Head to head prospective comparison of quantitative lung scintigraphy and segment counting in predicting pulmonary function of lung cancer patients undergoing video-assisted thoracoscopic lobectomy

Elite Arnon-Sheleg ^{1*} , Ori Haberfeld ^{2,3*} , Ran Kremer ^{2,3} , Zohar Keidar ^{2,3} , Michal Weiler-Sagie ²
*Equal contribution
¹ Galilee Medical Center, Nahariya, ISRAEL,
² Rambam Medical Center, Haifa, ISRAEL
³ Rappaport Faculty of Medicine, Technion – Israel Institute of Technology, Haifa, ISRAEL
Word count: 4635
Corresponding author:
Elite Arnon-Sheleg MD
Elite.arnon@gmail.com tel: 972-50-7887611
ORCID ID 0000-0001-8978-42021
Running title: Post-operative lung function prediction in lobectomy patients

ABSTRACT

Prediction of post-operative pulmonary function in lung cancer patients before tumor resection is essential for patient selection for surgery and is conventionally done with a non-imaging segment counting method (SC) or a two-dimensional planar lung perfusion scintigraphy (PS). The purpose of this study was to compare quantitative analysis of PS to single photon emission computed tomography/computed tomography (SPECT/CT) and to estimate the accuracy of SC, PS and SPECT/CT in predicting post-operative pulmonary function in patients undergoing lobectomy.

Methods: Seventy-five non-small cell lung cancer (NSCLC) patients planned for lobectomy were prospectively enrolled (68% males, average age 68.1±8 years). All patients completed pre-operative forced expiratory volume capacity (FEV1), diffusing capacity of the lung for carbon monoxide (DLCO), Tc99m-MAA lung perfusion scintigraphy with PS and SPECT/CT quantification. A subgroup of 60 patients underwent video-assisted thoracoscopic (VATS) lobectomy and measurement of post-operative FEV1 and DLCO. Relative uptake of the lung lobes estimated by PS and SPECT/CT were compared. Predicted post-operative FEV1 and DLCO were derived from SC, PS and SPECT/CT. Prediction results were compared between the different methods and the true post-operative measurements in patients who underwent lobectomy.

Results: Relative uptake measurements differed significantly between PS and SPECT/CT in right lung lobes, with a mean difference of -8.2±3.8, 18.0±5.0 and -11.5±6.1 for right upper, middle and lower lobes respectively (p<0.001). The differences between the methods in the left lung lobes were minor with a mean difference of -0.4±4.4 (p>0.05) and -2.0±4.0 (p<0.001) for left upper and lower lobes respectively. No significant difference and strong correlation (R=0.6-0.76, p<0.001) were found between predicted post-operative lung function values according to SC, PS, SPECT/CT and the actual post-operative FEV1 and DLCO.

Conclusions: Although lobar quantification parameters differed significantly between PS and SPECT/CT, no significant differences were found between the predicted post-operative lung function results derived from these methods and the actual post-operative results. The additional time and effort of SPECT/CT

quantification may not have an added value in patient selection for surgery. SPECT/CT may be advantageous in patients planned for right lobectomies but further research is warranted.

Key Words: Lung function, perfusion, SPECT/CT, VATS lobectomy, lung cancer

INTRODUCTION

Lung cancer is the most common cause of death among oncologic patients worldwide (1). Resection is the treatment of choice for early stage non-small cell lung cancer (NSCLC) (2). Due to a common risk factor (smoking), many lung cancer patients suffer from coexisting lung disease resulting in reduced pulmonary functions, increased risk of peri-operative morbidity and mortality (3).

Estimation of the respiratory reserve is an essential element of pre-operative evaluation. Candidates for lung resection undergo respiratory evaluation by pulmonary function testing with measurement of FEV1 (forced expiratory volume in 1 second) and DLCO (diffusing capacity of the lungs) (3,4). Patients with FEV1 or DLCO<80% of predicted value are defined as high risk patients and require estimation of the pulmonary function after the operation, which is achieved by calculating the predicted post-operative FEV1 and DLCO (ppoFEV1 and ppoDLCO) (5,6). A predicted value of <30% is considered a significant risk for peri-operative mortality or morbidity and thus the operation is contraindicated (5). The predicted post-operative lung function can be calculated simply by multiplying the pre-operative FEV1 or DLCO with the fractional number of lung segments that will remain after the operation (7). This method, called segment counting (SC), is considered reliable, but some studies have found that it is inaccurate as it ignores the possibility that some of the segments have reduced function and tends to underestimate the ppoFEV1 (7,8).

Radionuclide perfusion lung scanning with technetium-99m-labeled macroaggregate of albumin (Tc-99m MAA) can be used to estimate and quantify the regional distribution of lung function. The contribution of a lobe or an entire lung can be determined by drawing regions-of-interest on planar perfusion images. Typically, the data from quantitative radionuclide perfusion scans are reported as the percent of function contributed by the six lung regions: upper third, middle third and lower third of each hemithorax. These data, combined with the preoperative lung function value and the location and planned extent of surgical resection, permit a calculation of the ppoFEV1/DLCO value. The ppoFEV1 derived from planar perfusion scintigraphy (PS) has shown fair correlation with the spirometry-measured postoperative FEV1 in pneumonectomy patients (9); however, less is known about using perfusion scintigraphy to estimate post-lobectomy lung function. Single photon emission computed tomography (SPECT) can provide tomographic images of lung perfusion. The comparison of SPECT (without concomitant CT) and

PS has shown no significant advantage in post-operative lung function prediction (10-,12), possibly due to attenuation effects and the inability to trace the lobar anatomic boundaries since the lung fissures are not visible in the study. In recent years several studies have attempted to compare the post-operative prediction of lung function between PS and single photon emission computed tomography/computed tomography (SPECT/CT) perfusion scans with various methodologies (13-,19). Most of these studies had small numbers of lobectomy patients and some did not compare the prediction results to the actual post-operative lung function tests. Some of the studies found SPECT/CT based calculations to be superior but some showed no difference from planar imaging.

This study aimed to compare lung function quantification with PS and SPECT/CT and to estimate the accuracy of SC, PS and SPECT/CT for the prediction of post-operative lung function, in a selected and homogeneous group of early stage NSCLC patients undergoing video-assisted thoracoscopic lobectomies (VATS).

MATERIAL AND METHODS

Patients admitted for VATS lobectomy / bilobectomy due to NSCLC with reduced pulmonary function tests (FEV1 or DLCO<80% of predicted) were included in the study. Seventy-five patients were prospectively enrolled from December 2016 to April 2018 (age 68.1±8 years, 51 males (68%), 66 smokers (88%). The study was approved by the Institutional Ethics Committee, and all subjects signed informed consent forms.

All of the included patients underwent pre-operative spirometry (for FEV1) and pulmonary diffusing capacity test (DLCO) 1-14 days before surgery (preFEV1 and preDLCO) and had reduced lung function tests (FEV1 or DLCO<80% of predicted). Lung perfusion scan was performed 1-5 days before surgery after a slow intravenous injection of 150 MBq Tc-99m MAA with the patient in the supine position. Imaging data was acquired on a dual head gamma camera (Discovery 670, GE Healthcare, Milwaukee, USA) using a low-energy high resolution (LEHR) parallel hole collimator and an energy window of 140 keV \pm 10 % for emission counts. PS consisted of static posterior and anterior acquisition of 500 k counts on a 256 x 256 matrix with a square pixel size of 1.74 mm. SPECT was acquired with projection data every 6 degrees for 360 degrees of rotation with a matrix of 128 x 128, a square pixel size

of 4.45 mm, and an acquisition duration of 15 seconds per projection. SPECT acquisition was followed by a helical CT scan at a peak voltage of 120 kV, and adaptive tube current (50 to 180 mA using GE Smart mA with noise index of 24.6). The pitch was 1.375 with 1 s per rotation. Image slice thickness was 3.75 mm and the matrix size was 512 x 512 for a 50 cm diameter transverse field of view. CT was reconstructed using filtered back-projection and a soft-tissue filter. SPECT was reconstructed with CT attenuation correction using an ordered subset expectation maximization (OSEM) algorithm with 2 iterations, 10 subsets, Butterworth post-filtering (order 10, cutoff frequency 0.48 cm⁻¹), and an isotropic voxel size of 4.45 mm. PS was processed for quantitative perfusion analysis using automatic software provided by the Xeleris workstation (GE Healthcare). The software divides both lungs into 3 regions of interest and calculates the relative uptake in each region (zone) using the geometric mean of the anterior and posterior images (Fig. 1A). In the right lung the upper, middle and lower zones correspond with the right upper lobe (RUL), right middle lobe (RML) and right lower lobe (RLL) respectively. In the left lung the upper zone and half of the middle zone correspond to the left upper lobe (LUL) and the lower zone, and half of the middle zone corresponds to the left lower lobe (LLL). Quantitative analysis of the SPECT/CT images data was done with semi-automatic software, Qlung[©] provided by GE (Fig. 1B). The software requires the reader to mark the lung fissures in (at least) two places for each fissure on the CT images. The software then automatically draws volumetric regions of interest (VOIs) for each lobe and calculates its relative uptake. The relative uptake was calculated for all 5 lobes in both methods (PS and SPECT/CT).

The predicted post-operative lung function values (ppoFEV1 and ppoDLCO) were calculated by three methods:

SC – calculated by multiplying the preoperative lung function tests with the predicted fraction of segments the patient will have after resection (8). The total number of segments in both lungs is 19 (3 in the RUL, 2 in RML, 5 in RLL, 5 in LUL and 4 in LLL).

ppoFEV1 or ppoDLCO = preFEV1 or preDLCO x (19-number of excised segments)

19

PS – calculated by multiplying the preoperative lung function tests with the predicted residual functioning lung according to the planar quantification (20).

SPECT/CT – calculated similarly to PS predicted values using the percentage of perfused lung to be resected based on the SPECT/CT quantification.

Using the predicted lung function results from SC and PS, patients with either ppoFEV1 or ppoDLCO<30% were defined as very high risk patients and were excluded from surgical treatment.

Of the 75 enrolled patients, a subgroup of 60 patients underwent VATS lobectomies. Following the operation, all of the patients in this subgroup underwent additional lung function tests, including FEV1 and DLCO (postFEV1 and postDLCO), within a month from the time of operation, at the same facility where the pre-operative tests were done. The subgroup's patient characteristics are detailed in Table 1.

Results of the post-operative lung function tests were compared to the predicted values according to the three different methods specified.

Statistical Methods

Quantitative variables were presented as mean \pm SD and range. Qualitative variables were described with frequencies and percentages.

Statistical analysis was performed with IBM SPSS Statistics version 25.0.

The agreement between quantitative measures was done by Bland–Altman analysis using a scatter plot for the difference of paired measures and the average of each pair. Limits of agreement were defined as mean of difference \pm 2 SD. Paired sample t-test was used for comparisons between the quantitative measures and Pearson's correlation coefficient test was used to evaluate the relationship between those measures. Normal distribution of the measures or of the differences between the paired measures were described with histograms and tested with the One-sample Kolmogrov-Smirnov test. Normality was tested

as preliminary assumption for the Pearson's correlation coefficient test and the paired sample t-test. Alpha less than 5% was considered significant. 2-sided significant level was presented, unless noted.

RESULTS

Comparison of Relative Uptake Quantified by PS and SPECT/CT

The relative uptake was calculated for each lung lobe using the PS and SPECT/CT quantification in all of the patients. The mean relative uptake calculated by PS and SPECT/CT and the difference between them is shown in Table 2. A significant difference was found between the quantitative methods in all of the lung lobes except for the LUL. PS consistently showed higher relative uptake in the RML (mean difference $_{\text{(PS-SPECT/CT)}} = 18.0\pm5.0$, p<0.001) and consistently lower results for the RUL and RLL (mean difference $_{\text{(PS-SPECT/CT)}} = -8.2\pm3.8$ and -11.5±6.1 respectively, p<0.001). A minor but significant difference was found between the methods in the LLL (mean difference $_{\text{(PS-SPECT/CT)}} = -2.0\pm4.0$, p<0.001) and no significant difference was found in the LUL (mean difference $_{\text{(PS-SPECT/CT)}} = -0.4\pm4.4$, p>0.05). A difference >10% in lobar quantification between the methods was observed in 26 patients (35%) in the RUL, 69 patients (92%) in the RML, 47 patients (63%) in the RLL, 3 patients (4%) in the LUL and 5 patients (7%) in the LLL.

Despite the significant difference in relative uptake calculated by PS and SPECT/CT, there was a good correlation between the two methods in all of the lung lobes, excluding the RML (Fig. 2). The correlation was stronger in the LUL, LLL and RUL ($R=0.67,\,0.77$ and 0.64 respectively, p<0.001) and moderate in the RLL (R=0.49 p<0.001). Weak correlation with borderline significance was found for the RML (R=0.22 p=0.57).

Comparison of Predicted Post-Operative Lung Function Calculated according to SC, PS and SPECT/CT and the Actual Post-Operative Results:

In the subgroup of 60 patients who underwent VATS lobectomies, 31 patients (52%) underwent lobectomy of the right side and 29 underwent left lobectomies (48%). Most of the lobectomies were of the LUL (21, 35%) and RUL (19, 32%) and only three patients underwent RML lobectomies (5%) (Table 1).

The mean ppoFEV1 and ppoDLCO measurements calculated using SC were 58.6±13.9 and 54.2±13.9 respectively. The mean ppoFEV1 and ppoDLCO were 60.8±14.0 and 56.5±15.3 when calculated by PS, and 60.4±13.6 and 55.7±13.4 when calculated with SPECT/CT. The actual mean post-operative lung function results were FEV1 of 60.8±15.7 and DLCO of 55.4±14.3. Significant correlation was found between the predicted FEV1 and DLCO and the post-operative results for all three methods (Fig. 3). The

ppoFEV1 calculated by SC showed the strongest correlation to the actual post-operative value (R=0.76 p<0.001), while SPECT/CT derived ppoDLCO calculation had the strongest correlation to the post-operative value (R= 0.64 p<0.001). Bland-Altman plots showed no significant differences between predicted and post-operative values for all 3 methods (Fig. 4), with the lowest limits of 95% confidence interval shown by SC for FEV1 (-18.4-22.9) and SPECT/CT for DLCO (-20.6-21.5).

Comparison between the values predicted by the different methods and the post-operative measurements showed similar results in patients undergoing either right or left side lobectomy, with correlation coefficients of 0.74, 0.70 and 0.71 (p<0.001) for SC, PS and SPECT/CT respectively in right lung lobectomies and 0.80, 0.76 and 0.80 (p<0.001) respectively for left lung lobectomies. Comparison between the methods according to the lobes resected showed similar results in all of the lobes excluding the RML where the ppoFEV1 and ppoDLCO calculated by PS were lower than the results by SC and SPECT/CT and lower than the actual post-operative results (Supplemental Fig. 1), though a statistical analysis was not possible since only three patients underwent RML lobectomies.

DISCUSSION

In this prospective study in a homogenous population of patients with localized NSCLC planned for VATS lobectomy, although significant differences were shown between the relative lobar uptake quantified by PS and SPECT/CT in the right lung lobes, no significant differences were found between these methods for predicting post-operative lung function.

These results are consistent with some of the previous studies comparing the role of tomographic techniques such as SPECT/CT to PS (summarized in Table 3) and were validated in this study using strict methodology in patient selection, an advanced SPECT/CT derived lung segmentation method, a single facility for lung function testing, and a single surgical method. Previous studies comparing these methods included patients undergoing several types of procedures, including pneumonectomy, lobectomy and segmentectomy and several surgical methods, including thoracotomy and VATS (10,11,17,18). Our study population was homogenous, containing only patients undergoing VATS lobectomies, since in patients undergoing a pneumonectomy, PS is sufficient for assessing the relative uptake of the whole lung. VATS lobectomy was the only surgical method used in the current study in order to avoid differences in patient

recovery process after thoracoscopic procedures and open thoracotomies, differences which can affect postoperative lung function tests.

Several previous studies did not compare the scintigraphy-derived results with actual postoperative lung function tests, and some evaluated only FEV1 as a measure of the patients lung function
(14,15,18,19,21). In this study the predicted results (ppoFEV1 and ppoDLCO) according to the different
quantification methods were compared to the post-operative tests, which are considered to be the gold
standard value, in a subgroup of 60 patients. We included in our lung function assessment both FEV1 and
DLCO, since FEV1 is considered to be the standard reference value but recent studies have shown that
DLCO has a better correlation with survival after lobectomy for lung cancer patients (22,23). All patients in
the VATS lobectomy subgroup underwent lung function tests before and after surgery and the tests were
conducted at a specified and limited time period pre- and post-surgery. Since results of lung function tests
can vary significantly between different facilities, all of the lung function tests in our study were conducted
in a single facility.

The SPECT and CT scans in this study were acquired sequentially, thus avoiding errors of misregistration and enabling attenuation correction of the SPECT data. SPECT/CT quantitative assessment of the lung perfusion was performed using the Qlung® semiautomatic software which divides the lung into VOI's for each lobe according to the actual lung fissures, thus ensuring that even in patients with significant anatomical changes the segmentation is correct. Other commercial software from different vendors are available for lobar segmentation and will need to be validated separately. Some of the previous studies acquired the SPECT and the CT scans at different time points and co-registered both data sets later (14,16). This could cause misregistration errors. Other studies used different methods of segmentation of the SPECT/CT data into the lung lobes, for example the study by Kovacevic-Kusmierek *et al* (17) used the CT for finding landmarks, such as the position of the tracheal bifurcation or the fourth rib, for the location of the lung fissures, since the low dose CT did not visualize the fissures themselves. This method can introduce lung segmentation errors in patients with unusual lung anatomy, especially in patients suffering from gross emphysematous or fibrotic changes.

The comparison between the relative lobar uptake according to PS and SPECT/CT showed significant differences in the quantitation of the right lung lobes but minor differences in the left lung lobes.

The difference between the methods was most pronounced in the RML with a mean difference of 18.0±5.0 and a difference >10% found in 92% of the patients. This is probably due to the inability of PS to differentiate between the RML and the remainder of the right lung. Similar results were shown in Suh's, Genseke's and Provost's studies (18,19,24).

Although significant differences were found between the quantification methods, no such difference was shown when calculating the predicted post-operative lung function according to the different methods in the VATS lobectomy subgroup, including the simple non-imaging SC method. SC had a slightly better performance in predicting the postFEV1 values and SPECT/CT in predicting the postDLCO values, but these were minor differences. We did find a difference however, in the prediction values for both FEV1 and DLCO between the PS method and the remainder of the methods in RML lobectomy patients, but these could not be statistically proven due to the small number of patients in this group. Suh's study showed similar results but only a small portion of patients in the study underwent post-operative lung function tests (only 9 out of 55 patients) (18).

The major limitation of our study was a relatively small number of patients, especially patients undergoing RML lobectomies.

CONCLUSIONS

Lobar quantification is significantly different between PS and SPECT/CT in the right lung lobes.

SC, PS and SPECT/CT showed similar performance in prediction of post-operative FEV1 and DLCO.

SPECT/CT may have an added value in patients planned for right lung lobectomies but further research in a larger patient cohort is needed.

Compliance with Ethical Standards

Conflict of interest: The authors declare that they have no conflict of interest.

Statements of human rights: All procedures performed in studies involving human participants were in

accordance with the clinical standards of the institutional and national research committees and with the

1964 Helsinki declaration and its later amendments or comparable clinical standards.

Statement on the welfare of animals: This article does not contain any studies with animals performed by

any of the authors.

Informed consent: Informed consent was obtained from all individual participants included in the study.

Clinical Trial Registration: Clinical trial registration was waived by the Institutional Ethics Committee, as

participation in the trial had no consequences on patient management.

KEY POINTS

Question: Is SPECT/CT based quantification of perfusion scintigraphy different from planar based

quantification and which method of predicting post-operative lung function in lobectomy patients more

accurate?

Pertinent findings: In this prospective study in 75 patients, SPECT/CT based quantification of lung function

was significantly different from planar based quantification in the lobes of the right lung. No significant

differences were found between predicted lung function calculated with a non-imaging segment counting

method (SC), planar perfusion scan, SPECT/CT and the actual post-operative values in a subgroup of 60

patients.

Implication for patient care: Prediction of post-operative lung function in lung cancer patients who are

candidates for lobectomy can be achieved with the simple non-imaging SC method in most patients.

Quantitative lung scintigraphy with SPECT/CT quantification should be considered for right lobectomies

over planar-based quantification.

13

REFERENCES

- [1] Torre LA, Siegel RL, Jemal A. Lung cancer statistics. *Adv Exp Med Biol.* 2016;893:1–19.
- [2] Maconachie R, Mercer T, Navani N, McVeigh G. Lung cancer: diagnosis and management: summary of updated NICE guidance. *Br Med J.* 2019;11049.
- [3] Bolliger CT, Koegelenberg CF, Kendal R. Preoperative assessment for lung cancer surgery. *Curr Opin Pulm Med*. 2005;11:301–306.
- [4] Little AG, Rusch VW, Bonner JA, et al. Patterns of surgical care of lung cancer patients. *Ann Thorac Surg.* 2005;80:2051–2056.
- [5] Brunelli A, Charloux A, Bolliger CT, et al. ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients (surgery and chemo-radiotherapy). *Eur Respir J.* 2009;34:17–41.
- [6] 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(5 Suppl):e166S-e190S.
- [7] Zeiher BG, Gross TJ, Kern JA, Lanza LA, Peterson MW. Predicting postoperative pulmonary function in patients undergoing lung resection. *Chest.* 1995;108:68–72.
- [8] Bolliger CT, Gückel C, Engel H, et al. Prediction of functional reserves after lung resection:

 Comparison between quantitative computed tomography, scintigraphy, and anatomy. *Respiration*.

 2002;69:482-489.
- [9] Corris PA, Ellis DA, Hawkins T, Gibson GJ. Use of radionuclide scanning in the preoperative estimation of pulmonary function after pneumonectomy. *Thorax*. 1987;42:285–291.
- [10] Mineo TC, Schillaci O, Pompeo E, Mineo D, Simonetti G. Usefulness of lung perfusion scintigraphy before lung cancer resection in patients with ventilatory obstruction. *Ann Thorac Surg.* 2006;82:1828-1834.
- [11] Piai D, Quagliatto Jr R, Toro I, et al. The use of SPECT in preoperative assessment of patients with lung cancer. *Eur Respir J*. 2004;24:258-262.
- [12] 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.

- [13] Yoshimoto K, Nomori H, Mori T, et al. Prediction of pulmonary function after lung lobectomy by subsegments counting, computed tomography, single photon emission computed tomography and computed tomography: a comparative study. *Eur J Cardio-thoracic Surg.* 2009;35:408-413.
- [14] Ohno Y, Koyama H, Nogami M, et al. State-of-the-art radiological techniques improve the assessment of postoperative lung function in patients with non-small cell lung cancer. *Eur J Radiol*. 2011;77:97-104.
- [15] 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.
- [16] Nagamatsu Y, Sueyoshi S, Sasahara H, et al. Predicting exercise capacity after lobectomy by single photon emission computed tomography and computed tomography. *Gen Thorac Cardiovasc Surg*. 2016;64:537-542.
- [17] Kovacević-Kuśmierek K, Kozak J, Pryt Ł, 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.
- [18] Suh M, Kang YK, Ha S, et al. Comparison of two different segmentation methods on planar lung perfusion scan with reference to quantitative value on SPECT/CT. *Nucl Med Mol Imaging*. 2017;51:161-168.
- [19] Genseke P, Wetz C, Wallbaum T, et al. Lung cancer pre-operative quantification of pulmonary function using hybrid-SPECT / low-dose-CT: A pilot study. *Lung Cancer*. 2018;118:155–160.
- [20] Markos J, Mullan BP, Hillman DR, et al. Preoperative assessment as a predictor of mortality and morbidity after lung resection. *Am Rev Respir Dis.*, 1989;139:902–910.
- [21] Le Roux PY, Leong TL, Barnett SA, et al. Gallium-68 perfusion positron emission tomography / computed tomography to assess pulmonary function in lung cancer patients undergoing surgery.

 Cancer Imaging, 2016;16:24.
- [22] Cerfolio RJ, Bryant AS. Different diffusing capacity of the lung for carbon monoxide as predictors of respiratory morbidity. *Ann Thorac Surg.* 2009;88:405–411.

- [23] Brunelli A, Refai MA, Salati M, Sabbatini A, Morgan-Hughes NJ, Rocco G. Carbon monoxide lung diffusion capacity improves risk stratification in patients without airflow limitation: evidence for systematic measurement before lung resection. *Eur J Cardiothorac Surg.* 2006;29:567–570.
- [24] Provost K, Leblond A, Gauthier-Lemire A, Filion E, Bahig H, Lord M. Reproducibility of lobar perfusion and ventilation quantification using SPECT/CT segmentation software in lung cancer patients. *J Nucl Med Technol.* 2017;45:185–192.

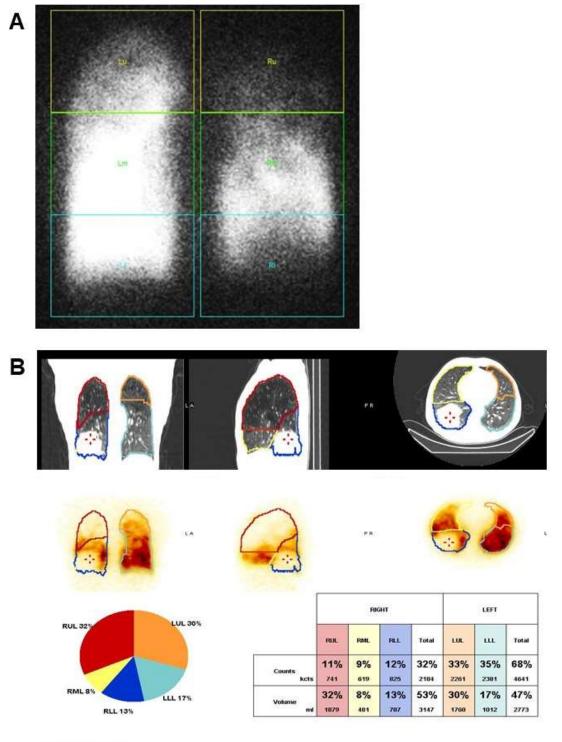


Figure 1

Figure 1: The methods of quantitative analysis of perfusion images in a patient with a RLL tumor. **(A)** Posterior view of the planar study with automatic lung division into 6 zones. **(B)** GE Qlung[©] quantitative analysis of SPECT/CT.

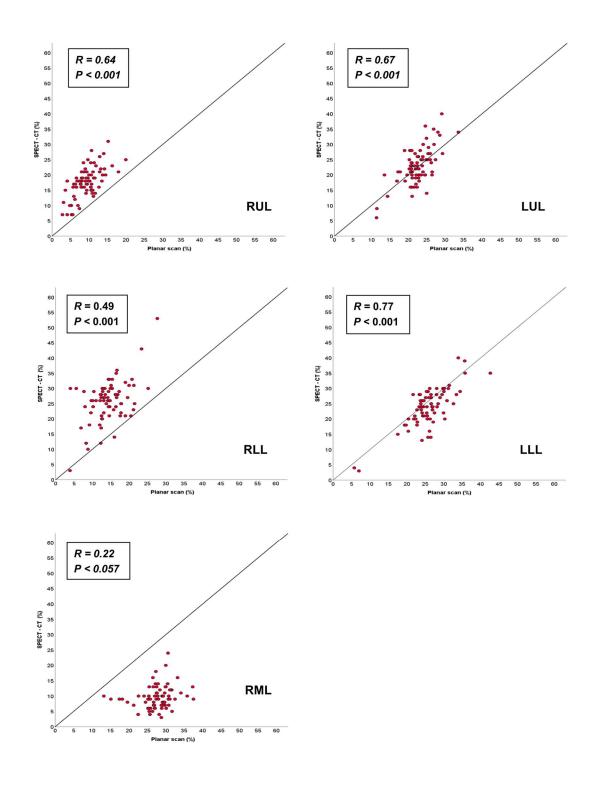


Figure 2

Figure 2: Correlation between relative uptake calculated by PS and SPECT/CT for each lobe (n=75).

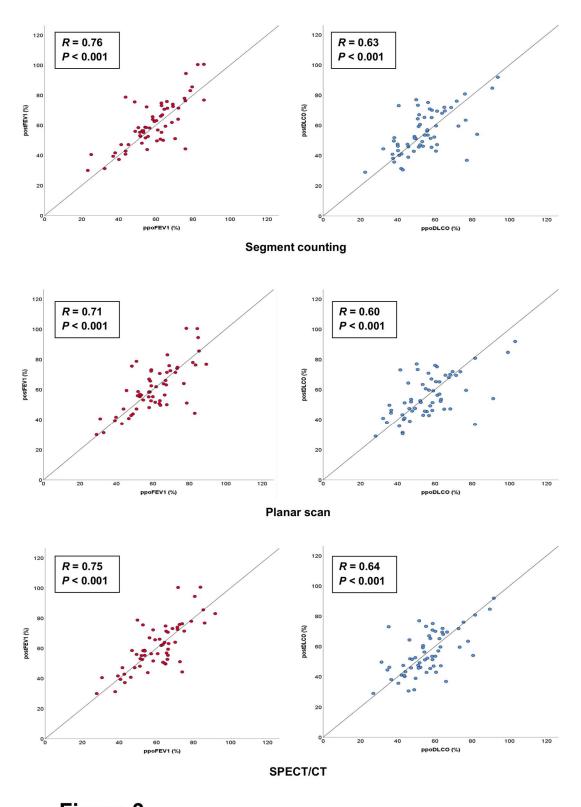


Figure 3

Figure 2: Completion between analysis of an about an artist EFV1 and DLCO for the 2 model to it the WATS

3: Correlation between predicted and post-operative FEV1 and DLCO for the 3 methods in the VATS lobectomy subgroup (n=60).

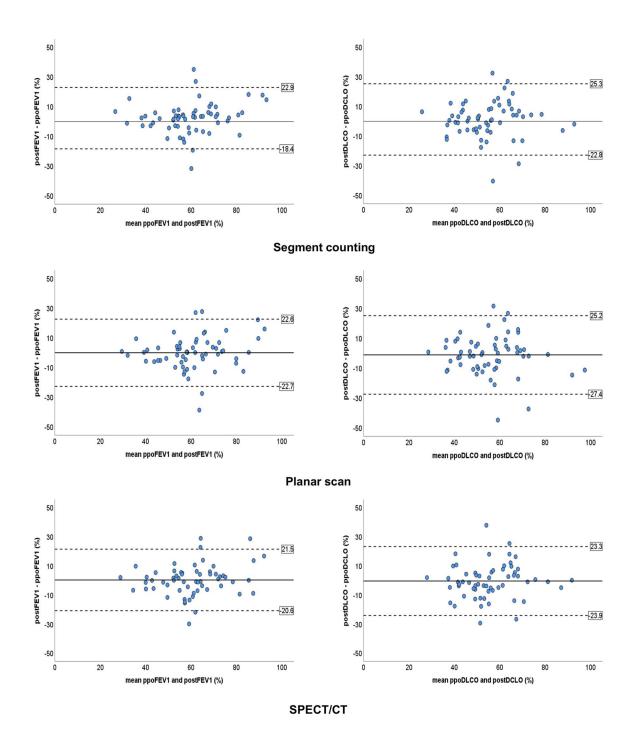
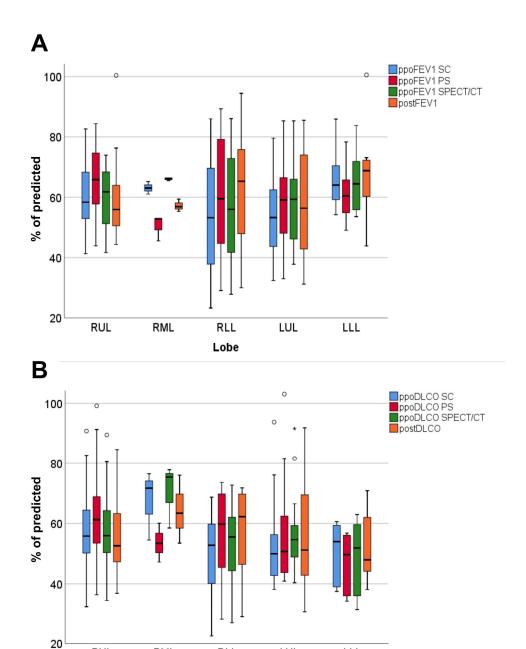


Figure 4

Figure 4: Bland-Altman plots comparing predicted and post-operative FEV1 and DLCO for the 3 methods in the VATS lobectomy subgroup (n=60).



Supplemental Figure 1

RML

RLL

Lobe

RUL

Supplemental Figure 1: Box plot chart comparing the predicted and post-operative FEV1 **(A)** and DLCO **(B)** according to the resected lobes in the VATS lobectomy subgroup (n=60). The thick line in the middle of the box represents the median. The top and bottom box lines show the first and third quartiles. The whiskers show the maximum and the minimum values, with the exceptions of outliers (circles) and extremes (asterisks). Outliers are at least 1.5 box lengths from the median and extremes are at least three box lengths from the median.

LUL

LLL

Table 1: VATS subgroup patient characteristics (n=60).

	N (%)	Average	Range
Surgery side, Right	31 (52%)		
RUL lobectomy	19 (32%)		
RML lobectomy	3 (5%)		
RLL lobectomy	8 (13%)		
LUL lobectomy	21 (35%)		
LLL lobectomy	8 (13%)		
RUL+RML lobectomy	1 (2%)		
Pre-operative FEV1		74.5±18	32-109
Pre-operative DLCO		68.9±17	31-127
Post-operative FEV1		60.8±15.7	30-101
Post-operative DLCO		55.4±14.3	29-92

Table 2: Relative uptake of the lung lobes according to the planar and SPECT/CT and the difference between the methods (n=75).

	Planar		SPECT/CT		Mean Difference	2-sided
						Significance
	Mean	Range	Mean	Range		
RUL	9 (±3)	3 - 20	18 (±5)	7 - 31	-8.2 (±3.8)	<0.001
RML	27 (±4)	13 - 37	10 (±4)	3 - 24	18.0 (±5.0)	<0.001
RLL	14 (±5)	2 - 27	26 (±7)	3 - 53	-11.5 (±6.1)	<0.001
LUL	23 (±4)	11 - 34	23 (±6)	6 - 40	-0.4 (±4.4)	0.05 NS
LLL	26 (±6)	6 - 43	24 (±7)	3 - 40	2.0 (±4.0)	<0.001

NS = No significance

Table 3: Studies comparing methods of lung quantification

Author	Year	Study Method (Prospective/Re trospective)	Number of Patients	Number of Pneumonectom y/Lobectomy	Comparison to post-operative tests	Scan Methods compared	Optimal Method
Piai (11)	2004	Prospective	26	13/13	Yes	PS vs. SPECT	PS=SPECT
Mineo (10)	2006	Prospective	39	11/28	Yes	PS vs. SPECT	PS=SPECT
Yoshimoto (13)	2009	Prospective	37	0/37	Yes	SC vs. CT and SPECT/CT	CT and SPECT/CT
Ohno (14)	2011	Prospective	229	14/215*	Yes	CT vs. MRI, PS, SPECT and Co-registered SPECT/CT	CT, MRI and SPECT/CT
Toney (15)	2014	Retrospective	17	NA	No	PS vs. SPECT-CT	NA
Kovacevic- Kusmierek (17)	2015	NM	70	47/23	Yes	SC vs. PS, SPECT and SPECT/CT	PS
Le Roux (21)	2016	Retrospective	22**	1/13**	No	PS vs. Q PET-CT	NA
Nagamatsu (16)	2016	Prospective	18	0/18	Yes	SC vs. Co-registered SPECT/CT	SC = Co- registered SPECT/CT
Suh (18)	2017	Prospective	55	2/32* (21 – no surgery)	Yes (9 patients)	PS (AP & PO) vs. SPECT/CT	SPECT/CT
Genseke (19)	2018	Retrospective	39	NM (32 – no surgery)	No	PS vs. SPECT/CT	NA
Current study	2019	Prospective	75	60	Yes (60 Patients)	SC vs. PS and SPECT/CT	SC=PS=SPECT /CT

NA = Not applicable, no gold standard test used. NM = Not mentioned. SC = Segment Counting. FS = Functional segments according to fiber-optic bronchoscopy. CT = Quantitative Computed Tomography. MRI = Perfusion MRI. PS = Perfusion Scintigraphy with planar quantitation. AP = Anterior-Posterior. PO = Posterior-Oblique. SPECT = Perfusion Scintigraphy with SPECT quantitation. SPECT-CT = Perfusion Scintigraphy with SPECT-CT quantitation. Co-registered SPECT-CT = CT and SPECT performed separately and co-registered with software.

^{*} Including segmentectomy or bi-lobectomy in the lobectomy group

^{**} Only 16 patients underwent both Q PET/CT and planar scan. 13 lobectomy, 4 segmentectomy, 1 pneumonectomy, 4 no operation.