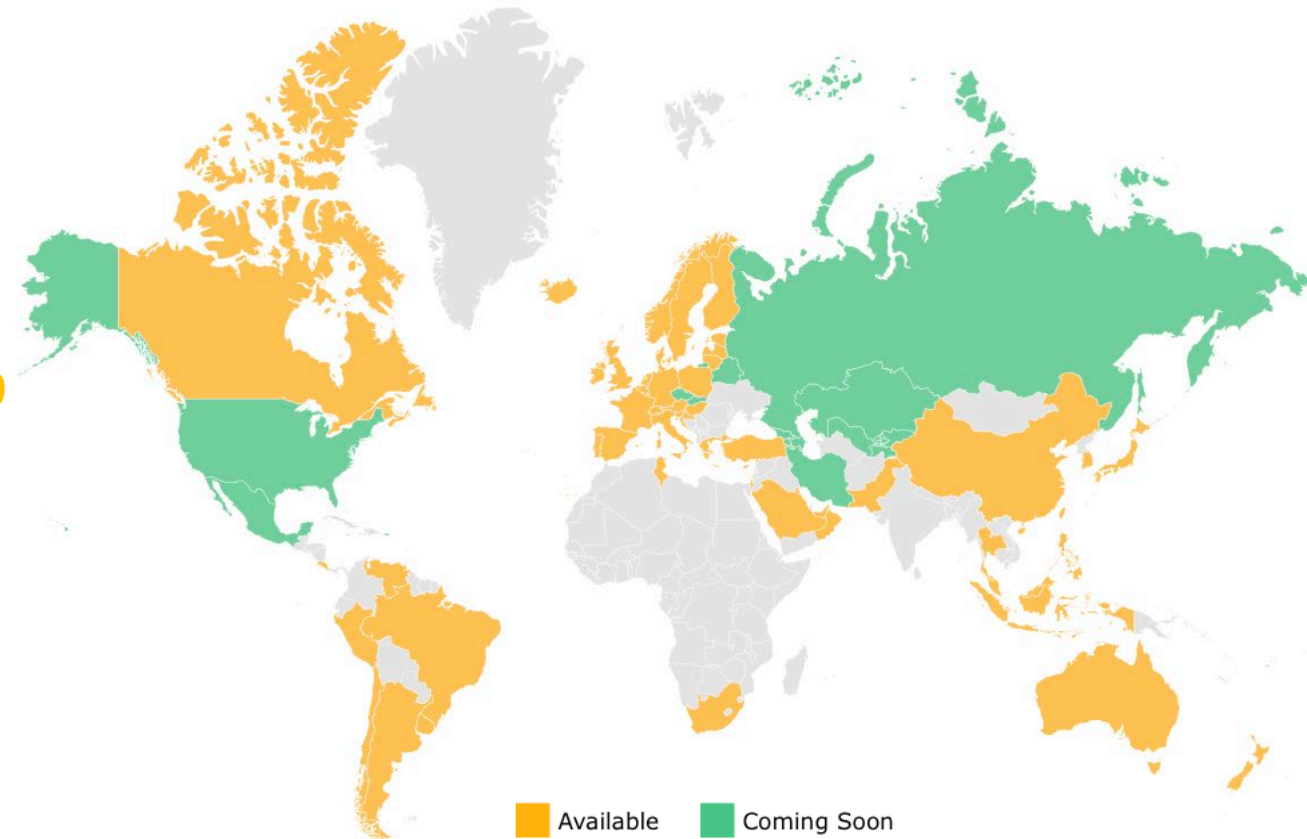
Technegas was introduced to the medical community **in 1986**¹



Technegas revenues are generated **in 59 countries** via a combination of direct and distributor sales models



Over **4.2 million** patient procedures to date



1. Wiebe LI, et al. Current Radiopharmaceuticals 2010; 3(1): 49-59

Advantages of Technegas

Technegas provides clinically superior outcomes to its competitors

- Better clinical results at a fraction of the high radiation doses used in CTPA (angiograms)
- No contraindications
- More accurate and sensitive measurement in diagnosing pulmonary embolism
- Particularly effective when CTPA is contraindicated e.g. renal impairment
- Improved patient comfort and tolerance with only 3-4 breaths required for delivery
- Allows for 3D images and regional quantification
- Named as the preferred ventilation imaging agent of choice in the European Association of Nuclear Medicine Guidelines

IP/Generic protection

- Technegas is a system - needs the generator, patient administrator set (PAS) and service capability
- R&D on 3rd generator generation underway set to extend IP protection

Competitive Nuclear Medicine Products

Product	Comparison to Technegas
Xenon 133	<ul style="list-style-type: none">▪ Patient has to continually re-breathe gas causing patient discomfort / anxiety▪ Can't provide 3D images▪ Costly air-handling infrastructure required in order to administer
DTPA	<ul style="list-style-type: none">▪ Inferior images in patients with obstructive lung disease (COPD)

Existing Market Development Strategy

- Sales and marketing program targeting referring respiratory physicians
- Implemented educational programs for Distributors
- Updating Technegas distribution contracts to include detailing to respiratory physicians
- Leveraging New Complementary Technologies
- Strengthening relationships with KOL's and industry bodies
- Guideline Development
- Product Renewal & Enhancements
- Sponsoring pilot clinical trials targeting expanded indications
- Introduction of new products by leveraging off of existing network - Ultralute™



Technegas – The Canadian Case Study

Canada is Cyclopharm's largest single country market

Market leader for diagnosing PE

14 consecutive years of PAS growth

Represents a strong indicator of USA acceptance

Xe-133 rapidly displaced by early adopters

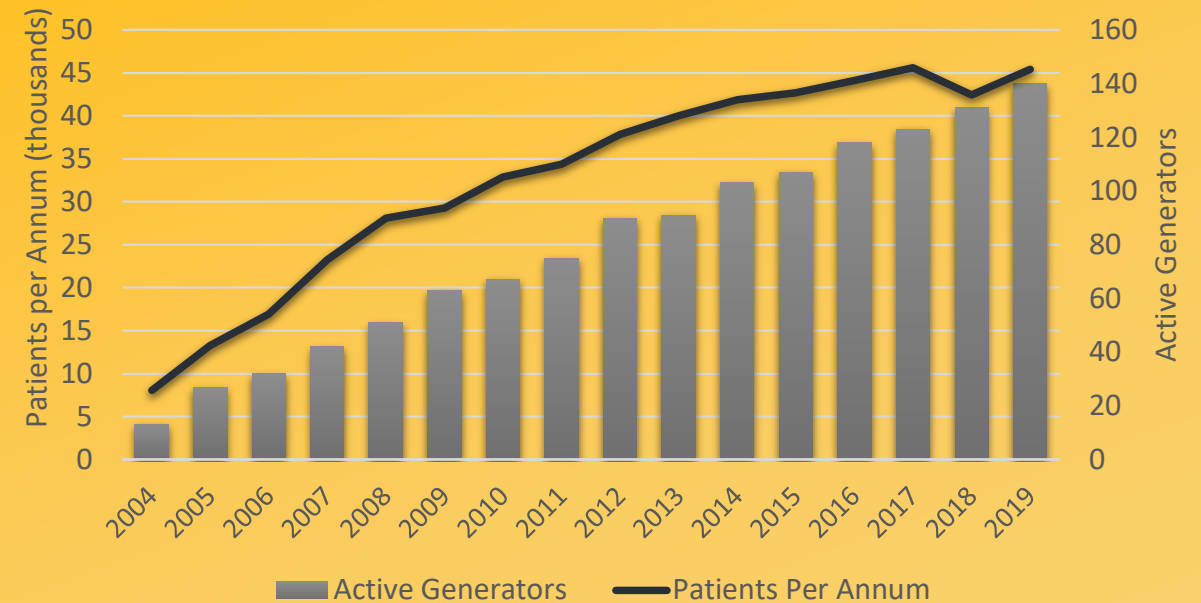
Direct correlation with the number of active generators and annual consumable sales

Market driven by public healthcare sector

Market launch initiated province by province, leveraging off pilot sites

The Generator and Consumable Relationship

Technegas Growth - Canada



What the guidelines say about **Technegas**:

Endorsed by the guidelines from the European¹⁻² and the Canadian³ Associations of Nuclear Medicine (EANM & CANM)

- “ Using 99m-Tc-Technegas is according to clinical experience better than the best aerosols ”
- “ Technegas facilitates interpretation, particularly in COPD”
- “ For ventilation, 99m-Tc Technegas is the best-aerosol particularly in patients with COPD ”
- “ Liquid aerosols are inferior for SPECT and should not be used unless Technegas is not available ”
- “ The best widely available agent for ventilation is 99m-Tc-Technegas ”
- “ Because of the very small particle size, this agent is distributed in the lungs almost like a gas and deposited in alveoli by diffusion, where they remain stable, thus providing the best possible images for ventilation SPECT ”
- “ Another advantage is that only a few breaths are sufficient to achieve an adequate amount of activity in the lungs, reducing time and personnel exposure to radiation ”
- “ Technegas is considered the agent of choice in the COPD population as there is less central airway deposition, better peripheral penetration, and it does not wash out as quickly as traditional aerosols ”

1. Bajc M, et al. Eur J Nucl Med Mol Imaging 2019; [Epub ahead of print]: <https://link.springer.com/content/pdf/10.1007%2Fs00259-019-04450-0.pdf>

2. Bajc M, et al. Eur J Nucl Med Mol Imaging 2009; 36(8): 1356-70; https://eanm.org/publications/guidelines/gl_pulm_embolism_part1.pdf

3. Leblanc M, et al. CANM 2018; https://canm-acmn.ca/resources/Documents/Guidelines_Resources/MasterDocument_Final_Nov_21_incl-Exec-Sum_ver3_Dec.%2012_.pdf 2.a

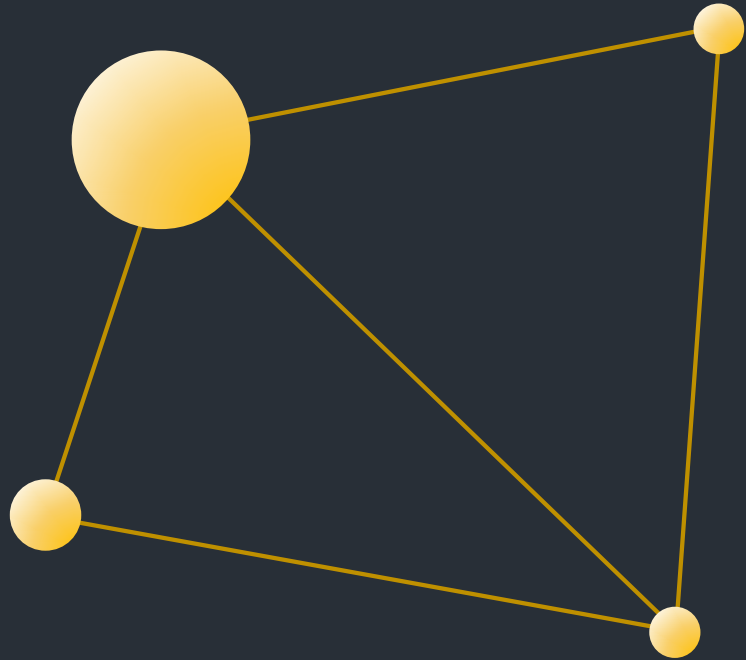
Technegas in the recent literature

66% of references citing Technegas in the past 24 months are for indications Beyond PE

1. King GG, et al. Dismantling the pathophysiology of **asthma** using imaging. Eur Respir Rev 2019; 28(152): pii: 1801111
2. Yang L, et al. Changes in ventilation and perfusion following lower lobe endoscopic lung volume reduction (**ELVR**) with endobronchial valves in severe COPD. Clin Respir J 2019; [Epub ahead of print].
3. Kjellberg M, et al. Ten-year-old children with a history of **bronchopulmonary dysplasia** have regional abnormalities in ventilation perfusion matching. Pediatr Pulmonol 2019; 54(5): 602-609
4. Paludan JPD, et al. Improvement in image quality of Tc-99m-based ventilation/perfusion single-photon emission computed tomography in patients with **chronic obstructive pulmonary disease** through pretest continuous positive airway pressure treatment. World J Nucl Med 2019; 18(2): 185-186
5. Myc LA, et al. Role of medical and molecular imaging in **COPD**. Clin Transl Med 2019; 8(1): 12
6. Ling T, et al. Ventilation/perfusion SPECT/CT in patients with severe and rigid **scoliosis**: An evaluation by relationship to spinal deformity and lung function. Clin Neurol Neurosurg 2019; 176: 97-102
7. Farrow CE, et al. SPECT Ventilation imaging in **asthma**. Semin Nucl Med 2019; 49(1): 11-15
8. Mortensen J, et al. Lung scintigraphy in **COPD**. Semin Nucl Med 2019; 49(1): 16-21
9. Sanchez-Crespo A, et al. Lung VQ SPECT in **infants and children** with nonembolic chronic pulmonary disorders. Semin Nucl Med 2019; 49(1): 37-46
10. Bajc M, et al. Ventilation/Perfusion SPECT Imaging - Diagnosing other **cardiopulmonary diseases** beyond PE. Semin Nucl Med 2019; 49(1): 4-10
11. Sanchez-Crespo A, et al. Lung scintigraphy in the assessment of **aerosol deposition and clearance**. Semin Nucl Med 2019; 49(1): 47-57
12. Bailey DL, et al. V/Q SPECT - Normal Values for **Lobar Function** and Comparison With CT Volumes. Semin Nucl Med 2019; 49(1): 58-61
13. Lawrence NC, et al. Ventilation perfusion single photon emission computed tomography: Referral practices and diagnosis of acute pulmonary embolism in the quaternary clinical setting. J Med Imaging Radiat Oncol 2018; 62(6): 777-780.
14. Leblanc M, et al. CANM Guidelines for Ventilation/Perfusion (V/P SPECT) in pulmonary embolism. www.canm-acnm.ca/guidelines
15. Hsu K, et al. Endoscopic Lung Volume Reduction in **COPD**: Improvements in Gas Transfer Capacity Are Associated With Improvements in Ventilation and Perfusion Matching. J Bronchology Interv Pulmonol. 2018; 25(1): 48-53
16. Dimastromatteo J, et al. Molecular imaging of pulmonary diseases. Respir Res 2018; 19(1): 17
17. Jögi J, et al. Diagnosing and **grading heart failure** with tomographic perfusion lung scintigraphy: validation with right heart catheterization. ESC Heart Fail 2018; 5(5): 902-910
18. Waxman AD, et al. Appropriate use Criteria for Ventilation-Perfusion imaging in Pulmonary embolism : Summary and Excerpts. J Nucl Med 2017; 58(5): 13N-15N
19. Isidoro J, et al. Radiation dose comparison between V/P SPECT and CT-angiography in the diagnosis of pulmonary embolism. Phys Med 2017; 41: 93-96
20. Righini M, et al. Diagnosis of acute pulmonary embolism. J Thromb Haemost. 2017; 15: 1251-1261
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27. Provost K, et al. Reproducibility of **lobar perfusion and ventilation quantification** using SPECT/CT segmentation software in lung cancer patients. J Nucl Med Technol 2017; 45(3): 185-192
28. Metter DF, et al. Current status of ventilation-perfusion scintigraphy for suspected pulmonary embolism. AJR Am J Roentgenol 2017; 208(3): 489-494
29. Stubbs M, et al. Incidence of a single subsegmental mismatched perfusion defect in SPECT and planar ventilation/perfusion scans. Nucl Med Commun 2017; 38(2): 135-140
30. El-Barhoun EN, et al. Reproducibility of a **semi-quantitative lobar pulmonary ventilation** and perfusion technique using SPET and CT. Hell J Nucl Med 2017; 20(1): 71-75

Pulmonary Imaging With

TEC  NEGAS™

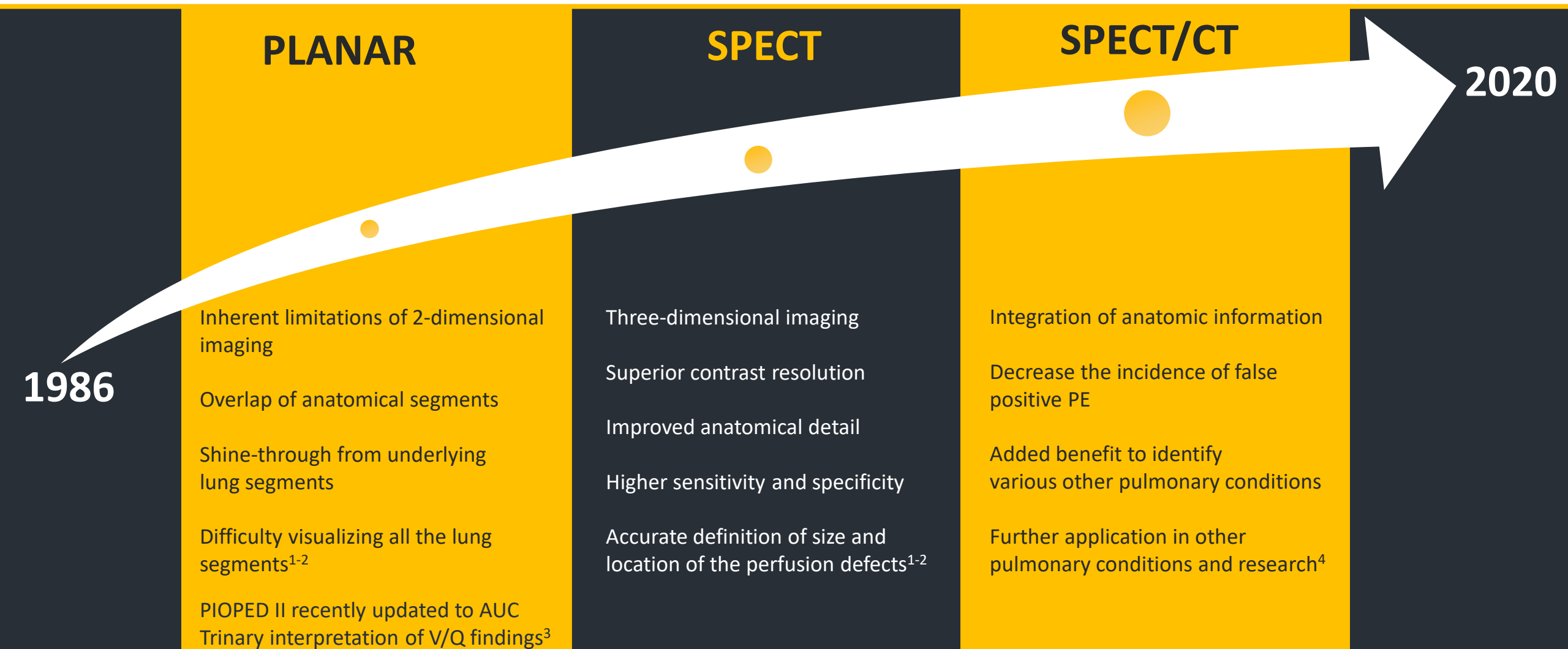


Evolution of Functional Lung Ventilation Imaging

- Improvements in 3D imaging techniques, hybrid imaging and the advent of analytical software have dramatically improved the sensitivity and specificity in functional lung imaging with Technegas
- Traditionally used in the diagnosis of Pulmonary Embolism, nuclear medicine functional lung ventilation imaging utilising improved imaging techniques are expanding the potential clinical utility for Technegas
- The following Technegas images underscore the advancement in complementary technology Cyclopharm is leveraging today:



Nuclear Medicine Imaging Technology Has Evolved Beyond CTPA in Diagnosing PE



1. Gutte H, et al. Nucl Med Commun 2010; 31: 82-86

2. Roach PJ et al. Semin Nucl Med 2010; 40:397-407

3. Waxman AD, et al. J Nucl Med 2017; 58: 13N-15N

4. Roach PJ, et al. J Nucl Med 2013; 54:1588–1596

Radiation Dosimetry

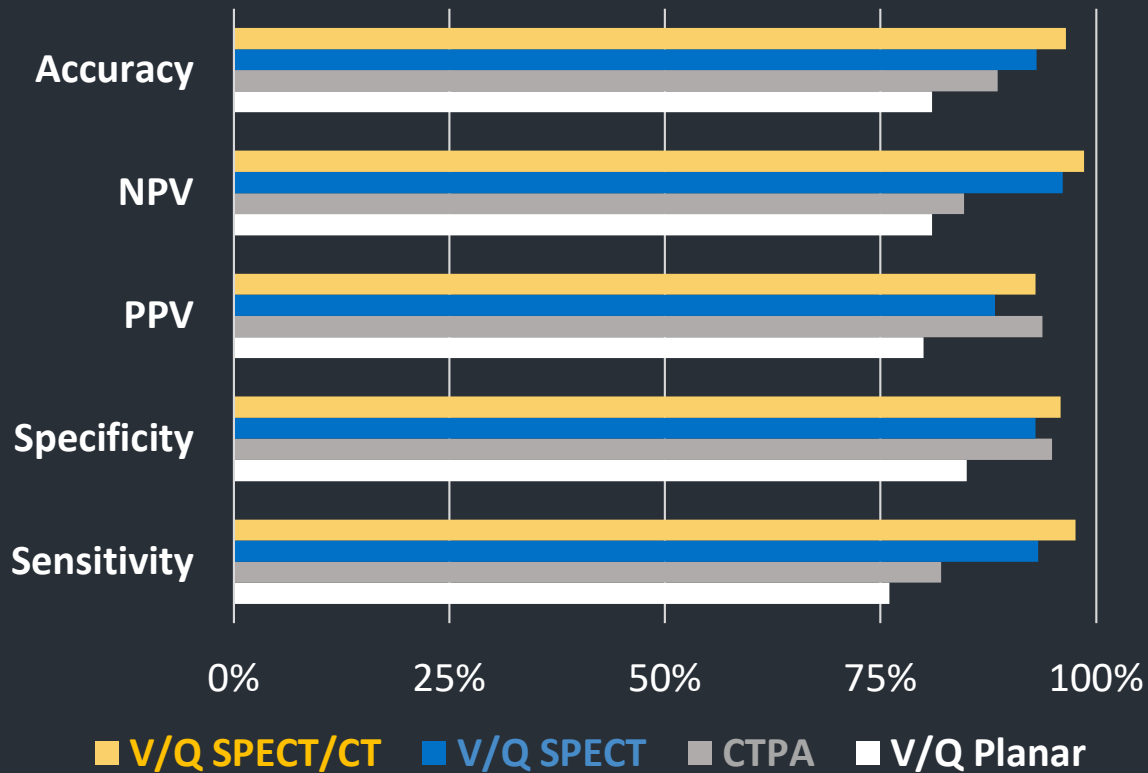
A nuclear medicine V/Q scan is exponentially lower in dose than CTPA

Technique	Effective dose (mSv/MBq)	Effective dose (mSv)	Breast absorbed dose (mGy)	Lung absorbed dose (mGy)
Ventilation Technegas (20MBq) ¹⁻³	0.015	0.30	0.13	2.2
Ventilation ^{99m} Tc-DTPA (20MBq) ¹⁻²	0.007	0.14	0.04	0.30
Ventilation ¹³³ Xe (800MBq) ¹	0.0014	1.12	0.09	0.89
Perfusion MAA (120MBq) ¹⁻³	0.012	1.44	0.60	7.92
Low dose CT non-contrast ⁴	NA	~ 1.00	-	-
CTPA 16 slice ¹	NA	14.4	10-20	10
CTPA 64 slice ^{1,3}	NA	19.9	22	20

Table: Radiation dosimetry data were sourced from Bajc M et al 2009 ¹; Schembri GP et al 2010 ², Isidoro J et al 2017 ³ and Ling IT et al 2012 ⁴.

1. Bajc M, et al. Eur J Nucl Med Mol Imaging 2009; 36(8): 1356-1370
2. Schembri GP, et al. Semin Nucl Med 2010; 40: 442-454
3. Isidoro J, et al. Phys Med 2017; 41: 93-96
4. Ling IT, et al. Intern Med J 2012; 42(11): 1257-1261

Nuclear Medicine provides better diagnostic outcomes in Diagnosing PE



V/Q SPECT and V/Q SPECT/CT have shown that V/Q SPECT/CT is **superior** in most clinical settings with better overall diagnostic performance¹.

In situation of acute PE, chronic PE pregnancy, paediatrics and the COPD population, V/Q SPECT, with or without low-dose CT, can be considered as a first-line investigation to detect PE³ due to:



Its higher accuracy, sensitivity and negative predictive value when compared to CTPA³

Its low radiation and no adverse reactions³

Table: Diagnostic ability of V/Q SPECT/CT¹, V/Q SPECT¹, CTPA¹ and V/Q Planar² to detect PE (adapted from Hess and al, 2016¹ and from Reinartz et al, 2004²)

1. Hess S, et al. Semin Thromb Hemost 2016; 42(8): 833-845
 2. Reinartz P, et al. J Nucl Med 2004; 45: 1501-1508
 3. Leblanc M, et al. CANM guidelines; Nov 2018: www.canm-acmn.ca/guidelines

Reclaiming and Expanding Pulmonary Imaging

Education

Educating referring physicians to the facts, benefits and capabilities of nuclear medicine will bring back lung imaging to nuclear medicine

Utilizing Available Technology

Leveraging the state of the art techniques to include SPECT, SPECT-CT & Quantification Software

CYC Research Strategy Beyond PE

Exploring new methods and techniques to engage specialists and develop new clinical applications

CYC Publication Strategy Beyond PE

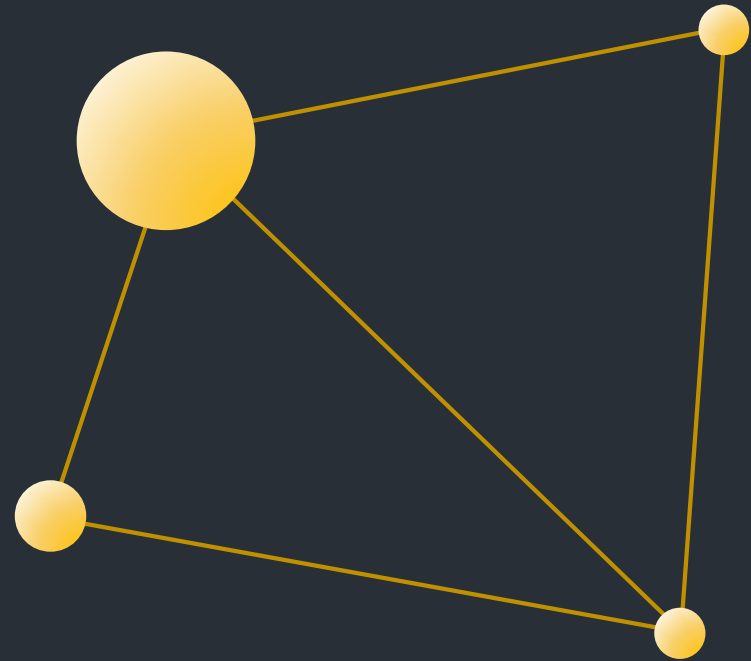
Extending the reach of journal articles beyond the nuclear medicine community.... i.e. Respiratory Medicine, Emergency Medicine & Cardiology



CANM
ACMN

The Canadian Association of Nuclear Medicine
Association canadienne de médecine nucléaire





Technegas

Expanding Indications



Technegas – Global Indication Expansion

- ✓ Applications in chronic disease has the potential to dwarf the use of Technegas in Pulmonary Embolism
- ✓ In 2015 Cyclopharm commenced a clinical program targeting Technegas indication expansion to include:

Chronic Obstructive Pulmonary Disease

- 30x the size of total PE market
- **1 in 7 Australians** over the age of 40
- In 2008, the total economic impact of COPD was estimated to be **\$98.2 billion** of which **\$8.8 billion** was attributed to financial costs and \$89.4 billion to the loss of wellbeing.
- COPD is a leading cause of death and disease burden after heart disease, stroke and cancer
- Global estimates show that COPD will be the **third leading cause of death by 2030**

Lung Reduction Intervention

- Application in determining ventilation pre and post lung reduction intervention

Asthma

- 334 million people globally
- **1 in 9** Australians have asthma
- **\$655 million** was spent on asthma in 2008-9; which is 0.9% of all direct health spend on diseases.
- **34%** of people report that asthma interferes with their daily living, and **21.8%** of people aged 15-25 required time off work, school or study due to their asthma

CTEPH

- Ventilation/Perfusion imaging is recommended
- Up to **40 million** patients globally

Clinical Call for Action

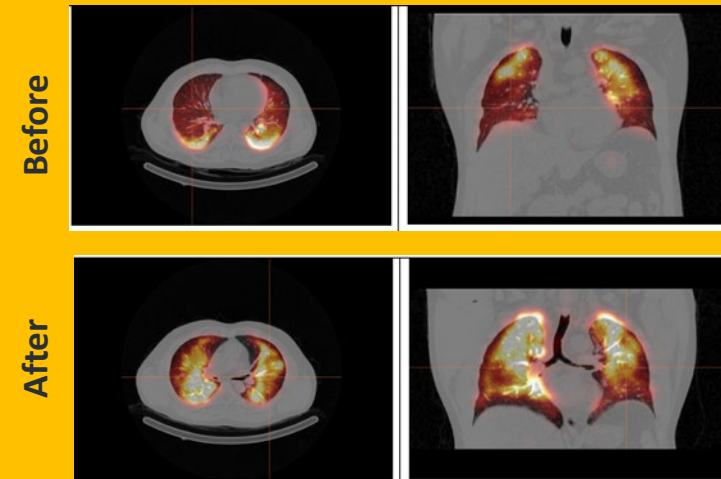
A new way of thinking about respiratory Medicine

Lancet Commission - After asthma: redefining airways disease, September 2017

Executive Summary:

*Progress in reducing hospital admissions and mortality in people with asthma have **stalled in the past 10 years**. This Lancet Commission examines where we are in the understanding of this heterogeneous syndrome and where we need to go to **kickstart a new era of examining, monitoring, treating, and ultimately preventing airways diseases**. The Commissioners recommend to **deconstruct airway disease into component parts before planning treatment with a focus on traits that are identifiable and treatable**. This approach will require **a complete change in how we think about airways diseases with the goal of achieving real precision treatment with better patient outcomes**. In addition, **primary prevention and disease-modifying interventions need to become a more important ambition**. It is unacceptable that people still die from asthma attacks in 2017.*

Functional ventilation imaging using Technegas may provide useful biomarker information in assessing baseline diagnosis and response to therapy in respiratory disease



Assessing Response to Monoclonal
Therapy using Technegas

Technegas SPECT/CT Images provided by HMRI

Hybrid V/Q SPECT/CT

V/Q SPECT provides **functional** information on ventilation and perfusion of the lungs^{1,2}

Low-dose CT provides **anatomical** information such as fissures delineation³

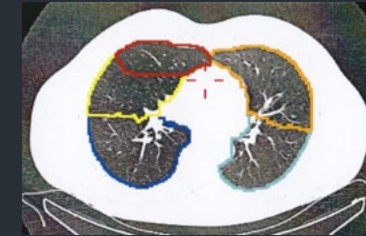
Combination of functional and anatomical information allow for objective results through **quantitative software**^{2,3}



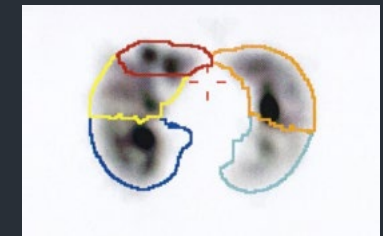
Ventilation SPECT



Low-dose CT



Fused SPECT/CT



Lobar distribution of ventilation

	RIGHT				LEFT		
	RUL	RML	RLL	Total	LUL	LLL	Total
Counts	27%	11%	28%	66%	24%	10%	34%
kcts	254	103	261	617	227	95	321
Volume	24%	9%	25%	57%	26%	17%	43%
ml	1256	456	1321	3033	1364	914	2278

Percentages, volumes and counts of individual lobes (Images and 3D quantification provided by MMI)

IMPROVES DIAGNOSTIC CAPABILITIES AND OFFERS ANATOMICALLY-BASED QUANTIFICATION OF LOBAR CONTRIBUTION FOR INTERVENTIONAL THERAPIES

1. Reinartz P, et al. J Nucl Med 2004; 45: 1501-1508
2. King GG, et al. Semin Nucl Med 2010; 40(6): 467-473
3. Provost K, et al J Nucl Med Technol 2017; 45(3): 185-192

Treatment response in asthma patient

Case 1

CLINICAL HISTORY

Male patient of 25 years old with life-long asthma

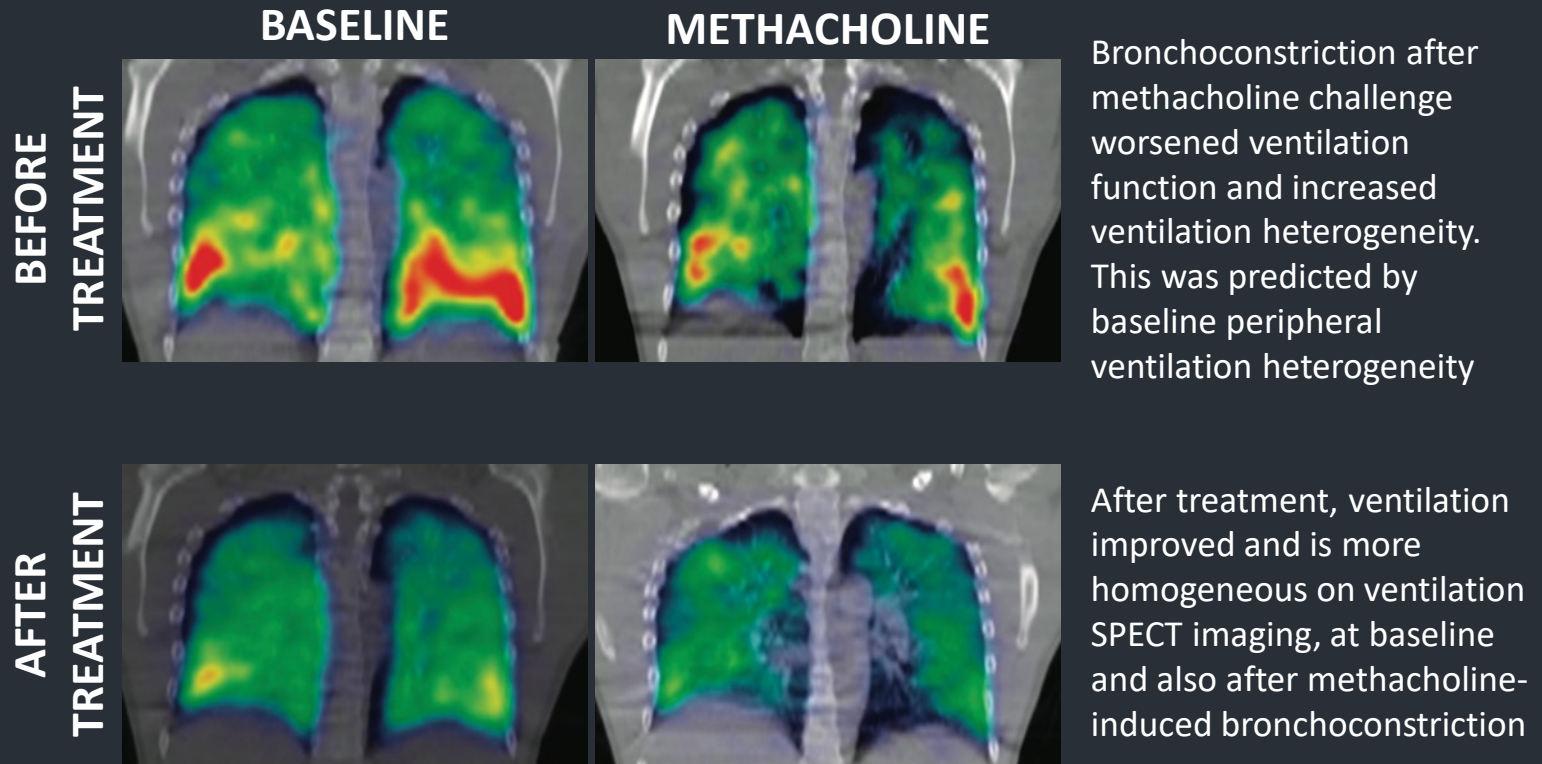
REFERRAL

Evaluation of asthma treatment efficacy

PROTOCOL

Ventilation SPECT/CT imaging at baseline and after methacholine challenge before and after asthma treatment

Images and data were kindly provided by the Woolcock Institute of Medical Research



Bronchoconstriction after methacholine challenge worsened ventilation function and increased ventilation heterogeneity. This was predicted by baseline peripheral ventilation heterogeneity

After treatment, ventilation improved and is more homogeneous on ventilation SPECT imaging, at baseline and also after methacholine-induced bronchoconstriction

VENTILATION SPECT/CT TO MONITOR TREATMENT RESPONSE IN PATIENTS WITH LIFELONG ASTHMA

Planning lung volume reduction surgery

Case 2

CLINICAL HISTORY

Male patient of 64 years old with emphysema

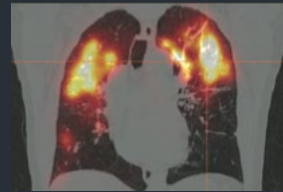
REFERRAL

Assessment of lung ventilation function before planning endoscopic lung volume reduction

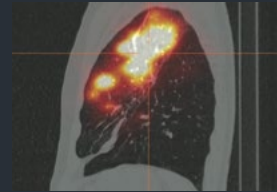
PROTOCOL

VQ SPECT/CT imaging with Technegas as ventilation agent

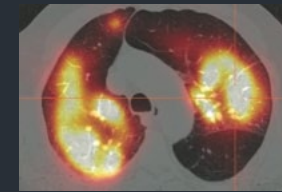
Images and data were kindly provided by Macquarie Medical Imaging



CORONAL FUSION



SAGITTAL FUSION



UPPER LOBES
TRANSVERSE
FUSION



LOWER LOBES
TRANSVERSE
FUSION

The ventilation SPECT/CT scan reveals the function of the lower lobes is severely affected. The left oblique fissure is intact so the left lower lobe should be a good target lobe for endobronchial valves insertion.

Assessment for collateral ventilation was confirmed using CHARTIS assessment tool during the procedure.

Decision: 3 valves were inserted into the left lower lobe.

VENTILATION RELATIVE UPTAKE [%]		
	Right	Left
UPPER	45 %	36 %
MIDDLE	12 %	N/A
LOWER	3 %	4 %
TOTAL	60 %	40 %

Lobar 3D quantification provided by Hermes

VENTILATION SPECT/CT AS A TOOL TO ASSIST IN PREDICTING FUNCTIONAL LUNG VENTILATION PRIOR TO LUNG VOLUME REDUCTION



BUILDING FOR GROWTH