Volumetric evaluation of the lung expansion following resection: a stereological study

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Abstract

Objective: Following lung resection, the thoracic cavity may be filled partially or completely by the remaining pulmonary tissue. To our knowledge, no study has yet evaluated this volumetric change in thoracic content using high resolution computed tomography (HRCT) scans. We aimed to evaluate the volume changes of the lungs using HRCT scans during the preoperative and postoperative periods. Methods: In this study, we took HRCT scans of 25 patients preoperatively and 3 months after the resection. All patients were male and their mean age was 59.6 (40—75) years. The volume and volume fraction of individual pulmonary lobes were estimated by superimposing point-counting grids on the preoperative and postoperative HRCT scans. Results: The means of total lung volume in all patients were 6.40 ± 1.40 l and 4.92 ± 1.21 l in the preoperative and postoperative periods, respectively. While 30.79 ± 10.64% of pulmonary tissue was resected in expanded patients, the pulmonary tissue was diminished volumetrically by 18.51 ± 15.96% postoperatively. Volumetric analyses showed that the remaining structures increased its volume by 12.28%. Thereby, almost 50% of the resected pulmonary tissue was recovered volumetrically by the remaining tissues. Conclusions: Present results showed that the volume and volume fraction of the total lung and individual lobes could be estimated practically on HRCT scan using the method proposed in this study. The obtained data not only provided information about actual postoperative progress but also information for predicting the possible postoperative course in patients prior to the resection.

Keywords: Lung cancer; Resection; Volume; Volume fraction; High resolution computed tomography

1. Introduction

Lung resection elicits a number of anatomical changes within the thoracic cavity. Physiological compensation for the loss of lung tissue is achieved by various mechanisms. The thoracic cavity may be filled partially or completely by the remaining pulmonary tissue following the resection [1]. As we were unable to find a study evaluating these volumetric changes in thoracic content using high resolution computed tomography (HRCT) scans, we decided to perform an HRCT scan study in the preoperative and postoperative periods applying the combination of the Cavalieri principle of stereological methods.

The volume of biological structures can be estimated by combining sectional radiological imaging techniques with the Cavalieri principle of volume estimation as described previously [2—4]. The human organs do, however, vary widely in size. Several factors contribute to this variation. Factors related to growth, such as gender and physical size, are thought to influence the maximal size of an individual’s organs [5,6]. Simply comparing the organ volumes or the volumes of lobes between two groups (i.e. control and experimental groups) will not provide reliable data. However, the volume fraction of a component within a reference volume is a simple and very widely used parameter in biomedical science [7—9], which can be used to express the proportion of a phase or component within the whole structure. Hence, it is possible to use this proportion to compare the organ size and any part of an organ between the groups.

In the present study, we examined the volume of the individual lobes of the lungs and total lung volume. We also estimated the volume fraction of an individual lobe within the total lung volume using a technique namely volume fraction, one of the modern stereological methods [9]. We analysed the relationship between the volume of the resected portion of the lung and the expanded tissue volume
following resection. Further analyses of resection size and lung expansion interactions were performed.

2. Materials and methods

The Ethic Committee of the Faculty of Medicine, Ondokuz Mayis University, approved this study. Lung cancer resection was carried out in 25 patients, in our clinic, over a period of 2 years. The surgery had been done by one surgeon (A.B.) and the same surgical approach had been applied for all patients. All patients were males and their age, weight and height were 59.6 (40—75) years, 65 (54—75) kg and 1.74 (1.56—1.90) m, respectively. Patients underwent right upper lobectomy (10), left upper lobectomy (7), bilateral upper lobectomy (1), right lower lobectomy (3), left lower lobectomy (2), right pneumonectomy (2) and left pneumonectomy (1). In the presented study, we did not include the patients suffering from the chronic obstructive pulmonary disease, emphysema and obstructive atelectasis to obtain homogenous groups.

High resolution computed tomography scans of patients were taken before the resection and 3 months after surgery using a high-resolution scanner (Toshiba Aquilion, Japan) without contrast medium during the inspiration phase of respiration and with the patient in supine position. CT scans of the thorax in axial plane were obtained applying the following parameters: kV 120, mAS 250. The slice thickness was 1 mm with intervals varying between 7 and 14 mm. The consecutive sections were printed on films using the most appropriate contrast showing the fissures of lung to distinguish the lobes. The volume and volume fraction of individual pulmonary lobes were estimated by applying the point-counting grids to the preoperative and postoperative HRCT scans.

The films were placed on a negatoscope and a transparent square grid test system with d = 0.4 cm between test points was superimposed, randomly covering the entire image frame (Fig. 1). The point-counting grid which is composed of crosses was superimposed randomly to cover the entire area of the lung sectional images and the numbers of intersections (i.e. upper right corner of the crosses) making contact with the lung tissue were counted on consecutive HRCT images.

The outer contours of lung including the airspaces and lung tissue were counted on consecutive HRCT images. The volume fraction of an X phase within a Y reference volume is simply expressed as follows:

\[ V_V(X, Y) = \frac{\text{Volume of } X\text{ phase in } Y\text{ reference space}}{\text{Volume of } Y\text{ reference space}} \]  

(2)

where the \( V_V(X, Y) \) indicates volume fraction of X phase within the Y reference volume. Using this approach, \( V_V(\text{hippocampus, brain}) \), \( V_V(\text{epidural haematoma, total brain volume}) \) and \( V_V(\text{lobe, lung}) \) can be estimated. Volume fraction ranges from 0 to 1 and is often expressed as a percentage [9].

In the light of the above information, the same points counted for the volume estimation were also used for the estimation of volume fraction of a lobe within the lung using the following simple formula:

\[ V_V(\text{lobe, lung}) = \frac{\sum P_{\text{lobe}}}{\sum P_{\text{lung}}} \]  

(3)

where \( \sum P_{\text{lobe}} \) is the total number of points hitting any part of the lobe of interest, and \( \sum P_{\text{lung}} \) is the total number of points hitting lobes of the lungs. The right middle lobe was regarded as part of the right superior lobe. The obtained value is the volume fraction of any lobe within the total lung volume and is expressed as a percentage. The application of the described approaches for the estimation of volume and volume fraction are presented in Table 1.

The coefficient error (CE) of stereological estimations was determined using the formula reported by Gundersen and Jensen [13]. All calculations and other related data were obtained as a spread sheet using Microsoft Excel. After the initial setup and preparation of the formulae, the point counts, formulae and other data were entered for each subject and the final data obtained automatically.
3. Results

We divided 25 patients into two groups, namely expanded and nonexpanded groups according to the results of volumetric analysis on postoperative HRCT scans. The expanded group is composed of 19 patients whose remaining lung tissues showed expansion 3 months after surgery (Fig. 2A and B). The nonexpanded group consists of 6 patients without any apparent lung tissue expansion following surgery (Fig. 2C and D).

The mean total lung volume in all patients were $6.40 \pm 1.40 \text{l}$ and $4.92 \pm 1.21 \text{l}$ in the preoperative and postoperative period, respectively. The difference was statistically significant ($P < 0.05$). The details are presented in Table 2. Prior to surgery, the remaining volume of intact lung was predicted for all patients, and for the expanded and nonexpanded groups. The results were $4.58 \pm 1.56$, $4.37 \pm 1.07$ and $5.25 \pm 1.24$, respectively (Fig. 3), showing no statistically significant difference between the expanded and nonexpanded groups ($P > 0.05$). There was a high correlation between the predicted remaining lung volume and expanded volume of the lung following surgery ($r = 0.704; P < 0.01$).

The mean forced expiratory volume in 1 second (FEV1) values in all patients were $2.46 \pm 0.75 \text{l}$ and $1.85 \pm 0.58 \text{l}$ in the preoperative and postoperative periods, respectively, this difference being statistically significant ($P < 0.001$). From the mean values of the two groups before and following surgery presented in Table 2, it is clear that there is a statistically significant difference between the expanded and nonexpanded groups’ FEV1 values ($P < 0.001$). No correlation was found between the lung tissue volumes and FEV1 values ($P > 0.01$).

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### Table 1

An example of the application of volume and volume fraction method described in the present study

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Total numbers of points ($\sum P_{\text{lobe}}$) = 745 482 332 433

SU = 5 cm; SL = 1.35 cm; d = 0.4 cm; t = 1 cm (thickness + interval = 0.1 + 0.9 = 1); $\sum P_{\text{total lung}}$ = 1982.

\[
\begin{align*}
V_{\text{right superior lobe}} &= \frac{SU}{d} \times \sum P_{\text{right superior lobe}} = \frac{5}{0.4} \times 745 = 1635 \text{ cm}^3 \\
V_{V\text{(right superior lung)}} &= \frac{\sum P_{\text{right superior lobe}}}{\sum P_{\text{lung}}} = \frac{745}{1982} = 0.374 = 37.4\%
\end{align*}
\]

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Fig. 2. Thoracic roentgenograms of two patients. (A) Preoperative and (B) postoperative X-ray film of a patient who showed expansion of lung; (C) preoperative and (D) postoperative X-ray film of a patient who did not show expansion of lung.
An amount of $30.79\pm 10.64\%$ pulmonary tissue was resected in all patients; the pulmonary tissue was diminished volumetrically in $18.51\pm 15.96\%$ postoperatively. The mean percentage of resected pulmonary tissues in both groups before and following surgery are shown in Table 2 and amount to $30.79\pm 10.64\%$ and $20.33\pm 7.12\%$ for the expanded and nonexpanded groups, respectively (Fig. 4). This difference is statistically significant ($P < 0.05$).

### 4. Discussion

In animal models, the surgical removal of a lung lobe or lobes substantially diminishes diffusion capacity by reducing the total number of alveoli and the associated vasculature available for gas exchange. The immediate challenge in pneumonectomized animal is to maintain adequate gas exchange following resection of lung tissue. Physiological compensation for the loss of lung mass is achieved primarily through two mechanisms: enhancement of diffusion capacity in the remnant lung and/or generation of new pulmonary gas exchange units [1].

The decline in lung function varies with the extent of the resection. The forced expiratory volume in 1 second has been shown to fall by an average of $34–36\%$, the forced vital capacity (FVC) $36–40\%$ and the maximum oxygen consumption (VO$_2$ max) $20–28\%$. If a lobectomy is performed, the FEV1 has been shown to decrease by an average of $9–17\%$, the FVC $7–11\%$ and the VO$_2$ max $0–13\%$ [14–16].

A quantitative lung scan allows calculation of functional remaining parenchyma after surgery and the predicted postresection forced expiratory volume in 1 second value. Correlations between the predicted and observed postresection FEV1 values have proved to be good, although there is a tendency to underestimate postoperative function. Our results did not, however, show a correlation between the tissue volume and FEV1 values. This might be due to the fact that the number of patients was not adequate to allow a quantitative result showing correlation.

Scintigraphy is also a noninvasive technique for evaluating the contribution of each lung to the overall pulmonary function. Based on the common assumption that pulmonary ventilation and perfusion show a similar distribution pattern, both ventilation and perfusion lung scintigraphy can be employed for the assessment of residual pulmonary function [17,18].

![Fig. 3. Graph showing the volumetric changes in total pulmonary tissue in both groups. PreTLV, preoperative total lung volume; PRLTV, predicted remaining lung tissue volume; PostTLV, postoperative total lung volume.](image1)

![Fig. 4. Graph showing the percentage change in resected tissue size and expansion response to the surgery. RLL, resected lung lobe; PostVC, postoperative volume change; ELV, expanded lung volume.](image2)
The value of the pulmonary function test may underestimate the functional capacity following resection as determined by exercise testing. The degree of functional loss appears to be less in individuals with poor baseline lung function [14—16].

In this situation, scintigraphic studies and quantitative lung scan procedures allow lung functional values to be predicted while neglecting the compensatory lung growth and complications postoperatively. Apart from the approaches available for assessing lung tissue volume, we did not find a study evaluating the tissue volume on routine sectional radiological images. Hence, the present study evaluated the volume changes between preoperative and postoperative periods and the relations with lung functions by applying stereological methods to the HRCT scans of the thorax.

Compensatory lung growth was not observed in some patients. In addition to the given amount of resected pulmonary tissues, postoperative follow-up showed that the remaining tissues increased their volumes by 18.51 ± 15.96% to fill the thoracic cavity in the expanded group. Hence, over 50% of the resected pulmonary tissues were recovered volumetrically by the remaining tissues. However, following the lung resection in the nonexpanded group, the pulmonary tissues were diminished in volume by 12.56 ± 7.02%. Postoperative pleural thickening and atelectasis are two of the causes of the decline in total compliance of the thorax. Changes in lung function after thoracotomy and lung resection occur because of mechanical effects on the thoracic wall and tissue loss due to resection. There is a strong possibility that the postoperative progress could not be predicted because of the extremely heterogenous nature of patients in terms of preoperative pulmonary and general status and performed operations.

To our knowledge, no study has examined the relationship between resected tissue size and expanded lung volume using imaging techniques. In this context, there is little information on the interaction between the resection and expansion of remaining lung. In the present study, we obtained quantitative information about the total and individual lobe volumes of the lung. Our results indicate that the volume of total lung or individual lobes could be estimated easily using the combination of HRCT scans and the Cavalieri principle. Moreover, the volume fraction of an individual lobe within the whole lung could also be assessed using the stereological methods.

Stereological methods provide some data to the researcher making appropriate changes to the sampling procedures. When the coefficient of error of these measurements is high, it can generate obvious problems in accuracy and hence interpretation. These problems may arise if too few slices or too few points are taken into account. The observer is eligible to change the spacing of points in the grid or the number of slices available in any sectional study to obtain a reasonable CE value. It is important to note that the appropriate grid size and number of slices required for an object under study is determined at the beginning, there is no need to calculate the CE value for repeated sessions [2,3].

In the presented study, the mean of CE was 4%; it should be less than 5% [13]. This reflects the adequacy of the sectioning and the density of the points in the grid. The CE reflects the efficiency of the applied stereological method i.e. Cavalieri volume estimation. Moreover, the CE of the estimations could be decreased as well as 1% by means of increasing the section number or using dens point-counting grids. However, this will increase the required time for the estimation of the volume and volume fraction of the lung. Hence, the researcher may choose a target CE for efficient volume estimation.

The estimation of the volume and volume fraction using the stereological approach applied in this study provides unbiased data about the volumetric quantities of the lung. The values obtained in this way are reliable and reproducible. Moreover, the stereological approach could be easily applied without altering routine radiological imaging techniques and the obtained data show little inter-observer variation [3,4,10,11].

Our results show that the volume and volume fraction of the total pulmonary tissues and individual lobes could be evaluated practically on HRCT scans using the method proposed in this study. We, however, suggest that a comparative study evaluating the volume changes estimated by stereological methods and by a scintigraphic approach would provide a judgment about which method is the most suitable to apply.

Acknowledgement

We thank to Ms Brenda Vollers for language correction and referees for their productive contributions.

References

Appendix A. Conference discussion

**Dr T. Grodzki (Szczecin, Poland):** It’s always refreshing to listen to some mathematics at the end of a thoracic session, and I’d like to thank you for this interesting approach, but I have some difficulties with understanding its practical use. I don’t understand the terms ‘compensated’ or ‘uncompensated.’ Do you mean that those 6 patients were not fully expanded within the chest cavity? Am I right?

**Dr Basoglu:** According to the postoperative results, we divided, and postoperatively, the HRCT scans, we divided them. The cause of the uncompensated group may be because of atelectasis or other complications postoperatively.

**Dr Grodzki:** My second point of slight criticism is that your method treats the lung as an anatomical specimen, and we know that it’s a functional, living organ, and you know, as we all know, that FEV1 not only depends on the volume but on the status of the bronchus, on the drugs, rehabilitation, etc. That’s why I’m a little bit doubtful if the practicality of this method will be widely appreciated.

**Dr Basoglu:** I wanted to show that we suggest this method to evaluate the volume changes.

**Dr E. Pompeo (Rome, Italy):** In your study there is one important assumption, which is that only the volume changes are important for the outcome. As every one of us knows, the outcome of an operated patient depends also on the density of the lung and the volume variation depends on the change in density, which can be due to atelectasis or even to the elastic properties of the lung itself. I think that you should add in your study another important variable, which is the change in tissue density.

**Dr Basoglu:** Could you repeat, please?

**Dr Pompeo:** You evaluated only volume changes in your study.

**Dr Basoglu:** Yes.

**Dr Pompeo:** This is interesting; however, I believe that it is important also to evaluate the elastic properties of the lung, which can vary in every patient and which can influence the outcome after lung resection. This variable also should be included in this kind of study because tissue density is important as well as volume changes.