Accuracy and precision of perfusion lung scintigraphy versus ^{133}Xe-radiospirometry for preoperative pulmonary functional assessment of patients with lung cancer

Denis Mariano-Goulart[1], Eric Barbotte[2], Célia Basurko[2], F. Comte[1], Michel Rossi[1].

[1] *Department of Nuclear Medicine. Montpellier University Hospital, Montpellier, France.*

[2] *Department of Statistics and Epidemiology, Montpellier University Hospital, Montpellier, France.*

Communicating author:

Nam : Denis Mariano-Goulart

Address: Service Central de Médecine Nucléaire, CHU Lapeyronie,

371 avenue du Doyen Gaston Giraud, 34295 Montpellier Cedex 5, France

Telephone number: +33-467-338-598

Fax number: +33-467-338-465

E-mail: d-mariano_goulart@chu-montpellier.fr

Abstract. *Purpose:* This study sought to determine whether ^{133}Xe-radiospirometry (XRS) successfully selects patients able to undergo lung resection without postoperative respiratory complication and whether perfusion lung scintigraphy (PLS) is likely to provide a similar selection of patients for certain stages of the tumor. *Methods:* Two hundred and eighty-four patients with resectable lung cancer underwent preoperative assessment of postoperative forced expiratory volume in one second (FEV_1) by XRS and PLS. Correlations, the Bland and Altman analysis and contingency tables were used to analyze the difference between the two predictive techniques. *Results:* One hundred and sixty patients underwent lung resection on the basis of XRS preoperative testing only. None of them developed respiratory insufficiency. Despite a close correlation, the limits of agreement between predicted FEV_1 by XRS and PLS exceeded ± 0.3 L/s. For tumor stages T1Nx and T2N0, PLS underestimated postoperative FEV_1 whereas it overestimated this parameter for stages III. *Conclusion:* The agreement between XRS and PLS is unacceptable, whereas XRS accurately selects patients able to undergo lung resection without postoperative pulmonary insufficiency. When only PLS is available, higher thresholds for patients with stage III cancers and lower thresholds for those with stage I cancers should be used to decide on operability.

Key Words: Radiospirometry – Xenon - perfusion – 99mTc albumin – Pulmonary resection – Lung cancer.

Introduction

When indicated, surgical resection offers the best chance for cure in patients with non-small cell lung carcinoma. However, the transitory increase in the dead space to tidal volume ratio during the postoperative period may be responsible for postoperative respiratory insufficiency in patients with impaired preoperative lung function [1]. This heightens the need for both efficient postoperative care and an accurate selection of patients who are likely to undergo lung resection without severe postoperative respiratory complications [2, 3]. Several studies have pointed out that global spirometric tests fail to detect the patients that are at high risk of postoperative complications, particularly among those with chronic obstructive pulmonary disease [1, 4]. Nevertheless, these tests are recommended by several guidelines before pulmonary resection [5, 6], and criteria for selecting patients who should be able to tolerate lung resection have been proposed on the basis of these tests [7, 8]. When these criteria are not fulfilled, assessment of regional lung function by quantitative imaging is required. Most studies and guidelines suggest that pulmonary resection is feasible in patients with a predicted postoperative FEV_1 of 30-40% or more of the normal value [1, 3, 9, 10], or 1-1.2 L/s [11, 12]. Quantitative computed tomography scanning has shown promising results, but this method is not yet widely used [2, 3, 13, 14]. More usually, radionuclide techniques, including lung ventilation or perfusion scintigraphy, are employed for the assessment of postoperative pulmonary function [11, 15, 16].

Since the use of functional vital capacity (FVC) does not improve the accuracy of patient selection [18], the regional measurement of forced expiratory volume in the first second (FEV_1) is regarded as the most reliable spirometric index of pulmonary insufficiency and has been chosen by most investigators to assess operability. With the use of a spirometer and a large field-of-view gamma-camera, equilibrium ^{133}Xe-radiospirometry allows simultaneous measurements of the global FEV_1 and regional lung activities that are proportional to the volumes of the pulmonary lobes. Thus measurements of changes in regional activities in the first second of maximal forced expiration provide a direct assessment of regional FEV_1. Along with bronchospirometry, which is invasive, ^{133}Xe-radiospirometry is considered as the method of first choice for the assessment of preoperative pulmonary function [18-27]. However, the widespread clinical use of this technique is impeded by the difficulties of performing a spirometric test with a gaseous isotope in routine clinical settings.

Alternatively, calculations based on measurements of regional activities on static ventilation radionuclide scans have been used to estimate preoperative FEV_1. However, Tc-99m aerosols or ultrafine carbon particles cannot be delivered to poorly ventilated peripheral respiratory bronchioles and the physical decay of 81m-krypton occurs before an equilibrium distribution can be attained. Thus the uptake of these static ventilation agents can only be regarded as an indirect means to assess regional FEV_1 measured during unforced breathing. Since airway hypoxia leads to vasoconstriction of peripheral pulmonary arteries, static ventilation and perfusion lung scintigraphies generally show a similar distribution of activity in patients with no isolated perfusion defects. Previous studies have compared the capacity of static perfusion and ventilation studies for predicting postoperative lung function and reported no significant difference in accuracy, with a trend toward technetium-99m macroaggregated albumin (^{99m}Tc-MAA) perfusion scintigraphy as the most reliable method in routine settings [1, 28, 29].

Using postoperative spirometric measurements as a gold standard, however, some authors have pointed out the high imprecision of perfusion lung scintigraphy in predicting postoperative residual pulmonary function for pneumectomies as well as for lobectomies [10, 30-35]. This method may be appropriate for measuring the precision of preoperative predictions, but it does not directly address the problem of preventing postoperative respiratory insufficiency. Since perfusion scintigraphy remains in routine use for the assessment of operability, these results illustrate the need to confirm the accuracy of this method for determining the risk of postoperative pulmonary insufficiency among patients scheduled for lung resection.

The goals of this study were therefore twofold. First, we sought to determine whether ^{133}Xe-radiospirometry actually succeeds in selecting patients able to undergo lung resection safely. Second, we investigated whether the simpler perfusion lung scintigraphy is likely to provide a similar selection of patients for certain stages of cancer, which would justify its use in place of ^{133}Xe radiospirometry.

Materials and methods

Patients

Two hundred and eighty-four patients (60 females and 224 males, mean age 64±10 years, range 38-84 years) referred for isotopic preoperative pulmonary functional assessment were prospectively included in the study. Ethical approval was obtained from the Ethics Committee of the School of Medicine. All patients were affected by squamous cell carcinoma or adenocarcinoma and scheduled for lobectomy or pneumectomy. The international system for staging lung cancer [36] was used to classify the anatomic extent of the disease. Mean T and N values were respectively 2.3±1 (range 1-4) and 0.9±1 (range 0-3). None of the patients presented known distant metastasis when the perfusion scintigraphy and the radiospirometry were performed (M=0). The number of patients included in the study with respect to T and N descriptors is shown in Table 1. Using the international stage grouping classification schema, this corresponds to 105 patients (37 %) with IA or IB, 54 patients (19 %) with IIA or IIB, 66 patients with IIIA (23 %) and 59 patients (21 %) with IIIB.

In the patient population, the primary tumor was located almost as often in the right lung (141 patients, 25% in the upper lobe, 20% in the lower lobe, 5 % in the middle lobe) as in the left lung (143 patients, 28 % in the upper lobe, 21 % in the lower lobe, 1 % in the lingular segments). Thirty-nine patients had a history of previous lung surgery regarding the right lung (12 upper lobectomies, 5 lower lobectomies, 1 middle lobectomy and 2 pneumectomies) or the left lung (8 upper lobectomies, 7 lower lobectomies and 4 pneumectomies). Given the six patients with a history of pneumectomy, the results described for the whole study population were evaluated in a population of 278 patients only when the possibility of another pneumectomy was under consideration.

All patients underwent ^{133}Xe-radiospirometry, immediately followed by a perfusion lung scintigraphy. The results from the perfusion scintigraphy were not used to decide whether the patients would undergo lung surgery. According to usual guidelines [3, 9], the decision to operate was based on ^{133}Xe-radiospirometric assessment, when the predicted postoperative FEV_1 was above a threshold defined as 1 L/s or 35% of the normal FEV_1 evaluated with respect to the gender, height and age of the patient [37]. Postoperative complications were prospectively monitored and were defined as any cardiovascular or pulmonary trouble that required special treatment within 1 month of the operation. This included postoperative ventilation support > 24 h, reintubation for respiratory failure, acute carbon dioxide retention, pneumonia and atelectasis.

Scintigraphic assessment of regional pulmonary function

Dynamic scintigraphic studies were recorded using a large field-of-view dual-head gamma camera (DST-XL, SMVi, Buc, France) with low-energy high-resolution parallel-hole collimators. All ventilation images were acquired in a 64x64 matrix. The patient was installed in the seated upright position in front of the radiospirometer. The two detectors of the gamma-camera were facing the back of the patient, in the left (LPO) and right posterior oblique (RPO) incidences. These incidences were chosen to minimize the differential attenuation of the ^{133}Xe signal from the different lobes. Next, 1110 MBq (30 mCi, that is 3mCi/L) of ^{133}Xe gas was introduced into a closed rebreathing spirometer (Ventil-Con II; RadX, Houston, Texas) equipped with a CO_2 absorber and oxygen supply.

After becoming accustomed to the mouthpiece and nose clip, the patient was instructed to breathe normally at the usual rate for at least 3 minutes to reach equilibrium. During this phase, FVC measurements were performed. Once equilibrium was reached, the FEV_1 measurements were recorded as planar dynamic LPO, and RPO scintigraphic data were acquired at five images/s for 20 seconds. This acquisition was followed by a washout phase during which the patient inspired room air. The expired mixture of ^{133}Xe and room air was vented to a charcoal trap ventilation system. Washout images were recorded every 2 seconds for 2 minutes, but were not used for this study. Last, with the subject still connected to the spirometer and the camera in the same position, 185 MBq (5 mCi) of ^{99m}Tc-macroaggregated albumin were injected intravenously and static perfusion images were acquired in a 128x128 matrix.

Image treatment and analysis

First, the dynamic images recorded during FEV_1 measurement were summed and a threshold corresponding to 30% of the maximal pixel activity in the resulting image was used to set the background pixel values to zero. This image was used to define six regions of interest (ROI) corresponding to the upper lobes, the lower lobes, the middle lobe and the two lingular segments. To improve accuracy and reproducibility, the ROIs were defined using the segmental reference chart proposed by Magnussen et al. [38]. The two images corresponding to this reference chart for left and right posterior oblique views were automatically translated and scaled to fit the summed images of the lung activity (Fig. 1).

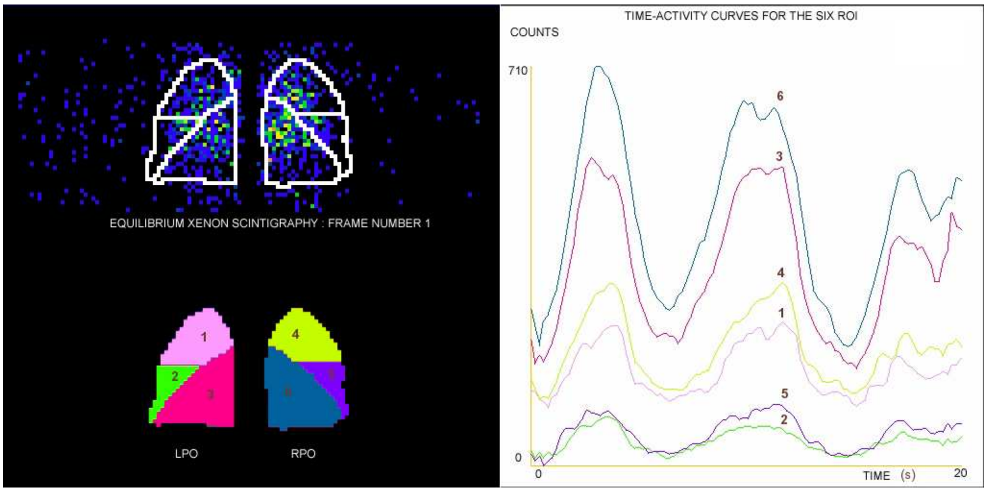

Figure 1

Then, for each dynamic image corresponding to a time interval of 0.5 seconds, the values of the pixels belonging to a given ROI were summed to derive six time-activity curves (TAC). Because the images were acquired at equilibrium and the half-life of ^{133}Xe is relatively long compared with the duration of the test (T=5.24 days), the activities measured in these TACs were proportional to the volumes of each pulmonary lobe. The coefficient of proportionality was computed by comparing the global FEV_1 and the corresponding variation of activity within the two lungs. Thus measurements of the variation of activity within a given ROI during 1 second of forced expiration following maximal inspiration provided a direct measurement of regional FEV_1, for each of the six lobes studied. These measurements of FEV_1 were termed radiospirometric measurements (RS-

FEV_1). Similarly, the same ROIs were applied to the static left and right posterior oblique perfusion scintigraphic images. The relative function of each lobe was estimated by the ratio of the activity in the corresponding ROI to the total lung activity. Regional lung function was then estimated to be the product of the relative function of a given pulmonary lobe and the global FEV_1 measured during the radiospirometric test. These measurements of FEV_1 were termed perfusion measurements (P-FEV_1) and compared with the radiospirometric measurements.

Statistical analysis

The mean value ± standard deviation (SD) and the range characterize the distributions of the parameters. Statistical significance was defined as *p*-value < 0.05. Continuous data were compared with a paired Student's t-test or a paired Wilcoxon's test, as appropriate. Agreements between predicted postoperative parameters provided by perfusion lung scintigraphy and ^{133}Xe-radiospirometry were assessed using the Bland and Altman method. The limits of agreement of the two methods were defined as the mean difference ±1.96 standard deviation of the differences. The consequences of these limits of agreement were explored by computing positive and negative predictive values for the two methods with the previously defined threshold. A ROC curve analysis was performed to determine the threshold for lung perfusion scintigraphy that would prevent any lung resection that had been rejected using ^{133}Xe-radiospirometry. Last, in order to investigate whether the (T, N) staging could explain the differences in FEV_1 assessments by the two scintigraphic methods, these differences were divided into quartiles to perform a Pearson χ^2 test and a Mantel-Haenszel χ^2 test for trend.

Results

Spirometric results and immediate outcome after surgery

For the whole population, the mean global FVC and FEV_1 were respectively 3.13±0.72 L (range: 1.21-5.28 L) and 2.02±0.59 L/s (range: 0.88-4.51 L/s). One hundred and sixty patients (56 %) of the 284 included had a predicted postoperative FEV_1 assessed by ^{133}Xe-radiospirometry that was above the operability threshold; these patients underwent lung surgery within 1 month of the scintigraphic assessment of regional pulmonary function. The surgical resection included 82 right lobectomies (32 upper lobectomies, 19 lower lobectomies, 7 middle lobectomies and 24 pneumectomies) and 78 left lobectomies (34 upper lobectomies, 19 lower lobectomies and 25 pneumectomies). The patients who underwent pneumectomy had predicted RS-FEV_1 = 1.26 ± 0.31 (range 0.73 – 2.21) as assessed by radiospirometry and P-FEV_1 = 1.26 ± 0.29 (range 0.72 – 2.14) as assessed by perfusion scintigraphy. For the patients who had a lobectomy, the predicted postoperative FEV_1 values were RS-FEV_1 = 1.81 ± 0.53 (range 0.74 – 3.45) and P-FEV_1 = 1.81 ± 0.59 (range 0.82 – 3.76), respectively. No patient developed respiratory insufficiency or required supplemental oxygen at the time of hospital discharge. The postoperative course was uneventful for 151 patients. Nine patients (5.6 %) died within the first month of surgery. The complications responsible for these fatal outcomes were postoperative septic shock (5 patients who benefited from neoadjuvant chemotherapy), cardiogenic shock (3 patients) and acute bleeding (1 patient).

Correlations in the whole population

In the whole population studied, the intraclass correlation coefficient between preoperative P-FEV_1 and RS-FEV_1 assessed for pneumectomy was 0.90 (95% confidence interval: 0.88-0.92), showing a very good global agreement between perfusion scintigraphy and ^{133}Xe-radiospirometry (Fig. 2).

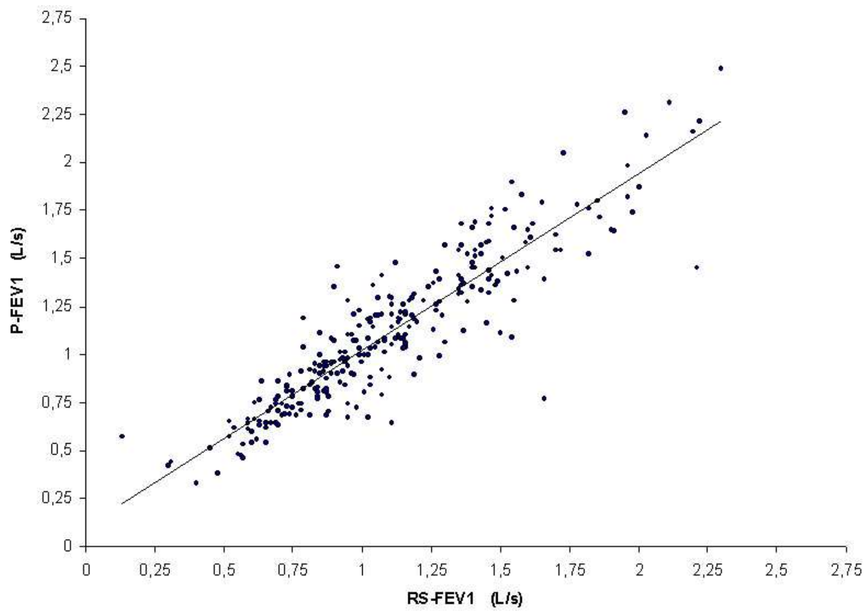

Figure 2.

The differences D_1 between P-FEV_1 and RS-FEV_1 assessed for pneumectomy ranged from –0.89 to 0.55 L/s (Fig. 3). The mean difference was 0.014 ± 0.17 L/s and the limits of agreement were –0.32 to 0.34 L/s. The Wilcoxon test showed that D_1 was significantly different from zero, although this difference was relatively small (*p*<0.03; median difference = 0.015 L/s).

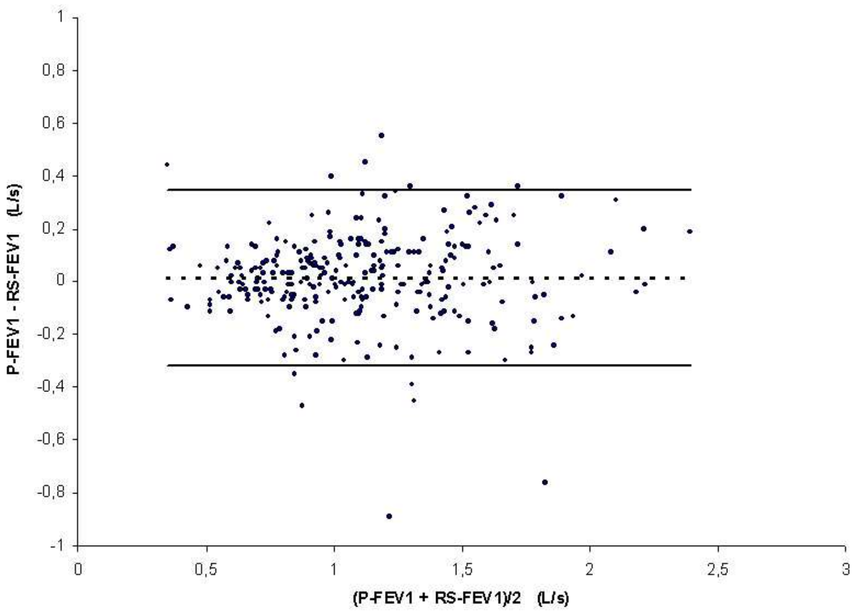

Figure 3.

Similar means and limits of agreement were found when D_1 was evaluated for the two subgroups corresponding to right and left pneumectomies.

When a lobectomy was scheduled, the intraclass correlation coefficient between P-FEV_1 and RS-FEV_1 was 0.94 (95% confidence interval: 0.92-0.95) for all the patients included in the study, confirming the very good global agreement between perfusion scintigraphy and ^{133}Xe-radiospirometry (Fig. 4). The differences D_2 between P-FEV_1 and RS-FEV_1 assessed for lobectomy ranged from –0.85 to 0.72 L/s (Fig. 5). The mean difference was 0.011 ± 0.21 L/s and the limits of agreement were –0.39 to 0.41 L/s. The Wilcoxon test showed that D_2 was not significantly different from zero, although this difference was relatively small (*p*=0.06; median difference = 0.03 L/s).

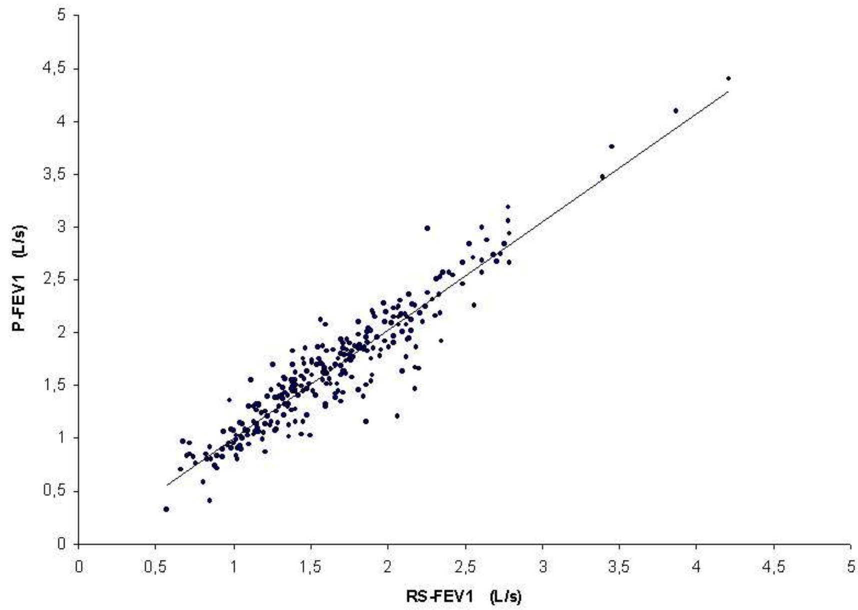

Figure 4

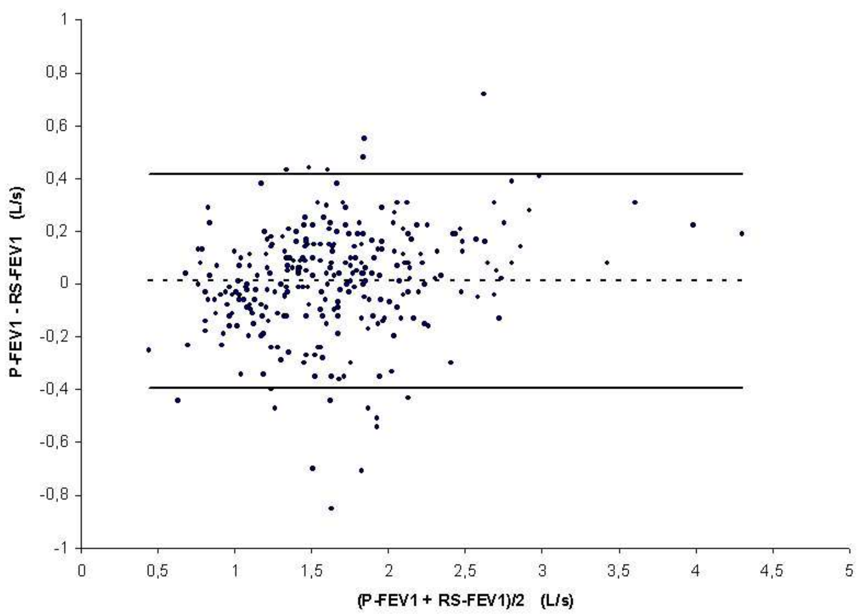

Figure 5.

Similar means and limits of agreement were found when D_2 was evaluated for the subgroups corresponding to lower and upper lobectomies, as well as for the right and left lungs.

Tables 2 and 3 show the number of patients that would have been accepted or rejected for a lung resection using the previously defined threshold. According to the preoperative results provided by ^{133}Xe-radiospirometry, 56% of the patients would have been accepted for pneumectomy and 91% for lobectomy. Of the 15 patients for whom radiospirometric analysis did not allow pneumectomy whereas perfusion scintigraphy did, nine underwent lobectomy without postoperative complication, and six were denied surgery. For those six patients, the difference P-FEV_1 – RS-FEV_1 averaged 0.31 ± 0.13 L/s (range: 0.16-0.55 L/s). To prevent any pneumectomy that would have been rejected using ^{133}Xe-radiospirometry, the threshold for perfusion scintigraphy was 1.46 L/s. On the other hand, the only patient who was denied lobectomy, whereas P-FEV_1 was above the threshold, had similar predictive FEV_1 by the two methods (1.06 and 0.94 with perfusion scintigraphy and radiospirometry, respectively).

The positive predictive values for the perfusion lung scintigraphy were 90% for pneumectomy (95% confidence interval: 83-93) and 99.6 % for lobectomy (95% confidence interval: 96-99); the negative predictive values were 88% (95% confidence interval: 83-94) and 71% (95% confidence interval: 55-86), respectively.

Links with the anatomic extent of the lung cancer

Stage T, as well as the international stage grouping classification, was significantly linked with the difference in the assessment of FEV_1 by perfusion scintigraphy and ^{133}Xe-radiospirometry (p = 0.01 and p = 0.03, respectively) when a pneumectomy was scheduled. For pneumectomies, perfusion scintigraphy underestimated postoperative FEV_1 when T=1 or for stages IA and IB. On the contrary, for T=4 and for stages IIIA or IIIB, perfusion scintigraphy overestimated postoperative FEV_1 in comparison with ^{133}Xe-radiospirometry. All but one of the patients who were denied surgery with P-FEV_1 suggesting operability had IIIB tumors. The Mantel-Haenszel test showed evidence of a linear quantitative relationship between the differences and the grouped stages (p = 0.01). A similar tendency occurred when stage N was studied alone or when a simple lobectomy was scheduled. In these situations, however, no significant link between the difference in predicted FEV_1 and the staging could be proven by our data (p = 0.07-0.09 for T or grouped stages when a lobectomy was scheduled and p = 0.22-0.52 for N stages whatever the surgery).

Discussion

Using postoperative measurements of FEV_1 as a gold standard, most authors have reported an overall imprecision and inaccuracy of perfusion scintigraphy in the assessment of postlobectomy residual pulmonary function, with errors greater than 15% leading to significant postoperative mortality [12]. Some authors have reported significant overestimations of postoperative FEV_1 [30,34], whereas others have pointed out several limitations including a systematic underestimation of postoperative FEV_1 [28, 11]. Thus, previous studies stated that a predictive preoperative FEV_1 of around 0.7-0.8 L/s should not be considered a total contraindication to surgery, whereas an operability threshold of predicted postoperative FEV_1 equal to 1.2-1.3 L/s should be chosen, especially for left pneumectomies or upper lobectomies where the margin of uncertainty is greater [11].

The key clinical point, however, is not so much to verify that perfusion lung scintigraphy can predict postoperative FEV_1 as it is to determine whether this technique is able to reliably identify the patients with an increased risk of pulmonary insufficiency during the postoperative period. Moreover, even if postoperative measurements of FEV_1 may be regarded as a gold standard, this parameter is often difficult to measure with high reproducibility when, as in the present work, the study population is living in a large geographic area. For this reason, the immediate postoperative outcome was used to determine whether scintigraphic methods can actually succeed in selecting patients able to undergo lung resection safely.

In the present study, operability was decided on using predicted postoperative FEV_1 assessed by ^{133}Xe-radiospirometry only, with the threshold value that is generally used with lung perfusion scintigraphy [1,3,9,10,11]. None of the 160 patients who underwent lobectomy or pneumectomy developed postoperative respiratory insufficiency or a need for supplemental oxygen. This justifies the use of ^{133}Xe-radiospirometry as a gold standard to evaluate the results provided by perfusion lung scintigraphy in the selection of patients scheduled for surgery, although the study design did not allow us to draw conclusions about the seven patients (2.5% of the population) who were denied pneumectomy or lobectomy on the basis of radiospirometric measurements, whereas lung perfusion suggested operability.

Perfusion lung scintigraphy can be regarded as accurate, as the mean difference between predicted postoperative FEV_1 by this technique and by ^{133}Xe-radiospirometry remained small (for pneumectomies) or not significantly different from zero (for lobectomies). But the limits of agreement for predicted postoperative FEV_1 were greater than ± 0.3 L/s for pneumectomies as well as for lobectomies. This agreement did not depend on the lobe in which the tumor was located. Therefore, the differential attenuation of the ^{133}Xe signal from the different lobes does not significantly alter the measurements when posterior oblique incidences are used. In the population of this study, this poor agreement would have led to a high error rate in rejecting patients for surgery (12% for pneumectomies and 29% for lobectomies), mainly for patients with IA, IB and T1Nx lung tumors. These results are consistent with those published by Giordano et al. [11]. On the other hand, perfusion lung scintigraphies were found to overestimate postoperative FEV_1 for patients with IIIA or IIIB lung tumors, possibly because of a decrease in lung perfusion that is not due to the hypoxic vasoconstriction reflex [41]. Further studies are required to check this hypothesis, but our results indicate that if only lung perfusion scintigraphy is available, operability thresholds equal to or possibly lower than 1L/s for IA, IB and T1Nx lung tumors should be used. On the other hand, when a pneumectomy is scheduled to cure IIIA or IIIB cancers, higher thresholds of up to 1.4-1.5 L/s are necessary to prevent any lung resection that would be rejected using ^{133}Xe-radiospirometry.

Conclusion

The data presented in this study confirm that, whatever the lung surgery scheduled, ^{133}Xe-radiospirometry reliably identifies those patients with no increased risk of pulmonary insufficiency during the postoperative period. In clinical centers where ^{133}Xe-radiospirometry is unavailable, preoperative pulmonary function testing may be performed with perfusion lung scintigraphy, provided that higher thresholds are used to decide on operability in patients with advanced lung cancers. Last, as recently suggested [42], the results of this study point out the need for further research to determine whether it is possible to use lower thresholds for ^{133}Xe-radiospirometry, in order not to deny surgery to patients who are able to tolerate it.

References

1. Dunn WF, Scanlon PD. Preoperative pulmonary function testing for patients with lung cancer. Mayo Clin Proc. 1993; 68:371–377.
2. Gierada DS, Yusen RD, Villanueva IA, Pilgram TK, Slone RM, Lefrak SS et al. Patient selection for lung volume reduction surgery. Chest. 2000; 117:991–998.
3. Mazzone PJ, Arroliga AC. Lung cancer: Preoperative pulmonary evaluation of the lung resection candidate. Am J Med. 2005; 118: 578–583.
4. Mohr DN, Jett JR. Preoperative evaluation of pulmonary risk factors. J Gen Intern Med. 1988; 3:277–287.
5. Zibrak JD, O'Donnel CR, Marton K. Indications for pulmonary function testing. Ann Intern Med. 1990; 112:763–771.
6. American College of Physicians. Preoperative pulmonary function testing. Ann Intern Med. 1990; 112-793–794.
7. Tisi GM. Preoperative evaluation of pulmonary function: validity, indications, and benefits. Am Rev Respir Dis. 1979; 119:293–310.
8. Putnan JB, Lammermeier DE, Colon R, McMurtrey MJ, Ali MK, Roth JA. Predicted pulmonary function and survival after pneumectomy for primary lung carcinoma. Ann Thorac Surg. 1990; 49:909–914.
9. British Thoracic Society and Society of Cardiothoracic Surgeons of Great Britain and Ireland Working Party. Guidelines on the selection of patients with lung cancer for surgery. Thorax. 2001; 89-108.

10. Beckles MA, Spiro SG, Colice GL, Rudd RM. The physiologic evaluation of patients with lung cancer being considered for resectional surgery. Chest. 2003; 123:105S-114S.

11. Giordano A, Calcagni ML, Meduri G, Valente S, Galli G. Perfusion lung scintigraphy for the prediction of postlobectomy residual pulmonary function. Chest. 1997; 111:1542–1547.

12. Boysen PG, Block AJ, Olsen GN, Moulder PV, Harris JO, Rawitscher RE. Prospective evaluation for pneumectomy using the 99m-technetium quantitative perfusion lung scan. Chest. 1977; 72:422-425.

13. Wu MT, Pan HB, Chiang AA, Hsu HK, Chang HC, Peng NJ et al. Prediction of postoperative lung function in patients with lung cancer: comparison of quantitative CT with perfusion scintigraphy. AJR Am J Roentgenol. 2002; 178:667–672.

14. Ashton RW, Jett JR. Screening for non-small cell lung cancer. Semin Oncol. 2005; 32: 253–258.

15. Bria WF, Kanarek DJ, Kazemi H. Prediction of postoperative pulmonary function following thoracic operations: value of ventilation-perfusion scanning. J Thorac Cardiovasc Surg. 1983; 86-186–192.

16. Markos J, Mullan BP, Hillman DR, Musk AW, Antico VF, Lovegrove FT et al. Preoperative assessment as a predictor of mortality and morbidity after lung resection. Am Rev Respir Dis. 1989; 139:902–910.

17. Wahi R, Mc Murtrey MJ, DeCaro LF, Mountain CF, Ali MK, Smith TL et al. Determinant of perioperative morbidity and mortality after pneumectomy. Ann Thorac Surg. 1989; 48:33–37.

18. Veneskoski T, Sovijarvi A. 133Xe radiospirometry in prediction of ventilatory function and vital capacity after pneumectomy in patients with endobronchial tumor. Ann Chir Gynaecol. 1985; 74:256–260.

19. Arborelius M, Fajgelj A, Lassen N, Lindell SE, Miorner G, Svanberg L. Bronchospirometry or Xe133 radiospirometry in the study of regional lung function. Strahlentherapie. 1967; 65:440–445.

20. Miorner G. 133 xe-radiospirometry. A clinical method for studying regional lung function. Scand J respir Dis. 1968 ; 64 :1–84.

21. Korhonen O, Poppius H. Comparison of 133 Xenon radiospirometry with moving detectors and bronchospirometry. Scand J respir Dis. 1971; 52:63–66.

22. Gustafsson MT, Kjellman B, Lundstrm NR, Mortensson W. Xe-radiospirometry for evaluation of congenital malformations of pulmonary arteries. Pediatrics. 1971; 47:529–536.

23. Lindell SE. 133-Xe-radiospirometry: prediction of lung function after pulmonary resection. Scand J Clin Lab Invest. 1974; 34:289–292.

24. Kristersson S. Preoperative evaluation of differential lung function (133Xe-radiospirometry) in bronchial cancer. Scand J respir Dis. 1974; 85:110–117.

25. Kampmann H, Matthys H, Bitter F, Adam WE, Konjetzko N. Scintigraphic radio-spirometry. Methods and indications. Rofo. 1975; 122:50–54 (in German).

26. Veneskoski T, Sovijarvi A. Prediction of ventilatory function after subtotal lung resection using preoperative dynamic spirometry and radiospirometry. Eur J Respir Dis. 1986; 68:167–172.

27. Ikonen T, Harjula ALJ, Kinnula V, Savola J, Sovijarvi AR. Selective assessment of single-lung graft function with 133Xe radiospirometry in acute rejection and infection. Chest. 1996; 109:879–884.

28. Wernly JA, DeMeester TR, Kirchner PT, Myerowitz PD, Oxford DE, Golomb HM. Clinical value of quantitative ventilation-perfusion lung scans in the surgical management of bronchogenic carcinoma. J Thorac Cardiovasc Surg. 1980; 80:535–543.

29. Cordiner A, De Carlo F, De Gennaro R, Pau F, Flore F. Prediction of postoperative pulmonary function following thoracic surgery for bronchial carcinoma. Angiology. 1991; 42:985–989.

30. Sangali M, Spiliopoulos A, Megevand R. Predictability of FEV1 after pulmonary resection for bronchogenic carcinoma. Eur J Cardiothorac Surg.1992; 6 :242–245.

31. Kikuchi K, Ishii Y, Kitamura S. Prediction of postoperative lung function in patients with lung cancer and chronic obstructive disease. Nippon Kyobu Shikkan Gakkai Zasshi . 1996; 34:1071–1076.

32. Zeiher BG, Gross TJ, Kern JA, Lanza LA, Peterson MW. Predicting postoperative pulmonary function in patients undergoing lung resection. Chest. 1995; 108:68–72.

33. Izquierdo JM, Pac JJ, Casanova J, Vara F, Cortes J, Fombellida et al. Lung resection surgery in patients with functional limits. Arch Bronconeumol. 1995; 31:328–332 (in Spanish).

34. Giordano A, Calcagni ML, Massaro M. Scintigraphic prediction of residual lung function following lobectomy: the use of posterior oblique views. In: BergmannH, Sinzinger H, eds. Isotopes in clinical medicine and research. Basel: Birkhauserr Verlag AG. 1995; 379–384.

35. Wang SC, Fischer KC, Slone RM, Gierada DS, Yusen RD, Lefrak SS et al. Perfusion scintigraphy in the evaluation for lung volume reduction surgery: correlation with clinical outcome. Radiology. 1997; 205:243–248.

36. Mountain CF. Revisions in the international system for staging lung cancer. Chest. 1997; 111:1710–1717.

37. Roca J, Burgos F, Sunyer J, Saez M, Chinn S, Anto JM et al. References values for forced spirometry. Eur Respir J. 1998; 11(6):1354–1362.

38. Magnussen JS, Chicco P, Palmer AW, Mackey DW, Magee M, Murray IP et al. Enhanced accuracy and reproducibility in reporting of lung scintigrams by a segmental reference chart. J Nucl Med. 1998; 39:1095–1099.

39. Bria WF, Kanarek DJ, Kazemi H. Prediction of postoperative pulmonary function following thoracic operations. Value of ventilation-perfusion scanning. J Thorac Cardiovasc Surg. 1983; 86:186–192.

40. 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.

41. Von Euler US, Liljestrand G. Observations on the pulmonary arterial blood pressure in the cat. Acta Physiol Scand. 1946, 12:301–320.

42. Linden PA, Bueno R, Colson YL, Jaklitsch MT, Lukanich L, Mentzer S et al. Lung resection in patients with preoperative FEV1 < 35% predicted. Chest. 2005; 127:1984–1990.

Figure legends

Fig. 1. Definition of the regions of interest and time-activity curves showing volumes of each pulmonary lobe versus time, during a ^{133}Xe-radiospirometric test.

Fig. 2. Predicted postoperative FEV_1 for pneumectomy, assessed by perfusion scintigraphy (P-FEV_1) versus ^{133}Xe-radiospirometry (RS-FEV_1).

Fig. 3. Plot of the predicted postoperative FEV_1 difference for pneumectomy (perfusion scintigraphy minus ^{133}Xe-radiospirometry) against the mean obtained by the two methods. Solid lines represent the limits of agreement. The dashed line represents the mean difference.

Fig. 4. Predicted postoperative FEV_1 for lobectomy, assessed by perfusion scintigraphy (P-FEV_1) versus ^{133}Xe-radiospirometry (RS-FEV_1).

Fig. 5. Plot of the predicted postoperative FEV_1 difference for lobectomy (perfusion scintigraphy minus ^{133}Xe-radiospirometry) against the mean obtained by the two methods. Solid lines represent the limits of agreement. The dashed line represents the mean difference.

Table 1. Number of patients included in the study with respect to T and N stages

	T1	T2	T3	T4	All T
N0	68	37	17	18	140
N1	11	26	11	12	60
N2	4	34	17	16	71
N3	0	1	8	4	13
All N	83	98	53	50	284

Table 2. Number of patients with predictions of postoperative FEV_1 compatible or not with pneumectomy, using assessment by perfusion scintigraphy or by ^{133}Xe-radiospirometry

Pneumectomy	RS-FEV_1 > FEV_{LIM}	RS-FEV_1 < FEV_{LIM}
P-FEV_1 > FEV_{LIM}	141	15
P-FEV_1 < FEV_{LIM}	14	108

P Perfusion lung scintigraphy, *RS* ^{133}Xe-radiospirometry
FEV_1 Forced expiratory volume in 1 second
FEV_{LIM} 1 L/s or 35% of the normal global FEV_1 for the patient

Table 3. Number of patients with predictions of postoperative FEV_1 compatible or not with lobectomy, using assessment by perfusion scintigraphy or by ^{133}Xe-radiospirometry

Lobectomy	RS-FEV_1 > FEV_{LIM}	RS-FEV_1 < FEV_{LIM}
P-FEV_1 > FEV_{LIM}	249	1
P-FEV_1 < FEV_{LIM}	10	24

P Perfusion lung scintigraphy, *RS* ^{133}Xe-radiospirometry
FEV_1 Forced expiratory volume in 1 second
FEV_{LIM} 1 L/s or 35% of the normal global FEV_1 for the patient