Quantitative Computerized Two-Point Correlation Analysis of Lung CT Scans Correlates With Pulmonary Function in Pulmonary Sarcoidosis

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Background: Chest CT scans are commonly used to clinically assess disease severity in patients presenting with pulmonary sarcoidosis. Despite their ability to reliably detect subtle changes in lung disease, the utility of chest CT scans for guiding therapy is limited by the fact that image interpretation by radiologists is qualitative and highly variable. We sought to create a computerized CT image analysis tool that would provide quantitative and clinically relevant information.

Methods: We established that a two-point correlation analysis approach reduced the background signal attendant to normal lung structures, such as blood vessels, airways, and lymphatics while highlighting diseased tissue. This approach was applied to multiple lung fields to generate an overall lung texture score (LTS) representing the quantity of diseased lung parenchyma. Using deidentified lung CT scan and pulmonary function test (PFT) data from The Ohio State University Medical Center's Information Warehouse, we analyzed 71 consecutive CT scans from patients with sarcoidosis for whom simultaneous matching PFTs were available to determine whether the LTS correlated with standard PFT results.

Results: We found a high correlation between LTS and FVC, total lung capacity, and diffusing capacity of the lung for carbon monoxide ($P < .0001$ for all comparisons). Moreover, LTS was equivalent to PFTs for the detection of active lung disease. The image analysis protocol was conducted quickly (< 1 min per study) on a standard laptop computer connected to a publicly available National Institutes of Health ImageJ toolkit.

Conclusions: The two-point image analysis tool is highly practical and appears to reliably assess lung disease severity. We predict that this tool will be useful for clinical and research applications.

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Abbreviations: DLCO = diffusing capacity of the lung for carbon monoxide; ILD = interstitial lung disease; LTS = lung texture score; NIH = National Institutes of Health; PFT = pulmonary function test; TLC = total lung capacity; TPCF = two-point correlation function

Pulmonary function testing currently is the standard tool for objectively assessing lung disease severity in pulmonary sarcoidosis¹ and other chronic parenchymal and alveolar lung diseases.^{2–6} High-resolution chest CT imaging is highly reproducible and is very sensitive for detecting lung pathology.⁷ Unlike pulmonary function tests (PFTs), which are subject to variability in patient effort and ethnicity, technical variables such as laboratory methodology, and different interpretive algorithms,⁸ lung CT scan results are highly reproducible. However, the current approach to interpretation of CT scan results, which depend on

radiologists, is poorly standardized and qualitative for both clinical and research applications in patients with interstitial lung disease (ILD).⁹ At present, there is no convenient, well-standardized, radiologist-generated CT image analysis approach that provides a quantitative assessment of lung disease. Thus, an efficient, objective, and quantifiable approach to chest CT image analysis is needed.

Previous attempts to quantify the severity of ILD, particularly fibrotic lung disease, based on computer-aided CT image analysis were of limited utility. In general, prior studies have reported modest correlations

between radiographic features (eg, lung attenuation) and pulmonary function parameters,¹⁰⁻¹² leading the authors of these studies to conclude that computer CT image analysis is relatively insensitive to textural changes, such as ground glass and reticular abnormalities.¹⁰ Thus, to account for textural characteristics of the lung related specifically to disease while minimizing the noise related to normal features, including blood vessels, airways, and other contiguous structures, we evaluated a two-point correlation function (TPCF)-based approach to quantify the severity of diseased lung using conventional-resolution CT images. To this end, we developed a proprietary plug-in program that can be operated on the publicly available National Institutes of Health (NIH) ImageJ toolkit (<http://rsbweb.nih.gov/ij/index.html>) to produce a lung texture score (LTS) reflecting the overall burden of lung disease. To validate this tool, we compared the LTS to well-standardized pulmonary function results and to conventional (radiologist) image analysis.

MATERIALS AND METHODS

Patient Population

The Ohio State University Medical Center's Information Warehouse is an honest broker for deidentified patient data, including image files and PFT results. The authors obtained written permission to use the data. Using "sarcoidosis" and *International Classification of Disease, 9th Edition* code 135 as search terms, we found and analyzed 71 consecutive chest CT scan studies (with 5-mm slice thickness and no contrast agent use) from patients with sarcoidosis who had simultaneous (same-day) PFT results available. No patient was analyzed more than once.

CT Scan Visual Scoring

CT images were evaluated by a fellowship-trained thoracic radiologist (M. K.) using a picture archiving and communication

system workstation (Agfa-Gevaert Group). The radiologist was blinded to all clinical and image analysis data. The lungs were divided into upper (aortic arch to apex), mid (bottom of aortic arch to top of the right inferior pulmonary vein), and lower (right inferior pulmonary vein to posterior costophrenic recess) lung zones. Each lung was considered separately. The images were evaluated for the presence and profusion of the following morphologies: nodules, fibrosis (areas of honeycomb lung or central bronchovascular bundle thickening), consolidation (pulmonary density that obscured the underlying lung parenchyma), ground glass (increased pulmonary density that did not obscure the underlying parenchyma), and reticular (intralobular lines) or linear (septal thickening) pattern. A profusion score for each morphologic abnormality was assigned to each lung zone based on the percentage of the lung zone involved, as follows: 0 for 0%, 1 for 1% to 25%, 2 for 26% to 50%, 3 for 51% to 75%, and 4 for $\geq 76\%$. A nodule profusion score was based on the number of nodules per zone, as follows: 0 for no nodules, 1 for one to five, 2 for six to 10, 3 for 11 to 15, and 4 for ≥ 16 . Each lung was considered separately, so the maximum total score for a study patient was 120 (20 per zone $\times$ 3 zones/lung $\times$ 2 lungs).

Computer CT Image Analysis

The lungs were segmented using Hounsfield units, and a TPCF-based approach (Fig 1) was used to quantify the proportion of diseased lung, using a proprietary plug-in program that can be operated on the publicly available NIH ImageJ toolkit. The LTS derived from these analyses represents the percentage of the lung parenchyma exhibiting nonuniform texture (Fig 1). Briefly, our TPCF-based approach, LTS, is adapted from the field of material sciences.¹³ In material sciences, while calculating TPCF, samples from a given section of material (metal, alloy, etc) are compared with samples from another section in question, and the TPCF measures the correlation between the two sample populations. During our LTS calculations using a TPCF-based approach, rather than measuring the correlation between the sections (pixels in our images), we measured the mismatches for a given CT scan study. Hence, LTS calculations could be explained by the following steps (Fig 1):

1. For a given chest CT image (Fig 1A) using the Hounsfield units (eg, between $-1,000$ and -200), lungs are segmented (Fig 1B). During this segmenting operation, the ratio between the segmented lung tissue volume and the overall CT scan volume (lung ratio) is also calculated. We then convert the values in this volume from 16 bits (65,535 gray levels) to 8 bits (256 gray levels) and enhance their contrast using histogram equalization. Both 16- to 8-bit conversion and histogram equalization operations are already available as built-in functionality of the NIH ImageJ toolkit, and we invoke these methods programmatically.
2. Within this given lung volume, the pixel values are converted from 8 to 4 bits (16 gray levels). This conversion is a simple Java bit shift operation that we invoke for each pixel within our volume, and we only keep the most significant 4 bits. Then, for each pixel (Fig 1C) in this volume (Fig 1D), comparisons are made between the surrounding neighbors. That is, the gray levels between pixels are compared to determine whether they mismatch based on a predetermined threshold. Here, starting from a central pixel, if we were to compare pixels 1 step away in every direction (x-axis, sagittal; y-axis, transversal; z-axis, axial), we would be making 27 comparisons ($3 \times 3 \times 3$) per pixel. Comparisons between pixels could be made in any distance (eg, a 3-pixel distance would be 343 comparisons). Using this logic, mismatches for each pixel are thresholded (eg, if there is $> 60\%$ mismatch with surrounding pixels, this pixel is counted as a mismatch).

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FIGURE 1. Schematic representation of the two-point correlation function-based approach (lung texture score). A, Lung texture score accepts chest CT scan studies in DICOM (digital imaging and communications in medicine) format as input. B, Using Hounsfield units, lungs are segmented, and the segmented lung volume is raster scanned. The red square represents the lung field to be analyzed. C, During this scan, each pixel is compared with its neighbors' in various distances within a threshold. D, This process is repeated for the entire lung segment. E, All mismatches for each pixel that are integrated throughout the volume are summed at individual pixel level, which are later added to the volume of mismatches.

The mismatches (Fig 1E) are then simply added for the given lung volume, and this integrated value is turned into a ratio of mismatches for the entire volume. The final value of LTS is calculated by dividing the mismatch ratio by the lung ratio.

Statistical Analysis

Data were analyzed with SAS version 9.2 (SAS Institute, Inc) and Stata 10 (StataCorp LP) statistical software. Scatterplots and Pearson correlations were used to show the direction of the

relationship between the LTS and PFT variables. Logistic regression was used to determine whether the LTS is a good predictor of sarcoidosis. Comparisons of the areas under the receiver operating characteristic curves were done through the logit model to determine whether LTS is superior to PFT for detection of sarcoidosis.

RESULTS

Two-Point Correlation Analysis of CT Images Reduces Background Signal From Normal Lung Structures

The image analysis tool effectively eliminates the background noise represented by normal contiguous lung structures (eg, blood vessels, airways). The signals from alveolar and interstitial compartments are highlighted (Fig 2).

LTS Strongly Correlates With PFT Results

A higher LTS is shown to correlate strongly with the inverse of the FVC % predicted, total lung capacity (TLC), and diffusing capacity of the lung for carbon monoxide (DLCO) (Figs 3A-C). It is reflected by Pearson coefficient (r) and $P < .0001$ for all comparisons.

Correlations Between LTS and PFT Remain Significant After Reducing Image Intensity Precision

Sixteen-bit images were converted to 4-bit images during our calculations. This implies that lower-dose CT images (less radiation exposure, but higher signal-to-noise ratio) may be suitable for LTS analyses.

Radiographic Sarcoidosis Features and Corresponding LTS

In support of the notion that CT image analysis will detect distinct pulmonary sarcoidosis phenotypes,

FIGURE 2. Two-point correlation analysis of CT images highlights diseased lung. The image on the left is produced by filtering out the tissues other than the lungs. The image on the right is a result image that shows the calculated features for every pixel from the source image. Areas marked by 1 (green arrows) highlight example regions of interest with enhanced discrimination between normal and abnormal lung tissue. Areas marked by 2 (red arrows) highlight example regions of interest with enhanced discrimination between normal blood vessels and adjacent diseased lung.

LTS is elevated in patients with predominantly ground glass, fibrotic, nodular, or reticular CT image patterns (Fig 4). Results of qualitative and semiquantitative analyses of pulmonary sarcoidosis disease manifestations with corresponding PFT and LTS results are shown in Table 1. Using a binary approach for the radiographic detection of active pulmonary sarcoidosis, wherein 11 studies are shown to have minimal (eg, a single nodule) or no evidence of active pulmonary disease (no lung disease), we sought to determine whether LTS was comparable to PFT results for the detection of active pulmonary sarcoidosis. As shown in Figure 5, LTS is equivalent to TLC and superior to FVC for the detection of active pulmonary disease.

DISCUSSION

Despite ready access to highly automated and reproducible high-quality images available from lung CT scans,¹⁴ CT image analysis is currently of limited utility for assessing the severity of pulmonary sarcoidosis because of the subjective and nonquantifiable nature of the radiologist's interpretation of ILD severity. As such, subtle changes in CT image characteristics are typically ignored in the context of clinical sarcoidosis research. The current study indicates that a novel TPCF analysis of CT images strongly correlates with PFT (FVC, TLC, and DLCO), which is the current standard for estimating lung disease severity in patients with pulmonary sarcoidosis.^{15,16}

Currently available clinical end points for sarcoidosis research all have their limitations. For instance, patients often report a paradoxical worsening of their quality of life despite treatments that effectively prevent lung disease progression. On the other hand, patients can remain asymptomatic with normal lung function despite obvious progression of pulmonary sarcoidosis based on radiographic criteria. A more objective measure of the overall burden of pulmonary disease is needed to guide clinical decision-making and research. By eliminating the large background signal generated by normal lung structures (blood vessels, lymphatics, airways), the computerized two-point correlation analysis described herein assesses changes in radiographic texture related to interstitial and alveolar processes. Thus, this quantitative approach is expected to objectively detect changes in the overall burden of parenchymal and alveolar lung disease.

Another potential advantage of the computerized TPCF approach is the potential to reduce the intensity of radiation exposure required to generate useful CT images. In this regard, high-resolution CT scans with a high signal-to-noise ratio are generally regarded as superior to conventional CT images for detecting

FIGURE 3. Correlation between LTS and lung function. The LTS calculated from the CT images reflects the amount of irregularity within the lungs (ie, the percentage of irregular [textured] lung within the overall lung volume for the given CT image). A-C, Higher LTS negatively correlates with FVC % predicted ($r = -0.76$), TLC ($r = -0.61$), and DLCO ($r = -0.57$), respectively. $P < .0001$ for all comparisons, indicating very strong correlations. DLCO = diffusing capacity of the lung for carbon monoxide; LTS = lung texture score; TLC = total lung capacity.

changes in lung disease severity in patients with ILD, such as sarcoidosis. However, there is a growing concern about the long-term risks attendant to the higher levels of radiation exposure when using serial CT scans for the assessment of disease progression.¹⁷ Although the retrospective nature of the current study does not allow us to determine the minimal radiation dose required to attain a strong correlation with standardized PFT results, we are able to show strong correlations between the LTS and FVC, TLC, and DLCO while using 4 bits. Being able to work with 16 gray levels suggests LTS is robust regarding signal-to-noise ratio and should work with low-dose scans. We plan to investigate this in a later study.

There is reason to believe that computer-aided image analyses improve the detection of subclinical lung disease. Computer-aided CT image analysis was recently shown to detect subtle changes in lung texture attendant to early asymptomatic ILD using low-dose CT scan studies.¹⁸ Likewise, the current data

indicate that LTS is equivalent to FVC and TLC for the detection of lung disease. In terms of quantifying lung disease severity, we speculate that the LTS provides a measure of lung disease burden that is complementary to standard physiologic metrics.

In addition to the study design limitations inherent in retrospective image analysis, a number of other questions are raised by these compelling results. Our analysis was confined to a single institution using similar CT scanners and protocols, and a larger cohort would be necessary to confirm the preliminary associations between abnormal LTS and the diverse sarcoidosis disease phenotypes (eg, nodular, ground glass, fibrotic) reported herein. In this regard, further optimization of the protocol may lead to even stronger correlations between LTS and objective measures of lung function in sarcoidosis and other lung diseases. To further enhance the performance of this image analysis tool, future studies should start with the raw image data to optimize the protocol for the purpose

FIGURE 4. A-D, Lung CT scan image is shown on the left and the corresponding image after conversion using the computer-generated two-point correlation function approach is shown on the right. A, Conforms to "normal lung." B, Conforms to "fibrosis." C, Depicts "ground glass" infiltrates. D, Represents "nodular lung disease." CT image score detects diverse pulmonary sarcoidosis disease manifestations. Patients with sarcoidosis with predominant fibrotic, nodular, and reticular radiographic disease manifestations and a disease-free control subject were analyzed using the two-point correlation approach to derive an overall LTS. As shown, a higher LTS is associated with each disease phenotype, indicating that each radiographic phenotype contributes to the overall LTS. See Figure 3 legend for expansion of abbreviation.

Table 1—Results of Qualitative and Semiquantitative Analyses of Pulmonary Sarcoidosis Disease Manifestations With Corresponding PFT and LTS Results

Case No.	RUL	LUL	RML	LML	RLL	LLL	FVC	TLC	DLCO	FVC/DLCO	LTS
1	F4	F4	F2,N4	F2,N4	F1,N1	N2,F1	64	72	52	43	57.47748
2	0	0	0	0	0	0	101	86	77	11.6	33.68263
3	0	0	0	0	0	0	67	79	62	37.3	44.70803
4	N3,F2	N2,F1	N4,F1	N2,F1	N1	F1,N2	106	105	76	36.2	37.33333
5	0	0	0	0	0	0	84	84	83	18.5	42.76827
6	F1	F2	F2	F2	N2,G2	F1,G1	86	84	76	32.6	56.10561
7	N1	0	0	0	F1	F1	83	84	88	23.4	39.91684
8	0	0	F1,G1	G1	F1	F2,R2	69	78	89	27.7	45.98765
9	0	0	N4	N2	0	0	93	103	65	24.9	38.93617
10	N4	N4	N1,C1	N4,C1	C1,N4	C1,N4	69	80	47	35.4	63.93443
11	N4	N4	N4,R4	N4,R2	N4	G4	82	72	62	30.2	45.16129
12	0	0	0	0	0	0	98	103	76	23.4	36.27797
13	N1	N1	N1	N1	G1	G1	102	104	81	27.5	39.4669
14	N1	N1	N2	F1,N2	N1,F1	0	77	71	65	27.5	59.10653
15	F1	N1	R1,F1	N1	R1	G1	68	66	60	28	53.94495
16	G2,F1	G3	F2	G1	F1,G1	0	70	79	83	33.5	48.50187
17	F1	F1,N1	G1,F1	G1	0	C1	60	74	56	42.4	46.81583
18	R2,N1	R1	F2	F1	R1,N1	R1,F1,N1	85	95	60	39.3	50.47468
19	F4	F3,G1	F1,G1	F1	F2	F3	60	66	38	38	54.92372
20	0	0	0	0	0	0	99	97	78	22.5	40.39634
21	0	0	0	0	0	0	70	88	86	37.6	44.86572
22	0	N1	N1,G1	0	N1	N1,G2	103	100	86	22	35.41667
23	F3	F2	F3,N2	F2,N1	G1	G1	82	87	81	30.6	44.57478
24	N1	N1	F2	F2	N1	0	59	67	65	47	53.05868
25	0	0	0	0	0	0	112	109	79	29.2	39.1411
26	F4,N1	F2	F2,N3	F3,N1	F2,N2	F1,C1,N2	55	66	35	39.2	64.71545
27	0	0	0	0	0	N1	99	94	67	20.2	34.91686
28	N3	N3	N1	N2	F1,N1,R1	F1,R1	88	92	52	36.9	41.90031
29	0	0	0	0	N1	0	106	108	72	25.5	25.85551
30	0	0	0	F1	F1	F1	79	76	47	26.3	40.58824
31	0	0	0	0	0	0	96	97	100	29	35.17139
32	F4	F3	F3	F3,N1	G2	G2	80	83	62	28.7	46.37188
33	F2	F2	N2,F1	F1,N1	N1	N1	59	81	63	55.5	49.71751
34	N4,F1	N4	N4,F1	N4	N2	N2	84	85	46	36	43.24324
35	N1	0	F2	F2	F1,R1,N1	F1,N2	70	82	53	40.2	57.3487
36	N1,F1	F1	F1,N1	N1,F1	G1,N1	G1,N1,F1	60	74	75	43.4	61.59754
37	N4,F1	N3,F1	N4	N4,F1	F1,N2	F1,C1	74	72	50	23.5	44.00585
38	0	0	0	N1	C1	0	36	89	28	67.5	69.78967
39	F1,G2	F1,N1,G1	F1,N1	F1,N4	F2	F2	53	77	47	60.8	50.9901
40	F2	F2,N1	F2	F2,N1	F1	F1	70	74	55	29.5	58.18182
41	0	0	0	0	0	0	98	101	64	40.6	39.24303
42	N1,F1	F1,N1	F2,N2	F1,N2	F2,N1	F1,N1	63	102	95	45.3	45.32225
43	R1	0	G2,N4,F2	N4,F1	F1,G1	N4,G3,R3	70	77	79	28.7	58.54701
44	F3,N1	0	F2,C1	F1,N2	F1,R1,N1	F1,N1	83	79	60	34.1	50.26525
45	F3,N4	F2,N4	F4,N4	F3,N4	G3	G3	76	85	81	35.5	46.42314
46	F1	0	F1,G1	C1	F1	F1	66	73	68	29.3	45.07042
47	0	0	0	0	0	0	81	95	89	37.5	41.41145
48	R4	R2,N2	F1,N4,R3	F1,N2,R1	F3,R1	F1,R1	82	90	58	37.2	50.67385
49	F1	F1	F1	N1,F1	F1	0	68	87	80	41.1	49.4152
50	G2,N1	G2	F2,G1	G1,N1	F1	0	74	77	76	32.8	45.36082
51	0	0	N1	0	0	0	79	84	81	24.1	41.89017
52	0	0	0	0	N1	0	94	94	72	33.3	40.54054
53	F1	0	F1	F1	F1	F1	76	83	76	32.9	44.08759
54	N1	N1	N4,F2	N4,F1	F2	F2	79	78	38	29.8	54.48276
55	F3,N1	F3	F2,C1,N2	F1,N2	F1	F1	57	63	35	52.3	66.71368
56	0	0	F1	0	F1	0	88	91	71	29.6	43.18182
57	R1	N1	F2	N1,G1	0	R1,N1	71	70	57	29.4	59.26493
58	F3	F3	F4	F3	G3	G2	74	87	77	38.9	45.23196
59	G4	G3,N1	C2,G3	N1,G3	G3	G2,C1	73	74	71	29.6	43.58974
60	F1,N2	F1	G1,N4,F1	G1,F1	0	F1	78	99	45	32.1	47.59174

(Continued)

Table 1—Continued

Case No.	RUL	LUL	RML	LML	RLL	LLL	FVC	TLC	DLCO	FVC/DLCO	LTS
61	F1,R1,N1	0	R2,N1	N1	R1	N1	92	89	91	34.5	31.48148
62	N4,G1	N4	N3,G1	N3	G1,N1	N2	79	81	52	30.5	47.77948
63	G2,N1	G1	G3	N1	G3	G3	61	66	66	35.8	48.10659
64	F2,N4	F1	N4,F1	N4,F1	N4	N1	83	66	79	8.3	44.69697
65	F1,N1	N4,F1	F1,G1,N1	F1,N3,G1	G1,N1,R1	G2,R1	72	69	60	32.9	47.4934
66	0	0	N4	N3	N2	N1	116	116	90	26.6	39.19717
67	G1	0	F1	F1	F1	F2,R1	72	80	84	32.3	53.0343
68	0	0	0	0	F1	F1	79	82	67	29.7	41.14286
69	0	0	F1	F1	F1	F1	66	81	50	40.5	47.4026
70	0	N1	0	0	0	0	76	81	66	25.3	48.29545
71	0	0	0	0	0	0	84	97	71	42.4	44.38687

Symbol-finding scoring: F (fibrosis, honeycomb lung), 0 = 0%, 1 = 1%-25%, 2 = 26%-50%, etc; C (consolidation), 0 = 0%, 1 = 1%-25%, 2 = 26%-50%, etc; N (nodule), 0 = no nodule; 1 = 1-5 nodules, 2 = 6-10 nodules, 3 = 11-15 nodules, 4 = ≥ 16 nodules; G (ground glass), 0 = 0%, 1 = 1%-25%, 2 = 26%-50%, etc; R (reticular/linear), 0 = 0%, 1 = 1%-25%, 2 = 26%-50%, etc. DLCO = diffusing capacity of the lung for carbon monoxide; LLL = left lower lobe; LML = left middle lobe; LTS = lung texture score; LUL = left upper lobe; PFT = pulmonary function test; RLL = right lower lobe; RML = right middle lobe; RUL = right upper lobe; TLC = total lung capacity.

of minimizing radiation exposure while further improving the detection of changes in lung texture related to ILD and perhaps obstructive lung disease. With respect to the latter, our unpublished data suggest that lower LTS scores correspond to emphysema severity. Finally, we speculate that the correlation between LTS and DLCO in patients with sarcoidosis may be influenced by the upper-lobe predominance of the disease, as confirmed by expert radiologist analysis (Table 1), which tends to preserve DLCO compared with ILDs affecting the lower lobes (eg, interstitial pulmonary fibrosis). As such, we expect that improved correlation with DLCO could be achieved by weighting the image analysis on the basis of the severity of apical and basilar lung disease severity.

In summary, the novel TPCF-based CT image analysis approach strongly correlates with severity of pulmonary sarcoidosis based on standard PFT criteria,

and these correlations were obtained using relatively low grayscale resolution (16 gray levels) images. This implies that the computer image analysis approach could reduce the risks of radiation exposure while providing a more objective assessment of disease progression for clinical and research applications. Another benefit of this approach is the demonstrated efficiencies in terms of computer power, expense, and time. Specifically, the analysis can be conducted within 1 min on a conventional laptop computer using the NIH open source ImageJ toolkit along with our ImageJ Java software plug-in. Additional studies are needed to determine whether the TPCF approach is effective for other interstitial and obstructive lung diseases.

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Dr Erdal: contributed to the design of the study, data collection and analysis, and drafting of the manuscript.

Dr Crouser: contributed to the design of the study, data analysis, and drafting of the manuscript.

Mr Yildiz: contributed to the data analysis for the manuscript.

Dr King: contributed to data analysis and drafting of the manuscript.

Mr Patterson: contributed to data analysis for the manuscript.

Dr Knopp: contributed to data interpretation and revisions to the manuscript.

Dr Clymer: contributed to the design of the study, data analysis, and revisions to the manuscript.

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FIGURE 5. ROC analysis of LTS, FVC, and TLC for the detection of active pulmonary sarcoidosis. LTS is shown to be equivalent to TLC and FVC for the detection of active pulmonary sarcoidosis. ROC = receiver operating characteristic. See Figure 3 legend for expansion of other abbreviations.

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