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Original Article

# Usability and Feasibility of Chest Perfusion Computed Tomography in Differentiating Small Cell Lung Cancer and Non-Small Cell Lung Cancer

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## ABSTRACT

**Objective:** We aimed to investigate to usability and feasibility of perfusion computerized tomography (PCT) in differentiating small cell lung cancer (SCLC) from non-small cell lung cancer (NSCLC).

**Methods:** Between September 2013 and February 2022, 42 patients with a detected lung mass took part in the present study. All patients went through PCT examination, and data regarding permeability (PMB), blood flow (BF), and blood volume (BV) of the tumor were acquired. These parameters along with mass diameter of the tumors were compared in both cancer types.

**Results:** Maximum tumor diameter was measured as 48 ± 11 mm in average in the SCLC cases and 49 ± 15 mm in the NSCLC cases ($P = .892$). There was a correlation at a moderate level between the tumor's maximal diameter and PMB ($r = .49$, $P = .020$). Regarding tumor PMB values, there was a meaningful variation between the 2 tumor groups (SCLC: 16.4 ± 3.6 mL/100 mL/min; NSCLC: 5.1 ± 2.8 mL/100 mL/min; $P = .001$). No further meaningful differences were observed among the BF- and BV-related comparisons.

**Conclusion:** Among the perfusion parameters in lung PCT, PMB can be used to distinguish the NSCLC from SCLC in patients who were diagnosed with lung cancer.

**Keywords:** Computed tomography, perfusion imaging, SCLC, NSCLC

## INTRODUCTION

Lung carcinoma is the most prevalent type of cancer on the planet regarding the incidence and mortality. While mortality rates for nearly all cancers have been decreasing over the years, the rate of death from lung cancer is on the rise. Lung cancer, which takes the first row regarding cancer-related deaths in developed countries, is most often diagnosed in an inoperable phase.[1] Lung carcinoma is categorized under 2 main histological types of lung carcinoma: small cell and non-small cell. The classification has a meaningful influence on the curation and prognosis of the disease.[2] Treatment decisions, concerning whether surgery, chemoradiotherapy or more than 1 therapy method will be used, depend on the stage of the tumor.[3]

Perfusion computerized tomography (PCT), which has been introduced to the field of oncology in recent years, is a favorable CT technique, enabling the functional assessment of the tissue vascularity. Also, this method reveals tumor angiogenesis, and thus, it can evaluate the aggressivity of the tumor non-invasively and quantitatively.[3-5] Moreover, applications such as lesion characterization concerning benign–malign discrimination, identification of occult malignancies, and evaluation of therapeutic efficacies of various treatment methods take place within the clinical uses of PCT.[6]

The perfusion CT application is a CT technology enabling the functional assessment of the tissue vascularity.[3] On the other hand, when it is considered that the functional changes occur before the morphological changes

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following treatment, techniques such as perfusion CT enable earlier evaluation of the efficacy of the treatment when compared to the other conventional methods.[7]

Although PCT was primarily developed for assessment of the cerebral perfusion, it is a non-invasive technique that has particularly come into use in the field of oncology recently. Among its oncological applications, cancers such as liver cancer, lung cancer, head–neck tumors, colorectal carcinoma, prostate carcinoma, pancreatic neoplasms, and lymphoma are present.[3,8]

In our study, we aimed to investigate the usability and feasibility of PCT in differentiating small cell lung cancer (SCLC) from non-small cell lung cancer (NSCLC).

## METHODS

### Participants

Between September 2013 and February 2022, 42 patients with confirmed lung masses on CT imaging enrolled in this study. Our study has been approved by the ethics committee of Atatürk University (September 11, 2013 no.: B.30.2.ATA.0.01.00), and the study was conducted in accordance with the Declaration of Helsinki. The participating patients were informed about the study and provided their written consent.

The study stipulated the following criteria for the patients to be included in the research: absence of administration of radiotherapy or chemotherapy; absence of allergy to contrast material; absence of severe heart, liver, and renal failure; and not being diagnosed with the simultaneous presence of any other tumor.

The exclusion criteria for the patients were as follows: benign pathology report (n = 2); disapproval of the biopsy procedure (n = 3); and lesion diameter smaller than 1 cm (n = 1).

**MAIN POINTS**

- In our study, we aimed to investigate the usability and feasibility of perfusion computerized tomography (PCT) in differentiating small cell lung cancer (SCLC) from non-small cell lung cancer (NSCLC).
- There was a moderate correlation between maximum tumor diameter and permeability (PMB) of the tumor ($r = 0.49$, $P = .020$).
- **The PMB was found to be considerably higher in patients with SCLC (SCLC:** 16.4 ± 3.6 mL/100 mL/min; NSCLC: 5.1 ± 2.8 mL/100 mL/min; $P = .001$).
- Our study supports the consideration of chest PCT imaging method as an additional imaging tool which can support the differentiation of the tumor's subtype as SCLC and NSCLC.

### Perfusion Computerized Tomography Protocol

Examinations of PCT were carried out with a dual-source Multidetector computed tomography (MDCT) scanner of 256-slice (Somatom Definition Flash, Siemens Healthcare, Forchheim, Germany). The scan area was limited to the single lung lobe in which the tumor was located. The patients had to lie motionless on the table while the iodinated contrast material, 50 mL of iopromide, was being quickly injected (Ultravist 370 mg/mL, Bayer Schering Pharma, Berlin, Germany) followed by 50 mL saline. Injection was performed with an automated injector (MCT Plus; Medrad, Pittsburgh, Pa., USA) above 12.5 s with a rate of 4 m/s through intravenous. As scanning parameters, 80 kVp tube potential, 100 mAs/rot effective tube current, 25 scans, an alternating scan direction, 1.5 s travel time between one terminal point and the other on the table, 39 seconds examination time in total, 128 × 0.6 mm slice acquisition (with the use of z-flying spot), and 0.28 seconds Gantry rotation time were used. The patients had to breathe slightly and slowly as much as possible during the perfusion scan. Three millimeter slice thickness with 3 mm increments and tissue convolution kernel with moderate smoothness (B20f) served to conduct image reconstruction. The dose mitigation was put into use. Each patient's average size of radiation CT dose index and dosage–length product (DLP) of PCT scans were carried out. The efficacious PCT dose of radiation was evaluated through a technique that was suggested by the guidelines of the European Working Group regarding the CT quality requirements, which utilizes the DLP and a conversion factor for the rib cage, namely, $k$ = 0.015 mSv/(mGy cm).

### Image Analysis

A private workstation was used to manipulate the PCT data (Leonardo Volume Perfusion CT Body, Siemens). The highest slope method was used to calculate the perfusion. The related region of interest (ROI, range 20-42 $mm^2$) that was drawn manually was positioned in the diaphragm-level downward aorta to acquire the reference arterial input information. An automatic drawing of the curve of arterial time abatement was plotted. For future calculations, the software recorded this input information. There was a color diversity from purple to red in the functional maps with the former designating the bottom frontier and the latter designating the topmost frontier of the screen for blood flow (BF) (range of color from 0 to 100), blood volume (BV) (range of color from 0 to 15), and PMB (range of color from 0 to 50). For each tumor, the ROIs (range from 55 to 160 $mm^2$) were drawn by hand (Figures 1 and 2). To pull the ROI from a site in the tumor, the region with the highest contrast retention was chosen so as to avoid the enclosing vascular structures and

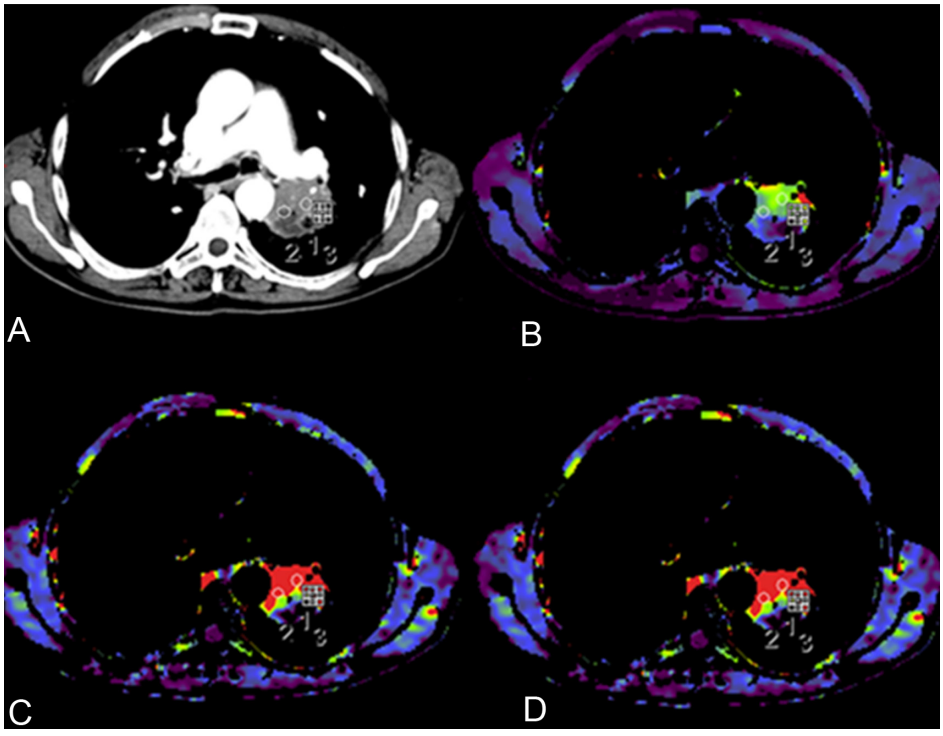


**Figure 1.** Conventional axial image (A), blood flow(B), blood volume (C) and permeability (D) maps in a patient with small cell lung cancer.

tissues. The ROIs taken out of the tumor were used to calculate BF (mL/100 g tissue/min), BV (mL 100 g tissue), and PMB (mL/100 mL/min). The diagnosis was established on the basis of a visual examination of the colored parametric: perfusion computerized tomography (CTP) maps. Two radiologists (S.E., a thoracoabdominal radiologist with 15 years of experience, and Ö.Ö., a radiologist with 4 years of experience) analyzed the visuals. They

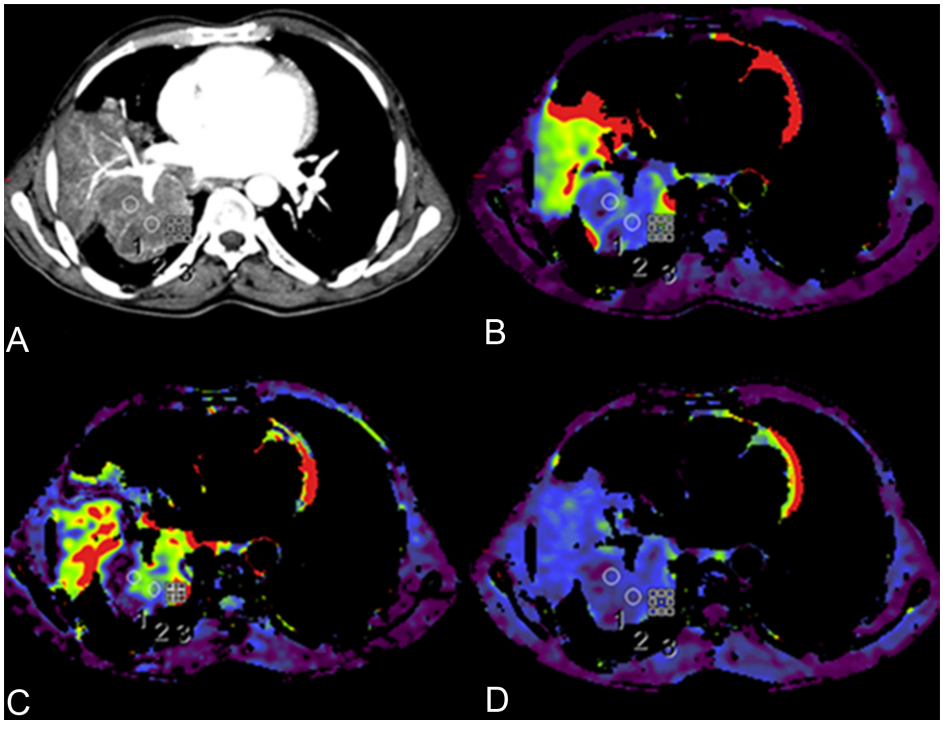


**Figure 2.** Conventional axial image (A), blood flow(B), blood volume (C) and permeability (D) maps in a patient with non-small cell lung cancer.

jointly considered that the visuals validated the quantitative analyses.

### Statistical Analysis

Distribution of data was evaluated using D'Agostino–Pearson test. Summary statistics were given as mean ± SD. Variables belonging to different perfusion parameters in 2 tumor groups were evaluated with the use of the independent *t* test. The Pearson correlation coefficient was utilized for perfusion parameters and tumor diameter correlation. If the *r* values were between 0.40 and 0.59, it was accepted that there was a moderate correlation between the variables. All 2-tailed *P* values were calculated, and a value lower than .05 was accepted as statistically significant. Evaluation of the whole statistical analyses was made on a computer using the statistical package program (Medcalc version 12, Mariakerke, Belgium).

## RESULTS

Our study included 36 patients, consisting of 32 males and 4 females. On average, the participants were aged 60.1 ± 10.2 years (44-90 years). The male participants' mean age was 59.9 ± 8.2 years and that of females was 61.3 ± 25 years. The results showed no difference regarding age in gender groups ($P = .226$).

In the patients included in the study, SCLC was detected in 11 patients and NSCLC in 25 patients histopathologically. The maximum tumor diameter (MTD) was measured to be 48.8 ± 11 mm on average in the SCLC cases and 49.4 ± 15 mm in the NSCLC cases. There was no statistically significant difference between the 2 malignancies in terms of MTD ($P = .892$).

As a result of the correlation analysis carried out between the MTD and PCT parameters, a moderate correlation was present between the MTD and the PMB of the tumor ($r = 0.49$, $P = .020$). There was no other meaningful relationship between the MTD and BF and BV.

The PMB was found to be considerably higher in patients with SCLC (SCLC: 16.44 ± 3.6 mL/100 mL/min; NSCLC: 5.13 ± 2.8 mL/100 mL/min; $P = .001$). Regarding BV values (SCLC: 15.18 ± 6.1 mL/100 g tissue; NSCLC: 14.88 ± 8.1 mL/100 g tissue; $P = .940$) and BF values (SCLC: 45.38 ± 11.2 mL/100 g tissue/min; NSCLC: 35.53 ± 20.1 mL/100 g tissue/min; $P = .090$), the 2 tumor groups showed no meaningful differences (Figure 3). The relationships between the MTD and perfusion values of the SCLC and NSCLC groups are shown in Table 1.

## DISCUSSION

In this study, we found that PMB values differ in patients with SCLC and NSCLC. However, perfusion parameters such as BV and BF did not show any statistically significant difference.

Histologically, we can divide lung cancer into 2 primary groups: SCLC and NSCLC. The type of NSCLC is more

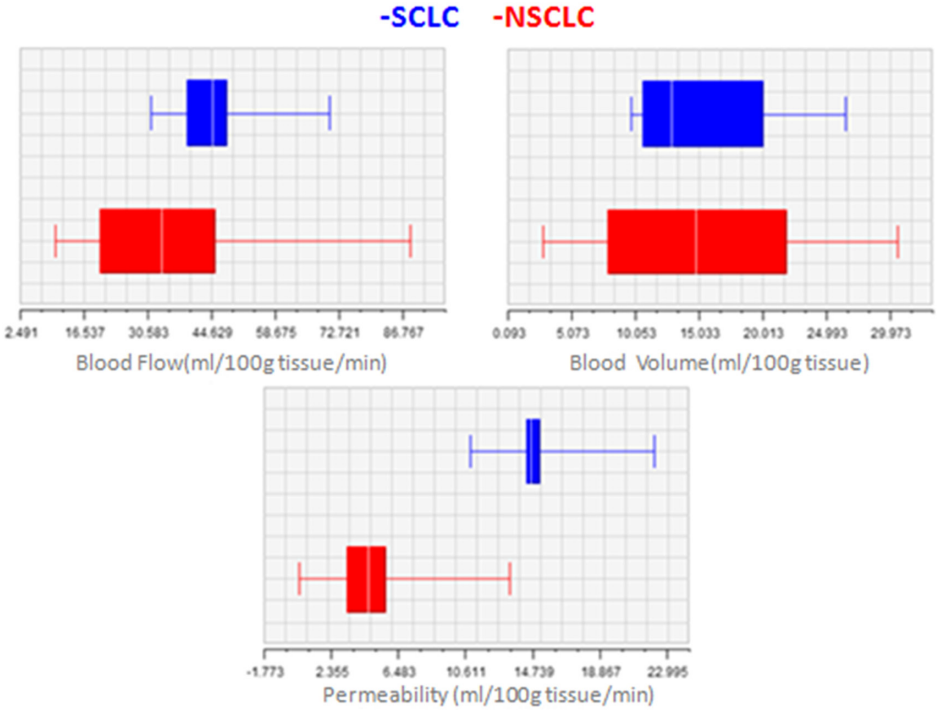


**Figure 3.** Data regarding the comparison of the perfusion parameters presented as box-plots.

**Table 1.** Different Imaging Parameters of the Tumors Belong to Small Cell Lung Cancer and Non-Small Cell Lung Cancer Groups and Corresponding *P*-values

| | All (n = 36) | SCLC (n = 11) | NSCLC (n = 25) | *P* |
|---|---|---|---|---|
| Maximum tumor diameter (mean, mm) | 49.2 ± 14.50 | 48.80 ± 11 | 49.4 ± 15 | .892 |
| Blood flow (mean, mL/100 mL/min) | 38.49 ± 18.32 | 45.38 ± 11.20 | 35.53 ± 20.10 | .090 |
| Blood volume (mean, mL/100 mL) | 14.97 ± 7.52 | 15.18 ± 6.10 | 14.88 ± 8.10 | .940 |
| Permeability (mean, mL/100 mL/min) | 8.53 ± 6.10 | 16.44 ± 3.60 | 5.13 ± 2.80 | **<.001** |

common than the SCLC. This classification is based on histological features and has utmost importance regarding the clinical approach and prognosis. The reason for gathering the various cancer types in the "non-small cell" group is the similar clinical approach and the prognosis of those tumors.[2,9] The type of tumor considerably determines the treatment of primary lung cancer.[10]

Non-invasive functional imaging methods have been used increasingly in practice as routine clinical applications in diagnosis, phasing, and follow-up of the lung cancer until today.[11] Computerized tomography, which is used preferably for diagnosis, provides images that enable assessments of the location, size, and relations with the adjacent structures by creating volume models suitable for making morphological and anatomical analyses with sagittal and coronal sections. Perfusion computerized tomography is a promising modality for non-invasive in vivo characterization of tumor vascularity.[12-14] Lung tumors that have perfusion at higher rates are more sensitive to radio chemotherapy compared to those that have perfusion at lower levels.[13] Measurement of perfusion, reproducibility, motion artifacts, and resolution are technical advantages of PCT over MR perfusion in the lungs.

The technique used in perfusion imaging in CT is based on the viability of the tumor. It can be evaluated using PCT that depends on the examination of time and density curves obtained in successive scans following the iodinated contrast material injection.[15-21] Due to the assessment of a limited number of transverse sections within the tumor, this method was restricted. Therefore, during therapy, it impeded thorough evaluation of the current angiogenesis in large tumors along with the comparability of follow-up tests. This restriction was eliminated with the development of PCT, which enabled the assessment of the whole tumor mass without the necessity of limiting the volume of interest.[12,22,23]

In our study, a statistically significant difference was determined between SCLC and NSCLC concerning PMB values in patients who had lung cancer. According to this result, the PMB values of the SCLC patients were higher when compared to those of the NSCLC patients. However, the absence of any difference between the SCLC and NSCLC patients regarding the other perfusion parameters such as BF and BV showed that the dynamic changes such as BF and BV were similar in patients with SCLC and NSCLC, despite the increasing PMB in the SCLC cases. Additionally, another result of our study was the presence of a moderate correlation between the maximum diameter of the tumor and the tumor PMB in the NSCLC patient group. There is no information regarding the PMB features of these tumor types in the literature. We think that differences in PMB in those are associated with the histopathological features of those tumor types.

Our study had some limitations. The primary one was the relatively low participation of the patient population. As was suggested in studies performed with a similar number of patients in the literature, the results should be confirmed in series with a higher number of patients. Second, our quantitative results depended on the deconvolution model recommended for the data analysis by the manufacturer company. Therefore, our results were not comparable to the preceding PCT studies performed with different mathematical and statistical approaches. Third, since the results were obtained by the co-decision of 2 observers in PCT measurements, the probable diversified intra- and interobserver evaluations were not investigated.

As a conclusion, our study supports the consideration of chest PCT imaging method as an additional imaging tool which can support the differentiation of the tumor's subtype as SCLC and NSCLC.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Atatürk University (Date: September 11, 2013, Number: B.30.2.ATA.0.01.00/).

**Informed Consent:** Approval was obtained from the hospital management where patient data was used.

**Peer-review:** Externally peer-reviewed.

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Interpretation – Ö.Ö., S.E.; Literature Search – Ö.Ö., S.E.; Writing Manuscript – Ö.Ö., S.E.; Critical Review – Ö.Ö., S.E.

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