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Original Article

A Comparison of Gross Tumour Volumes between 18-FDG PET-CT Scan and CECT Scan in Radiation Planning of Locally Advanced Unresectable Oral Cavity Cancers

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Abstract

Introduction: *Head and neck cancers are the seventh most cancer with 30% from Indian population, of which 16% are oral cavity cancers .70% patients present with locally advanced unresectable disease with substantial risk of cervical node metastasis for which CTRT is the definitive treatment. Detecting metastatic cervical nodes with conventional imaging techniques has limitations which are solved by noninvasive 18F FDG PET CT Scan. Using PETCT scan to delineate the GTV of primary tumor and nodal is compared with planning CECT in this study.*

Objectives: *To define radiation planning volumes (Gross tumor volume for tumor and lymph nodes) with 18F FDG PETCT compared to CECT scan.*

Material and Methods: *25 biopsy proven patients with oral cavity tumors were assessed prospectively for a study period of 2 years from 2020 to 2022 in a single tertiary cancer institute. All the patients underwent PETCT scan and was registered to planning CECT scan where the volumes are compared in cc.*

Statistical Analysis: *paired T test with all correlations done using chi square test with $p<0.05$ considered statistically significant.*

Results: *Of all 25 patients, 88% males and 12 % female patients with most fall below 51 years 81%(15) and 10%(10) above 51 years. Out of all subsites Buccal mucosa 52%, Oral tongue 32% , retro molar trigone 8%,alveolus 8% and floor of mouth 4%. Most patients have squamous cell carcinoma as histology. On assessing GTV volumes of primary tumor and nodes in planning CECT scan and fused 18F-FDG PET CT scan the mean volume GTV P(primary) of CECT scan is 61.07 cm3 with standard deviation of 55.704cm3 and on PETCT mean is 47.80 cm3 with standard deviation of 29.783 cm3, p value <0.037 with mean difference of 13.26cm3. The mean of GTV N (nodal) in CECT is 20.41 cm3 with standard deviation of 18.719cm3 compared to PET mean of 16.29 with standard deviation of 16.678cm3, p value <0.007 with the mean difference of 4.11cm3.*

Conclusion: *On reviewing the above results, using FDG PET CT scan in planning CECT scan may decrease the GTV p and GTV n, which further may decrease the planning volume.*

Keywords: *Oral cavity cancers, Radiotherapy, GTV delineation, PETCT GTV delineation, CECT GTV delineation, Target Volumes, PETCT Vs CECT GTV.*

Introduction

Globally, Head and Neck Cancer ranks as the seventh most prevalent cancer, affecting approximately 878,000 patients annually. In India alone, the annual incidence ranges from 0.2 to 0.25 million cases, contributing significantly to the global burden, with 57.5% of cases originating from Asia, particularly India. Within India, Head and Neck Cancer accounts for 30% of all cancer cases1[1].Oral cavity cancers are more prevalent in Asian, especially in south and southeast Asia predominantly in India [2] which affects around 370,000 individuals worldwide, with approximately 135,000 cases occurring in India, constituting nearly one-third of the global incidence. Notably, Oral Cancer stands as the most prevalent cancer among men in India, comprising 16% of all cases, and the fourth most common among women, comprising 4.6% of all cases with concerning trend emerges with 70% of Oral cavity cancers diagnosed at advanced stages resulting in a mere 20% five-year survival rate3[3]. Treatment modalities are contingent upon tumor stage and nodal disease burden, necessitating a multidisciplinary approach for early stage oral cancer while definite chemo radiation became standard of care for unresectable oral cancers4[4]. Oral cavity carries a substantial risk of cervical lymph node metastases which impacts survival[5] and, often undetected due to their small size, prompting routine elective irradiation to clinically uninvolved nodal targets in definitive (chemo)radiotherapy[6]. Conventional imaging techniques like CT and MRI have limitations in differentiating metastatic from non-metastatic lymph nodes[(6,7)],which always needed a Ultrasound guided fine needle aspiration for confirmation[8] which made impossible to assess every node, however a mere radiological criteria to identify metastatic nodes is addressed [8] still underscoring the need for molecular imaging modalities like18F- FDG-PETCT(18F fluorodeoxyglucose positron emission tomography computer tompography) [26].As most locally advanced oral cancer patients with nodal burden receive concomitant radiotherapy as definitive treatment , which impacts quality of life with acute and late toxicities[26] with nutritional implications[11] which are decreased by limiting irradiated area with conformal radiation therapy planning by delineation of primary tumor ,positive nodes and nodal levels usually done on a planning CT scan[12]. Using FDG-PETCT for primary and nodal target delineation in radiotherapy planning, potentially altering treatment strategies for one in every four patients compared to conventional imaging[13,14,15]. The impact of improved nodal detection by FDG-PET/CT on radiotherapy outcomes needs further investigation, which this prospective analysis aims to compare the GTV

volumes delineated in planning CT scan and by using PET CT scan in radiation planning of oral cavity cancers.

Material and Methods

Patient Selection

Patients of oral cavity cancers who attended between 2020 to 2022 at department of Radiation Oncology from a single tertiary cancer institute in Hyderabad, India are assessed prospectively and observed. A 25 Histologically proven squamous cell carcinoma/adenocarcinoma/adenosquamous carcinoma of oral cavity with PS of 0-2 aged between 20-70years with TNM stage T1 to T4, N1to N3 patients are included with proper informed written consent. Patients with metastatic, multiple malignancy, prior radiation and renal failure contrast allergic patients are excluded.

Ethical Consideration

The analysis was conducted according to principles of ethics for medical research and approved by Institutional Ethic Committee (reference no ECR/300/Inst/AP/2013/RR-16).

Aim

To investigate the benefits of PET/CT on defining radiotherapy planning volumes of head and neck cancer patients compared planning CECT (Contrast enhanced computer tomography) scan.

Objective

Define RT planning GTV (Gross tumor volume for tumor and lymph nodes) with 18-FDG PET-CT scan findings compared to CECT scan at diagnosis.

Work up

Pre- treatment evaluation including detailed history and physical examination done. Local examination of the oral cavity for the extent of the disease and neck for any clinically palpable lymph nodes. Base line tests are done including Hemogram, Blood sugar, Kidney function test, Liver function test. Biopsy for histopathological confirmation and after taking proper informed consent, Patient is advised to get a CECT scan neck and 18F-FDG PET CT Scan not exceeding the interval gap over 1 week. According to AJCC 8th edition oral cavity TNM staging[13], clinical staging is done by CECT neck as T, N and M as well with 18F-FDG PETCT Scan in treatment position. Prior to the initiation of radiation, a careful oral and dental evaluation, including a panoramic radiograph, should be performed.

CECT neck for tumor and nodal staging.18-FDG PET CT Scan for staging and in CD in DICOM format for fusing with planning CT scan.

Treatment Planning

CT simulation with IV contrast 50ml/kg body is done in all patients with proper immobilization with head and neck ray cast. CT scan is imported to the treatment planning system (TPS) for planning radical radiotherapy using conventional or conformal radiation technique. CD with PET CT scan in DICOM format of the patient is imported and fused with the planning CT scan with minimum margin of error. GTV P and GTV N are contoured in planning CT scan and volume is measured in cc. With the help of PET CT scan another GTV P(figure 1A &1B)and GTV N is contoured and volumes in cc is measured for both. The clinical target volume (CTV) is defined as per radiation planning guidelines for the stage and subsite for IMRT planning by TMH guideline [4]and DAHANCA Gregoire V[12] guidelines for contouring twenty-five. Patients are treated with IMRT radiation technique for 66-70gy, 2G per fraction in thirty-three -35 fractions 5 days per week with concomitant chemotherapy with cisplatin (@40 mg/m^2) or carboplatin (AUC 2) as per NCCN[4,16].

Methods of Measurement

Volume (cm^3) is measured by contouring the GTV and measuring the volumes in eclipse software of Varian systems.

Statistical Methods

The objective is to compare the GTV P and GTV N of CECT scan PET CT and analysis was done

by Paired t test. All correlations are done using the chi square test. $p<0.05$ was considered statistically significant. All potential prognostic factors were analyzed. Graphical presentations like pie charts and bar diagram were used.

Results

Among the cohort of twenty-five patients under study, a notable gender distribution is observed, with 88% being male and 12% female. The majority of patients, comprising 81% (15 individuals), are below the age of fifty-one, while 10% (10 individuals) fall above this threshold. Analysis of the anatomical subsites affected reveals a distribution where Buccal Mucosa accounts for 52% of cases, followed by Oral Tongue at 32%, Retro Molar Trigone at 8%, Alveolus at 8%, and Floor of Mouth at 4% (table 1). Histologically, the predominant pathology observed among these patients is squamous cell carcinoma, indicating a common underlying etiology. Upon assessment of Gross Tumor Volume (GTV) volumes derived from planning Contrast-Enhanced Computed Tomography (CECT) scans and fused 18F-Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography (PET-CT) scans, distinct differences in tumor volumes are noted. The mean volume of GTV Primary (GTV P) derived from CECT scans is calculated at 61.07 cm^3, with a standard deviation of 55.704 cm^3. In contrast, the mean GTV P volume obtained from PET-CT scans is notably lower at 47.80 cm^3, with a standard deviation of 29.783 cm^3(figure 2A). Statistical analysis reveals a significant difference between the two modalities, with a p-value of less than 0.037 and a mean difference of 13.26 cm^3(figure 2A). Similarly, evaluation of GTV Nodal (GTV N) volumes demonstrates variations between CECT and PET-CT imaging modalities. The mean GTV N volume derived from CECT scans is measured at 20.41 cm^3, with a standard deviation of 18.719 cm^3, while the mean GTV N volume from PET-CT scans is slightly lower at 16.29 cm^3, with a standard deviation of 16.678 cm^3. Statistical analysis reveals a significant discrepancy between the two techniques, with a p-value of less than 0.007 and a mean difference of 4.11 cm^3(figure 2B). These findings underscore the importance of selecting appropriate imaging modalities and accurately delineating tumor volumes to optimize treatment planning and therapeutic outcomes for patients with Oral cavity Cancer.

Diagnosis of Study Population:

Diagnosis	No. of Subjects	Percentage
Retro Molar Trigone	2	8.0%
Oral Tongue	8	32.0%
Buccal Mucosa	13	52.0%
Alveolus	2	8.0%
Total	25	

Table 1: Distribution of Anatomical Subsites Affected by Head and Neck Cancer This table illustrates the distribution of anatomical subsites affected by Head and Neck Cancer among a total of 25 patients. Buccal Mucosa accounts for the highest percentage of cases at 52%, followed by Oral Tongue at 32%, Retro Molar Trigone at 8%, Alveolus at 8%, and Floor of Mouth at 4%.

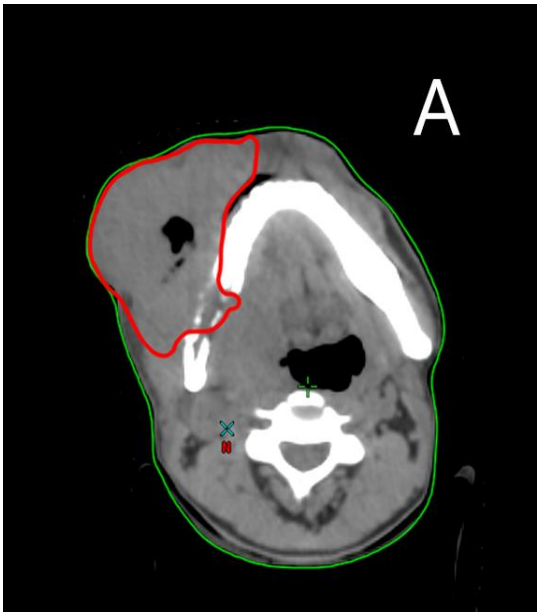

Figure A: GTV P Visualization from CECT Scan in Carcinoma of the Right Buccal Mucosa.

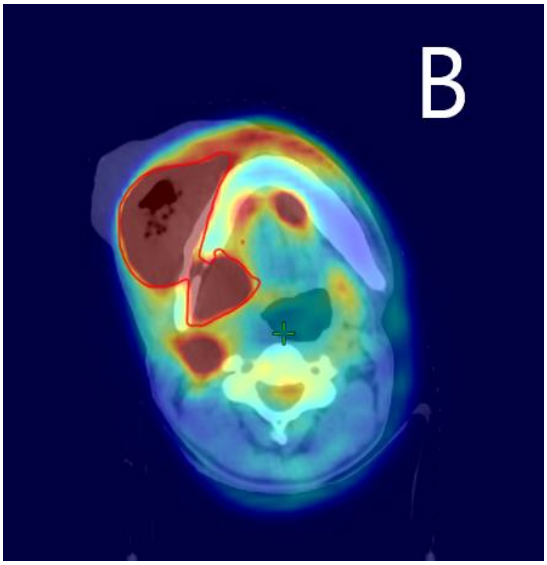

Figure B: GTV P Visualization from PET-CT scan Registered with Planning CECT.

The tumor volume is highlighted in red color for enhanced visibility. The GTV P delineation provides a detailed visualization of the extent and distribution of the tumor within the right buccal mucosa region, aiding in treatment planning and therapeutic decision-making for patients diagnosed with carcinoma in this anatomical site.

GTV P (red) Gross tumor volume Primary, CECT-contrast enhanced computed tomography.

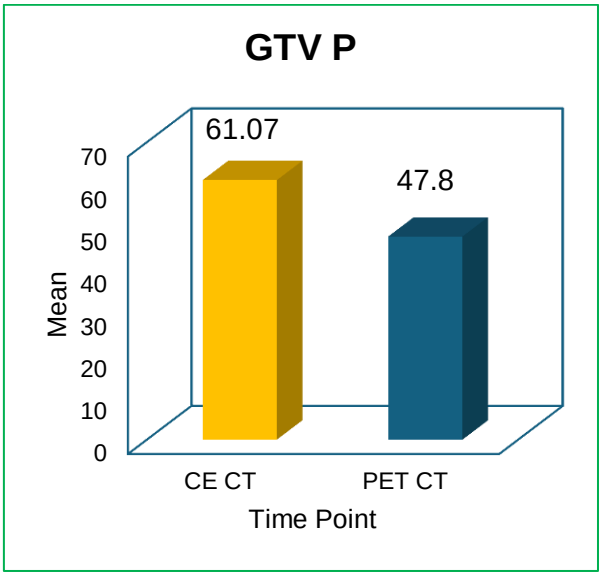

Figure 2 A: Assessment of GTV P Volumes from Planning CECT and Fused 18F-PET-CT Scans.This figure illustrates the assessment of GTV volumes obtained from planning CECT scans and fused 18F-PET-CT scans. The mean volume of GTV P derived from CECT scans is visualized alongside the mean GTV P volume obtained from PET-CT scans. Statistical analysis highlights a significant difference between the two modalities, with a p-value of less than 0.037, indicating distinct differences in tumor volumes.

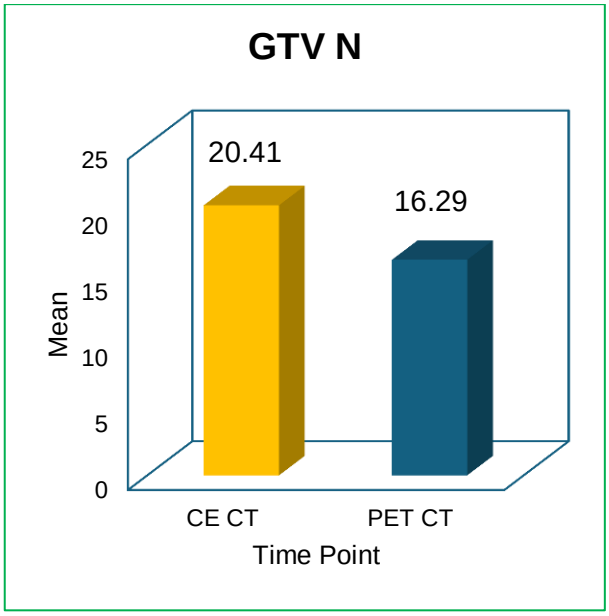

Figure 2B: Evaluation of GTV N Volumes from CECT and PET-CT Imaging Modalities This figure illustrates the evaluation of GTV N volumes obtained from CECT and PET-CT imaging modalities. The mean GTV N volume derived from CECT scans is compared to the mean GTV N volume from PET-CT scans. Statistical analysis highlights a significant discrepancy between the two techniques, with a p-value of less than 0.007 and a mean difference of 4.11 cm3.

Discussion

The study aims to analyze the comparison of the volumes of the GTV p and GTV n in planning CT scan alone and 18 FDG PET scan when fused in planning CT scan in oral cavity tumors such as lip, buccal mucosa, oral tongue, gingivobuccal sulcus, alveolus, hard palate, and retro molar trigone which are the sub-sites of the oral cavity.

A total of twenty-five patients are taken into study with various sub-sites in oral cavity tumors. In

which males are 88% (22) predominant than females 12% (3). Most of the patients fall in age below 51yrs with15(81%) and 10(19%) above 51 yrs. Out of all sub-sites, patients with buccal mucosa are 13(52%), oral tongue are 8(32%), retro moral trigone are 2(8%), alveolus are 2(8%) and floor of mouth are 1(4%). Most of the patients have well differentiated squamous cell carcinoma as histology followed by moderately differentiated squamous cell histology and poorly differentiated squamous cell carcinoma.

Staging a tumour plays a key role in managing oral cavity tumour. Staging is done as tumour(T), node(N) and metastasis(M) according to AJCC 8th edition and staged accordingly based on them[17]. Accurate staging of tumours helps in choosing appropriate treatment which benefits the patient. As the years pass, modalities in detecting the tumour have evolved from x-rays to CT scans, MRI, and PET CT scans by understanding the tumour pathology. In clinical practice, the conventional diagnostic strategy of HNSCC patients includes detailed physical examination and endoscopy followed by imaging modalities such as neck ultrasound, neck MRI and neck-chest CT for the assessment of disease extent and diagnosis of synchronous second primary tumors (SPTs). Recent studies have shown that 18F-FDG PET-CT is more accurate than conventional staging in HNSCCs, thus resulting in a change of therapeutic management in about one-third of patients [18]. A metanalysis done by Seong-Jang Kim suggested the low sensitivity and moderate specificity of 18FDG PET CT scan in detecting nodal metastasis in head and neck cancers [19].

External beam radiotherapy plays a significant role in both unresectable and as adjuvant therapy in oral cavity tumours. It reduces morbidity and preserves the functional anatomy of the surrounding organs with minimal adverse effects. Radical chemo-radiation is the primary mode of treatment in unrespectable oral cavity tumours. With the change in era, radiation techniques also evolved from conventional to conformal planning sparing normal OAR's which reduces the acute and chronic toxicities.

Over the course of time defying the volumes of the tumour has become much easier using CT scan in planning radiation, yet it has its own pitfalls in defining tumour and nodal metastasis which may increase or decrease the treating volume on the patient. Treating the higher volumes may increase the toxicities and may be difficult in continuing the treatment. And treating lower inaccurate volumes may lead to recurrences. Overcoming such issues and defining appropriate and accurate volumes to the tumour and nodes fusing of other imaging techniques may help. Such imaging includes MRI and 18 FDG PET CT scan. Yet using MRI may give false negative results. Therefore 18 FDG PET CT scans are used in this study to determine tumour volumes compared to MRI as a study conducted by Yeşim Ceylan[20].

All the patients in the study group underwent CECT scan and PET CT scan within a week to avoid errors due to delay in imaging. On comparing the tumor(T) of PET CT scan to the CECT neck, statically there is a correlation of PET CT scan in staging compared to the CECT neck with p value <0.001 which is considered as significant and PET CT scan can be used in staging tumors. On comparing the nodal staging of PET CT scan with the CECT neck, it also revealed the significant correlation of the PET CT with CECT neck. A study by Johannes Czernin suggested that PET CT has an advantage in staging tumours[21].

The tumor volumes of the primary tumor GTVp and nodal volumes GTVn which are measured in CECT of planning and FDG PET CT scan when fused with planning CT scan. As the result revealed, the GTVP of primary tumor is more in CECT when compared to FDG PET CT scan when fused with planning Ct. Which declares that GTVp volume when fused with PET CT gives a lesser volume when compared to CECT and can help in deliver optimal radiation which decreases the radiation toxicities.

The GTVn volumes when compared revealed the lesser volumes when fused with PET CT and the higher volumes by CECT in planning CT when compared. In the initial experience of Daisne et al., gross tumour volume (GTV) delineated from 18F-FDG PET was closest to the pathologic GTV from surgical specimens, and significantly smaller than GTV delineated by CT and MRI [20]. Further applications of 18F-FDG PET-CT for radiotherapy planning are under clinical investigation and include the possibility of directing dose escalation to 18F-FDG-avid sub-volumes of the tumor as well as adapting the radiotherapy plan during treatment thanks to the information on the biological and molecular tumor changes induced by therapy [21].

Conclusion

Based on the results of the study, it is concluded that using 18F-FDG PET CT scan with the planning CECT scan may decrease the volumes of the GTV p and GTV n. However, response to the PET CT based planning must be assessed to predict the outcomes and toxicities.

Limitations

Smaller sample size, to predict the exact outcome higher sample size may be required.

Obtaining PET CT images to fuse with planning CT in treatment position.

It is a single institutional study, and results would vary with multi-institutional study, as our most our patients belong to low socioeconomic, poor nutritional status and social factors.

Conflict of interest

No author is benefited from the study and has no conflict of interest related to this manuscript.

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