Technical Validation, Clinical Applications, and Future Directions Across Perfusion Assessment, V/Q Mismatch, PE Detection, BLVR/LVRS Planning, and Precision Lung Surgery

CT:VQ—A Contrast-Free Breakthrough in Regional Pulmonary Ventilation and Perfusion Imaging

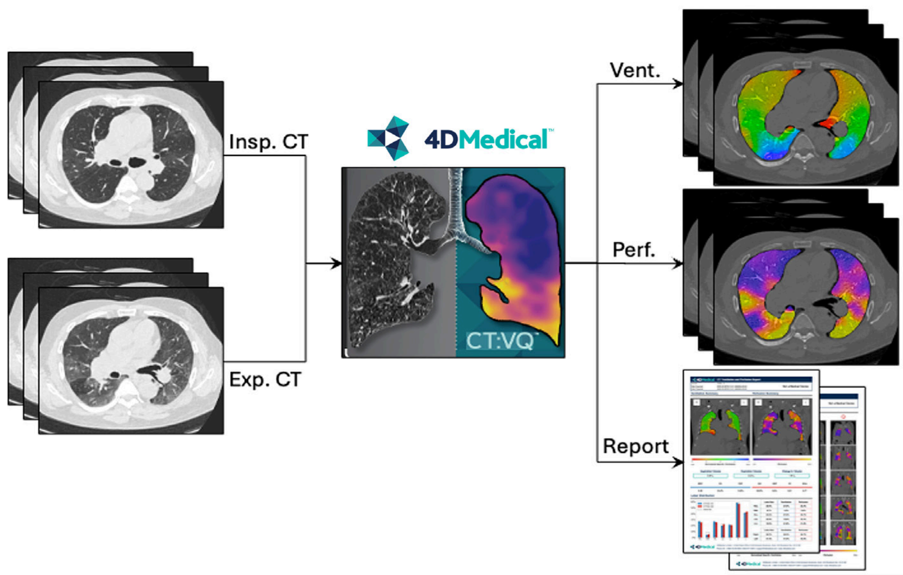
1. INTRODUCTION

Ventilation-perfusion (V/Q) imaging is foundational for evaluating pulmonary physiology across a wide spectrum of diseases-from pulmonary embolism and COPD to lung volume reduction interventions. For decades, clinical V/Q assessment has relied almost exclusively on nuclear medicine imaging, most commonly single-photon emission computed tomography (SPECT). While widely used, SPECT requires radiotracers, introduces logistic and operational burdens, and provides relatively low spatial resolution.

CT Ventilation–Perfusion (CT:VQ) represents a major technological inflection point. Recently cleared by the U.S. Food and Drug Administration, CT:VQ enables **fully non-contrast, tracer-free,** regional ventilation and perfusion imaging derived from standard paired inspiratory–expiratory CT scans.

KEY FEATURES OF CT:VQ

- Requires **no contrast** or **radioisotopes**
- Uses routine, widely available CT images
- Produces **quantitative, 3D, high-resolution maps** of ventilation and perfusion
- Allows simultaneous assessment of structure, ventilation, perfusion, and V/Q mismatch
- Integrates seamlessly into clinical evaluation of pulmonary conditions such as COPD and pulmonary embolism, and into procedural workflows including bronchoscopic lung volume reduction (BLVR) and lung volume reduction surgery (LVRS)



Its capability for high-fidelity physiologic characterization positions CT:VQ not merely as an alternative to SPECT, **but as a revolutionary technology that unifies multiple imaging needs into a single CT-based workflow.**

The following sections synthesize the technical and clinical validatory evidence supporting CT:VQ, highlight emergent applications in perfusion defect detection, V/Q mismatch, and collateral ventilation, and summarize a quantitative, CT-based approach for LVRS patient selection. Data on file; peer reviewed examples in this paper are have been accepted and will be published at ATS 2026.

2. TECHNICAL VALIDATION OF CT:VQ

2.1 Quantitative Concordance with Dual-Energy CT Perfusion[1]

- CT:VQ perfusion closely matched Dual-Energy CT (DECT) perfusion maps in COPD subjects.
- Uniform and high lobar-specific concordance between the imaging methods.
- CT:VQ is a non-contrast alternative that quantifies regional perfusion.

CT:VQ-derived perfusion has been directly benchmarked against dual-energy CT (DECT) iodine maps, widely regarded as one of the most physiologically robust and validated imaging surrogates for regional pulmonary blood volume (PBV). DECT-generated PBV maps are commonly used in research and select clinical settings because they provide a contrast-based quantification of regional perfusion; thus, they serve as an ideal reference standard for evaluating a non-contrast technique such as CT:VQ.

To assess concordance between the two modalities, a quantitative analysis was performed using a well-characterized COPD cohort (N = 58). For each subject, relative lobar perfusion was computed by taking the total CT:VQ perfusion signal within each anatomical lobe and normalizing it to the total perfusion signal across the lungs. The same procedure was applied to the DECT generated PBV maps.

Across all lobes and all subjects, the agreement between CT:VQ and DECT-PBV was exceptionally strong, with a Pearson correlation coefficient of r = 0.921 for relative lobar perfusion (**Figure 2**). Lobar-specific correlation values are summarized in **Table 1** and uniformly demonstrate high concordance between modalities. This level of agreement indicates that CT:VQ reliably captures the same physiologic perfusion distribution measured with DECT iodine imaging.

Importantly, CT:VQ achieves this without the need for iodinated contrast, dual-energy CT technology, or the specialized post-processing workflows required for PBV volume mapping. As a result, CT:VQ reduces cost, workflow complexity, and patient risk while preserving fidelity to physiologic perfusion patterns. This makes it far more scalable for routine clinical use and broad research deployment.

These results support CT:VQ as a non-contrast alternative to DECT that can quantify regional perfusion accurately and with meaningful clinical relevance.

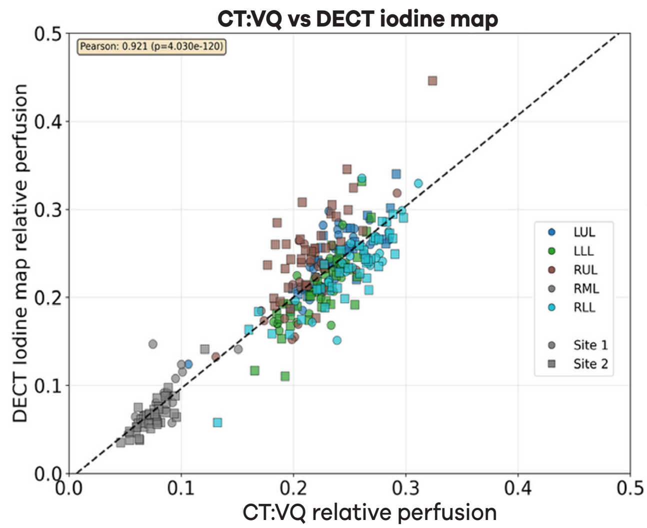


Figure 2: *Correlation between relative lobar perfusion assessed by CT:VQ and DECT iodine maps.*

Lung region	Pearson correlation n=58 subjects, N=290 lobes
All lobes	0.921, p<0.001
RUL	0.752, p<0.001
RML	0.770, p<0.001
RLL	0.858, p<0.001
LUL	0.806, p<0.001
LLL	0.788, p<0.001

Table 1: *Combined and individual correlations of relative lobar perfusion between CT:VQ and DECT.*

2.2 CT:VQ Perfusion & Ventilation Agreement with SPECT V/Q[2–5]

- **Robust, multi-site validation of CT:VQ against SPECT V/Q across relevant patient groups: subacute PE, small airways disease, and lung volume reduction candidates.**
- **CT:VQ has strong, quantitative agreement with SPECT with lobar and cohort-specific correlations reported.**
- **Practical advantages: CT:VQ reproduces regional V/Q patterns without radiotracers, nuclear equipment, or complex workflows.**

CT:VQ was validated directly against the clinical standard, SPECT ventilation–perfusion (V/Q) imaging. Validation included patients with subacute pulmonary embolism, chronic obstructive or small-airways disease, and individuals evaluated for lung volume reduction therapy, representing clinical scenarios where accurate regional V/Q assessment is essential.

Fifty-six subjects with paired inspiratory/expiratory CT and SPECT were analyzed across four international clinical sites. Before CT:VQ processing, the CT component of the SPECT exam was anatomically registered to the patient's diagnostic CT to ensure precise lobe-level comparison. For each subject, relative lobar ventilation and perfusion were calculated by taking the total signal within each anatomic lobe and normalizing to total lung signal, allowing a direct, distribution-based comparison between modalities.

Pearson linear regression demonstrated strong agreement between CT:VQ and SPECT for both ventilation ($r = 0.833$, $p<0.001$) and perfusion ($r = 0.857$, $p<0.001$) (**Figure 3**), comparable to correlations between SPECT-VQ and DECT or Xe-MRI[3–5]. Lobar-level correlations and cohort-specific correlations between CT:VQ and SPECT are tabulated in **Table 2** and **Table 3.**

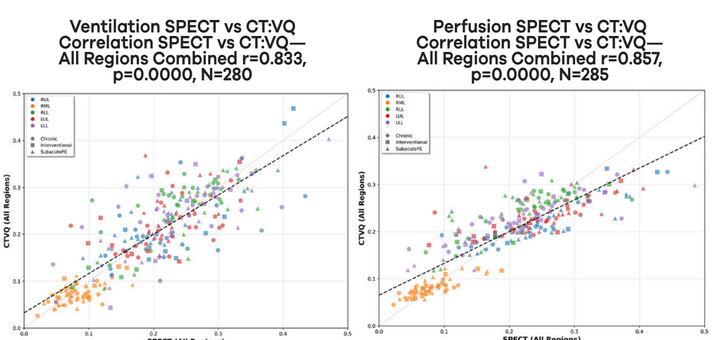


Figure 3: *Correlation between relative lobar ventilation (left) and perfusion (right) assessed by CT:VQ and SPECT. Dashed line = best linear fit. Gray line = line of unity.*

These results show that CT:VQ captures similar regional ventilation and perfusion patterns to SPECT, but without the need for radiotracers, dedicated nuclear imaging equipment, or complex acquisition workflows. Because CT is already widely available and routinely obtained in PE, COPD, and planning populations, CT:VQ has the potential to provide high resolution functional lung imaging at dramatically lower cost and complexity. Multi-site validation further confirms robustness across scanners, institutions, and disease phenotypes, supporting CT:VQ as a scalable alternative to SPECT.

Lung region	Ventilation Pearson correlation n=56 subjects n=280 lobes	Perfusion Pearson correlation n=57 subjects n=285 lobes
All lobes	0.833, p<0.001	0.857, p<0.001
RUL	0.679, p<0.001	0.834, p<0.001
RML	0.613, p<0.001	0.806, p<0.001
RLL	0.734, p<0.001	0.812, p<0.001x$
LUL	0.482, p<0.001	0.656, p<0.001
LLL	0.744, p<0.001	0.822, p<0.001

Table 2: *Lobar-level correlations between CT:VQ and SPECT.*

Cohort Group	Ventilation Pearson correlation	Perfusion Pearson correlation
Interventional	0.853, p<0.001, n=40	0.879, p<0.001, n=40
Chronic	0.805, p<0.001, n=135	0.878, p<0.001, n=135
Subacute PE	0.864, p<0.001, n=110	0.825, p<0.001, n=110

Table 3: *Cohort specific correlations between CT:VQ and SPECT.*

2.3 Pivotal Reader Study Performance: CT:VQ vs SPECT[2]

- **Pivotal, prospective, multi-center reader study with six expert radiologists compared CT:VQ perfusion maps to SPECT in PE, chronic lung disease, and lung volume reduction therapy candidates.**
- **CT:VQ perfusion distributions are visually consistent with SPECT, supporting clinical interpretability and positioning CT:VQ as a viable, high-resolution, non-nuclear alternative.**

In a rigorous, prospective, multi-center performance assessment, perfusion (Q) images generated from non-contrast paired inspiratory and expiratory CT scans using CT:VQ software were compared directly with single-photon emission CT (SPECT) perfusion images by expert radiologists. This comparison was performed in clinical conditions involving subjects with subacute pulmonary embolism, chronic lung diseases, and those undergoing lung volume reduction therapy. Six radiologists ("readers"), with an average of 24.3 years of experience, who routinely review V/Q studies, conducted evaluations on n=77 subjects who underwent paired inspiratory/expiratory chest CT and SPECT V/Q scans. Perfusion images were assessed for lung perfusion across six zones on a monotonic scale (1 = absent to 5 = well perfused). Inter-modality reader agreement was analyzed using Kendall's Tau (τ). The similarities in perfusion intensity distributions across modalities were also compared by radiologists in a side-by-side view (1 = no agreement to 5 = excellent agreement) for each lung zone and reported as mean ± standard deviation (SD).

Reader results demonstrated that CT:VQ perfusion maps had excellent ordinal agreement with SPECT across all lung zones as demonstrated in the confusion matrices (**Figure 4**). Additionally, radiologist-rated perfusion intensity agreement scores were high, with mean ratings above 3 for each reader and exceeding 4 when averaged, signifying good to excellent inter-modality agreement (**Table 4**).

Overall, the analyses showed strong correlations between CT:VQ and SPECT, with Kendall's τ values of 0.702–0.765 (all $p < 0.001$). Reader assessments were similarly favorable, with average inter-modal perfusion agreement ratings between 4.32 and 4.43 on a five-point scale.

In conclusion, readers found CT:VQ perfusion distributions visually consistent with SPECT, supporting the modality's clinical interpretability and confirming that CT:VQ is a viable, high-resolution, non-nuclear alternative to SPECT.

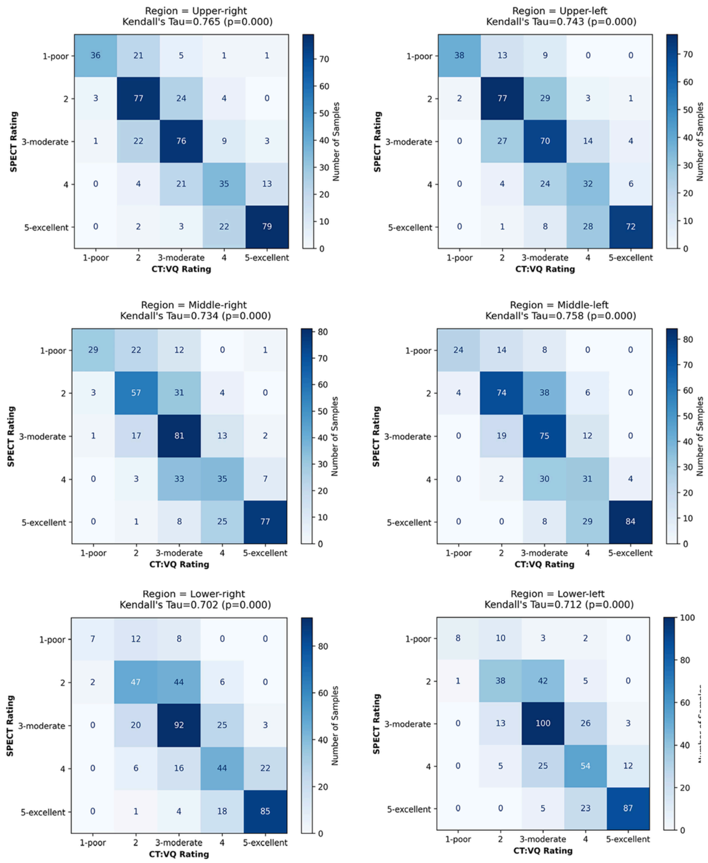


Figure 4: *Confusion matrices for the reader perfusion ratings between SPECT and CT:VQ. Kendall's Tau, p-value, and lung region are reported.*

Lung Zone	Inter-Modality Reader Agreement (τ)	Radiologist-Averaged Perfusion Rating (Mean ± SD)
ULZ	0.743	4.32 ± 0.95
MLZ	0.758	4.32 ± 0.90
LLZ	0.712	4.34 ± 0.89
URZ	0.765	4.43 ± 0.86
MRZ	0.734	4.38 ± 0.87
LRZ	0.702	4.33 ± 0.95

Table 4: *Inter-modality reader agreement of regional perfusion was assessed using Kendall's Tau over all reads and SPECT/CT:VQ scan pairs, for each lung zone.*

2.4 CT:VQ Correlation with Physiologic Markers (DLCO & Spirometry)[2]

- **Perfusion–DLCO: CT:VQ Perfusion variability showed stronger inverse correlation with DLCO than SPECT suggesting** greater sensitivity to gas-exchange impairment.
- **Ventilation–airflow: CT:VQ Ventilation** correlated inversely with airflow obstruction.
- CT:VQ agrees with SPECT on regional heterogeneity and shows more robust links to physiologic impairment.

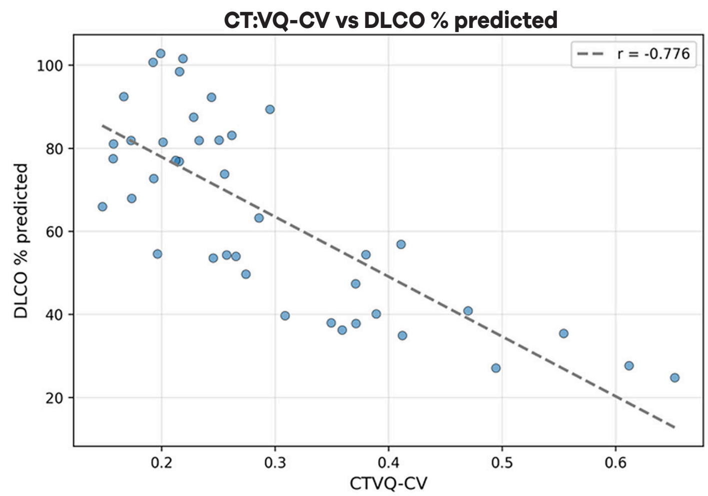
Ventilation and perfusion heterogeneity biomarkers were computed from CT:VQ and SPECT V/Q images and compared to pulmonary function tests (PFTs) across cohorts with subacute pulmonary embolism, chronic obstructive or small-airways disease, and patients evaluated for lung volume reduction therapy. A total of n=46 subjects with spirometry, DLCO, and paired inspiratory/expiratory chest CT plus SPECT V/Q were analyzed.

Perfusion and ventilation heterogeneity was computed as the coefficient of variation of the ventilation and perfusion distributions for both modalities (Qcv, Vcv). These markers were correlated with PFT parameters including FEV1/FVC (n=45) and DLCO % predicted (n=41).

CT:VQ perfusion heterogeneity (Qcv) showed a strong negative correlation with DLCO ($\rho = -0.78$, $p < 0.001$; n = 41) (Figure 5, left). By comparison, SPECT Qcv demonstrated a more moderate negative correlation with DLCO ($\rho = -0.62$, $p < 0.001$; n = 41) (**Figure 5**, right).

These findings suggest improved sensitivity to gas-exchange abnormalities relative to SPECT, potentially due to higher spatial resolution and lower artifact susceptibility. CT:VQ ventilation heterogeneity metrics also showed moderate and statistically significant inverse correlations with airflow obstruction, where CT:VQ Vcv vs FEV1/FVC yielded a Pearson correlation of $\rho = -0.553$ ($p < 0.001$, n=45).

Across multiple functional domains, CT:VQ demonstrated robust relationships with physiologic impairment measured by DLCO and spirometry. The combination of high spatial resolution, non-contrast acquisition, and strong physiologic validity supports CT:VQ as a scalable, high-fidelity alternative to nuclear medicine V/Q imaging for regional lung-function assessment.



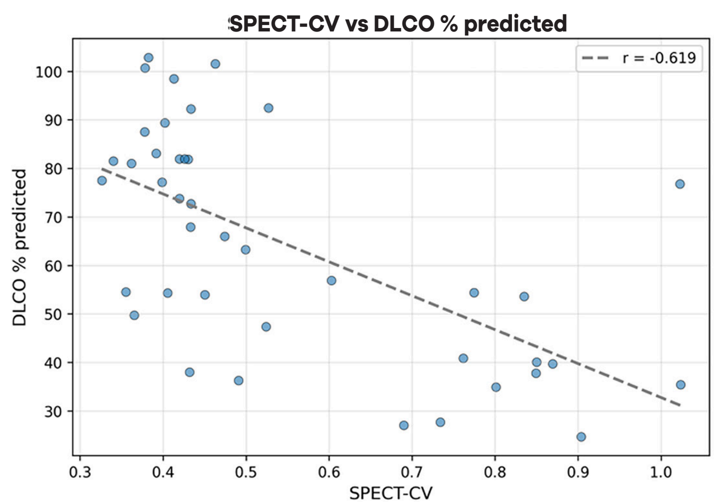


Figure 5: *Top: CT:VQ perfusion coefficient of variation vs DLCO% predicted. Bottom: SPECT perfusion coefficient of variation vs DLCO% predicted.*

2.5 CT:VQ for Evaluation of Individuals with Post-Acute Sequelae of SARS-CoV-2 and Dyspnea[1]

- **CT:VQ may reveal perfusion abnormalities not detected by standard tests in post-acute sequelae of SARS-CoV-2-related dyspnea.**
- **Despite normal baseline spirometry, and largely unremarkable conventional inspiratory CT, the dyspnea group showed significantly higher perfusion heterogeneity and perfusion defect percent on CT:VQ.**

Post-Acute Sequelae of SARS-CoV-2 (PASC) affects an estimated 10% of those recovering from COVID-19, with dyspnea being one of the common symptoms affecting up to 41% of those with PASC. Despite extensive physiologic testing and imaging, the etiology of dyspnea in most of those with PASC remains unclear. A study at Tufts Medical Center was conducted to describe ventilation and perfusion abnormalities seen on computed tomography imaging utilizing functional respiratory imaging.

Participants 18 years of age or older reporting persistent symptoms of dyspnea, fatigue, or exercise intolerance at least 3 months after their primary SARS-CoV-2 infection and healthy controls were enrolled. For each participant, symptom surveys, quality of life scores, pulmonary function testing (PFTs), six minute walk test (6MWT), and non-contrast CT chest images were obtained. CT images were analyzed using CT:VQ software, which estimates ventilation and perfusion parameters in lung tissue by analyzing mapped CT derived Hounsfield units within paired non-contrast inspiratory and expiratory CT images. Variables were analyzed using the Mann Whitney U test and results were reported as median and interquartile range.

Seven individuals with PASC and dyspnea were compared to 18 individuals with no dyspnea. Those with dyspnea were older and had a lower perception of their own current overall health as assessed by the EQ-5D-5L questionnaire (Table 5). Baseline PFTs and 6MW distance were normal and were not significantly different between the 2 groups. Despite relatively unremarkable baseline inspiratory CT chest imaging, perfusion heterogeneity and perfusion defect percent were significantly higher in the dyspnea compared to the non-dyspnea cohort.

Individuals with PASC and dyspnea demonstrate normal conventional CT chest imaging and pulmonary function testing but may have underlying perfusion abnormalities that can be detected with non contrast chest imaging using CT:VQ software. These observations are consistent with emerging evidence from a larger cohort evaluated at Brooke Army Medical Center (BAMC), which enrolled 35 healthy, active individuals with persistent dyspnea at least three months after COVID-19 infection. In that study, high-resolution CT:VQ analysis similarly revealed functional abnormalities (perfusion defects and heterogeneity) despite normal PFTs (Table 5). These findings reinforce that subtle regional ventilation and gas-exchange impairments may persist undetected by standard testing.

Taken together, results from both the Tufts and BAMC cohorts support the growing recognition that post COVID respiratory symptoms may reflect regional ventilation or perfusion abnormalities that are not evident on conventional PFTs or standard CT interpretation. Additional study and expanded multi-site analyses are warranted to confirm these physiologic signatures, understand their mechanisms, and determine their clinical significance.

	BAMC Dyspnea Cohort (N=68)	Tufts PASC Dyspnea Cohort (N=7)	Tufts No Dyspnea Cohort (N=18)	P-value (Tufts patients)
Age, years	-	**55 (53.5 - 62)**	**29 (23.3 - 47.3)**	**0.014**
Height, cm	-	162.6 (160 - 167.6)	163.8 (160 - 172.1)	0.951
Weight, Kg	-	74.8 (65.3 - 80.5)	70.3 (63.6 - 78.2)	0.649
BMI	-	27.5 (25 - 29.2)	25.8 (24 - 27.3)	0.36
EQ-5D-5L	-	**50 (27 - 66)**	**84 (75 - 92.5)**	**0.005**
FVC, %	96 (90-105)	113 (95.5 - 123)	114 (96 - 125)	0.785
FEV1, %	91 (82-101)	106 (94 - 123)	106 (95 - 112)	0.69
FEV1/FVC ratio, %	77 (73-83)	75 (71.5 - 82)	80 (72.3 - 84.8)	0.59
TLC, %	96.1 (89-105)	97 (85.5 - 100.5)	102.5 (88.3 - 108.8)	0.237
DLCO, %	86.7 (74.7-95.2)	91 (77.5 - 104)	102.5 (95.3 - 107.5)	0.164
6MWD, %		90 (78.5 - 92.5)	75.5 (62 - 82)	0.32
End Inspiratory Volume, L	4.9 (3.8-5.8)	4.7 (3.7 - 5.1)	4.6 (3.8 - 6.2)	0.53
End Expiratory Volume, L	2.5 (2.1-3.2)	2.2 (1.9 - 2.4)	2.2 (1.6 - 2.7)	0.98
Volume Change, L	2.0 (1.5-2.8)	2.4 (1.4 - 2.8)	2.4 (1.9 - 3.4)	0.389
Mean Specific Ventilation	0.64 (0.4-0.7)	0.7 (0.6 - 1)	1 (0.7 - 1.2)	0.5
Ventilation Heterogeneity	55.4 (46.7-60.7)	47.7 (42 - 55.3)	44.9 (40.4 - 49.5)	0.62
Ventilation Defect Percent	15.9 (12.9-18.7)	10.6 (9.3 - 13.9)	11.2 (8.7 - 12.7)	0.93
Perfusion Heterogeneity	36.1 (29.8-40.4)	**38.6 (34.5 - 45.2)**	**32 (29.1 - 36.4)**	**0.047**
Perfusion Defect Percent	4.10 (1.9-7.1)	**3.6 (2.6 - 5)**	**1.4 (0.3 - 3)**	**0.04**

Table 5: *Patient demographics and CT:VQ metrics compared between the two cohorts.*

3. FUTURE DIRECTIONS IN CT:VQ: PERFUSION DEFECTS, V/Q MISMATCH, AND COLLATERAL VENTILATION

3.1 Automated Pulmonary Embolism Detection[1]

- **For PE assessment, a highly sensitive, screening/triage approach is being tested and could augment current PE imaging where contrast or nuclear resources are limited.**
- **CT:VQ's non-contrast perfusion mapping detected perfusion defects with AUC 0.90 and 100% sensitivity.**

The current diagnostic pathway for pulmonary embolism (PE) is marked by overuse in low-risk patients and under-diagnosis in high-risk settings. Since 2004, CT pulmonary angiography (CTPA) utilization has increased by roughly 450%, while diagnostic yield has fallen from ~15% to 3–10% across large networks meaning most patients undergo iodinated contrast exposure without PE confirmation. At the same time, constraints on serial contrast imaging in renal impairment contribute to missed disease in hospitalized populations, with reports of 53.6% misdiagnosis and autopsy studies showing undiagnosed PE in 37.9% of ICU deaths. These inefficiencies are amplified by the limited specificity of D-dimer testing in groups that critically need accurate triage such as oncology patients (~9-fold higher PE risk) and in pregnancy, where PE accounts for 9–15% of maternal mortality. Concerns about contrast load and radiation in these populations can delay treatment, while technical pitfalls (e.g., suboptimal bolus timing) and nuclear medicine logistics further impede care. Together, these gaps underscore the need for an anatomically precise, scalable diagnostic modality that preserves accuracy while reducing reliance on iodinated contrast. CT:VQ, which extracts regional ventilation and perfusion information from standard breath-hold CT scans, offers the potential to identify perfusion defects without intravenous contrast or radiotracers.

In this preliminary study, CT:VQ perfusion images were used to investigate a fully automated approach for pulmonary embolism detection. Fifty-eight participants were included: individuals with radiologist-confirmed PE (n=12), healthy controls (n=17), and subjects with COPD (n=29). All underwent paired inspiratory and expiratory CT imaging, from which CT:VQ computed 3D perfusion maps. An example from a subject with a confirmed right middle lobe PE along with CT:VQ outputs is shown in **Figure 6**. Automated in-house proprietary algorithms were then applied to the CT:VQ outputs to identify perfusion defects.

The CT:VQ-based model demonstrated strong early diagnostic performance. It achieved an AUC of 0.90 and correctly identified every subject with confirmed PE, resulting in 100% sensitivity. Importantly, the algorithm produced three dimensional visualizations of suspected embolic regions, enabling clear localization of perfusion defects often consistent with known embolic anatomy. These outputs highlight the potential diagnostic value of CT:VQ, particularly for detecting subsegmental or regional perfusion deficits.

Taken together, the findings suggest that automated PE detection from non-contrast CT perfusion maps is feasible, highly sensitive, and capable of highlighting specific lung regions affected by perfusion abnormalities. By removing reliance on contrast material and nuclear imaging workflows, CT:VQ offers a scalable pathway for PE assessment that could expand access in settings where traditional imaging is constrained. With further clinical validation, this approach may evolve into a practical, rapid, and low-risk screening or triage tool, augmenting rather than replacing existing imaging standards and supporting faster decision-making in acute care environments.

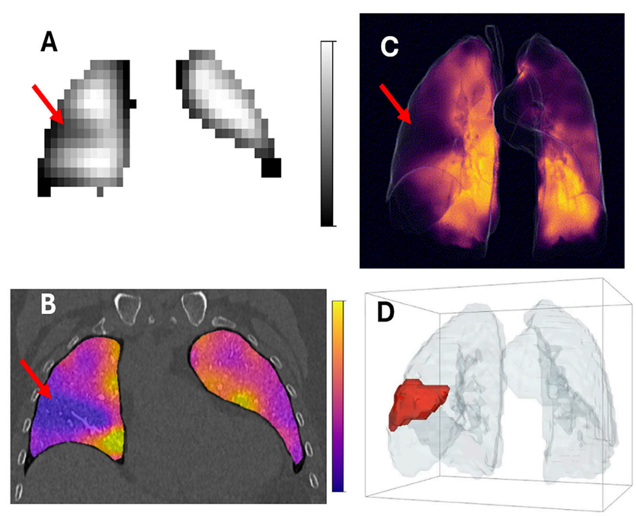


Fig 6: *Example from a subject with a confirmed right middle lobe PE (red arrows point to the PE). A) Nuclear medicine SPECT coronal slice displaying the PE defect. B) CT:VQ coronal slice displaying the PE defect. C) 3D perfusion render from CT:VQ. D) PE model output for PE defect as 3D rendering (red).*

3.2 3D V/Q Mismatch Detection and Correlation with Gas Transfer[1]

- **CT:VQ classification identified shunts, dead space, and matched defects with 3D maps detailing regional functional lung impairment.**
- **V/Q abnormal fractions from CT:VQ correlated strongly with DLCO indicating CT-derived metrics reflect gas-exchange deficits.**
- **CT:VQ distinguished disease phenotypes thereby supporting routine, non-contrast functional lung mapping and more personalized treatment planning.**

Ventilation–perfusion matching is a fundamental requirement for efficient pulmonary gas exchange, and disruptions in this relationship can profoundly impair respiratory function. Historically, evaluating V/Q matching has required nuclear medicine ventilation perfusion imaging or contrast-based modalities, each of which presents limitations related to spatial resolution, availability, cost, radiation exposure, and workflow complexity. Using CT:VQ, it is possible to extract quantitative ventilation and perfusion information from paired non-contrast inspiratory and expiratory CT scans, enabling the generation of fully three-dimensional V/Q maps without the need for radiotracers or contrast agents. To evaluate the clinical utility of using CT:VQ to assess V/Q mismatch, CT:VQ-derived ventilation and perfusion values were combined voxel by voxel to classify lung tissue into physiologically meaningful categories reflecting shunt, dead space, and matched defects. Shunt was defined as preserved perfusion with impaired ventilation, dead space as preserved ventilation with impaired perfusion, and matched defects as concurrent reductions in both processes. These maps provided a detailed depiction of regional functional impairment across the lungs (**Figure 7**).

Across the entire cohort of 46 patients, the proportion of lung identified as shunt or dead space demonstrated significant correlations with DLCO ($p < 0.001$). The most robust association was observed when shunt, dead space, and matched defects were combined into a single abnormal category as total V/Q abnormal fraction, which explained a substantial portion of the variability in DLCO ($r^2 = 0.68$, $p < 0.001$, **Figure 7D**). This relationship indicates that the CT-derived V/Q metrics reflect underlying physiologic impairment and capture the functional consequences of ventilation or perfusion deficits.

The functional characterization offered by CT:VQ also revealed important differences between patient groups. Individuals undergoing assessment for pulmonary intervention exhibited markedly higher levels of shunt, dead space, and matched defects compared with participants with subacute PE or chronic lung disease, consistent with their more advanced regional dysfunction. These imaging findings demonstrate that CT-based V/Q mapping can discriminate between disease phenotypes and identify the severity and distribution of physiologic impairment with high spatial detail.

Taken together, these results show that ventilation–perfusion matching can be derived directly from standard, non-contrast CT scans and that the resulting metrics reflect clinically meaningful deficits in gas exchange. By visualizing the distribution of V/Q mismatch throughout the lungs, CT:VQ extends CT imaging beyond structural assessment and into functional characterization, enabling more precise evaluation of respiratory disease. This capability provides an opportunity to integrate functional lung mapping into routine clinical workflows and to support more personalized treatment planning, particularly in conditions where regional heterogeneity drives symptoms and therapeutic response.

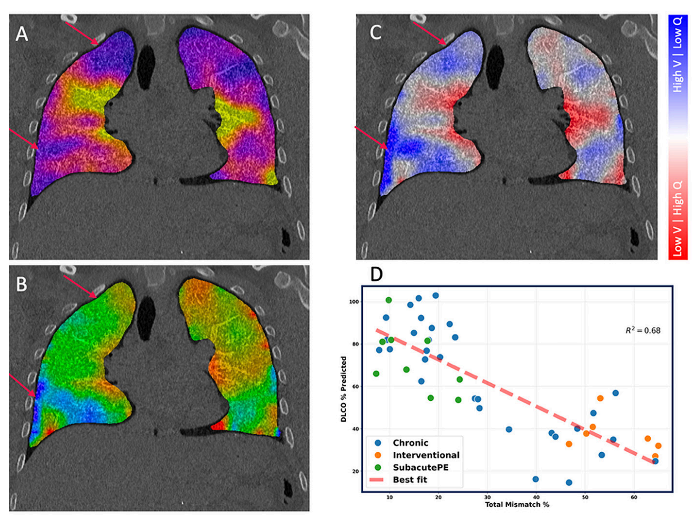


Fig 7: *Example from a subject with confirmed PE in the right upper lobe and right middle lobe (red arrows).* ***A)*** *Perfusion image from CT:VQ.* ***B)*** *Ventilation image from CT:VQ.* ***C)*** *VQ matching image derived from CT:VQ.* ***D)*** *Relationship between total mismatch defects and DLCO in the cohort.*

3.3 Advanced Collateral Ventilation Prediction in BLVR Planning[1]

- **BLVR success depends on lack of collateral ventilation (CV); current gold standard CV assessment (Chartis) is invasive and sometimes inconclusive.**
- **CT:VQ measurements fed into a model validated against Chartis resulted in 97% accuracy (AUC 0.94; sensitivity 0.90; specificity 1.0)**
- **Individualized CV prediction enables more confident BLVR candidate selection.**

Bronchoscopic lung volume reduction (BLVR) has emerged as a less invasive alternative to surgical interventions for advanced emphysema, relying on one-way endobronchial valves to induce lobar collapse and reduce hyperinflation. Yet, the success of BLVR hinges on the absence of collateral ventilation (CV), airflow that bypasses the target airway through incomplete fissures and prevents effective collapse. Although the Chartis system is currently the clinical gold standard for CV evaluation, it requires an invasive bronchoscopic procedure and is not always feasible or conclusive. There is growing interest in determining whether advanced imaging modalities can offer a more accessible, non-invasive, and reliable means of predicting CV before a patient is brought to the bronchoscopy suite.

This prospective study explored whether CT:VQ could improve pre-procedural CV assessment. Thirty adults undergoing evaluation for BLVR completed paired inspiratory and expiratory CT scans. Measurements from CT:VQ were used to predict the probability of each lobe boundary being CV-positive.

The imaging approach, assessed against Chartis, yielded a high predictive accuracy, where the model identified CV+ and CV- subjects with 97% accuracy, achieving an AUC of 0.94, sensitivity of 0.90, and specificity of 1.0 (Figure 8). Repeated stratified k-fold validation produced a stable mean accuracy of 94%, reinforcing the robustness of the result. Beyond its quantitative strength, the model generated individualized probability estimates of CV, enabling a clearer understanding of which fissures, and which patients, were at highest risk of valve treatment failure.

These findings point toward a meaningful shift in BLVR planning. By integrating high-resolution structural and functional information from standard CT scans, clinicians may be able to assess collateral ventilation with a level of precision that rivals invasive testing while eliminating the procedural burden, cost, and uncertainty associated with bronchoscopic assessment. As BLVR continues to expand as a therapeutic option for emphysema, these imaging-based methods offer a pathway to more confident patient selection, more predictable outcomes, and a more streamlined workflow across interventional pulmonology programs.

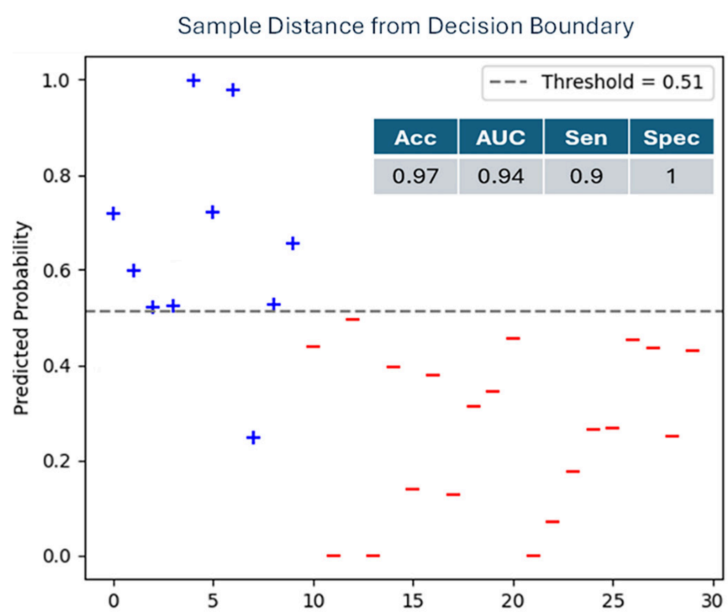


Fig 8: *The predicted probability of each subject being CV-positive (+) based on the model. Blue crosses represent CV-positive individuals, while red dashes(-) individuals as per Chartis.*

4. QUANTITATIVE CT-BASED PREDICTORS OF LVRS OUTCOMES[6]

- **LVRS outcomes are variable and current selection tools (visual CT, perfusion scintigraphy) lack robust, actionable thresholds.**
- **Pre-op signature of high upper-zone emphysema plus very low upper-zone CT:VQ perfusion identified patients more likely to improve FEV1, DLCO, and 6MWD.**
- **Combined CT thresholds outperformed traditional measures and raised the LVRS response rate.**

Lung volume reduction surgery (LVRS) remains one of the few interventions capable of producing substantial physiological and quality-of-life improvements for patients with advanced emphysema. Yet, despite the clear potential benefit, response to LVRS is highly variable, and selecting patients who will truly benefit from the procedure continues to challenge clinicians. Traditional selection methods, including visual CT assessment and nuclear medicine perfusion scintigraphy, provide only partial insight and lack validated thresholds for decision-making. As care teams increasingly seek tools that can identify patients most likely to improve, CT:VQ in combination with functional Lung Density Analysis (LDAf) offers a promising pathway to improved patient selection.

In this preliminary study, fifty individuals with upper-lobe–predominant emphysema who underwent bilateral LVRS were retrospectively evaluated using paired inspiratory and expiratory non-contrast CT scans. These imaging data enabled computation of both structural disease burden and functional perfusion patterns across lung zones. The goal was to determine whether specific CT:VQ and LDAf signatures could reliably predict which patients would achieve clinically meaningful improvement in FEV1 following surgery.

Patients who experienced significant post-operative improvement, defined as a ≥ 250 mL gain in FEV1, consistently demonstrated two defining features prior to surgery: high upper-zone emphysema and markedly low upper-zone perfusion. When evaluated together, these parameters identified a subgroup with substantially higher likelihood of improvement in FEV1, DLCO, and six-minute walk distance (Figure 9). Using the combined CT thresholds (≥ 50% upper-zone emphysema and ≤ 8% upper-zone perfusion) improved the procedure response rate from 46% to 76%. These results also align with prior interventional studies showing that severely perfusion-deficient upper lobes are more responsive to volume reduction.

Beyond predictive performance, the study highlights the practical value of a CT-only evaluation workflow. Because both LDAf and CT:VQ metrics are derived from standard non-contrast CT scans, this approach eliminates reliance on nuclear perfusion imaging, reduces time and cost, and streamlines the pre-operative work-up. By providing high-resolution, zone-specific quantification of both emphysema burden and perfusion, CT-based evaluation offers a more holistic representation of regional lung dysfunction, an essential factor in determining whether volume reduction will meaningfully restore respiratory mechanics.

In summary, this work demonstrates that combined CT-derived emphysema and perfusion metrics can substantially strengthen LVRS patient selection. The approach identifies a physiologically compelling signature, structurally destroyed and functionally under-perfused upper lobes, that corresponds to improved post-operative outcomes. While larger multicenter validation will be valuable, these findings point toward a more precise, scalable, and clinically practical pathway for LVRS decision-support, positioning quantitative CT as a powerful tool for guiding high-stakes therapeutic interventions.

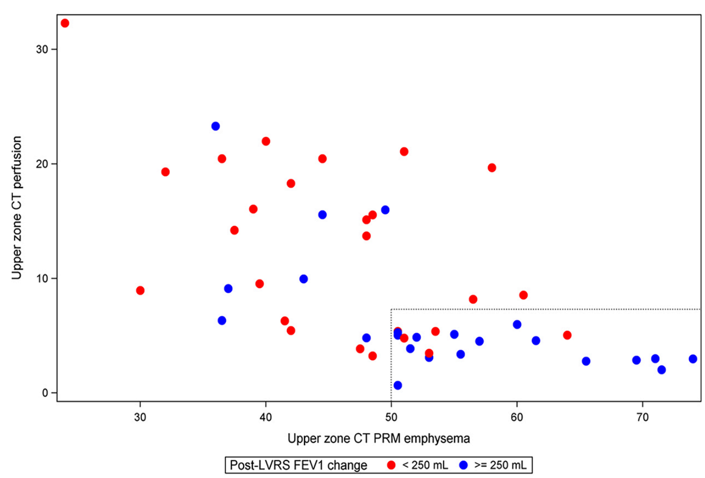


Fig 9: *Post-LVRS FEV1 improvement as function of upper zone quantitative emphysema and upper zone CT:VQ relative perfusion.*

5. CASE STUDIES AND CLINICAL VIGNETTES

Thromboembolic Conditions

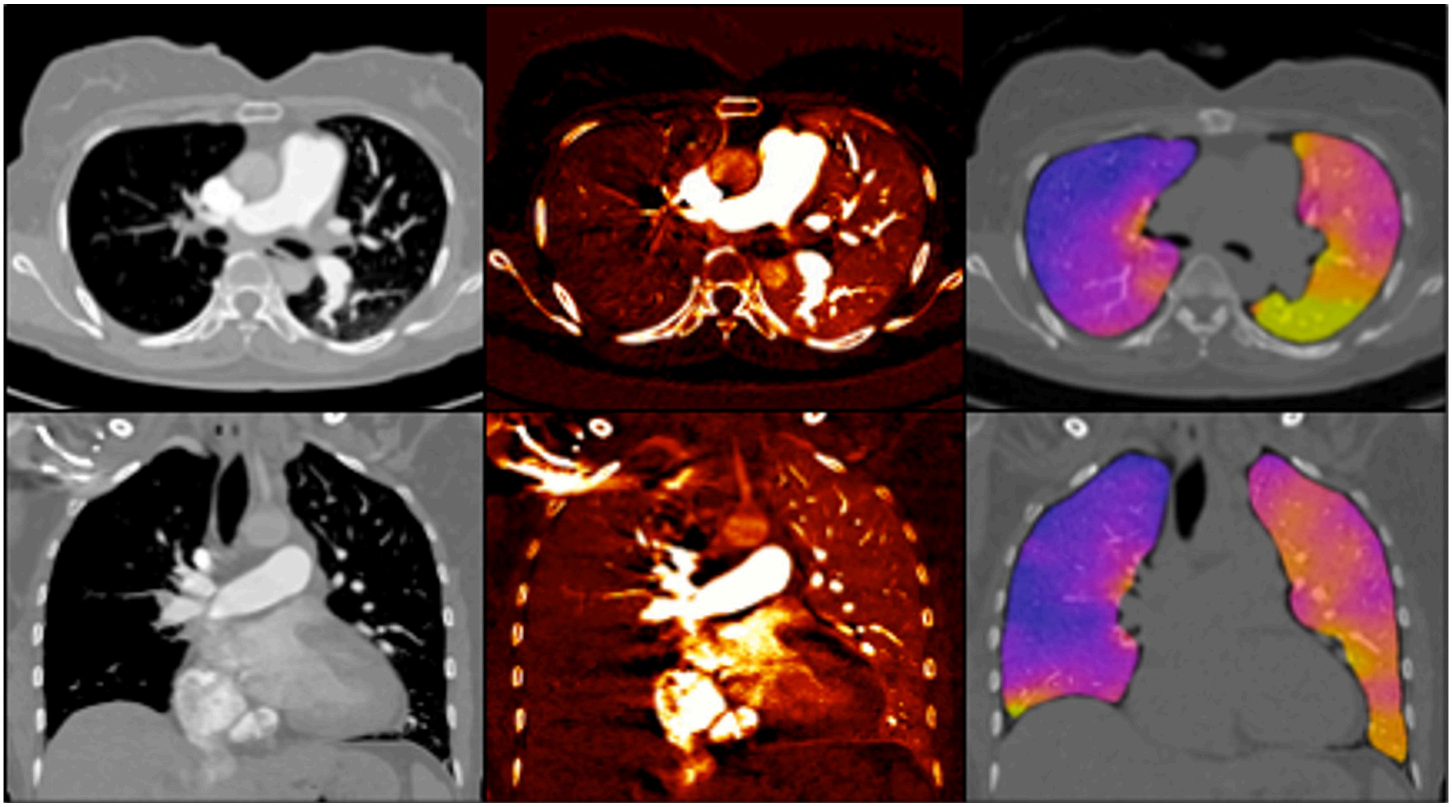


Fig 10: *CTEPH with distal right chronic PE and proximal stricture in Right PA: Axial and coronal CTPA, DECT, and Non-contrast CT:VQ images (acquired prior to contrast injection) showing strong correlation of reduced right lung perfusion.*

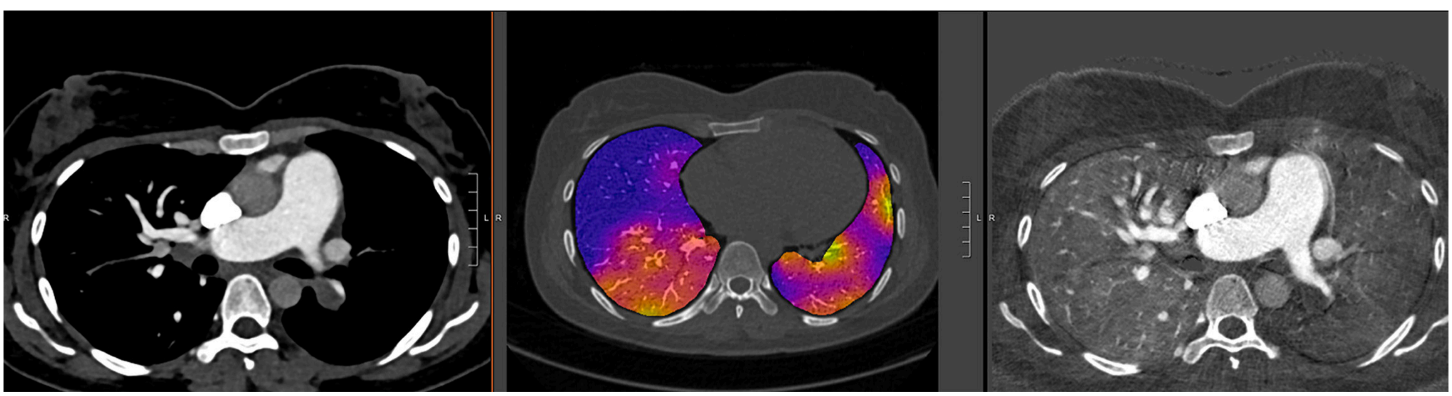
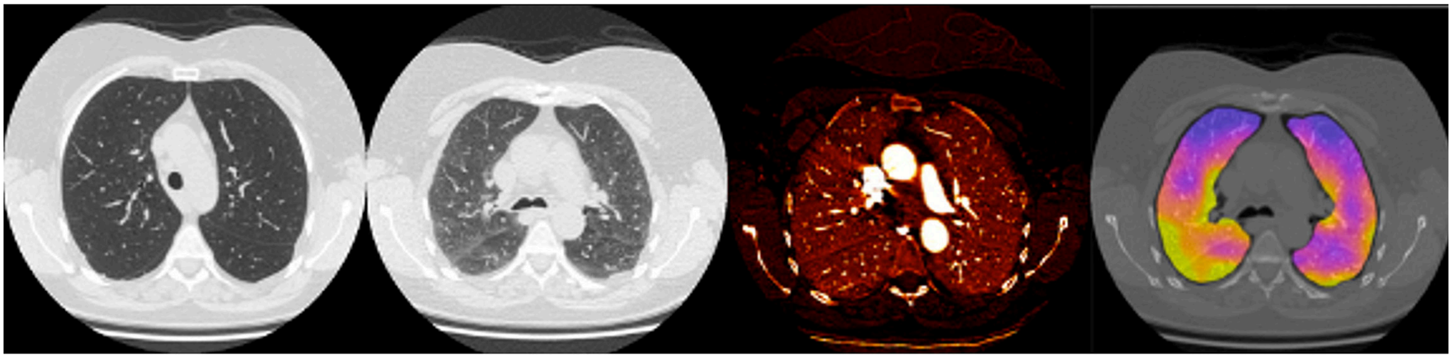
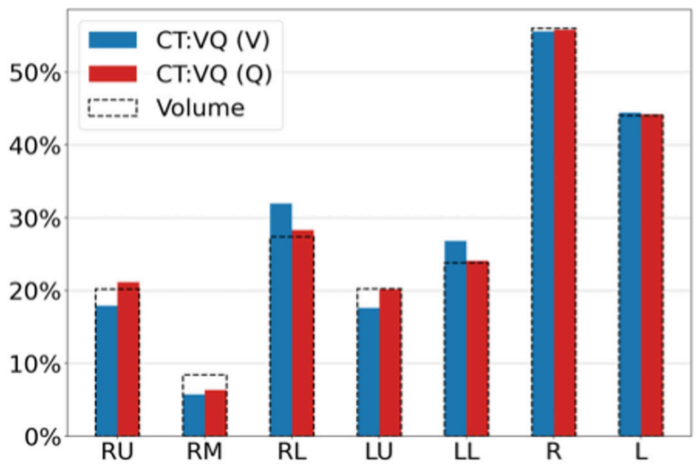


Fig 11: *CTEPH with large subacute left thrombus and chronic right thrombus and narrowing: Axial CTPA, Non-Contrast CT:VQ, and DECT images.*

Thromboembolic Conditions



Lobar Distribution



	Lobe Size	Ventilation	Perfusion
RUL	20.2%	17.9%	21.2%
RML	8.4%	5.7%	6.3%
RLL	27.4%	31.9%	28.3%
LUL	20.2%	17.6%	20.1%
LLL	23.8%	26.8%	24.1%

	Lobe Size	Ventilation	Perfusion
Right	56.0%	55.6%	55.8%
Left	44.0%	44.4%	44.2%

Fig 12: *Axial standard CT, DECT, and CT:VQ quantitative report in patient ruled out for PE or chronic lung disease showing well matched ventilation and perfusion qualitatively and quantitatively.*

Chronic Disease/Pulmonary Interventions

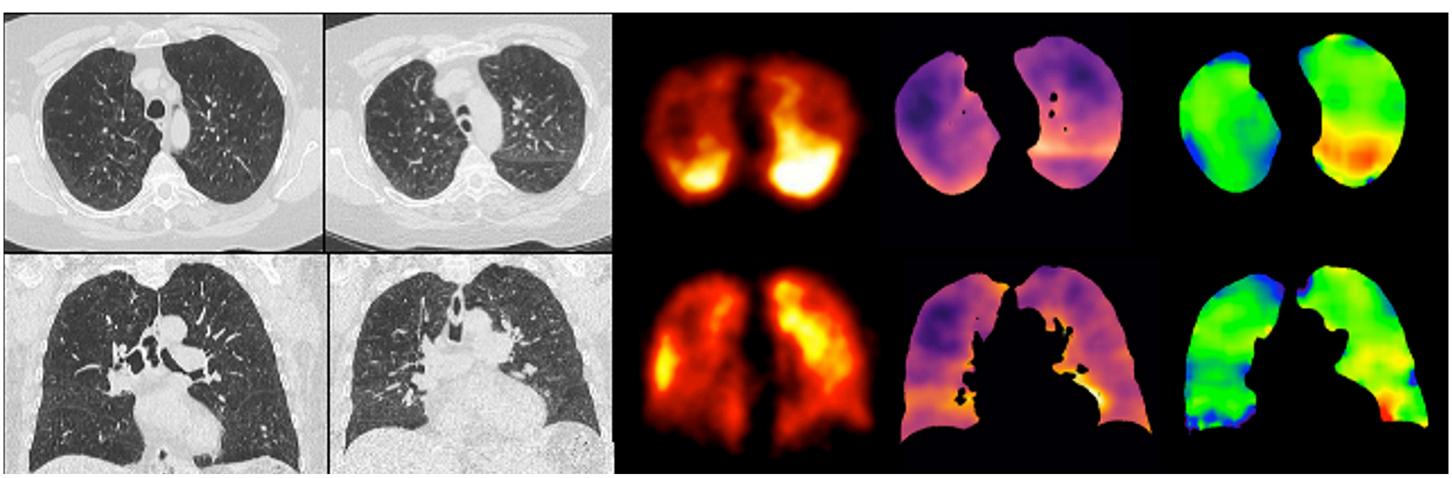


Fig 13: *HRCT-derived CT-VQ image show improved assessment of target lobes Bronchoscopic Lung Volume Reduction (BLVR) compared to SPECT VQ without the use of injected or inhaled contrast.*

Chronic Disease/Pulmonary Interventions

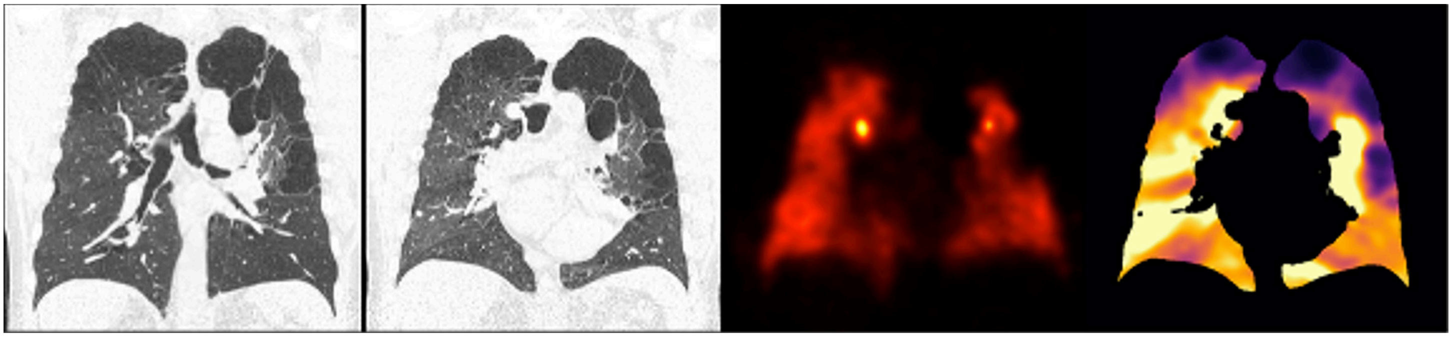


Fig 14: *Standard assessment of pre-operative Lung Volume Reduction Surgery (LVRS) patients combining quantitative emphysema and perfusion assessment from routine non-contrast CT predict improved outcomes compared to SPECT.*

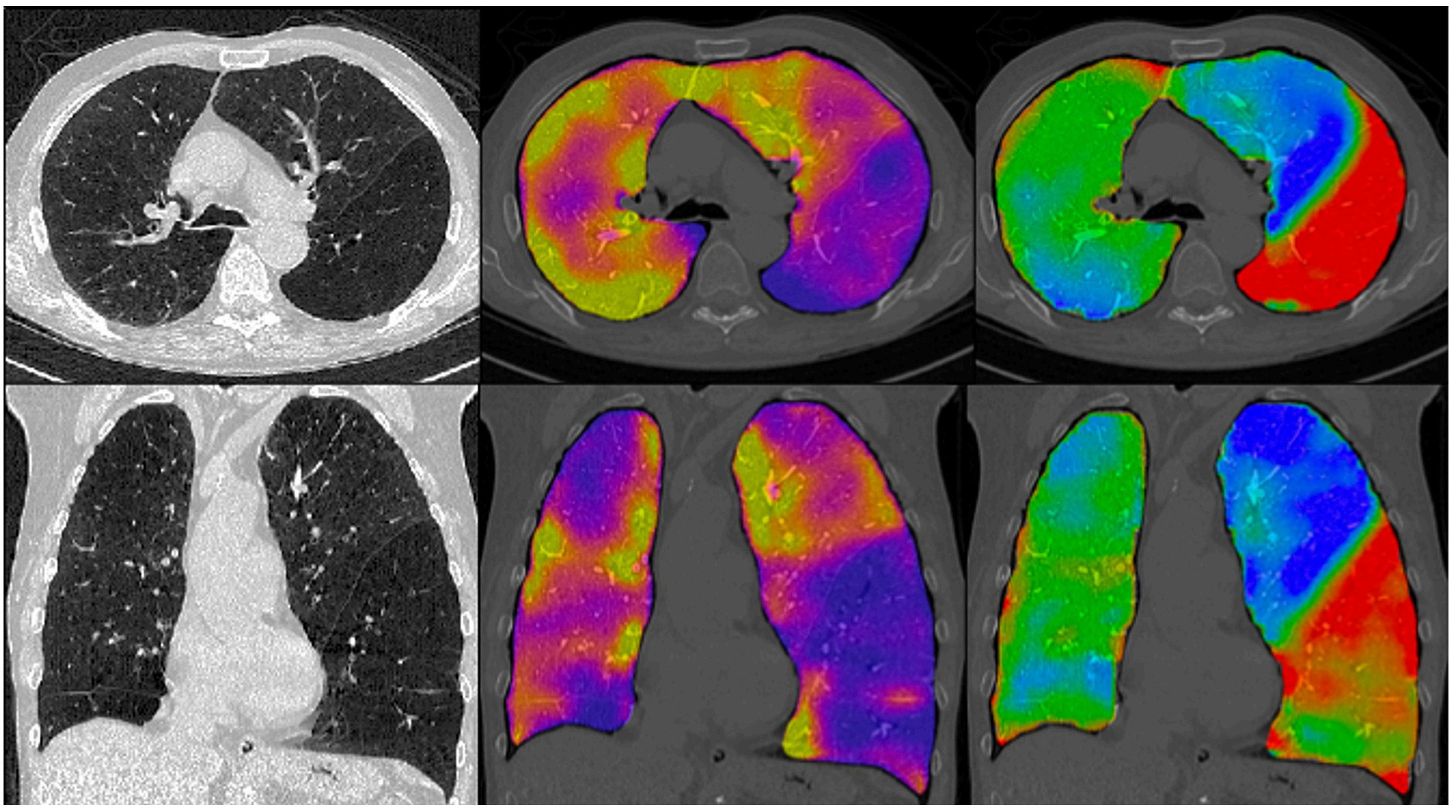


Fig 15: *COPD Emphysema Left lower lobe Coronal and axial non-contrast images in patient COPD with LLL emphysema and enlargement showing matching VQ defect, but unexpected significant perfusion defect and resulting dead space in RUL driving optimal interventional strategy.*

6. CONCLUSION

CT:VQ represents a novel, transformative step in thoracic imaging, replacing tracer-based nuclear medicine studies and enabling high-resolution, contrast-free regional pulmonary physiology from routine CT scans. As demonstrated in the studies in this paper, CT:VQ values and images contribute to many clinical areas:

- **Strong correlation with SPECT and DECT perfusion**
- **Superior physiologic sensitivity to gas-exchange impairment**
- **Robust visualization of V/Q mismatch**
- **Accurate automated PE detection**
- **Accurate collateral ventilation prediction**
- **Quantitative enhancements to LVRS and BLVR candidate selection**

CT:VQ technology is both novel and nascent, with the studies listed representing some of the early clinical utility studies. Continued exploration into new applications will unlock new possibilities in thoracic imaging. By unifying structural imaging with physiologic function, CT:VQ stands to redefine how clinicians diagnose, phenotype, and manage pulmonary disease offering a faster, safer, more accessible, and more quantitative alternative to nuclear imaging.

7. REFERENCES

1. Based on accepted peer-reviewed abstract to be pubslished at ATS 2026.
2. Data on file, 4DMedical.
3. Si-Mohamed S, Moreau-Triby C, Tylski P, Tatard-Leitman V, Wdowik Q, Boccalini S, et al. Head-to-head comparison of lung perfusion with dual-energy CT and SPECT-CT. Diagnostic and Interventional Imaging 2020;101:299–310. https://doi.org/10.1016/j.diii.2020.02.006.
4. Strotzer QD, Heidemanns S, Mayr V, Stuerzl R, Meiler S, Schmidt D, et al. Head-to-Head Comparison of Dual-Source and Split-Beam Filter Multi-Energy CT versus SPECT/CT for Assessing Lobar Lung Perfusion in Emphysema. Radiology: Cardiothoracic Imaging 2023;5:e220273. https://doi.org/10.1148/ryct.220273.
5. Doganay O, Matin T, Chen M, Kim M, McIntyre A, McGowan DR, et al. Time-series hyperpolarized xenon-129 MRI of lobar lung ventilation of COPD in comparison to V/Q-SPECT/CT and CT. Eur Radiol 2019;29:4058–67. https://doi.org/10.1007/s00330-018-5888-y.
6. Based on a study currently submitted for peer-review.

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