

A Prospective Study Comparing Dosimetry between Computed Tomography (CT) based Radiation Planning and Positron Emission Computed Tomography (PET-CT) based Radiation Planning in Treatment of Non-Metastatic Non Small Cell Lung Carcinoma

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Abstract

Background: To evaluate dosimetry between CT based radiation planning and PET-CT based radiation planning. **Material & Methods:** Histologically proven 40 cases of locally advanced non-small cell carcinoma of lung were accrued for the prospective study. Contrast enhanced planning CT images and PET images were acquired. Target volume delineation, organs of interest & radiation planning were performed in Eclipse V 14.5 followed by dosimetric comparison among GTV, PTV and OARs. A p-value of <0.05 was considered significant. **Results:** The mean of GTV were 141.18 ± 119.76 cc in CT and 115.54 ± 91.02 cc in PET-CT based and the difference was statistically significant ($p=0.03$). The mean of CTV were 313.91 ± 180.87 cc in CT and 260.81 ± 148.83 cc in PET-CT based and the difference was statistically significant ($p=0.03$). The contralateral lung mean dose was statistically very significant ($p<0.01$) among both the 3D-CRT plans which were 8.49 Gy in CECT based planning and 9.53 Gy in PET CT based planning. The heart mean dose was also statistically significant ($p=0.03$) among the plans which were 17.90 Gy in CECT based planning and 17.06 Gy in PET CT based planning. Mann-Whitney U test showed the CT based PTV D90 was 58.20 Gy vs 57.58 Gy in PET CT based planning ($p=0.02$). PTV V95 were also comparable in both of the plans ($p=0.02$). **Conclusions:** GTV measured using PET-CT, may be greater or lesser than the CECT-based GTV. PET-CT-based contouring is more accurate for identifying tumour margins and new lymph node volumes.

Keywords: Dosimetry- PET-CT based radiation planning- Non-metastatic NSCLC

Asian Pac J Cancer Prev, 24 (7), 2543-2550

Introduction

Lung cancer has highest number (1,796,144) of mortality among all forms of cancers worldwide. As per GLOBOCON 2020 data (World, 2020), lung is the second most common (11.4%) malignancy worldwide in both sexes. In India, according to GLOBOCON 2020 data (India, 2020), lung cancer is 4th most common cancer (5.5%) with male predominance. The global incidence of lung cancer is increasing at a rate of 0.05% per year, thus becoming the leading cause of cancer mortality in most countries (The MPOWER package, warning about the dangers of tobacco. Geneva: WHO; 2011. WHO Report on The Global Tobacco Epidemic, 2011). As per internal audit, non-small cell lung cancer cases are about 8-9% of total cases and among them 90% are either inoperable or locally advanced in our institute. Lack of awareness

regarding chest symptoms is probably the foremost cause of such presentation in advanced stage. Improvement of loco-regional control can play a role in prolonging patient survival in inoperable locally advanced cases. Recent investigations have revealed the advantages of PET-CT in different clinical situations such as staging and treatment response assessment (Kubicek and Heron, 2011; Ung YC et al., 2011). CT imaging is now the only imaging method accepted for radiation treatment planning because attenuation characteristics of tissue for high-energy photons needed for precise dose calculation, could be only identified using CT data (Arriagada et al., 1991). 18F-fluoro-2-deoxy-D-Glucose (FDG) positron emission tomography (PET) is a useful tool in helping staging accuracy and treatment planning (Ung YC et al., 2011). FDG-PET is superior to computed tomography (CT) alone in the staging of lung cancer (Kubicek and

Heron, 2011; MacManus et al., 2001). The combined PET/CT information has been shown to have greater staging accuracy than PET imaging alone (De Wever et al., 2007). A combined PET-CT acquisition is now the standard method of acquiring FDG-PET images for baseline staging and radiotherapy treatment planning (RTP) who are being considered for radical intent treatment (De Wever et al., 2007; Ung YC et al., 2011). This study aimed to compare dosimetry between CT based radiation planning and PET-CT based radiation planning in patients with non-metastatic non-small cell lung carcinoma.

Materials and Methods

At the Department of Radiotherapy, MCH, histologically proven cases of carcinoma of lung were registered and accrued for the prospective study. Prior to starting treatment, radiologic assessment of gross tumour volume was done by CECT scan and PET-CT scan. CT Planning images were acquired on the Philips Brilliance 16 Slice CT Simulator with the patients in predetermined treatment position with aid of proper immobilisation and positioning devices using IV contrast injection iohexol/omnipaque according to body weight over 1-2 minutes (assessing blood for urea, creatinine report). PET-CT was also performed on the Siemens Biograph 6 PET-CT scanner (equipped with a 16 slice CT scanner, 24 detector ring PET scanner and a common custom flat table) in the identical CT simulation position for each patient. After completion of CT scan, delineation and planning were done using the CT images on Eclipse (version 14.5).

Target volume delineation

Target Volumes and Organs of Interest were made to the 1993 International Commission on Radiation Units & Measurements report (ICRU)-62 document for a complete description of the various target volume definitions (GTV, CTV and PTV). Right lung, left lung, composite lung, heart, esophagus, spinal cord, brachial plexus, liver volume was delineated based on the clinical scenario and tumor location ("Perez and Brady, Principles and Practice of Radiation Oncology, 7th edition 2019; 48:1083,"). The planning CECT and PET-CT images were transferred to Varian SOMAVISION virtual simulation software (True Beam SN3279). The two images were fused together by point matching (mainly on manubrium sterni, xiphisternum, bifurcation of trachea and splenic point) followed by auto matching and manual matching in few cases, if required. Two GTVs contours and two planning target volume (PTV) contours were outlined by the same radiation oncologist for each patient. CT-based delineation was done with standardized window settings (De Ruysscher et al., 2017), W= 1600 and L = - 600 for parenchyma and W= 400 and L = 20 for mediastinum. The first volumes were defined exclusively from the anatomic data provided by CT (GTV_CT) and the second volumes were defined from composite images based on CT and FDG data (GTV_PET). The GTV_CT consisted of the pulmonary gross tumor (GTV-P) and mediastinal nodes (GTV-N). The GTV-P included the primary tumor seen on CT. Similarly FDG based target volume definition

was created by visual GTV contouring by using a clinical protocol that integrated all relevant clinical information, the reports of the nuclear medicine physician and radiologist at standardized window setting (De Ruysscher et al., 2017). All sets of image were crosschecked by one Nuclear Medicine faculty in the same contouring station regarding image fusion and whether uptake is significant or not. No mathematical algorithm such as a fixed standard uptake value or the 40% threshold was used to delineate the GTV in the PET scan data set. Rather, we followed the suggestion made at the Lung Cancer Meeting in Barcelona (Mac Manus et al., 2006), that all the available information together with the best clinical judgment should be used to guide the delineation of the GTV in co-registered PET-CT scans. Auto contours may provide consistent contours, but was strictly avoided in our study due to factors other than tumor activity such as patient biological factors and technical factors (Konert et al., 2015). The CTV (both PET-CT & CECT based) were incorporated the GTV and a volumetric margin of 7 mm to account for microscopic tumor extension. Internal target volume (ITV) were incorporated around CTV with 7 mm radical margin and 10 mm cranio-caudal margin and planning target volume (PTV) was contoured with a margin of 5 mm around ITV (Kataria et al., 2014). In patients with huge atelectatic lung adjacent to the GTV-P, only the areas with increased FDG uptake were considered part of the GTV-P. The GTV-N of GTV_CT included only those lymph nodes considered to be involved. Lymph nodes were considered to be involved when they demonstrated increased FDG uptake or had a short axis ≥ 10 mm in diameter on CT.

The dose was prescribed to the ICRU reference point with lung inhomogeneity corrections. The plans were optimized to maximize the dose to the PTV while limiting the dose to normal tissue. The PTV was intended to receive $\geq 95\%$ and $\leq 107\%$ of the prescribed dose. Radical RT planned with 60 Gy over 30 fractions by 3D-CRT with field in field technique, with the dose-limiting constraints of the organs at risk. The cumulative dose-volume histogram was calculated separately for the GTV and organs at risk, such as the heart, spinal cord, and healthy lung parenchyma. A beam's-eye-view display was used to ensure optimal target volume coverage and normal tissue sparing with color wash. Two separate planning were generated for each patient, which was cross-checked by expert faculty of our department and modified accordingly by the same physicist faculty. Identical beam profiles were used in both the plans with few modifications where it was absolutely needed and finally plans were approved for dosimetric analysis. From each patient GTV, CTV, PTV volumes were calculated. From both PTV & GTV D_{90} , D_{95} , D_{100} , V_{90} , V_{95} were calculated separately. Dmean, Dmax and volumes receiving 30 Gy for heart were collected. Opposite lung V20, Mean lung dose and V20 were calculated. Dmean and V35 for esophagus and Dmax for spinal cord were assessed. All collected and properly tabulated data were analysed with the help of IBM standard statistical software SPSS version 23. Descriptive statistics were analysed by simple statistical test. Then Box-whisker plot was made to assess the pattern of distribution of data set using gender and tumor site

as constant. As the data set was skewed in nature, non-parametric test was done for calculating the association. Both Pearson chi-squared test and Mann-Whitney U test were done for comparing the means.

Results

The baseline demographic and clinical characteristics were tabulated in Tables 1 and 2. Mean age was 57.72 ± 7.67 years (median- 60.50) and among them 32 (80%) were above 50 years of age; 31(77.5%) patients were smoker. The mean tumor size was 5.66 ± 1.91 cm (median- 5.18 cm) and 24 (60%) patients were adenocarcinoma variant of NSCLC. After PET CT scan, tumor size downgraded in 11 (27.5%) patients, where 14 (35%) patients became upgraded in nodal stage. Overall AJCC 8th stage grouping became upstaged in 6 (15%) patients and only 2 (5%) became downstaged. Mean PET SUV_{max} was 13.16 ± 3.90 . After Contouring in two sets of images, Gross tumor volume separately changed in 36 (90%) patients. Among them primary tumor decreased in half of the cases and lymph node increased in 9 (22.5%)

Table 1. Demographic Characteristics of Study Population (n=40)

| Variable | Number of Patients (n=40) | Percentage |
|-------------------------|--------------------------------------|------------|
| Age (Years) | Mean- 57.72, Median- 60.50, SD- 7.67 | |
| ≤50 years | 8 | 20 % |
| >50 years | 32 | 80% |
| Gender | | |
| Male | 28 | 70.00% |
| Female | 12 | 30.00% |
| Addiction Status | | |
| Smoker | 31 | 77.50% |
| Non-smoker | 9 | 22.50% |
| Affected side | | |
| Right | 16 | 40.00% |
| Left | 24 | 60.00% |
| ECOG-Performance Status | | |
| PS-0 | 33 | 82.50% |
| PS-1 | 7 | 17.50% |

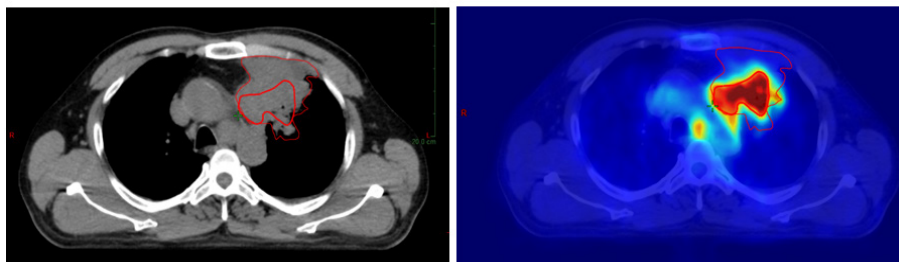


Figure 1. Planning CECT, PET-CT & Fusion Image Shows Gross Tumor Volume

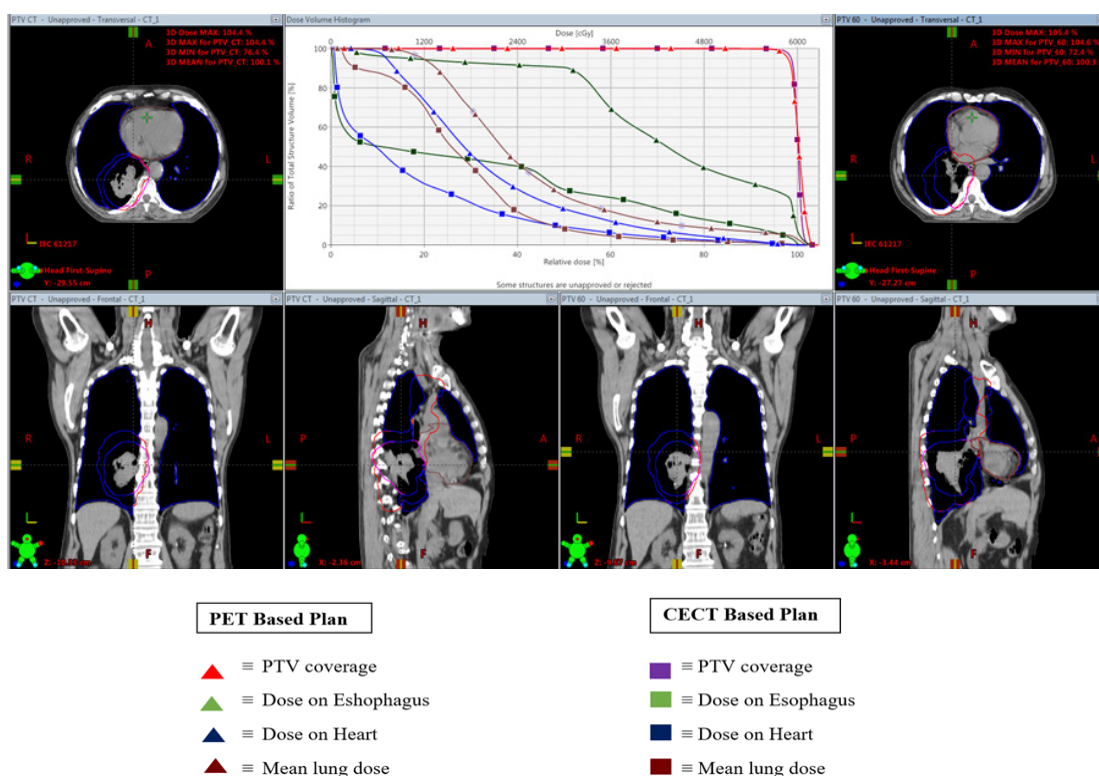


Figure 2. DVH of Esophagus & Heart and Contouring of Tumor at Different Sections

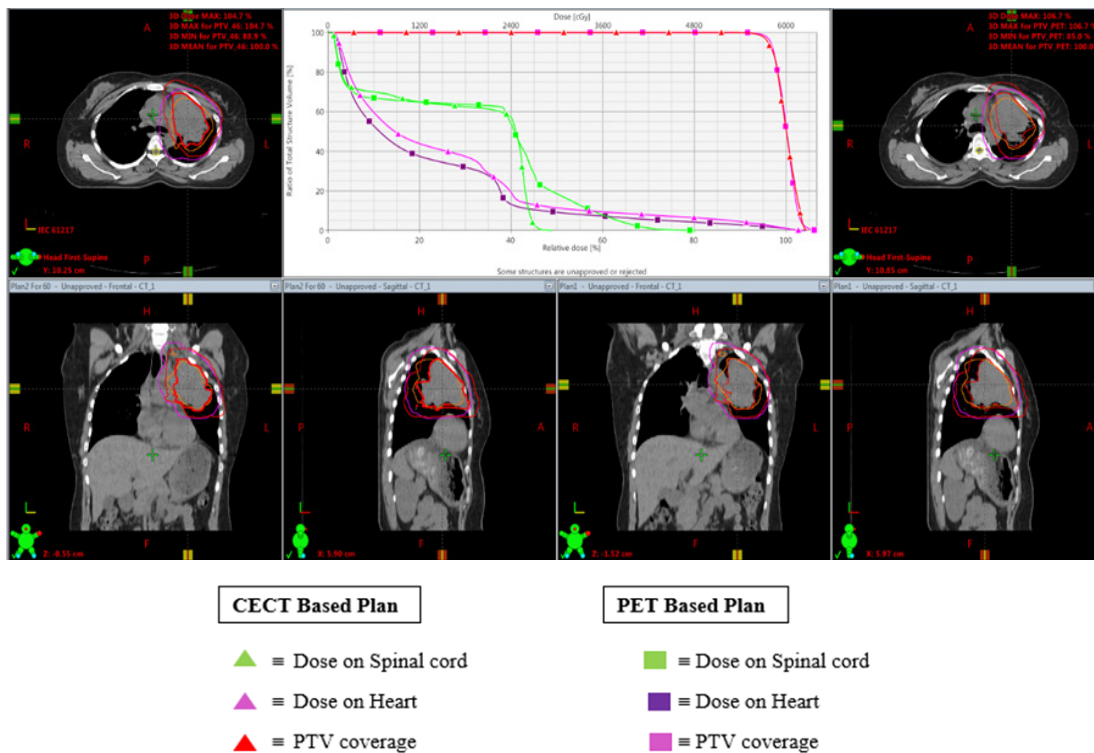


Figure 3. DVH of Heart & Spinal Cord and Contouring of Tumor at Different Sections

Table 2: Tumor Characteristics of Study Population (n=40)

| Variable | Number of Patients (n=40) | Percentage (Median) |
|------------------------------|---------------------------------------|---------------------|
| Tumor size (mm) | Mean- 56.65, Median- 51.85, SD- 19.07 | |
| Tumor Site | | |
| Upper Lobe | 19 | 47.50% |
| Middle / Lower Lobe | 21 | 52.50% |
| Histologic subtype | | |
| Squamous Cell CA | 13 | 32.50% |
| Adenocarcinoma | 24 | 60% |
| NSCLC-NOS | 3 | 7.50% |
| T Stage | | |
| T1c | 4 | 10% |
| T2a | 3 | 7.50% |
| T2b | 13 | 32.50% |
| T3 | 10 | 25% |
| T4 | 10 | 25% |
| Nodal (N) Stage | | |
| N0 | 4 | 10% |
| N1 | 6 | 15% |
| N2 | 24 | 60% |
| N3 | 6 | 15% |
| Tumor Stage Group (AJCC 8th) | | |
| IIA | 4 | 10% |
| IIB | 6 | 15% |
| IIIA | 7 | 17.50% |
| IIIB | 20 | 50% |
| IIIC | 3 | 7.50% |

patients. Only 4 (10%) patients had minimal gross tumor volume change or similar type of contouring. 3 out of 4 (7.5%) patients had decreased the volume. Cause of GTV volume decrease was atelectasis around lung tumor and GTV volume increase were additional tumor detected ± new node identified. The volume receiving 90% of the dose (D_{90}) is statistically significant ($p=0.02$) in PET CT based planning. Percentage of volume receiving $\geq 95\%$ of prescribed dose (V_{95}) were also comparable in both of the plans and statistically significant ($p=0.02$). Dose that covers 95% (D_{95}) of the PTV is also comparable ($p=0.06$). The volumetric mean of the gross tumor of both the plans were statistically significant ($p=0.03$) where

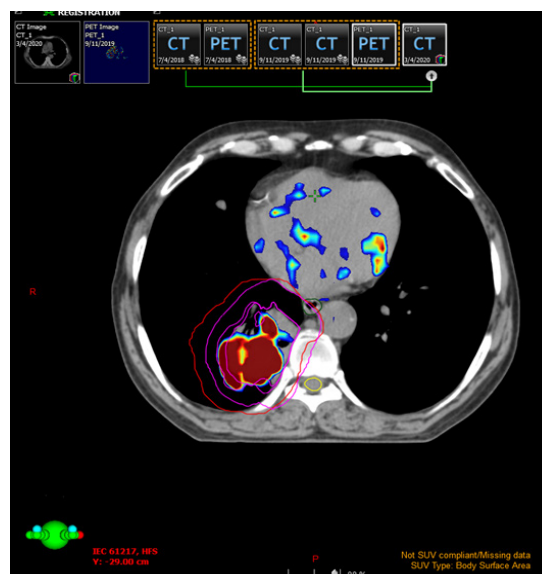


Figure 4. PET-CT Shows FDG Avid Lung Tumor

Table 3. Tumor Specific Dosimetric Analysis of Gross Tumor Volume (GTV)

| Parameters | CT Based Mean ± SD | PET Based Mean ± SD | p Value |
|-----------------------|-----------------------|------------------------|---------|
| Volume (cc) | 141.18 ± 119.76 | 115.54 ± 91.02 | 0.03 |
| D ₉₀ (Gy) | 58.96 ± 0.54 | 58.89 ± 0.68 | 0.53 |
| D ₉₅ (Gy) | 58.61 ± 0.59 | 58.60 ± 0.72 | 0.16 |
| D ₁₀₀ (Gy) | 56.65 ± 2.31 | 55.77 ± 5.25 | 0.06 |
| V ₉₀ (%) | 99.90 ± 0.35 | 99.24 ± 1.69 | 0.41 |
| V ₉₅ (%) | 99.51 ± 1.19 | 99.47 ± 1.19 | 0.81 |

planning CECT based mean was 141.18 cc and PET based mean was 115.54 cc. Dose that covers 100% (D₁₀₀) of the GTV is also comparable (p=0.06). Tumor Specific gross tumor volume analysis was tabulated in Table 3. The contralateral mean lung dose was statistically very significant (p<0.01) among both the plans which were 8.49 Gy in planning CECT based planning and 9.53 Gy in PET CT based planning. The heart mean dose was also statistically significant (p=0.03) among the plans which were 17.90 Gy in planning CECT based planning and 17.06 Gy in PET CT based planning. Volumetric analysis of organ at risks was tabulated in Table 4. The mean of clinical target volume were 313.91 cc in CT based where 260.81 in PET CT based, which was also statistically significant (p=0.03). The CT based PTV D₉₀ (Dose that covers 90% of the PTV) was 58.20 Gy where 57.58 Gy in PET CT based, which was statistically significant (p=0.02). Percentage of volume of PTV receiving ≥95% of prescribed dose (V₉₅) were also comparable in both of the plans and statistically significant (p=0.02). Dose that covers 95% of the PTV (D₉₅) were also comparable significantly but not statistically significant (p=0.06). The comparison of means of PTV & OARs for both the plans was summarized in Tables 4 and 5.

Discussion

Control of local tumour burden is the single most important factor to ensure long-term disease-free survival and increase overall survival rate in NSCLC. To improve the local control, adequate tumour coverage with correct tumour margin contouring, adequate tumour coverage with proper radiation planning technique and precise radiation delivery with motion management are required. Due to unavailability of 4D CT scan, precise radiation was delivered by incorporating an internal target volume, in accordance with published literature (Kataria et al.,

Table 4. Organ at Risk (OAR) Specific Dosimetric Interpretation

| Parameters | CT Based Mean ± SD | PET Based Mean ± SD | p Value |
|-------------------------------|-----------------------|------------------------|---------|
| Mean Lung Dose (Gy) | 15.98 ± 4.82 | 15.57 ± 4.26 | 0.38 |
| Lung V ₂₀ (%) | 32.80 ± 16.46 | 29.63 ± 9.50 | 0.55 |
| C/L Lung Mean (Gy) | 8.49 ± 2.96 | 9.53 ± 3.13 | <0.01 |
| Heart Mean (Gy) | 17.90 ± 5.51 | 17.06 ± 8.17 | 0.03 |
| Heart V ₃₀ (%) | 21.92 ± 11.07 | 18.71 ± 11.14 | 0.26 |
| Esophagus Mean (Gy) | 20.56 ± 8.64 | 22.14 ± 10.77 | 0.15 |
| Esophagus V ₃₅ (%) | 27.31 ± 15.64 | 30.93 ± 21.75 | 0.55 |
| Spinal cord Dmax (Gy) | 38.51 ± 8.97 | 37.61 ± 12.72 | 0.09 |

2014). GTV delineation needs to be accurate (Figure 1) in 3D-CRT planning otherwise local recurrence or increased normal organ doses may occur, due to underestimated or overestimated contours respectively. Addition of functional imaging like 18F-FDG PET-CT helps in accurate target volume delineation (TVD) based on uptakes. Dose escalation can be attempted sparing the OAR only if the target volume is accurate and relatively small. A meta-analysis by Tolozaet al., (2003) reports the sensitivity and specificity for mediastinal staging to be 84% and 89% respectively for FDG-PET and 57% and 84%, respectively, for CT. In a recent prospective study, it was reported that 30% of patients with locally advanced NSCLC became ineligible for curative radiotherapy because of detection of either distant metastatic disease or intrathoracic disease too extensive for radical radiation (Mac Manus et al., 2001).

The integration of PET and CT scans allows the simultaneous use of biologic and anatomic imaging data. Lardinois et al., 2003 reported the added benefit of integrating PET/CT compared to either PET or CT separately or to visual correlation in 49 patients. Integrated PET-CT provided additional information in 41% of cases, beyond that provided by conventional visual correlation of PET and CT. CT scan based radiation treatment planning may overestimate or underestimate the targeted treatment volumes, because of the inability to differentiate between neoplastic and benign tissues. In some anatomic sites, e.g prostate, contouring CTV is a relatively uncomplicated task compared to a lung cancer site, where confounding radiologic uncertainties such as small lymph nodes of questionable significance, areas of atelectasis, and operative scarring surround CT scan images, resulting in varying degrees of uncertainty in delineating the target

Table 5. Tumor Specific Dosimetric Analysis of Planning Target Volume (PTV)

| Parameters | CT Based Mean | PET Based Mean | Pearson Chi-Square test p Value | Mann-Whitney U Test p Value |
|---------------------------|-----------------|-----------------|---------------------------------|-----------------------------|
| PTV Volume (cc) | 621.13 ± 395.94 | 558.41 ± 222.48 | 0.12 | 0.12 |
| PTV D ₉₀ (Gy) | 58.20 ± 0.94 | 57.58 ± 2.25 | 0.02 | 0.02 |
| PTV D ₉₅ (Gy) | 57.47 ± 0.98 | 56.39 ± 4.30 | 0.06 | 0.06 |
| PTV D ₁₀₀ (Gy) | 53.25 ± 2.21 | 51.73 ± 7.53 | 0.55 | 0.55 |
| PTV V ₉₀ (%) | 99.58 ± 0.63 | 98.48 ± 3.29 | 0.90 | 0.9 |
| PTV V ₉₅ (%) | 95.72 ± 4.18 | 95.07 ± 6.01 | 0.02 | 0.02 |

volumes leading to a final PTV. To resolve the issue, PET scan was employed by some (Choi NC et al., 2000) to contour biologic target volume to refine the final treatment volume. Initial studies incorporating PET into treatment planning have been reported (Kiffer et al., 1998). Some have arbitrarily advocated the FDG-avid volume as the region encompassed by the 50% intensity level relative to the tumor maximum intensity (Arriagada et al., 1991; Le Chevalier et al., 1994), whereas Bradley et al., (2004) and TMH data (Tibdewal et al., 2021) employed the 40% intensity level. Paulino and Johnstone (2004) suggested in an editorial autocontouring all areas with a standardized uptake value (SUV) of 2.5. The debate has become even more compelling in the era of image-guided radiation therapy.

It is difficult to correctly differentiate the margins between the incompletely expanded lung parenchyma (e.g. atelectasis, obstructive pneumonia) and tumour by using conventional CT scan in NSCLC patients. So, CT based planning may lead to incorrect target delineation thus insufficient dose coverage of the target volume or may cause more damage to surrounding normal tissue. As per the Radiation Therapy Oncology Group guidelines, only involved nodes are to be treated (Bradley et al., 2012). On the other hand, 18F-FDG PET-CT scan correctly distinguishes between the atelectasis and lung cancer, leading to adequate radiation dose delivery to precise target volume. Thus, it helps to control local tumour burden effectively sparing surrounding normal tissues from inadvertent radiation injury (Abramyuk et al., 2009). Our findings showed that for 40 NSCLC patients with criteria of $V_{95\%} > 95\%$ and $D_{95\%} > 95\%$, CT-based plan of about 80% of them, did not cover the treatment volume defined by scan based. We found that Gross tumor volume separately changed in 36 (90%) patients. Among them primary tumor decreased in half of the cases and lymph node increased in 9 (22.5%) patients. Gross tumor volume reduced because of atelectasis around lung tumor and GTV was increased because of additional tumor detected \pm new node identified (Figure 4). The PTV D_{90} (dose that covers 90% of the PTV) ($p=0.02$), PTV V_{95} (percentage of volume of PTV receiving $\geq 95\%$ of prescribed dose) ($p=0.02$), the contralateral mean lung dose ($p<0.01$), heart mean dose ($p=0.03$) were statistically significant (Table 5). We preferred Mann-Whitney U results as the final interpretation owing to its higher power. During planning we noticed how spinal cord was critically saved when the PET based planning were done in centrally located lung tumor with appropriate beam arrangement (Figure 3). In another few patients in left lung tumor heart dose was also reduced with PET CT based planning (Figure 2). We also observed the contralateral lung dose increased where mediastinal lymph node was positive and decreased in CT based planning. Our study showed that dose of heart and opposite lung and esophagus can be critically managed with proper tumor control. The 18F-FDG can accurately identify tumour boundaries by differentiating the tumour from incompletely expanded lung tissue e.g. atelectasis; thus the GTV of primary tumour volume is decreased on the 18F-FDG PET-CT-based contouring. Although the GTV of primary tumour

on 18F-FDG PET-CT can be increased because of the inability to identify tumour boundaries near the chest wall and mediastinum. Also, GTV Lymph node can be increased because the mediastinal node more than 1 cm on cross-section was considered involved and included in the GTV lymph node. Due to high negative predictive value of the 18F-FDG PET-CT, accurate identification of the uninvolved nodes is possible hence GTV lymph node is decreased and elective lymph node irradiation can be avoided.

Bradley et al., 2012 have studied that the GTV lymph node was changed in 50% patients (total patients-34) on 18F-FDG PET-CT contouring. So, the treatment of the involved fields are treated and risk of elective nodal failure becomes low. Another study have found change of treatment volume in 62% patients (45 out of 73) using 18F-FDG PET-CT (Vanuytsel et al., 2000). Deniaud-Alexandre et al., (2005) have shown a change of GTV in 50% patients with an increase and a decrease in 26% and 23% of them, respectively in 18F-FDG PET-CT based RT planning (total 92 patients). Hicks et al., (2001) have documented GTV changes in 25% patients in their study of 153 patients. In our study of 18 patients, 88.8% patients have shown GTV change of primary tumour volume and 89% patients have shown GTV change of lymph node on 18F-FDG PET-CT. This higher than expected percentage of GTV change may be attributed to small sample size. The reduction in GTV lymph node using PET-CT was statistically significant. In our study, when same RT plan of CECT was applied on the 18F-FDG PET-CT, dose coverage was found to be suboptimal in 50% patients necessitating replanning. On the other hand, Nestle et al., (1999) have shown a change of plan in 35% patients to avoid suboptimal dosing. Kiffer et al., (1998) and Vanuytsel et al., (2000) needed replanning in 26.7% and 62% patients, respectively, for optimum coverage. Our study has shown replanning in 50% (nine) patients which is similar to other studies. The oesophagus, heart, and spinal cord mean doses are expected to increase with identification of new mediastinal lymph nodes. Similarly, normal organ doses are expected to decrease if the tumour volume decreases. The contralateral lung mean dose was statistically very significant ($p<0.01$) among both the planning CECT based planning and PET CT based planning. The heart mean dose was also statistically significant ($p=0.03$) in our study. Parameters like MLD were decreased on 18F-FDG PET-CT-based RT planning as shown by Bradley et al., 2012. On the other hand, parameters of OAR doses like MHD was increased whereas lung V20, MLD, and MED were decreased as shown by Vanderwel et al., (2000)'s study. Yin et al., (2013) have documented that OAR doses' parameters e.g. including MED, MHD, and V30 were increased in patients with increased GTV node whereas MLD, V20, and the maximum spinal cord dose were decreased on 18F-FDG PET-CT-based RT planning. Deniaud-Alexandre et al., (2005) have shown decreased MSD where the remaining OAR doses was dependent on the volume change in PET-CT based planning. Additionally, OAR dose reduction also resulted in reduction of primary tumor GTV. OAR dose changes corresponded to change of GTV of lymph

node as explained already. The clinical implications of the statistically significant dosimetric advantages have been translated into clinical gain or not will be analysed over two year follow up as the magnitude of the dose difference is low.

Though sample size of our study was 40 patients with a skewed distribution, it was a prospective single intuitional study, where every imaging including PET CT and Planning CECT scan were done in presence of resident doctor. Contouring were done by single resident and cross-checked by senior experienced faculty of the institution. Single physicist planned each patient in both sets of images to reduce interpersonal observational bias; it increases strength of the study. All patients were planned by 3D-CRT; no IMRT/VMAT was done. Having this said, we exclude IMRT cases to maintain uniformity across the study plans and few literature has also shown the non-inferiority of 3D CRT over IMRT in lung cancer treatment planning (Hu et al., 2016).

In conclusion, GTV, measured using PET-CT, may be greater or lesser than the CECT-based GTV. PET-CT-based contouring is more accurate for identifying tumour margins and new lymph node volumes. Non-18F-FDG avid nodes detected on the PET-CT can be omitted to avoid elective nodal irradiation to spare adjacent OAR. Although, PET-CT integration in daily clinical practice is quite challenging. There are many unfulfilled gaps in technical, administrative and financial aspects. Continuous efforts are being made to utilize the full potential of this exciting technology using standardized guidelines. Our study finding complies with the published literature. Small sample size and dosimetric nature of this study, however, are the main drawbacks. More and more randomised trials with bigger sample size involving multiple centres with multiple techniques (IMRT, VMAT) are the need of the hour to form a standard consensus guideline for using PET-CT in routine practice.

Author Contribution Statement

Concepts: Mandal Bidyut, Basu Abhishek, Manna Amitabha; Design: Mandal Bidyut, Basu Abhishek, Manna Amitabha, Mondal Janmenjoy Chakraborty Ipsita, Addway Chakraborty. Definition of intellectual content: Mandal Bidyut, Manna Amitabha, Mondal Janmenjoy, Ghosh Debjit, Chakraborty Ipsita. Literature search: Basu Abhishek, Manna Amitabha, Mondal Janmenjoy, Ghosh Debjit. Clinical studies: Mandal Bidyut, Basu Abhishek, Manna Amitabha, Mondal Janmenjoy, Ghosh Debjit, Chakraborty Ipsita, Addway Chakraborty. Experimental studies: Mandal Bidyut, Basu Abhishek, Manna Amitabha, Mondal Janmenjoy, Ghosh Debjit, Chakraborty Ipsita, Addway Chakraborty. Data acquisition: Mandal Bidyut, Basu Abhishek, Mondal Janmenjoy, Chakraborty Ipsita, Addway Chakrabort. Data analysis: Basu Abhishek, Manna Amitabha, Mondal Janmenjoy. Statistical analysis: Mandal Bidyut, Mondal Janmenjoy, Ghosh Debjit, Chakraborty Ipsita, Basu Abhishek. Manuscript preparation: Mandal Bidyut, Basu Abhishek, Manna Amitabha, Mondal Janmenjoy. Manuscript editing: Basu Abhishek, Mondal Janmenjoy,

Ghosh Debjit, Chakraborty Ipsita, Addway Chakraborty. Manuscript review: Mandal Bidyut, Basu Abhishek, Manna Amitabha. Guarantor: Basu Abhishek, Mondal Janmenjoy, Ghosh Debjit, Chakraborty Ipsita, Addway Chakraborty.

Acknowledgements

We acknowledge the utmost co-operation from our patients & hard work of the Physicist & Nuclear Medicine team and fellow colleagues.

Ethical Clearance

Approved by Institutional Ethics Committee (Reg. No.- ECR/287/Inst/ WB/2013) Medical College, Kolkata, 88, College Street, Kolkata 700073, West Bengal, India, Ref. No.- MC/KOL/IEC/NON-SPON/222/01-2019, dated 05/01/2019

Presentation at a meeting

Presented at 10th Annual Conference of Indian Society for Study of Lung Cancer (NALCCON 2020) and awarded Best E-poster presentation; Organisation – ISSLC (Indian Society for Study of Lung Cancer). Place – Max Institute of Cancer Care, New Delhi, India. Date – 26.09.2020 – 27.09.2020

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