Special Article

PET/CT in Oral Cavity and Oropharyngeal Cancer in Post Therapy Setting

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^{18}F-FDG PET/CT is an immerging tool for follow-up a head and neck cancer patients. Accurate PET/CT interpretation in a post therapy setting is crucial for proper management. However, there are many limitations in post therapy settings. For example, variable degree of normal physiologic uptake is noted. Physiologic processes cannot be identified by symmetrical FDG uptake in a post therapy setting. The present article demonstrates case series including asymmetrical, abnormal, or unusual patterns of FDG uptake within the oral cavity and oropharyngeal structures in both benign and malignant conditions.

Keywords: *PET/CT, Oral cavity and oropharyngeal*

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^{18}F-fluoro-2-deoxy-D-glucose (^{18}F-FDG) positron emission tomography (PET)/computed tomography (CT) plays an important role for evaluation of head and neck cancer patients in both staging and restaging. Residual or recurrent tumor, either at the primary site or in neck nodes occurs in up to 50% of patients with advanced tumors[1]. Early detection of residual or recurrent disease may allow early intervention, usually in the form of surgical salvage[2] and may potentially offer a survival advantage. PET/CT is a highly sensitive tool to detect recurrent disease, especially in squamous cell carcinoma of head and neck with a high sensitivity and moderate specificity[3-6]. Recently published data from meta-analysis confirm that PET has a highly accurately role for detecting residual or recurrent head and neck squamous cell carcinoma with positive and negative predictive values of 75% (95% CI, 68-82%) and 95% (95% CI, 92-97%) respectively[7]. In addition, Pantvaidya et al reported a 38.7% change in management because of the additional PET/CT to conventional methods of assessment[8].

PET/CT scan seems to be a new technology in Thailand. The cost per scan is very expensive. Although reimbursement in Thailand at this time does not cover head and neck cancer patients, there are many articles as described above that reveal the usefulness of PET/CT in these patients, especially in post therapy settings.

There is a variable degree of FDG uptake in normal structures such as tongue muscles and lymphoid tissue in the Waldeyer's ring that may confuse interpretation and lead to false-positive results[9,10]. Although FDG uptake in primary neoplasm is usually greater than that seen in the most metabolically active normal structures, overlap between tumor and physiologic uptake may confound interpretation. In addition, the interpreting physician relies on symmetry to differentiate between physiologic and pathologic FDG accumulation. However, physiologic processes cannot be identified by symmetrical FDG uptake in post therapy setting. Post therapy changes complicate its interpretation. Accurately PET/CT interpretation in the post therapy setting is very important and leads to proper management.

In the present article, the author will focus on therapy-related changes with illustrations of a case series, including asymmetrical, abnormal, or unusual patterns of FDG uptake within the oral cavity and oropharyngeal structures in both benign and malignant conditions.

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PET/CT interpretation in post treatment changes

Treatment options for head and neck cancer patients are surgery, chemotherapy, radiation therapy, and combination of these treatments, depending on location, staging, and patient decision. Imaging plays

an important role in both initial staging and restaging. To date, there have been no consensus studies to determine the optimal surveillance interval in head and neck cancer patients. Agarwal et al[11] from the University of Pittsburgh medical center performed surveillance of head and neck cancer patients with PET/CT at 2, 5, 8, and 14 months after treatment. If questionably abnormal finding is seen, additional PET/CT scan will be performed three months later. Qoun et al[12] from Stanford University medical center published a reasonable consensus of opinion for surveillance in head and neck cancer patients. At 1-2 months after complete therapy, CT scan or MRI was done first. If no evidence of suspect site was found, baseline PET/CT was performed beginning at three months after completion therapy. Subsequent surveillance PET/CT scan are scheduled either depending on clinical suspicion or at regular intervals such as every six months for the first 18 months and annually thereafter. In NCCN (National Comprehensive Cancer Network) guideline v1. 2009, PET scan and cross sectional imaging such as CT or MRI is recommended as baseline post treatment imaging at minimum 12 weeks after treatment in some cancers, such as oropharynx and larynx, with advanced T (T3-4) and N (N2-3) stages. If a PET/CT is performed and negative for persistent cancer, further cross sectional imaging is an optional.

In a post therapy setting, surgery-related changes involve distortions of anatomic planes, ensuring functional asymmetry and artifacts from metals. Reconstructive procedures such as grafts or flaps cause further complicated imaging interpretation because of confusing surgical anatomy. Fused ^{18}F-FDG PET with CT scan shows overall higher accuracy than either ^{18}F-FDG or CT alone. Knowledge about the surgical procedures is very important for accurate PET/CT interpretation.

Muscles of the tongue and floor of the mouth may demonstrate diverse and unpredictable patterns of FDG uptake. In the absence of a history of oral cavity and oropharyngeal cancer and evidence of abnormality detectable on the accompanying CT scan, interpretation of the tongue muscle uptake is likely to represent physiologic uptake rather than malignancy process (Fig. 1).

In the patient with a history of treated oral cavity and oropharyngeal cancer, FDG uptake in the tongue should be carefully reviewed and interpreted (Fig. 2-4). Definitive diagnosis between physiologic uptake and malignant process cannot be made based on only the degree of FDG uptake on PET findings.

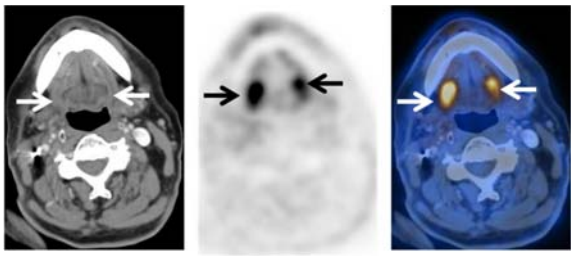

Fig. 1 Axial images of a PET/CT study in patient with a history of treated head and neck cancer show normal FDG uptake within the tongue. (arrow) without demonstrable mass on corresponding slices CT scan

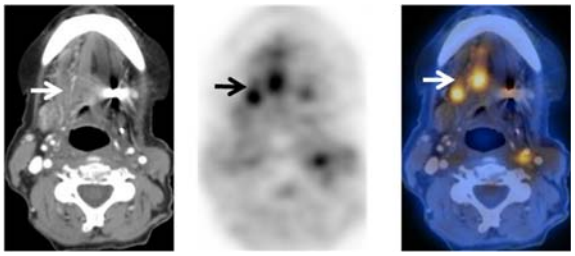

Fig. 2 A79-year-old female with a history of tongue cancer status post left hemiglossectomy, left partial pharyngectomy and left neck dissection followed by radiation therapy. CT scan, PET scan and fused PET/CT scan shows focally increased uptake at the tongue muscle (arrow) without any discrete mass on the accompanying contrast enhanced CT scan. These findings are interpreted as physiologic uptake

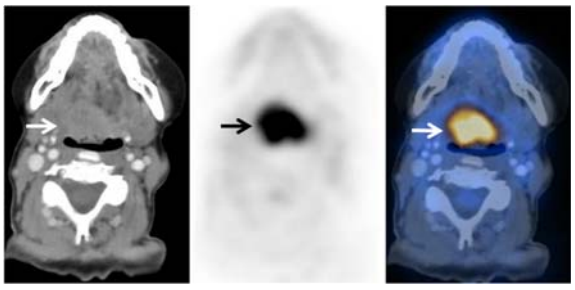

Fig. 3 Base of the tongue (BOT) cancer in a 79-year-old female presented with right BOT mass. Axial images of a PET/CT scan shows intense FDG uptake (SUV_{max} 15) corresponding with a large, lobulated enhancing mass at the BOT on contrast enhanced HRCT scan, consistent with malignant process. These findings proved to be squamous cell carcinoma

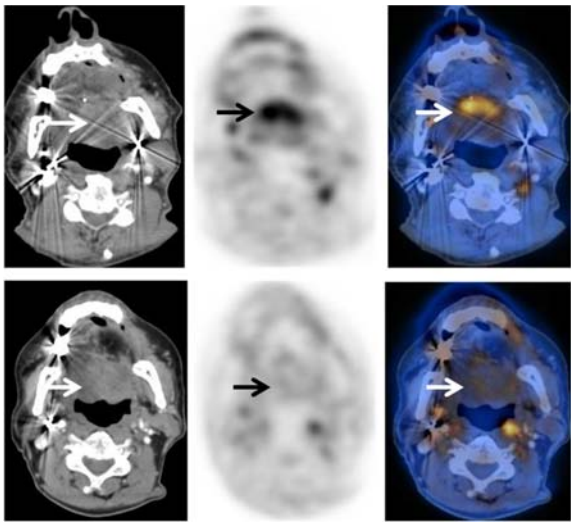

Fig. 4 Post surgical inflammatory change of the tongue in a 73-year-old male with a history of recurrent FOM cancer status post extensive surgery 5 months earlier
Upper row: axial images of a PET/CT scan shows diffusely increased FDG uptake (SUV_{max} 6.0) at the glossectomy surgical suture without corresponding any discrete mass on accompanying contrast enhanced HRCT scan, likely to be post surgical inflammatory change in nature
Lower row: A follow-up PET/CT scan at 5 months was obtained. There has been an interval resolution of increased FDG uptake at the glossectomy site

The accompanying HRCT findings help to identify an abnormal enhancing lesion. However, artifact from surgical clips as well as dental metallic may obscure anatomic details on HRCT. Sequential follow-up PET/CT scan is also helpful for differential post-operative change from recurrent tumor (Fig. 4).

The degree of FDG uptake may reflect patient activity during or immediately preceding the uptake phase. Kathula et al[13] reported intense FDG uptake (SUV_{max} 24) in patient who chewing gum before FDG injection. These findings are similar to patient demonstrating in Fig. 5.

Conversely, tongue cancer sometimes shows only a faint FDG uptake, which is interpreted as physiologic uptake (Fig. 6). In this case, tongue cancer is detected by only physical examination. Both FDG PET and contrast enhanced HRCT fail to detect an abnormality. Contrast enhanced HRCT scan is difficult to evaluate enhancing mass in this region due to dental artifact. It is uncommon for SCCA of the tongue that does not show appreciable FDG uptake. Low-grade tumor such as mucoepidermoid tumor or adenoid cystic carcinoma may demonstrate only faintly or mildly increased FDG uptake. In these settings, clinical and physical examination correlation as well as a closed follow up PET-CT is recommended for the best result. It is well known that PET scan has limitation to detect small size tumor (less than 5-8 mm). However, the resolution is better in newer model, which may approach resolution of 2-5 mm.

Inflammatory and infectious process demonstrate intense FDG uptake (Fig. 4, 7) and may lead to a false positive scan, especially for unfamiliar readers. In most cases 4-6 weeks after surgery seems to be an appropriate timing to evaluate residual tumor on PET/CT scan. In some instances, inflammation from extensive surgery may last longer than many months. Continued close follow-up PET/CT within three months and correlation with physical examination is recommended. Biopsy should be performed to exclude the possibility of recurrent tumor.

Radiation therapy (RT) may either leads to an increased or decreased FDG uptake in the organs

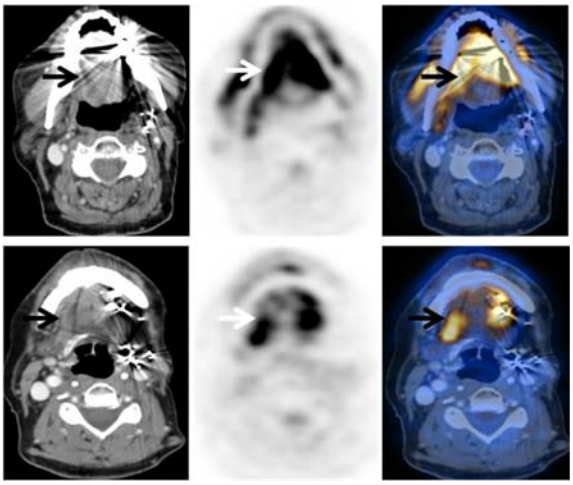

Fig. 5 A 59-year-old male with a history of left tongue cancer status post surgery, combination therapy with chemo- and radiation therapy 3 years earlier. Two slices of axial images of a PET/CT study demonstrate increased FDG uptake within the tongue, particularly in its extrinsic muscles (arrow) without any evidence of a discrete mass seen on the corresponding contrast enhanced CT scan, most consistent with physiologic uptake. Of note, the patient was later reported to be chewing gum during the incubation period of FDG uptake

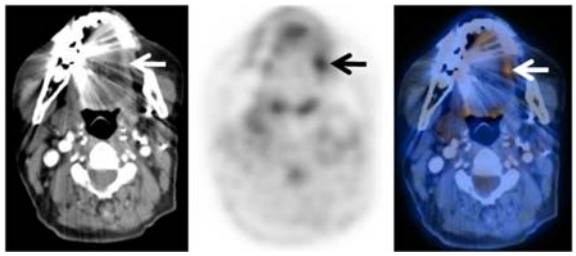

Fig. 6 A second primary tumor in the left lateral tongue in a 72-year-old patient with a history of alveolar ridge cancer status post surgery for 3 months. Axial images of PET/CT scan shows focally increased FDG uptake at the left lateral tongue (SUV_{max}3.9), without any evidence of discrete mass on contrast enhanced CT scan. This finding was initially interpreted as physiological tongue uptake. However, the physical examination showed a palpable mass in this region, biopsy at the left lateral tongue on the next day confirmed a second primary tumor in the left lateral tongue. Tumor size was 0.9 cm

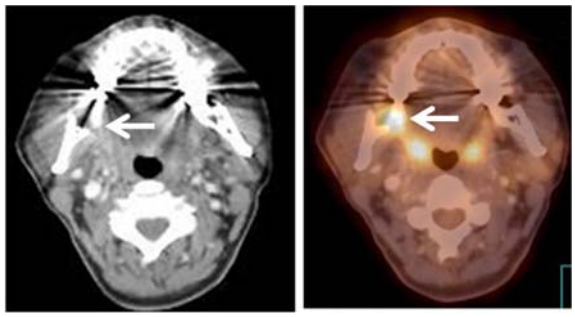

Fig. 7 A 55-year-old female with a history of gum cancer underwent wide excision and marginal mandibulectomy for 2 weeks. CT scan and fused PET/CT scans show increased FDG uptake (arrow) at right lower gum with SUV_{max} of 3.7. No soft tissue or bone mass is demonstrated on accompanying slices CT scan

included within the radiation field depending on timing. Timing between the end of radiation therapy and the scan appears to affect the accuracy of PET/CT in identifying residual disease. In the past, there used to be a disagreement on when to perform PET/CT scan after completion of the therapy[4,14-16]. Nowadays, the optimal timing of PET/CT scans has been determined to be 8-12 weeks after completion of treatment to achieve the most accurate results than earlier time point[17-19].

Most inflammatory process usually shows diffuse uptake in the radiation field. When an inflammatory process has been resolved, there is relatively decreased FDG uptake in the organs included in the radiation field (Fig. 9, 10). Misinterpretation as increased FDG uptake in the normal physiologic contralateral sided is possible and leads to the wrong diagnosis.

There is no consensus about cut off value of SUV to definitively differentiate between pathologic and physiologic normal structures. Kapoor et al, mentioned an average SUV of 3 is generally used as a guide to indicate neoplasm[20] while Wong et al,

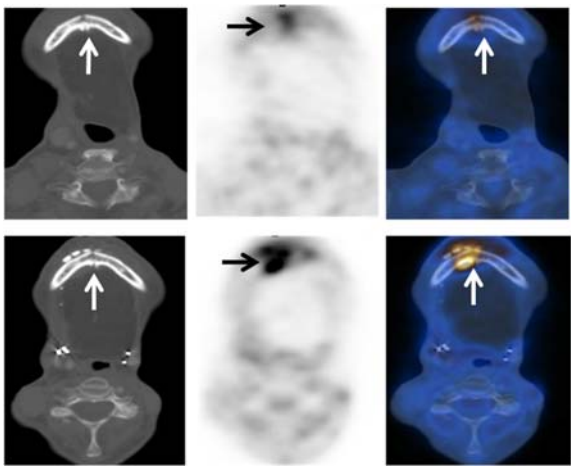

Fig. 8 Inflammation of the mandible in a 71 year- old male with a history of recurrent BOT cancer treated with chemotherapy, radiation therapy and surgery for 3 months

Upper row: Axial images of a PET/CT scan shows a focal area of increased FDG uptake (SUV_{max}4.3) in the mid mandible anteriorly where multiple implant screws in place (arrow), without evidence of bony destruction on the corresponding slices of CT scan. Given the patient's history of recent surgery and no definitively bony destruction on the HRCT scan, these findings may represent inflammatory process. Closed follow-up PET/CT scan is recommended

Lower row: A follow-up PET/CT scan at 3 months later shows increased in intensity and extension of the prior lesion in the mid mandible and again no bony destruction is seen on the corresponding slices of CT scan (arrow). Given the significant degree of FDG uptake, recurrent tumor cannot definitively excluded. CT guided biopsy at the mandibular symphysis was done. Pathological revealed fibrous tissue with acute and chronic inflammation without malignancy cell

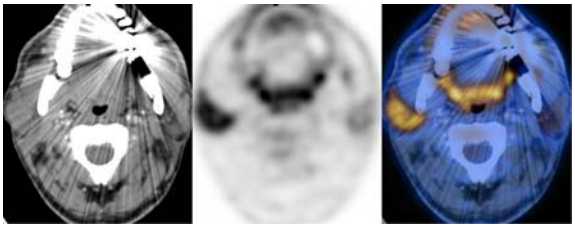

Fig. 9 Asymmetrical FDG uptake at the salivary gland in patient with a history of left buccal cancer treated with surgery and radiation therapy. FDG uptake at the right salivary gland is a normal finding. Relatively decreased uptake at the left salivary gland from prior radiation therapy is observed

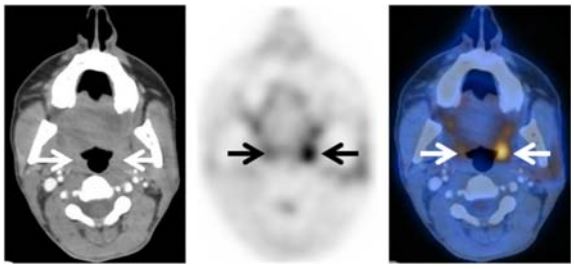

Fig. 10 Post treatment changes in the right tonsil in a 33-year-old female with a history of right submandibular gland cancer status post resection follow by radiation therapy for 5 months. Axial images of a PET/CT study shows asymmetrical FDG uptake in the tonsils (arrow), left more than right, without any appreciable mass on the accompanying CT scan. Given the patient has a history of prior radiation therapy to the right neck, these findings were interpreted as post treatment change in the right tonsil and subman-dibular gland

recommended an optimal SUV of 3.2 to determine the presence of malignancy[3].

Osteonecrosis of the mandible is a rare complication occurrence after RT and chemotherapy of oral cavity and oropharyngeal cancer. Most of the patients do not have any symptom in an early stage. Once the disease progresses, pain, diminished or complete loss of sensation, fistula, and infection are the most common symptoms. Pathologic fracture can occur as the compromised bone is unable to appropriately undergo repair at the involved sites. Osteonecrosis may demonstrate increased FDG uptake (Fig. 8), which is similar to recurrent tumor. Biopsy should be performed for definitive diagnosis and proper management.

Conclusion

PET/CT is an emerging tool for follow-up head and neck cancer patient. PET/CT interpretation in post therapy settings is challenging. Knowledge about variation of physiologic uptake, prior treatment, as well as limitation of PET/CT scan is helpful for accurate interpretation.

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การใช้ PET/CT ในผู้ป่วยมะเร็งช่องปากและคอหอยหลังช่องปากภายหลังการรักษา

อาภากร โฆษิตวัฒนฤทธิ์

^{18}F-FDG PET/CT เป็นเครื่องมือที่มีประโยชน์ในการติดตามผู้ป่วยมะเร็งศีรษะและลำคอภายหลังการรักษา การแปลผลภาพ PET/CT มีผลในการตัดสินใจให้การรักษาผู้ป่วย แต่อย่างไรก็ตามในผู้ป่วยที่ได้รับการรักษาแล้ว การแปลผลภาพ PET/CT มีข้อจำกัดหลายอย่าง เช่น physiologic uptake ที่มีความหลากหลาย รวมถึงความสมมาตรของการ uptake อาจจะเปลี่ยนไปภายหลังให้การรักษา ในบทนิพนธ์นี้ได้รวบรวม case series แสดงการจับสาร ^{18}F-FDG ในบริเวณช่องปากทั้งในภาวะ benign และมะเร็ง