4DMedical files FDA submission for CT:VQ™

26 May 2025

Highlights

- 4DMedical files FDA 510(k) submission for CT:VQ™, a non-contrast CT-based lung imaging software product for assessing both ventilation (V) and perfusion (Q) in the lungs
- CT:VQ™ represents a revolution in ventilation perfusion imaging, solving key clinical and logistical limitations across all forms of nuclear ventilation perfusion imaging
- Compelling clinical validation package, demonstrating equivalence (or superiority) to SPECT ventilation perfusion across multiple lung conditions
- 4DMedical expects to capture 100% of the one million nuclear ventilation perfusion scans performed annually
- CT:VQ™ is expected to align with the Company's existing CT LVAS™ CPT code (USD $650), supporting rapid clinical adoption
- Provides the potential to grow the current ventilation perfusion market into new applications in disease monitoring and screening, due to the wide availability of CT infrastructure
- When including days spent with the applicant, the average time for FDA 510(k) decision is approximately 120 days
- 4DMedical will hold an investor webinar tomorrow, Tuesday 27 May 2025 at 11am AEST

Melbourne, Australia, **26 May 2025**: 4DMedical Limited (ASX: 4DX, "4DMedical", or the "Company"), a global leader in respiratory imaging technology, today announces that it has received an acknowledgement letter from the U.S. Food and Drug Administration (FDA) confirming the filing of an FDA 510(k) submission for CT:VQ™.

Ventilation Perfusion (VQ) scans

A ventilation perfusion (VQ) scan is a specialised nuclear medicine procedure that evaluates both the airflow (ventilation) and blood flow (perfusion) in a patient's lungs. This diagnostic test creates images that show how well air and blood are distributed throughout the lungs, which helps doctors identify areas where there might be an imbalance between ventilation and perfusion.

A VQ scan is highly effective in diagnosing several lung conditions. Its primary use is detecting pulmonary embolism (blood clots in the lungs), a serious, potentially life-threatening condition that requires prompt diagnosis and treatment. Beyond pulmonary embolism, VQ scans are valuable for assisting physicians with a wide range of conditions. For example, chronic thromboembolic pulmonary hypertension (CTEPH), a condition where persistent blood clots lead to high blood pressure in the lung vessels. VQ scans also help evaluate regional lung function in patients with chronic obstructive pulmonary disease (COPD), asthma, or other airway diseases by showing areas of poor ventilation or altered blood flow.

A nuclear VQ scan is performed in two parts, typically on the same day, in a single appointment, with two discrete components. For the ventilation portion, the patient breathes in a radiotracer, which travels through the airways and allows the specialised gamma camera to create images of air distribution in the patient's lungs. For the perfusion portion, a different radiotracer is injected into the patient and travels through the bloodstream to the lungs, allowing the gamma camera to capture images of blood flow patterns. The entire procedure usually takes 45-90 minutes.

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4DMedical's ventilation perfusion scan – CT:VQ™

4DMedical's CT:VQ™ represents a revolution in ventilation perfusion imaging, enabling quantitative VQ data and visualisations to be extracted from a routine CT scan, without the need for any radiotracer or contrast agent. It achieves this by measuring both the regional motion and local density changes of lung tissue.

CT:VQ™ solves key clinical and logistical limitations across all forms of nuclear VQ imaging:

- No radiotracers – improved scheduling and accessibility
- Simplified workflows – integrated into routine CT imaging without any additional infrastructure
- Higher resolution and quantification without artifacts caused by clumping or leakage of contrast
- Large install base – leverages the ~14,500 installed CT scanners across the U.S. healthcare system, including rural and smaller healthcare facilities, which may not have existing nuclear VQ infrastructure

Commercial opportunity for CT:VQ™

Over one million nuclear VQ scans are performed annually in the U.S. alone, with an average reimbursement rate of approximately USD $1,150 per scan. This translates to an initial addressable market of more than USD $1.1 billion annually in the U.S., and estimated at over USD $2.6 billion globally.

With the clinical and logistical advantages CT:VQ™ has over traditional nuclear VQ imaging modalities, 4DMedical believes it can rapidly capture a significant part of this market, and over time expects to displace 100% of all nuclear VQ scans. Management also anticipates that the introduction of CT:VQ™ into the market will drive long-term growth in demand for ventilation perfusion scans beyond the traditional nuclear VQ indications.

Analysing both ventilation and perfusion together can provide superior diagnostic information compared to assessing either parameter alone, revealing crucial VQ mismatches, enabling precise differential diagnosis, and accurately evaluating regional lung function in ways impossible with isolated functional measurements. While conventional nuclear medicine VQ scans offer valuable diagnostic capabilities for conditions like pulmonary embolism, CTEPH, and pre-surgical assessment, their broader application remains constrained by practical limitations: limited access to the specialised gamma cameras, and potentially limited hours of operation of nuclear medicine departments, handling of radiotracers, and other resource constraints.

CT:VQ™ overcomes these barriers by extracting both ventilation and perfusion data from routine CT scans, a widely available imaging modality, thereby making comprehensive lung assessment more accessible for both established VQ indications and potentially new applications in disease monitoring and screening. This innovation has the potential to transform pulmonary care by enabling healthcare providers without nuclear medicine facilities, or those with limited scheduling availability, to offer a comprehensive functional lung assessment.

Reimbursement pathway for CT:VQ™

Reimbursement pathways in the United States are expected to align with the Company's existing CT LVAS™ CPT code (USD $650), which will support rapid clinical adoption and recurring revenue from both hospital and outpatient imaging providers.

Hospitals with inpatients managed under Diagnosis Related Group (DRG) payments, a classification system that groups patients with similar diagnoses and treatment plans for billing and reimbursement purposes, receive a fixed payment for each patient irrespective of the final cost of treating that patient. As a result, the improved economics of a non-contrast CT-based ventilation perfusion assessment will also support adoption for this segment of the market.

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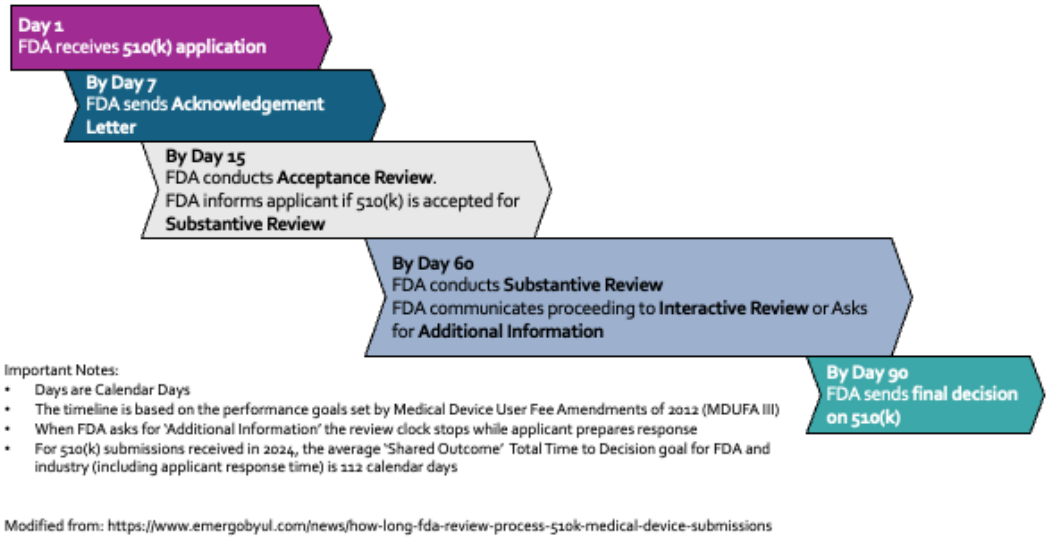
FDA 510(k) submission overview and regulatory pathway

The FDA's 510(k) process enables medical devices to achieve market clearance by demonstrating "substantial equivalence" to a predicate device already cleared in the United States.

4DMedical's submission for CT:VQ™ leverages its FDA-cleared CT LVAS™ product (CT Lung Ventilation Analysis Software) as the predicate device for the ventilation component. In addition, CT:VQ™ has been benchmarked against SPECT imaging, which is widely recognised as the state-of-the-art nuclear medicine approach to lung perfusion imaging.

The FDA has a statutory obligation to make a final decision on 510(k) submissions within 90 calendar days. However, this period typically extends if additional information is requested, during which time the review clock stops until the applicant responds. When including days spent with the applicant, the average time for FDA 510(k) decision is 112 days.

Figure 1: Timeline of FDA 510(k) review



Modified from: https://www.emergobyul.com/news/how-long-fda-review-process-510k-medical-device-submissions

Clinical evaluation study results strongly support 510(k) submission

The submission follows extensive technical development, internal validation, and regulatory documentation. It marks the culmination of years of research into functional CT-based lung imaging, and the convergence of high-resolution anatomical and functional data in a single imaging session.

SPECT imaging has long been considered the reference method for functional lung assessment due to its ability to provide spatially resolved maps of both ventilation and perfusion. As such, it serves as a suitable benchmark for validating CT:VQ™. However, SPECT is limited by lower spatial resolution, logistical constraints, and human radiation exposure, whereas CT:VQ™, as a software layer, offers a fast, high-resolution and readily available alternative that can be generated from existing routine CT data.

The performance of CT:VQ™ was validated by directly comparing it to SPECT across a wide range of patients. To thoroughly assess the performance of CT:VQ™, the Company employed three complementary approaches:

I. Standalone device performance assessment: quantitative comparison
II. Reader performance assessment: qualitative assessment
III. Case-based review

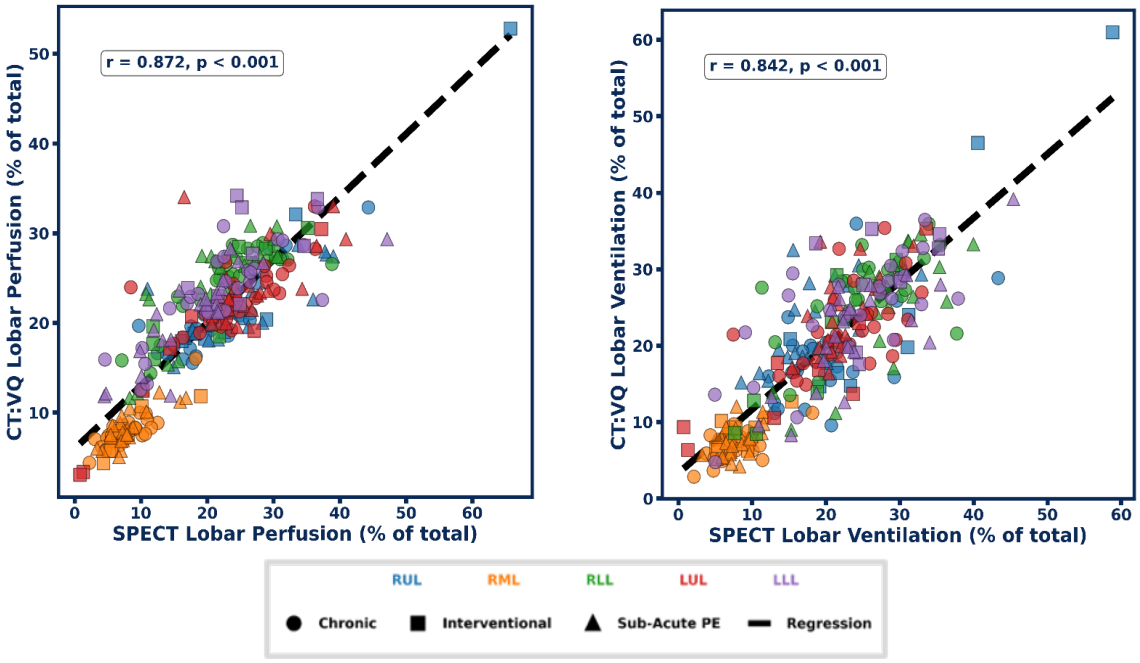
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I. Standalone device performance assessment: quantitative comparison

The regression analysis below provides lobar-level comparison of (A) perfusion and (B) ventilation between SPECT and CT:VQ™. Each data point represents the ventilation or perfusion in a lobe as a percentage of the total ventilation or perfusion in the lungs. Both perfusion and ventilation display strong positive correlation (r=0.872 and r=0.842) with high statistical significance.

This data highlights strong quantitative agreement between SPECT and CT:VQ™, across both ventilation and perfusion. Lobar ventilation % and lobar perfusion % are important measures in daily clinical use and are used regularly as part of planning and decision-making process ahead of lung surgery and lung valve placement procedures.



II. Reader performance assessment: qualitative assessment

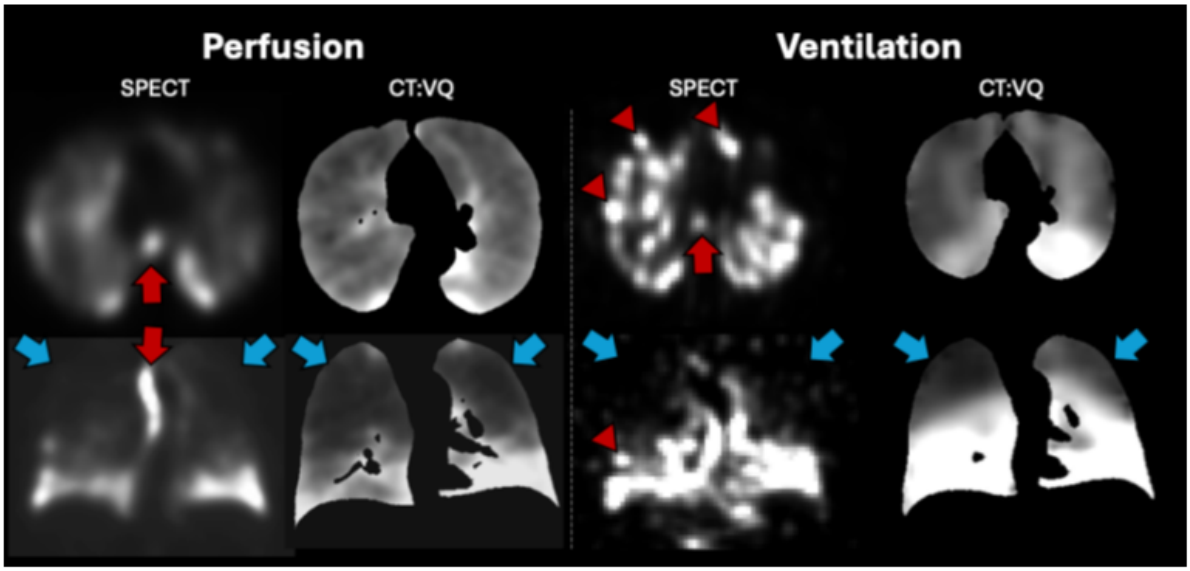
For this assessment, expert radiologists and nuclear medicine physicians rated the regional distribution of function on CT:VQ™ and SPECT using a standardised 5-point ordinal scale. The reader study confirmed that clinicians consistently rated CT:VQ™ perfusion images as having good to excellent agreement with SPECT across all lung zones, with very strong inter-modality correlation.

III. Case-based review

Case reviews further highlighted CT:VQ™ advantages, including higher spatial resolution and the absence of common SPECT artifacts, demonstrating its diagnostic equivalence and enhanced image quality for assessing regional lung function.

Below is a case study for a COPD subject showing selected axial (top row) and coronal (bottom row) perfusion (left panels) and ventilation (right panels) images from SPECT and the CT:VQ™:

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Concordance of defects (blue arrows); Artifacts (red arrows)

This case contains two matching ventilation perfusion defects (i.e. loss of both ventilation and perfusion) in the upper regions of both the left and the right lung. This type of matched defect is common in subjects with COPD. The ventilation and perfusion defects are marked with blue arrows, in both the perfusion (left) and ventilation (right). As can be seen, both the SPECT and CT:VQ™ images show the same upper lung matched defects. In addition, red arrows identify imaging artifacts present in the SPECT perfusion and SPECT ventilation images. These artifacts can present as high-intensity areas caused by concentration or accumulation of contrast, for example, caused by swallowing inhaled contrast and having it collect in the oesophagus.

Summary of validation

By combining quantitative metrics, expert interpretation, and clinical case studies, the Company has provided a comprehensive validation of CT:VQ™ to the FDA. Findings suggest that CT:VQ™ reliably replicates SPECT ventilation perfusion assessments, while offering practical advantages in workflow, higher resolution, shorter acquisition time, and compatibility with routine non-contrast CT, positioning CT:VQ™ as a compelling non-nuclear alternative for ventilation and perfusion imaging for use in clinical practice.

Early customer interactions with CT:VQ™

As previously announced, the Company has commercial contracts for CT:VQ™ for use in clinical trials at Brooke Army Medical Center (the U.S. Department of Defense's largest facility and only Level 1 trauma center) and with several companies undertaking clinical trials of their pre-release products.

Clinicians assisting in the assessment of CT:VQ™ have noted the benefits of having access to pulmonary ventilation and perfusion derived from readily available non-contrast CT scans, with considerable interest in early adoption. 4DMedical attended ATS 2025 (American Thoracic Society; the largest meeting of lung physicians and researchers in the U.S.) last week, and at that meeting received overwhelmingly positive feedback.

For example, Dr. Kyle Hogarth, Professor of Medicine and Director of Bronchoscopy and Interventional Pulmonary at University of Chicago Medicine, said: "*I am excited about being able to image perfusion in my patients without the delays and logistical challenges of nuclear imaging. I'm already ordering a non-contrast CT on these patients: I want to maximize the data from each scan, and this allows me to do that.*"

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Commercially, CT:VQ™ represents a strategic play that enables our sales teams, for the first time, to be selling a product that is a replacement for one that is already in established clinical pathways. For clinicians, their interest has come from being able to add the software assessment to CT scans they were already ordering, as part of their routine clinical workup of many pulmonary patients, yielding richer information on the function of their lungs with the minimum impact to their operational workflow.

Investor Webinar

4DMedical will hold an investor webinar tomorrow, Tuesday 27 May 2025 at 11am AEST, where Dr Andreas Fouras will provide further information, and host a Q&A session, in relation to CT:VQ™.

Please register in advance using the following links:

Phone registration: https://s1.c-conf.com/diamondpass/10047546-qpjld5.html
Webcast: https://ccmediaframe.com/?id=a2ozxVzA

After registering, you will receive a confirmation email containing information about joining the webinar or dial-in details for those who would prefer to join by telephone.

4DMedical MD/CEO and Founder Andreas Fouras said:

This FDA submission marks a defining moment in 4DMedical's journey. CT:VQ™ has the potential to completely transform how respiratory disease is diagnosed and managed — offering clinicians a faster, more convenient, and more accessible tool for functional lung assessment. Importantly, CT:VQ™ uses widely available CT infrastructure, making it a scalable solution that can quickly meet the enormous unmet demand in pulmonary imaging.

This is a rare opportunity. Because of inherent advantages of CT:VQ™ across economics and workflow, to win this huge market, we only need to show equivalence between CT:VQ™ and SPECT. Qualitative and quantitative data from our trials strongly support equivalence between CT:VQ™ and SPECT. Additionally, case studies illustrated key advantages of CT:VQ™, including greater spatial resolution, higher signal to noise ratio, and the absence of common SPECT-related artifacts. Layer on top the practical advantages in workflow, and integration with widely available existing CT-based evaluations, and it is clear we have a product that can rapidly disrupt the existing market and even grow clinician demand for complete functional lung imaging in other patient populations.

–ENDS–

Authorised by the 4DMedical Board of Directors.

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About 4DMedical

4DMedical Limited (ASX:4DX) is a cutting-edge global medical technology company revolutionizing respiratory care. By harnessing advanced imaging and AI-powered solutions, 4DMedical delivers unprecedented insights into lung function, enabling earlier and more precise diagnoses of respiratory diseases.

At the heart of 4DMedical's innovation is its patented XV Technology®, a groundbreaking platform that dynamically quantifies ventilation throughout the lungs as patients breathe. This technology underpins the company's FDA-cleared XV Lung Ventilation Analysis Software (XV LVAS®) and its CT LVAS™, empowering physicians to detect and monitor regional airflow abnormalities with unparalleled sensitivity.

4DMedical's solutions integrate seamlessly into existing hospital infrastructure via its Software as a Service (SaaS) model, transforming routine imaging into powerful diagnostic tools.

In December 2023, 4DMedical expanded its leadership in medical imaging with the acquisition of **Imbio**, a pioneer in artificial intelligence solutions for chronic lung and cardiothoracic diseases. Imbio's AI-driven platforms enhance physician productivity, improve diagnostic precision, and support personalized care, aligning seamlessly with 4DMedical's mission to redefine respiratory healthcare.

To learn more, please visit www.4dmedical.com

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