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THE EFFECT OF USING PET-CT FUSION ON TARGET VOLUME DELINEATION AND DOSE TO ORGANS AT RISK IN 3D RADIOTHERAPY PLANNING OF PATIENTS WITH NSSLC

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Non–small-cell lung cancer, Radiation therapy, Target delineation, FDG-PET.

Abstract

Background: three-dimensional conformal radiation therapy (3DCRT) planning remains the standard option in the management of locally advanced NSSCL, a technique that makes the radiation oncologist face the challenge of target volume delineation based on CT scan alone, which will eventually affect target volume coverage, i.e. gross tumor volume (GTV) and planning target volume (PTV), as well as dose to the surrounding normal tissues at risk.

Purpose: To prospectively study the impact of fusing 18F-fluoro-deoxy-2-glucose hybrid positron emission tomographic (FDG-PET) images with CT images on the planning target volume (PTV) delineation, target coverage, and critical organ dose in radiation therapy planning of non–small-cell lung carcinoma.

Methods and Materials: Twenty patients with Stages I–III NSCLC were referred to our radiotherapy department in the period between Jan 1st 2015 and Aug 30, 2016, planned for treatment via radiotherapy alone or with concurrent chemo-radiation. Each patient underwent a planning CT with immobilization devices. FDG-PET scan was ordered for every patient and done in the department of nuclear medicine very soon after or before the day of CT simulation. Both the CT and PET/CT image data sets were fused and used in the radiation treatment planning workstation for contouring. Each FDG-PET study was reviewed with the interpreting nuclear radiologist before tumor volumes were contoured. A three-dimensional conformal radiation therapy (3DCRT) plan was calculated based on contours done on the CT scan only. A second plan based on the fused PET/CT images was generated. The PTV was defined by a 20 mm margin around the GTV. The two 3DCRT plans for each patient were compared with respect to the GTV, PTV, mean lung dose, volume of normal lung receiving >20 Gy (V20), and mean esophageal dose.

Results: The FDG-PET findings altered the AJCC TNM stage in 6 of 20 (30%) patients; 2 patients were diagnosed with metastatic disease based on FDG-PET and received palliative radiation therapy. Of the 18 patients who were planned with 3DCRT, PET clearly altered the radiation therapy volume in 10 (66%), for example, PET helped to distinguish tumor from atelectasis in all 4 patients with atelectasis. Unsuspected nodal disease was detected by PET in 2 patients, and 1 patient had a separate tumor focus detected within a different lobe of the lung. Increases in the target volumes led to increases in the dose to organs at risk (mean lung dose, V20, and mean esophageal dose). Decreases in the target volumes in the patients with atelectasis led to decreases in these normal-tissue toxicity parameters.

Conclusions: Radiation targeting with fused FDG-PET and CT images resulted in modifications in radiation therapy planning in over 50% of patients by comparison with CT targeting. The future plan of having a PET-CT simulator in our department will make it possible to have the planning CT and PET-CT done on the same day and in the same position, eliminating all the difficulties faced during the fusion process.

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Introduction

Despite all the efforts made the prognosis of patients with inoperable non–small-cell lung cancer (NSCLC) is poor with published 5-year survival rates ranging from 6% to 32% for Stage I and II patients receiving radiation alone and 17% for Stage III patients receiving both chemotherapy and radiation (1– 3). Following a high radiation doses of _60 Gy, still local failure as determined by biopsy occurs in up to 83% of Stage III patients, indicating a need to improve local tumor control (4).

Positron emission tomography (PET) has become widely used in oncology over the last decade in different fields. In patients with suspected or proven NSCLC, FDG-PET is used primarily for the diagnostic evaluation of pulmonary nodules, for staging the mediastinum, and for detection of distant metastases. FDG-PET has consistently been shown to be more accurate than computed tomography (CT) in determining mediastinal nodal status.
A meta-analysis by Toloza et al. reports the sensitivity and specificity for mediastinal staging to be 84% and 89%, respectively, for FDG-PET and 57% and 84%, respectively, for CT (5).

Materials and methods

In the period between Jan 1st 2015 and Aug 30, 2016, twenty patients with Stages I–III NSCLC were enrolled in this study; they were planned for treatment via radiotherapy alone or with concurrent chemo-radiation.

Each patient was required to have pathologic confirmation of NSCLC and a Zubrod performance status of 0–1. Patients had Stage I–III disease with no evidence of metastatic disease detected by history and physical examination, routine laboratory testing, CT of the chest and upper abdomen (to include the liver and adrenal glands), and bone scintigraphy. Patients previously treated with chemotherapy were included because this study was designed primarily to determine the impact of PET on radiation therapy target volumes**.**

Planning

Each patient underwent a volumetric CT scan and immobilized before the CT using Redi-Foam alpha cradle in supine position with arms overhead .Three fiducial markers were placed on the patient skin for localization of the reference point, 2 lateral and 1 anterior, CT images were then obtained as 3-mm sections through the entire thorax.
The CT images were then transferred to the planning work station where normal tissues contoured on the CT data set.

Normal-tissue contours included the right lung, left lung, esophagus (from the carina to the esophagogastric junction), spinal cord, and heart. After the normal tissues were contoured, each CT data set was copied to maintain two separate data sets for three-dimensional planning: CT alone and PET/CT fusion data sets.

First the CT-alone data set was contoured and planned by the treating physician and a dosimetrist without knowledge of the PET scan results, in an effort to reduce bias. The GTV consisted of the primary tumor and any regional lymph nodes seen on CT with short-axis diameter_10 mm or more. Lung window settings were used to contour the primary tumor in each case, and mediastinal window used to define lymph nodes. The PTV consisted of the GTV plus a volumetric margin of 20 mm; this data set was used to generate a comparison treatment plan for each patient, but was not used for treatment.

PET/CT images were then registered on the planning system and fused with the copied CT images, after reviewing the PET images with a nuclear radiologist; the same treating physician generated gross tumor volume (GTV) and planning target volume (PTV) contours for each patient. The GTV included the primary tumor seen on both CT and PET and any clinically involved regional lymph nodes. Lymph nodes were considered tumor if they demonstrated increased FDG uptake or measured_10 mm or more in short-axis dimension on CT. In patients with atelectatic lung adjacent to gross primary tumor, only the areas with increased FDG uptake were considered part of the GTV. The PTV consisted of the GTV plus a volumetric 20-mm margin. Noninvolved elective nodal regions were not intentionally targeted.

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Both the CT-planned and the PET/CT-planned data sets underwent 3DCRT planning by separate dosimetrists. The dosimetrists were provided with the following guidelines: the total dose to be prescribed to the isocenter, and a block margin of 7 mm beyond the PTV; in addition, the PTV was to receive _95% of the prescribed dose. Plans were optimized to maximize dose to the PTV while limiting dose to normal tissues.

The two treatment plans for each patient were compared with respect to the contoured GTV, PTV, and normal tissues receiving radiation. For the purpose of defining differences in GTV and PTV contours, "significant" differences were predefined as tumor and/or nodal regions that were included as GTV/PTV within one data set, but not the other, or the difference in the volume of the GTV/PTV being 25% or more. Minor differences in contours of the same tumor and/or nodal volume with a value of 25% or less between data sets were considered "minimal".
Mean lung dose (MLD), the volume of normal lung receiving _20 Gy (V20), and mean esophageal dose (MED) are reported to summarize predictions of normal-tissue toxicity.

Results

Between January 2015 and August 2016, 20 patients were enrolled in this prospective pilot study at our institution. Assigned clinical stages at referral (without PET information) included 2 patients with T1N0M0 carcinomas, 2 with T1N1, 4 with T1N2M0, 6 with T2N2M0, 3 with T3N2M0, 1 with T1N3, 1 with T2N3, and 1 with T4N2M0 cancers. The addition of PET altered the AJCC TNM clinical stage in 6 patients (30%) (Table 1). PET identified unsuspected distant metastasis (M1 disease) in 2 patients. One had intrapulmonary metastases, and the other had bone metastases. Both received palliative radiation therapy.

Eighteen patients received definitive 3DCRT planned with the PET/CT fusion images. Of these 18 patients, PET significantly altered the GTV in 10 (66%) patients. PET helped to delineate tumor within regions of atelectasis in 4 patients, reducing the GTV for each. PET increased the GTV significantly in 3 patients; a second right upper-lobe lesion was included in 1 patient (T4 disease), and additional unsuspected regional nodal disease was included in 2 patients.

Three patients with tumor-related atelectasis were included. The addition of PET did not change the assigned stage in any of these patients. However, the PET/CT fusion data clearly helped to delineate tumor from atelectatic lung, reducing the GTV, PTV, MLD, and MED, accordingly.

Table 2 demonstrates the changes in the GTV, PTV, and normal-tissue radiation doses when the PET/CT-based plans are compared to the CT-based treatment plans. In the patients with atelectasis, decreases in the GTV led to reduced radiation doses to the lung and esophagus. With increases in GTV because of the detection of additional gross primary or nodal disease, the doses to normal tissues were increased, as were the probabilities of normal-tissue complication. A summary of FDG-PET changes in TNM stage and contoured GTV is given in Table 3.

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Table 1. Alteration in TNM staging by PET

CT stage	PET/CT stage
Stage IA T1N0 (n = 2)	T1N0(n=2)
Stage II T1N1(n=2)	T1N1 (n=1) T1N2 (n=1)
Stage IIIA T1N2(n=4) T2N2(n=6) T3N2(n=3)	T1N2(n=4) T2N2(n=4) T4N2(n=1) T2N3(n=1) T3N2(n=2) T3N2M1(n=1. Bone mets)
Stage IIIB T1N3(n=1) T2N3(n=1) T4N2(n=1)	T2N3(n=1) T2N3(n=1) T4N2M1(n=1. Lung mets)

Table 2. Alteration in target volumes and normal tissue doses: CT vs. PET/CT

Patient #	*Target Volumes*				*Normal tissue doses*					
	GTV(cm3)		PTV(cm3)		MLD(Gy)		V20(%)		MED(Gy)	
	CT	PET/C	CT	PET/CT	CT	PET/CT	CT	PET/CT	CT	PET/CT
Significant GTV decrease (Atelectasis)										
1	254	184	835	543	12.5	7.7	29%	15%	42	22
2	465	120	985	520	19	13	32.2%	28.5%	39	26
3	370	99	920	430	20.3	15.2	28.5%	16.3%	29.2	24.8
4	510	267	1206	566	21	14.6	35%	21%	34	25
Significant GTV increase										
5	42	78	215	365	13.1	15.6	24%	29.5%	5.8	8.2
6	110	190	367	628	15.2	18	21%	30.4%	17.5	26.4
7	68	375	140	930	10.7	20.3	18%	27.6%	7	41
8	270	456	550	1020	17	19.5	23.3%	35.6%	35	38
9	95	163	274	468	8.6	12.8	10.6%	13.4%	5.5	8.4
10	73	220	145	647	6.5	13.4	9.7%	25%	10.3	17.8
Minimal GTV change										
11	145	132	446	439	12	14.2	21%	22%	24	25.3
12	130	124	405	394	22.7	21.4	19.6%	19.2%	16	17.5
13	36	53	155	164	11.8	13.4	12.2%	13.6%	4.1	4.6

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14	274	265	742	713	14.8	14.3	27%	25.8%	34	31
15	98	85	324	316	11.5	10.9	16%	14.7%	7.4	7
16	64	71	214	220	8.2	8.5	12.3%	12.6%	0	1.3
17	452	471	963	987	17.8	18.4	35.6%	36.7%	41	42.3
18	321	317	784	769	15.7	15.3	31%	28.6%	35	34.2

Abbreviations: CT _ computed tomography; PET_ positron emission tomography; GTV _ gross tumor volume; PTV _ planning target volume; MLD _ mean lung dose; MED _ mean esophageal dose.

Conclusion

The results of this prospective trial show that FDG-PET has an impact on the management of patients with NSCLC. In addition to the alteration of the clinical TNM stage, FDG-PET simulation may have a therapeutic impact by identifying additional gross disease that needs to be included within the high-dose volume. Our prospective data and the reported literature suggest that in 30–60% of these patients treated with definitive radiation therapy, the use of PET simulation will enhance precision in coverage of the GTV, PTV, as well as affecting dose delivered to normal tissues.

The future plans of having a PET/CT simulator assigned for radiotherapy simulation and planning is thought to eliminate all the difficulties in the fusion and registration process.

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