

Fusion Imaging - A Retrospective Study of 10 Different Cases

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Abstract

Objective: Positron emission tomography (PET) – computed tomography (CT) is a unique combination of the cross-sectional anatomic information provided by CT and the metabolic information provided by PET, which are acquired during a single examination and fused. The role of PET-CT with fluoro-deoxy-glucose (FDG) in the staging of head and neck cancer, metastasis, recurrence, differential diagnosis and treatment outcome.

Materials and Methods: A retrospective case analysis of 10 subjects was carried out among the cancer patients at Mahavir cancer hospital and research institute, Jaipur. The images of all the cases were analysed and the advantages disadvantages of the different modalities are reviewed in detail.

Conclusion- PET-CT seen to show highest sensitivity and specificity in all the indications that are taken in account for the study.

Keywords: PET-CT, Positron emission tomography, FDG (fluoro-deoxy glucose), staging of cancer, specificity.

Introduction

Computed tomography (CT) and magnetic resonance (MR) imaging are the standard imaging techniques used for the evaluation of a patient with head and neck cancer. They provide structural information at a high spatial resolution and are therefore used routinely in the initial staging of tumors in these patients. On the other hand, CT and MR imaging rely on certain criteria, such as nodal size and contrast-enhancement patterns, that are not very specific.

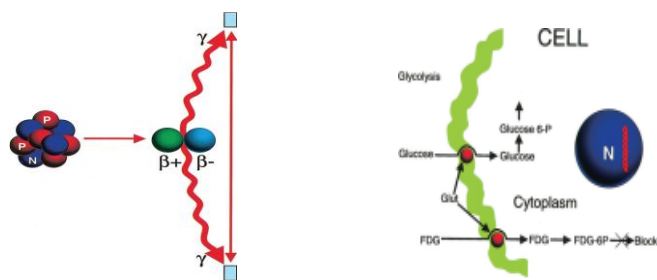
And after radiation and/or chemotherapy, changes in tumor metabolism precede morphologic changes. Similarly, after radical surgery or radiation therapy for head and neck malignancies, normal tissue planes are altered substantially. Therefore, CT and MRI are useful for initial T-staging, since their high spatial resolution and soft-tissue contrast can demonstrate subtle abnormalities and accurately delineate tumour volume but has relatively poor specificity in the assessment of residual or recurrent disease following radical therapy. Positron emission tomography (PET), on the other hand,

helps evaluate tumor metabolism, and the information obtained is essentially independent of tumor location and lesion size.¹

PET/CT has been shown to have better sensitivity and specificity for pathologic cervical nodes than MRI and CT, likely because the latter rely on nodal size and contrast-enhancement criteria which are not specific and can miss metastases in normally sized nodes.

FDG PET-CT plays an important role in identifying disease in lymph nodes in unexpected locations (upper mediastinum and axillae) and detecting unsuspected distant metastatic disease. PET-CT has an advantage over conventional imaging, in this setting, because of its whole-body coverage and its sensitivity to lesions that may be missed by conventional imaging such as subtle bone metastases that may not be detectable on a routine CT scan.¹

PET is based on the detection of annihilation photons (gamma) released when radionuclides, such as F-18, carbon-11, and oxygen-15, emit positrons (beta +) that undergo annihilation with electrons (Fig 1). The photons thus released have energies of 511 keV (0.511 MeV) and are detected by coincidence imaging as they strike scintillation crystals made of bismuth germinate (BGO), lutetium oxyorthosilicate (LSO), or gadolinium silicate (GSO).



Annihilation reaction - Positrons (beta+) released from the nucleus of FDG annihilate with electrons (beta-), releasing two coincidence 511-keV photons (gamma),

which are detected by scintillation crystals (blue rectangles). N - neutron, P - proton.

Uptake of FDG - FDG is a glucose analog that is taken up by metabolically active cells by means of facilitated transport via glucose transporters (*Glut*) in the cell membrane. In the cell cytoplasm, FDG undergoes phosphorylation to form

FDG-6-phosphate (*6P*), which, unlike glucose, cannot undergo further metabolism and becomes trapped within the cell. *N*- nucleus.²

The effect of increased glycolysis in malignant cells was first described by Otto Warburg in 1924 and is known as Warburg effect: it is proportional to their metabolic activity. Tumor cells take up glucose by facilitated transport using glucose transporters (GLUT). It then undergoes glycolysis with formation of pyruvate under aerobic conditions. FDG is initially phosphorylated like glucose, but unlike glucose-6- phosphate, FDG-6-phosphate cannot undergo further metabolism and thus gets trapped and accumulates within metabolically active tumor cells. This accumulation of FDG-6-phosphate within the cell, combined with a higher concentration of neoplastic cells in a tumor, form the basis for the successful use of FDG in PET tumor imaging.³

For these reasons, PET with the glucose analogue fluorodeoxyglucose (FDG) has been used successfully for the assessment of tumor aggressiveness, for staging of nodal disease in the neck, for treatment evaluation, and for detection of recurrent disease in patients with head and neck cancer. Unfortunately, the lack of anatomic detail remains a major limitation of PET as it was used.

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whole-body coverage and its sensitivity to lesions that may be missed by conventional imaging such as subtle bone metastases that may not be detectable on a routine chest or abdominal CT scan.

Combined PET/CT is a recent imaging technique that permits almost synchronous image acquisition and exact co-registration of anatomic and metabolic data sets. Use of PET/CT fusion imaging in patients with head and neck cancer improves the anatomic localization of abnormalities identified on PET images alone. While it would have been ideal to have histopathologic results available in all cases.

For these reasons, PET/CT fusion imaging is highly recommended in the evaluation of patients with head and neck malignancies.

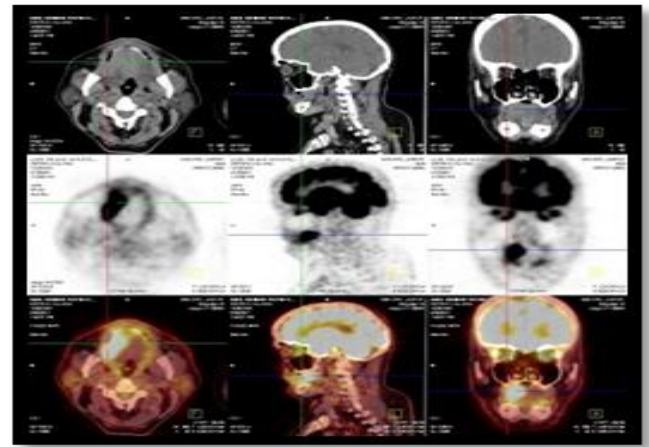
Since the spatial resolution of FDG-PET is limited to 4-10mm, its ability to precisely localize small tumours or microscopic tissue involvement is often diminished in the head and neck region. Tumours with low metabolic rate and poor avidity for FDG uptake may also be difficult to characterize on PET scans.⁴

Indications of PET/CT –

T – stage - An early tumour may have poor FDG uptake and its detection on the scan may be obscured by cross contamination of physiologic activity from surrounding tissues – the so-called ‘spillover effect’.⁵

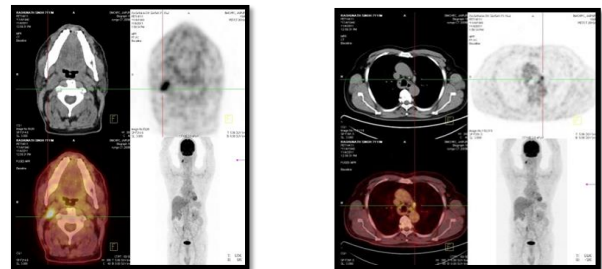
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Hypermetabolic 5.4*2.2*2.7cm lesion on right lateral border of anterior 2/3rd of tongue and base of the tongue. SUV – 11.94.

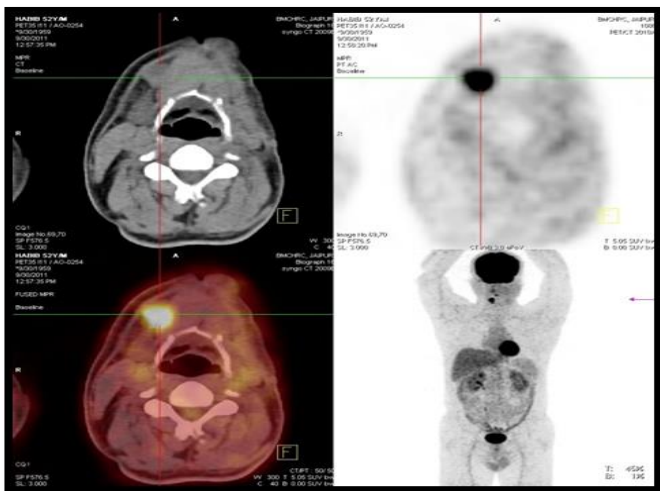
N- stage The spread of disease to regional lymph nodes is the most important prognostic factor in squamous cell carcinoma of the head and neck. PET has been shown to be superior to conventional imaging modalities for the detection of regional nodal metastases. PET/CT bridges this gap by combining metabolic and anatomic information and allows for the most accurate assessment of regional nodal metastases.



Hypermetabolic lymph nodes of cervical level II and pulmonary nodes with increased SUV.

M- stage - Approximately 10% to 15% of patients with primary HNSCC will have distant metastases. The most common sites of involvement are the lungs, followed by the liver and skeletal system. The presence of distant metastases may indicate a need for additional therapeutic measures, whereas overlooked distant metastases can lead to inappropriately aggressive treatment. In most

patients, distant metastatic lesions will be clinically silent.⁴



T4N1M0 of left buccal mucosa and treated by segmental mandibulectomy & MND with concurrent RT. On followup PET/CT - Hypermetabolic mass in right side of submental region, may be recurrence or metastasis. H/D – metastasis.

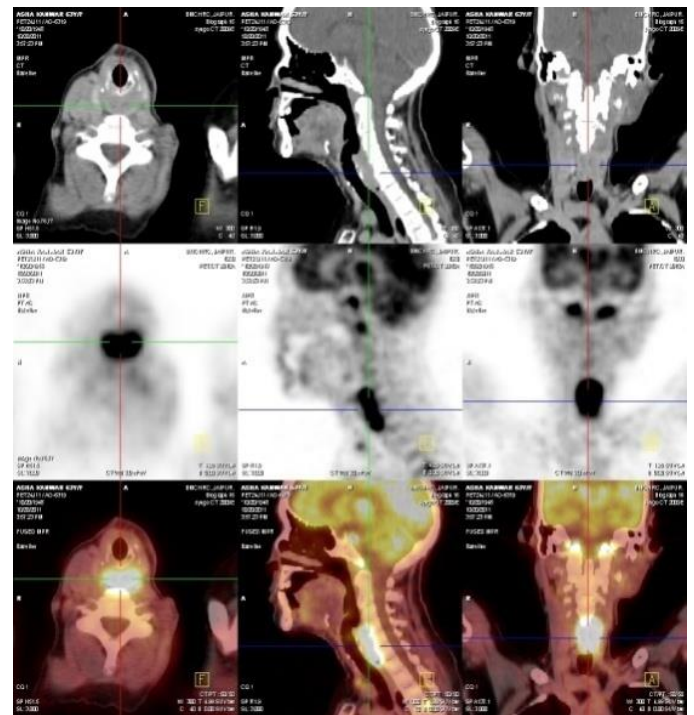
Recurrence

Recurrence of head and neck cancer has a poor prognosis. With earlier detection of recurrence, it is possible that survival could be improved. Previous reports have shown the high accuracy of PET in staging head and neck cancer and in identifying tumor recurrence. Conclusion of the study conducted by Val et al was that the PET can detect head and neck tumor recurrence when it may be undetectable by other clinical methods. FDG-PET permits highly accurate detection of head and neck cancer recurrence in the post therapy period.³

Patients with recurrent, early-stage HNSCC who undergo salvage surgery have a 70% 2-year relapse-free survival, whereas those with recurrent, advanced-stage HNSCC undergoing surgical salvage have just a 22% 2-year relapse-free survival. Early diagnosis and accurate identification of recurrent HNSCC are therefore critically

important for successful treatment.⁶ Post-treatment surveillance for the recurrence of head and neck squamous cell carcinoma (HNSCC) is a diagnostic challenge. Tissue distortion from radiation and surgery can obscure early detection of recurrence by conventional follow-up approaches such as physical examination, CT, and MRI. Several studies have shown that 18F-FDG PET may be an effective technique for the detection of persistent, recurrent, and distant metastatic HNSCC after treatment.

The results of our study confirmed the high effectiveness of 18F-FDG PET/CT in assessing for recurrence of HNSCC in patients who have been considered cured of the disease. Findings of this study suggest that 18F-FDG PET/CT is more accurate than conventional follow-up physical examinations alone in such patients. The systematic use of PET/CT at 12 month of the usual follow-up could be proposed, but cost-effectiveness and survival impact remain to be evaluated.⁷



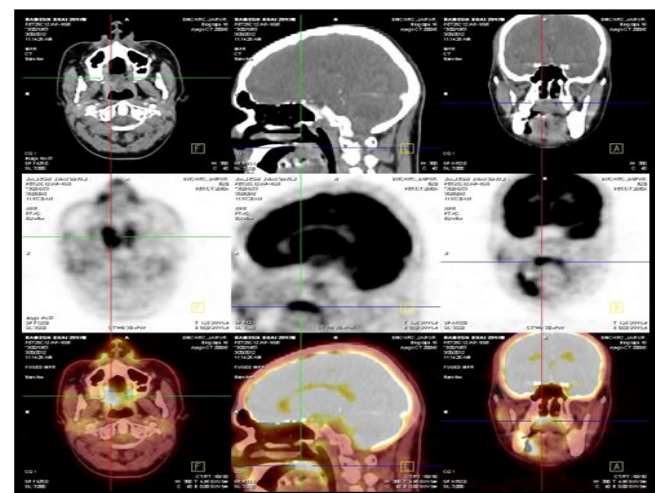
Patient has been treated for poorly differentiated malignancy of left parotid gland and treated by RND 6

months back and undergone Pet/ct for a lump in the neck. On PET/CT - Hypermetabolic mass in posterior region of cricoid at the upper end of cervical esophagus with SUV – 16.06

Unknown primary tumors

Patients with HNSCC sometimes present clinically with an enlarging neck mass for which FNA reveals metastatic SCC. In most cases, the primary tumor will be found by physical exam, cross-sectional imaging, or endoscopic evaluation. PET/CT helped identify more primary tumors (33%) than CT (18%) or PET (24%) alone.²

Differential diagnosis - Inflammation and infection are common treatment sequelae that may increase FDG uptake in certain tissues; hence, the addition of CT to PET is especially important in these situations in order to distinguish truly pathologic areas from postirradiated tissue.⁸



Hypermetabolic mass on right submanibular, sublingual & soft palate. On delayed scan soft palate shows SUV – 5.56 as compared to 7.76 initially.

Surveillance

Second primary - Patients treated for primary HNSCC have a high rate (3% to 5% per year) of developing second primary tumors. This most likely is because of the widespread distribution of toxic effects from tobacco and

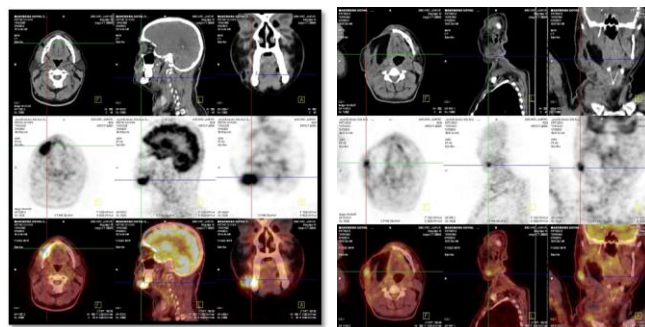
alcohol. Second cancers can occur around the same time as the primary (synchronous) or 6 months or more after the primary (metachronous). The major sites of involvement are the Head and neck, lung, and esophagus. Posttreatment surveillance can diagnose these second primary lesions earlier and more accurately allowing for potentially higher cure rates. Pet and PET/CT have proven to be the modalities of choice for surveillance of patients with HNSCC.

There has been significant recent interest in the use of integrated PET/CT for radiotherapy planning. When compared with CT, PET/CT has been shown to more accurately assess gross target volume (GTV), which is essential to IMRT. PET/CT is superior to conventional imaging modalities for radiation treatment planning, allowing for improved tumor coverage and sparing of normal tissues.

Monitoring treatment response assessment of patients during and after therapy is vital to determine whether an alternate therapeutic approach is needed or whether additional therapy is warranted. PET/CT is therefore a useful tool for monitoring treatment response in HNSCC and for restaging recurrences including nodal disease and distant metastases.⁴

Treatment outcome

In chemotherapy usually after 2 cycles it is advisable to check the status of the disease where in surgical treatment PET/CT should be done after 4-6 weeks to rule out any residual or secondaries.



Hypermetabolic mass in right buccal mucosa & sublingual area with SUV – 9.95. After 6 weeks of treatment by hemimandiblectomy with RND, PET/CT done which shows healing phase without any recurrence, metastasis and residual disease.

Physiological uptake

A number of physiologic variants are commonly encountered, including normal physiologic uptake in the head and neck, heart, breast, thymus, liver, spleen, gastrointestinal tract, genital system, urinary collecting system, bone marrow, muscles, brown adipose tissue and in the active muscles after injection of radionuclide. It is important to instruct patient not to talk during the uptake phase, since excessive talking may cause prominent activity in the laryngeal structures, tongue musculature etc.⁹

Disadvantages of PET/CT –

First, the PET/CT scanner is more like a tunnel than a doughnut, so claustrophobia is a problem for some patients.

Use of intravenous contrast for the CT scan can cause artifacts in the reconstruction of the PET images. This is because the iodine component of intravenous contrast absorbs the lower-energy CT x-rays much more efficiently than the high-energy, 511- keV photons emitted during PET imaging.

Motion artifacts can be amplified with PET/CT. A specific and important facet of this is respiratory motion. Because the patient is breathing during the PET study, it is important to perform the CT scan in a manner that best matches the positioning of the diaphragm and adjacent organs, in order to optimize registration of the two data sets.⁵

Limitations of PET-CT

Variable FDG uptake in normal structures such as nasal turbinates, pterygoid muscles, salivary glands, extra-

ocular muscles, and lymphoid tissues of the adenoids and Waldeyer ring may result in difficulty interpreting the PET-CT scan. This may result in false-positive findings. Similarly, normal uptake of FDG in contracting muscles, as for example in tense/ anxious patients or in talkative patients, may also lead to false-positive findings.

Tumors with inherently low FDG uptake such as the majority of salivary gland tumors and those tumors with significant necrosis (with lower amounts of metabolically active malignant tissue) can potentially yield false negative or equivocal results.

Conclusion - The development of tumor-specific ligands will enhance the usefulness of PET-CT in the detection of early-stage tumors and in the evaluation of tumors with low FDG avidity. Successful treatment outcome for patients with head-and-neck cancer will be more likely thanks to better predictive abilities, as well as better differentiation of tumor from radiation reaction and/or scar, and by improved abilities to precisely localize the tumor.¹⁰

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