10.21761/jms.v9i01.01

RESEARCH ARTICLE

Radiotherapy Planning of Carcinoma Esophagus - Role of PET Fusion with CT Scan

Brijesh Bhagwan Maheshwari[1], Arvind Kumar Chauhan[2] , Piyush Kumar[2*], Jitendra Nigam[3], Silambarasan NS[4], Navitha S[4], Pavan Kumar[2], Ayush Garg[3]

ABSTRACT

Introduction: Oesophageal cancers are treated with a multimodality approach. The concept of organ preservation has led to concurrent chemoradiation becoming the standard of care in cervical as well as mid-thoracic oesophageal tumors. Radiotherapy can be delivered by various conventionall and with conformal techniques. Defining target volumes adequately is important in radiotherapy planning and delivery of treatment as esophageal and gastroesophageal cancers have a high propensity of loco-regional recurrence. The present study aims to evaluate and compare the dosimetry parameters in patients with cancer esophagus planned on CT-based contours and PET-CT fusion-based contours by conformal technique.

Material and Methods: In 50 biopsy-proven cases of cancer esophagus and gastroesophageal junction were selected in our institute between February 2021 to July 2022. After immobilization, spiral CT for simulation was performed. Thereafter, PET was performed in the same treatment position as in CT imaging protocol. The (DICOM) images were transferred to the eclipse treatment planning system (TPS) and registered. Gross tumor volume was contoured on CT and PET-CT scans, followed by CTV contouring. Volumetric margin given depending on the institutional protocol to account for microscopic tumor extension and mean motion of the lesion to generate planning target volume (PTV). Two PTV volumes were finally contoured that is PTV - PTV-CT and PTV - PET-CT. The organs at risks (bilateral lungs, heart, spinal cord) were generated in accordance with the radiation therapy oncology group (RTOG) protocol and dose constraints given as per QUANTEC. The dose prescribed to PTV-CT and PTV-PETCT in the range of 45 to 59.4Gy, depending upon the site in 25 to 33 fractions.

Two plans (groups 1 and 2) were generated for comparison and were optimized to maximize the dose to the PTV and limit the dose to normal tissue. PTV dosimetric parameters evaluated were V95, D2, D50, D95, D98, Dmax, Dmean, conformity index and homogeneity index. Dosimetric parameters evaluated for OARs were both lungs combined (D-mean, D-max, V-5, and V-20), heart (D-mean, D-max, and V-40) and spinal cord (D-max). Statistical analysis was done using paired T-test. A comparison of mean value of dosimetric parameters and *p-value* was done.

Results: The mean age is 61 years, with male to female ratio 0.7:1. The most common subsite is the mid-thoracic esophagus (46%). Histopathology seen was squamous cell carcinoma (88%) and adenocarcinoma (12%) with a majority having moderately differentiated grade (80%). Median standardized uptake value is 14.9 and the mean is 14.8 (range 0–37.4). The variation of gross tumor size and gross tumor volume on PET-CT scan as compared to CT scan ranged from -1.7 cm (-44.7%) to 2.7 cm (55.1%) and from -11.9 cm^3 (-28.6%) to 13.2 cm^3 (36.8%) which was not statistically significant (p = 0.38 and p = 0.41, respectively). There was a difference of 18% in the detection of nodes by PET CT scan as compared to CT scan which was statistically significant (p = 0.0001). Increased PTV was seen in 26% of patients (p=0.0001). No difference in dosimetric parameters of PTV was found in terms of V9, D2, D50, D95, D98, Dmax, and Dmean. Similarly, no statistical difference was found in the CI and HI of both plans. Dosimetric parameters of both lungs show statistically significant differences in D mean (14.73 *vs* 16.13 Gy; p = 0.0005) and V5 (89.16 *vs*. 28.4 Gy; p = 0.0056). Dosimetric parameters in the heart did not show a statistically significant difference. Dmax for the spinal cord in both groups was within dose constraints (38.7 *vs* 39.1 Gy) with no statistically significant difference (p = 0.22).

Conclusion: Delineation of primary gross tumor is better with PET fusion than as compared to CT alone. Further, PET-CT scans detect more lymph nodes than CT alone. Therefore, by incorporating PET–CT scans in radiotherapy planning of carcinoma esophagus, more accurate and precise treatment planning can be done, which will lead to fewer chances of geographical miss and less chances of loco-regional failure.

Keywords: Cancer Oesophagus, Radiotherapy, PET-CT SCAN.

How to cite this article: Maheshwari BB, Chauhan AK, Kumar P, Nigam J, Silambarasan NS, Navitha S, Kumar P, Garg A. Radiotherapy Planning of Carcinoma Esophagus - Role of PET Fusion with CT Scan. SRMS J Med Sci. 2024;9(1):1-8.

Source of support: Nil

Conflict of interest: None

Submission: 02-01-2024; **Acceptance:** 03-02-2024; **Published:** 30-06-2024

[1]Senior resident, [2]Professor, [3]Associate Professor, [4]Assistant Professor

Department of Radiation Oncology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India.

Corresponding Author: Piyush Kumar, Professor, Department of Radiation Oncology, Shri Ram Murti Smarak Institute Of Medical Sciences, Bareilly, Uttar Pradesh, India, e-mail: piykumagr@gmail.com

INTRODUCTION

Oesophageal cancers are treated with a multimodality approach, which may comprise surgery, radiotherapy and chemotherapy depending upon the stage and site. With the introduction of the concept of organ preservation, concurrent chemoradiation has become the standard of care in cervical as well as mid-thoracic oesophageal tumors.

Radiotherapy can be delivered by various techniques like conventional and conformal techniques like 3-dimensional conformal radiotherapy (3D-CRT), intensity modulated radiotherapy (IMRT), or volume modulated arc therapy (VMAT). Doses of radiotherapy are based on the site and stage of the tumor. It plays a major role in deciding the treatment outcome of a patient. Defining the target volumes adequately is of utmost importance in radiotherapy planning and delivery of treatment as esophageal and gastroesophageal cancers have high propensity of loco regional recurrence most commonly occurring in loco regional lymph nodes which can be because of geographical miss in planning target volume which includes the gross tumor along with potential nodes involved occur by intra-observer error with the help of computed tomography (CT) scan.

Some reports demonstrated that less than 15% of nodes are greater than 1-cm and that average size difference between involved and uninvolved nodes are frequently not significantly different. Imaging modalities like positron emission tomography-computed tomography (PET-CT) scan has also shown an estimated sensitivity of only 67% for detecting nodal metastasis.[1] Therefore, it is not appropriate to rely exclusively on any one single imaging technique. Incorporating PET with CT scan in target volume delineation and planning may help in defining areas of tumor as well as lymph nodes adequately and it is advisable to include these imaging modalities to accurately define areas of subclinical spread, however literature is sparse, and supporting evidence is limited, to declare the superiority of PET-CT based planning in cancer esophagus patients.[2]

The present study aims to evaluate dosimetry parameters in patients of cancer oesophagus planned on CT based contours and PET-CT fusion-based contours by conformal technique.

MATERIAL AND METHODS

In 50 biopsy proven cases of cancer esophagus and gastroesophageal junction were selected in our institute between February 2021 to July 2022.

Patient Selection

Inclusion criteria

Carcinoma oesophagus and gastro-oesophageal junction patients with histopathology proven squamous cell carcinoma and adenocarcinoma; age > 18 years; Karnofsky performance scale above 70; no history of previous malignancy; no previous thoracic radiotherapy

Exclusion criteria

Patients with prior or synchronous malignancy; distant metastasis.

All patients were planned and delivered standard radiotherapy to gross tumor and regional lymph nodes at a dose range of 45 to 59.4 Gy depending upon the site in 25 to 33 fractions over 6 to 7 weeks

Randomization

Two plans were generated based on CT and PET contours.

Group I

Radiotherapy was planned on CT based contours by conformal (IMRT or 3D CRT) technique.

Group II

Radiotherapy was planned on PET based contours conformal (IMRT or 3D CRT) technique.

Pre-treatment Evaluation

Complete history and physical examination; baseline hematological tests (hemogram, renal function tests, liver function tests); random plasma glucose; PET-CT scan, (The patient were fasting for a minimum of 6 hours before the injection of FDG. The patient rested until the examination to decrease muscle uptake. Blood glucose levels was checked and recorded).

Radiotherapy Planning and Technique

Immobilisation and CT simulation

Patients were placed in the supine position with arms placed accordingly depending on the site of oesophagus and immobilised using 4-point thermoplastic cast. Radio-opaque fiducial markers were placed depending on the anatomical location of the disease.

Patients were aligned with help of three perpendicular laser beams installed in the room. Intravenous injection of hexa-opaque iodine based dye was given to all patients according to a standard protocol with 30 s before acquisition followed by volumetric CT. Spiral CT was performed using slice thickness of, 1.5 and 3 mm.

FDG-PET images

18F-fluoro-deoxy-D-glucose image acquisition was performed with Seimens Biograph MCT flow 64 slice 3 ring LSO-PET CT scanner. An intravenous injection of about 8 Mill curie of FDG was given 60 minutes before the examination. The patient was placed in the treatment position same as in CT imaging protocol. All PET images were interpreted by experienced nuclear physicians. Foci of visually abnormal FDG uptake were considered to represent viable active tumor. Less intense foci were scored as tumor if a corresponding small abnormality was identified on CT images.

Image acquisition and registration

After planning CT and PET scan, the images were acquired in Digital imaging and communication in medicine (DICOM) format. The DICOM images were transferred to the eclipse treatment planning system (TPS).

CT and FDG PET fusion

Image registration was done on eclipse treatment planning system. 18F-fluoro-deoxy-D-glucose-positron emission tomography (FDG-PET) images were then fused with the CT images.

Contouring

Gross tumor volume (GTV) consisted of oesophageal gross tumor and gross lymph nodes which were contoured on CT and PET-CT scan and were named as GTV-CT (primary), GTV–CT (node) and GTV–PET CT (primary), GTV-PET CT (node).

Clinical target volume (CTV) including CTV–CT (primary), CTV–CT (node) and CTV–PET CT (primary), CTV–PET CT (node) were contoured as per guidelines.

A volumetric margin was given depending on the institutional protocol to account for microscopic tumor extension, mean motion of the lesion to generate planning target volume (PTV). Two PTV volumes were finally contoured that is PTV-CT and PTV-PET-CT. The first volumes were defined exclusively from the anatomic data provided by CT, and the second volumes were defined from composite images using CT and PET fusion. Lymph nodes were considered to be involved in PET, only when they demonstrated increased FDG uptake or had a short axis of 10 mm in diameter on CT. A standardized uptake value (SUV) of 2.5 was used to supplement visual assessment in this study

Dose prescription

The dose prescribed to PTV-CT and PTV-PETCT in the range of 45 to 59.4 Gy depending upon the site in 25 to 33 fractions.

Organs at risk (OARs)

The OAR's included bilateral lungs, heart, spinal cord and liver. The OARs were generated in accordance with the radiation therapy oncology group (RTOG) protocol. Dose constraints were given to each organ as per QUANTEC.[3]

Bilateral lungs - V20 < 20%; V20 < 30%; D-mean < 20 Gy

Heart - D-mean < 26; V25 < 10%

PRV spine- D-max < 50 Gy

Treatment planning

Treatment planning was done on eclipse treatment planning system (version 13.6), varian medical system, using intensity modulated radiotherapy technique. Planning was done by 6MV energy and 7- field (0º, 51 º, 102 º, 153 º, 204 º, 255 º and 306 º) technique.

Calculation algorithm was analytical anisotropic algorithm (AAA).

Plan evaluation

Two plans were generated for comparison and were optimized to maximize the dose to the PTV and limit the dose to normal tissue. Dose–volume histograms (DVHs) corresponding to the delivered IMRT plans was generated and evaluated.

PTV dosimetric parameters for evaluation were as follows: PTV receiving 95% dose was designated as PTV (V95), dose given to 2, 50, 95 and 98%, PTV was designated as PTV (D2, D50, D95 and D98, respectively), maximum dose to the PTV (Dmax), and mean dose to the PTV (Dmean), conformity index (CI) and homogeneity index (HI).

The CI is defined as, CI = TV/PTV where TV was the volume of reference dose (95%) inside the PTV. CI value closer to 1 indicates a conformal plan. The HI is defined as HI = (D2% D98%)/D50%, where D2%, 98% and 50% of the PTV volume. HI value closer to 0 indicates a homogeneous plan. To normalize the plan the planning goal had homogeneity between -5% and +7% (95–107%).

Dose constraints of OAR were also checked with following parameters for

- Both lungs combined (D-mean, D-max, V-5, and V-20)
- Heart (D-mean, D-max, and V-40)
- Spinal cord (D-max)

Following evaluation of DVH results were done.

The mean value was taken for V95, D2, D50, D95, D98, Dmax, Dmean, HI, CI of PTV on CT scan and PET-CT scan. Comparison of mean value of dosimetric parameters was done and statistical analysis was done using paired T-test.

The mean was taken for V20, V-5, Dmax, Dmean of both lungs on CT scan and PET-CT scan and statistical analysis was done using paired T-test. Comparison of mean value of dosimetric parameters and *p-value* was calculated. Percentage difference of lung volume on CT scan and PET-CT scan was calculated.

The mean was taken for V40, Dmax, Dmean of heart on CT scan and PET-CT scan and statistical analysis was done using paired T-test. Comparison of mean value of dosimetric parameters and *p-value* was done. Percentage difference of heart volume on CT scan and PET-CT scan was calculated.

The mean was taken for Dmax of spinal cord on CT scan and PET-CT scan and statistical analysis was done using paired T-test. Comparison of mean value of dosimetric parameters and *p-value* was done.

RESULTS

The mean age in the present study population is 61 years with most common presentation in 5th and 6th decade. Male to female ratio is 0.7:1. The most common subsite is mid thoracic esophagus (46%); Table 1.

All patients had complaint of difficulty in swallowing solid food (Table 2). Around 76% of patients had some or the other addiction either tobacco intake (smoking or tobacco chewing or both) or alcohol intake. Most common general clinical presentation was pallor (62%) followed by supraclavicular nodes (10%); Table 3.

The histopathology seen was squamous cell carcinoma (88%) and adenocarcinoma (12%) with majority having moderately differentiated grade (80%).

Median standardized uptake value in the present study group is 14.9 and mean 14.8 (range 0–37.4).

Gross Tumor Volume and Length

CT scan showed an increase in gross tumor size in 22 (44%) patients and reduction in 26 (52%) patients on CT scan when compared to PET-CT scan and no change or difference seen in 2 (4%) of patients.

The variation of gross tumor size and gross tumor volume on PET-CT scan as compared to CT scan ranged from -1.7 (-44.7%) cm to 2.7 cm (55.1%) and from -11.9 cm^3 (-28.6%) to 13.2 cm^3 (36.8%) which was not statistically significant $p = 0.38$ and $p = 0.41$, respectively.

Nodal status

In this present study of 50 patients CT was able to detect lymph nodes in 23 (46%) patients compared to PET-CT where detection of lymph nodes was in 32 (64%) patients. There was a difference of 18% in detection of nodes by PET-CT scan as compared to CT scan which was statistically significant ($p = 0.0001$).

Table 1: Table showing subsite wise distribution of tumor.

S. No	Subsite	Number (%)
1.	Gastro oesophageal junction	7 (14%)
2.	Cervical oesophagus	02 (04%)
3.	Upper thoracic oesophagus	10 (20%)
4.	Mid thoracic oesophagus	23 (46%)
5.	Lower thoracic oesophagus	08 (16%)

Table 2: Table representing the chief complaints.

S. No	Chief complaints	Number (%)
1.	Difficulty in swallowing solid food	50 (100%)
2.	Difficulty in swallowing solid food and liquid	27 (54%)
3.	Pain in chest	03 (06%)
4.	Loss of appetite	16 (32%)
5.	Generalized weakness	40 (80%)
6.	Weight loss	26 (52%)
7.	Others	27 (54%)

Planning Target Volume (PTV)

PTV were increased due to additional detection of lymph nodes. The increased PTV was seen in 26% patients ($p = 0.0001$)

Dosimetric Parameters of PTV

No difference in dosimetric parameters of PTV was found in terms of V95, D2, D50, D95, D98, D max and Dmean. Similarly, no statistical difference was found in CI and HI of both plans

Dosimetric Parameters of Organs at Risk

Dosimetric parameters of both lungs shows statistical significant difference in Dmean (14.73 *vs* 16.13 Gy; $p = 0.0005$) and V5 (89.16 *vs* 28.4 Gy; $p = 0.0056$) (Table 4).

Dosimetric parameters in heart in terms of Dmean, Dmax and V40 did not show statistical significant difference (Table 5).

Dmax for spinal cord in both groups were within dose constraints (38.7 *vs* 39.1 Gy) with no statistical significant difference ($p = 0.22$).

DISCUSSION

The role of PET-CT scan is established in staging but remains controversial in planning the radiotherapy as well as contouring the tumor volumes. PET-CT with its

Table 3: General clinical presentation of patients.

S. No.	General clinical presentation	Number (%)
1.	Pallor	31 (62%)
2.	Icterus	02 (04%)
3.	Clubbing	03 (06%)
4.	Dyspnoea	03 (06%)
5.	Supraclavicular nodes	05 (10%)

Table 4: Table showing dosimetric parameters of both lungs

S. No	Parameters	CT-SCAN	PET-CT	p-value
1.	D-mean	14.73	16.13	0.0005
2.	D-max	55.87	55.87	0.49
3.	V-5	74.4	78.78	0.0056
4.	V-20	89.16	28.4	0.17

Table 5: Table showing dosimetric parameters of heart

S. No.	Parameters	CT-SCAN	PET-CT	p-value
1.	D-mean	20.19	20.73	0.06
2.	D-max	50.19	60.87	0.1
3.	V-40	15.34	15.41	0.42

ability to detect the tumor and nodal metastasis based on tumor metabolic activity can be utilised for more accurate and precision target volume delineation and radiotherapy planning.

Standardized uptake value

Little *et al*[4] in his study to ascertain the role of PET-CT in superficial tumors, in which 58 superficial oesophageal cancer patients were studied he which he observed that positron emission tomography is not indicated in staging superficial oesophageal cancer. Ceullar *et al*[44] in a study determining the utility of FDG-PET/CT in the clinical staging of early-stage oesophageal cancer in 79 patients suggested that FDG-PET/CT is not useful in the TNM staging of primary adenocarcinoma of the oesophagus in cTis and cT1. Similarly, in our study we found that 4 patients out of 50 had zero SUV with no uptake in FDG-PET and on upper GI endoscopy finding tumor was of size 2 to 3 cm each and growth was also seen on CT scan. This could be because, these patients may belong to Tis or T1 stage and tumor cells have not develop the metabolic activity to be diagnosed on PET-CT.

Blackstock *et al*[5] in his study to determine the impact of 18-F-FDG PET in staging and prognosis of patient with locally advanced oesophageal cancer observed and stated that on correlation of CT-detected subcentimeter intrathoracic/intraabdominal lymph nodes with increased uptake with FDG-PET was the most common reason for upstaging, occurring in 9 of 39 patients (23%). Similarly in our study the PTV volume was increased (clinically upstaged) in 9 (18%) of the patients due to incorporation of sub-centimetric nodes found on in CT scan which showed a significant uptake on PET-CT scan this is due to PET-CT has more sensitivity to detect tumor metastasis in lymph nodes as compared to any other radiological investigation which lead to upstaging of oesophageal cancer.

Gross Tumor Volume and Length

Zobotto *et al*[6] in his study to see the impact of fused PET and CT images with conformal radiotherapy on 34 patients, observed that volume (GTV) was decreased by CT and FDG image fusion in 12 patients (35%) and increased in 7 patients (21%). The GTV reduction was more than 25% in 4 patients owing to a reduction in the length of the oesophageal tumor. The GTV increase was >25% with FDG-PET in 2 patients. While Jimenez *et al*[7] in a study to compare the volumes and tumor lengths defined by fused PET/CT *vs*. CT simulation, found a non-statistically significant difference between CT- and PET/CT-based GTVs.

Shi *et al*[8] did a study on 72 patients to compare the Gross Target volumes based on diagnostic PET/ CT for primary oesophageal cancer found no significant difference in the displacement cranio-caudal direction in any comparison between two different GTVs (p = 0.178–0.771) but Grange *et al*[9] did a study to evaluate the contribution of single PET-CT in the treatment position to RTP found significant larger PET-GTV in 12 cases in smaller in 6 cases compared to CT scan.

Contradictory to these studies Konski *et al*[10] in a study to evaluated the impact of PET compared with CT simulation in the planning of radiation fields for patients with oesophageal carcinoma concluded that length of tumors were significantly longer as measured by CT scan compare with PET scans. Similarly, in our study when GTV length was compared on CT as well as PET-CT scan it was seen that no statistically significant difference was found. On addition of PET to CT scan GTV was increased in 26 (52%) patients decreased in 22 (44%) patients while it was same in 4 % of the patient with *p-value* of 0.38. Size difference was >20% in 6 patients in PET-CT compared to CT and was > 20% in 7 patients in CT compared to PET-CT this is because the PET-CT has the ability to differentiate between the oesophageal wall thickness and presence of tumor metabolic activity, this differentiation is not possible in CT scan.

Grange *et al*[9] in his retrospective study of 19 patients observed that mean gross tumor volume on CT was 67.8 cm^3 and mean GTV volume on PET-CT was 72.4 cm^3 and mean volume increase with PET-CT was 13.1 and mean volume decrease with PET-CT was 11.7 which were clinically insignificant. In 15 patients Kalyanasundaram *et al*[11] in his study to find the dosimetric impact of PET-based gross tumor volume (GTV) delineation over CT-based GTV delineation for carcinoma oesophagus on 15 patients, observed that by addition of PET to CT there was a reduction of volume of GTV in 12 patients and increased in 3 patients. Where as in our study we observed that the mean GTV volume on CT was 55.13 cm^3 and mean GTV volume on PET-CT was 55.34 cm^3 and mean volume increase in 52% patients with PET-CT was 4.4 cm^3 in and mean volume decrease in 48% patients was 4.0 cm^3 which came out to be clinically insignificant because on PET-CT tumor volume delineation is based upon FDG uptake where on CT scan it is based upon contrast enhancement which is less accurate as compared to PET-CT delineation.

Gupta *et al*[12] in his study to assess the early use of PET/CT among GEJ patients in a regionalized setting and identify factors contributing to disparity in access did a retrospective cohort study of adults with GEJ between 2012 and 2014 from the Population Registry of Oesophageal and Stomach Tumors found that PET/CT use has been increased from 2012 to 2014 and that

the majority of EC/GEJ patients being considered for curative therapy received PET/CT. PET/CT appears to confer a potential survival benefit similarly in our out of 7 patients of GEJ we found that by incorporation of PET to CT there was increase in tumor length in 5 patients and decrease was seen in 2 patients and FDG-PET was able to detect lymph nodes in 6 patients while CT scan was able to detect nodes in only 3 patients. Since GEJ has high chances of recurrence and lymph node metastasis and geographical miss it is very important to incorporate PET with CT scan.

Gross Tumor Node

Yoon *et al*[13] compared the accuracy of fluorine 18-fluorodeoxyglucose (FDG) PET and CT for detection of primary tumor and metastasis to individual lymph node groups and stated that FDG-PET is more sensitive than CT for depicting nodal metastases in patients with squamous cell carcinoma of the oesophagus. Gamal *et al*[14] evaluated the efficacy of PET-CT in diagnosing and staging of oesophageal carcinoma and compared it with CECT which he concluded that CT was able to detect lymph nodes in 4 patients and PET-CT was able to detect lymph nodes in 8 patients.

Choi *et al*[15] studied 61 patients in which 382 lymph nodes were dissected out of which 100 were found to be malignant FDG PET showed a sensitivity of 57%, a specificity of 97%, and an accuracy of 86% for determining whether a lymph node group harboured metastasis. However, CT detected only 18% of the metastatic lymph node groups ($p < 0.001$) and showed an accuracy of 78%, which was significantly lower than that of FDG PET ($p < 0.001$). In terms of staging, it was seen that nodal staging by FDG-PET was correct in 83% (40/48) of the patients. Both CT (60%, 29/48; $p < 0.001$) were less accurate.

In the present study of 50 patients with the help of CT scan was able to detect lymph nodes in 23 (46%) patients and PET-CT was able to detect lymph nodes in 32 (64%) patients. There was a statistically significant difference i.e ($p < 0.0001$) and of 18% in detection of nodes by PET-CT scan as compare to CT scan. this was because in 18% of the patients there was a larger PTV volume in PET-CT fusion as compared to CT scan alone therefore the planning treatment volume was increased in those 9 patients. Since, specificity of FDG-PET is more compared to CT scan in detection of lymph nodes therefore, statistically significant difference was seen.

Liu *et al*[16] studied patterns of lymph node metastases from oesophageal squamous cell carcinoma (ESCC) using 18F-FDG-PET/CT. on 75 patients and observed that most common site of nodal is to right para-tracheal lymph nodes followed by para-oesophageal lymph nodes. Munch *et al*[17] in a retrospective study analysing patterns of lymph node metastases and their correlation with the primary tumor using FDG-PET/CT scans in which 76 patients were studied in which he found that the most common site of nodal metastasis was para oesophageal followed by para-tracheal, supra clavicular and hilar lymph nodes.

In the present study, it was observed that the most common location of lymph nodes were para tracheal followed by hilar and the para-oesophageal lymph nodes because the most common site of presentation in our study was mid thoracic oesophagus and the most common draining lymph node of site are para-tracheal and para-oesophageal nodes.

Planning Target Volume (PTV)

In a study of 15 patients Kalyanasundaram *et al*[11] observed that by addition of PET to CT there PTV showed significant reduction ($p < 0.05$) in volume while considering only PET, whereas Guo *et al*[18] in his prospective study on 18 patients observed statistically significant difference in PTV, PTV-PET>PTV-CT ($p = 0.000–0.048$)). Similarly in our study also we found significant difference in PTV volume, PTV-PET>PTV-CT with $p < 0.0001$ it is because of number of nodes which were significantly more in PET compared to CT and were included in PTV.

Dosimetric Parameters of PTV

Muijs *et al*[19] observed that, the incorporation of PET information in the radiation planning did not result in statistically significant differences in any of the dosimetric factors analysed similarly in our study we didn't find any significant difference in PTV dosimetric parameters (V95, D2, D50, D95, D98, Dman, Dmax) because all patients were planned with IMRT technique and PTV parameters were achieved in both plans as per ICRU 83[20] and hence there was no much difference in dosimetry parameters in both the plan.

Dosimetric Parameters of Lung

Leong *et al*[21] in a prospective study to evaluate the impact of FDG-PET on CT-based radiotherapy treatment planning for oesophageal cancer found no significant difference on average in radiation doses to lungs. Zobotto *et al*[6] observe that the percentage of total lung volume receiving 20 Gy was reduced after PET-CT image fusion in 12 patients and percentage of total lung volume receiving 20 Gy was increased after PET-CT image fusion in 13 patients.

Muijs *et al*[19] found that by incorporation of PET to CT there is significant increase in V_{20} ($p < 0.003$) and there is significant decrease in V_{20} ($p < 0.000$). Kalyanasundaram *et al*[11] observed that in the study while comparing the lung doses, it was found that 11 out of 15 patients (73%)

showed decrement in left lung doses, 12 out of 15 patients (80%) showed decrement in right lung V20% doses and 13 patients (87%) showed decrement in right lung V10% doses. Where as in our study we observed out of 50 patients 48 were able to achieve $D_{mean} \leq 20$ Gy in CT scan but only 43 were able to achieve $D_{mean} \leq 20$ Gy in PET scan. Since majority of cases in our study were of thoracic oesophagus and PTV was overlapping with lung and we have to give priority to PTV which caused increased in lung dose.

Dosimetric parameters of heart

Muijs *et al*[19] in 21 patients observed that the dose at V_{40} was increased in 6 patients and was decreased in 15 patients. Kalyanasundaram *et al*[11] observed that mean reduction in heart mean dose with respect to heart mean dose in CT was significant with *p-value* of 0.031 and heart V30% doses showed insignificant difference $p = 0.69$. Zobotto *et al*[6] in his study on 34 patients After CT-PET image fusion, the percentage of total heart volume receiving 36 Gy increased in 11 patients and decreased in 12 patients. Similarly in our study we found insignificant difference in heart parameters ($D_{mean\ and}\ V_{30})_{as}$ majority of the cases were of thoracic oesophagus and PTV was overlapping with heart and we have to give priority to PTV which caused increased in heart dose.

Dosimetric Parameters of Spinal Cord

Zobotto *et al*[6] in his study on 34 patients found comparable maximal dose to the spinal cord with a mean of 43 Gy with CT alone vs. 42.6 Gy with CT-PET similarly in our study we found insignificant and comparable maximal dose to spinal cord with mean of 38.7 Gy on CT scan and 39.03 Gy on PET-CT scan as IMRT planning was done in both plan achieving dose constraints.

Advantage of PET-CT over CT scan

Cheung *et al*[22] did systematically review of published data on the efficacy of PET-CT in the radiotherapy planning process of patients with oesophageal carcinoma in which 37 studies were included comprising a total sample size of 1921 patients found that primary tumor detection rate of 92.7% and for lymph node staging, sensitivity and specificity ranged from 0 to 100% for sensitivity and 71% to 100% for specificity. He also observed that PET-CT significantly reduced inter-/intra-observer variability and increased observers' confidence in GTV delineation and no under-dose was reported on PET-based treatment volume.

Similarly in a study a systematic review on the role of FDG-PET/CT in tumor delineation and radiotherapy planning in patients with oesophageal cancer by Muijs *et al*[19] found that FDG-PET was able to identify most primary tumors, with a sensitivity and specificity for the detection of metastatic lymph nodes of 30–93% and 79–100%. The use of FDG-PET/CT resulted in changes of target volumes, and consequently in changes in treatment planning. In our study we didn't find any significant difference in gross tumor volume primary but there was significant difference seen in detection of gross node with the help of PET fusion with CT scan it also helped in integration of nodes which were subcentimetric in CT scan but showed high SUV in PET-CT scan.

In the present study, significant change in target volume delineation was seen due to higher specificity of lymph node detection by fusion of PET to CT scan which helped in prevention of geographical miss in our planning therefore PET-CT should be incorporated as an essential investigation not only in staging and diagnosis of oesophageal cancer but also in radiotherapy planning of carcinoma oesophagus to provide a better disease free survival to patients.

CONCLUSION

The present study concludes that with PET-CT fusion better delineation of primary gross tumor is possible as compared to CT alone. Further, PET-CT scan has more sensitivity in lymph node detection than CT alone, therefore by incorporating PET–CT scan in radiotherapy planning of carcinoma oesophagus more accurate and precise treatment planning can be done which will lead to less chances of geographical miss and less chances of loco regional failure.

REFERENCES

1. Kitajima K, Nakajo M, Kaida H, Minamimoto R, Hirata K, Tsurusaki M, *et al*. Present and future roles of FDG-PET/CT imaging in the management of gastrointestinal cancer: an update. Nagoya J Med Sci. 2017 [cited 2023 Mar 12];79(4):527–43. Available from: http://dx.doi.org/10.18999/ nagjms.79.4.527
2. Zygogianni A, Kyrgias G, Kouvaris J, Pistevou-Gompaki K, Kouloulias V. A new role of PET/CT for target delineation for radiotherapy treatment planning for head and neck carcinomas. Hell J Nucl Med. 2012 [cited 2023 Mar12];15(2):139–43.Available from:https://pubmed.ncbi. nlm.nih.gov/ 22833861/
3. Bentzen SM, Constine LS, Deasy JO, Eisbruch A, Jackson A, Marks LB, Ten Haken RK, Yorke ED. Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC): an introduction to the scientific issues. Int J Radiat Oncol Biol Phys. 2010 Mar 1;76(3 Suppl):S3-9. doi: 10.1016/j.ijrobp.2009.09.040. PMID: 20171515; PMCID: PMC3431964.
4. Little SG, Rice TW, Bybel B, Mason DP, Murthy SC, Falk GW, *et al*. Is FDG-PET indicated for superficial esophageal cancer? Eur J Cardiothorac Surg. 2007 [cited 2023 Mar 12]; 31(5):791–6. Available from: https://pubmed.ncbi.nlm.nih.gov/17337344/
5. Blackstock AW, Farmer MR, Lovato J, Mishra G, Melin SA, Oaks T, *et al*. A prospective evaluation of the impact of 18-F-fluoro-deoxy-D-glucose positron emission tomography staging on survival for patients with locally advanced esophageal

cancer. Int J Radiat Oncol Biol Phys. 2006 [cited 2023 Mar 12]; 64(2):455–60. Available from: https://pubmed.ncbi.nlm.nih.gov/16213103/

6. Moureau-Zabotto L, Touboul E, Lerouge D, Deniaud-Alexandre E, Grahek D, Foulquier J-N, *et al*. Impact of CT and 18F-deoxyglucose positron emission tomography image fusion for conformal radiotherapy in esophageal carcinoma. Int J Radiat Oncol Biol Phys. 2005 [cited 2023 Mar 12];63(2):340–5. Available from: https://pubmed.ncbi. nlm.nih.gov/16168829/
7. Jimenez-Jimenez E, Mateos P, Aymar N, Roncero R, Ortiz I, Gimenez M, *et al*. Radiotherapy volume delineation using 18F-FDG-PET/CT modifies gross node volume in patients with oesophageal cancer. Clin Transl Oncol. 2018 [cited 2023 Mar 12]; 20(11):1460–6. Available from: https://pubmed.ncbi.nlm.nih.gov/29721766/
8. Shi J, Li J, Li F, Zhang Y, Guo Y, Wang W, *et al*. Comparison of the gross target volumes based on diagnostic PET/CT for primary esophageal cancer. FrontOncol.2021;11:550100.Availablefrom:http://dx.doi.org/10.3389/fonc.2021.550100
9. le Grange F, Wickers S, Warry A, Warrilow J, Bomanji J, Tobias JS. Defining the target in cancer of the oesophagus: direct radiotherapy planning with fluorodeoxyglucose positron emission tomography-computed tomography. Clin Oncol (R Coll Radiol). 2015 [cited 2023 Mar 12]; 27(3):160–7. Available from: https://pubmed.ncbi.nlm. nih.gov/25540907/
10. Konski A, Doss M, Milestone B, Haluszka O, Hanlon A, Freedman G, *et al*. The integration of 18-fluoro-deoxy-glucose positron emission tomography and endoscopic ultrasound in the treatment-planning process for esophageal carcinoma. Int J Radiat Oncol Biol Phys. 2005 [cited 2023 Mar 12];61(4):1123–8. Available from: https://pubmed.ncbi.nlm.nih.gov/15752892/
11. Kalyanasundaram K, Vellaiyan S, Shanmugam S. Dosimetric impact of positron emission tomography-based gross tumor volume (GTV) delineation over conventional CT-based GTV delineation for carcinoma oesophagus. J Radiother Pract. 2020 ,20(3):1–7
12. Gupta V, Kulanthaivelu R, Metser U, Ortega C, Darling G, Coburn N, *et al*. Acceptance and disparities of PET/CT use in patients with esophageal or gastroesophageal junction cancer: Evaluation of mature registry data. Front NuclMed.2022;2.Available from: http://dx.doi.org/10.3389/fnume.2022.917873
13. Yoon YC, Lee KS, Shim YM, Kim B-T, Kim K, Kim TS. Metastasis to regional lymph nodes in patients with esophageal squamous cell carcinoma: CT versus FDG PET for presurgical detection prospective study. Radiology [Internet]. 2003 [cited 2023 Mar 12];227(3):764–70. Available from: https://pubmed.ncbi.nlm.nih.gov/12773680/
14. Gamal GH. Does PET/CT give incremental staging information in cancer oesophagus compared to CECT? Egypt J Radiol Nucl Med. 2019;50(1). Available from: http://dx.doi.org/10.1186/s43055-019-0114-8
15. Choi Y, Choi JY, Hong TH, Choi Y-L, Oh D, Woo SY, *et al*. Trimodality therapy for locally advanced esophageal squamous cell carcinoma: the role of volume-based PET/CT in patient management and prognostication. Eur J Nucl Med Mol Imaging. 2022 [cited 2023 Mar 15];49(2):751–62. Available from: https://pubmed.ncbi.nlm.nih.gov/ 34365522/
16. Liu C-J, Cheng JC-H, Lee J-M, Cheng M-F, Tzen K-Y, Yen R-F. Patterns of nodal metastases on 18F-FDG PET/CT in patients with esophageal squamous cell carcinoma are useful to guide treatment planning of radiotherapy. Clin Nucl Med. 2015[cited2023Mar15];40(5):384–9.Availablefrom: https://pubmed.ncbi.nlm.nih.gov/25674870/
17. Münch S, Marr L, Feuerecker B, Dapper H, Braren R, Combs SE, *et al*. Impact of 18F-FDG-PET/CT on the identification of regional lymph node metastases and delineation of the primary tumor in esophageal squamous cell carcinoma patients. Strahlenther Onkol. 2020 [cited 2023 Mar 12]; 196(9):787–94. Available from: http://dx.doi.org/ 10.1007/s00066-020-01630-y
18. Guo YL, Li JB, Shao Q, Li YK, Zhang P. Comparative evaluation of CT-based and PET/4DCT-based planning target volumes in the radiation of primary esophageal cancer. Int J Clin Exp Med. 2015 Nov 15;8(11):21516-24.
19. Muijs CT, Beukema JC, Pruim J, Mul VE, Groen H, Plukker JT, *et al*. A systematic review on the role of FDG-PET/CT in tumor delineation and radiotherapy planning in patients with esophageal cancer. Radiother Oncol [Internet]. 2010 [cited 2023 Mar 12];97(2):165–71. Available from: https://pubmed.ncbi.nlm.nih.gov/20541273/
20. Hodapp N. The ICRU Report 83: prescribing, recording and reporting photon-beam intensity-modulated radiation therapy (IMRT). Strahlenther Onkol [Internet]. 2012 [cited 2023 Mar 12];188(1):97–9. Available from: https://pubmed.ncbi.nlm.nih.gov/22234506/
21. Leong T, Everitt C, Yuen K, Condron S, Hui A, Ngan SYK, *et al*. A prospective study to evaluate the impact of FDG-PET on CT-based radiotherapy treatment planning for oesophageal cancer. Radiother Oncol [Internet]. 2006 [cited 2023 Mar12];78(3):254–61. Availablefrom: https://pubmed.ncbi.nlm.nih.gov/16545881/
22. Cheung, G. S. M. Contribution of PET–CT in radiotherapy planning of oesophageal carcinoma: A review. Radiography (London, England: 1995), 19(3), (2013) 259–269.