HRCT-Approximated Perfusion is Comparable to Nuclear Perfusion Imaging in Severe COPD

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Published in:
American Journal of Respiratory and Critical Care Medicine

DOI:
10.1164/rccm.202303-0463LE

Publication date:
2023

stable spirometry values close to LLN and increasing residual volume/TLC (13).

Neonatal medicine changed dramatically during the 1980s, with fundamental technological and medical advances (1). Thus, to evaluate an EP-born subject's risk of later lung disease, birth decade, as well as neonatal clinical course, need to be considered. We have previously presented growth charts for FEV_1 based on data from three cohorts born EP during the 1980s, 1990s, and 2000s, depicting parallel trajectories from mid-childhood to adulthood at levels clearly below those of term-born individuals, but with smaller deficits with each birth decade (4). To fully understand the consequences of continuously evolving neonatal treatment and survival rates, we must follow representative groups into late adulthood and encourage collaborative efforts to pool data, such as the RECAP (https://recap-preterm.eu/) and PELICAN (https://thepelican.network/) networks.

The strengths of the study are the population-based design with individually matched control subjects, relatively high follow-up rates, and free access to health care for all children, reducing risks of socioeconomic bias. The main limitation is the cohort size, a situation shared with most studies in this area (5). Only two-thirds of the participants performed post-bronchodilator spirometry, complicating COPD classification.

In conclusion, EP-born adults in their fourth decade of life have widespread lung function impairments affecting both airways and alveolar components, partly compatible with criteria listed for pre-COPD or possibly representing a unique EP lung phenotype. We need longer follow-up to settle this, but the current findings represent a premonition of what to expect. Adult chest physicians must pay attention to the early life history of their patients. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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High-Resolution Computed Tomography-approximated Perfusion Is Comparable to Nuclear Perfusion Imaging in Severe Chronic Obstructive Pulmonary Disease

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To the Editor:

Bronchoscopic lung volume reduction with one-way endobronchial valves (EBVs) in patients with severe hyperinflation and emphysema has been shown to significantly improve lung function, quality of life, and exercise capacity (1, 2). With this therapy, the most diseased lobe is occluded with EBVs to induce a lobar atelectasis, thus reducing hyperinflation. Using quantitative computed tomography (CT) scan

Supported by Lung Foundation Netherlands grant 5.1.17.171.0.

Originally Published in Press as DOI: 10.1164/rccm.202303-0463LE on May 16, 2023

Table 1. Results of Comparison between Perfusion Scintigraphy and Computed Tomography Perfusion Approximation Analysis and between Single-Photon Emission Computed Tomography–Computed Tomography and Computed Tomography Perfusion Approximation Analysis

	Perfusion Scintigraphy	PXT				
n = 207	Perfusion Mean ± SD (%)	Perfusion Mean ± SD (%)	Difference (%) ± SD (%)	*P* Value	95% Limits of Agreement	Intraclass Correlation Coefficient (95% CI)
Left lung	49 ± 9	48 ± 8	0.6 ± 3.5	0.02	−6.19, 7.33	0.96 (0.94–0.97)
Right lung	51 ± 9	52 ± 8	−0.6 ± 3.5	0.02	−7.33, 6.19	0.96 (0.94–0.97)
	SPECT	**PXT**				
n = 85	Perfusion Mean ± SD (%)	Perfusion Mean ± SD (%)	Difference (%) ± SD (%)	*P* Value	95% Limits of Agreement	Intraclass Correlation Coefficient (95% CI)
Left lung	48 ± 9	46 ± 8	1.5 ± 3.5	<0.01	−5.4, 8.5	0.95 (0.91–0.97)
Right lung	52 ± 9	54 ± 8	−1.5 ± 3.5	<0.01	−8.5, 5.4	0.95 (0.91–0.97)
LUL	23 ± 10	22 ± 9	1.6 ± 3.4	<0.01	−5.1, 8.3	0.96 (0.92–0.98)
LLL	25 ± 11	25 ± 9	0 ± 3.2	0.46	−6.4, 6.3	0.97 (0.96–0.98)
RUL	22 ± 12	21 ± 10	1.4 ± 3.9	<0.01	−6.2, 8.9	0.96 (0.94–0.98)
RML	6 ± 4	6 ± 4	0 ± 2.5	0.49	−4.9, 4.9	0.88 (0.82–0.93)
RUL + RML	28 ± 12	27 ± 10	1.4 ± 3.4	<0.01	−5.3, 8.1	0.97 (0.95–0.98)
RLL	24 ± 10	27 ± 9	−2.9 ± 3.2	<0.01	−9.0, 3.2	0.95 (0.70–0.98)

Definition of abbreviations: CI = confidence interval; LLL = left lower lobe; LUL = left upper lobe; PXT = computed tomography perfusion approximation analysis; RLL = right lower lobe; RML = right middle lobe; RUL = right upper lobe; SPECT = single-photon emission computed tomography.

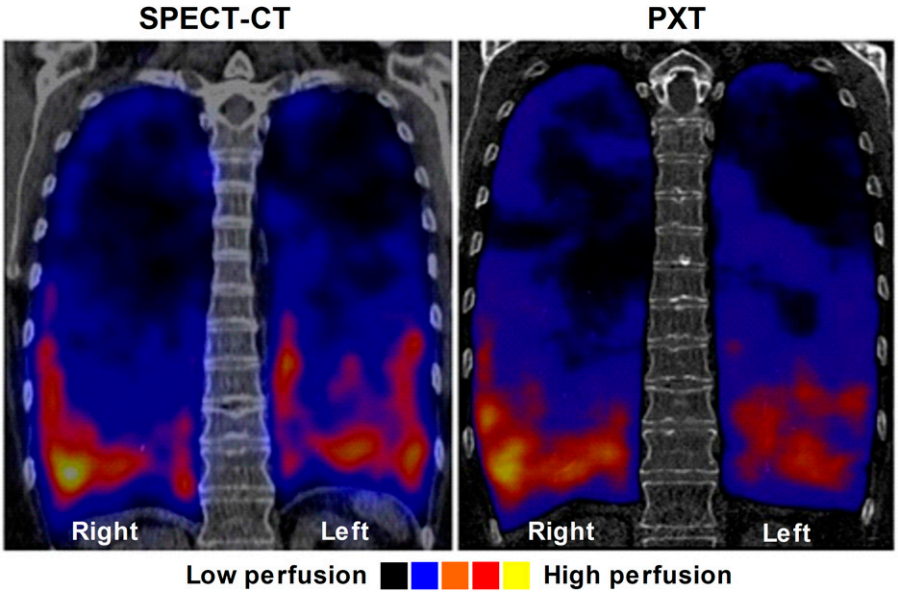

Figure 1. Example of a patient with the results of perfusion on a lobar level measured with both single-photon emission computed tomography–computed tomography (SPECT-CT) and CT perfusion approximation analysis (PXT). The figure shows the coronal view of matched SPECT and CT (left) and the comparable image of the heatmap acquired with PXT (right). Perfusion is distributed mainly in the lower lobes. Lobar data of SPECT versus PXT: right upper lobe, 11% versus 12%; right middle lobe, 3% versus 6%; right lower lobe, 37% versus 37%; left upper lobe, 9% versus 10%; left lower lobe, 40% versus 35%.

analysis, the key features of a treatment target lobe can be accurately assessed: emphysema distribution and severity, as well as fissure completeness score as a surrogate for absent interlobar collateral ventilation (3–5). In addition, assessment of lung and lobar perfusion is important to select the optimal treatment target lobe, especially in case of a homogeneous emphysema distribution or multiple potential targets (3). Patients with low target lobe perfusion and high perfusion in the ipsilateral lobe are better responders to EBV therapy with regard to exercise capacity (6). Perfusion distribution can be estimated using regular scintigraphy with technetium-99m–labeled microalbumin aggregates. However, this planar technique does not accurately assess the lobar distribution. Lobar perfusion can also be quantified with single-photon emission computed tomography (SPECT) or dual-energy contrast-enhanced CT scans (7, 8). Nevertheless, these perfusion techniques require additional scans, radiation exposure, and costs. A significant relationship between the pulmonary small vessels as assessed with quantitative CT scan analysis and perfusion scintigraphy has already been described (9). New artificial intelligence (AI)-based algorithms can quantify lobar perfusion distribution from the available high-resolution computed tomography (HRCT) and can provide a complete information package for optimal EBV target lobe selection in just one diagnostic procedure (3). Therefore, in this study, we investigated whether AI perfusion distribution approximated from an inspiratory HRCT provides information similar to that provided by perfusion scintigraphy and SPECT-CT.

Methods

We included all patients with severe chronic obstructive pulmonary disease who were screened for EBV treatment and who underwent both HRCT and planar perfusion scintigraphy (time frame 2014–2019) or SPECT-CT (time frame 2019–2022). We performed two separate analyses to compare both planar perfusion scintigraphy and SPECT-CT with approximated CT perfusion.

All patients provided written informed consent regarding the use of their data for future scientific purposes, which was approved by the medical ethics committee of the University Medical Center Groningen (METC2016.483) and Maastricht University Medical Center (METC2018-0868).

Thirona's CT perfusion approximation analysis (PXT; patent application no. 17/004073) was performed to estimate pulmonary perfusion from HRCT scans (LungQ version 3.0.0; Thirona) (10). PXT is an AI-based deep learning algorithm designed to recognize pulmonary perfusion and detect chronic perfusion defects from a single noncontrast CT scan by automatically combining information regarding the parenchymal tissue, pulmonary arteries, and veins, and it can provide anatomical quantification (i.e., perfusion per lung, lobe, or [sub-]segmental). In this study, PXT scores were quantified for the left and right lungs and each of the individual lobes.

Perfusion scintigraphy and SPECT-CT were performed after injection of technetium-99m macroaggregated albumin. For perfusion measured with SPECT-CT, scans were processed with quantitative lung application software (GE Healthcare NM/CT 87 or Siemens Symbia T Series with LungVQ algorithm, Lung Analysis Suite version 1.0) to provide perfusion per lobe.

To compare the two methods, the intraclass correlation coefficient (two-way mixed, absolute agreement, average measures) was computed. The Bland-Altman method was used to calculate the mean difference of PXT and the perfusion in each lung (for perfusion scintigraphy) and each lung and all lobes separately (for SPECT-CT) and calculate the 95% limits of agreement.

Results

We included 292 patients with severe chronic obstructive pulmonary disease (69% female; mean age, 62 $\pm$ 23 yr; body mass index, 24 $\pm$ 4 kg/m^2; FEV_1, 27 $\pm$ 8% predicted; residual volume, 237 $\pm$ 49% predicted). Of these, 207 underwent perfusion scintigraphy plus HRCT, and 85 underwent SPECT-CT plus HRCT.

Perfusion scintigraphy versus PXT comparison. The mean percentage of perfusion of the left lung was 49 $\pm$ 9% compared with 48 $\pm$ 8% with the PXT method, and for the right lung, it was 51 $\pm$ 9% versus 52 $\pm$ 8% (Table 1). The mean difference between perfusion and PXT for both lungs was 0.6 $\pm$ 3.5% ($P = 0.018$). The intraclass correlation coefficient was 0.92 ($P < 0.01$), and the 95% limits of agreement ranged from $-$6.19% to 7.33% (Table 1).

SPECT-CT versus PXT comparison. The perfusion measured with SPECT-CT of the separate lobes varied from 6 $\pm$ 4% to 28 $\pm$ 12%, and with PXT, it varied from 6 $\pm$ 4% to 27 $\pm$ 10%. The intraclass correlation coefficient varied from 0.88 in the middle lobe to 0.97 in the left lower lobe (Table 1). An example of an individual case that shows the perfusion with both SPECT-CT and PXT is provided in Figure 1.

Clinical usability of PXT compared with SPECT-CT. Of the 85 patients who underwent SPECT-CT analysis for lung volume reduction evaluation, 38 patients actually underwent a lung volume reduction treatment (33 treatments with one-way valves; 5 patients underwent surgical lobectomy). The treatment target lobe identified by SPECT-CT and PXT was identical in all these patients.

Discussion

Pulmonary perfusion distribution approximated from an HRCT scan using the novel AI-based PXT method provides information similar to the current perfusion standard of care using either regular perfusion scintigraphy or SPECT-CT. There is a high correlation between the perfusion scintigraphy and PXT for the left and right lungs separately and between SPECT-CT and PXT for all lobes separately.

To our knowledge, the present study is the first to compare quantitative CT perfusion with perfusion scintigraphy for both the left and right lungs and on a lobar level. The high correlation and small mean difference between PXT and SPECT-CT make this novel quantitative analysis a valuable addition to the already used quantitative HRCT scan analysis with information regarding fissure completeness, lobar volumes, and emphysema destruction score.

We found a slight difference in perfusion per lung and per lobe. This may be due to the fact that the methods are quite different. Perfusion measured by PXT uses data from pulmonary arteries, veins, and parenchymal tissue to provide information about chronic perfusion defects, whereas nuclear perfusion imaging is a dynamic method and provides the actual distribution of the blood throughout the lung. Furthermore, for lobar comparison, SPECT-CT is the reference test in this study. However, the automated software used to identify lungs and lobes may also exhibit a certain margin of error.

The use of PTX has not yet been prospectively validated for use in clinical practice. In our patient group, there was no difference in target lobe selection of the patients who were treated. We expect that the reported differences between perfusion scores are not clinically relevant because the differences are small and perfusion is generally used in addition to other quantitative measurements. We, therefore, think that the selection of the treatment target lobe will not be different. However, this is an important subject that should be confirmed in other studies.

In conclusion, quantitative CT–approximated perfusion using AI-based software (PXT) is highly comparable to perfusion scintigraphy and SPECT-CT to determine the perfusion per lung and on a lobar level. This novel technique is a valuable addition to the current reports of quantitative CT scan analysis in patients eligible for lung volume reduction treatment to guide optimal treatment target lobe selection and save additional testing, radiation, and costs. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Acknowledgment: The authors thank Annick Willems van Beveren and Aafke van Erp-Zeilstra for the SPECT-CT analysis.

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Optimal Threshold of FEV_t/FVC Ratio for Detection of Airflow Limitation Associated with Structural Lung Disease

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To the Editor:

Airflow obstruction in adults is defined by a lower than normal FEV_1/FVC ratio. The selection of the 1-second time point for the numerator is somewhat arbitrary but has stood the test of time as the most commonly accepted metric. Several other time thresholds for the numerator have been evaluated in the past, including $FEV_{0.5}$ and $FEV_{0.75}$, but these are not used in clinical practice in adult pulmonary medicine. Some of these subsecond measures are used in children younger than 6 years of age (1, 2). Similarly, time thresholds beyond 1 second such as FEV_3 have also been assessed, and these may aid in the detection of small airway disease in those whose FEV_1/FVC is normal (3–5). The accuracy of these thresholds for the detection of lung disease has, however, not been compared. We aimed to evaluate the discriminative accuracy of FEV over a range of time (FEV_t) over a wide range for the detection of clinically meaningful thresholds of emphysema and small airway disease detected on computed tomography (CT).

Methods

We evaluated participants enrolled in the Genetic Epidemiology of COPD (COPDGene) study, a multicenter cohort study of current and

Supported by NIH/NHLBI R01HL151421 (S.P.B. and A.N.), UH3HL155806 (S.P.B.), K01HL163249 (S.B.), U01 HL089897, and U01 HL089856. COPDGene is also supported by the COPD Foundation through contributions made to an industry advisory board that has included AstraZeneca, Bayer Pharmaceuticals, Boehringer Ingelheim, Genentech, GlaxoSmithKline, Novartis, Pfizer, and Sunovion.

Author Contributions: Study concept and design: S.P.B.; acquisition, analysis, or interpretation of data: all authors; drafting of the manuscript: S.P.B.; critical revision of the manuscript for important intellectual content: all authors; statistical analysis: S.B.; study supervision: all authors.

Originally Published in Press as DOI: 10.1164/rccm.202302-0205LE on June 7, 2023