



Contribution of Open Mouth Technique in ^{18}F -FDG PET/CT Imaging in Patients with Malignant Lip Neoplasm

Dudak Malign Neoplazmı Tanılı Hastaların ^{18}F -FDG PET/CT Görüntülemesinde Ağız Açık Pozisyonlamanın Katkısı

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Manisa Celal Bayar University Faculty of Medicine, Department of Nuclear Medicine, Manisa, Turkey

Abstract

Objectives: ^{18}F -fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) plays an important role in evaluating head and neck cancers. However, localization and size evaluation in this region can be rough due to the multitude of the anatomic structures and physiologic uptakes. The aim of this study was to evaluate malignant lip lesions with the contribution of open mouth (OM) imaging technique at PET/CT.

Methods: Fifty-six patients with malignant lip neoplasm underwent ^{18}F -FDG PET/CT imaging. Each patient was imaged twice as whole-body PET/CT with routine closed mouth (CM) position; and OM head and neck image, standardized with a special device. Lesion maximum standard uptake value (SUV_{max}), localization, size, and involvement of lymph nodes were evaluated.

Results: Lesion localization was correctly detected in 100% of the OM images. Lesion size in PET/CT was compared with clinical, radiological (magnetic resonance imaging and CT) and/or histopathological results and the size measurement was coherent at 47.1% and 95.6% for CM and OM images, respectively. It was observed that OM acquisition did not contribute additionally in detecting regional lymph node metastasis. Forty-one PET/CT scans with CT artifacts due to dental amalgams were evaluated and 46.3% dimensional and 53.7% localization errors were detected in the CM position. There was no statistically significant difference between OM and CM SUV_{max} ($p>0.05$).

Conclusion: We concluded that additional OM head and neck imaging is useful and necessary to accurately determine the localization and size of the tumor, thus enhancing the value of PET/CT in staging, treatment response assessment, and restaging of patients with malignant lip cancer with or without dental amalgam.

Keywords: Malignant lip neoplasm, open mouth technique, ^{18}F -FDG PET/CT

Öz

Amaç: Baş-boyun malignitelerinin değerlendirilmesinde ^{18}F -florodeoksiglukoz (FDG) pozitron emisyon tomografisi/bilgisayarlı tomografi (PET/CT) oldukça önemli bir yere sahiptir. Ancak bu bölgede yerleşimli anatomik yapıların çokluğu ve fizyolojik tutulum sıklığı nedeniyle lokalizasyon ve boyut değerlendirilmesinde güçlük yaşanabilmektedir. Bu çalışmada amaç, dudak malign neoplazmı evrelemesi amacıyla ^{18}F -FDG PET/CT çekilen hastalarda, ağız açık (AA) pozisyonlamanın primer tümörün lokalizasyon ve boyut değerlendirilmesine katkısını araştırmaktır.

Yöntem: Temmuz 2017-Ocak 2020 tarihleri arasında kliniğimizde dudak malign neoplazmı evrelemesi endikasyonu ile ^{18}F -FDG PET/CT çekilen 56 hasta çalışmaya dahil edilmiştir. Hastalara rutin uygulanan ağız kapalı (AK) pozisyonda tüm vücut ^{18}F -FDG PET/CT görüntülemesi yapılmıştır. İlk görüntülemenin hemen ardından, özel aparat ile AA'lığı standardize edilerek AA pozisyonda ek baş-boyun görüntüleri alınmıştır. Her iki görüntüde lezyon maksimum standartlaştırılmış alım değeri (SUV_{maks}), $\text{SUV}_{\text{ortalama}}$, lezyon boyutu, lezyon lokalizasyonu ve lenf nodu metastazı varlığı karşılaştırılmıştır.

Address for Correspondence: Gözde Mütevelizade MD, Manisa Celal Bayar University Faculty of Medicine, Department of Nuclear Medicine, Manisa, Turkey

Phone: +90 532 471 32 62 **E-mail:** gozdemutevelizadee@gmail.com ORCID ID: orcid.org/0000-0001-5986-8777

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Bulgular: Lezyon lokalizasyonu AA görüntülerin tamamında doğru tespit edildi. Lezyon boyutu değerlendirme açısından PET/BT görüntüleri, radyolojik, klinik ve histopatolojik veriler ile karşılaştırıldı; AK ve AA görüntülerde sırasıyla %47,1 ve %95,6 uyumlu olarak saptandı. AA görüntülemenin lenf nodu varlığını saptamada ek katkısı olmadığı izlendi. Kırk bir PET/BT görüntüsünde dental amalgamlara ait BT artefaktı mevcut olup, AK pozisyonda %46,3'ünde boyut ve %53,7'sinde lokalizasyon uyumsuz olarak saptandı. AA ve AK görüntülerde lezyon SUV_{maks}'ı açısından istatistiksel olarak anlamlı bir fark izlenmedi (p>0,05).

Sonuç: Dudak malign neoplazmı tanısı ile evreleme, yeniden evreleme ve tedaviye yanıt değerlendirme amacıyla çekilen ¹⁸F-FDG PET/BT görüntülerinde AA olarak yapılacak olan ek görüntülemenin, tümörün lokalizasyonunun ve boyutunun daha doğru belirlenmesinde faydalı ve gerekli olduğu sonucuna varılmıştır.

Anahtar kelimeler: Dudak malign neoplazmı, ağız açık pozisyonlama, ¹⁸F-FDG PET/BT

Introduction

Lip and oral cavity malignancies are the 16th most common neoplasms in the world, with nearly 355,000 new diagnoses and over 177,000 deaths in 2018 (1). Lip cancers are mostly seen in the 5th and 6th decades and are six times higher in males than in female patients. Lip cancers constitute 12% of head and neck cancers (HNC) and 25%-30% of oral cavity cancers. Lower lip cancer accounts for 88%-98% of lip cancers. The vast majority of lesions are located on the vermilion border of the lower lip. More than 95% are squamous cell carcinomas (SCC) and 70% are well differentiated. Basal cell carcinomas constitute 13% of upper lip cancers and less than 1% of lower lip cancers (2). Lip cancers are important diseases as they can affect patients' quality of life and cause cosmetic problems (3). Distant metastases due to lip carcinomas occur very rarely. Because it can be easily noticed by virtue of its localization, in 93% of patients, the tumor is at an early stage when diagnosed (4). Recurrence may develop in 15.1% of patients, and this is due to large size tumor and poor differentiation (5). The main risk factors associated with lip and oral cavity cancers are tobacco use, betel quid chewing, alcohol consumption, poor oral hygiene, low fruit and vegetable dietary habit, high exposure to ultraviolet light, radiotherapy, human papilloma virus infection and genetic factors (6,7). The major prognostic factor in lip carcinomas is the presence of cervical lymph node metastasis. The probability of cervical lymph node spread during diagnosis is between 2 and 16% in lower lip cancers (8). The gold standard treatment is neck dissection and resection of the primary tumor in the presence of lymph node metastasis (9). Accurate localization of a malignant neoplasm and early detection of cervical lymph node metastases play a critical roles in the management and survival of patients with this disease. Clinical examination and anatomical imaging with ultrasound (USG), computed tomography (CT) or magnetic resonance imaging (MRI) have proven to be of limited value for the correct staging of the cervical lymph nodes (10). The use of 2-deoxy-2-[¹⁸F] fluoro-D-glucose positron emission tomography/computed tomography

(¹⁸F-FDG PET/CT) is important in the initial assessment of early-stage and advanced-stage head and neck carcinomas. In the evaluation of primary lesions, nodal disease and distant metastases, sensitivity and specificity of ¹⁸F-FDG PET/CT were found to be superior to those of traditional imaging methods (11). Correct evaluation of the size and localization of the lesion is important in lip carcinomas because it affects treatment planning and follow-up parameters. Usually, clinical examination underestimates the actual thickness of the tumor and lymph node involvement (10). Studies have shown that ¹⁸F-FDG PET/CT has higher accuracy, sensitivity and positive predictive value than CT and MRI in determining the width and depth of the primary tumor (12). However, because of the closeness of anatomical structures of the head and neck region and increased physiologic uptake of ¹⁸F-FDG in this area, the spatial resolution of ¹⁸F-FDG PET/CT examination of the oral cavity and lip carcinoma may not be sufficient. ¹⁸F-FDG PET/CT shows high sensitivity but rather low specificity and weak spatial and anatomical resolution. Hence, it is often difficult to localize lip and oral cavity lesions with high accuracy. Therefore, some additional positional techniques may be useful for evaluating lip carcinomas.

We evaluated correct localization, width and depth of malignant lip neoplasms with the contribution of open mouth (OM) imaging technique at ¹⁸F-FDG PET/CT.

Materials and Methods

Fifty-six patients (17 women, 39 men; mean age 69±11.5 years) with histopathologically proven malignant lip neoplasm underwent ¹⁸F-FDG PET/CT (Philips, True Flight Select, USA) imaging in our clinic approximately 2017-2021 were included in the study. Manisa Celal Bayar University Faculty of Medicine Local Ethics Committee (decree number: 20.478.486/1069) approval was required and written informed consent was obtained from all patients. Patients fasted for at least 6 h and their blood glucose concentrations were measured to confirm the levels were below 200 mg/dL. Whole body images of the patients were taken after the 60 min resting phase following

intravenous injection of 370-555 MBq (10-15 mCi) ^{18}F -FDG. The patients spent the resting period without moving or speaking in a quiet room. Combined (fusion) whole body images of the patients in mouth close positions were acquired 60 min after intravenous injection of 5.2 MBq/kg ^{18}F -FDG. CT acquisition (16 slice; 120 kVp; 80 mA) was immediately followed by multibed PET acquisition (lutetium yttrium orthosilicate crystals; 3-dimensional 3D acquisition; 180 s per bed position; 5 bed positions). PET images were reconstructed using 3D ordered subsets expectation maximization as appropriate, in conjunction with the parameters described for the clinical protocol. Attenuation was corrected by the CT images obtained after ^{18}F -FDG injection. Intravenous contrast material was not used for the PET/CT scan. Immediately after, additional OM head and neck image acquired by a 50 mL syringe to standardize the position. A syringe was placed between the teeth to ensure correct and standardized immobilization (Figure 1). The acquisition was performed with quiet respiration for 5 min. All data were evaluated by two experienced nuclear



Figure 1. A 69 year old woman presented with lower lip squamous cell carcinoma. Additional open mouth head and neck image acquired by a 50 mL syringe placed between the teeth to ensure correct and standardized immobilization

medicine physicians blinded to each other, on a computer display in 3 orthogonal planes (i.e., axial, coronal, and sagittal). The observers did not have any information about the results of the conventional imaging modalities (USG, CT, MRI) and clinical examination findings. Closed mouth (CM) and OM scans were analyzed separately. Lip lesions were analyzed semiquantitatively according to maximum standard uptake value (SUV_{max}). The SUV_{max} was calculated automatically by software, as the ratio of the maximum tissue concentration of ^{18}F -FDG (kBq/mL) in the structure delineated by the region of interest to the activity injected per gram body weight of the patient (kBq/g). The PET/CT images suggested lymph node involvement in the case of any focal ^{18}F -FDG uptake greater than the background activity and correspond to nodular structures on CT. Lesion SUV_{max} , SUV_{mean} , lesion size, lesion localization and presence of lymph nodes were evaluated in OM and CM images. Findings were compared and correlated with radiological, histopathological and clinical findings.

Statistical Analysis

Data were recorded in the SPSS 21.0 data analysis program; lesion SUV_{max} , SUV_{mean} , lesion size, lesion localization and lymph node presence were compared between OM and CM images ($p < 0.05$ was considered as statistically significant).

Results

Lesion SUV_{max} , SUV_{mean} , lesion size and localization and presence of lymph nodes were evaluated both on OM and CM images. We calculated the lesion size by measuring the depth and wideness of the lesion. Since 10 patients had restaging and treatment response evaluation ^{18}F -FDG PET/CT, 68 images were included in the statistical evaluation. All the results were compared and correlated with radiological, histopathological and clinical findings. No statistical significant difference was detected between OM and CM SUV_{max} ($p > 0.05$) (Table 1). This revealed that openness or closure of the mouth did not affect SUV_{max} .

Distant metastasis was found in 13 of the 56 patients included in our study. There were 5 lung, 2 bones, 5 axillas and/or mediastinal lymph nodes and 1 lung and liver metastasis. There was no effect of mouth position on the detection of distant metastasis, as expected. Regional lymph node metastasis was not observed in 31 images (46%), whereas in 37 (54%) ^{18}F -FDG PET/CT images regional lymph node metastasis was detected. The presence of lymph nodes was correctly detected in all OM patients. While the presence of lymph nodes was correctly detected in 83.8% of CM patients, it was found to be inconsistent in 16.2%. It was observed that OM imaging

	n	Minimum	Maximum	Mean	Standard deviation	p
CM SUV _{max}	68	1.50	36.60	7.8618	7.59617	0.506
OM SUV _{max}	68	1.20	38.30	7.7632	8.13391	
CM SUV _{mean}	68	0.50	12.70	2.1015	1.95437	0.325
OM SUV _{mean}	68	0.40	22.40	1.9206	2.75180	
Valid n (listwise)	68	-	-	-	-	-

(p<0.05 was considered significant), CM: Closed mouth, OM: Open mouth, SUV_{max}: Maximum standard uptake value

		Frequency	Percent	Valid percent
CM lesion size	Incorrect	36	52.9	52.9
	Correct	32	47.1	47.1
	Total	68	100.0	100.0
OM lesion size	Incorrect	3	4.4	4.4
	Correct	65	95.6	95.6
	Total	68	100.0	100.0

CM: Closed mouth, OM: Open mouth

had no additional contribution in detecting lymph nodes. ¹⁸F-FDG PET/CT images were compared with the clinical, radiological (MRI and CT) and/or histopathological results in terms of lesion localization and dimension evaluation. Lesion size was correctly detected in 95.6% of OM images, but lesion size was correctly detected in only 47.1% of CM images (Table 2). OM positioning is much more correlated with the clinical findings on the basis of lesion size. While the lesion localization was detected correctly in all OM images, the localization assessment was incorrect in 57.4% of the CM images (Table 3). OM images are much more accurate in detecting both localization and the dimension of the lesions (Figure 2).

Forty-one PET/CT scans (60.3%) had CT artifacts due to dental amalgams. When these images are evaluated, 46.3% dimensional error is detected in the CM position, while this number decreases to 7.3% in the OM position. Similarly, 53.7% localization error was detected in the CM position in 41 images, but no error was determined in the localization evaluation in the OM position (Figure 3). Ten patients had more than one ¹⁸F-FDG PET/CT imaging. Two patients were imaged 3 times and 8 patients were imaged 2 times with PET/CT. One of these patients did not accept surgery, tumor growth was observed at follow-up and re-evaluated with PET/CT. The other 9 patients had various metastatic lesions and were treated with chemotherapy, radiotherapy, or chemoradiotherapy.

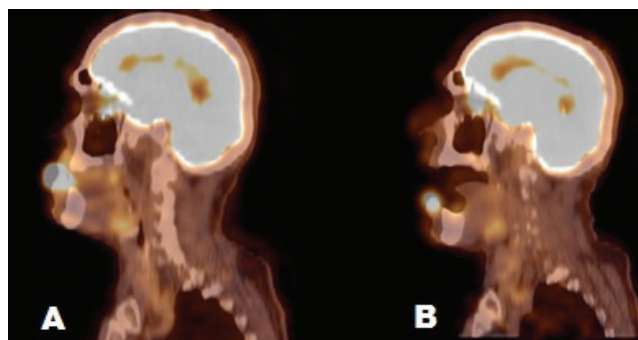


Figure 2. Closed (A) and open (B) mouth fused sagittal ¹⁸F-FDG PET/CT images of a 61 year old man with lower lip squamous cell carcinoma. Open mouth positioning helped to identify the lesion size and localization. SUV_{max}: Maximum standard uptake value, PET: Positron emission tomography, CT: Computed tomography, FDG: Fluorodeoxyglucose

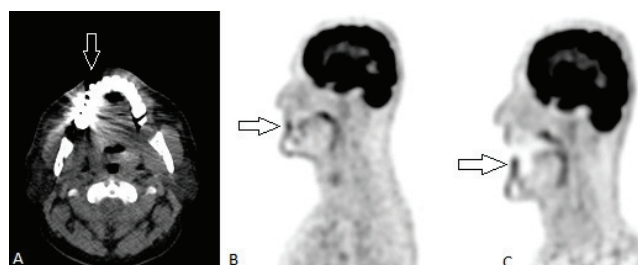


Figure 3. Sixty-four year old man presented with lip squamous cell carcinoma had dental amalgam artifact, which results in blind areas (arrow) at axial CT images (A). PET images were evaluated instead of CT and PET/CT due to amalgam artifact. Identification the localization of the very small lesion (arrow) in CM position is contradictory (B). The size and the localization of the lesion is unclear. It is easy to clearly identify the localization of the lesion (arrow) to the lower lip as his mouth is open at sagittal PET images (C)

PET: Positron emission tomography, CT: Computed tomography, CM: Closed mouth

Discussion

Lip cancer is usually diagnosed earlier than other carcinomas of the oral cavity because it is easier to notice. The surgical treatment of lip cancer involves excision of the entire tumor while leaving an adequate margin of healthy tissue. The prognosis in patients diagnosed with lip carcinoma depends on the stage of the disease. The greater the

Table 3. Difference of closed mouth and open mouth imaging in terms of lesion localization assessment

		Frequency	Percent	Valid percent
CM lesion localization	Incorrect	39	57.4	57.4
	Correct	29	42.6	42.6
	Total	68	100.0	100.0
OM lesion localization	Correct	68	100.0	100.0
	Total	68	100.0	100.0

CM: Closed mouth, OM: Open mouth

thickness of the tumor, the higher the probability of lymph node metastasis (13). Therefore, it is critical to determine the size and thickness of the tumor correctly while staging (14). ^{18}F -FDG PET/CT plays an important role in evaluating HNC. However, localization and size evaluation of this region can be difficult due to the multiplicity of the anatomic structures and increased physiologic uptake of ^{18}F -FDG. PET/CT shows high sensitivity but rather low specificity and weak spatial and anatomic resolution. Therefore, it is often difficult to localize lip and oral cavity lesions with high accuracy. PET/CT plays an important role in the management of patients with HNC. The diagnostic success of PET/CT in different cancers compared to PET or CT alone is now an indisputable fact, and PET/CT has become the most important cancer imaging modality (15). Imaging methods in HNC make an important contribution to clinical examination. Various techniques and positioning methods have been studied to provide an optimal image of scanning methods in HNCs. OM imaging technique in oral cavity tumors was first described by Henrot et al. (16) in 2003. They indicated that OM technique allows a better visualization, especially in oral cavity lesions that cannot be localized because of CT artifacts due to dental amalgams. Henrot et al. (16) described dynamic maneuvers such as Puffed Cheek Technique, the modified Valsalva maneuver, phonation and The OM technique during the CT shoot. They have showed that the OM technique is especially effective in evaluating the CT images of patients with oral cavity and oropharynx tumors with dental amalgam, because of the attenuation created by the X-ray beam as it crosses dental amalgam (16). Kumar et al. (17) also evaluated the similar techniques (puffed-cheek, OM, modified valsalva maneuver, phonation) to better identify the lesions on PET/CT in HNC patients. They underlined that the OM technique is especially useful when a tumor of the oral cavity is not clearly visible because of dental amalgam artifact (17). Metal artifacts affect the image quality and give different results in OM and CM scans. Forty-one PET/CT scans (60.3%) had CT artifacts due to dental amalgams

in our study. In these patients, when comparing the OM and CM images, we observed that the OM scans are much more accurate in detecting both localization and the dimension of the primary lesions.

Pentenero et al. (12) evaluated the accuracy of PET/CT in oral SCC patients. They concluded that PET/CT scan showed good accuracy in determining tumor width and depth. They used the additional OM position, which revealed an increased space between the oral structures and provided a much clearer visualization (12).

Cistaro et al. (18) evaluated usefulness of the OM technique in patients with oral cavity carcinomas. They found that for anatomic localization and detection of tumor extent, OM images always resulted in better visualization than conventional CM images. They also found that in four patients, tumors were not detected using the CM technique but were correctly evaluated with the OM method because of better discrimination of the adjacent anatomical structures. They found no difference between the two techniques in terms of lymph node involvement, which was similarly concluded in our study. They included 34 patients with oral cavity tumors in their studies, and only one of them had lip cancer. Our study is the first and only to compare two techniques in patients with lip cancer homogeneously (18).

Lymph node involvement is the most important prognostic factor in patients with lip cancer, studies show that 5-year survival rates are reduced to approximately 50% in patients with nodal disease (19). Regional spread of lower lip carcinoma is unlikely, but death is mostly the result of uncontrolled disease in the neck. The role of elective neck dissection for treating lip cancer is controversial. Most surgeons do not recommend elective neck dissection for lower lip cancer. Onercl et al. (13) showed that tumor thickness correlated well with cervical lymph node metastasis in lower lip cancer. They showed that the risk of metastatic cervical lymph node increased if the primary lesion was above 5 mm (14). Supporting this data, in our study, all patients with cervical lymph node metastases had a tumor size above 5 mm. Regional lymph node metastasis was observed in 37 (54%) ^{18}F -FDG PET/CT images in our study and we found that OM imaging has no additional contribution to the detection of metastatic cervical lymph nodes.

When evaluating images of patients with HNC, optimal patient preparation technique can also help decrease unexpected ^{18}F -FDG uptake. To prevent non-pathologic increase orofarengal activity, patients are asked not to speak or chew during the waiting period and after ^{18}F -FDG injection. In our study, we informed all patients that

they should spend the waiting period under appropriate conditions. All patients were kept in the waiting room under optimized waiting conditions. Patients stayed in waiting rooms with a similar room temperature, and they were instructed not to use mobile phones, not to chew gum and not to talk.

Although lip cancer is usually an easily recognizable malignancy, some small and deeply located lesions may not be anatomically distinguishable. Especially in these patients, the location and extension of lesions are evaluated more easily from the OM positioning technique.

Since the primary treatment of lip cancer is surgery, it is critical to determine the extent of the lesion accurately (20,21). In our study, we observed that the OM images are very guidance for the surgeon who will perform the surgery in terms of determining the surgical margins. As seen in the results of our study, compared to conventional PET/CT imaging, OM PET/CT scanning improves the assessment of tumor localization and extent in the patients with carcinoma of the lip.

Study Limitations

Our study had several limitations: (1) The radiological images of the patients were in the form of MR or CT, and there was no single standard imaging method, (2) histopathological data were in the form of excision or wide resection, and there was no standard surgical procedure in this respect, (3) the number of patients was relatively small.

Conclusion

We conclude that additional OM head and neck imaging is useful and necessary for the accurate determination of the localization and size of the tumour, thus enhancing the value of PET/CT in staging, re-staging and response to the treatment of malignant lip neoplasms. We recommend routine OM positioning in patients with lip cancer to avoid additional X-ray exposure. Since it may be difficult to stand still with OM position during whole-body imaging, an additional OM head and neck scan is a good option for patients. We suggest that appropriate positioning techniques will also have beneficial results in other head and neck malignancies such as oral cavity, tongue, buccal mucosa, gingival mucosa, and oropharynx.

Ethics

Ethics Committee Approval: Manisa Celal Bayar University Faculty of Medicine Local Ethics Committee (decree number: 20.478.486/1069).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: G.M., C.S., Concept: G.M., C.S., Y.P., G.G., E.S., Design: G.M., C.S., Y.P., G.G., E.S., Data Collection or Processing: G.M., C.S., Analysis or Interpretation: G.M., C.S., Y.P., Literature Search: G.M., G.G., E.S., Writing: G.M., G.G., E.S.

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