Int J Clin Exp Med 2019;12(1):735-743
www.ijcem.com /ISSN:1940-5901/IJCEM0072413

Original Article

^{18}F-FDG PET/CT in diagnosis and staging of tongue squamous cell carcinoma

Dong Zheng[1,2*], Lixuan Niu[3*], Jun Fei[2], Ke Li[2], Jiahe Tian[1]

[1]Department of Nuclear Medicine, General Hospital of PLA, Beijing, China; [2]Department of Radiology, 306 Hospital of PLA, Beijing, China; [3]Department of Oral and Maxillofacial Surgery, School and Hospital of Stomatology, Peking University, Beijing, China. [*]Equal contributors.

Received January 9, 2018; Accepted September 12, 2018; Epub January 15, 2019; Published January 30, 2019

Abstract: The aim of the present study was to evaluate the application value of ^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET/CT in the diagnosis and staging of tongue squamous cell carcinoma. In 52 patients with tongue squamous cell carcinoma confirmed by pathology, there were 34 males and 18 females (age, 22-78 years; mean age, 52.2 years). ^{18}F-FDG PET/CT manifestations of the 52 patients were retrospectively analyzed; TNM staging and histopathological differentiation grading of the 52 patients were assessed according to postoperative pathology, and associations between ^{18}F-FDG uptake and differentiation or staging of tongue squamous cell carcinoma were examined. Preoperative staging was prospectively reviewed and the results were compared with those of postoperative pathological staging. The results showed that the majority of patients were at middle or advanced stage (28/52) when newly diagnosed. The lesions were mostly located in the middle or middle-posterior part of the tongue (38/52). The sensitivity of PET/CT in diagnosing tongue squamous cell carcinoma was 92.3%. There were no statistically significant differences in the maximum Standardized Uptake Value (SUV_{max}) in the well, moderate-well and moderate degree of tongue carcinoma cell differentiation (P = 0.109). The SUV_{max} in stage III or IV patients was statistically significantly higher than that in stage I or II (P = 0.000). There was an excellent correlation between the result of preoperative PET/CT and postoperative pathological staging (Kappa = 0.859, P = 0.000). The accuracy of PET/CT in staging tongue squamous cell carcinoma was 90.4% (47/52). Conclusions can be drawn that the SUV_{max} correlates well with the stage of the tongue squamous cell carcinoma but not with the degree of de-differentiation. FDG PET/CT is highly sensitive for the diagnosis and highly accurate for pre-surgical staging of tongue squamous cell carcinoma and is a highly accurate noninvasive imaging approach for the pre-surgical diagnosis and staging.

Keywords: Tongue squamous cell carcinoma, ^{18}F-FDG, positron-emission tomography and computed tomography, stage

Introduction

Oral tongue carcinoma is one of the most common oral and maxillofacial malignant tumor and the first most common type of oral cancers worldwide [1]. Previous studies have shown that oral cancer ranked the 21st among Chinese population in 2009-2011 [2]. The incidence has a clear upward trend in recent years. The American Cancer Society recently predicted that in the new cases of malignant tumors, oral cavity cancers would rank 10th in 2017 [3]. While preoperative staging is extremely important for the treatment and prognosis judgment of oral tongue carcinoma, currently, CT or MRI are usually used for tongue cancer preoperative routine examination, and more relevant research have been introduced [4, 5]. Studies have showed that CT or MRI only provides morphological assessment of tongue cancer and thus is unable to detect micro-metastasis within lymph nodes. Instead, PET/CT, PET combining CT, could provide both accurate anatomical and useful metabolic information of tongue cancer and has been increasingly used in diagnosis of tumors at present. FDG PET-CT imaging in Head and Neck Squamous Cell Carcinoma has multiple applications including staging, radiotherapy planning, treatment adaptation, response assessment, and recurrence detection [6-8]. However, the use of FDG PET-CT for staging HNSCC remains controversial [9, 10]. In

Table 1. Patient characteristics and tumor features of the tongue carcinoma study population (N = 52)

Characteristic	N Patients (%)
Gender	
Male	34 (65.4%)
Female	18 (34.6%)
Age, years (mean 52.2, range 30-75)	
≥ 60	12 (23.1%)
≥ 40 or <60	35 (67.3%)
< 40	5 (9.6%)
Subsite	
Anterior	6 (11.5%)
Middle	24 (46.2%)
Posterior	4 (7.7%)
Anterior-middle	2 (3.8%)
Posterior-middle	15 (28.8%)
Overall	1 (1.9%)
Tumor differentiation	
Well	17 (32.7%)
Well-Moderate	19 (36.5%)
Moderate	16 (30.8%)
AJCC stage	
I	11 (21.6%)
II	13 (25.0%)
III	13 (25.0%)
IV	15 (28.8%)
Gross morphology	
Exophytic	26 (50%)
Other	26 (50%)

most of the studies, patients usually comprise many different forms of cancer, such as oropharynx, oral cavity, hypopharynx, larynx, paranasal sinuses. The study with PET/CT concerning just at the tongue squamous cell carcinoma is rare. A previous study on patients with oral tongue carcinoma [11] showed that the accuracy of preoperative staging using MRI alone, PET/CT alone and combined MRI-PET/CT were 33.3%, 72.2% and 72.2%, respectively. It implies that PET/CT alone could important in the preoperative staging of oral tongue carcinoma. But the study evaluated just 18 cases, which is a small sample size. Accordingly, the results might be a certain degree of error. Then, our study enrolling so many tongue squamous cell carcinoma patients (52 cases) confirmed by pathology retrospectively analyzed the clinical characteristic, PET/CT imaging, pathological data and prospectively reviewed preoperative staging of them in order to further explore the value of PET/CT in the diagnosis and staging of tongue squamous cell carcinoma.

Materials and methods

Patients

Our study had Institutional Review Board approval. Patients with complaint of tongue ulcer, white spots or mass, pain or movement disorders underwent PET/CT in our hospital between June 2014 to December 2015 were included in this study. Eligibility criteria included the following: 1) Patients possessed biopsy-proven tongue squamous cell carcinoma. 2) Patients had not previously been treated for carcinoma. 3) Patients underwent whole-body PET/CT examination in our center as well as the images had good quality. Patients satisfying at least one of the following criteria were excluded: 1) Tongue carcinoma radical surgery was not performed after PET/CT examination. 2) Patients had concurrent second primary malignancies. In total, 52 patients (34 men, 18 women; mean age 52.2 years, range 22-78 years) were enrolled. Among them, there were 17 cases of well differentiated squamous cell carcinoma, 16 cases of moderate differentiated squamous cell carcinoma and 19 cases of moderate-well differentiated squamous cell carcinoma. The average duration of 52 patients from the onset of symptoms to diagnosis of the disease were 5.7 month. The main complaints were chronic tongue ulcer or white patch (26 cases) and tongue mass (26 cases). (Patient and tumor characteristics are listed in **Table 1**).

^{18}F-FDG PET/CT examinations

All patients fasted for at least 6 h before the PET/CT study. None of the patients had a blood glucose level exceeding 130 mg/dL before ^{18}F-FDG injection, and no intravenous contrast agent was used. A body-weight-adapted dose of ^{18}F-FDG was injected intravenously (370-555 MBq) and scanning began 60 ± 10 min later. During the 60 min required for tracer distribution and uptake, patients were orally hydrated (approximately 500 ml of water) and they were asked to void their bladder before scanning. All

Table 2. SUV_{max} of primary tumor differences in various differentiation

Tumor differentiation	n	$\bar{X} \pm S$	χ^2 value	*P* value
Well	17	5.52 ± 3.21		
Moderate-Well	19	6.97 ± 4.08		
Moderate	16	7.99 ± 3.89	4.425	0.109

Table 3. SUV_{max} of primary tumor differences in various stage

Stage	n	$\bar{X} \pm S$	χ^2 value	*P* value
I	11	3.04 ± 1.06		
II	13	5.30 ± 1.64		
III	13	8.63 ± 3.46		
IV	15	9.33 ± 4.06	26.9	0.000

patients were placed supine. The scans were acquired with the patients immobilized. PET scanner integrated with a dual section helical CT scanner (Somatom Emotion; Siemens Medical Solutions) was used to acquire and coregister PET and CT images in succession. Six to eight bed positions were used and the acquisition time was 2-2.5 min per position. CT imaging began at the vertex and progressed to the upper thigh (40-100 mAs; 120 kV; 5 mm slice thickness) and PET scanning followed immediately over the same body region. CT data were used for attenuation correction and images were reconstructed using a standard ordered-subset expectation maximization algorithm. The axial spatial resolution was 6.5 mm at the center of the field of view.

Imaging and data analysis

All PET/CT images were reviewed at a workstation using fusion software (Syngo, Siemens Medical Solutions) that provided multiplanar reformatted images in transverse, coronal and sagittal planes. PET/CT fusion images, PET images and CT images of the same patient were analyzed frame by frame. The obtained images were visually analyzed independently by two experienced radiologists blinded to any clinical information. Interobserver disagreements were resolved by consensus. Visual analysis and semi-quantitative analysis had been employed. Spherical regions of interest were placed over the pathological raised uptakes on PET/CT images to obtain the maximum Standardized Uptake Value (SUV_{max}). The diagnostic criteria for tongue carcinoma and lymph node metastasis were: focal lesion exhibited increased ^{18}F-FDG uptake, $SUV_{max} \geq 2.5$ or radioactivity greater than liver tissue uptake. PET/CT preoperatively staging was compared with the postoperative pathological diagnosis according to the 8th Edition American Joint Committee on Cancer (AJCC) staging criteria [12].

Statistical analysis

Kruskal-Wallis rank-sum were used to determine the significance of SUV_{max} differences among well, moderate-well and moderate differentiation of cancers of the tongue. Kruskal-Wallis rank-sum and an unpaired t test with a Bonferoni correction were used to determine the significance of SUV_{max} differences among stage I, stage II, stage III and stage IV. PET/CT diagnosis for the stage of 52 patients with oral tongue carcinoma was compared with the postoperative pathological diagnosis. κ values were used as the index to measure the degree of consistency. κ value ≥ 0.75 indicated an excellent degree of consistency while κ value was < 0.4 indicated a poor level of consistency level. All quantitative data were expressed as mean ± standard deviation ($\bar{X} \pm S$) and statistical analyses were done using SPSS Software (version 17.0 for Windows). A *P* value < 0.05 was considered statistically significant.

Results

Diagnosis of tongue carcinoma with ^{18}F-FDG PET/CT

Of the 52 cases of malignant lesions, there were three false negatives. The sensitivity of fasting ^{18}F-FDG PET/CT for the diagnosis of tongue carcinoma were 92.3%. These three false negatives observed were all in stage I cancers and small ulcerative. PET/CT would be somewhat limited in early ulcerative cancer states. Primary lesions were located in the anterior part of the tongue in 6 cases, 24 cases of middle, 4 cases of posterior , 2 cases of middle-anterior, 15 cases of middle-posterior and 1 case involving all parts. The maximum diameter of the tumor was between 0.6-7.8 cm (mean 3.3 cm). 9 cases of cancer invaded lingual-septum. Of the 52 cases, only 10 cases had been detected by plain CT scan (5 cases slightly low-density, 5 cases slightly high-density), resulting in a sensitivity of only 19.2% for CT.

Table 4. SUV_{max} of primary tumor multiple comparison in various stage

Compare groups	$\bar{R}_i$-$\bar{R}_j$	$\sigma_{\bar{R}i-\bar{R}j}$	Z_{ij}	*P* value
I *vs* II	2.26	1.21	1.50	0.067
I *vs* III	5.59	1.21	3.15	0.000
I *vs* IV	6.29	1.17	3.20	0.000
II *vs* III	3.33	1.21	2.51	0.006
II *vs* IV	4.03	1.12	3.09	0.001
III *vs* IV	0.70	1.12	1.62	0.533

SUV_{max} of primary tumor differences in various differentiations

The mean ± standard deviation of SUV_{max} for Moderate (n = 16), Moderate-Well (n = 19), Well (n = 17) differentiated groups were 7.99 ± 3.89 (range 2.53-14.2), 6.97 ± 4.08 (2.14-19.18), and 5.52 ± 3.21 (1.86-12.07), respectively. There were no significant differences among moderate, moderate-well and well differentiated tongue carcinoma groups (X^2 = 4.425, P = 0.109) (**Table 2**).

SUV_{max} of primary tumor differences in various stage

Primary tumor resection or combined with cervical lymph node dissection were adopted in total 52 cases. The SUV_{max} of stage I (n = 11), stage II (n = 13), stage III (n = 13) and stage IV (n = 15) was 3.04 ± 1.06 (range 1.29-11.02), 5.30 ± 1.64 (3.24-7.32), 8.63 ± 3.46 (2.87-14.21), and 9.33 ± 4.06 (11.37-22.51), respectively. Because of the heterogeneity of variances, Kruskal-Wallis rank-sum test of four independent samples was used, showing a significant difference among stage I, stage II, stage III and stage IV (P < 0.0001, **Table 3**). Using the unpaired t test with Bonferroni correction, there were significant differences between stage I and stage III (P < 0.05/6 = 0.008), stage I and stage IV (P < 0.008), stage II and stage III (P < 0.008), stage II and stage IV (P < 0.008). However, there was no significant difference between stage I and stage II (P = 0.067), stage III and stage IV (P = 0.533, **Table 4**).

Correlation between preoperative PET/CT and postoperative pathological staging

In total, 12 cases of stage I, 12 cases of stage II, 15 cases of stage III (**Figure 1**) and 13 cases of stage IV (**Figure 2**) were identified at the preoperative staging of tongue cancer by PET/CT assessment.

Confirmation of the PET/CT results by postoperative pathology (staging), 11 cases of stage I, 13 cases of stage II, 13 cases of stage III and 15 cases of stage IV were identified by postoperative pathology.

Comparison between the PET/CT staging results and pathological diagnosis Showed that there was an excellent correlation between the result of preoperative PET/CT and postoperative pathological staging (Kappa = 0.859, P = 0.000). The accurate rate for staging of oral tongue carcinoma using PET/CT was 90.4% (47/52) (**Table 5**).

There were three PET/CT underestimated stage cases due to false negative of micrometastasis lymph node, while the two overestimated cases were result of false positive of brown fat and reactive lymph node uptake respectively.

Discussion

Biopsy is the main basis for the diagnosis of tongue squamous cell carcinoma, however, it is an invasive exam after all. Although patients had symptoms of pain, ulcer or induration earlier, the time of diagnosis was mostly in the middle and late stage. In this study, the average duration of 52 patients from the onset of symptoms to diagnosis of the disease were 5.7 month and more than half of the patients at stage three or four (54%, 28/52). While the higher the stage is, the greater the difficulty of surgery is and the worse the prognosis of patients is [13-15]. So the early diagnosis of tongue cancer is extremely important. The ideal way to achieve early diagnosis is through a noninvasive approach that is easily accepted by patients. Imaging is undoubtedly the best choice. Previous studies have used CT and MRI for diagnosis and staging. In contrast to these morphological imaging modalities which only scan a selectively localized region, PET/CT can rapidly accomplish a whole-body image one time, thus displaying all the lesions that uptake the radiopharmaceutical. Through combining metabolic and morphological assessment of lesions with significant improvements in diagnostic accuracy, PET/CT has had a considerable impact on diagnosis, staging, patient management of oncology and so on in the past

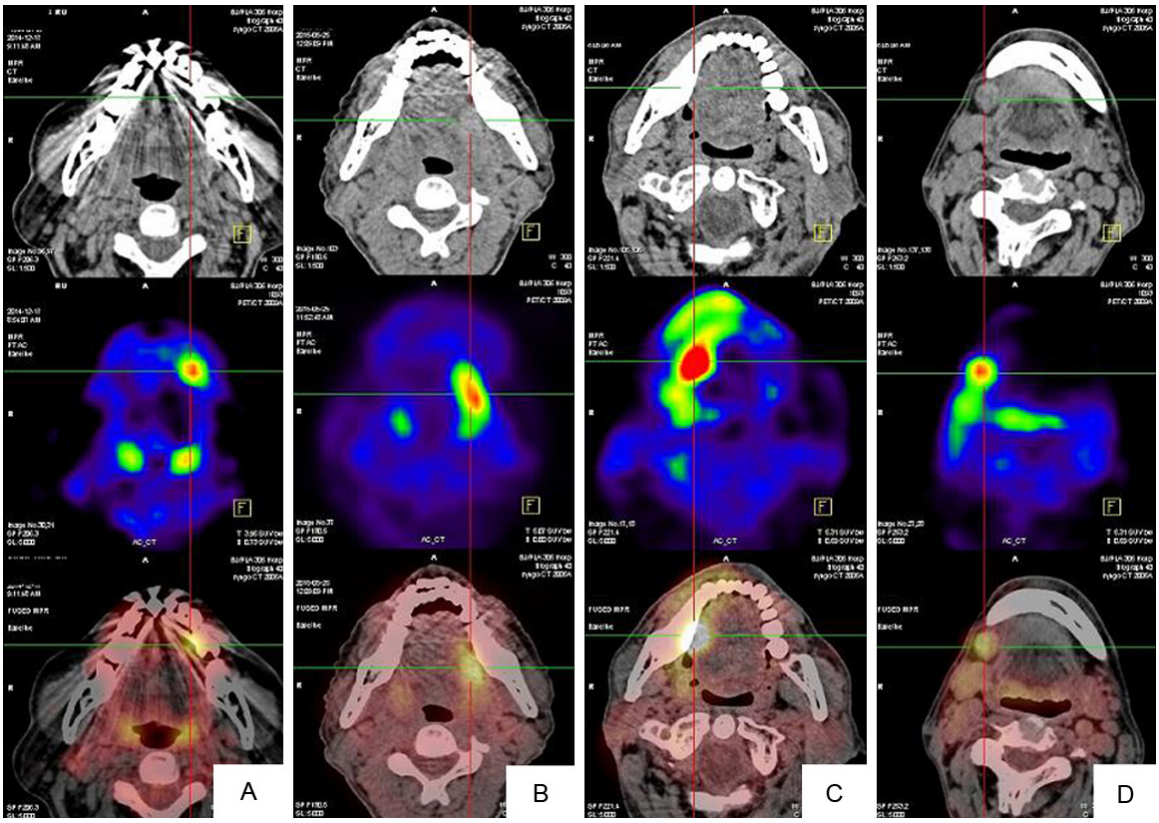

Figure 1. Seventy-year-old female with stage I show local increased uptake in the anterior-middle of left lingue margin (A). Fifty-six-year-old male with stage II show local increased uptake in the middle of left lingue margin (B). Fifty-seven-year-old male with stage III show local increased uptake in the middle of right lingue margin (C), and there is intense hypermetabolic activity of one ipsilateral metastasis lymph node (D).

decade [16]. The maximum standardized uptake value (SUV_{max}), a semiquantitative simplified measurement of the tissue deoxyglucose metabolic rate measured on FDG-PET/CT, could be a parameter for evaluating the degree of tissue metabolic activity and the proliferation rate of tumor cell [17]. So, it is conducive to early detection of tumors. In this group of cases, SUV_{max} of 49 cases were increased in different degrees (mean 7.02 ± 3.8, range 2.5-19.2). The sensitivity of PET/CT in diagnosing oral tongue carcinoma was reached 92.3%. There were three false negatives, their gross forms were ulcer type. The course of them was about 3 months. Inequality of their Sites comprised apex linguae, middle of left margin, middle-posterior of right margin. The tumors that are small (< 1 cm) may be missed because of partial volume averaging related to the resolution limits of the PET/CT apparatus [18-20]. Of these three cases, two were well differentiation, one moderate-well differentiation. It was suggested that false negative might be related to the higher degree of cell differentiation. On the other hand, it was suggestive that chronic small ulcer lesions should be highly vigilant. These false negatives observed were only in stage I cancers. So, the diagnostic accuracy of the approach would be somewhat limited in early ulcerative cancer states. Even if the PET/CT examination was negative in ulcerative cases, the biopsy should be performed.

CT is frequently poorly sensitive to detecting tongue carcinoma within the soft tissues due to its suboptimal contrast soft resolution. The present study showed that the CT diagnostic sensitivity of tongue carcinoma was only 19.2%. So plain CT scan could not act as diagnostic tool alone for tongue carcinoma.

Theoretically, the lower differentiation of tumor cell tends to the more actively proliferating and the higher radioactive isotope uptake. While the correlation between SUV and tumor differ-

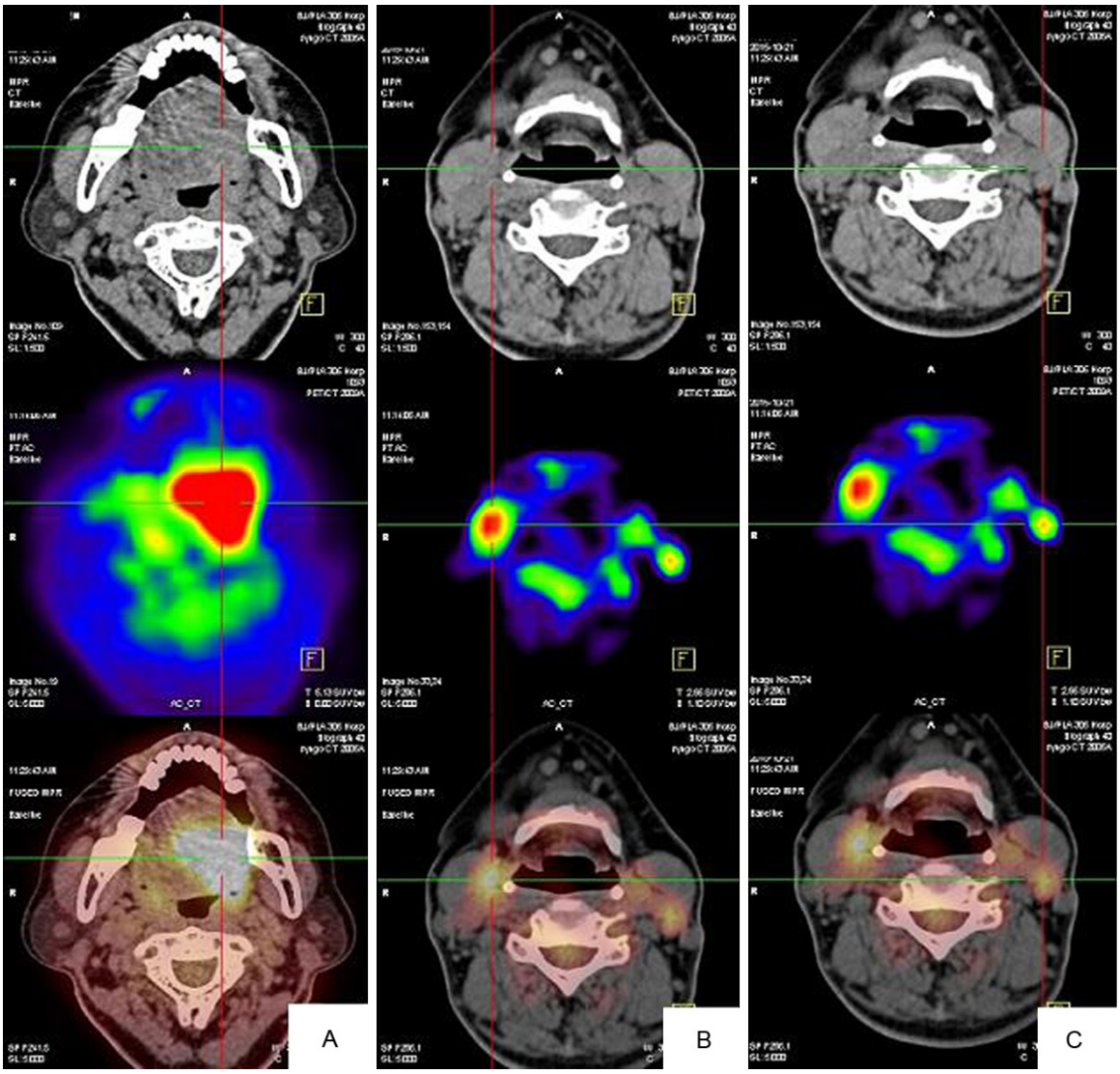

Figure 2. Fifty-nine-year-old female with stage IV show local intense hypermetabolic tumor in the middle -posterior of left lingue body, involving ipsilateral palatine tonsil and nuclei fibrous linguae (A). Moderately hypermetabolic activity of metastasis lymph node on the right side (B). Mildly hypermetabolic activity of metastasis lymph node on the left side (C).

entiation is still controversial. Early data reported by Dylan Jones *et al.* [21] showed that the SUV_{max} of ^{18}F-FDG PET/CT had nothing to do with cell differentiation. Our studies showed a similar result. The mean SUV_{max} for well, moderate-Well and moderate differentiation groups were 5.52, 6.97 and 7.99, respectively. There was no significant difference among the three groups. But the value of them were rising. No significant difference might be due to a lack of sample size.

The correlation between the SUV_{max} and the staging of tongue cancer had not been reported before. The present study reveals that there is a significant difference among stage I, stage II, stage III and stage IV. The higher the value of SUV_{max} implies the poorer staging of tongue cancer. The SUV_{max} of stage I add stage II, stage III add stage IV was 4.26 ± 1.8 and 9.0 ± 3.7, respectively. The former was significant smaller than the latter. Preoperative staging was made on the basis of extent of primary tumor, metastasis in cervical lymph nodes and distant metastasis. The diagnostic criteria for AJCC stage III (T3N0M0 or T1-3N1M0), T3 means the extent of primary tumor is bigger than 4 cm. According to our studies, when primary lesion is

Table 5. Correlation between preoperative PET/CT and postoperative pathological staging

PET/CT staging	Postoperative pathological staging				Total
	I	II	III	IV	
I	11		1		12
II		11		1	12
III		2	12	1	15
IV				13	13
Total	11	13	13	15	52

Kappa = 0.859, P = 0.000.

less than 4 cm, if its SUV_{max} value is higher than 6.06 (the biggest SUV_{max} of the group of stage I add stage II is 4.26 add 1.8 equal 6.06, note: 4.26 is the mean, 1.8 is the standard deviation), which indicated that the cancer is at least in stage III, then the possibility of lymph node metastasis is greater and observation must be extremely careful to avoid missed diagnosis. Accurate preoperative staging of tongue carcinoma is extremely important for selection of the surgical procedure, comprehensive treatment plans and prognosis assessment. A few earlier studies have made preoperative staging through imaging methods. Wang et al. [22] evaluated the value of imaging in preoperative staging of 36 patients with oral tongue carcinoma and indicated that the MRI, CT diagnostic accuracy of staging was 90.5%, and 61.9%, respectively. Another Wang *et al.* [23] concluded that PET alone diagnostic accuracy of staging was 85.7% through studying about 10 patients. However, the systematic study of staging by PET/CT has rarely been reported yet. Our study shows that PET/CT diagnostic accuracy of preoperative staging was 90.4%, which is higher than CT or PET alone examination respectively and similar to MRI examination.

Cervical lymph nodes mostly spindle-shaped, most of its longest diameter is longitudinal. Because CT image is always transverse, it sometime does not reflect the true size of lymph nodes. On the other hand, normal size lymph node metastases in the head and neck can not be detected by CT scan. The above factors reduced the accuracy rate of staging in tongue carcinoma. MRI scanning has high soft tissue resolution and may be used to perform multifaceted and multiscan sequence scanning, which may provide a signal comparison between different imaging modalities. So MRI is considered the optimal technique for evaluating tongue carcinomas compared with computed tomography [24]. But a long clinical assessment time (normally 30-45 min), which is prone to poor image quality for artifacts, a small and limited scan range are its disadvantage in accurate staging of oral tongue carcinoma. The main criterion to consider lymph nodes as metastatic by MRI and CT is the size. However, this approach is of limited value since that metabolic change precedes morphologic change in metastatic lesions. PET which find lesion through metabolic change has proven to have priority over conventional imaging modalities to detect lymph node metastasis [25, 26]. In our study, there were three metastasis lymph nodes which considered normal on CT exhibited increased FDG uptake. However, on PET alone image, the anatomical structure is unclear. Physiological muscle and brown fat uptake can make identification of pathology difficult. The differentiation between inflammation, infection and nodal metastasis is sometimes challenging in interpretation as all these situations may show an increased ^{18}F-FDG uptake. While, PET/CT is the optimal diagnostic modality which provide a PET and CT fusion image showing the increased metabolism of the tumor and the anatomical localization simultaneously. Our study showed an excellent correlation between the result of preoperative PET/CT and postoperative pathological staging (Kappa = 0.859). It is of great significance for the treatment selection and prognosis judgment.

In sum, there is an excellent correlation between the result of preoperative PET/CT and postoperative pathological staging. The SUV_{max} of the primary tumor by FDG-PET/CT scanning may be definitely associated with stages and uncertainty correlated with differentiation in tongue squamous cell carcinoma. FDG PET/CT is highly sensitive for the diagnosis and highly accurate for pre-surgical staging of tongue squamous cell carcinoma and is a highly accurate noninvasive imaging approach for the pre-surgical diagnosis and staging. It will become a routine method in diagnosis and staging of tongue squamous cell carcinoma with which may aid with guiding the selection of treatment options and improve prognosis.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Jiahe Tian, Department of Nuclear Medicine, General Hospital of PLA, 28 Fuxing Road, Beijing 100853, China. Tel: +8613910554175; E-mail: tianjh301@163.com

References

[1] Rui-Pionheiro A, Jose LL, Enrique JS, Jorge RS and Carlos I. A pioneering epidemiological study investigating the incidence of squamous cell carcinoma of tongue in a portuguese population. Med Oral Patol Oral Cir Buca 2012; 17: e550-e554.

[2] Chen W, Zheng R, Baade PD, Zhang S, Zeng H, Bray F, Jemal A, Yu XQ and He J. Cancer statistics in China, 2015. CA Cancer J Clin 2016; 66: 115-132.

[3] Rebecca LS, Kimberly DM and Ahmedin J. Cancer statistics, 2017. CA Cancer J Clin 2017; 67: 7-30.

[4] Kwon M, Moon H, Nam SY, Lee JH, Kim JW, Lee YS, Roh JL, Choi SH and Kim SY. Clinical significance of three-dimensional measurement of tumour thickness on magnetic resonance imaging in patients with oral tongue squamous cell carcinoma. Eur Radiol 2016; 26: 858-865.

[5] Juliano A, Moonis G. Computed tomography versus magnetic resonance in head and neck cancer: when to use what and image optimization strategies. Magn Reson Imaging Clin N Am 2018; 26: 63-84.

[6] Troost EG, Schinagl DA, Bussink J, Oyen WJ and Kaanders JH. Clinical evidence on PET-CT for radiation therapy planning in head and neck tumours. Radiother Oncol 2010; 96: 328-334.

[7] Schwartz DL, Macapinla HA and Weber RS. FDGPET staging of head and neck cancer-can improved imaging lead to improved treatment. J Natl Cancer Inst 2008; 100: 688-689.

[8] Bussink J, Van Herpen CM, Kaanders JH and Oyen WJ. PET-CT for response assessment and treatment adaptation in head and neck cancer. Lancet Oncol 2010; 11: 661-669.

[9] James WF, Benjamin D, Heloisa PS, Barry AS, Val JL, Gary HL, R. Edward C, Richard W, John CP, Norbert A, Lawrence HE, W. Warren S, David S, Dominique D, Mark G and Anthony FS. Recommendations on the use of ^{18}F-FDG PET in oncology. J Nucl Med 2008; 49: 480-508.

[10] Fleming J AJ, Smith SP Jr, Paul CM, Hall NC, Daly BT, Agrawal A and Schuller DE. Impact of [^{18}F]-2-fluorodeoxyglucose-positron emission tomography/computed tomography on previously untreated head and neck cancer patients. Laryngoscope 2007; 117: 1173-1179.

[11] Chen W, Zhang C, Zhang S, Liang L, Zhang B, Liu C, Zhang Z and Liang C. Application value of MRI combined with positron emission tomography PET/CT in diagnosis and preoperative staging of tongue squamous cell carcinoma. J Med Imaging Radiat Oncol 2015; 59: 170-178.

[12] Doescher J, Veit JA, Hoffmann TK. The 8 th edition of the AJCC cancer staging manual: updates in otorhinolaryngology, head and neck surgery. HNO 2017; 65: 956-961.

[13] Mücke T, Kanatas A, Ritschl LM, Koerdt S, Tannapfel A, Wolff KD, Loeffelbein D, Kesting M. Tumor thickness and risk of lymph node metastasis in patients with squamous cell carcinoma of the tongue. Oral Oncol 2015; 53: 80-84.

[14] Erickson LA. Squamous cell carcinoma of the tongue. Mayo clin Proc 2017; 92: 1171-1172.

[15] Sagheb K, Kumar V, Rahimi-Nedjat R, Dollhausen M, Ziebart T, Al-Nawas B and Walter C. Cervical metastases behavior of T1-2 squamous cell carcinoma of the tongue. J Maxillofac Oral Surg 2017; 16: 300-305.

[16] Kitajima K, Suzuki K, Senda M, Kita M, Nakamoto Y, Onishi Y, Maeda T, Yoshikawa T, Ohno Y and Sugimura K. FDG-PET/CT for diagnosis of primary ovarian cancer. Nucl Med Commun 2011; 32: 549-553.

[17] Yagi S, Yahata T, Mabuchi Y, Tanizaki Y and Kobayashi A. Primary tumor SUV_{max} on preoperative FDG-PET/CT is a prognostic indicator in stage IA2-IIB cervical cancer patients treated with radical hysterectomy. Mol Clin Oncol 2016; 5: 216-222.

[18] Pentenero M, Cistaro A, Brusa M, Ferraris MM, Pezzuto C, Carninon R, Colombini E, Valentini MC, Giovanella L, Spriano G and Gandolfo S. Accuracy of 18F-FDG-PET/CT for staging of oral squamous cell carcinoma. Head Neck 2008; 30: 1488-1496.

[19] Port JL, Andrade RS, Levin MA. Positron emission tomographic scanning in the diagnosis and staging of non-small cell lung cancer 2 cm in size or less. J Thorac Cardiovase Surg 2005; 130: 1611-1615.

[20] Ng SH, Yen TC, Liao CT, Chang JTC, Chan SC, Ko SF, Wang HM and Wong HF. ^{18}F-FDG PET and CT/MRI in oral cavity squamous cell carcinoma: a prospective study of 124 patients with histologic correlation. J Nucl Med 2005; 46: 1136-1143.

[21] Jones D, Al-Momani H, Griffith DG, Naguib N, Lewis WG, Havard T and Escofet X. Histological grade/differentiation and ^{18}-FDG PET/CT in oesophageal cancer. Gastroenterology 2013; 144: S515-519.

[22] Wang D, Liu WC, Luo ZB. Comparison of CT and MRI in preoperative diagnosis and staging of

tongue cancer. J Guangdong Med Col 2012; 30: 492-496.
[23] Wang SH, Tang AW, Qiao HX. Metastasis of the neck lymph nodes in patients with tongue squamous cell carcinomas: a comparison of PET with histopathology. Chin J Med Imaging Technol 2003; 19: 30-31.
[24] Iwai H, Kyomoto R, Ha-Kawa SK, Lee S and Yamashita T. Magnetic resonance determination of tumor thickness as predictive factor of cervical metastasis in oral tongue carcinoma. Laryngoscope 2002; 112: 457-461.
[25] Admas S, Baum RP, Stuckensen T, Bitter K and Hör G. Prospective comparison of ^{18}F-FDG PET with conventional imaging modalities (CT, MRI, US) in lymph node staging of head and neck cancer. Eur J Nucl Med 2007; 25: 1255-1260.
[26] Mayoral M, Paredes P, Domènech B, Fusté P, Vidal-Sicart S, Tapias A, Torné A, Pahisa J, Ordi J, Pons F and Lomena F. ^{18}F-FDG PET/CT and sentinel lymph node biopsy in the staging of patients with cervical and endometrial cancer. Role of dual-time-point imaging. Rev Esp Med Nucl Image Mol 2017; 36: 20-26.