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Reproducibility of lobar perfusion and ventilation quantification using a SPECT/CT segmentation software in lung cancer patients

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Abstract

Planar perfusion scintigraphy with Tc99m-labelled macroaggregated albumin (Tc99m-MAA) is often used for pre-therapy quantification of regional lung perfusion in lung cancer patients, particularly in patients with poor respiratory function. However, subdividing lung parenchyma in rectangular regions of interests, as done on planar images, is a poor reflection of true lobar anatomy. New tridimensional methods using SPECT and SPECT/CT have been introduced, including a semi-automatic lung segmentation software (Hermes Medical Solutions). The present study evaluates inter- and intraobserver agreement of quantification using a SPECT/CT software, and compares results of regional lung contribution obtained with SPECT/CT and planar scintigraphy.

Methods: Thirty (30) lung cancer patients underwent ventilation perfusion (V/Q) scintigraphy with Tc99m-MAA and Tc99m-Technegas. Regional lung contribution to perfusion and ventilation was measured on both planar scintigraphy and SPECT/CT using a semi-automatic lung segmentation software by two observers. Interobserver and intraobserver agreement for SPECT/CT software were assessed using intra-class correlation coefficient (ICC), Bland Altman plots, and absolute differences of measurements. Measurements from planar and tridimensional methods were compared using paired sample t-tests, and mean absolute differences.

Results: ICC were in the excellent range (above 0.9) for both interobserver and intraobserver agreement using the SPECT/CT software. Bland Altman analyses showed very narrow limits of agreement. Absolute differences were below 2.0%

in 96% of both interobserver and intraobserver measurements. There was a statistically significant difference between planar and SPECT/CT methods (P<.001) for quantification of perfusion and ventilation for all right lung lobes, with a maximal mean absolute difference of 20.7% for the right middle lobe. There was no statistically significant difference for quantification of perfusion and ventilation for left lung lobes using both methods, however absolute differences reached 12.0%. Total right and left lung contribution were very similar using both methods, with a mean difference of 1.2% for perfusion and 2.0% for ventilation. **Conclusion:** Quantification of regional lung perfusion and ventilation using a SPECT/CT-based lung segmentation software is highly reproducible. This tridimensional method yields statistically significant differences in measurements for right lung lobes when compared to planar scintigraphy. We recommend that SPECT/CT based quantification be used for all lung cancer patients undergoing pre-therapy evaluation of regional lung function.

Key words

Lobar quantification – Pulmonary perfusion – Pulmonary ventilation – Scintigraphy – SPECT/CT

Introduction

Quantification of regional lung perfusion with Tc99m-labelled macroaggregated albumin (Tc99m-MAA) is commonly used to evaluate pulmonary function in patients with lung cancer prior to volume reduction surgery (*1,2*), or radiotherapy(*3*). It allows estimation of the impact of treatment on forced expiratory volume in one second (FEV1) in those with borderline pre-therapy lung function(*4,5*). The current most widely used method for quantification of regional lung function uses planar perfusion scintigraphy. In this method, the lung parenchyma is subdivided into 6 equal-sized rectangular regions of interest (ROIs). Calculation of relative percentage of counts for each lung region is obtained from the geometric mean on anterior and posterior views, thus approximating lobar contribution. However, rectangular ROIs are a poor representation of true lobar anatomy(*5*).

With the advent of hybrid imaging, new methods of tridimensional lung segmentation using SPECT and SPECT/CT have been introduced, offering anatomically based quantification of lobar contribution for perfusion studies(*6-8*), or combined perfusion and ventilation (V/Q) studies(*9,10*). Recently, a semi-automatic lung segmentation software using SPECT/CT (Hermes Hybrid 3D Lung Lobe Quantification, Hermes Medical Solutions) has been developed. However, reproducibility of measurements obtained with this software in a clinical setting has not been studied, nor has feasibility of SPECT/CT quantification in a group of patients with a high prevalence of underlying lung disease, such as nonsurgical candidates undergoing radiotherapy.

In the present study, we will evaluate the feasibility and the inter- and intraobserver agreement of lung quantification using this software, as well as compare results of regional lung contribution obtained with those of traditional planar method for V/Q studies.

Materials and Methods

We included thirty (30) consecutive lung cancer patients (14 females and 16 males with a mean age 68.2 years, range 52 to 80 years) referred to our Nuclear Medicine Department for pre-radiotherapy evaluation of lung function from April 2015 to June 2016. The institutional review board approved this study, and all subjects signed an informed consent form. Patient characteristics are detailed in Table 1.

Ventilation and perfusion scintigraphy were performed on the same day with inhalation of Tc99m-Technegas (Cyclomedica, mean dose 577 MBq placed in crucible), and intravenous injection of Tc99m-MAA (mean dose 292 MBq). Ratio of perfusion to ventilation count rates was superior to 4 in all patients. All studies were performed on a dedicated SPECT/CT camera (Discovery NM/CT 670, GE Healthcare). SPECT only acquisition was done for the ventilation study, while a SPECT/CT acquisition with attenuation correction was performed for the perfusion study. Planar anterior and posterior acquisitions were done for both ventilation and perfusion studies. SPECT acquisition parameters included a 20% energy window centered at 140 keV, a 128x128 matrix, acquisition of 60 total

frames over 360 degrees, with time per projection of 28 seconds for the ventilation acquisition and 17 seconds for the perfusion acquisition. Acquisitions were performed using a low energy high resolution (LEHR) parallel hole collimator, and zoom factor of 1.28. SPECT reconstructions were performed using an iterative 3D ordered-subsets expectation maximization algorithm (HRECON version 1.1C, Hermes Medical Solutions) with 3 iterations, 6 subsets, and filtering with 3D Gaussian filter (1.25 cm full width at half maximum). A helical CT acquisition was performed during free breathing, immediately before the perfusion SPECT acquisition. CT parameters included a voltage of 120 kV, a current of 150 mA, a 0.5 s rotation time, a pitch of 1.375, 16x0.625mm collimation, and a reconstruction with a 1.25 mm slice thickness using a filtered back projection algorithm and soft tissue filter. There was no intravenous contrast injection. Estimated effective doses for SPECT acquisitions was 3 mSv CT acquisition was 2 mSv. SPECT and SPECT/CT images were reviewed for adequate co-registration. Planar ventilation images were visually assessed for the presence of central deposition of Technegas.

Quantification with planar scintigraphy was performed using the Hybrid Viewer Lung Quantification software (Hermes Medical Solutions), which subdivides each lung into 3 rectangular ROIs, and computes relative contribution (percentage) of each ROI from the geometric mean of counts on anterior and posterior views (example shown in Figure 1A). Tridimensional quantification with SPECT and SPECT/CT was performed using the Hermes Hybrid 3D Lung Lobe

Quantification software (Hermes Medical Solutions). The workflow in this software consists of the following steps: 1) automatic CT-based lung volume detection through a region growing algorithm, 2) semi-automatic delimitation of lung fissures (the user defines 6 points along each lung fissure on multiple reconstructed CT slices in the sagittal plane), and 3) software computation of 5 volumes of interest, one for each lobe (right upper, right middle, right lower, left upper and left lower lobes).

Ventilation and perfusion studies are co-registered to CT with mutual information algorithm and identical frame of reference, respectively. Volumes of interest are applied to co-registered V/Q SPECT data, and the relative contribution (percentage) of each lobe is computed for both ventilation and perfusion. A 3D rendering of CT-based volumes of interest is displayed along with the quantification results (example shown in Figure 1B-C).

SPECT/CT-based segmentation was performed for both ventilation and perfusion studies for all patients by observer 1 (K.P.), and once for perfusion by observer 2 (A.G.L.). Repeat measurements for observer 1 were done at least one week apart to minimize recall bias. Observers were blinded to any previous measurement.

Interobserver and intraobserver agreement were assessed using two-way random, absolute agreement, single measures intra-class correlation coefficients (*11*) for results of tridimensional quantification of perfusion and ventilation, respectively.

For both the inter- and intraobserver analyses, absolute differences between measurements were calculated, as well as mean absolute difference for each lobe. Bland-Altman plots were also done for interobserver analysis (*12*).

The quantification results of the left middle third on planar scintigraphy were redistributed equally between the left upper and left lower third to allow comparison with the left upper and left lower lobes respectively for the tridimensional method (Appendix I). The quantification results on planar scintigraphy for the right lung ROIs were compared directly (i.e. upper third with right upper lobe, middle third with right middle lobe, and lower third with right lower lobe). Comparison of results for total right and total left lungs, as well as lobar quantification obtained by planar and SPECT/CT studies (using results from observer 1) was performed using paired sample t-tests for both ventilation and perfusion. Subgroup analysis was performed for patients with and without central deposition of Technegas on planar ventilation study. *P* values <.05 were considered statistically significant. Mean absolute differences for the results obtained from both methods were also calculated. Statistical analyses were performed with SPSS (version 24.0.0.0).

Results

Semi-automatic segmentation using the SPECT/CT-based software was feasible in 29 of the 30 patients, taking on average 5 to 10 minutes per patient. We

excluded one patient due to failure of automatic lung contour detection (see discussion).

Mean measurements obtained by planar and SPECT/CT, mean absolute differences between the two methods, as well as *P* values from paired sample t-test comparing both methods are shown for perfusion and ventilation in Table 2 and Table 3, respectively.

The right/left lung differentials obtained by the planar and the tridimensional methods were not statistically different for the perfusion studies (Table 2), but were statistically different for the ventilation studies (Table 3). However, no statistically significant difference was found when only the subgroup of patients without central deposition of Technegas (n=18) was considered (Table 3).

For lobar quantification of both perfusion and ventilation, there was a statistically significant difference in values obtained by the planar and tridimensional methods for right upper, right middle, and right lower lobes, while there was no statistically significant difference for left upper and left lower lobes, as shown in Tables 2 and 3. For left lung lobes, one third of patients had an absolute difference greater than 5.0% between quantification measurements of the two methods.

When considering only the lobe of clinical interest for each patient (e.g. left upper lobe quantification for a patient with left upper lobe tumor), there was a statistically significant difference in measurements obtained by SPECT/CT and planar methods (*P* = .04), with a mean absolute difference of 7.1% for perfusion

(min 0.2%, max 22.8%). For both perfusion and ventilation, absolute differences between total right and left lung contribution measured with planar and tridimensional methods were very small. However, absolute differences were much higher for individual lobar values, especially for right lung lobes, with a maximal absolute difference for the right middle lobe of 36.0% for perfusion and 29.7% for ventilation (Tables 2 and 3).

Comparison of interobserver measurements revealed very small mean absolute differences (0.3 to 1.0%), as well as ICC in the excellent range (Table 4). Bland-Altman plots show narrow limits of agreement for all measurements (Figure 2).

ICC for intraobserver measurements was also excellent (>0.9) for all lobes, and for total right and left lungs, with very small mean absolute differences between repeated measurements (0.3-1.3%) (Table 5).

Absolute differences of <2.0% were found in 96% of repeated interobserver and intraobserver measurements (Figures 3 and 4).

Discussion

Quantification of lobar perfusion and ventilation using SPECT and SPECT/CT with a semi-automatic segmentation algorithm has excellent inter- and intraobserver agreement. This method yields statistically and clinically significant differences when compared to segmentation with planar scintigraphy for right

lung lobes, with an absolute difference of up to 36.0%. Although differences in values for left lung lobes were not statistically significant, they can be considered clinically significant, with absolute differences of greater than 5.0% in one third of patients, and maximal absolute differences of 12.0 %. We can hypothesize that such differences could alter the clinical management of certain patients.

In practice, the left lung is often subdivided in 3 ROIs when planar images are used for quantification. For the purpose of this study, the contribution of the left middle region of interest was redistributed equally to the left upper and left lower thirds. This redistribution more closely approximates true left lung anatomy, with more or less equal-sized upper and lower lobes. This may explain the lack of statistically significant difference when we compare quantification results for the left lung lobes from planar and SPECT/CT segmentation techniques.

Delineation of volumes of interest from the CT acquisition more accurately represents individual patient anatomy. Therefore, V/Q quantification obtained from those volumes of interest is more likely to represent the true lobar contribution to perfusion and ventilation than the arbitrarily defined rectangular subdivisions drawn on planar scintigraphy. Furthermore, on planar images, extraneous activity may not be easily excluded from the quantification. Examples include tracheobronchial deposition of Tc99m-Technegas, thyroid and gastric activity from free pertechnetate, and residual vascular activity on Tc99m-MAA studies. Additionally, in some cases, the right and left lungs cannot be easily

separated with the preset rectangular ROIs (example in Figure 5). Tridimensional segmentation with SPECT/CT overcomes these limitations by only considering the activity corresponding to true lung parenchyma. For these reasons, we believe that planar-based quantification should be abandoned in favor of SPECT/CT or SPECT in centers without access to hybrid cameras.

A number of studies have investigated manual tridimensional lung segmentation techniques using SPECT or SPECT/CT for both preoperative(*6-8,10,13-15*) and pre-radiotherapy(*16,17*) patients. Only a few studies investigated semi-automatic algorithms for total lung and lobar segmentation using SPECT/CT in preoperative patients(*9,18*). No studies had previously compared results to those obtained with planar scintigraphy, or evaluated interobserver and intraobserver agreement on patient studies. In our study, we demonstrated the excellent reproducibility of the semi-automatic segmentation technique in a population with a high prevalence (63%) of underlying lung disease, which makes visualisation of lung anatomy more challenging. We can hypothesize that we would obtain even more reproducible results in patients with unaltered lung parenchyma, such as most preoperative patients.

Quantification based on perfusion scintigraphy only, as opposed to combined V/Q scintigraphy, has been used by some groups(*7,8,18*), with few studies having investigated the role of ventilation scintigraphy on prediction of post-treatment FEV1(*9,10*). However, at our institution, combined V/Q scintigraphy is

routinely performed to exclude underlying thromboembolic disease in cancer patients referred for quantitative perfusion lung scintigraphy. In our cohort, one patient had an incidental finding of pulmonary emboli.

Multiple non-nuclear medicine imaging techniques have been described for evaluation of lung perfusion, including MRI, CT pulmonary angiography, and double-energy CT with parenchymal iodine mapping (*19*). Although accurate, widespread use of these techniques for perfusion quantification has been restricted by limited accessibility, as well as contraindications and risk inherent to iodine contrast injection. These CT-based techniques also have substantially higher radiation doses to patients compared to nuclear medicine techniques.

The semi-automatic lung segmentation software used in this study allows simple and rapid quantification of both perfusion and ventilation studies in a single streamed workflow, taking on average 5 to 10 minutes per patient. Some limitations of this technique include occasional difficult visualization of lung fissures on free breathing CT, although this occurred in a minority of patients and did not significantly influence inter or intraobserver agreement, as shown in our results. In our study, CT was acquired during free-breathing to match perfusion acquisition. In patients with suboptimal fissure visualisation, it would have been possible to use a previous diagnostic CT and co-register it for lung segmentation, however, this was not done to ensure uniformity of method across patients, and to avoid difference in lung volumes on CT and SPECT acquisitions. Another

limitation of the software is that the automatic lung contour detection is sometimes more difficult when lung density is highly heterogeneous, for example with presence of extensive bullae mixed with areas of fibrosis. As previously mentioned, one patient had to be excluded due to failure of the software to detect lung contours. This was found to be due to an endobronchial density which prevented the region growing algorithm from functioning correctly. A disadvantage of SPECT/CT-based methods is dependence on tomographic acquisition and hybrid camera, which can increase imaging cost.

Limitations of this study also include a small number of patients, who were all non-surgical candidates with a high prevalence of underlying lung disease. He et al.(*9*) have described accurate prediction of post lobectomy lung function in 305 patients using semiautomatic lung segmentation algorithm. Further work is needed to evaluate whether results obtained with the tridimensional technique yield more accurate prediction of post-treatment FEV1 than traditional planar scintigraphy in patients undergoing radiotherapy. It would also be interesting to take into account the actual radiation therapy treatment fields in quantification of regional parenchymal perfusion and prediction of post-therapy FEV1.

Conclusion

Tridimensional lung lobar quantification can easily be performed using SPECT/CT acquisitions and a semi-automatic segmentation software for both perfusion and ventilation studies. This segmentation technique demonstrates

excellent interobserver and intraobserver agreement. Results obtained with this method differ significantly from those obtained with planar scintigraphy, especially for right lung lobes. We recommend that SPECT/CT-based quantification be used for all lung cancer patients undergoing pre-therapy evaluation of regional lung function. Further studies are needed to evaluate prediction of post-radiotherapy FEV1 with this technique, and whether quantification of perfusion or ventilation yield the most accurate results.

Financial disclosures

None

Disclaimer

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References

1. Brunelli A, Kim AW, Berger KI, Addrizzo-Harris DJ. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest.* 2013;143:e166S-190S.

2. Mazzone PJ. Preoperative evaluation of the lung cancer resection candidate. *Expert Rev Respir Med.* 2010;4:97-113.

3. Marks LB, Hollis D, Munley M, et al. The role of lung perfusion imaging in predicting the direction of radiation-induced changes in pulmonary function tests. *Cancer.* 2000;88:2135-2141.

4. Garrity ER. Clinical applications of pulmonary nuclear medicine In: Henkin RE, Boya D, Dillehay GL, Karesh SM, Halama JR, Wagner RH, eds. *Nuclear Medicine* 2nd ed. St. Louis Mosby; 2006 1349-1350.

5. Royal HD. Pulmonary imaging for nonthromboembolic disease In: Henkin RE, Boya D, Dillehay GL, Karesh SM, Halama JR, Wagner RH, eds. *Nuclear Medicine* 2nd ed. St. Louis Mosby 2006:1423-1438.

6. Knollmann D, Meyer A, Noack F, Schaefer W. CT-based 3D vs. planar derived quantification of pulmonary lobar perfusion in preoperative lung cancer patients with borderline lung function. *J Nucl Med.* 2012;53:604.

7. Kovacevic-Kusmierek K, Kozak J, Pryt L, et al. Perfusion lung scintigraphy for the prediction of postoperative residual pulmonary function in patients with lung cancer. *Nucl Med Rev Cent East Eur.* 2015;18:70-77.

8. Toney LK, Wanner M, Miyaoka RS, Alessio AM, Wood DE, Vesselle H. Improved prediction of lobar perfusion contribution using technetium-99m-labeled macroaggregate of albumin single photon emission computed tomography/computed tomography with attenuation correction. *J Thorac Cardiovasc Surg.* 2014;148:2345-2352.

9. He W, Zhai W, Avondo J. The clinical value of novel Hybrid 3D Lobar Quantification SPECT Lung ventilation/perfusion scan in predicting remaining lung function for lobectomy lung cancer patients. *J Nucl Med.* 2016;57:244.

10. Imaeda T, Kanematsu M, Asada S, et al. Prediction of pulmonary function after resection of primary lung cancer. Utility of inhalation-perfusion SPECT imaging. *Clin Nucl Med.* 1995;20:792-799.

11. McGraw K, Wong S. Forming inferences about some intraclass correlation coefficients. *Psychol Methods* 1996;1:30-46.

12. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet.* 1986;1:307-310.

13. Hirose Y, Imaeda T, Doi H, Kokubo M, Sakai S, Hirose H. Lung perfusion SPECT in predicting postoperative pulmonary function in lung cancer. *Ann Nucl Med.* 1993;7:123-126.

14. Knollmann D, Meyer A, Noack F, Schaefer WM. Preoperative assessment of relative pulmonary lobar perfusion fraction in lung cancer patients. A rather simple three-dimensional CT-based vs. planar image-derived quantification. *Nuklearmedizin.* 2015;54:178-182.

15. Piai DB, Quagliatto R, Jr., Toro I, Cunha Neto C, Etchbehere E, Camargo E. The use of SPECT in preoperative assessment of patients with lung cancer. *Eur Respir J.* 2004;24:258-262.

16. Yin L, Shcherbinin S, Celler A, et al. Incorporating quantitative single photon emission computed tomography into radiation therapy treatment planning for lung cancer: impact of attenuation and scatter correction on the single photon emission computed tomography-weighted mean dose and functional lung segmentation. *Int J Radiat Oncol Biol Phys.* 2010;78:587-594.

17. Yin Y, Chen JH, Li BS, et al. Protection of lung function by introducing single photon emission computed tomography lung perfusion image into radiotherapy plan of lung cancer. *Chin Med J (Engl).* 2009;122:509-513.

18. Knollmann D, Avondo J, Meyer A, Schaefer W. CT-based 3D quantification of relative pulmonary lobe perfusion from SPECT in preoperative lung cancer patients: Comparing a manual and a semi-automatic approach. *J Nucl Med.* 2016;57:1731.

19. Thieme SF, Johnson TR, Reiser MF, Nikolaou K. Dual-energy lung perfusion computed tomography: a novel pulmonary functional imaging method. *Semin Ultrasound CT MR.* 2010;31:301-308.

Figures

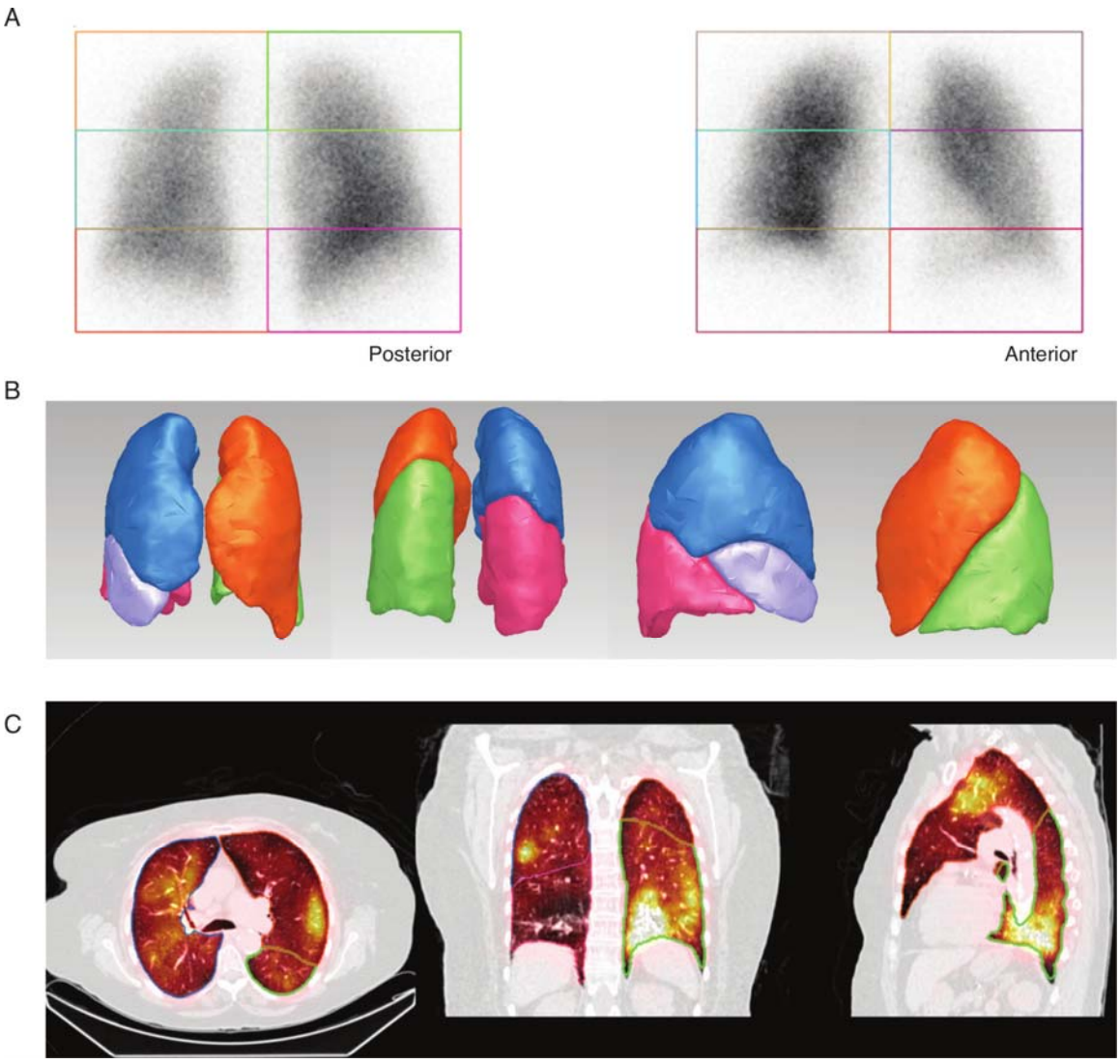

Figure 1. Quantification of perfusion using the planar method (A) and the semi-automatic SPECT/CT-based lung segmentation software (B-C).

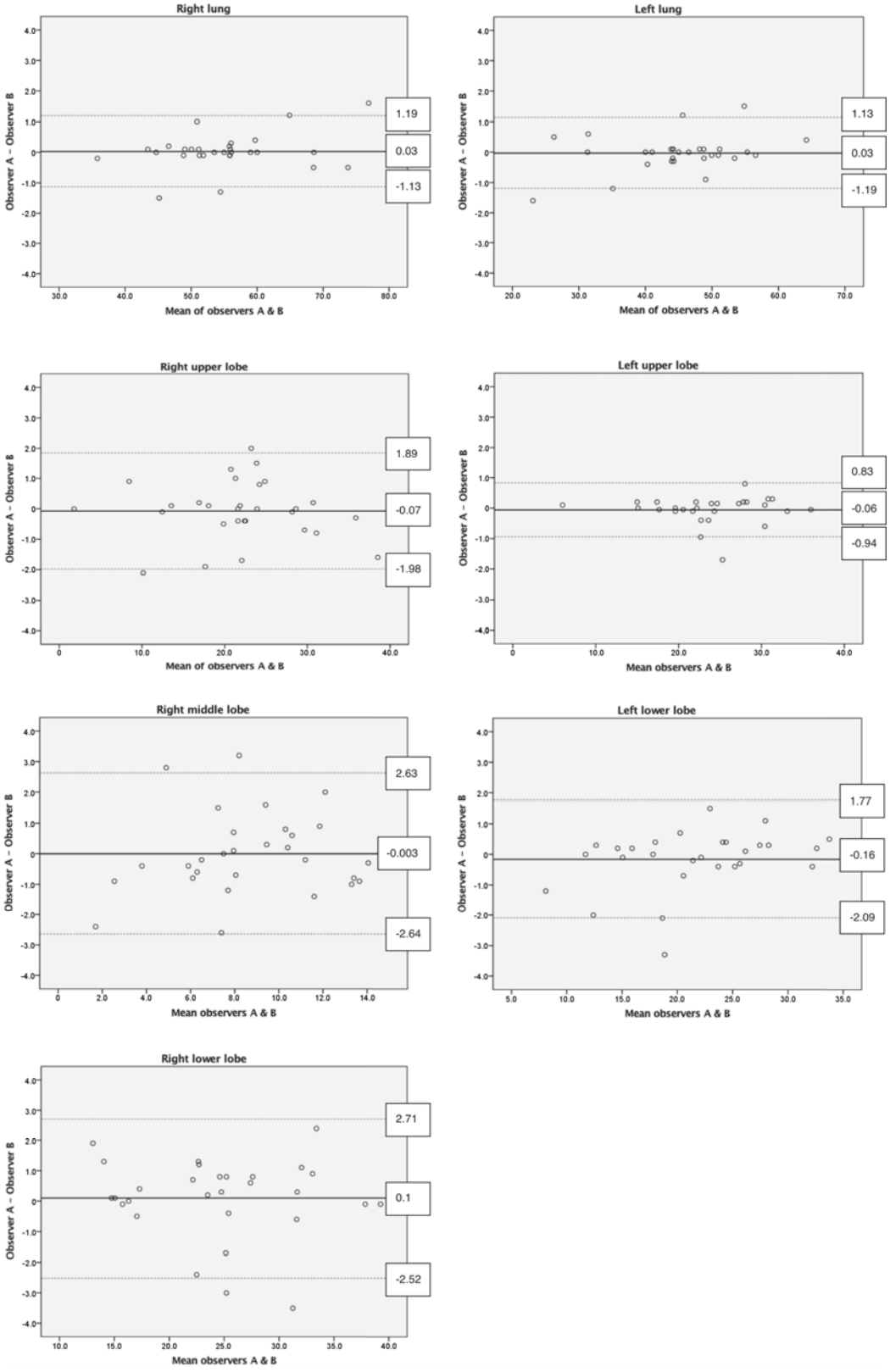

Figure 2. Bland Altman plots for interobserver measurements of total lung and lobar perfusion using SPECT/CT.

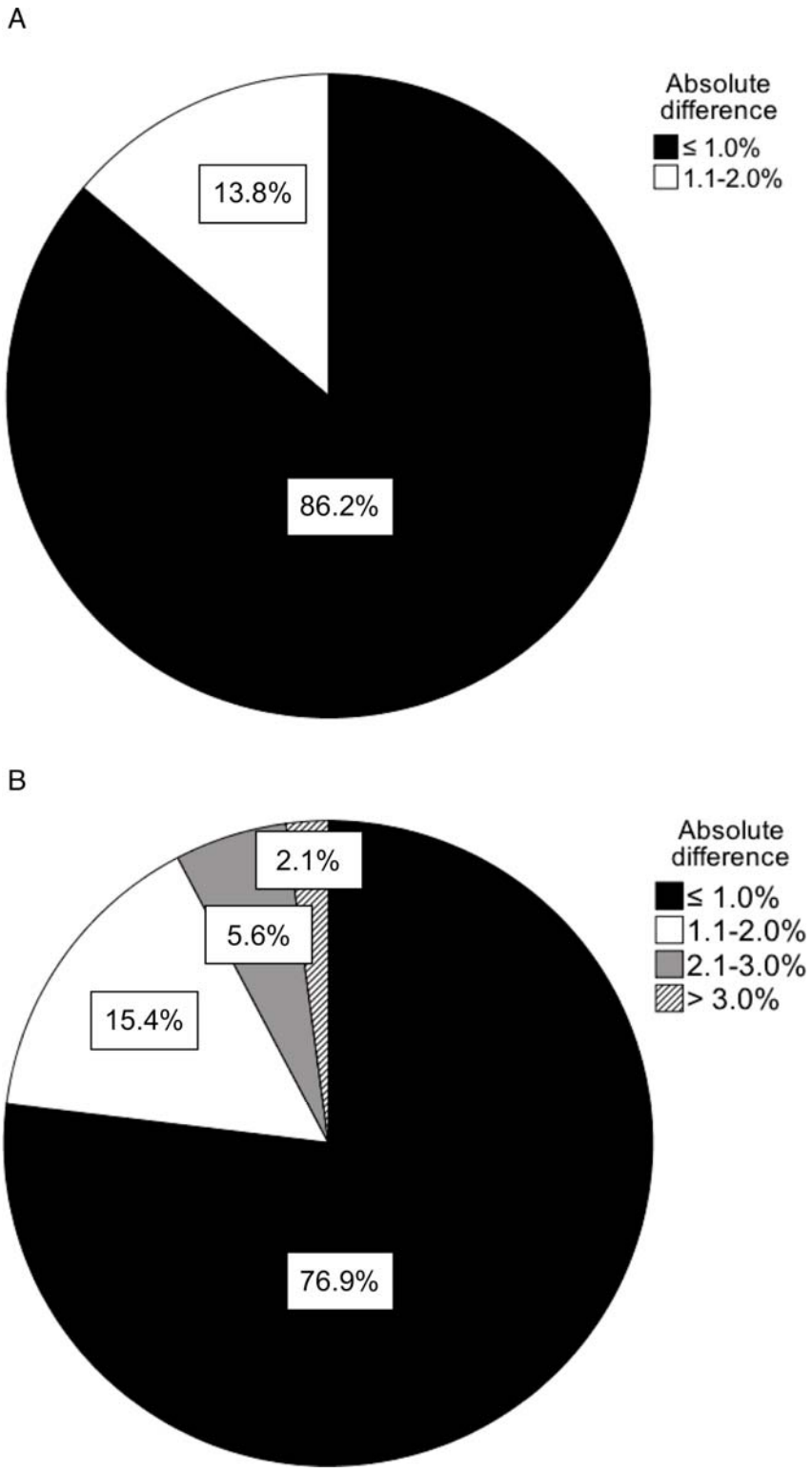

Figure 3. Absolute differences for interobserver measurements of total lung (A) and lobar (B) contribution using SPECT/CT.

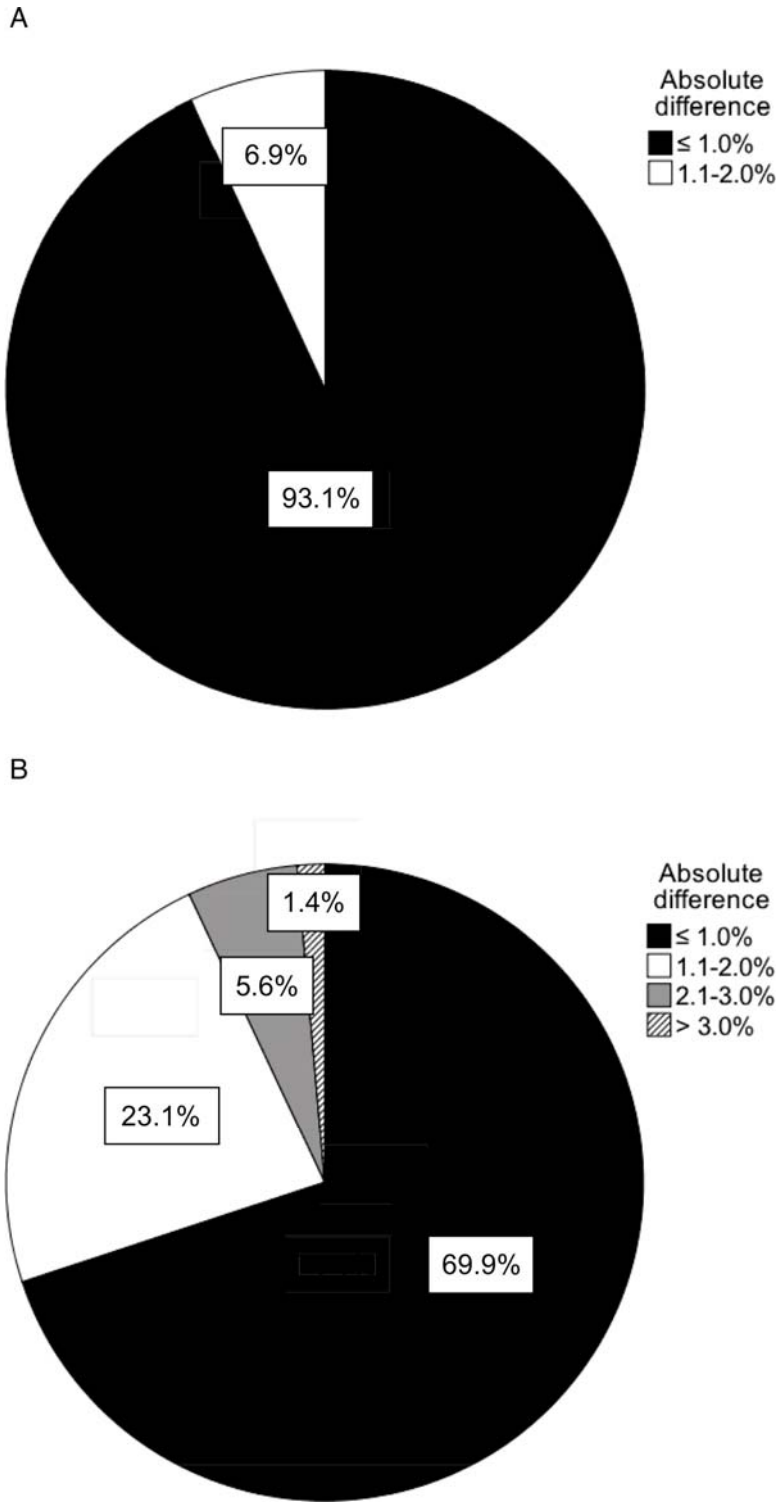

Figure 4. Absolute differences for intraobserver measurements of total lung (A) and lobar (B) contribution using SPECT/CT.

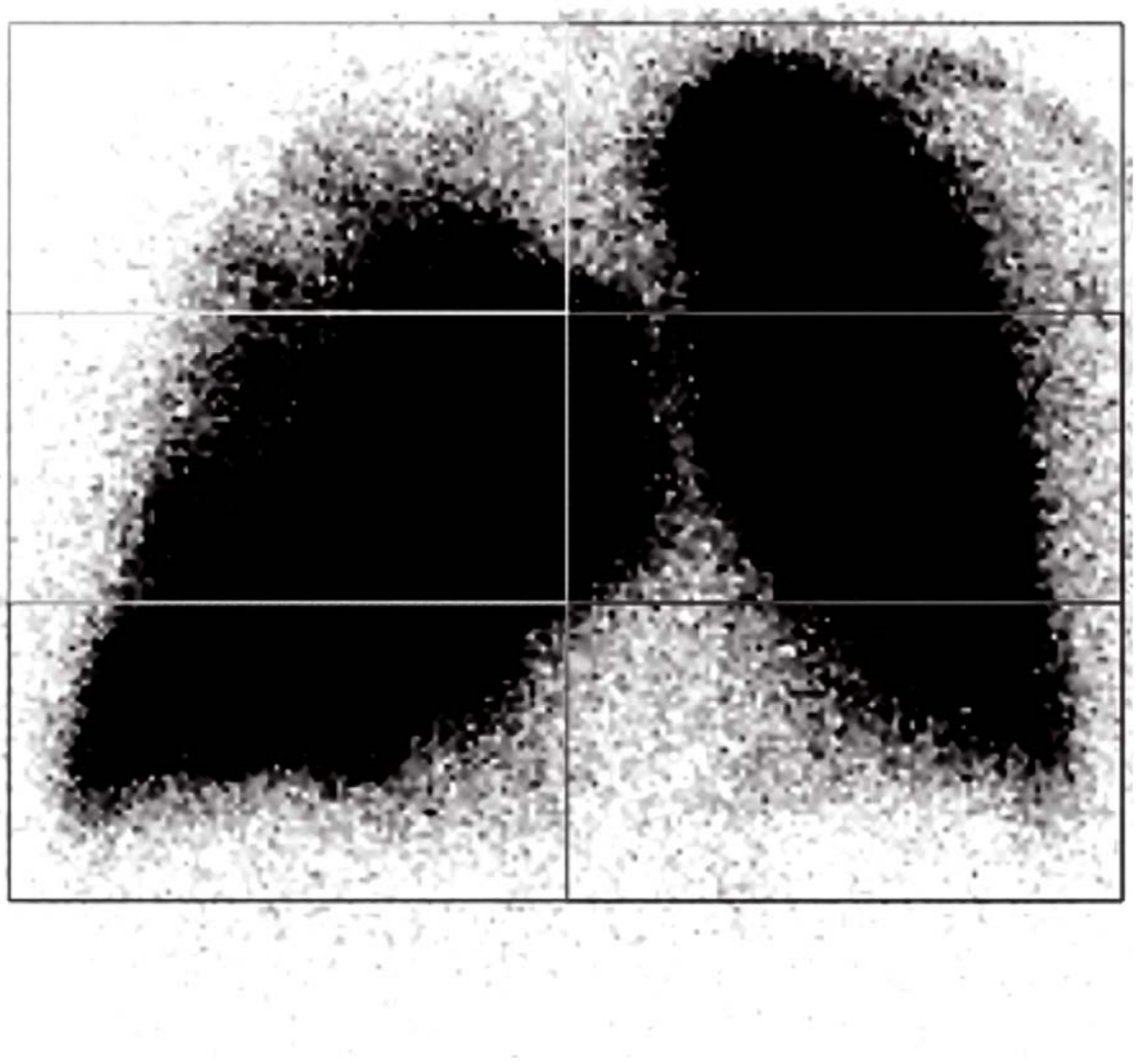

Figure 5. Example of inadequate segmentation on planar scintigraphy due to right lung parenchyma overlying midline. There is also prominent vascular activity, partly included in left upper and left middle lung regions (anterior view showed, image contrast increased).

Tables

Table 1. Patient characteristics

Patient (n=30)	Age & Sex	Site of primary tumor	Underlying lung disease	Central deposition of Technegas
1	79M	LUL	Severe emphysema	Present
2	80F	LUL	None	Absent
3	61M	LLL	None	Absent
4	79F	LUL	None	Present
5	62F	RLL	Moderate emphysema	Absent
6	53F	RML	Severe emphysema	Present
7	73M	LUL	Severe emphysema	Present
8	70M	RLL	Severe emphysema	Present
9	74M	RUL	Severe emphysema	Absent
10	79F	LUL	None	Absent
11	52F	Mediastinum	None	Absent
12	65M	LUL	Severe emphysema	Absent
13	63M	RLL	Moderate emphysema	Absent
14	75F	RUL	None	Absent
15	60F	RUL	None	Absent
16	70M	RLL	Severe emphysema	Absent
17	69M	LLL	Severe emphysema	Present
18	69M	LUL	Moderate emphysema	Absent
19	56M	RUL	Severe emphysema	Present
20	75M	LUL	Multifocal infiltrates	Absent
21	69M	LUL	Severe emphysema	Present
22	69F	RLL	None	Absent
23	65F	RUL and RLL	None	Absent
24	80M	LUL	Moderate emphysema	Absent
25	74M	RLL	Moderate emphysema	Absent
26	70M	LLL	Severe emphysema	Present
27	64F	RLL	Moderate emphysema	Present
28	56F	RLL	None	Absent
29*	55F	LUL	Severe emphysema	Present
30	67F	LUL	None	Present

*excluded patient

Table 2. Comparison of lobar, total right and total left lung quantification values on planar method and SPECT/CT perfusion studies

	Mean (planar)	**Mean (SPECT/CT)**	**Mean absolute difference (MAD) (min-max)**	***P* value**
R	54.8	55.1	1.2 (0-3.4)	.15
L	45.2	44.9	1.2 (0-3.4)	.15
RUL	11.9	22.2	10.7 (2.1-22.8)	< .001
RML	29.4	8.7	20.7 (11.1-36.0)	< .001
RLL	13.5	24.6	11.1 (0.3-23.6)	< .001
LUL	22.7	23.9	3.2 (0-10.6)	.63
LLL	21.5	21.3	3.7 (0-10.8)	.31

R= total right lung, L= total left lung, RUL = right upper lobe, RML = right middle lobe, RLL = right lower lobe, LUL = left upper lobe, LLL = left lower lobe

Table 3. Comparison of lobar, total right and total left lung quantification values on planar method and SPECT/CT ventilation studies

	Mean (planar)	**Mean (SPECT /CT)**	**Mean absolute differences (MAD) and *P* values**					
			All patients (n=29)		*No central deposition* (n=18)*		*Central deposition (n=11)*	
			MAD (min-max)	*P* value	MAD (min-max)	*P* value	MAD (min-max)	*P* value
R	54.6	56.0	2.0 (0-8.8)	.01	1.9 (0.1-8.8)	.13	2.2 (0.4-6.0)	.02
L	45.4	44.0	2.0 (0-8.8)	.01	1.9 (0.1-8.8)	.13	2.2 (0.4-6.0)	.02
RUL	11.8	20.6	8.8 (0.2-19.2)	< .001	9.1 (0.2-19.2)	< .001	8.3 (4.9-13.6)	< .001
RML	27.3	9.3	18.0 (10.6-29.7)	< .001	17.9 (12.5-27.0)	< .001	18.2 (10.6-29.7)	< .001
RLL	15.5	26.1	10.9 (0.2-12.0)	< .001	10.4 (0.2-17.3)	< .001	11.8 (2.4-27.3)	< .001
LUL	21.7	22.3	3.6 (0-12.0)	.82	3.2 (0-12.0)	.87	4.3 (0.1-11.5)	.63
LLL	22.4	22.0	3.5 (0-11.1)	.22	3.4 (0-11.1)	.27	3.6 (0.1-9.8)	.57

R= total right lung, L= total left lung, RUL = right upper lobe, RML = right middle lobe, RLL = right lower lobe, LUL = left upper lobe, LLL = left lower lobe
*Subgroup analyses were performed for patients with and without central deposition of Technegas.

Table 4. Interobserver measurements for quantification on SPECT/CT perfusion studies

	Mean (min-max)	**Mean absolute difference (MAD) (min-max)**	**ICC** (95% confidence interval)**	**SEM*** for ICC**
R	55.1 (35.8-76.9)	0.3 (0-1.6)	0.998 (0.996-0.999)	0.810
L	44.9 (23.1-64.2)	0.3 (0-1.6)	0.998 (0.996-0.999)	0.810
RUL	21.9 (1.8-38.5)	0.7 (0-2.1)	0.993 (0.984-0.997)	1.321
RML	8.7 (1.7-14.1)	1.0 (0-3.2)	0.922 (0.841-0.963)	1.832
RLL	24.6 (13.1-39.3)	0.9 (0-3.5)	0.984 (0.966-0.992)	1.830
LUL	23.8 (6.0-36.0)	0.3 (0-1.7)	0.990 (0.979-0.995)	1.278
LLL	21.5 (8.1-33.8)	0.6 (0-3.3)	0.989 (0.977-0.995)	1.390

R= total right lung, L= total left lung, RUL = right upper lobe, RML = right middle lobe, RLL = right lower lobe, LUL = left upper lobe, LLL = left lower lobe
** ICC= intraclass correlation coefficient
*** SEM= standard error of the mean

Table 5. Intraobserver measurements for quantification on SPECT/CT ventilation studies

	Mean (min-max)	**Mean absolute difference (MAD) (min-max)**	**ICC** (95% confidence interval)**	**SEM*** for ICC**
R	56.0 (46.3 -74.0)	0.4 (0 -1.6)	0.997 (0.994-0.999)	0.798
L	44.0 (26.1 -53.7)	0.4 (0 -1.7)	0.997 (0.994-0.999)	0.798
RUL	20.7 (7.7 -33.8)	1.3 (0 -3.5)	0.956 (0.910-0.979)	2.312
RML	9.3 (0.5 -14.6)	0.9 (0 -3.4)	0.943 (0.882-0.973)	1.661
RLL	26.0 (13.9 -42.2)	0.8 (0 -2.3)	0.989 (0.977-0.995)	1.443
LUL	22.3 (7.3 -33.1)	0.3 (0 -1.3)	0.989 (0.977-0.995)	1.174
LLL	22.0 (10.0-33.3)	0.6 (0 -3.3)	0.989 (0.976-0.995)	1.205

R= total right lung, L= total left lung, RUL = right upper lobe, RML = right middle lobe, RLL = right lower lobe, LUL = left upper lobe, LLL = left lower lobe
** ICC= intraclass correlation coefficient
*** SEM= standard error of the mean

Appendix I

Schematic representation for comparison of quantification measurements on planar scintigraphy and SPECT/CT