^{18}FDG PET-CT standardized uptake value for the prediction of radiation pneumonitis in patients with lung cancer receiving radiotherapy

YONG ZHANG[1], YONGHUA YU[1], JINMING YU[1], ZHENG FU[2], TONGHAI LIU[3] and SHOUFANG GUO[2]

Departments of [1]Radiation Oncology, [2]Nuclear Medicine and [3]Imaging Physics, Shandong Tumor Hospital and Institute, Jinan, Shandong 250117, P.R. China

Received October 9, 2014; Accepted July 7, 2015

DOI: 10.3892/ol.2015.3637

Abstract. The present study aimed to determine if the standardized uptake value (SUV) determined with ^{18}F-FDG PET-CT can be used to predict radiation pneumonitis (RP) in lung cancer patients who receive radiotherapy. A total of 40 patients with non-small cell lung cancer received ^{18}F-FDG PET-CT examinations prior to and following radiotherapy. The average SUV of lung tissue prior to and following radiation were measured at differing radiation doses. SUV differences between patients with and without RP, and the SUV ratio of the irradiated lung tissues compared with that of non-irradiated lung tissues (L/B) were compared. There were no differences in the mean SUV between the RP and no RP groups prior to radiotherapy. There were also no significant differences in the mean SUV of lung tissue within groups or between the no RP and RP groups with radiation doses of <5 Gy, 5 to ≤14.9 Gy and 15 to ≤34.9 Gy (all P>0.05) following radiotherapy. There were, however, statistically significant differences in the mean SUV of lung tissue within groups or between the no RP and RP groups with doses of ≥60 Gy prior to therapy and 35 to ≤59.9 Gy and ≥60 Gy following therapy (all P<0.05). When the L/B ratio was ≥3, the incidence of RP was 50%, and when the L/B ratio was ≥2.5 the incidence was 40.7%. When the L/B ratio was <2, there were no cases of RP. In conclusion, the present study indicates that ^{18}F-FDG PET-CT can be used to predict RP by L/B ratio.

Introduction

Lung cancer is a common malignancy, and radiotherapy is an essential method of treatment. Radiation pneumonitis (RP) is the most common dose-limiting complication in lung cancer radiotherapy, and 13 to 37% of lung cancer patients develop RP following radiotherapy (1). RP often leads to irreversible pulmonary fibrosis, and the prognosis of significant RP is poor, with ~50% of patients succumbing within 2 months of diagnosis (2). Thus, it is of great importance to predict the occurrence of RP accurately.

^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET-CT) can diagnose disease at the molecular level prior to the occurrence of anatomical structural changes, identified through observing changes in metabolism. RP is an inflammatory reaction within irradiated lung tissues in response to radiation injury (3,4), and as such may be detectable by ^{18}F-FDG PET-CT. However, there have been no studies regarding whether the standardized uptake value (SUV) and its changes can predict the occurrence of RP.

The purpose of the present study was to determine if ^{18}F-FDG PET-CT is useful for the prediction of RP in patients with non-small cell lung cancer (NSCLC) who receive radiotherapy.

Patients and methods

Patients. A total of 40 patients (27 males and 13 females) with NSCLC treated with radiotherapy between January 2004 and June 2007 at the Department of Radiation Oncology of Shandong Tumor Hospital and Institute (Jinan, China) were included in the present study. The average age of the patients was 63 years (range, 39-82 years), and 22 patients were >60 years of age and 18 were ≤60 years of age. The inclusion criteria were: i) A diagnosis of NSCLC confirmed by cytology or pathology; ii) no prior surgery for the disease; iii) no pericardial effusion, pleural effusion, diabetes mellitus, anemia or cardiopulmonary insufficiency; iv) a Karnofsky performance scale score of ≥70; and v) a ^{18}F-FDG PET-CT examination performed within 4 weeks of treatment and at 6-10 weeks after treatment. Patients found to have RP prior to the second ^{18}F-FDG PET-CT examination were excluded. Written informed consent was obtained from all patients and ethical approval was obtained from the ethics committee of Shandong Tumor Hospital and Institute.

Treatments. All patients were treated with three-dimensional (3D) radiation therapy using a Varian 2100C linear

Correspondence to: Dr Yonghua Yu, Department of Radiation Oncology, Shandong Tumor Hospital and Institute, 440 Jiyan Road, Jinan, Shandong 250117, P.R. China
E-mail: yonghuaqyu@163.com

Key words: lung cancer, computed tomography, positron emission tomography, standardized uptake value, radiation pneumonitis

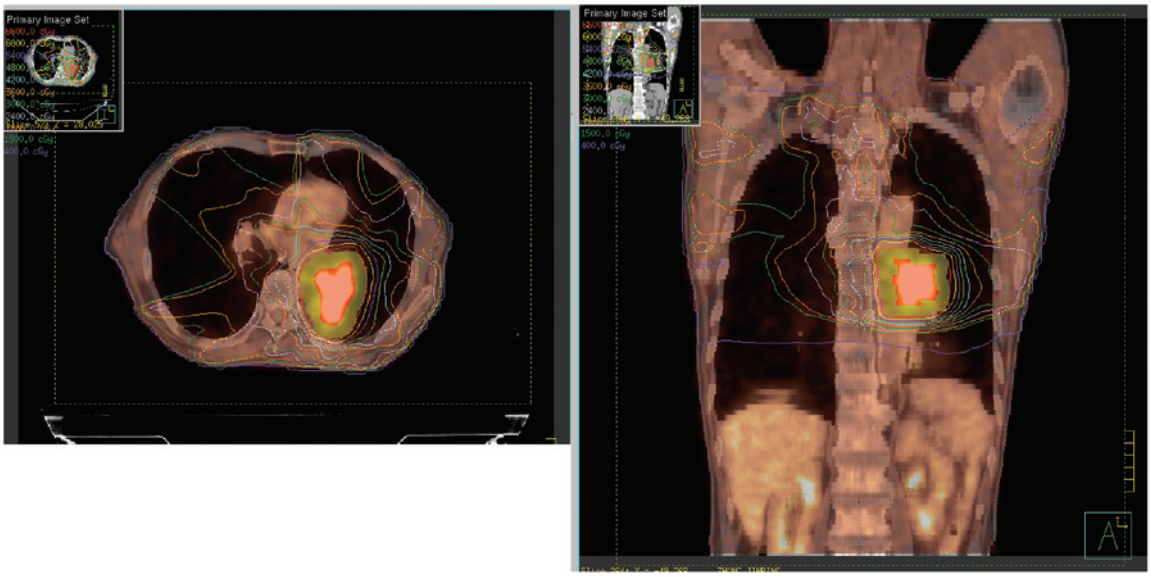

Figure 1. Dose curves derived from ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography image fusion with the treatment planning systems. The planning treatment volume receiving different doses are shown by different color isodose lines: 66 Gy (red), 60 Gy (yellow), 54 Gy (purple), 48 Gy (green), 42 Gy (light blue), 36 Gy (orange), 30 Gy (dark green), 24 Gy (gray), 18 Gy (orange), 12 Gy (dark green) and 4 Gy (purple).

accelerator with a 15-MV beam (Varian Medical Systems, Inc, Milpitas, CA, USA). The target was outlined by radiotherapists and radiologists according to CT combined with ^{18}F-FDG PET-CT findings, and included the primary pulmonary lesion and metastatic lymph modes. The clinical target volume was a 10-15-mm expansion of the edge of the target area. Radiotherapy was administered five times per week at 1.8-2.0 Gy per time, for a total dose of 60-66 Gy. Patients also received 3-4 cycles of a platinum-based chemotherapy combined with paclitaxel (135 mg/m^2), gemcitabine (1,000 mg/m^2) and vinorelbine (25 mg/m^2). The agents were administered by i.v. drip on days 1 and 8 of each 21-day cycle.

^{18}F-FDG PET-CT. The ^{18}F-FDG PET-CT scanner and FDG synthesis modules were produced by GE Healthcare (Pittsburgh, PA, USA). FDG with a radiochemical purity of >95% was derived from the cyclotron. The blood glucose level of the patients was <6 mmol/l prior to the examination. Patients were injected with ^{18}F-FDG (7.4 MBq/kg) in an antecubital vein and then rested for 60 min, remaining quiet for 6 h. A row-spiral CT scan (scanning parameters: 140 kv; 90 mA; pitch, 0.75; table speed, 15 mm/rotation; after -5 mm, 50-cm primary field of view) was performed, followed by a full-body PET-CT (after -4.25 mm, 50-cm apparent field of view; mean beds, 6; 4 min/bed; checking time, 30 min) from the top of the cranium to the top of the femur using a GE Discovery LS PET-CT scanner (GE Healthcare).

PET cross-sectional, coronal and sagittal image reconstructions were performed using the two-dimensional acquisition ordered subsets-expectation maximization method in a LERWAS workstation using CT attenuation correction data, and were fused with CT images on a multi-level and multi-image basis. The mean SUV of lung tissue was measured by two or more nuclear medicine physicians according to the 3D conformal radiotherapy treatment planning system: <5 Gy, 5 to ≤14.9 Gy and 15 to ≤34.9 Gy, 35 to ≤59.9 Gy and ≥60 Gy equal dose curves corresponding to the anatomy prior to and following radiotherapy. The SUV of three defined points (the distance between any two points being ≥10 mm) of lung tissue enveloped by the dose curves >10%, 10 to 20%, 20 to 50%, 50 to 90% and >90% corresponding to ≤5 Gy, 5 to ≤14.9 Gy, 15 to ≤34.9 Gy, 35 to ≤59.9 Gy and ≥60 Gy, respectively, were measured. Next, the mean of the three points within the framework of the lung tissue was used to indicate the SUV. The dose curves derived from ^{18}F-FDG PET-CT image fusion with the Eclipse™ treatment planning systems (Varian Medical Systems, Inc. Palo Alto, CA, USA) are illustrated in Fig. 1.

Follow-up. Patients were followed-up every 2 or 3 months after the treatment and received physical examinations, tests of liver and kidney function and tumor markers, chest X-rays and enhanced chest CT scans.

Statistical methods. The mean SUV of the RP group and the no RP group prior to and following irradiation were compared by t-test. The comparison of the rates of RP was performed by χ^2 test. All statistical analyses were performed with SPSS, version 12.0 (SPSS, Inc., Chicago, IL, USA). P<0.05 was considered to indicate a statistically significant difference.

Results

Follow-up. In April 2008, the follow-up rate was 100%, with a median follow-up time of 13.5 months (range, 9-23 months). Among the 40 patients, 8 developed RP (≥grade 2) following treatment, which accounted for 20% of the whole group. Patient data are summarized in Table I. The Criteria of the Radiation Therapy Oncology Society of the United States was used as the standard to diagnose RP, and the detailed grades are shown in Table II (5)

Table I. Patient characteristics.

Characteristic	RP group	No RP group	P-value
Patients, n	8	32	0.043
Age, years	63	61	2.546
Gender, n			
Male	5	22	0.046
Female	3	10	0.032
Smoking history, n			
≤20 years	3	13	0.054
≥20 years	6	18	0.032
Tumor location, n			
Upper	3	11	0.210
Middle	2	8	0.036
Lower	3	13	0.041
GTV, cm^3	156	148	6.354
Mean lung volume, cm^3	3218	3276	9.012
Pathological type, n			
Squamous carcinoma	3	13	0.037
Adenocarcinoma	5	19	0.026
Tumor stage, n			
I-II	3	15	0.025
III-VI	5	17	0.031
V20, n			
≤25%	1	6	0.044
25% <V20 <35%	2	17	0.015
≥35%	5	9	0.086
MLD, n			
≤15 Gy	3	18	0.047
>15 Gy	6	14	0.562
Time to development of RP, days			
Mean	82.4	78.4	0.947
Range	78-86	60-83	0.032
Interval between PET and radiotherapy, days			
Mean	42	44	6.451
Range	28-56	28-60	1.011
Radiation dose, Gy			
Mean	65.6	62.8	7.518
Range	60-72	60-72	6.312
Chemotherapy, n			
Single agent	0	2	5.138
Combined	8	30	0.087

RP, radiation pneumonitis; GTV, gross tumor volume; V20, volume of lung receiving at least 20 Gy; MLD, mean lung dose; PET, positron emission thermography.

SUV prior to radiotherapy. There were no statistically significance differences in the mean SUV between the no RP group and the RP group who received radiation at doses of <5 Gy, 5 to ≤14.9 Gy and 15 to ≤34.9 Gy and 35 to ≤59.9 Gy (all P>0.05). However, there were statistically significant differences in the mean SUV of lung tissue within (t=1.98, P=0.029; t=2.32, P=0.018) or between (t=2.13, P=0.025; t=2.42, P=0.015) the no RP and RP groups with radiation doses of 35 to ≤59.9 Gy and ≥60 Gy, respectively (Tables IV and V). of the group with a radiation dose of ≥60 Gy compared with the

Table II. Radiation therapy oncology group pneumonitis toxicity criteria.

Grade	Clinical symptoms
0	None
1	Asymptomatic or mild symptoms (dry cough); slight radiographic appearances
2	Moderate symptomatic fibrosis or pneumonitis (severe cough); low grade fever; patchy radiographic appearances
3	Severe symptomatic fibrosis or pneumonitis; dense radiographic changes; intermittent O_2; requires steroids
4	Severe respiratory insufficiency; continuous O_2; assisted ventilation
5	Mortality

mean SUV of lung tissue of the other groups. A summary of the mean SUV data is shown in Tables III and IV.

SUV following radiotherapy. There were no statistically significant differences in the mean SUV of lung tissue within groups or between the no RP and RP groups with radiation doses of ≤5 Gy, 5 to ≤14.9 Gy and 15 to ≤34.9 Gy (all P>0.05). However, there were statistically significant differences in the mean SUV of lung tissue within groups or between the no RP and RP groups with radiation doses of 35 to ≤59.9 Gy and ≥60 Gy (intergroup: t=2.13 and 2.42; P=0.025 and 0.015, respectively; within group: t=1.98 and 2.32; P=0.029 and 0.018, respectively) (Tables IV and V).

L/B ratio. When the L/B ratio was ≥3, the incidence of RP was 50%, and when the L/B ratio was ≥2.5, the incidence was 40.7%. The differences compared with the 20% incidence of the whole group were statistically significant (χ^2=4.18 and 4.92; P<0.05). When the L/B ratio was ≥2.5, the incidence of RP was 25%, and the difference compared with the whole group was not statistically significant (χ^2=0.41; P>0.05). At an L/B ratio of ≥2.5, all the lung tissues received an exposure dose of ≥35 Gy (lung tissues circumscribed by the 50% equal dose curve). Taking the L/B ratio of ≥2.5 as the standard, the predictive sensitivity and specificity for RP were 72.7 and 90.9%, respectively (Tables V and VI).

Volume of lung receiving at least 20 Gy (V20) and mean lung dose (MLD). When the V20 was ≤25%, 25% <V20 <35%, and ≥35%, the incidence of RP was 14.3, 13.6 and 33.3%, respectively. When the MLD was ≤15 Gy and >15 Gy, the incidence of RP was 11.5 and 27.3%, respectively. There were no statistically significant differences in the occurrence of RP between a V20 ≥35% and MLD >15 Gy, V20 ≥35% and L/B ≥2.5, and MLD >15 Gy and L/B ≥2.5 (χ^2=0.18, 0.33 and 1.27, respectively; P>0.05).

Discussion

RP, which has a big effect on lung function and quality of life in patients, is the most common dose-limiting complication of radiation therapy (6). Although the occurrence of RP has been known about for a number of years, it is difficult to predict when it will occur. The ability to provide early adjunctive therapy to high-risk patients may improve a patient's quality of life and survival. The present study investigated whether FDG PET-CT can predict the occurrence of RP based on the SUV.

Studies have shown that the occurrence of RP is associated with the susceptibility, exposure dose and volume. Graham *et al* (7) analyzed 99 patients with NSCLC who received 3D radiotherapy and found that the incidence of RP of a grade ≥2 was associated with the V20 (P=0.001). In this study, the incidence of fatal RP was 4%. However, the single patient who succumbed to RP had a V20 of 22%, which is considered to be safe. Similarly, patients with a lower V20 developed RP of grade ≥3. However, numerous patients with a higher V20 in the study did not develop RP. Kwa *et al* (8) analyzed the dose-volume histograms of 540 patients with lung cancer and breast cancer who received radiotherapy; 73 developed RP of a grade ≥2 and there was a significant statistical difference between lung cancer and breast cancer RP (P=0.02). The present results are similar to those of other studies; with an increase in V20 and MLD, the incidence of RP increased. It has been hypothesized that patients are safe from RP when the V20 is <25%, however, in the present study, one case of RP of grade ≥2 occurred. These data indicate that the V20 is not adequate for predicting RP.

PET-CT can provide information on the metabolism and pathophysiology of pathological changes. In particular, PET-CT is superior to CT for the formation of precise radiotherapy plans, reducing the development of radiation injury, evaluating the therapeutic effect, and identifying residual tumors and fibrosis subsequent to chemotherapy. Furthermore, ^{18}F-FDG PET-CT is able to detect the inflammation and fibrosis caused by radiotherapy (9-11). ^{18}F-FDG PET-CT can visualize and quantitate endotoxin-induced pneumonitis in normal healthy volunteers (12) and in patients affected by cystic fibrosis (13). The main characteristic of RP is the presence of leukocytes migrating from the blood to the irradiated lung tissues; therefore, on FDG-PET imaging, the more intense the inflammatory response, the greater the FDG uptake (12).

To date, no conclusions have been made with regard to whether FDG PET-CT can predict the occurrence of RP. Guerrero *et al* (14) examined 36 patients with esophageal carcinoma 4-12 weeks after completion of radiotherapy with ^{18}F-FDG PET-CT and found a linear association between the radiation dose and normalized FDG uptake in the lung. The slope rate range of the linear association was 0.0048-0.069. The present study analyzed the SUV of 40 patients who received PET-CT examination prior to and following radiotherapy, and found no statistical significance in lung tissues anywhere except for lung tissue enveloped by 90% of the isodose curve. The SUV of lung tissue enveloped by 90% of the isodose curve is higher than in other areas, as it is close to the tumor. In the current study, there were no statistically significant differences in the average SUV of lung tissue within groups or between the no RP and RP groups with radiation doses of <5 Gy, 5 to ≤14.9 Gy and 15 to ≤34.9 Gy (all P>0.05). However, there were statistically significant

Table III. Lung tissue SUV of radiation pneumonitis group prior to and following radiotherapy.

SUV of lung tissue at different exposures	Prior to radiotherapy	Standard deviation	Following radiotherapy	Standard deviation	P-value
≥60 Gy	0.68	0.042	1.47	0.285	0.025
35 to ≤59.9 Gy	0.44	0.026	0.97	0.154	0.015
15 to ≤34.9 Gy	0.45	0.021	0.65	0.120	6.051
5 to ≤14.9 Gy	0.41	0.018	0.58	0.058	4.025
≤5 Gy	0.39	0.022	0.44	0.036	1.337

Exposure doses of different lung tissues were calculated by the isodose curve. SUV, standardized uptake value.

Table IV. Lung tissue SUV of the no radiation pneumonitis group prior to and following radiotherapy.

SUV of lung tissue at different exposures	Prior to radiotherapy	Standard deviation	Following radiotherapy	Standard deviation	P-value
≥60 Gy	0.67	0.038	1.02	0.246	0.029
35 to ≤59.9 Gy	0.46	0.023	0.76	0.125	0.018
15 to ≤34.9 Gy	0.42	0.018	0.61	0.112	1.084
5 to ≤14.9 Gy	0.42	0.015	0.52	0.048	3.052
≤5 Gy	0.38	0.016	0.42	0.032	0.059

Exposure doses of different lung tissues were calculated by the isodose curve. SUV, standardized uptake value.

Table V. Numbers of patients from the radiation pneumonitis group who received different radiotherapy exposures.

Ratio	≥60 Gy	35 to ≤59.9 Gy	15 to ≤34.9 Gy	5 to ≤14.9 Gy	P-value
L/B ≥3	4	0	0	0	0.026
2.5 ≤L/B <3	4	3	0	0	0.018
2 ≤L/B <2.5	0	5	3	0	0.625
1 ≤L/B <2	0	0	5	8	2.054

L/B is the mean standardized uptake value (SUV) of radiated lung tissues/the average SUV of non-radiated lung tissues. The value of non-radiated lung tissues is equal to that of local lung tissues with an exposure dose of ≤5 Gy (the lung tissues that are non-circumscribed by the 10% equal dose curve).

Table VI. Numbers of patients from the no radiation pneumonitis group who received different radiotherapy exposures.

Ratio	≥60 Gy	35 to ≤59.9 Gy	15 to ≤34.9 Gy	5 to ≤14.9 Gy	P-value
L/B ≥3	4	0	0	0	0.025
2.5 ≤L/B <3	6	6	0	0	0.015
2 ≤L/B <2.5	19	15	5	2	0.952
1 ≤L/B <2	3	11	27	30	4.051

L/B is the mean standardized uptake value (SUV) of radiated lung tissues/the average SUV of non-radiated lung tissues. The value of non-radiated lung tissues is equal to that of local lung tissues with an exposure dose of ≤5 Gy (the lung tissues that are non-circumscribed by the 10% equal dose curve).

differences in the mean SUV of lung tissue within groups or between the no RP and RP groups with radiation doses of 35 to ≤59.9 Gy and ≥60 Gy. There was no marked change in lung tissues with an exposure dose of ≤35 Gy at 6-10 weeks

after radiotherapy. The mean SUV of lung tissues was higher in the no RP group and the RP group following exposure to 35 to ≤59.9 Gy or ≥60 Gy, compared with other exposure doses. This indicates that the SUV of lung tissue is correlated with the radiation dose.

As the SUV is affected by individual differences, in order to compare the difference in the SUV of lung tissue in different exposure regions, the L/B ratio (the SUV of radiated lung tissue/the SUV of non-radiated lung tissue) was examined. When the L/B ratio was ≥3, the incidence of RP was 50%, and when the L/B ratio was ≥2.5, the incidence was 40.7%. The differences compared with the 20% incidence of the whole group were statistically significant (χ^2=4.18 and 4.92; P<0.05). When the L/B ratio was ≥2.5, the incidence of RP was 25%, and the difference compared with the whole group was not statistically significant (χ^2=0.41; P>0.05). At an L/B ratio of ≥2.5, all the lung tissues received an exposure dose of ≥35 Gy (lung tissues circumscribed by the 50% equal dose curve). Based on these findings, adjuvant therapy should be administered to patients when the L/B ratio is ≥2.5, and when it is 2 ≤L/B <2.5, patients should be observed closely. In the present study, when the V20 was <25%, one patient developed RP, but the L/B ratio was ≥2.5. When the L/B ratio was <2, there were no cases of RP. This shows that FDG PET-CT can predict RP through the molecular metabolism of the lung tissue itself, which is different from dose and volume factors. Thus, it is superior to the V20 method, as it avoids the effect of individual dose susceptibility. When the L/B ratio is ≥3, the region exposure is ≥60 Gy; that is, in the lung tissue enveloped by the 90% isodose curve, SUV is affected by the uptake value of the tumor itself and the tumor regression region. Thus, we suggest that for the prediction of RP, the L/B ratio of lung tissues should be located outside the 90% isodose curve.

In the present study, the FDG uptake in lung tissue following irradiation was associated with the radiation dose. ^{18}F-FDG PET-CT can be used to predict RP using the L/B ratio, and the L/B ratio is positively correlated with the occurrence of RP. The importance of variation in individual susceptibility for RP was shown in this study.

References

1. Clade L, Pérol D, Ginestet C, Falchero L, Arpin D, Vincent M, Martel I, Hominal S, Cordier JF and Carrie C: A prospective study on radiation pneumonitis following conformal radiation therapy in non-small-cell lung cancer: Clinical and dosimetric factors analysis. Radiother Oncol 71: 175-181, 2004.
2. Schild SE, Stella PJ, Geyer SM, Bonner JA, McGinnis WL, Mailliard JA, Brindle J, Jatoi A and Jett JR; North Central Cancer Treatment Group: The outcome of combined modality therapy for stage III non-small-cell lung cancer in the elderly. J Clin Oncol 21: 3201-3206, 2003.
3. Fajardo LF, Berthrong M and Anderson RE: Radiation Pathology. Oxford University Press, New York, pp200-206, 2001.
4. Robets CM, Foulcher E, Zaunders JJ, Bryant DH, Freund J, Cairns D, Penny R, Morgan GW and Breit SN: Radiation pneumonitis: A possible lymphocyte-mediated hypersensitivity reaction. Ann Intern Med 118: 696-700, 1993.
5. Cox JD, Stetz J and Pajak TF: Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys 31: 1341-1346, 1995.
6. Magaña E and Crowell RE: Radiation pneumonitis successfully treated with inhaled corticosteroids. South Med J 96: 521-524, 2003.
7. Graham MV, Purdy JA, Emami B, Harms W, Bosch W, Lockett MA and Perez CA: Clinical dose-volume histogram analysis for pneumonitis after 3D treatment for non-small-cell lung cancer (NSCLC). Int J Radiat Oncol Biol Phys 45: 323-329, 1999.
8. Kwa SL, Lebesque JV, Theuws JC, Marks LB, Munley MT, Bentel G, Oetzel D, Spahn U, Graham MV, Drzymala RE, *et al*: Radiation pneumonitis as a function of mean lung dose: An analysis of pooled data of 540 patients. Int J Radiat Oncol Biol Phys 42: 1-9, 1998.
9. Hicks RJ, Kalff V, MacManus MP, Ware RE, Hogg A, McKenzie AF, Matthews JP and Ball DL: (18)F-FDG PET-CT provides high-impact and powerful prognostic stratification in staging newly diagnosed non-small cell lung cancer. J Nucl Med 42: 1596-1604, 2001.
10. Yan R, Song J, Wu Z, *et al*: Detection of myocardial metabolic abnormalities by 18F-FDG PET/CT and corresponding pathological changes in Beagles with local heart irradiation. Korean J Radiol 16: 919-928, 2015.
11. Akhurst T, Downey RJ, Ginsberg MS, Gonen M, Bains M, Korst R, Ginsberg RJ, Rusch VW and Larson SM: An initial experience with PDG-PET in the imaging of residual disease after induction therapy for lung cancer. Ann Thorac Surg 73: 259-264, 2002.
12. Chen DL, Ferkol TW, Mintun MA, Pittman JE, Rosenbluth DB and Schuster DP: Quantifying pulmonary inflammation in cystic fibrosis with position emission tomography. Am J Respir Crit Care Med 173: 1363-1369, 2006.
13. Chen DL, Rosenbluth DB, Mintun MA and Schuster DP: FDG-PET imaging of pulmonary inflammation in healthy volunteers after airway instillation of endotoxin. J Appl Physiol (1985) 100: 1602-1609, 2006.
14. Guerrero T, Johnson V, Hart J, Pan T, Khan M, Luo D, Liao Z, Ajani J, Stevens C and Komaki R: Radiation pneumonitis: Local dose versus [18F]-fluorodeoxyglucose uptake response in irradiated lung. Int J Radiat Oncol Biol Phys 68: 1030-1035, 2007.