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# Role of 18F-FDG-PET/CT Scanning in Management of Patients with Locally Advanced Head and Neck Cancer

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***Abstract:***
*Purpose: to compare between 18F-FDG-PET/CT versus CT scan in staging, target volumes delineation, and monitoring response to therapy in patients with locally advanced Head and Neck Squamous cell carcinoma treated by concurrent radiotherapy with systemic therapy.*
*Patients and Methods: 31patients with histologically confirmed primary HNSCC were enrolled. All patients had planning CT and combined PET/CT in treatment position. All the GTVs (for the primary and nodal disease) were defined from both 18F-FDG-PET/CT (GTV- PET) and CT (GTV- CT). A 40% intensity level relative to the tumor maximum (SUV max) was used to delineate the margins of the GTV- PET.The CTVs, as well as the PTVs, were created from the GTV s. All volumes had been measured and expressed in cubic centimeters. PET-CT and CT scan had been performed 12 weeks after completion of treatment.*
*Results: PET resulted in change of stage for 3 cases, 2 was up staged to metastatic disease (1 of them was excluded and patient was treated with palliative intent) and 1 was down staged. GTVs delineated using CT scan (C-GTV) were larger than those delineated using combined PET/CT scan (PET-GTV) with median volume of 31.71cc compared to 15.13cc of (C-GTV) and (PET-GTV) respectively with high statistical significance (P < 0.001). The PTV-Boosts volumes ranged 48.52 - 157.92 cc and 47.31 - 155.8 in PTV-CT-Boost and PTV-PET-Boost respectively, with larger PTV- CT- Boost median (96.23 cc)versus(93.58 cc) for PET/CT(P<0.001).No statistically significant difference in the volumes when applied to nodal GTVs, CTVs and PTVs. PET/C and detecting residual disease yet this was not statistically significant (P= 0.824).*
*Conclusion: the use of PET/CT resulted in change of disease's stage, the primary tumor and nodal GTVs were changed with the implementation of combined PET/CT; that translate into a smaller and statistically significant difference in GTV of the primary tumor and PTV- boost, however, such difference in the volumes was not statistically significant when applied to nodal GTVs, CTVs and PTVs. PET/CT is superior than traditional imaging modality in evaluating response to therapy and detecting residual disease.*

***Keywords:*** *(18F-FDG-PET/CT scanning, Locally Advanced Head and Neck cancer, GTV- PET, GTV- CT, target volumes delineation, gross tumor volume)*

## 1. Introduction

Head and neck cancers account for approximately 4% to 5% of all the malignant diseases (1). Head and neck squamous cell carcinoma (HNSCC) comprises the vast majority of head and neck cancer (HNC). Unfortunately, at the time of initial diagnosis more than 50% of patients already present with regional nodal metastases or even distant metastases. For all stages, the 5-year survival is approximately 50%. Of patients for whom therapy fails, 90% will have recurrent disease within the first 2 years after treatment (2).

Oncologic imaging plays an important role in head and neck cancers as imaging findings can aid significantly detection, staging, restaging, and therapy response assessment of these tumors ***(1,2)***. Positron Emission Tomography (PET) has found its role in the diagnosis, staging, prognosis, treatment planning and evaluation of treatment response. The incorporation of PET in radiotherapy treatment planning has revolutionized the field of radiation oncology***.***

With the introduction of advanced radiotherapy treatment techniques like 3-D conformal radiotherapy (3-D CRT) and intensity modulated radiotherapy (IMRT), it is of utmost importance to delineate the target volume precisely in order to achieve a good tumor control**.** As of now, CT is the most used imaging modality for 3-D treatment planning as it provides information about the tissue densities in the form of electron density which is required for radiotherapy dose calculation. To utilize PET in radiotherapy, it should be fused either with CT or MRI. An integrated PET-CT is the best option, it provides precise localization of lesions and improves the standardization of volume delineation compared with that of CT alone [3]**.** Using PET-CT in radiotherapy planning reducing inter observer variability in target delineation, and modifying the extension of tumor volumes including gross (GTV), clinical (CTV) and planning target volumes (PTV) and consequently allowing additional dose escalation for both primary tumor and regional lymph nodes. In some cases, the intent of treatment could also change from curative to palliative if distant metastases have been detected by PET [1,4]**.** The aim of this study is to compare between combined 18F-FDG-PET/CT versus CT scan in Staging, target volumes delineation, and monitoring response to therapy in patients with locally advanced Head and Neck Squamous cell carcinoma treated by concurrent radiotherapy and systemic therapy.

## 2. Patients and Methods

### *2.1. Patients Eligibility*

Between January 2013 and March 2015, 30 patients with primary histologically confirmed squamous cell carcinoma of the head and neck were prospectively enrolled in the study. Their ages ranged between 18 and 70 years old, all had measurable disease of stages III, IV A, IV B, classified according to the International Union Against Cancer staging criteria (7th edition 2010). Performance status according to ECOG scale was ≤ 2. All patients provided informed consent for treatment. The study was approved by the Ethical Committee of Scientific Research- Faculty of Medicine- Ain Shams University.

All patients had pretreatment evaluation including: Complete medical history, Complete physical examination, assessment of the performance status according to ECOG scales, full E.N.T examination and endoscopy. Biopsies from the primary lesion and lymph nodes were performed for histopathological confirmation. CBC, renal functions, liver function, serum electrolytes, and creatinine clearance were evaluated. All patients underwent diagnostic C.T scan and/or MRI of primary site and regional lymph nodal areas. Pretreatment dental evaluation and prophylaxis, nutritional assessment as well as audiogram were done.

### *2.2. 18F-FDG-PET/CT and CT Image Acquisition*

All the patients were immobilized with a customized thermoplastic mask fixed to a flat tabletop. PET/CT was done using a standard procedure. Each patient, who had fasted for ≥6 h, and in absence of antidiabetic therapy, was injected with 18F-FDG, images were obtained 60–80 min after injection. The scan was performed with a dedicated PET-CT scanner. The field of view of PET/CT is from the skull to the thigh.PET/CT acquisition was performed in the treatment position. The data sets obtained and imported on a workstation treatment planning system. Each patient, immediately after PET/CT scanning, underwent RT planning CT in the same position as that used for PET/CT. All treatment planning CT scans sent to the same workstation treatment planning system.

### *2.3. Delineation of Target Volumes*

Radiotherapy volumes treated; were the extent of the tumor at diagnosis according to ICRU 62 report. Physical examination, Contrast-enhanced CT and/or MRI, ± Endoscopic findings of the primary tumor and regional disease had been used to tailor the radiotherapy portals and target volumes.GTV: gross tumor volume (primary or nodal disease), CTV (clinical target volume): including GTV + margin (according to the site), potential routes of spread and the entire lymphatic drainage of the neck. PTV (the planning target volume): is CTV+ 3-5mm margin.

All the GTVs (for the primary and nodal disease) were defined from both 18F-FDG-PET/CT (GTV- PET) and CT (GTV-CT). The CT-based GTV was drawn without the information from the FDG-PET scans. The 18F-FDG-PET–positive regions were interpreted as malignant on the emission images. A 40% intensity level relative to the tumor maximum (SUV max) was used to delineate the margins of the GTV PET.The CTVs, as well as the PTVs, were created from the GTV s. All volumes had been measured and expressed in cubic centimeters.

All patients were included in a follow-up program that began 2 months after RT completion, PET-CT and CT scan with contrast enhancement had been performed in the third month of follow-up (12 weeks after completion of treatment). Response was evaluated according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1

The Primary objective was to analyze the differences in tumor volumes obtained by the two modalities of measurement during conformal radiotherapy planning, CT and combined 18F-FDG-PET/CT, while the Secondary objectives were to evaluate the impact of using PET/CT on changing the pretreatment staging obtained by traditional imaging modalities (CT and/ or MRI), And to evaluate metabolic response using PET/CT versus radiological response using CT scan.

*2.4. Results*

30 patients, 23 men (76.7%) and 7 women (23.3%) were prospectively enrolled in the study between January 2013 and March 2015. The age ranged between 25-70 year, the median age was 54.5 year and a mean age of 53.13 ± 10.41. Regarding the primary site, 10 patients (33%) had nasopharyngeal carcinoma, 7 patients (23.3%) with cancer of the oropharynx. 6 (20%) patients had oral cavity tumors, 3 patients (10%) had laryngeal cancer, another 3 patients (10%) presented with carcinoma of the hypopharynx while only one patient had maxillary sinus carcinoma represents 3.3% of the cases. In the beginning of the study, we included one patient with stage IVA glottic carcinoma but this patient was excluded because PET/CT up staged his status to be IVc with lung metastases so the patient was treated with palliative intent.

| | No. | % |
|---|---|---|
| **Gender** | | |
| Male | 23 | 76.7 |
| Female | 7 | 23.3 |
| **Age (years)** | | |
| ≤50 | 9 | 30.0 |
| >50 | 21 | 70.0 |
| Min. – Max. | 25.0 – 70.0 | |
| Mean ± SD. | 53.13 ± 10.41 | |
| Median | 54.50 | |
| **Performance Status** | | |
| ECOG 0 | 9 | 30.0 |
| ECOG 1 | 18 | 60.0 |
| ECOG 2 | 3 | 10.0 |
| **Smoking** | | |
| Non-smoker | 9 | 30.0 |
| Smoker | 21 | 70.0 |

*Table 1: Demographic data of the patients*

| Site | No. | % |
|---|---|---|
| **Hypopharynx** | 3 | 10.0 |
| **Para nasal Sinus** | 1 | 3.3 |
| **Oropharynx** | 7 | 23.3 |
| **Oral Cavity** | 6 | 20.0 |
| **Nasopharynx** | 10 | 33.3 |
| **Larynx** | 3 | 10.0 |

*Table 2: Distribution of the studied cases according to site of primary disease*

10 patients accounting for 33.3% had stage III disease and 20 patients (66.7%) with clinical stage IV, 15 (50%) of them had stage IVA and 5 patients (16.7%) presented with stage IVB. Compared to PET staging shown in table (3), there were 11 patients with stage III disease accounting for 36.7%, and 19 patients (63.3%) had stage IV disease (13 patients had stage IVA).

| | Clinical Stage | | PET- Stage | |
|---|---|---|---|---|
| | No. | % | No. | % |
| III | 10 | 33.3 | 11 | 36.7 |
| IV | 20 | 66.7 | 19 | 63.3 |
| IVA | 15 | 50 | 13 | 43.3 |
| IVB | 5 | 16.7 | 5 | 16.7 |
| IVC | | | 1 | 3.3 |

*Table 3: Distribution of the studied cases according to clinical stage compared to PET stage (n = 30)*

The PET/CT scanning resulted in down staging of 1 case with carcinoma of the larynx from stage IVA to stage III as the nodal stage was changed to N1by PET, the suspicious lymph node on the right side of the neck seen in CT scan was proved to be negative by FNAC confirming the PET results. Another case was up staged from IVA to IVC as PET showed active lesion in D4 dorsal vertebra.

PET resulted in change of stage for 3 cases, 2 was up staged to metastatic disease (1 of them was excluded and patient was treated with palliative intent) and 1 was down staged as shown in (Table 4) comparing the 2 modalities of diagnosis and pretreatment staging.

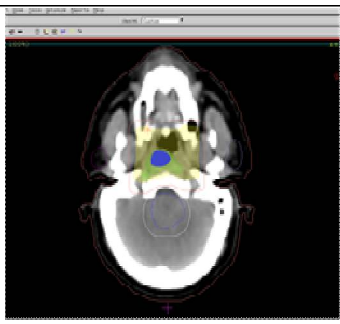
| No. of case | Site | Clinical stage | PET stage |
|---|---|---|---|
| 1(excluded) | Larynx | T4N1M0<br>Stage IVA | T4N1M1 (lung)<br>Stage IV C |
| 2 | Larynx | T3N2M0<br>Stage IVA | T3N1M0<br>Stage III |
| 3 | Nasopharynx | T4N1M0<br>Stage IVA | T4N1M1 (bone)<br>Stage IVC |

*Table 4: Changes of pretreatment clinical stage related to PET/CT*

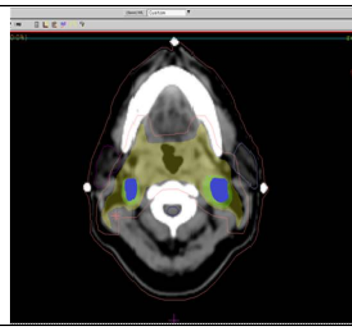
Table (5) shows that GTVs delineated using CT scan (C-GTV) were larger than those delineated using combined PET/CT scan (PET-GTV) with median volume of 31.71cc compared to 15.13cc of (C-GTV) and (PET-GTV) respectively with high statistical significance **(P < 0.001)**. (PET-GTV) was smaller than (C-GTV) by a mean of 15.5 cc which represents 47.3% reduction in the gross tumor volume using PET/CT compared to clinical and traditional imaging modalities.

| | C-GTV | PET-GTV | Wx | p |
|---|---|---|---|---|
| Min. – Max. | 2.82 – 70.20 | 3.20 – 59.24 | 4.659* | <0.001* |
| Mean ± SD. | 32.78 ± 18.18 | 17.27 ± 12.52 | | |
| Median | 31.71 | 15.13 | | |
| **Change** | ↓15.5 | | | |
| **% of change** | ↓47.3% | | | |

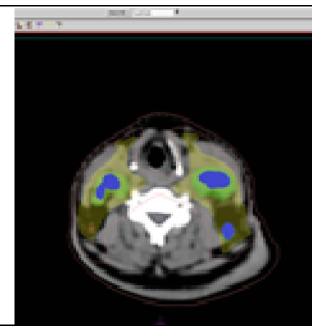
*Table 5: Descriptive analysis of the studied cases according to Gross tumor volumes using CTscan (C-GTV) versus PET/CT (PET-GTV) (n = 30)*
*p: p value for Wilcoxon signed ranks test for comparing between C-GTV and PET-GTV*
**: Statistically significant at p ≤ 0.05*



A: GTV-PET/CT (blue)versus GTV- CT (green) of nasopharyngeal lesion



B: GTV-PET/CT (blue)versus GTV- CT (green) of lymph nodes of neck level II



C: GTV-PET/CT (blue)versus GTV- CT (green) of lymph nodes of neck level III/ and V

*Figure 1: GTVs at Nasopharynx and different levels of neck nodes basins*

The clinical target volumes delineated using CT scan (CT based CTV) and PET/CT scan (PET-CTV) were compared, the PET-CTV was smaller than CT based CTV but yet non-statistically significant (P= 0.14).The PTVs drown using CT scan were comparable to PTVs delineated using PET/CT scan (P= 0.221).

(Table 6): The PTV-Boosts (phase 3) delineated to boost the gross tumors were also compared, they ranged 48.52 - 157.92 cc and 47.31 - 155.8 in PTV-CT-Boost and PTV-PET-Boost respectively with PTV- CT- Boost median of 96.23 cc which was **larger** than the PTV-PET-Boost median 93.58 cc with high statistical significance (P <0.001)

| | PTV-CT-Boost | PTV-PET-Boost | Wx | p |
|---|---|---|---|---|
| Min. – Max. | 48.52 - 157.92 | 47.31 - 155.8 | 4.782* | <0.001* |
| Mean ± SD. | 98.99 ± 30.83 | 96.83 ± 30.85 | | |
| Median | 96.23 | 93.58 | | |

*Table 6: Descriptive analysis of the studied cases according to Planning target volumes Boosts (PTV-CT-Boost) versus (PTV-PET-Boost)*
*p: p value for Wilcoxon signed ranks test for comparing between C-GTV and PET-GTV*
**: Statistically significant at p ≤ 0.05*

The clinically detected gross tumor volumes of the enlarged neck lymph nodes (C-GTV-LN) were almost of the same volumes as those detected by PET/CT scan with slightly larger median volume of (C-GTV-LN) compared to PET-GTV-LN without statistical significance (P=0.171) and (P= 0.062) for left and right neck nodes respectively.

The complete clinical responses detected using CT scan and or MRI compared to that detected using PET/CT scan were similar in both groups (53.3% in each). One of the cases had complete clinical response but residual lesion in oropharynx was detected by PET/CT scan and confirmed by biopsy, this patient received additional radiation boost of 6 Gy after which she achieved complete resolution of the lesion as seen in the second follow up PET/CT scan. Another case of the nasopharynx had residual lesion seen in CT scan while PET/CT showed no suspicious lesion denoting complete response which was confirmed by biopsy that revealed no residual malignancy.

There were 2 cases evaluated by CT scan to have less than partial response (no response) while PET/CT scan showed evidence of partial response, by clinical examination the patient was labeled as having respectable disease and she underwent right partial glossectomy and bilateral neck dissection. The other case with oropharyngeal carcinoma had no clinical response but PET/CT scan evident partial response thereby these two cases were shifted to the partial response category under PET/CT group.

Progression were detected equally in 6 patients representing 20% of the cases using both modalities, one case showed local progression in the CT scan but local progression as well as lung metastases using PET/CT scan. There was no statistical significance between the two groups in spite of the differences detected by PET/CT scan as explained above (P= 0.824). (table 7).

| | Clinical Response | | PET- Response | | $\chi^2$ | p |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | | |
| Lost follow up (after 50Gy, in middle of phase II) | 1 | 3.3 | 1 | 3.3 | 2.268 | 0.824 |
| No Response | 2 | 6.7 | 0 | 0.0 | | |
| Partial | 5 | 16.7 | 7 | 23.3 | | |
| Complete | 16 | 53.3 | 16 | 53.3 | | |
| Progression | 6 | 20.0 | 6 | 20.0 | | |

*Table 7: Comparison between clinical response using CT scan vs PET/CT*
*$\chi^2$, p: $\chi^2$ and p values for Chi square test*
*$^{MC}$p: p value for Monte Carlo for Chi square test*

### 3. Discussion

The incorporation of PET in radiotherapy treatment planning has revolutionized the field of radiation oncology**.** The therapeutic index in radiation therapy can be improved with better target volume delineation. This is especially true in head and neck cancers where organs at risk are in close proximity to these targets and highly conformal therapies are often needed to minimize morbidity. In recent years, more research has been made in evaluating the clinical role of combined 18F-FDGPET/CT on target volume delineation in head and neck cancer. Although some groups report that 18F-FDG-PET/CT based delineation resulted in smaller tumor volumes than the CT-based volumes[(5-7)], others report that GTV defined with 18F-FDG-PET/CT was similar or even larger than their CT-based counterparts.[(8,9)]

The present study was performed to compare between 18F-FDG-PET/CT versus CT scan in staging, target volumes delineation, and monitoring response to therapy in patients with locally advanced head and neck squamous cell carcinoma treated by concurrent radiotherapy with systemic therapy.

Thirty patients - with histologically proven locally advanced head and neck squamous cell carcinoma- were included in this prospective study which was conducted between January 2013 and March 2015.This study has shown that the use of PET/CT in the staging work up, resulted in change of disease's stage for 3 cases. One patient with carcinoma of the larynx was down-staged from stage IVA to stage III as the nodal stage was changed to N1 instead of N2 using PET, the suspicious lymph node on the right side of the neck seen in CT scan was proved to be negative by FNAC confirming the PET results. Another 2 cases were up staged from IVA to IVC as PET had proven bone metastasis in one patient and lung metastasis in the other patient who was excluded from the analysis as the decision of his treatment was changed to be palliative therapy.

In an Indian study curried out recently, 30 patients of locally advanced head and neck cancer were analyzed from January 2014 to January 2016. PET scan changed the CT-based staging in seven cases (25.93%). Three cases (11.11%) were upstaged (III to IVA, IVA to IVC, and IVB to IVC) and four cases (14.81%) were down-staged by PET/CT scan (stage III to II). In two of their patients (7.4%), distant metastasis was seen and treatment approach was changed from curative to palliative.[(10)]**.**

Alessandra **Guido** and colleagues, evaluated 38 patients with head-and-neck cancer for the effect of the use of 18F-FDG-PET/CT in radiotherapy management. Combined 18F-FDG PET/CT determined a change in the tumor stage in 6 of 38 patients (15.78%).In 5 cases the CT-based nodal information was upstaged by the PET/CT data. In contrast, in 1 oropharyngeal cancer case, it resulted in downstaging [(5)].

Deantonio *et al*.2008,[(9)]analyzed the use of 18F-FDG-PET/CT images for staging and target volume delineation of patients with head and neck carcinoma; PET/CT imaging changed the TNM categories in 5 of 22 (22%) cases when compared with CT alone.

Wang *et al*. 2006, [(11)]evaluated 28 patients with head and neck carcinoma and the impact of FDG-PET fused with planning CT scans on tumor localization. PET/CT changed CT-based staging in 16 of 28 (57%) of patients**.**

In our study, fused 18F-FDG-PET/CT images produce different target volumes to those produced using conventional method CT, it was found that GTVs delineated using CT scan (C-GTV) were larger than those delineated using PET/CT (PET-GTV) scan in most of the cases (93.3%), while in 2 cases (6.67%) only the PET- GTV was greater than C-GTV unlike the results of ***Burela's*** study in which the GTV-PET was larger than GTV-CT in 15 cases (55.56%) and was smaller in 12 cases (44.44%). In our study, the median volume of C-GTV was 31.71cc and 15.13cc of PET-GTV compared to a median value of 11.31 $cm^3$ for GTV-CT in Burela's, while that of GTV-PET was 13.81 $cm^3$. GTV delineated on PET vs. CT scan for primary tumor and nodes showed no statistical significant change in the mean volumes (P = 0.803 for GTV primary, P = 0.589 for nodes)[10].

In our study, the volume difference between GTVs using CT scan versus PET/CT, was highly statistically significant for the primary tumor ((*P= <0.001).* but not significant for the nodal volumes (P=0.171 for left neck nodes and P= 0.062 for the right-side nodes).

Delouya et al. 2011,[12]studied twenty-nine patients with SCC of the head and neck to determine the impact of 18F-FDG-PET in radiotherapy target delineation and patient management, for head and neck squamous cell carcinoma, compared to CT alone. All gross tumor volumes of the primary (GTVp) and the suspicious lymph nodes (GTVn) were defined on CT (GTVp-CT) and 18F-FDG-PET/CT (GTVp-PET). Four patients who had previous diagnostic tonsillectomies were excluded, for the other 25 patients, GTVp-PET were smaller than the GTVp-CT in 80% of the cases, leading to a statistically significant volume difference (p = 0.001).No such volume change was observed (p = 0.08) for the lymph node. 18F-FDG-PET modified treatment management in three patients (Distant metastases were found in two patients and one had a newly diagnosed lung adenocarcinoma). These results are compatible with the current study.

Similarly, Guido et al. 2009[5], found that in 92% of cases, the CT-based GTVs were larger than the PET/CT-based GTVs.The average total GTV from the CT and PET/CT scans was 34.54 $cm^3$ (range, 3.56–109) and 29.38 $cm^3$ (range, 2.87–95.02), respectively (p < 0.05). Separate analyses of the difference between the CT- and PET/CT-based GTVs of nodal disease were not statistically significant. The comparison between the PET/CT-based and CT-based boost planning target volumes did not show a statistically significant difference.

***Paulino et al. (2005)***[6], investigated 40 patients and found changes in the GTV in 37 of 40 cases. Of the 40 patients, 30 had a decrease in GTV on PET/CT and 7 had an increase. However, in that study, the investigators fused both the CT portion of the PET-CT and the CT simulation images, thus introducing a possible source of error. Furthermore, a separate analysis of the data according to primary tumor and nodal disease was not provided.

***Heron et al. (2004)***[7], enrolled 21 patients with head-and-neck cancer. Overall, 80% of all patients presented with a change in the GTV delineation. The investigators performed a separate analysis of the primary tumor vs. nodal disease and found that in the primary tumor, the GTV was increased in 3 of 21 patients and decreased in 14. In the nodal stations, it was increased in 7 and decreased in 3 of 21 patients.

In our current study, The PTV-Boosts (phase 3) delineated to boost the gross tumors ranged between 48.52 - 157.92 cc and 47.31 - 155.8 in PTV-Boost and PTV-PET-Boost respectively with PTV- Boost median of 96.23 cc which was **larger** than the PTV-PET-Boost median 93.58 cc with high statistical significance (P <0.001).

Multiple studies have shown that PET/CT is superior to conventional anatomic imaging in assessment of tumor response and detection of residual tumor [13].

A systemic review and meta-analysis of 51 studies involving 2,335 patients- assessing the diagnostic performance of 18F- FDG PET with or without CT in post-treatment response assessment and/or surveillance imaging of head and neck squamous cell carcinoma- had been conducted by Gupta et al in 2011. They found that, the weighted mean (95% CI) pooled sensitivity, specificity, PPV and NPV of post-treatment FDG PET(CT) for the primary site was 79.9% (73.7-85.2%), 87.5% (85.2-89.5%), 58.6% (52.6-64.5%) and 95.1% (93.5-96.5%), respectively. Similar estimates for the neck were 72.7% (66.6-78.2%), 87.6% (85.7-89.3%), 52.1% (46.6-57.6%) and 94.5% (93.1-95.7%), respectively. The authors concluded that, the overall diagnostic performance of post-treatment FDG PET/CT for response assessment and surveillance imaging of HNSCC is good, but its PPV is somewhat suboptimal. Its NPV remains exceptionally high and a negative post-treatment scan is highly suggestive of absence of viable disease that can guide therapeutic decision-making. Timing of post-treatment imaging (≥ 12 weeks after completion of definitive therapy) has a significant, though moderate impact on diagnostic accuracy [14].

In the current study, the complete clinical responses detected using CT scan and or MRI compared to that detected using PET/CT scan were similar in both groups (53.3% in each). There were 2 cases evaluated by CT scan to have less than partial response (no response) while PET/CT scan showed evidence of partial response. Progression were detected equally in 6 patients representing 20% of the cases using both modalities, one case showed local progression in the CT scan but local progression and lung metastasis using PET/CT scan. There was no statistical significance between the two groups in spite of the differences detected by PET/CT scan as explained earlier in the results section (P= 0.824).

A study done by Andrade et al. 2006,[15] was performed for Post treatment assessment of response using FDG-PET/CT for patients treated with definitive radiation therapy for head and neck cancers. Regarding the detection of residual disease, the overall sensitivity and specificity of FDG-PET/CT was 76.9% and 93.3%, respectively, compared with 92.3% and 46.7% for contrast-enhanced CT. The accuracy of FDG-PET/CT was 85.7%, compared with 67.9% for CT alone. All false-negative (n = 3) and false-positive (n = 1) FDG-PET/CT results occurred between 4 and 8 weeks after treatment. At 8 weeks or later after treatment, the specificity of CT was 28%, compared with 100% for FDG-PET/CT. It was concluded that, the metabolic-anatomic information from co-registered FDG-PET/CT provided the most accurate assessment for treatment response when performed later than 8 weeks after the completion of radiation therapy. FDG-PET/CT excelled by a higher specificity and overall diagnostic performance than CT imaging alone. These results support a potential clinical role of FDG-PET/CT in the early assessment of therapy response after definitive radiation therapy.

**4. Conclusion & Recommendations**

Our study has shown that the use of PET/CT in the staging work up, resulted in change of disease's stage for 3 cases. One patient was down-staged and 2 cases were up staged. Combined PET/CT imaging -utilizing anatomical and biological data- could improve target volume delineation and RT dosimetry and, likely, provide better locoregional control in head-and-neck cancer while sparing the surrounding normal tissues. In our study, the primary tumor and nodal GTVs were changed with the implementation of combined PET/CT; that translate into a smaller and statistically significant difference in the mean volume of the GTV of the primary tumor and PTV- boost delineation, however, such difference in the volumes was not statistically significant when applied to nodal GTVs, CTVs and PTVs.

PET/CT is superior than traditional imaging modality in evaluating response to therapy and detecting residual disease yet this was not statistically significant (P= 0.824).

Larger multicenter studies are needed to ascertain whether combined 18F-FDG-PET/CT in target delineation can influence the main clinical outcomes, such as toxicity reduction, dose escalation to smaller volumes without compromising local control, and survival.

We recommend to perform combined PET/CT in the GTV delineation of all head-and neck cancer patients as implementation of combined PET/CT imaging has the potential to improve primary tumor and nodal basins staging, target delineation and clarify uncertain lesions.

The role of novel PET tracers, designed to depict biological characteristics such as hypoxia (18-F fluoromisonidazole =FMISO), protein synthesis (11C-methionine, MET), and cell proliferation (32-deoxy-32-(18) F-fluoro-thymidine, FLT) in HNC patient care, seems to be a good field for future researches. One or more of these tracers may one day facilitate functional imaging-based individualization of treatment strategies.

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