Dosimetric analysis of normal tissue toxicity in 3D conformal radiotherapy planning with fused PET-CT imaging in non-small cell lung carcinoma

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Abstract

Introduction: The prime modality for inoperable NSCLC is radiation therapy and or chemo-radiation and better results can be achieved by a higher dose of radiation. However dose escalation is difficult due to presence of critical and dose limiting sensitive structures in the vicinity of lung. Therefore success of radiotherapy in such tumors solely depends on the selective delivery of adequate dose to target with minimal irradiation of surrounding structures. The precision in target and normal tissue delineation needs to be achieved. So the aim of this study is to explore the possibility of using fused PET-CT images for accurate target and normal tissue delineation in 3D-conformal radiotherapy planning in patients of carcinoma lung (NSCLC) who are referred to us for radical radiotherapy.

Materials and Methods: It's a hospital based prospective study in which 14(n) cancer patients who had biopsy proven NSCLC and were referred to us for radical radiotherapy. After CT simulation and FDG-hybrid PET data sets were transferred to CMS planning system. The co-registration was done in Focal Pro using an auto fusion, 3D rotation and translation rigid body program, and the fiducial markers. The gross tumor volume (GTV), planning target volume (PTV) and normal tissue parameters were defined using the CT data and PET-CT data. 3D-CRT plans were generated for both CT data and PET-CT data sets and dosimetric analysis was done for same.

Results: The mean age was 65 yrs, 78.5% (11) patients are male and 21.5 % (3) are female. The registration of fused images of PET with planning CT scan decreased the gross tumor volume (GTV) in 10 patients (71.42%), decreased volume in 4 patients (28.58%). The 3D-CRT planes were modified in 5patients (35%). CT-PET planning did not reduce the radiation fields in all patients. When all constraints of the lung, esophagus, and spinal cord were taken into account, normal tissue exposure was reduced with use of CT-PET. V20 decreased from 31.86% ± 4.17% to 28.66% ± 4.23% ($p = 0.2676$) and MLD was 17.08 ±1.94 Gy to 15.53 ± 2.02 Gy ($p <= 0.06763$). MED decreased from 18.11 ± 2.5 Gy to 15.11 ± 3.9 Gy ($p =0.0085$)

Conclusion: Our findings extend the conclusion of observational studies in which FDG-PET has already been used to improve delineation of GTV and normal tissue parameters. The tumor volume and normal tissue irradiation parameters were significantly reduced. It showed 35% alteration in radiotherapy treatment plan. PET-CT should be incorporated.

Keywords: NSCLC, PET-CT, 3D-CRT, Normal tissue toxicity.

Introduction

Lung cancer is the most common cancer in the world and accounts for nearly 13% of all new cancer diagnoses in both sexes combined[1,2] and currently is the leading cause of cancer related deaths worldwide.[3] The lung cancer incidence in India is 2-14.6 per 1,00,000 in males and 0-3.7 per 1,00,000 in females.

Non small cell lung cancer (NSCLC), is the most common type of lung cancer. The treatment options for NSCLC depend on stage, extent of cancer and may consist of surgery, radiotherapy, chemotherapy and or biologic therapy. Definitive radiotherapy alone or chemo-radiotherapy is indicated for approximate 40% of patients presenting with newly diagnosed NSCLC. The radiotherapy is a localized form of treatment and can be delivered with advanced techniques such as Three Dimensional conformal Radiotherapy (3D-CRT), Intensity Modulated Radiotherapy (IMRT) with or without Gating, SRS/SRT etc, have a single objective to achieve therapeutic objective while sparing uninvolved structures. Thus a radio-therapeutic intervention must deliver a lethal dose to the target volume while maintaining subclinical dose to the surrounding healthy tissues.

Due to complex anatomical structure and its peculiar location in thoracic cavity especially due to proximity to some critical organs such as heart, esophagus, spinal cord etc. pose as a challenge for radiation dose delivery.

In Three Dimensional conformal Radiotherapy (3D-CRT), CT/MR images are reconstructed three dimensionally and beam is shaped with multileaf collimator thus, minimizing irradiation of the organ at risk. This technique promises high precision dose delivery to the target and better sparing of normal tissues of the organ at risk. It also predicts more accurately the toxicity of given course of radiation therapy

With the advent of three-dimensional conformal radiation therapy (3D-CRT), traditional portals target volumes, and beam arrangements have been questioned. 3D-CRT plan evaluation is more complex than 2D isodose curve evaluation. It is extremely important not to exceed the maximum doses tolerated by sensitive and

intrathoracic structures such as lung, oesophagus, spinal cord, and heart. Dose-volume histograms (DVHs) for all normal organs in the chest are evaluated for dose and volume of irradiation. DVH analysis still is been developed, but preliminary results indicate that it can predict the development of complications such as pneumonitis and lead to improved and more objective treatment planning.

Lung Toxicity: The lung is a parallel organ and lung injury from irradiation is related to both dose and volume effect. Toxicity to the respiratory system is a common side effect and result in significant morbidity. The toxicities are essentially preventable by avoiding irradiation to significant portion of the lung. Radiation induced lung injury was first recognized as a distant clinical entity by Grover, Christit and Merrit in 1923. Warren and Spencer in 1950 extensively described the pathological changes in the lung following radiation therapy.

Our knowledge of lung tolerance has expanded greatly through information obtained from 3DCRT. As a result, there are several parameters reported that are predictive of pneumonitis. The mean lung dose (MLD) is most simple parameter and is clinically useful. The volume of total lung receiving above a certain dose is reported as V20 (>20Gy) or V30 (>30Gy).[4,5]

Lung toxicity is a common side effect and result in significant morbidity. It is extremely important not to exceed the maximum doses tolerated by lung while dose escalation. With the advancement of 3D-CRT planning, DVH analysis several parameters were studied as predictor of pneumonitis. Munley[5] and Maguire in their respective studies showed, Mean Lung Dose (MLD) to be simple and clinically useful parameter where Graham et al concluded V20 is useful parameter.

Esophageal Toxicity: Esophageal toxicity is one of the principal complications occurring after radiotherapy for carcinoma of the lung. The incidence of esophageal toxicity has been reported to be > 5% to up to 100%, with a spectrum of injury ranging from acute self-limited reactions to late life-threatening complications.
The risk of esophageal toxicity must, at least in part, depend on the dose and volume irradiated. Many studies have attempted to relate the 3D dosimetric parameters to esophageal injury. MED, V45 parameters appear to be useful dosimetric predictors of radiation esophagitis.

Spinal Cord Toxicity: In spinal cord the most widely observed clinical dose limits are 45 Gy in 22–25 fractions of 1.8-2 Gy, and the tolerance dose (TD5) of 50 Gy often is recommended as the maximum level when cord segments of less than 10 cm are irradiated
Marcus and Million showed that, at 45 GY, the incidence of radiation myelitis is < 0.2 %. No volume effect is supported by current clinical data.[6]

Traditionally treatment planning for these patients has been based on CT scan alone. In many cases, CT scan provides excellent morphologic information but lack the ability to distinguish between benign and malignant disease or biological activity, also cannot rule out metastatic disease in normal size lymph node.

18 F-fluoro-deoxy-2-glucose (FDG), Positron Emission Tomography (PET) scan is a functional imaging technique that visualizes the distribution of a glucose analog in vivo. Many tumor cells have an increased rate of glycolysis, leading to a increased uptake of FDG and provides the biological nature of disease.

The combination of CT and PET scan imaging's has significantly improved the ability to accurately map the distribution of cancer within the chest and newest generation of radiotherapy planning computers has the ability to take full advantage of both study types in the treatment planning process. This is done by co-registering or fusing the images from different planning studies in the three dimensions on the same display. In this way anatomic information provided by CT scan and cancer biological information provided by PET studies are combined in the computer in the view of getting most accurate possible radiation treatment volume with better sparing of surrounding tissues.

So the aim of this study is to explore the possibility of using fused PET-CT images for accurate target and normal tissue delineation in 3D-conformal radiotherapy planning in patients of carcinoma lung (NSCLC) who are referred to us for radical radiotherapy.

Materials and Methods

After initial evaluation, all 14 patients of NSCLC who are referred to us for radical radiation therapy and fulfill other set criteria of patient selection included in this prospective study.

In all patients the simulation was done in supine position with neck rest, hands above the head, abducted and normal breathing. Same position is maintained throughout simulation, CT scan, PET scan procedure. The isocenter was chosen for each patient, lasers are marked so that it will help in proper patient positioning and external radio-opaque markers placed for future reference.

During acquisition of the CT images, patients were instructed to maintain steady, shallow breathing, Spiral CT was performed using a slice thickness of 3.3 mm and inter slice spacing of 3.3 mm throughout the volume containing the tumor and fiducial markers to encompass the entire thorax and upper abdomen. The voxel dimensions in this region were 0.9 mm x 0.9 mm x3 mm.

PET imaging was commenced after 1 hour of injection. Immediately before the PET imaging was begun, patients were asked to urinate and empty the bladder fully. Fiducial markers were secured to the same skin locations as used for CT. The patient was placed in treatment position, using the same neck rest and a flat Perspex top on the PET couch. FDG-hybrid

PET images were acquired in 64 gantry steps, 20 seconds/view with an energy window of 20% around 511 KeV.

Acquisition was performed with a matrix size of 128 X 128, as a 1hr 30mins single tomographic study. Transaxial slices were reconstructed using ordered-subsets, maximum likelihood iterative technique. A calculated attenuation correction and a three-dimensional (3D) post reconstruction, low-pass filter were applied to the data, which were then resliced into transaxial, coronal, and sagittal planes for visual assessment. Voxels were cubic, measuring 4.6 mm on each side. Transaxial data were sent via a DICOM protocol to the CT simulation workstation for image co-registration.

CT and FDG-hybrid PET data sets were co-registered with Focus (Computerized Medical Systems, Version 4.33.02) using an auto fusion, 3D rotation and translation rigid body program, and the fiducial markers. In all cases, the total conjugate deviation between matched points was less than 5 mm. Registration was confirmed by verifying that images of the markers were overlaid in the fused images. Additional visual confirmation of anatomic registration was sought in cases where the myocardium was FDG avid.

For all patients, the gross tumor volume (GTV), planning target volume (PTV) and normal structures such as oesophagus, lungs, spinal cord were defined using the CT data and PET-CT data. This was done in two separate sessions. For CT planning, the GTVct was the primary tumor on the lung window (width 1600, length -800) and lymph nodes ≥1 cm on mediastinal setting (width 400, length 40),

For CT-PET planning, the anatomic sites of the pathologic zones on the PET scan were delineated on the CT scan. This was done using a visual fusion technique (33). The localization of the abnormal lymph nodes on the PET images was correlated with the lymph node zones on the CT images.

If the PET scan was negative in the mediastinum and the CT scan was positive, the mediastinum was considered not to harbor cancer cells and was not included in the CT-PET GTV. The volumes of primary tumor and abnormal lymph node areas were assessed by CT only. When the lymph nodes were abnormal on PET but negative on CT, the corresponding anatomical location of particular lymphnode within the mediastinum was taken as the GTV, to avoid the problems of tumor size determination on PET.

The PTV was defined as the GTV with a 1-cm margin in all directions for both CT- and CT-PET–based treatment planning. No elective nodal RT was done. The body surface and lungs were contoured automatically by the treatment planning system. For the calculation, normal tissue parameters were defined.

After contouring, both data sets are transferred to CMS planning system (Computerized Medical System, XiO TPS, Version 4.33.02), a three-dimensional conformal treatment plan was done using the PTVct and PTVct-pet for all patients, both to deliver 60 Gy in 30 fractions to the PTV, according to the International Commission on Radiation Units and Measurements Report 50 guidelines.

Dosimetric values were calculated on the basis of dose–volume histograms and dose distributions on each axial CT plan for both CT- and CT-PET–base planning.

For the tumor and pathologic lymph nodes, we analyzed the GTV and PTV. For the lung, the V20 and MLD were analyzed as predictors of radiation pneumonitis.[27,46] For the esophagus, the volume of the esophagus receiving 45 Gy (V45), Dmax and mean esophageal dose were analyzed as predictors of early and late esophageal toxicity.[90,35] For spinal cord, the volume receiving 45 Gy (V45), maximum dose received (Dmax), mean dose received.

All patients were analyzed and results are expressed as the mean ± standard error of the mean. Statistical differences between paired parameters from CT vs. CT-PET plans were evaluated with the Wilcoxon signed rank test for statistical analysis. Differences were considered to be significant when the two-tailed p-value was <0.05.

Results

We analyzed 14 patients who are biopsy proven NSCLC and referred to us for radical radiotherapy. After studying the various aspects of the patients included in our series the following observations were made.

Table1: Patient demographics and clinical characteristics

Mean Age (years)	**Range (years)**
65.7	54-82
Sex	**Number of patients (%)**
Male	11(78.5)
Female	3(21.5)
Kornafsky score	
70-80	7(50)
80-90	5(35)
90-100	2(15)
Weight loss	
Yes	6(43)
No	8(57)
Personal habits of patient	
Smoking	10(71)
No smoking	4(29)
Alcohol	6(37.5)
Stage of cancer	
IIB	3(22)
IIIA	5(35)
IIIB	6(43)
Histopathology	

SCC	1(7)
Adenoca	6(43)
Adeno-squamus	1(7)
NSCLC (not specified)	6(43)
Location:	
RUL	
RLL	3(22)
LUL	2(15)
LMZ	1(7)
LLL	4(28)
Mediastinal LN	
Yes	12(85)
No	2(15)
History of	

Chemotherapy	
Received chemotherapy	11(78)
No chemotherapy	3(22)

Impact on Target Delineation: For all 14 patients, GTV was 123.91 cm^3 by CT and 93.67 cm^3 by PET ($p < 0.042$). We divided the patients on the basis of increase/decrease the GTV volume. In GTV increase group (10 patients) GTV was 135.34 cm^3 by CT and 88.37 cm^3 by PET ($P<0.0019$). (Table 2)

For all 14 patients, PTV was 316.51 cm^3 by CT and 255.60 cm^3 by PET ($p < 0.049$). In GTV increase group (10 patients) GTV was 343.73 cm^3 by CT and 239.51 cm^3 by PET ($P<0.0019$). (Table 2)

Table: 2 Target volume parameters

Target Volumes				
Patients no.	**CT**	**GTV (cc) CT- PET**	**CT**	**PTV (cc) CT-PET**
GTV decrease:				
1	29.67	22.05	129.07	96.07
2	35.43	21.6	149.62	110.89
3	354.38	295.97	808.38	718.26
4	234.85	44.3	506.48	169.62
5	39.67	21.72	117.73	75.9
8	139.6	103.3	319.66	240.96
9	149.12	116.11	376.08	298.12
12	37.22	26.78	211.79	114.21
13	290.9	202.93	659.63	446.25
14	42.57	28.97	158.85	124.81
MEAN	135.34	88.37	343.73	239.51
SD	120.56	94.15	242.72	203.58
SEM	38.12	29.77	76.75	64.38
P	p<= 0.0019		p<= 0.0019	
	W+ = 55, W- = 0, N = 10,		W+ = 55, W- = 0, N = 10,	
GTV increase:				
6	18.93	36.83	101.09	154.35
7	204.16	206.02	466.88	484.88
10	130.15	142	404.54	455.39
11	97.24	111.44	307.64	348.05
MEAN	112.62	124.0725	320.0375	360.6675
Total (14)				
MEAN	123.41	93.67	316.51	255.60
SD	99.32	80.11	205.87	181.39
SEM	28.71	23.23	57.83	51.47
P	p<= 0.04187		p<= 0.04944	
	W+ = 85, W- = 20, N = 14,		W+ = 84, W- = 21, N = 14,	

Table 3: Summary of FDG-PET impact on stage and target volumes.

1.	GTV volume decrease	10/14	71.42%
2.	GTV volume increase	4/14	28.58%
3.	3D-CRT plan change	5/14	35%

Lung

CT-PET information led to a significant decrease in all dosimetric factors analyzed (Table 4). For all 14 patients, the V20 decreased from 31.86% ± 4.17% when only CT data were used to 28.66% ± 4.23% with CT-PET ($p = 0.2676$). The MLD was 17.08 ±1.94 Gy

with CT and 15.53 ± 2.02 Gy with CT-PET (p <= 0.06763). (Table 4)

In GTV increase group (10 patients), the V20 decreased from 33.54% ± 4.52% when only CT data were used to 26.87% ± 3.67% with CT-PET (p <= 0.0039). The MLD was 17.71% ± 1.98 Gy with CT and 14.72 ± 1.79 Gy with CT-PET planning (p <= 0.0039).

Table 4: Lung parameters

		Lung Volumes		**V20%**		**MLD (Gy)**	
				(Lungs-PTV)		(Lungs-GTV)	
Patients	**Rt Lung V**	**Lt Lung V**	**Total V**	**CT**	**CT-PET**	**CT**	**CT-PET**
GTV decrease:							
1	1123.4	1033.02	2156.42	13.18	9.18	8.23	6.46
2	2605.26	2283.58	4888.84	39.08	28.14	17.73	13.73
3	1558.42	1784.6	3343.02	58.87	43.04	29.86	27.14
4	1637.54	1380.22	3017.76	25.41	22.46	16.17	13.64
5	1085.68	852.41	1938.09	22.38	17.97	13.43	13.9
8	1336.3	1097.22	2433.52	39.08	33.64	19.87	13.12
9	1488.72	1374.68	2863.4	48.38	41.79	24.09	19.62
12	1671.31	1703.02	3374.33	28.98	16.1	14.01	10.85
13	2569.22	2039.94	4609.16	41.58	36.71	20.88	17.54
14	1066.2	935.74	2001.94	18.46	19.65	12.84	11.17
MEAN				**33.54**	**26.87**	**17.71**	**14.72**
SD				14.30	11.59	6.25	5.65
SEM				4.52	3.67	1.98	1.79
P				**p <= 0.003906**		**p <= 0.003906**	
GTV decrease							
6	1096.58	1094.34	2190.92	17.82	23.83	10.44	13.89
7	766.44	813.17	1579.61	65.43	70.47	33.81	34.98
10	1106.61	1983.17	3089.78	29.11	34.93	19.84	21.82
11	1364.41	1304.99	2669.4	41.58	47.24	23.23	24.02
MEAN				**38.49**	**44.12**	**21.83**	**23.68**
Total							
MEAN				**31.86**	**28.66**	**17.08**	**15.53**
SD				16.50	16.42	8.18	8.19
SEM				4.17	4.23	1.94	2.02
P				**p<=0.2676**		**p<=0.0676**	

Esophagus: The $V_{esophagus}$ 45 decreased from 18.46% ± 4.48% to 14.38% ± 4.95% (p = 0.0644), and the Dmax decreased from 48.59 Gy ± 3.94Gy to 44.25 Gy ± 4.88 Gy (p = 0.0494). The mean esophageal dose decreased from 18.11 ± 2.5 Gy to 15.11 ± 3.9 Gy (p =0.0085). [Table: 5]

For GTV decreased group, the $V_{esophagus}$ 45 decreased from 15.51% ± 4.2% to 8.58% ± 3.44% (p = 0.0019) and the Dmax decreased from 52.20 Gy ± 4.96 Gy to 44.46 Gy ± 6 Gy (p = 0.0019). The mean esophageal dose decreased from 18.45 ± 2.3 Gy to 13.21 ± 2.24 Gy (p = 0.0019).

Spinal Cord: The $V_{spinal\ cord}$ 45 decreased from 6.33% ± 3.41% to 5.61% ± 3.28% (p = 0.0812), and the Dmax decreased from 31.36 Gy ± 4.14 Gy to 25.99 Gy ± 4.78 Gy (p = 0.0579). The mean spinal cord dose decreased from 15.22 ± 2.98 Gy to 12.51 ± 2.68 Gy (p =0.0579). [Table: 6]

For GTV decreased group, the V45 decreased from 4.38% ± 3.78% to 2.5% ± 2.48% (p = 0.25) and the Dmax decreased from 32.81Gy ± 4.28 Gy to 23.06 Gy ± 3.8 Gy (p = 0.0019). The mean spinal cord dose decreased from 14.94 ± 3.27 Gy to 10.55 ± 2.16 Gy (p = 0.0019).

Table 5: Esophagus parameters

Patients No.	Volume	V45 %		MED (Gy)		Dmax (Gy)	
	(cc)	CT	CT-PET	CT	CT-PET	CT	CT-PET
GTV decrease:							
1	57.2	0	0	9.51	7.42	29.51	16.82
2	32.37	30.6	24.7	25.3	21.58	63.18	60.79
3	31.13	31.23	23.39	28.07	23.4	63.84	61.72
4	24.16	0	0	10.22	7.48	39.64	27.47
5	25.69	3.82	1.33	14.53	9.9	57.11	56.68
8	34.01	25.43	21.38	24.72	17.49	61.31	60.96
9	31.97	24.25	13.46	22.95	19.63	65.85	63.83
12	40.85	24.85	0	19.27	6.8	67.05	38.52
13	37.9	14.95	1.54	21.94	15.03	50.06	41.41
14	21.26	0	0	7.95	3.36	24.41	16.41
MEAN		15.51	8.58	18.45	13.21	52.20	44.46
SD		13.31	10.87	7.34	7.09	15.70	18.99
SEM		4.2	3.44	2.3	2.24	4.96	6
P		p <= 0.001953		p <= 0.001953		p <= 0.001953	
GTV increase							
6	33.3	0	0	3.26	3.83	38.05	41.47
7	20.99	38.39	41.74	29.7	31.21	63.84	64.64
10	26.79	43.98	46.11	32.55	35.77	63.93	65.84
11	40.61	43.28	47.87	29.78	31.38	65.34	66.18
MEAN		31.41	33.93	23.82	25.55	57.79	59.53
Total (14)							
MEAN		18.46	14.38	18.11	15.11	48.59	44.25
SD		15.66	17.05	9.85	10.61	19.70	20.49
SEM		4.48	4.95	2.5	2.9	3.94	4.88
P		p <= 0.06445		p <= 0.008545		p <= 0.04944	

Table 6: Spinal cord parameters

Patients	Total Vol	V45 %		Dmax (Gy)		Mean Dose(Gy)	
	(cc)	CT	CT-PET	CT	CT-PET	CT	CT-PET
GTV decrease:							
1	13.69	0	0	22.98	21.78	7.02	6.56
2	15.4	5.6	0.15	45.71	43.97	12.68	7.38
3	11.91	38.04	24.85	44.25	30.45	31.14	21.1
4	22.4	0	0	37.76	24.17	12.91	9.91
5	10.18	0	0	11.77	9.86	34.42	22.42
8	12.31	0	0	38.3	25.67	14.87	11.32
9	11.77	0	0	40.12	37.93	16.98	13.36
12	13.97	0.12	0	47.62	12.43	7	2.67
13	20.17	0	0	28.18	17.33	10.08	8.41
14	8.84	0	0	11.37	7.01	2.3	2.33
MEAN		4.38	2.50	32.81	23.06	14.94	10.55
SD		11.96	7.85	13.52	12.02	10.35	6.84
SEM		3.78	2.48	4.28	3.8	3.27	2.16
P		p <= 0.25		p <= 0.001953		p <= 0.003906	
GTV increase:							
6	11.29	0	0	6.7	7.62	1.3	3.4
7	11.96	0	0	45.35	51.32	27.78	26.97

10	13.75	11.21	19.74	50.16	59.4	18.86	23.23
11	16.04	32.56	37.85	52.21	54.03	32.85	34.09
MEAN		10.94	14.40	38.61	43.09	20.20	21.92
Total14							
MEAN		6.33	5.61	31.36	25.99	15.22	12.51
SD		11.62	11.12	16.42	17.61	10.63	9.60
SEM		3.41	3.28	4.14	4.78	2.98	2.68
P		p <= 0.8125		p <= 0.05798		p <= 0.05798	

Conflict of Interest: nil

Discussion

The mean age of the study population was 65 years, whereas maximum and minimum ages of patients were 82 years and 54 years respectively. The male patients were slightly higher than female patients in the study (78.5% vs 21.5 %.

Published trials on the use of three-dimensional radiotherapy have demonstrated feasibility and reported promising results with limited toxicity. The University of Michigan was one of the pioneering institutions using three-dimensional radiotherapy. At that institution, Hazuka et al[7] have reported results of 88 consecutive patients with medically inoperable or locally advanced unresectable NSCLC treated with radiotherapy alone.

Bradley et al[8], reported on 207 patients with stage I-III inoperable bronchogenic carcinoma. The overall survival for the entire group at 1-and 2-years was 59% and 41%, respectively. A multivariate analysis revealed that most important prognostic factor was the volume of gross tumor. The tumor dose of 70 Gy or greater resulted in improved local control and cause-specific survival rates but overall survival was not improved.

In summery from above studies, Hazuka et al[7] emphasized on need for further dose escalation. Prospective radiation dose escalation studies such as Bradley et al,[8] have increased the total dose beyond 60 Gy using 3D-CRT and showed higher local control rates with dose escalation.

Impact of FDG-PET on radiation therapy volume delineation in NSCLC was published by Bradley et al,[9] 26 patients with Stages I–III NSCLC were studied. The FDG-PET findings altered the AJCC TNM stage in 8 of 26 (31%) patients; 2 patients were diagnosed with metastatic disease based on FDG-PET and received palliative radiation therapy. Of the 24 patients who were planned with 3DCRT, PET clearly altered the radiation therapy volume in 14 (58%), unsuspected nodal disease was detected by PET in 10 patients, Increases in the target volumes led to increases in the 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. He concluded that Radiation targeting with fused FDG-PET and CT images resulted in alterations in radiation therapy planning in over 50% of patients by comparison with CT targeting.

We planned the treatment for 14 patients using CT with and without FDG-PET information. The size of the primary tumor and lymph node areas were assessed by CT only and countered as GTV. The margins of 1 cm from the GTV to PTV were used. We omitted the elective nodal RT. In our series, one can see that differences in GTV exist for each plan comparison. (Table: 2) For all 14 patients, GTV was decreased from 123.91 cm^3 to 93.67 cm^3 ($p < 0.042$) and PTV was decreased from 316.51 cm^3 to 255.60 cm^3 ($p < 0.049$). Our findings can be compared with study by Van Der Wel et al.[10] where he reported a decrease in nodal GTV from 13.7 ± 3.8 cm^3 on the CT scan to 9.9 ± 4.0 cm^3 on the PET-CT scan (p=0.011).

Lung toxicity is a common side effect and result in significant morbidity. It is extremely important not to exceed the maximum doses tolerated by lung while dose escalation. With the advancement of 3D-CRT planning, DVH analysis several parameters were studied as predictor of pneumonitis. Munley[5] and Maguire in their respective studies showed, Mean Lung Dose (MLD) to be simple and clinically useful parameter where Graham et al concluded V20 is useful parameter.

Hirota et al,[11] from Japan treated 26 patients of NSCLC with 3D-CRT, 50-60 Gy concurrently with weekly administration of carboplatin and paclitaxel (40–45 mg/m2) were reviewed to establish dosimetric predictors of radiation esophagitis. The factors analyzed included the following: percentages of organ volumes receiving >40 Gy (V40), >45 Gy (V45), >50 Gy (V50), and >55 Gy (V55); the length of esophagus (*total circumference*) treated with >40 Gy (LETT40), >45 Gy (LETT45), >50 G (LETT50), and >55 Gy (LETT55); the maximum dose in the esophagus (Dmax); and the mean dose in the esophagus (Dmean). All factors except Dmax showed statistical correlation with radiation esophagitis. Good correlations were shown between radiation esophagitis and LETT45 ($p = 0.714$) and V45 ($p = 0.686$). He concluded the LETT45 and V45 appear to be useful dosimetric predictors of radiation esophagitis.

Marcus and Million showed that, at 45 GY, the incidence of radiation myelitis is < 0.2 %. No volume effect is supported by current clinical data.[6]

Van Der Wel et al[10] reported all dose–volume characteristics for the esophagus and lungs decreased in favor of PET-CT. The esophageal V45 (the volume of the esophagus receiving 45 Gy) decreased from 45.2% ± 4.9% to 34.0% ± 5.8% (p = 0.003), esophageal V55 (the volume of the esophagus receiving 55 Gy) from 30.6% ± 3.2% to 21.9% ± 3.8% (p= 0.004), mean esophageal dose from 29.8 ± 2.5 Gy to 23.7 ±3.1 Gy (p = 0.004), lung V20 (the volume of the lungs minus the PTV receiving 20 Gy) from 24.9% ± 2.3% to 22.3% ± 2.2% (p = 0.012), and mean lung dose from 14.7 ± 1.3 Gy to 13.6 ± 1.3 Gy (p = 0.004).

Considering all patients together in our study, incorporation of FDG-PET scan data in the RT planning reduced the radiation exposure of the lungs, esophagus and spinal cord significantly (Table: 4,5and 6). However, CT-PET planning did not reduce the radiation fields in all patients. In 10 patients, the radiation fields decreased with CT-PET planning, but in 4 patients, the fields increased. When all constraints of the lung, esophagus, and spinal cord were taken into account, normal tissue exposure was reduced with use of CT-PET. V20 decreased from 31.86% ± 4.17% to 28.66% ± 4.23% (p = 0.2676) and MLD was 17.08 ±1.94 Gy to 15.53 ± 2.02 Gy (p <= 0.06763). MED decreased from 18.11 ± 2.5 Gy to 15.11 ± 3.9 Gy (p =0.0085). Our findings were comparable with Van Der Wel et[10] al and Bradley et al.[9]

Our study therefore confirms the results of the literature. Using a dedicated PET scanner, our initial treatment plan was modified for 35% of patients. The main benefit of CT-PET fusion appears in the reduction of irradiated volume of surrounding critical structures including healthy lung parenchyma and a statistically significant reduction was observed. This marked reduction will allow an escalation of the total dose per target volume without increasing normal tissue toxicity.

Conclusion

In new era of conformal radiotherapy, 3D-CRT has been successfully used in various anatomical sites including lung and the dose escalation is possible to some level with acceptable normal tissue toxicity. Our findings extend the conclusion of observational studies in which FDG-PET has already been used to improve delineation of GTV and normal tissue parameters. The tumor volume and normal tissue irradiation parameters were significantly reduced. It showed 35% alteration in radiotherapy treatment plan. PET-CT should be incorporated in radiotherapy treatment planning whenever feasible.

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