



Role of quantitative planar lung perfusion scintigraphy and tomography in identifying target lobes in patients with emphysematous phenotype of advanced chronic obstructive pulmonary disease: a retrospective cross-sectional study

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Background: Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease. Despite optimal medical therapy and pulmonary rehabilitation, bronchoscopic and surgical lung volume reduction may still be necessary. Identifying the target lobe is crucial for the success of these treatments. This study aims to compare the role of quantitative planar lung perfusion scintigraphy (QPLPS) with quantitative lung computed tomography (StratX[®]), which is used in identifying the target lobe before the Zephyr[®] endobronchial valve (EBV) placement in patients with the emphysematous phenotype of advanced COPD.

Methods: A single-center retrospective cross-sectional study was performed in the Department of Pulmonology at the University of Health Sciences Turkey, Yedikule Chest Diseases and Thoracic Surgery Education and Research Hospital between June 2019 and June 2022. The study included 46 patients with the emphysematous phenotype of advanced COPD, who were all candidates for Zephyr[®] EBV therapy. The target lobes were assessed using the QPLPS and StratX[®] and the agreement between the methods was analyzed by the Kappa statistic method. Additionally, demographic characteristics, respiratory function tests, distributions of emphysema, and 6-minute walk test results of patients were recorded.

Results: The median age was 67 (42–80) years and 42 (91.3%) were male. In QPLPS, the perfusion percentages were $7.47\% \pm 3.31\%$, $9.59\% \pm 2.67\%$, and $13.32\% \pm 2.59\%$ for the 1st, 2nd and 3rd target lobes, respectively while in StratX[®], the voxel densities were $68.28\% \pm 9.16\%$, $63.79\% \pm 7.42\%$, and $60.69\% \pm 5.35\%$. In StratX[®], the fissure integrity (FI) at the target lobe was $76.25\% \pm 21.18\%$, $84.68\% \pm 17.67\%$, and $86.19\% \pm 13.19\%$, respectively. There was a significant agreement between the methods in identifying the first, second, and third target lobes in all patients (Kappa coefficient: 0.897, 0.700, and 0.522), and also in

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identifying the first and second target lobes in patients with heterogeneous (Kappa coefficient: 0.879, and 0.735), and homogeneous subgroups (Kappa coefficient: 0.919, and 0.672).

Conclusions: There is an agreement between QPLPS and StratX® in identifying the target lobe in patients with severe emphysema, including those with homogeneous diseases. However, StratX® may be preferred, considering that it also predicts FI.

Keywords: Bronchoscopic lung volume reduction (BLVR); chronic obstructive pulmonary disease (COPD); quantitative lung computed tomography (StratX®); quantitative planar lung perfusion scintigraphy (QPLPS)

Submitted Jan 20, 2024. Accepted for publication Jul 15, 2024. Published online Aug 19, 2024.

doi: 10.21037/qims-24-125

View this article at: <https://dx.doi.org/10.21037/qims-24-125>

Introduction

Emphysema is one of the two main phenotypes of advanced chronic obstructive pulmonary disease (COPD) and is characterized by abnormal permanent dilatation of air spaces distal to the terminal bronchioles, accompanied by the destruction of alveolar walls and without any fibrosis and destruction of lung parenchyma with decreasing lung elastic recoil (1). This leads to decreases in gas exchange, changes in airway dynamics, especially expiratory airflow, and hyperinflation. Hyperinflation affects the functioning of respiratory muscles, particularly the diaphragm, leading to reduced inspiratory respiratory muscle strength (2). These conditions can result in fatigue, dyspnea, and exercise intolerance.

Depending on pulmonary hyperinflation severity, it can be treated with bronchodilators, pulmonary rehabilitation, and lung volume reduction interventions. The limited outcomes of current medical treatments and the high postoperative morbidity and mortality rates of surgery in reducing hyperinflation have led to the development of new therapies (3). One of the novel options is bronchoscopic lung volume reduction (BLVR) with valves, coils, biological lung volume reduction, and thermal airway ablation. Randomized controlled trials have shown that BLVR improves pulmonary function, exercise tolerance, and quality of life in patients by reducing hyperinflation (4). Endobronchial valve (EBV), the most researched among BLVR methods, has been proven effective in patients with emphysema without interlobar collateral ventilation (5,6). The development of post-procedural lobar atelectasis has been demonstrated to be associated with survival in patients with EBV placement (7).

In general, an ideal candidate for EBV placement is a patient with severe COPD who has quit smoking,

remains symptomatic despite optimal medical therapy and pulmonary rehabilitation, and exhibits a heterogeneous distribution of emphysema (1). One of the parameters affecting the success of these treatments is the target lobe selection, and selecting the best target lobe avoids serious complications such as severe hypoxia, respiratory failure, and severe pneumothorax (8). Generally, the target lobe is the largest lobe with the highest emphysema score and/or the lobe with the lowest perfusion for heterogeneous or, relatively homogeneous emphysema (9). Current expert panel statements recommend 99mTc perfusion scintigraphy in all patients screened for selection of target lobe before BLVR (10). Quantitative computed tomography (CT) analysis is another method used to identify patients who are more likely to benefit from BLVR, and it has been widely employed in recent years (11).

We aimed to investigate whether there is an agreement between quantitative planar lung perfusion scintigraphy (QPLPS) and quantitative lung computed tomography (StratX®) in the identification of the target lobes. We present this article in accordance with the STROBE reporting checklist (available at <https://qims.amegroups.com/article/view/10.21037/qims-24-125/rc>).

Methods

Study design and setting

This retrospective cross-sectional study was conducted at the Department of Pulmonology in the University of Health Sciences Turkey, Yedikule Chest Diseases and Thoracic Surgery Education and Research Hospital, Istanbul, Turkey, which is a tertiary care center, between June 2019 and June 2022. Our center is one of the prominent referral hospitals in our country for lung volume reduction procedures.

Ethical approval of the study was obtained from the Ethics Committee of Yedikule Chest Diseases and Thoracic Surgery Education and Research Hospital (30.12.2021, Decision No. 2021-177). This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Patient data and records were retrieved from the hospital's automation system. The requirement for written informed consent was waived due to the retrospective nature of the study.

Study population

A total of 482 patients with severe emphysema between June 2019 and June 2022 were retrospectively analyzed. The inclusion criteria were selected as BLVR inclusion criteria, having both QPLPS and StratX[®] assessments, and being able to identify the appropriate target lobe with both methods in our study. BLVR treatment criteria are defined as: being between 40–75 years of age, having forced expiratory volume in 1 second (FEV1) 15–45% of predicted value, residual volume (RV) \geq 150% of predicted values, total lung capacity (TLC) $>$ 100%, partial pressure of arterial carbon dioxide $<$ 50 mmHg, partial pressure of arterial oxygen $>$ 45 mmHg (in room air), diffusing capacity of the lungs for carbon monoxide (DLCO) $>$ 20% of predicted value, the 6-minute walk test (6MWT) of at least 140 meters, systolic pulmonary artery pressure $<$ 50 mmHg in echocardiography, a pulmonary rehabilitation for at least 8 weeks before the procedure and an optimal bronchodilator treatment (12,13).

As exclusion criteria, lung volume reduction exclusion criteria, lack of StratX[®] assessment, and inability to identify an appropriate target lobe with both methods were included. The lung volume reduction exclusion criteria are defined as: ineligible on spirometry or plethysmography, severe conditioning deficiency, the presence of significant bronchiectasis or giant bulla, α 1-antitrypsin deficiency, pulmonary nodule requiring surgery, previous sternotomy or lobectomy, excessive sputum, severe hypoxemia and hypercapnia, pulmonary hypertension, persistent smoking, uncontrolled hypertension, cardiac dysrhythmia, heart failure [left ventricular ejection fraction (LVEF) $<$ 45%], and severe repeated infections of the lower airways (3,13).

Patients were initially excluded based on lung volume reduction exclusion criteria, subsequently evaluated in a multidisciplinary council for BLVR and lung volume reduction surgery (LVRS), and appropriate treatment was planned. The remaining ninety-eight patients, who met the EBV treatment criteria, were evaluated retrospectively. Of

these patients, 54 had QPLPS performed by the referral center and StratX[®] assessments to determine the target lobe before Zephyr[®] EBV placement. Additionally, in 8 patients assessed by both methods, no appropriate target lobe could be identified because all lobes had perfusion percentages greater than 20% (3) and voxel density on the StratX[®] below 50% (14); therefore, these patients were excluded from the study. Ultimately, 46 patients with determined target lobes who met the study criteria were included. A flow diagram is shown in *Figure 1*.

Data collection

Demographic characteristics, dyspnea scores, smoking history, respiratory function test results, distribution of emphysema, 6MWT distances, and QPLPS and StratX[®] reports were collected from electronic medical records.

QPLPS protocol

For perfusion scintigraphy, intravenously injected 99mTc-labeled macroaggregates of human albumin (99mTc-MAA) with a diameter of 15–100 μ m were used for microembolization of pulmonary precapillary arterioles and capillaries. The particle distribution defines regional lung perfusion. 222–370 MBq 99mTc-MAA was given by slow intravenous bolus injection over 30 seconds while the patient breathed normally in the supine position. The perfusion imaging was initiated when the infusion of 99mTc-MAA started. During imaging, patients lay supine and raised their arms above their heads to remain motionless throughout the imaging. Planar imaging was performed with six views (anterior, posterior, left and right posterior oblique, left and right anterior oblique) using General Electric Optima NM/CT 640 dual-head γ -camera (GE Healthcare, Wauwatosa, WI, USA). The γ -camera was equipped with a low-energy high-resolution collimator and included a 64 \times 64 matrix, 1,000 counts per view, with a 20% energy window centered on the 140 keV photopeaks.

Using the six views, regions of interest were obtained for the upper, middle, and lower zones. Counts from each zone were obtained, and thus the relative perfusion for each lobe was approximated. The target lobes were enumerated from the lowest perfusion to the highest perfusion scores.

StratX[®]

Thin-section high-resolution CT (HRCT) examination was

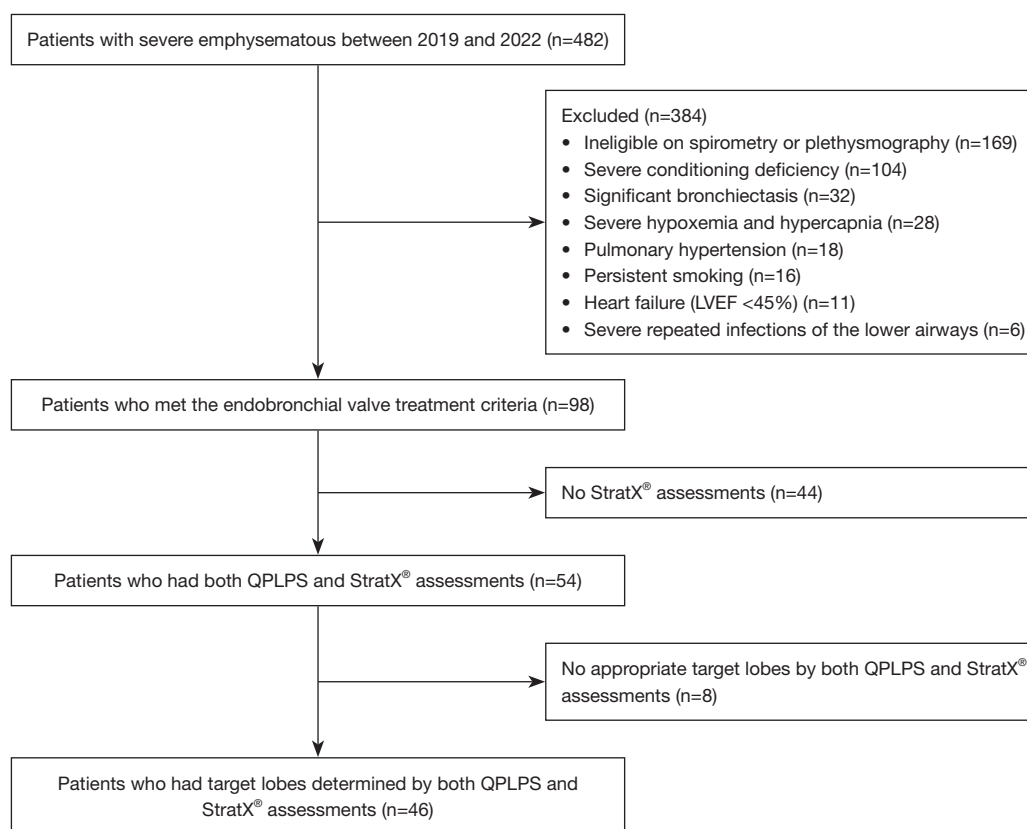


Figure 1 Flow diagram of the patient selection process. LVEF, left ventricular ejection fraction; QPLPS, quantitative planar lung perfusion scintigraphy; StratX®, quantitative lung computed tomography.

used in the selection of the lung lobe for the target lobe. CT scans of all cases were analyzed using the StratX® software. StratX® is a cloud-based quantitative CT analysis service provided by PulmonX Inc. (Redwood City, CA, USA) that gives clinically validated information on emphysema destruction [based on voxel density less than -950 and -910 Hounsfield units (HU)], fissure integrity (FI) and inspiratory volume. The files in the standard digital imaging and communications in medicine format following StratX® CT parameters were uploaded to the StratX® platform (12). The data were analyzed by algorithms yielding a report that is uploaded to the StratX® platform within 2–3 working days. Illustrations summarize voxel density, FI, and inspiratory lobar volume information. The distribution of voxel density was given in percentages for each lobe in the StratX® report and was divided into 4 subgroups: >70% (highest destruction score), 60–70%, 50–60%, and <50% voxel density. The voxel density was enumerated from the highest to the lowest for identification of the target lobe. The zone with the highest emphysematous destruction was considered the first target

lobe. A voxel density of less than 50% was an exclusion criterion for the target lobe. Heterogeneous emphysema was defined as a difference of 15% or greater in the destruction scores between the target lobe and the ipsilateral lobes (14). FI is divided into 3 subgroups: FI ≥95% (continuous black line), FI between 80% and 95% (continuous grey line), and FI <80% (dotted grey line). For the target lower lobes and the left upper lobe, oblique FI scores are utilized, whereas for the right upper lobe, FI is determined by considering the upper half of the right oblique fissure plus the horizontal fissure (Figure 2).

The HRCT and QPLPS images and the emphysematous destruction report of StratX® assessments of a representative patient are provided in Figure 3, and the interlobar FI of HRCT and StratX® images are shown in Figure 4.

Statistical analysis

Data analysis was performed using the SPSS 25 software program. Values were presented in frequency and

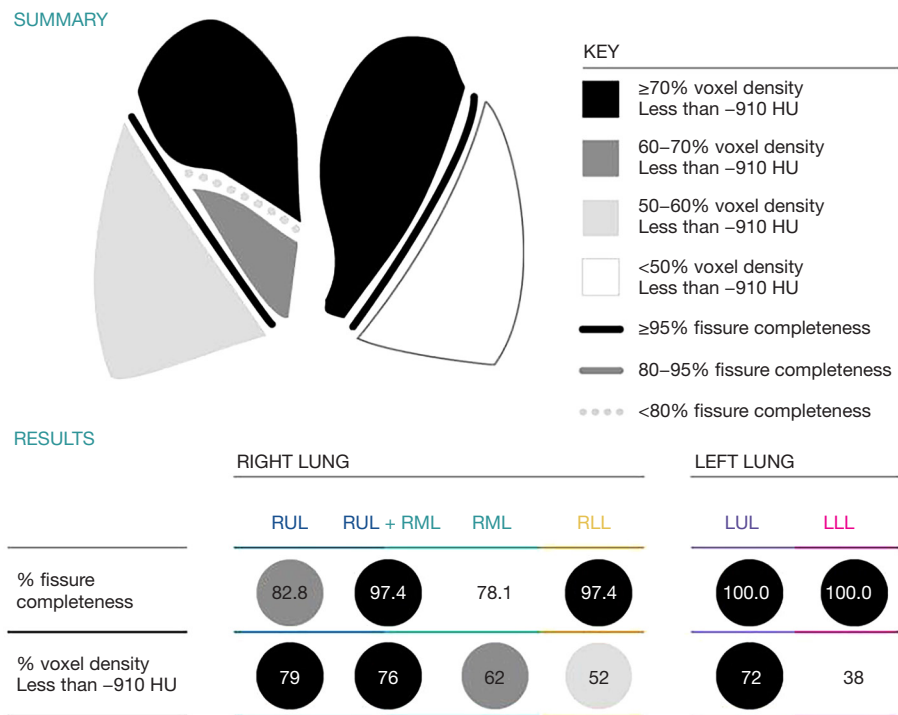


Figure 2 The StratX® lung report of our representative patient with severe emphysema in the bilateral upper lobe predominant and ≥95% complete bilateral major fissures. The black areas represent lobar destruction score values of ≥70% at -910 HU, dark grey areas represent lobar destruction score of 60–70%, light grey areas represent lobar destruction score of 50–60%, white areas represent lobar destruction score of <50%. The continuous black line represents fissures that are ≥95% complete, the continuous grey line represents fissures that are 80–95% complete, and the dotted grey line represents fissures that are below 80% complete. For the target lower lobes and the left upper lobe, oblique FI scores are utilized, whereas for the right upper lobe, FI is determined by considering the upper half of the right oblique fissure plus the horizontal fissure. StratX®, quantitative lung computed tomography; HU, Hounsfield units; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; FI, fissure integrity.

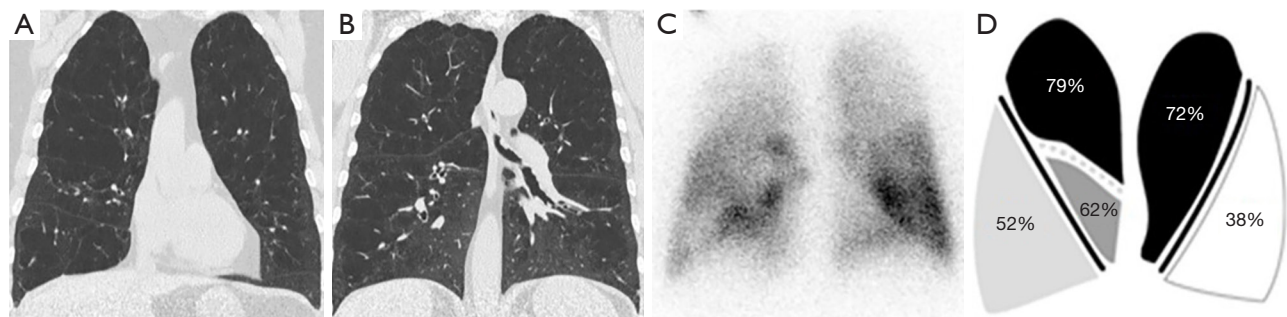


Figure 3 Images of an EBV candidate diagnosed with COPD. These images show severe, bilateral, upper-lobe predominant emphysema with complete major fissures. (A,B) The HRCT images show upper-lobe predominant heterogeneous emphysematous zones. (C) The perfusion scintigraphy shows lower diffusion zones in upper zones. (D) The StratX® lung report shows higher emphysematous destruction percentages (at -910 HU) and fissure integrity in upper lobes. EBV, endobronchial valve; COPD, chronic obstructive pulmonary disease; HRCT, high-resolution computed tomography; StratX®, quantitative lung computed tomography; HU, Hounsfield units.

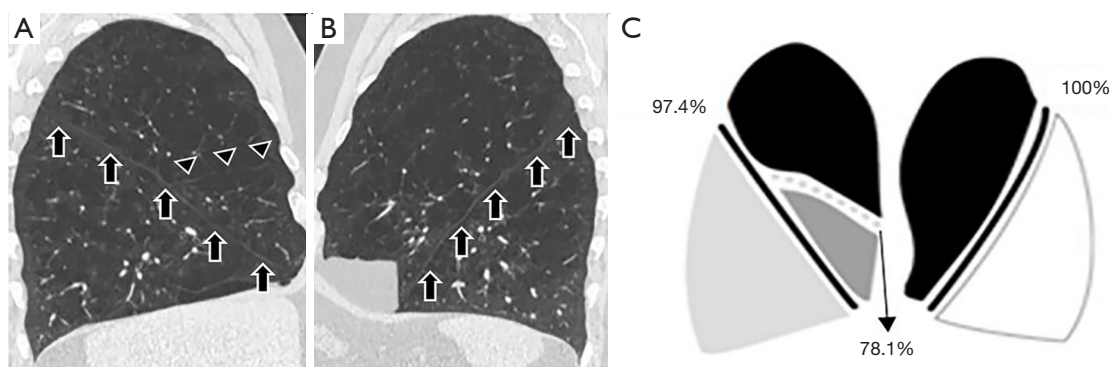


Figure 4 The HRCT and the StratX® images demonstrating interlobar FI. (A) The HRCT image shows visually that the right major fissure is intact (arrows), but the minor fissure is not (arrowheads). (B) The HRCT image shows visually that the left major fissure is intact (arrows). (C) The StratX® lung report shows that bilateral major FI is $\geq 95\%$ (continuous black line), and the right minor FI is $< 80\%$ (dotted grey line). HRCT, high-resolution computed tomography; StratX®, quantitative lung computed tomography; FI, fissure integrity.

Table 1 Demographics and functional characteristics of patients

Parameters	n (%) / median (min-max)
Age (years)	67 (42–80)
Sex (male)	42 (91.3)
Smoking (pack/year)	45 (16–120)
mMRC	3 (2–4)
Pulmonary function test	
FEV1, L	0.82 (0.39–1.82)
FEV1, %	27 (15–45)
FVC, L	2 (0.86–4.64)
FVC, %	54 (22–86)
FEV1/FVC, %	40.5 (28–57.1)
DLCO, mL/min/mmHg	3.29 (1.85–14.43)
DLCO, %	33.5 (22–118)
RV, L	4.94 (3.59–10.04)
RV, %	205 (150–424)
TLC, L	7.24 (5–12.09)
TLC, %	114.5 (102–181)
RV/TLC, %	72 (50–86)
6-minute walking distance (meter)	252.5 (150–480)
Distribution of emphysema*	
Heterogeneous	27 (58.7)
Homogeneous	19 (41.3)
Time after COPD diagnosis (months)	120 (60–264)

*, heterogeneous is defined as the difference in the destruction scores between the target and ipsilateral lobe was 15% or greater. mMRC, modified medical research council; FEV1, forced expiratory volume in 1 second; L, liter; FVC, forced vital capacity; DLCO, diffusing capacity of lungs for carbon monoxide; RV, residual volume; TLC, total lung capacity; COPD, chronic obstructive pulmonary disease.

percentages for categorical variables, and arithmetic mean, standard deviation or median, minimum, and maximum values for quantitative variables. In the absence of a pilot study in the literature related to our research, calculations were performed for the Kappa value corresponding to a moderate-substantial agreement level to determine the minimum sample size required for our study. The calculations indicated that 40 observations need to be included in the sample to achieve a power level of 0.81 ($\alpha=0.05$, $K_0=0$, $K_1=0.4$). The agreement between QPLPS and StratX® was analyzed by the Kappa statistic method. Two-sided P values were calculated, and the type I error rate was set at 0.05.

Results

Forty-six patients who had both QPLPS and StratX® assessments were included in the study. Forty-two (91.3%) patients were male, and the median age was 67 (42–80) years. The demographic characteristics, modified medical research council (mMRC) dyspnea scores, respiratory function test results, 6MWT distances, and distributions of emphysema of the patients were shown in *Table 1*.

Assessment of target lobe by QPLPS and StratX®

The QPLPS and StratX® methods assess four different target lobes for Zephyr® EBV treatment and determine the appropriate lobes. However, since the fourth target lobe could only be determined in two patients using these two methods, a separate kappa analysis for the fourth target

Table 2 Mean quantitative planar lung perfusion scintigraphy and StratX® values by target lobes

Method	Target lobe	Mean ± SD
Quantitative planar lung perfusion scintigraphy (% of pulmonary perfusion)	1st target lobe	7.47±3.31
	2nd target lobe	9.59±2.67
	3rd target lobe	13.32±2.59
StratX® (% voxel density less than <-910 HU)	1st target lobe	68.28±9.16
	2nd target lobe	63.79±7.42
	3rd target lobe	60.69±5.35

StratX®, quantitative lung computed tomography; SD, standard deviation; HU, Hounsfield units.

Table 3 Comparison between quantitative planar lung perfusion scintigraphy and StratX® for identification of target lobe

Quantitative planar lung perfusion scintigraphy	StratX®				Kappa coefficient	P value
	RUL	RLL	LUL	LLL		
1st target lobe (n=46)					0.897	<0.001*
RUL, n	24 [†]	0	1	0		
RLL, n	0	6 [†]	0	0		
LUL, n	1	1	5 [†]	0		
LLL, n	0	0	0	8 [†]		
2nd target lobe (n=42)					0.700	<0.001*
RUL, n	4 [†]	0	1	2		
RLL, n	2	5 [†]	1	0		
LUL, n	0	0	13 [†]	2		
LLL, n	0	0	1	11 [†]		
3rd target lobe (n=20)					0.522	<0.001*
RUL, n	3 [†]	0	2	0		
RLL, n	0	3 [†]	1	0		
LUL, n	0	3	4 [†]	0		
LLL, n	0	0	1	3 [†]		

*, indicates statistical significance; †, the values for which the target lobes determined by both methods were in agreement. StratX®, quantitative lung computed tomography; RUL, right upper lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; n, number of determined target lobes.

lobe was not conducted due to the limited number of cases. According to the QPLPS results, the involvement of the first, second, and third target lobes in perfusion

was 7.47%±3.31%, 9.59%±2.67%, and 13.32%±2.59%, respectively. As assessed by the StratX® results, the mean voxel density for the first, second, and third target lobes was 68.28%±9.16%, 63.79%±7.42%, and 60.69%±5.35%, respectively. The QPLPS and StratX® values selected based on the final target lobes are shown in *Table 2*. In StratX®, the FI of the target lobes was 76.25%±21.18%, 84.68%±17.67%, and 86.19%±13.19%, respectively.

Identified of target lobe by QPLPS and StratX®

The most common target lobes identified by both methods were the right upper lobe for the first target lobe and the left upper lobe for the second and third target lobes. The agreement between QPLPS and StratX® values for three different target lobes is shown in *Table 3*. StratX® results are presented according to the QPLPS results, and the number of target lobes identified is given. However, 43 out of 46 lobes (93.5%) in the first target lobe, 33 out of 42 lobes (78.6%) in the second target lobe, and 13 out of 20 lobes (65%) in the third target lobe were observed to be consistent. Furthermore, there was a statistically significant agreement between the methods in identifying the first, second, and third target lobes ($P<0.001$; Kappa coefficient: 0.897, 0.700, and 0.522, respectively). When target lobes were categorized according to emphysema heterogeneity, it was observed that there was a statistically significant agreement between the methods for target lobes in patients with both heterogeneous and homogeneous subgroups (*Tables 4, 5*).

BLVR treatment and follow-up

During the study period, the BLVR procedure could not be performed on 26 patients due to the coronavirus disease 2019 pandemic. Twenty patients were evaluated for Zephyr® EBV placement during the bronchoscopic procedure. In 5 cases, the Zephyr® EBV placement was canceled due to collateral ventilation observed in the Chartist™ Pulmonary Assessment System measurement and these patients had FI of less than 80% on StratX®.

Among the remaining 15 patients having no collateral ventilation, Zephyr® EBV was placed in 10 patients with FI ≥95% on StratX®. While 7 patients developed complete lobar atelectasis, 2 patients exhibited lung volume reduction without complete lobar atelectasis. In the remaining patient, no volume reduction was observed.

In 4 patients with FI between 80-95% on StratX®, Zephyr® EBV was placed, and complete lobar atelectasis

Table 4 Comparison between quantitative planar lung perfusion scintigraphy and StratX® for identification of target lobe in patients with heterogeneous emphysema

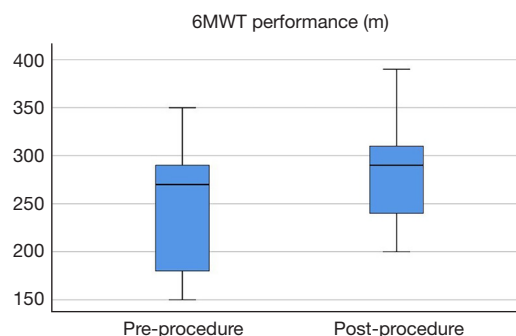
Quantitative planar lung perfusion scintigraphy	StratX [®]				Kappa coefficient	P value
	RUL	RLL	LUL	LLL		
1st target lobe (n=27)					0.879	<0.001*
RUL, n	15 [†]	0	0	0		
RLL, n	0	4 [†]	0	0		
LUL, n	1	1	3 [†]	0		
LLL, n	0	0	0	3 [†]		
2nd target lobe (n=16)					0.735	<0.001*
RUL, n	3 [†]	0	0	1		
RLL, n	1	1 [†]	0	0		
LUL, n	0	0	6 [†]	1		
LLL, n	0	0	0	3 [†]		

*, indicates statistical significance; †, the values for which the target lobes determined by both methods were in agreement. StratX®, quantitative lung computed tomography; RUL, right upper lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; n, number of determined target lobes.

Table 5 Comparison between quantitative planar lung perfusion scintigraphy and StratX® for identification of target lobe in patients with homogeneous emphysema

Quantitative planar lung perfusion scintigraphy	StratX [®]				Kappa coefficient	P value
	RUL	RLL	LUL	LLL		
1st target lobe (n=19)					0.919	<0.001*
RUL, n	9 [†]	0	1	0		
RLL, n	0	2 [†]	0	0		
LUL, n	0	0	2 [†]	0		
LLL, n	0	0	0	5 [†]		
2nd target lobe (n=26)					0.672	<0.001*
RUL, n	1 [†]	0	1	1		
RLL, n	1	4 [†]	1	0		
LUL, n	0	0	7 [†]	1		
LLL, n	0	0	1	8 [†]		

*, indicates statistical significance; †, the values for which the target lobes determined by both methods were in agreement. StratX®, quantitative lung computed tomography; RUL, right upper lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; n, number of determined target lobes.

**Figure 5** Boxplot illustrating pre- and post-procedural distances in the 6MWT. 6MWT, 6-minute walk test.

developed in 2 patients. In the remaining two patients, no volume reduction was observed.

The remaining patient with FI <80% on StratX®, Zephyr® EBV was placed. However, this patient was lost to follow-up and could not be evaluated for atelectasis.

The pre-procedural median mMRC score was 3 [2–4], and the average for the 6MWT distance was 247.14±64.77 meters for the 14 patients who underwent EBV placement. The pre-procedural mean values for FEV1 (liters, L), FEV1 (%), forced vital capacity (FVC) (L), and FVC (%) were 0.73±0.24, 25.29±6.73, 1.84±0.43, and 52±9.89, respectively. Furthermore, the pre-procedural median percentages for TLC, RV, and DLCO were 119.5% (106–164%), 216.5% (180–346%), and 32.5% (22–78%), respectively. Post-procedural pulmonary function tests could not be performed due to coronavirus disease 2019; however, the mMRC dyspnea scores and 6MWTs were monitored alongside radiological follow-ups. At the 1-year post-procedure follow-up, the post-procedural average for the 6MWT distance was 280±51.44 meters, and the median mMRC dyspnea score was 3 [2–3]. There was a significant improvement in the 6MWT results between pre- and post-procedure ($P<0.001$) (Figure 5). Given the equality of pre- and post-procedural median mMRC dyspnea scores, mean ranks were utilized. The mean rank for negative ranks was 4, whereas for positive ranks it was 0, signifying a substantial reduction in mMRC values ($P=0.008$).

Discussion

In our study involving COPD patients with severe dyspnea and emphysema, we found a high level of agreement between QPLPS and StratX® in determining the target lobe for

EBV placement. Although agreement was also observed in determining the second and third target lobes, the level of agreement slightly decreased. However, subgroup analysis revealed an agreement between both methods in determining the target lobe for patients with homogeneous emphysema.

Pathophysiologically, pulmonary parenchymal destruction leads to insufficient perfusion of damaged tissue and ventilation-perfusion mismatch, resulting in low perfusion scores; this suggests a correlation between areas of destruction and low perfusion regions. The MESA COPD study, which examined pulmonary microvascular loss, reported that even mild parenchymal destruction in COPD patients was correlated with a decrease in perfusion. Additionally, as the percentage of emphysema increased, perfusion progressively decreased (15). Hunsaker *et al.* (16) demonstrated a statistically significant correlation between lung perfusion scintigraphy and thoracic CT findings in assessing the severity and distribution of lung disease before LVRS. This study also concluded that separate preoperative thoracic CT and ventilation-perfusion scintigraphy assessments are nearly equivalent in predicting improvements in postoperative FEV1 measurements. Thomsen *et al.* (17) found a correlation between perfusion score and emphysema distribution in their study investigating the clinical success of EBV treatment. Before BLVR, it was recommended to undergo ^{99m}Tc perfusion scintigraphy and CT scans to evaluate emphysema morphology for target lobe selection (10). In our study, during target lobe selection, as the severity of emphysema increased in the StratX[®] which is a software program measuring the parenchymal destruction through HRCT images, perfusion in the same areas decreased in the QPLPS assessments. Accordingly, our study demonstrated a statistically significant agreement between both methods used for target lobe selection in identifying the target lobes before Zephyr[®] EBV placement. This agreement suggests that QPLPS and the StratX[®] program can be used interchangeably for target lobe selection before BLVR treatment.

Planar perfusion scintigraphy has some disadvantages such as the duration of the procedure taking approximately 30 minutes, the requirement for post-procedure social isolation (avoiding prolonged contact with infants and pregnant for 24 hours after administration) due to radioactive administration during the procedure, and the estimation of the zones assessed rather than the actual lobes. It may not be available in each hospital due to the need for experienced staff, equipment, and a nuclear medicine unit. In addition, a target lobe selection only

based on perfusion scanning does not provide an assessment of the lung parenchyma. However, StratX[®] stands out as a method that can evaluate lung parenchyma on existing HRCT scans without requiring additional intervention and can also identify target lobes based on areas with intense parenchymal destruction.

The heterogeneity of emphysema is used as one of the selection criteria for BLVR treatment, but its role is debated in current studies. The North American VENT study cohort reports that pre-procedural heterogeneous emphysema distribution is an important parameter in predicting post-procedural clinical and functional outcomes (14). Conversely, similar studies indicate that post-procedural outcomes do not significantly differ based on whether emphysema distribution is homogeneous or heterogeneous (18,19). However, selecting the target lobe in severe emphysema, particularly in patients with homogeneous disease, is known to be challenging. Therefore, it is suggested in studies that perfusion scintigraphy should be used in homogeneous patients (17). In our study, there is an agreement between StratX[®] and QPLPS in selecting target lobes not only in patients with heterogeneous emphysema but also in those with homogeneous emphysema. Although our results are limited by a small number of patients, this agreement suggests that StratX[®] may also be beneficial in selecting target lobes in patients with homogeneous emphysema.

In the study by Patel *et al.* (20), which investigated the role of imaging methods in determining the target lobe before BLVR treatment in 34 patients with advanced emphysema, perfusion measurements assessed by scintigraphy were compared with the results obtained from quantitative CT. The overall correlation between the perfusion/volume ratio determined via nuclear scintigraphy and the emphysema score calculated via CT was moderate. The correlation of emphysema destruction with perfusion/ventilation was strongest in the right upper lobe. Despite the lack of a strong correlation for all lobes, the authors suggested that the combined use of both methods provided a complementary role. In contrast, our results indicate that instead of being complementary, the two methods can be used interchangeably, and furthermore, due to the disadvantages of scintigraphy, StratX[®] may be preferred.

In patients undergoing scintigraphy alone, FI cannot be measured, and thus the presence of collateral ventilation is assessed by a Chartis[™] catheter during the procedure. One of the advantages of the quantitative tomographic assessment is that it also allows concurrent FI evaluation. This can help exclude those patients with significant collateral ventilation

as noted by StratX® and reduce the number of procedures in these patients with significant comorbidities. Fiorelli *et al.* (21) compared visual tomography and StratX® software for the assessment of FI and their StratX® report showed that an EBV can be used in patients with FI >95% without the use of a Chartis™ catheter. In our study, the correlation of StratX® with Chartis™ was 90% in patients with FI ≥95% and <80%, while the correlation was 50% in patients with FI between 80–95%. This suggests that StratX® can provide an additional advantage in patients with FI ≥95% and <80%, while the Chartis™ catheter should be used for patients with FI between 80–95%. However, prospective cohort studies with more patients are needed to support our results.

Our study has some limitations. The major limitation is the small number of patients and the retrospective nature of the study. Due to the limited number of patients, our study results cannot be generalized and applied to the entire population. However, these findings are valuable as they can shed light on future research with larger patient cohorts. Further studies with larger sample sizes are needed to validate and extend our findings to broader populations. As it was a retrospective study, the correlation between FI assessment via StratX® and collateral ventilation assessment via the Chartis™ catheter could not be evaluated. Another limitation was the comparison of planar scintigraphy with quantitative CT. Single photon emission computed tomography (SPECT) perfusion scintigraphy with 3-dimensional evaluation would have provided better results in identifying target lobes. However, our study was performed on planar perfusion because there is no recommendation for planar or SPECT quantitative scintigraphy in reference studies on pre-BLVR evaluation and only planar scintigraphy is available in our referral center.

Conclusions

In conclusion, we found that there is an agreement between QPLPS and StratX® used for target lobes selection before the Zephyr® EBV placement. Additionally, StratX® software provides similar contributions to target lobe selection in homogeneous emphysema as well as in heterogeneous emphysema. StratX® could be preferred as it allows evaluation using existing CT scans without requiring additional effort and assists in assessing fissure integrity.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://qims.amegroups.com/article/view/10.21037/qims-24-125/rc>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://qims.amegroups.com/article/view/10.21037/qims-24-125/coif>). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Yedikule Chest Diseases and Thoracic Surgery Education and Research Hospital (30.12.2021, Decision No. 2021-177). The requirement for written informed consent was waived due to the retrospective nature of the study.

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References

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease; 2024. Date of access: 01-06-2024. Available online: <https://goldcopd.org/2024-gold-report/>
2. Rochester DF, Braun NM. Determinants of maximal inspiratory pressure in chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1985;132:42-7.
3. Fishman A, Martinez F, Naunheim K, Piantadosi S, Wise R, Ries A, Weinmann G, Wood DE; National Emphysema Treatment Trial Research Group. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. *N Engl J Med* 2003;348:2059-73.

4. van Geffen WH, Slebos DJ, Herth FJ, Kemp SV, Weder W, Shah PL. Surgical and endoscopic interventions that reduce lung volume for emphysema: a systemic review and meta-analysis. *Lancet Respir Med* 2019;7:313-24.
5. Kemp SV, Slebos DJ, Kirk A, Kornaszewska M, Carron K, Ek L, et al. A Multicenter Randomized Controlled Trial of Zephyr Endobronchial Valve Treatment in Heterogeneous Emphysema (TRANSFORM). *Am J Respir Crit Care Med* 2017;196:1535-43.
6. Valipour A, Slebos DJ, Herth F, Darwiche K, Wagner M, Ficker JH, Petermann C, Hubner RH, Stanzel F, Eberhardt R; IMPACT Study Team. Endobronchial Valve Therapy in Patients with Homogeneous Emphysema. Results from the IMPACT Study. *Am J Respir Crit Care Med* 2016;194:1073-82.
7. Gompelmann D, Benjamin N, Bischoff E, Kontogianni K, Schuhmann M, Hoffmann H, Heussel CP, Herth FJF, Eberhardt R. Survival after Endoscopic Valve Therapy in Patients with Severe Emphysema. *Respiration* 2019;97:145-52.
8. Klooster K, Slebos DJ. Endobronchial Valves for the Treatment of Advanced Emphysema. *Chest* 2021;159:1833-42.
9. Valipour A. Valve therapy in patients with emphysematous type of chronic obstructive pulmonary disease (COPD): from randomized trials to patient selection in clinical practice. *J Thorac Dis* 2018;10:S2780-96.
10. Herth FJF, Slebos DJ, Criner GJ, Valipour A, Sciurba F, Shah PL. Endoscopic Lung Volume Reduction: An Expert Panel Recommendation - Update 2019. *Respiration* 2019;97:548-57.
11. Caviezel C, Froehlich T, Schneider D, Muehlematter U, Frauenfelder T, Guglielmetti LC, Opitz I, Weder W. Identification of target zones for lung volume reduction surgery using three-dimensional computed tomography rendering. *ERJ Open Res* 2020;6:e00305-2020.
12. Slebos DJ, Klooster K, Ernst A, Herth FJF, Kerstjens HAM. Bronchoscopic lung volume reduction coil treatment of patients with severe heterogeneous emphysema. *Chest* 2012;142:574-82.
13. Sciurba FC, Ernst A, Herth FJ, Strange C, Criner GJ, Marquette CH, Kovitz KL, Chiacchierini RP, Goldin J, McLennan G; VENT Study Research Group. A randomized study of endobronchial valves for advanced emphysema. *N Engl J Med* 2010;363:1233-44.
14. StratX® Lung Analysis Platform. Date of access: 01-06-2024. Available online: <https://pulmonx.com/stratx/>
15. Hueper K, Vogel-Claussen J, Parikh MA, Austin JH, Bluemke DA, Carr J, et al. Pulmonary Microvascular Blood Flow in Mild Chronic Obstructive Pulmonary Disease and Emphysema. The MESA COPD Study. *Am J Respir Crit Care Med* 2015;192:570-80.
16. Hunsaker AR, Ingenito EP, Reilly JJ, Costello P. Lung volume reduction surgery for emphysema: correlation of CT and V/Q imaging with physiologic mechanisms of improvement in lung function. *Radiology* 2002;222:491-8.
17. Thomsen C, Theilig D, Herzog D, Poellinger A, Doellinger F, Schreiter N, Schreiter V, Schürmann D, Temmesfeld-Wollbrueck B, Hippenstiel S, Suttorp N, Hubner RH. Lung perfusion and emphysema distribution affect the outcome of endobronchial valve therapy. *Int J Chron Obstruct Pulmon Dis* 2016;11:1245-59.
18. Valipour A, Herth FJ, Burghuber OC, Criner G, Vergnon JM, Goldin J, Sciurba F, Ernst A; VENT Study Group. Target lobe volume reduction and COPD outcome measures after endobronchial valve therapy. *Eur Respir J* 2014;43:387-96.
19. Schuhmann M, Raffy P, Yin Y, Gompelmann D, Oguz I, Eberhardt R, Hornberg D, Heussel CP, Wood S, Herth FJ. Computed tomography predictors of response to endobronchial valve lung reduction treatment. Comparison with Chartis. *Am J Respir Crit Care Med* 2015;191:767-74.
20. Patel R, Gangemi AJ, Dadparvar S, Zhao H, Zantah M, Pandya A, Dominguez Castillo E, Marron R, Patel M, Verga S, Zheng M, Patlakh N, Thomas J, Criner LYH, Marchetti N, Dass C, Criner GJ. Role of Quantitative SPECT/CT in Pre-Procedural BLVR Planning in Patients with Advanced Emphysema. *Am J Respir Crit Care Med* 2020;201:A5043.
21. Fiorelli A, Poggi C, Anile M, Cascone R, Carlucci A, Cassiano F, Andreotti C, Tiracorrendo M, Diso D, Serra N, Venuta F, Rendina EA, Santini M, D'Andrilli A. Visual analysis versus quantitative CT analysis of interlobar fissure integrity in selecting emphysematous patients for endobronchial valve treatment. *Interact Cardiovasc Thorac Surg* 2019;28:751-9.

Cite this article as: Demirkol B, Cortuk M, Tanriverdi E, Gul S, Eren R, Alcin G, Baydili KN, Cetinkaya E. Role of quantitative planar lung perfusion scintigraphy and tomography in identifying target lobes in patients with emphysematous phenotype of advanced chronic obstructive pulmonary disease: a retrospective cross-sectional study. *Quant Imaging Med Surg* 2024;14(9):6425-6435. doi: 10.21037/qims-24-125