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Evaluation of the impact of integrated [18f]-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography imaging on staging and radiotherapy treatment volume definition of non-small cell lung cancer

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SUMMARY

The aim of this study was to evaluate the impact of integrated positron emission tomography (PET)/computed tomography (CT) imaging on staging and radiotherapy treatment volume definition of non-small cell lung cancer (NSCLC). Thirty-nine patients with NSCLC referred to the Department of Radiation Oncology of Gulhane Military Medical Academy, for radical radiotherapy between June 2011 and December 2011 were enrolled in this study. All patients underwent integrated PET/CT imaging in treatment position for initial assessment. For patients deemed suitable for radical radiotherapy, CT-based and integrated PET/CT imaging based radiotherapy treatment plans were generated to comparatively evaluate dose-volume parameters of both plans. Of the 39 patients initially assessed with integrated PET/CT imaging, 29 patients (74.4%) were deemed suitable for radical radiotherapy with curative intent. Fifteen patients (38.5%) were upstaged after integrated PET/CT staging. Of the 29 patients treated with radical radiotherapy at our department using integrated PET/CT imaging based radiation treatment planning (RTP), gross tumor volume was decreased in 16 patients (55.2%) and increased in 13 patients (44.8%) by incorporating PET/CT into RTP. Integrated PET/CT imaging allows selection of patients eligible for radical radiotherapy along with tailoring of radiotherapy target volumes to prevent overtreatment and undertreatment.

Key words: *Non-small cell lung cancer, positron emission tomography, radiotherapy, treatment planning*

ÖZET

Entegre [18f]-fluoro-2-deoksi-D-glikoz (FDG) pozitron emisyon tomografi/bilgisayarlı tomografi görüntülemesinin küçük hücreli dışı akciğer kanseri evreleme ve radyoterapi tedavi hacim tanımlamasına etkisinin değerlendirilmesi

Bu çalışmanın amacı entegre pozitron emisyon tomografi (PET)/bilgisayarlı tomografi (BT) görüntülemesinin küçük hücreli dışı akciğer kanseri (KHDAK) evrelemesi ve tedavi hacmi tanımlamasına etkisinin değerlendirilmesidir. Haziran 2011 ile Aralık 2011 arasında KHDAK tanısıyla Gülhane Askeri Tıp Akademisi (GATA) Radyasyon Onkolojisi Anabilim Dalı'na yönlendirilen 39 hasta çalışmaya dahil edilmiştir. Başlangıç değerlendirmesi için tüm hastalara tedavi pozisyonunda entegre PET/BT görüntülemesi yapılmıştır. Radikal radyoterapi için uygun olduğu değerlendirilen hastalara BT tabanlı ve entegre PET/BT görüntülemesi tabanlı iki ayrı planlama, doz-hacim parametrelerinin bu iki planlamada karşılaştırılması için yapılmıştır. Entegre PET/BT görüntülemesiyle başlangıç değerlendirmesi yapılan 39 hastadan 29'u (%74.4) küratif amaçlı radikal radyoterapi için uygun olarak değerlendirilmiştir. Entegre PET/BT görüntülemesi sonrası 15 hastada (%38.5) evre atlaması görülmüştür. PET/BT'nin radyoterapi planlamasına dahil edilmesiyle kliniğimizde entegre PET/BT görüntülemesi tabanlı radyoterapi planlaması kullanılarak tedavi edilen 29 hastadan 16'sında (%55.2) gros tümör hacmi azalmış, 13 hastada (%44.8) ise artmıştır. Entegre PET/BT görüntülemesi, fazla ve eksik tedavinin engellenmesi için radikal radyoterapiye uygun hastaların seçimiyle birlikte radyoterapi hedef hacimlerinin şekillendirilmesine imkan sağlar.

Anahtar kelimeler: *Küçük hücreli dışı akciğer kanseri, pozitron emisyon tomografi, radyoterapi, tedavi planlaması*

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Introduction

Lung cancer is the leading cause of cancer-related death worldwide and non-small cell lung cancer (NSCLC) comprises 75% to 80% of all lung cancer cases (1). Radiotherapy plays a central role in the management of NSCLC. Local control rates are improved with dose escalation, however, escalating the total radiation dose requires accurate target definition (2,3). Computed tomography (CT), the conventional imaging modality used in radiation treatment planning (RTP) for NSCLC, may be insufficient to determine the target volume in some circumstances such as atelectasis due to poor contrast between tumor and normal tissues. Inclusion of entire atelectasis may result in larger treatment volumes in some patients leading to increased risk of treatment morbidity, which also limits the potential of dose escalation. Moreover, staging of the mediastinum with CT may not be accurate since the sole parameter to decide on lymph node involvement is a short axis diameter of 1 cm. In the study by Prenzel et al. 44% of lymph nodes <1 cm were reported to be malignant, whereas 77% of lymph nodes were benign (4). Thus, a major limitation of using CT alone in RTP for NSCLC is undertreatment owing to inaccurate mediastinal evaluation that may result in treatment failure. With the awareness of the uncertainity of CT to define treatment volumes in some circumstances, efforts have been focused on improving treatment volume definition by incorporating other imaging modalities.

Positron emission tomography (PET) with the glucose analog [18F]fluoro-2-deoxy-D-glucose (FDG) is a functional imaging modality which is increasingly being used in oncology for staging, restaging, assessing treatment response, predicting treatment outcomes, target definition, and follow up. Lungs comprise one of the most common tumor sites where 18-FDG PET is used for treatment volume definition. Incorporation of functional imaging data acquired by PET into RTP for NSCLC is important in overcoming uncertainties such as small mediastinal lymph nodes and atelectasis. Besides all these benefits, biological imaging and the concept of biological target volume (BTV) were introduced to increase cure rates through delivering higher doses to the subvolumes of the target with “dose painting” or “dose sculpting” (5-7).

Before the introduction of hybrid PET/CT scanners, incorporating PET into RTP without the integration of PET and CT was limited by the acquisition of data separately since this could be inherently error-prone in some steps. Integrated PET/CT imaging which allows the use of biological and anatomical imaging data together has been a major advance in the management of NSCLC. Compared to CT alone, PET alone and visual correlation of separate PET and CT, integrated PET/CT imaging has been shown to be superior in predicting the T status, N status and distant metastasis (8-16).

Accurate staging of patients with NSCLC provides important prognostic information and helps in therapeutic decision making. The use of integrated PET/CT for staging of patients with newly diagnosed NSCLC may help allocate patients to the optimal treatment approach. Detection of distant metastasis prevents overtreatment with surgery or definitive radical radiotherapy in some patients which allows avoiding the potential morbidity and mortality of these radical treatment approaches.

The rationale for incorporating PET/CT into RTP for NSCLC is to exploit the advantages of using both anatomical and metabolical data to determine the extent of disease more accurately. Integrated PET/CT improves differentiating normal tissue from the tumor by providing a greater contrast between benign and malignant tissues. This is particularly important in the presence of peritumoral atelectasis since poor demarcation of the tumor on CT limits precise target localization. Improving target definition with the incorporation of PET/CT in such cases may significantly reduce normal tissue exposure to excess radiation and thus dose escalation may be considered to increase the chances of cure. However, treatment volumes may also increase for some patients due to the inclusion of PET/CT-detected tumor involvement in mediastinal lymph nodes. In these patients, PET/CT imaging based RTP may prevent undertreatment by improving target definition with the potential to optimize treatment outcomes.

In this study, we evaluated the impact of integrated PET/CT imaging on staging and radiotherapy treatment volume definition of non-small cell lung cancer (NSCLC).

Material and Methods

Thirty-nine patients with NSCLC meeting the eligibility criteria of ≤65 years of age, pathologic confirmation of inoperable/unresectable NSCLC, Eastern Cooperative Oncology Group (ECOG) performance status of 0-1 and no previous radiotherapy to the thorax referred to Gulhane Military Medical Academy, Department of Radiation Oncology for radical radiotherapy between June 2011 and December 2011 were enrolled in the study. None of the patients had undergone previous integrated PET/CT imaging as part of the initial staging workup. Five patients with locally advanced disease received two to three courses of chemotherapy before radiotherapy. Baseline characteristics of the 39 patients are shown in Table I. Informed consents of all participants were obtained prior to study enrollment.

All patients underwent integrated PET/CT imaging in the treatment position for initial assessment. The combined PET/CT system (Discovery PET/CT 690, General Electric Medical System, Milwaukee, WI, USA) was used in the acquisition of integrated PET/CT images. After fasting for at least 6 hours, capillary blood glucose was measured to ensure that levels were below 150 mg/dl before intravenous FDG (370-555 MBq, 10-15 mCi) administration. Patients lay comfortably in supine position in a quiet and dimly lit room during the distribution phase. For scanning, patients were immobilized on a flat-panel carbon-fiber composite table insert in the treatment position with arms raised above head. Combined image acquisition was started 50-60 minutes after FDG injection. Firstly, an unenhanced CT scan with a slice thickness of 3.25 mm from the skull base to the proximal thigh was acquired using a standardized protocol with 120 kV, 30 mA. Subsequently, the PET scan was acquired in 3D mode from the skull base to the proximal thigh (6-7 bed positions, 3 minutes/position) without changing the patient’s position. Images were reconstructed using an ordered-subset expecta-

Table I. Baseline patient characteristics		
Characteristics	***Number of patients***	***%***
Gender		
Male	27	69.2
Female	12	30.8
Age (years)	Median 61 years (range 48-65 years)	
ECOG* performance status		
0	28	71.8
1	11	28.2
Histology		
Squamous cell carcinoma	14	35.9
Adenocarcinoma	11	28.2
Large cell carcinoma	2	5.1
NSCLC**, no further specification	12	30.8
Clinical stage before integrated PET/CT*** imaging		
IIA	5	12.8
IIB	6	15.4
IIIA	14	35.9
IIIB	14	35.9
T stage before integrated PET/CT*** imaging		
T2	6	15.4
T3	16	41.0
T4	17	43.6
N stage before integrated PET/CT*** imaging		
N0	8	20.5
N1	8	20.5
N2	12	30.8
N3	11	28.2

*: ECOG=Eastern Cooperative Oncology Group
**: NSCLC=Non-small cell lung cancer
***: PET/CT=Positron emission tomography/computed tomography

tion-maximization iterative algorithm. Emission images were corrected for measured attenuation using a segmented attenuation-correction algorithm. Images were displayed as whole-body reprojection images and as slices in three orthogonal planes (axial, coronal, and sagittal). After detailed evaluation of the integrated PET/CT images with an experienced nuclear medicine specialist, patients with distant metastasis or extensive locoregional disease precluding radical radiotherapy were allocated to receive palliative treatment. For patients deemed suitable for radical radiotherapy, the integrated PET/CT images were sent to the contouring workstation via network. These patients also underwent CT-simulation to generate both CT-based and integrated PET/CT imaging based radiotherapy treatment plans to comparatively evaluate dose-volume parameters of both plans.

For CT-simulation, all patients were immobilized using a Wing-Board (CIVCO, Kalona, IA, USA) with arms above head, and three fiducials were aligned on the patient's skin with the simulator lasers. Patients were scanned with 2.5 mm slice thickness at CT-simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK). The acquired images were sent to the contouring workstation via network. Advantage Sim MD simulation and localization software (Advantage SimMD, GE, UK) was used for contouring treatment volumes and critical organs. For gross tumor volume (GTV) definition on CT, pulmonary window settings were used to contour the pulmonary tumor and hilum and the predefined mediastinal window settings were used to contour the mediastinal lesions.

For integrated PET/CT imaging based RTP, we used the relative threshold method to define the GTV and created a 3D contour around voxels that are equal to or greater than 50% of the maximum voxel value inside a spherical region.

Any mediastinal lymph nodes with a diameter greater than 10 mm in the short axis were included in the GTV regardless of the standardized uptake value (SUV).

Margins for GTV to clinical target volume (CTV) were 6 mm for squamous cell carcinoma (SCC) and 8 mm for other histologic types. Tumor motion in superior-inferior (SI), anterior-posterior (AP), and left-right (LR) directions was assessed with the XVI Cone Beam CT (CBCT, X-ray Volume Imaging, Elekta, UK) imaging technology integrated with our linear accelerator (Synergy, Elekta, UK). The volumetric imaging and fluoroscopic monitoring data obtained by CBCT flat-panel technology allowed documenting tumor motion in three dimensions (SI, AP, LR) for each patient using the grids on the acquired images. In the generation of the planning target volume (PTV), individualized internal margins plus 5 mm setup margin was added to the CTV. Delineation and treatment planning procedures were performed by the same physician and physicist to improve consistency and concordance.

Two separate radiotherapy treatment plans were generated for each patient with PrecisePLAN (Elekta, UK) treatment planning system: one with CT-based planning and the other with integrated PET/CT imaging based planning. Dose-volume histograms were generated for all delineated structures in both plans of each patient. For the spinal cord maximum dose (Dmax) was calculated. For the heart, Dmean and percentage volume receiving a dose of 40 Gy or more (V40) was calculated. For the lungs, percentage of lung volume receiving a dose of 20 Gy or more (V20) and mean lung dose (MLD) was calculated. MLD was defined as the average dose to total normal lung volume. For the esophagus, mean esophageal dose (MED) was calculated. GTVs and aforementioned dose-volume parameters acquired from both plans were compared with each other using paired t test. Statistical Package for the Social Sciences, version 15.0 (SPSS, Inc., Chicago, IL) software was used for analysis and the level of significance was set at $p<0.05$.

PrecisePLAN (Elekta, UK) treatment planning system was used in generating the 2 separate three-dimensional conformal radiotherapy treatment plans for each patient. Beam organizations, wedges, and the beam angles were identical in both plans of the patients. Multileaf collimators were used to shape treatment fields when necessary. Primary objectives of planning were to achieve optimal normal tissue sparing while maintaining target coverage. Coverage of the CTV by the 95% isodose line was mandatory. PTV coverage with 95% isodose line was not achievable in some patients due to critical organ dose constraints. All patients were planned to receive a dose of 60 Gy in 30 fractions over 6 weeks using 6-18 MV photon beams. The use of concomitant weekly chemotherapy with cisplatin 40 mg/m^2 was planned for patients with locally advanced disease. Treatment was delivered using a linear accelerator (Synergy, Elekta, UK) allowing on-line setup verification under image guidance with kilo-Voltage Cone Beam Computed Tomography (kV-CBCT) (X-ray Volumetric Imaging (XVI), Elekta, UK) mounted on the LINAC gantry.

Results

Out of the 39 patients enrolled in the study, 10 patients (25.6%) including the five patients treated with chemotherapy before referral to our department were deemed unsuitable for curative treatment due to the detection of distant metastasis with integrated PET/CT imaging and these patients were allocated to receive palliative treatment. Thus, 29 patients (74.4%) with inoperable/unresectable NSCLC were treated with radical radiotherapy using integrated PET/CT imaging based radiation treatment planning (RTP).

Median tumor motion assessed using the volumetric imaging and fluoroscopic monitoring data acquired by XVI Cone Beam CT (CBCT, X-ray Volume Imaging, Elekta, UK) and corresponding median internal margins were 7 mm (range 3-11 mm), 4 mm (range 2-8 mm), and 3 mm (range 2-7 mm) in SI, AP, and LR directions, respectively.

GTV was altered in all 29 patients. In 16 patients (55.2%), GTV was reduced with the incorporation of integrated PET/CT imaging while it was increased in 13 patients (44.8%). The median decrease in GTV in 16 patients was 23.4% (range 12%-71%), whereas a median increase of 8.2% (range 3%-87%) was observed in 13 patients. Figure 1a-b shows the integrated PET/CT images of a patient with peritumoral atelectasis in sagittal and axial planes (Figure 1a-b). Figure 2a-b shows the treatment volumes (GTV, CTV,

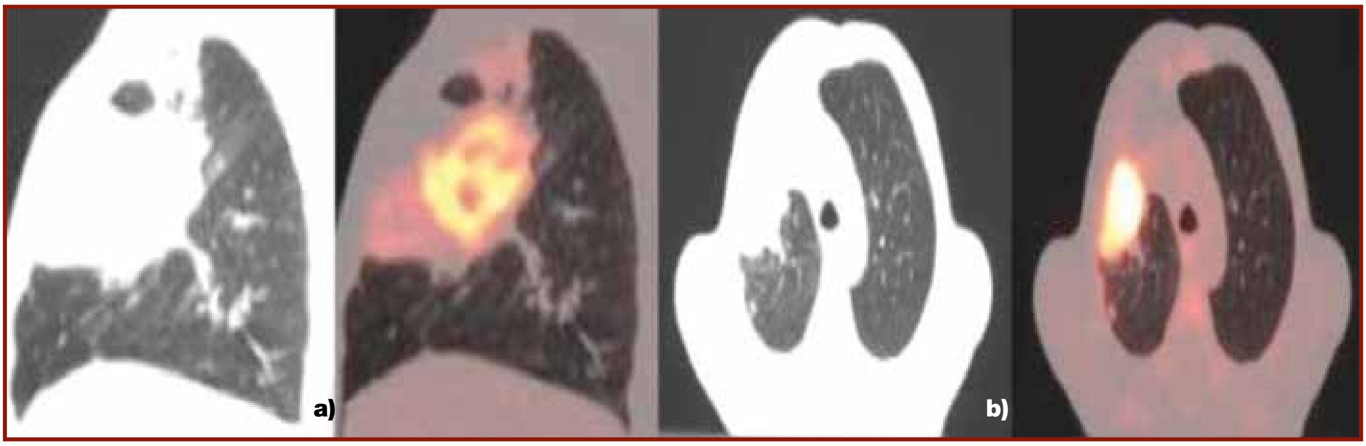

Figure 1 a,b. Integrated PET/CT images of a patient with peritumoral atelectasis in sagittal and axial planes. a) Integrated PET/CT images of a patient with peritumoral atelectasis in sagittal planes, b) Integrated PET/CT images of a patient with peritumoral atelectasis in axial planes

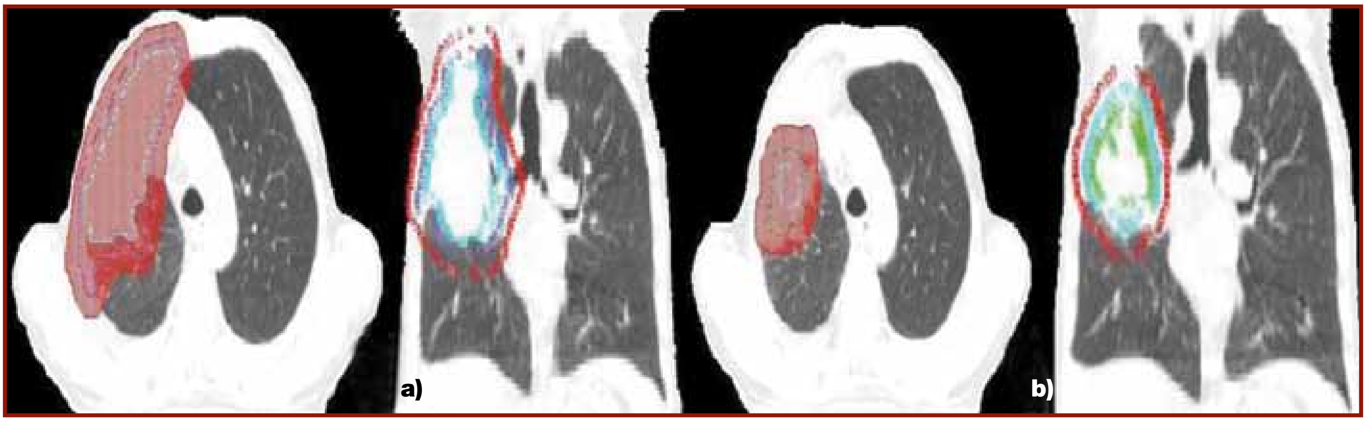

Figure 2 a,b. a) Treatment volumes (GTV, CTV, and PTV) of a patient with peritumoral atelectasis with CT-based RTP in axial and coronal planes. 2b) Treatment volumes (GTV, CTV, and PTV) of the same patient with peritumoral atelectasis with integrated PET/CT imaging based RTP in axial and coronal planes

and PTV) of a patient with peritumoral atelectasis with CT-based and integrated PET/CT imaging based RTP (Figure 2a-b).

Using integrated PET/CT imaging based RTP, all critical organ doses were significantly reduced in 16 patients with GTV reduction ($p<0.001$), and a statistically significant increase in critical organ doses was observed in 13 patients with GTV increase ($p<0.01$). Fifteen patients (38.5%) were upstaged with the incorporation of integrated PET/CT imaging while no downstaging was observed. Of these 15 patients, 10 patients were upstaged to stage IV due to the detection of distant metastasis with integrated PET/CT imaging. For the remaining 5 patients upstaged, 2 patients with stage IIA and 3 patients with stage IIB were upstaged to stage IIIB after integrated PET/CT imaging due to the detection of contralateral mediastinal lymph nodes. Figure 3 shows the integrated PET/CT images of a patient deemed unsuitable for radical radiotherapy due to adrenal metastasis (Figure 3). Dose-volume parameters of the total 29 patients and subgroups with GTV reduction and GTV increase are shown in Tables II, III, and IV, respectively.

Discussion

Functional imaging with the glucose analog [18F] fluoro-2-deoxy-D-glucose is increasingly being used in many steps of cancer management to improve

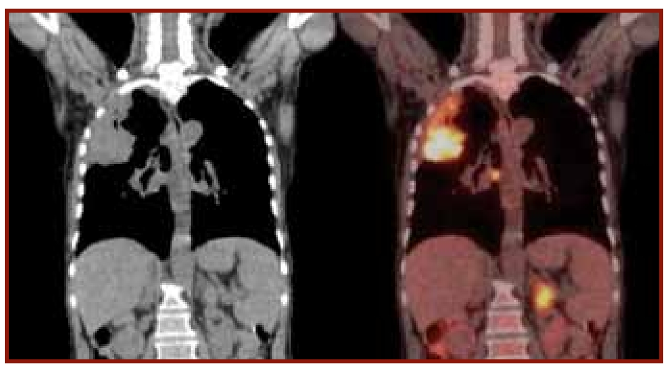

Figure 3 Integrated PET/CT images of a patient deemed unsuitable for radical radiotherapy due to adrenal metastasis

Table II. Dose-volume parameters for the total 29 patients

		Dose-volume parameter								
		GTV total (cc)	*GTV-tumor (cc)*	*GTV lymph node (cc)*	*V20 (%)*	*MLD (cGy)*	*Mean heart dose (cGy)*	*Heart V40 (%)*	*MED (cGy)*	*SCmax dose (cGy)*
CT-based RTP	Median	78	68	8	27.3	1973	1311	14.4	2189	4081
	Range	25-389	17-319	0-80	14.9-34.1	695-2312	578-1890	8.2-30	859-3437	3190-4208
Integrated PET/CT imaging based RTP	Median	61	52	7	24.1	1789	1190	13.8	2146	3678
	Range	22-299	15-293	0-68	13.1-34.1	611-2179	531-1678	7-28	639-3189	2897-4211

CT: Computed tomography, PET/CT: Positron emission tomography/computed tomography, RTP: Radiation treatment planning
GTV: Gross tumor volume, V20: Percentage of lung volume receiving a dose of 20 Gy or more, MLD: Mean lung dose (MLD)
HeartV40: Percentage of heart volume receiving a dose of 40 Gy or more, MED: Mean esophageal dose, SCmax dose: Spinal cord maximum dose

Table III. Dose-volume parameters for 16 patients with gross tumor volume (GTV) reduction

		Dose-volume parameter								
		GTV total (cc)	*GTV-tumor (cc)*	*GTV lymph node (cc)*	*V20 (%)*	*MLD (cGy)*	*Mean heart dose (cGy)*	*Heart V40 (%)*	*MED (cGy)*	*SCmax dose (cGy)*
CT-based RTP	Median	85	69.5	10.5	28	1973	1318	15	2377	4124
	Range	25-389	17-319	2.9-80	15-34.1	695-2312	578-1890	8.2-30	859-3437	3190-4208
Integrated PET/CT imaging based RTP	Median	60	48.5	7.5	22.5	1598	1157	12	2089	3483
	Range	22-257	15-197.5	2.6-68	13.1-29.1	611-1999	531-1601	7-28	639-3189	2897-3719
p (*)		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
% reduction with integrated PET/CT imaging based RTP	Median	23.4	24.3	14.3	20.3	17.4	14.8	14.9	15.3	14.2
	Range	12-71	12-47	7-38	4-30	1-31	7-22	2-33	1-26	8-25

*: Comparison of CT-based RTP and Integrated PET/CT imaging based RTP for dose-volume parameter reduction using the paired t test
CT: Computed tomography, PET/CT: Positron emission tomography/computed tomography, RTP: Radiation treatment planning
GTV: Gross tumor volume, V20: Percentage of lung volume receiving a dose of 20 Gy or more , MLD: Mean lung dose (MLD)
HeartV40: Percentage of heart volume receiving a dose of 40 Gy or more, MED: Mean esophageal dose, SCmax dose: Spinal cord maximum dose

treatment outcomes. The introduction of hybrid PET/CT scanners has further enhanced the utilization of integrated PET/CT imaging in RTP for lung cancer. By exploiting the advantages of using both anatomical and functional data, integrated PET/CT imaging has been shown to be superior in predicting the T status, N status and distant metastases compared to CT alone, PET alone and visual correlation (8-16). In our study, the use of integrated PET/CT imaging for initial assessment has changed the management of 10 patients (25.6%) from curative to palliative treatment and 15 patients (38.5%) were upstaged after integrated PET/CT staging. In the study by MacManus et al. 46 patients (30%) out of the total 153 patients with NSCLC were deemed unsuitable for radical treatment after FDG-PET staging (17). In the study by Kolodziejczyk et al. 25 (25%) of the total 100 patients with NSCLC were unsuitable for radical radiotherapy (18). Our results are consistent with the results of the studies by MacManus et al. and Kolodziejczyk et al. showing the benefit of functional imaging in selecting appropriate patients for curative treatment (17,18).

Target delineation has become more critical in the era of three dimensional conformal radiotherapy (3DCRT), intensity modulated radiation therapy

Table IV. Dose-volume parameters for 13 patients with gross tumor volume (GTV) increase

		Dose-volume parameter								
		GTV total (cc)	GTV-tumor (cc)	GTV lymph node (cc)	V20 (%)	MLD (cGy)	Mean heart dose (cGy)	Heart V40 (%)	MED (cGy)	SCmax dose (cGy)
CT-based RTP	Median	78	68	4.2	25.9	1973	1259	13.2	2168	3879
	Range	29-279	20-274	0-12	14.9-33.5	695-2100	617-1604	8.3-18.1	1589-2579	3411-4111
Integrated PET/CT imaging based RTP	Median	81	70	5	27	2019	1389	14	2217	4067
	Range	31-299	21-293	0-21	15.8-34.1	711-2179	690-1678	8.9-18.9	1699-2619	3568-4211
p (*)		<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
% increase with integrated PET/CT imaging based RTP	Median	8.2	8.3	14.5	4.1	3.6	4.4	4.2	3.6	3.1
	Range	3-87	2-87	4-75	2-13	1-8	1-12	2-7	2-7	2-11

*: Comparison of CT-based RTP and Integrated PET/CT imaging based RTP for dose-volume parameter increase using the paired t test
CT: Computed tomography, PET/CT: Positron emission tomography/computed tomography, RTP: Radiation treatment planning
GTV: Gross tumor volume, V20: Percentage of lung volume receiving a dose of 20 Gy or more , MLD: Mean lung dose (MLD)
HeartV40: Percentage of heart volume receiving a dose of 40 Gy or more, MED: Mean esophageal dose, SCmax dose: Spinal cord maximum dose

(IMRT) and image guided radiotherapy (IGRT); and incorporating functional data in RTP has been of crucial value for more accurate treatments. In our study, GTV was altered in all patients with the incorporation of integrated PET/CT imaging into RTP. In 16 patients (55.2%) a median decrease of 23.4% (range 12%-71%) was observed whereas an increase of 8.2% (range 3%-87%) was detected in 13 patients (44.8%) in GTV. The decrease in GTV turned into a statistically significant reduction in critical organ doses for the 16 patients in our study which affected the whole study group (Tables II, III). Although we used a standard radiotherapy schedule delivering a standard dose of 60 Gy, dose escalation may be considered if the critical organ dose reductions achieved with integrated PET/CT imaging based RTP allow further dose intensification. Delivering higher doses to the subvolumes of the target with “dose painting” or “dose sculpting” and escalating the total dose to PET-active tumor volumes has been reported and is an area of active investigation (5-7,19).

The selection of appropriate treatment volumes to delineate is an important concern in integrated PET/CT imaging based RTP and there is still no widely accepted consensus on using a fixed threshold value. Ciernik et al. suggested using a fixed threshold of 50% of the maximum activity which we used in this study (20). In the study by Wu et al. GTV defined by using the 50% threshold was the closest to the actual geometry (21). Bradley et al. used a fixed threshold of 40% while Paulino and Johnstone suggested autocontouring all areas with a SUV of 2.5 (22,23). Further studies are warranted to refine the optimal delineation procedure using functional data.

In conclusion, the introduction of integrated PET/CT imaging in NSCLC management is of crucial contribution not only by differentiating metastatic disease but also by tailoring radiotherapy treatment volumes to prevent overtreatment and undertreatment. By exploiting the advantage of compounding both functional and anatomical data to define treatment volumes accurately, the use of integrated PET/CT imaging is a promising tool to optimize treatment outcomes in patients with NSCLC.

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