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ORIGINAL RESEARCH ARTICLE

Role of PET CT in Radiotherapy Planning of Head and Neck Cancers

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ABSTRACT

Introduction: The use of new imaging modalities and combined chemoradiotherapy has resulted in significant improvements in treatment outcome for head and neck cancer patients. Presently, 3-D planning is standard in head and neck cancers and tissue volumes are delineated using computed tomography (CT) images. Role of positron emission tomography (PET) in radiotherapy planning is evolving. The PET/CT in radiotherapy planning may improve tumor delineation in terms of primary and nodal. The present study is designed to evaluate the role of PET-CT in radiotherapy planning of head and neck cancer and compare the dosimetric parameters for tumor and organs at risk between CT scan planning and PET-CT fusion planning.

Material and Methods: The present prospective study is of head and neck cancers was conducted in the department from August 2022 to January 2024. Histopathology proved squamous cell carcinoma head and neck cancers with age > 18 years and normal liver and kidney functions and not previously treated were selected. All patients were planned and delivered standard radiotherapy at a dose of 70 Gy in 35 fractions over 7 weeks. Two treatment plans were generated based on CT (group 1) and PET-CT (group 2) contours using intensity modulated radiotherapy technique (IMRT). Various dosimetric parameters of planning target volumes (PTV) and organs at risk (OAR) were evaluated for both groups. Collected data was analysed using standard statistical methods and the unpaired t-test was used to compare the means of both groups. *p-value* <0.05 was taken to be statistically significant.

Results: In the present study of 35 patients, majority of the patients were in the 7th decade of life with male predominance The commonest site involved was oropharynx (n = 13; 37.1%). T stage, N stage and overall stage, 17.1% cases were downstaged in PET CT. Total CTV (361.89 *vs* 355.96) and total PTV (692.33 *vs* 686.49) along with other PTV dosimetric parameters were slightly different in CT and PET CT which were not statistically significant. Similarly, various organs at risk did not show statistical difference in dosimetric parameters of both groups.

Conclusion: PET-CT supplementing radiotherapy planning contrast CT scan for tumor volume delineation has shown no statistical advantage in identifying the tumor more precisely in head and neck cancers. Cost-effectiveness and logistics associated with PET CT should be considered for radiotherapy planning.

Keywords: Head neck cancer, Radiotherapy planning, PET CT

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INTRODUCTION

Radiotherapy is used in combination with chemotherapy as a definitive organ function-preserving approach or after surgery as an adjuvant therapeutic modality.[1] Because locoregional recurrence is the most common pattern of failure in head and neck cancer patients, improvement in outcomes focuses on local disease control.[2] Over the years, the delivery of radiation therapy has improved with innovations that have reduced toxicity without compromising locoregional control. Among these advances, the development of intensity-modulated radiation therapy (IMRT) has represented a major turning point in the treatment of head and neck cancer patients.[3] IMRT is characterized by its highly conformal dose distribution with improved ability to treat target volumes to therapeutic doses while avoiding normal structures such as the salivary glands, DARS, spinal cord, and optic apparatus.[4-6]

The use of new imaging modalities and combined chemoradiotherapy in recent years has resulted in significant improvements in treatment outcomes for head and neck cancer patients. The precise definition of the target volumes (gross target volume [GTV], clinical target volume [CTV], and planning target volume [PTV]) is mandatory to develop optimal treatment plans. In modern radiation therapy practices, 3-D planning is standard and tissue volumes are delineated using computed tomography (CT) images. It provides both good anatomic detail for defining target volumes and the electron density data required for dose calculations. Although CT imaging provides adequate information for treatment planning in many cases, there are limitations in soft tissue definition and identification of physiologic subregions within tumors and normal tissues.[7,8]

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Positron emission tomography (PET) is now being incorporated into radiotherapy planning in some radiotherapy centers. The distinct advantage of PET/CT in radiotherapy planning is its potential to improve tumor delineation, reducing intra-observer and inter-observer variability and making treatment volumes more standard across individuals and institutions.[8] There is currently no officially recognized technique for best defining tumor volume using 18F- FDG-PET-CT, although recommendations for target delineation have been recently published.[9] Therefore, to evaluate the role of PET-CT in radiotherapy planning of head and neck cancer, the present study was designed to compare the dosimetric parameters for tumors and organs at risk between CT scan planning and PET-CT fusion planning

MATERIAL AND METHODS

The present prospective study of head and neck cancers was conducted in the department from August 2022 to January 2024.

Patient Selection

Inclusion criteria

Histologically proved squamous cell carcinoma head and neck cancer malignancies; Age >18 years; Karnofsky performance status >70, normal renal function tests, liver function tests.

Exclusion criteria

Patients with prior or synchronous malignancy who underwent prior surgery; distant metastasis; previously treated patients with radiotherapy.

All patients were planned and delivered standard radiotherapy at a dose of 70 Gy in 35 fractions over 7 weeks. Two plans were generated based on CT and PET-CT contours: -

- *Group I*

Delineation of all structures was done based on CT scan only.

- *Group II*

Delineation of all structures was done based on PET-CT fusion only.

Radiotherapy Planning and Technique

Immobilization

Patients were placed in the supine position with arms placed accordingly depending on the site of the esophagus and immobilized using 5-point thermoplastic cast. Radio-opaque fiducial markers were placed depending on the anatomical location of the disease.

CT simulation

Anatomic data acquired by a CT scan was performed in the treatment position. The patients were placed in the supine position using a neck rest, with the arms placed accordingly, depending upon the site of the tumor, and immobilized using a thermoplastic cast. Patients were aligned with the help of three perpendicular laser beams installed in the room. Fiducial markers were placed according to the site of the tumor. Intravenous injection of hexa-opaque iodine-based dye was given to all patients according to a standard protocol 30 seconds before acquisition, followed by volumetric CT. Spiral CT was performed using slice thicknesses of 1, 1.5 and 3 mm.

FDG-PET images

18F-fluoro-deoxy-D-glucose image acquisition was performed with Siemens Biograph MCT flow 64 slice three 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 the CT imaging protocol. Experienced nuclear physicians interpreted all PET images. 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 scans, 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). 18F-fluoro-deoxy-D-glucose-positron emission tomography (FDG-PET) images were then fused with the CT images.

FDG-PET threshold- The PET scans were evaluated at a signal intensity of 40% of the maximum threshold value after consulting the nuclear medicine specialist.

Treatment Planning

Treatment planning was done using the eclipse treatment planning system. Four gross tumor volume (GTV) contours; GTV-CT (primary), GTV-CT (node), GTV-PETCT (primary) GTV-PETCT (node), four clinical target volume (CTV) contours; CTV-CT(primary), CTV-CT (node), CTV-PETCT (primary), CTV-PETCT (node), and two planning volume (PTV) contours; PTV-CT and PTV-PETCT. The CT-based volumes were defined exclusively from the anatomic data provided by CT, and the PET-CT volumes were defined from composite images using CT and PET fusion. The GTV consisted of gross tumors and cervical lymph nodes. International Consensus

guidelines defined CTV. A volumetric margin was given depending on the institutional protocol to account for microscopic tumor extension mean motion of the lesion to generate PTV. The GTV nodal included only those lymph nodes considered to be involved. 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 the visual assessment by a qualified physician. Treatment planning was performed using the IMRT technique. Two plans were generated for comparison and were optimized to maximize the dose to the PTV and limit the dose to normal tissue. Calculation of dose distribution was systematically performed for each treatment plan. The cumulative dose–volume histogram was calculated accordingly on both these plans.

Dose prescription

The dose prescribed to PTV-CT and PTV-PETCT was 70 Gy in 35 fractions at 2 Gy per fraction.

Organs at risk (OARs)

The OARs were generated in accordance with the radiation therapy oncology group (RTOG) protocol. Dose constraints were given to each organ as per QUANTEC-Brainstem D_{max} <54 Gy; PRV-Spine D_{max} <50 Gy; Optic chiasma D_{max} <55 Gy, Mandible 1cc<70 Gy; Optic nerve D_{max} <55 Gy, Parotid gland D_{mean} <26 Gy; Cochlea D_{mean} <45 Gy; Eye D_{max} <50 Gy; Lips D_{mean} <30 Gy; The D_{max} for Brachial Plexus and D_{mean} for DARS was evaluated and no constraints were given.

Plan Evaluation

- Dose-volume histograms (DVHs) corresponding to the delivered IMRT plans were generated for each contoured plan.
- Both planning techniques were evaluated using a dose-volume histogram (DVH). PTV dosimetric parameters for evaluation were as follows: PTV receiving 95% dose was designated as PTV (V95). PTV was designated as PTV (D2, D50, and D98 respectively), the 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%).

Ethical Considerations

This study was conducted after getting an Ethical clearance certificate from the Institute's Ethics Committee (Ref No. SRMS IMS/ECC/2022/131).

Statistical Analysis

Collected data was analyzed using standard statistical methods and the unpaired t-test was used to compare the means of both groups. The *p-value* <0.05 was taken to be statistically significant.

RESULTS

In the present study of 35 patients, the majority of the patients were in the 7^{th} decade of life with male predominance. Male female ratio seen was 6:1. The commonest site involved was the oropharynx (n = 13; 37.1%), followed by the oral cavity (n = 11; 31.4%), larynx (n = 7; 20%), cervical lymphadenopathy with unknown primary (n = 2; 5.7%), hypopharynx (n = 1; 2.8%) and nasopharynx (n = 1; 2.8%).

Table 1: Group stage-wise distribution of patients

Group stage	*CT-scan*	*PET-CT*
I	0 (0%)	1 (2.8%)
II	4 (11.4%)	6 (17.1%
III	2 (5.7%)	2 (5.7%)
IVA	21 (60%)	19 (54.2%)
IVB	8 (22.8%)	7 (20%)

Table 2: Changes in group stage on PET-CT (as compared to CT-scan staging)

Upstaged	0 (0%)
Downstaged	6 (17.1%)
No change	29 (82.9%)

Table 3: Distribution of patients as per T-stage

Stage	*CT-Scan*	*PET-CT*
T0	3	3
T1	0	1
T2	5	7
T3	12	9
T4	15	15

Table 4: Changes in T-stage on PET-CT (as compared to CT-scan staging)

Upstaged	1 (2.8%)
Downstaged	6 (17.2%)
No change	28 (80%)

Table 5: Distribution of patients as per N-stage

Stage		*CT-Scan*	*PET-CT*
Node negative	N0	9	11
Node positive	N1	4	5
	N2	16	13
	N3	6	6

Table 6: Changes in N-stage on PET-CT (as compared to CT-scan staging)

Upstaged	5 (14.2%)
Downstaged	6 (17.1%)
No change	24 (68.5%)

Table 1 shows the stagewise distribution of cases. PET CT did not upstage any case, but in fact, 17.1% of cases were downstaged (Table 2).

T stage and N stage distribution and change in the stage due to PET CT is shown in Table 3-6

A comparison of gross tumor volume of primary (GTVP) and nodal (GTVN) for CT *versus* PET-CT is shown in Table 7.

A comparison of the clinical target volume of primary (CTVP) and nodal (CTVN) for CT versus PET-CT is shown in Table 8.

A comparison of the total clinical target volume of primary (Total CTV) and planning target volumes (PTV) for CT versus PET-CT is shown in Table 9.

Table 7: Comparing GTVP and nodal for CT *versus* PET-CT with volume differences (cc)

S. No.	*GTVP-CT*	*GTVP-PET-CT*	*DIFF (%)*	*GTVN-CT*	*GTVN-PET-CT*	*DIFF (%)*
1	25.4	18.3	-7.1 (-27.9%)	0	0	0 (0%)
2	16.2	28.1	11.9 (73.4%)	5.8	7.9	2.1 (36.2%)
3	26.8	28.7	1.9 (7.1%)	0	0.4	0.4 (0%)
4	42.6	15	-27.6 (-64.7%)	0	0	0 (0%)
5	20.1	23.3	3.2 (15.9%)	12.4	13.4	1 (8.1%)
6	19.7	15.6	-4.1 (-20.8%)	1.2	1.2	0 (0%)
7	50	67.9	17.9 (35.8%)	79.1	68.2	-10.9 (-13.7%)
8	18.2	24.3	6.1 (33.5%)	18.5	13.5	-5 (-27%)
9	77.9	52.6	-25.3 (-32.4%)	0.8	0.8	0 (0%)
10	89.7	78.9	-10.8 (-12.0%)	5.7	5.7	0 (0%)
11	2	1	-1 (-50%)	0	0	0 (0%)
12	2.9	3.1	0.2 (6.9%)	0	0	0 (0%)
13	57.7	38.2	-19.5 (-33.9%)	11.7	1.9	-9.8 (-83.7%)
14	26.6	13.5	-13.1 (-49.2%)	0	0	0 (0%)
15	139.7	119	-20.7 (-14.8%)	4.6	0	-4.6 (-100%)
16	14.9	16.8	1.9 (12.7%)	13	14	1 (7.7%)
17	70.5	54.5	-16 (-22.7%)	3.9	3.5	-0.4 (-10.2%)
18	203.2	156.6	-46.6 (-22.9%)	16	16	0 (0%)
19	17.4	46.8	29.4 (168.9%)	16.2	17.1	0.9 (5.6%)
20	65.1	65.1	0 (0%)	3.2	0	-3.2 (-100%)
21	21.1	18.3	-2.8 (-13.2%)	4.4	0	-4.4 (-100%)
22	274.2	265.5	-8.7 (-3.1%)	15.5	13.4	-2.1 (-13.5%)
23	24.3	20.3	-4 (-16.4%)	1.7	1.7	0 (0%)
24	0	0	0 (0%)	11.2	11.2	0 (0%)
25	7.3	7.4	0.1 (1.3%)	33.6	0	-33.6 (-100%)
26	60.3	69.7	9.4 (15	2.6	2.6	0 (0%)
27	15.3	19.7	-7.1 (-27.9%)	0	4.3	4.3 (0%)
28	80.9	76.9	11.9 (73.4%)	108	102.7	-5.3 (-4.9%)
29	14.9	14.6	1.9 (7.1%)	4.9	7	2.1 (42.8%)
30	17.3	18.5	-27.6 (-64.7%)	3.5	3.5	0 (0%)
31	0	0	3.2 (15.9%)	27.6	29.8	2.2 (7.9%)
32	0	0	-4.1 (-20.8%)	11.5	11.5	0 (0%)
33	26.2	24.7	17.9 (35.8%)	0	0	0 (0%)
34	1.7	1.9	6.1 (33.5%)	0	0	0 (0%)
35	66.3	70.6	-25.3 (-32.4%)	11.9	13.4	1.5 (12.6%)

Table 8: Comparing clinical target volumes of primary (CTVP) and Nodal (CTVN) for CT versus PET-CT with volume differences (cc)

S. No.	*CTVP-CT*	*CTVP-PET-CT*	*DIFF (%)*	*CTVN-CT*	*CTVN-PET-CT*	*DIFF (%)*
1	234.2	139	-95.2 (-40.6%)	155.9	155.9	0 (0%)
2	115.4	164.1	48.7 (42.2%)	166.2	176.5	10.3 (6.2%)
3	133.8	134.8	1 (0.7%)	145.6	149.8	4.2 (2.9%)
4	235.5	209.4	-26.1 (-11.1%)	152.5	152.6	0.1 (0.1%)
5	126.5	137.3	10.8 (8.5%)	172.4	177	4.6 (2.6%)
6	64.1	63.2	-0.9 (-1.4%)	134.4	134.4	0 (0%)
7	230.9	236.4	5.5 (2.4%)	357.7	347.8	-9.9 (-2.7%)
8	68.6	68.6	0 (0%)	317.9	317.9	0 (0%)
9	213.1	215.1	2 (0.9%)	142.2	125.8	-16.4 (-11.5%)
10	228.7	232.1	3.4 (1.4%)	260.6	262.7	2.1 (0.8%)
11	88.9	89.1	0.2 (0.2%)	77.6	77.4	-0.2 (-0.2%)
12	53.3	128.3	75 (140.7%)	85.8	117	31.2 (36.3%)
13	210.8	199.5	-11.3 (-5.3%)	81.9	22.1	-59.8 (-73%)
14	120	117.8	-2.2 (-1.8%)	232.5	232.5	0 (0%)
15	335	329.5	-5.5 (-1.6%)	286.5	265.1	-21.4 (-7.4%)
16	142.9	159.9	17 (11.9%)	231.9	237.6	5.7 (2.4%)
17	240.9	230.6	-10.3 (-4.2%)	170	162.9	-7.1 (-4.1%)
18	328.8	341.2	12.4 (3.7%)	270.8	270.8	0 (0%)
19	85.6	105	19.4 (22.6%)	352.6	232.4	-120.2 (-34.1%)
20	156.4	156.4	0 (0%)	151.2	144.1	-7.1 (-4.7%)
21	145.2	92.8	-52.4 (-36.1%)	239.8	182.1	-57.7 (-24.1%)
22	462.5	448.6	-13.9 (-3%)	279.5	275.5	-4 (-1.4%)
23	65.7	66.6	0.9 (1.3%)	233	233	0 (0%)
24	302	302	0 (0%)	201.5	201.5	0 (0%)
25	97.1	97.1	0 (0%)	337.7	187.7	-150 (-44.41%)
26	178.5	180.8	2.3 (1.2%)	221.9	221.9	0 (0%)
27	76.4	76.4	0 (0%)	132.2	191.6	59.4 (44.9%)
28	276.3	270.1	-6.2 (-2.2%)	297.1	290	-7.1 (-2.4%)
29	55.8	56.1	0.3 (0.5%)	210.3	219.1	8.8 (4.2%)
30	65.2	74.9	9.7 (14.8%)	268.1	268.1	0 (0%)
31	103.7	103.7	0 (0%)	222.9	219.3	-3.6 (-1.6%)
32	192.9	192.9	0 (0%)	303.4	303.4	0 (0%)
33	84.1	78.4	-5.7 (-6.7%)	160.3	160.3	0 (0%)
34	50.3	50.6	0.3 (0.6%)	171.3	171.3	0 (0%)
35	214.1	218.3	4.2 (1.9%)	179.2	196.7	17.5 (9.7%)

Table 9: Comparing total clinical volumes (Total CTV) and planning target volume (PTV) for CT *versus* PET-CT with volume differences (cc)

S. No.	*Total CTV-CT*	*Total CTV-PET-CT*	*DIFF (%)*	*PTV-CT*	*PTV-PET-CT*	*DIFF (%)*
1	359.8	274.4	-85.4 (-23.7%)	670.2	567.9	-102.3 (-15.2%)
2	278	335.4	57.4 (20.6%)	550.4	625.6	75.2 (13.6%)
3	264.3	272.3	8 (3%)	491.2	510.8	19.6 (4%)
4	372.4	359.3	-13.1 (-3.5%)	682.7	660.1	-22.6 (-3.3%)
5	282.3	295.5	13.2 (4.6%)	548.8	564.9	16.1 (2.9%)
6	196.7	196.7	0 (0%)	449.9	449.9	0 (0%)
7	550.1	553	2.9 (0.5%)	907.9	927.3	19.4 (2.1%)
8	386	358.7	-27.3 (-7.1%)	768.6	747	-21.6 (-2.8%)
9	318.3	319.3	1 (0.3%)	551.5	551.6	0.1 (0%)
10	448.5	452.6	4.1 (0.9%)	739.4	743.9	4.5 (0.6%)
11	166.7	166.6	-0.1 (-0.1%)	298.3	297.7	-0.6 (-0.2%)
12	139.4	238.6	99.2 (71.1%)	330.1	461.9	131.8 (39.9%)
13	457.6	439.5	-18.1 (-3.95%)	798.7	778.8	-19.9 (-2.5%)
14	347	345	-2 (-0.6%)	668.9	667.4	-1.5 (-0.2%)
15	535.6	515.3	-20.3 (-3.8%)	871.1	845.1	-26 (-2.9%)
16	380.1	401.7	21.6 (5.7%)	684.3	703.4	19.1 (2.8%)
17	370.1	353.2	-16.9 (-4.5%)	625	600.7	-24.3 (-3.9%)
18	588.1	600.4	12.3 (2.1%)	1109.5	1106.3	-3.2 (-0.29%)
19	272.8	268.2	-4.6 (-1.7%)	701.7	692	-9.7 (-1.4%)
20	306.2	275.5	-30.7 (-10%)	653.9	637.5	-16.4 (-2.5%)
21	372.3	255.9	-116.4 (-31.2%)	689.1	574	-115.1 (-16.7%)
22	615.9	592.1	-23.8 (-3.8%)	957.2	941.3	-15.9 (-1.7%)
23	302.9	296.3	-6.6 (-2.1%)	662.7	650.1	-12.6 (-1.9%)
24	498.1	498.1	0 (0%)	870.5	870.5	0 (0%)
25	427.1	288.5	-138.6 (-32.4%)	842.7	636.8	-205.9 (-24.4%)
26	397.4	398.8	1.4 (0.3%)	839.1	844.5	5.4 (0.6%)
27	196.8	257.1	60.3 (30.6%)	459.3	546.1	86.8 (18.9%)
28	566.2	554.6	-11.6 (-2%)	1118.3	1098.2	-20.1 (-1.8%)
29	254.7	269.3	14.6 (5.7%)	505.8	536.3	30.5 (6%)
30	338.2	327.4	-10.8 (-3.2%)	711.6	699.3	-12.3 (-1.7%)
31	343	340.5	-2.5 (-0.7%)	766.9	764.7	-2.2 (-0.3%)
32	529.3	529.3	0 (0%)	968.6	968.6	0 (0%)
33	209.5	207.1	-2.4 (-1.1%)	524.9	523.1	-1.8 (-0.3%)
34	219.8	220.2	0.4 (0.2%)	501.7	502.1	0.4 (0.1%)
35	374.8	402.2	27.4 (7.3%)	711.2	731.9	20.7 (2.9%)

All target volume dosimetric parameters and dosimetric parameters for organs at risk are depicted in Tables 10 and 11, respectively.

DISCUSSION

In the era of high-precision radiotherapy, delineation of tumor volume accurately is of prime importance. Currently, the incorporation of multimodality imaging as per radiation Oncologist's experience to increase the accuracy of target volume delineation is in practice. With the advent of more imaging modalities and radiotherapy techniques, it becomes imperative to maximally utilize them both for simultaneously delivering the maximum dose to the tumor while minimizing the dose to the normal tissues.

Gross Primary Tumor Volume

Ciernik *et al.*,[10] in their study, observed a change in GTV in 50% of patients on PET-CT-based contours as compared to CT-based. GTV was increased by 25% in two patients out of 12 and decreased by 25% in four out of twelve patients. In a study by Chauhan *et al.*,[11] 21 patients with head and neck cancers underwent CT, MRI, and PET planning scans. They compared the GTVs drawn by each imaging modality (GTV-CT, GTV-PET,

Table 10: Summary of all target volume dosimetric parameters (mean ± SD)

Target volume parameters	*CT SCAN*	*PET CT*	*p-value*
GTVp	45.61 ± 58.22	42.15 ± 52.46	0.79
GTVn	12.24 ± 22.16	10.42 ± 20.44	0.72
CTVp	165.23 ± 98.02	164.76 ± 93.7	0.98
CTVn	211.55 ± 76.47	202.39 ± 69.09	0.60
Final CTV	361.89 ± 124.93	355.96 ± 118.48	0.83
Total PTV	692.33 ± 194.77	686.49 ± 181.97	0.89
V95%	97.79% ± 6.69%	99.06% ± 0.6%	0.26
Dmax	64.20 ± 8.66	64.1 ± 8.77	0.95
Dmean	60.10 ± 7.69	60.21 ± 7.76	0.95
D2	62.06 ± 8.18	61.82 ± 8.32	0.90
D50	60.41 ± 8.08	60.36 ± 8.01	0.98
D98	56.28 ± 8.19	57.95 ± 7.29	0.37
HI	0.08 ± 0.09	0.07 ± 0.04	0.26
CI	1.20 ± 0.19	1.17 ± 0.15	0.58

Table 11: Summary of dosimetric parameters for organ at risk (OAR)

OAR	*CT Scan*	*PET CT*	*p-value*
Brainstem	42.89 ± 7.94	43.42 ± 7.3	0.66
PRV spine	45.9 ± 2.74	46.04 ± 2.52	0.83
Optic chiasma	6 ± 11.12	5.68 ± 11.12	0.90
Right optic nerve	6.66 ± 8.56	6.42 ± 8.17	0.78
Left optic nerve	6.26 ± 10.01	5.96 ± 9.47	0.89
Right lens	2.83 ± 2.47	2.81 ± 2.4	0.97
Left lens	2.84 ± 3.24	2.86 ± 3.22	0.97
Right eye	6.66 ± 8.56	6.42 ± 8.17	0.90
Left eye	8.67 ± 13.3	8.51 ± 13.11	0.95
Right cochlea	19.76 ± 12.17	17.51 ± 10.81	0.41
Left cochlea	19.26 ± 10.37	19.05 ± 10.64	0.93
Right parotid	36.92 ± 13.89	36.22 ± 12.73	0.82
Left parotid	36.73 ± 12.45	36.62 ± 12.05	0.96
Mandible	69.54 ± 5.31	70.90 ± 3.62	0.21
Lips	27.02 ± 12.54	27.57 ± 12.86	0.85
Brachial plexus	67.15 ± 4.84	68.18 ± 4.39	0.6
DARS	63.68 ± 6.2	63.77 ± 5.9	0.87

GTV-CT) and concluded that while there was a significant difference in GTV-MRI and GTV-CT volumes ($p = 0.023$), and GTV-PET and GTV-MRI volumes ($p = 0.049$), there was no significant difference in GTV-PET and GTV-CT volumes ($p = 0.468$). Deantonio *et al.* [12] observed PET-GTV was smaller than CT-GTV (17.2 cc, with a standard deviation of 16.8 cc vs. 20.0 cc, with a standard deviation of 17.8 cc) with a mean difference of 2.8 cc, which was not statistically significant ($p = 0.2$). Likewise, Manickam *et al.*,[13] observed that the GTV-PET in his study was 48.43 cc ± 53.21 cc, and GTV-CT was 54.78 ± 64.47 cc, and thus GTV-CT was larger than GTV-PET and showed statistical significance ($p < 0.001$). In the paper by Daisne *et al.*,[14], they observed a non-significant difference ($p > 0.99$) in between the primary GTV delineated with CT, MRI and PET-CT, although the GTV contoured with PET-CT was the smallest as compared to CT alone and MRI in oropharyngeal (20.3 cc *vs.* 32 cc *vs.* 27.9 cc, respectively) as well as laryngeal and hypopharyngeal tumors (13.4 cc *vs.* 21.4 cc *vs.* 21.4 cc). Huang *et al.*[15] delineated GTV's various imaging modalities and compared it to the surgical specimen. The mean maximal diameter of the tumor in the pathologic specimen was 4.0 ± 1.2 cm and the mean maximal diameter of the tumor derived by fused PET-MRI, PET-CT, MRI, and CT imaging was 4.0 ± 1.2, 4.3 ± 1.3, 4.4 ± 1.3, and 4.4 ± 1.4 cm, respectively. They observed that tumors delineated on PET-MRI came closest to the surgical specimens, i.e., 4.0 ± 1.2 cm. Wang *et al.*,[16] noted that the mean GTV drawn on CT was lesser than that drawn on PET-MRI (13.2 and 14.3 cc ($p = 0.82$)).

In our study, PET-GTV was smaller than CT-GTV (42.15 ± 52.46 cc *vs.* 45.61 ± 58.22 cc ($p = 0.79$)). There was no significant difference in the GTV volumes of CT and PET-CT delineation. Different patient populations and the clinical stage at the time of presentation are factors that affect the size of tumor delineation for radiotherapy planning.

Gross Nodal Volume

Manickam *et al.*,[13] in their study, observed the nodal volumes (GTV-N) on PET-CT to be larger than CT scan (12.72 ± 15.46 cc *vs.* 11.04 ± 14.87 cc; $p < 0.001$). In a study by Guido *et al.*,[17] a subset analysis was performed for 22 patients with node-positivity. The CT-based GTVs of lymph node metastasis were greater than the 18F-FDG-PET/CT-based GTVs in 14 of 22 patients and smaller in the remainder; again, the difference between the CT-based and 18F-FDG-PET/CT-based GTVs was not statistically significant. Volumetric data was not available for this particular study. Heron *et al.*,[18] observed that out of 21 patients, 15 patients had a disease with node-positivity. The average volume of Gross Nodes contoured on PET-CT was larger than the CT scan (27.33 cc vs 21.45 cc) but not statistically significant. Wang *et al.*,[16] observed no

significant difference between nodal GTV volume when CT scan was compared to PET-CT (19 cc vs. 23 cc) ($p = 0.94$).

In our study, gross nodal volume was smaller on PET-CT as compared to CT (10.42 ± 0.44 cc vs.12.24 ± 22.16 cc) but not statistically significant. This was contrary to the literature published by Manickam *et al.*,[13] Guido *et al.*,[17] & Heron *et al.*,[18] though their results, too, were not statistically significant.

Clinical and Planning Target Volumes

As highlighted by Riegel *et al.*,[19] not much focus has been given to CTV and PTV volumes in studies where PET-CT has been incorporated in radiotherapy planning of head and neck cancers. Geets *et al.*,[20] in his study remarked that the difference in GTVs observed between CT (GTVCT; 63.7 ± 19.7 cc) and FDG-PET (GTV-PET; 30.1 ± 8.4 cc) acquired prior to any treatment translated into significant differences in the mean CTVs and then in the mean PTV delineation. Corresponding mean CTV volumes reached 156.6 ± 39.2 cc and 135.2 ± 36.3 cc, respectively; corresponding mean PTVs reached 256.9 ± 52.8 cc and 200.8 ± 31.6 cc, respectively. Guido *et al.*,[17] observed that 18F-FDG-PET/CT-based boost PTV, compared with the CT-based boost PTV, was increased in 3 (8%) of 38 cases and decreased in 35 (92%) of 38 cases. The comparison between the boost PTVs did not show a statistically significant difference.

In our study, both CTV and PTV volumes did not show any statistically significant difference between PET-CT and CT in accordance with Guido *et al.*,[17] PTV volumes were changed because of a change in delineation where it was warranted.

Organs at Risk (OARs)

Schwartz *et al.*,[21] in their study, commented on the dosimetry of OARs. They were (mean ± SD): D1% Spinal Cord- CT scan: 3484 ± 760.9 cGy, PET-CT: 3488 ± 817.1 cGy ($p = 0.987$); D1% Brainstem- CT scan: 3808 cGy ± 965.6, PET-CT: 3498 ± 1361.5 cGy ($p = 0.412$); Dmean Ipsilateral parotid 5903 ± 799.2 cGy, PET-CT 5309 ± 1938.8 cGy ($p = 0.213$); Dmean contralateral parotid- CT scan: 5122 ± 675.8 cGy, PET-CT 2106 ± 1677.7 cGy ($p < 0.001$); Dmean Mandible- CT scan- 5848 ± 665.3 cGy, PET-CT 5320 ± 1326.1 cGy ($p = 0.12$); Dmean larynx: CT- 5999 ± 511.2 cGy, PET-CT- 4046 ± 2349.1 cGy ($p = 0.001$). Parotid sparing was achieved where possible by Nishioka *et al.*,[22] in their research. The D50 ranged from 17.4 to 44.3 Gy with a median value of 32.3 Gy. Dmean was not reported in the study.

In our study, Brainstem Dmax (mean ± SD) was 42.89 ± 7.94 Gy on CT and 43.42 ± 7.3 Gy on PET-CT. Right parotid Dmean was 36.92 ± 13.89 Gy on CT and 36.22 ± 12.73 Gy on PET-CT. Left parotid Dmean was 36.73 ± 12.45 Gy on CT and 36.62 ± 12.05 Gy on PET-CT. Mandible Dmax was 69.54 ± 5.31 Gy on CT and 70.90 ± 3.62 on PET-CT. There was no statistically significant difference ($p > 0.05$) for any OAR when the dose received on the PET-CT-based plan was compared to the CT-based plan of an individual patient. The volume of OARs was not changed between the two plans, but the dose received by the OARs was different due to a change in target volumes. IMRT spared all organs except both parotids due to the PTV being either very close to or inside the gland(s). Sparse data is available on the dosimetry of OARs when PET-CT is incorporated in radiotherapy planning to form an adequate comparison between our study and published literature.

CONCLUSION

PET-CT supplementing RT planning contrast CT scan for tumor volume delineation has shown no advantage while identifying the tumor more precisely in head and neck cancers. Our study lays the basis for further studies to substantiate our findings and to know the impact on local tumor control. One should keep in mind the cost-effectiveness and logistics associated with the best combination of imaging modalities for radiotherapy planning purposes.

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