Tongue depressor-assisted FDG PET/CT scans in oral cancer: a prospective study with a feasibility protocol

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Abstract

Background

F-18 Fluorodeoxyglucose positron emission tomography with computed tomography (FDG PET/CT) is a powerful tool in oral cancer. However, the oral cavity is a small cavity with complex components. An invasive cancer or post-therapy change frequently cause difficulty in interpretation. In this study, we established a tongue depressor (TD)-assisted FDG PET/CT protocol to solve this problem.

Methods

We enrolled 264 patients with oral cancers. Early and delayed images were acquired in each FDG PET/CT examination. A wooden tongue depressor was placed either between buccal mucosa and teeth or between tongue border and teeth in delayed image. TD placed delayed image was compared with early images to analyze the extent of tumor. The discrimination ratio (DR) of the tumor was calculated as: (images that can clearly distinguish features /all images) × 100%.

Results

In tongue cancer group, the DR of the tumors were 26.1% on early images and 99.3% on TD placed delayed images ($p < 0.001$). In buccal cancer group, the DR of the tumors were 10.9% on early images and 98.2% on TD placed delayed images ($p < 0.001$).

Conclusions

The TD-assisted FDG PET/CT protocol is patient-friendly and effective in analyzing the tumor when evaluating oral cancer.

Introduction

Head and neck cancers are one of the most common cancers globally. Among the cancers of the head and neck, tumors occurring in the oral cavity and oropharynx account for about 40% of cases [1, 2]. Precise tumor staging and restaging in oral cancer can provide a good treatment planning and decision making [3, 4]. This pre-treatment evaluation is commonly performed based on clinical examination, endoscopy and imaging examinations, such as computed tomography (CT) and/or magnetic resonance imaging (MRI). However, the oral cavity is a small cavity with complex components. Although CT and MRI provide high-quality images, the examinations are challenged by anatomical complexity of the head and neck and the presence of imaging artifacts [5].

F-18 Fluorodeoxyglucose (FDG) positron emission tomography (PET) is a better imaging technique than either CT or MRI [6–9]. PET alone, however, has lower spatial resolution than CT or MRI. PET/CT, PET combining CT, described by Beyer et al. [10], combines the anatomic detail provided by CT with F-18FDG PET metabolic information, thereby increasing accuracy in the detection of tumor [11]. Whole body F-18 FDG PET/CT has been well reported to be a powerful tool in staging and treatment planning of oral cancer, even in restaging in the case of recurrence and radiation therapy planning, which can effectively assist otolaryngologists and radiation oncologists on decision making [3, 12]. Tumor staging by whole-body FDG-PET may, in fact, supplement the conventional staging by means of CT/MRI and physical findings [13]. However, due to the scattering of high FDG-avid tumor activity, it interferes the judging of bounding between tumor and adjacent tissues. Even more, an invasive cancer or post-therapy change frequently disrupt the anatomical structure in this oral region and cause difficulty in the interpretation of an FDG PET/CT scan for disease extent evaluation.

An open-mouth method of F-18 FDG PET/CT scan in the staging of oral cancer had been reported by Cistaro et al. They found the open-mouth scan improved the anatomic tumor localization and extent and detection of tumor involvement in adjacent anatomic structures [14]. However, some patients with oral cancers suffered from severe limited mouth opening. Trismus is a significant complication of oral malignancies or its surgical and radiotherapy treatment, or both [15].

The purpose of this study was to design an easy and feasible tongue depressor (TD)-assisted method to solve this problem when evaluating patients with oral cancer using FDG PET/CT.

Materials And Methods

Patients

We enrolled 264 patients (male: 245, female: 19; age range: 33 to 94 years old) with oral cancers (group 1: tongue cancer [n = 138]; group 2: buccal mucosa cancer [n = 110]; group 3: others [lip, palate, gingiva, oropharynx, mouth floor & tonsil, n = 71]) between 2010 August and 2019 November. All patients received at least one F-18 FDG PET/CT examination. This study was approved by the Ethics Committee of Kuang Tien General Hospital (KTGH 10905). As all data were de-identified before analysis. Informed consent was obtained from all subjects.

Imaging technique of F-18 FDG PET/CT

Patients fasted for at least eight hours before examination and were instructed to stay silent and rest on the bed in the waiting room before administration of F-18 FDG and taking scan, to diminish F-18 FDG uptake by the muscles of tongue and vocal cords [16, 17]. All specifications of the 18F FDG PET/CT scan were carried out in accordance with the EANM procedure guidelines for tumour imaging (Eur J Nucl Med Mol Imaging (2015) 42:328–354).

Every patient was administered a weight-related dose of F-18 FDG (277–466 MBq) by intravenous injection. Before the scans, all metal objects such as necklaces, earring and prosthesis were removed. For all patients, a whole body PET/CT scan was acquired from the vertex of skull to the pelvis with 6–8 fields of view (15cm, 3mins each) using the PET/CT (Discovery ST, GE), combing a 16 slice CT scanner based on bismuth germanium oxide (BGO) detector PET tomography. PET was initiated immediately after the CT examination to use CT data for the attenuation correction of PET data (CT scan thickness, 3.3mm, 140kV; 30-auto A/s). Intravenous contrast was not used for the PET/CT scans.

Early 1-hour and delayed 3-hour images were acquired in each FDG PET/CT examination. On the early 1-hour PET/CT scan, the patients closed their mouth. On the delayed 3-hour PET/CT, the patients received the TD-assisted method depending on the location of FDG-avid lesion.

TD-assisted method

In the group 1 (patients with buccal mucosa cancer), a wooden TD was placed either between patient's buccal mucosa and teeth. In the group 2 (patients with tongue cancer), a wooden TD was placed either between patient's tongue border and teeth. In the group 3 (patients with other oral cancer), a wooden TD was placed either between patient's buccal mucosa and teeth or between patient's tongue and teeth depending on the judgment of nuclear medicine physician.

Figure 1 showed the TD positioning for the TD-assisted method. All patients could cooperate well and can tolerate TD placement. With this technique, the patients felt easy and no painful sensation. The informed consent from this patient was obtained for publication of identifying images in an online open-access publication.

Then, the delayed 3-hour image with TD placed was compared with the early 1-hour image. We analyzed features such as the feasibility of an accurate topographic localization of the tumor, evaluation of tumor extent and detection of tumor involvement with adjacent structures by at least 2 experienced nuclear nuclear medicine physicians and 1 otolaryngologist or radiation oncologist. The observers did not have any information about the results of CT and MRI scans if the patient had the examination. Any disagreement between the observers about the images findings were resolved by consensus.

For the F-18 FDG PET/CT scan, the invasion of bone by the tumor was suggested by two conditions: when F-18 FDG uptake was observed adjacent to a visible defect on CT images of the cortical bone or when F-18 FDG uptake was observed out of the cortical bone and within the bone marrow in the adjacent region, even without a detectable cortical erosion, as described by Goerres et. al [18]. All the patients underwent biopsy proved cancer as gold standard.

The discrimination ratio was calculated as: (patients being able to be clearly distinguished the characteristics of tumors /all patients) × 100%.

Statistical analysis

The McNemar test was used to determine if there were statistically significant differences between discrimination ratios on early 1-hour images without TD placed and those on delayed 3-hour image with TD placed. The datasets used and analyzed during the current study available from the corresponding author on reasonable request.

Results

The total numbers of scans were 316 times since some of the patients were performed the F-18 FDG PET/CT twice or more times for tumor recurrence, double cancers or secondary primary oral cancer.

Figures 2 showed examples of images without TD placed and with TD placed in the group 1–3, respectively.

The results of McNemar statistical test showed in Table 1. In the group of tongue cancer, the discrimination ratios of the tumors were 26.1% on early images without TD placed and 99.3% on delayed images with TD placed ($p < 0.001$). In the group of buccal cancer, the discrimination ratios of the tumors were 10.9% on early images without TD placed and 98.2% on delayed images with TD placed ($p < 0.001$). In the group of other oral cancers, the discrimination ratios of the tumors were 66.2% on early images without TD placed and 100% on delayed images with TD placed.

Table 1
Statistical results in three group.

	Total	Pre	Post	P-value
Tongue	138	36 (26.1%)	137 (99.3%)	< 0.001
Buccal	110	12 (10.9%)	108 (98.2%)	< 0.001
Other	71	47 (66.2%)	71 (100%)	-

Discussion

This study clearly disclosed that the TD-assisted FDG PET/CT protocol is easy and effective in analyzing the localization and extent of the tumor and detecting tumor involvement in adjacent structures when evaluating oral cancer.

In recent years, the incidence of oral cancer has increased significantly. Rebecca et al. reported in 2017 that oral cancer will rank tenth among new cases of malignant tumors [19]. Evaluating the extent of lesions is very important for the treatment and prognosis of oral cancer. CT or MRI is commonly used for routine examinations for oral cancer [20]. Studies have shown that CT or MRI can provide high-quality morphological assessment of oral cancer. However, the examinations are challenged by anatomical complexity of the head and neck and the presence of imaging artifacts [5]. Moreover, after oral cancer is treated, the complex anatomical structure of the area becomes more complicated due to changes after

surgery or radiation. The imaging landmarks and symmetry are lost, and the normal anatomical structure is significantly deformed, which distinguishes the changes after treatment from recurrence or residual tumors are challenging.

Instead, PET/CT could provide both accurate anatomical and useful metabolic information of oral cancer. F-18 FDG PET/CT is particularly useful for staging, restaging and radiotherapy planning as well as for assessment of treatment response in head and neck squamous cell carcinoma patients, due to its superior accuracy over clinical examination and conventional anatomic imaging such as MRI and CT examinations [21–23].

F-18 FDG PET/CT as compared with the MRI and CT image, FDG PET/CT has a high sensitivity in tumor detection and anatomic location [24]. The main limitations, especially in the post-treatment setting, are possible false positive results due to inflammation and the inability to detect microscopic disease [4].

However, the oral cavity is a small cavity with complex components including lips, buccal mucosa, tooth, gingiva, tongue, hard palate, floor of mouth, maxilla, mandible bones and some people with dental amalgam, etc. An invasive oral cavity cancer frequently disrupts the anatomical barrier in this region and causes difficulty in the interpretation of an FDG PET/CT study as a metabolic anatomical scan for disease extent evaluation. Some non pathological FDG uptake such as salivary glands' activity or muscle activity also interfere the interpretation of the tumor mapping [25–26]. Therefore, for a long time, the images of oral cancer patients have puzzled nuclear medicine physicians.

An open-mouth protocol in the staging of oral cancer had been developed at CT and F-18 FDG PET/CT examinations [14, 27]. Cistaro et al. reported that the open-mouth scan improved the anatomic tumor localization and extent and detection of tumor involvement in adjacent anatomic structures achieved by the standard F-18 PET/CT procedure. In addition, time of the examination (mid morning), relaxation of muscles before the compound was administered, and an upright position while the patient waited caused a reduction of the frequent equivocal physiologic uptake in the head and neck region. The open-mouth method does not influence the nodal staging. [14].

However, some patients with oral cancers suffered from severe limited mouth opening. Trismus is a significant complication of oral malignancies or its surgical and radiotherapy treatment, or both. Consideration must be given to its early diagnosis, to help in timely intervention and planning of preventive strategies [15].

An ideal examination technique for the assessment the oral cancers is the main issue for nuclear medicine doctor in the F-18 FDG PET CT scan. In this study, we designed a new TD-assisted method to resolve the aforementioned problem by using a wooden tongue depressor to place either between buccal mucosa and teeth or between tongue border and teeth when performing the F-18 FDG PET/CT scan on the delayed 3-hour image. In both groups of patients with tongue and buccal mucosal cancers, the discrimination ratio of tumors [(patients with being able to be clearly distinguished the characteristics of tumors /all patients) × 100%] were significantly higher on images with TD placed, compared with images

without TD placed ($p < 0.001$). In the group of patients with other cancers (lip, palate, gingiva, oropharynx, mouth floor & tonsil), the discrimination ratio of tumors were also higher on images with TD placed, compared with images without TD placed. The feasible, inexpensive and noninvasive TD-assisted FDG PET/CT method introduced in this study provided great benefits in diagnosing the tumor's border with separation from the adjacent anatomical structure (such as gum, tooth, palate, palatine tonsil, metal artifacts and dental amalgum). In addition, the TD-assisted FDG PET/CT method also has several advantages for patients with oral cancers:

1. easily performed by nuclear medicine physicians without spending longer time,

2. no harm and without painful sensation to patients,

3. increasing oral cavity space without artifact on the images due to low density of the wood material (about 0.35–0.5 g/cm^3),

4. easily reach a consensus between radiologists and otolaryngologists,

5. reproducibility.

Conclusion

The easy, feasible, inexpensive and noninvasive TD-assisted FDG PET/CT method provided great benefits in diagnosing the tumor's border with separation from the adjacent anatomical structure for patients with oral cancers. And we believe that the TD-assisted FDG PET/CT method will be easily accepted by the PET/CT apartments of the others hospital and will have a great result in the interpretation of the FDG PET/CT images for patients with oral cancer.

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Figures

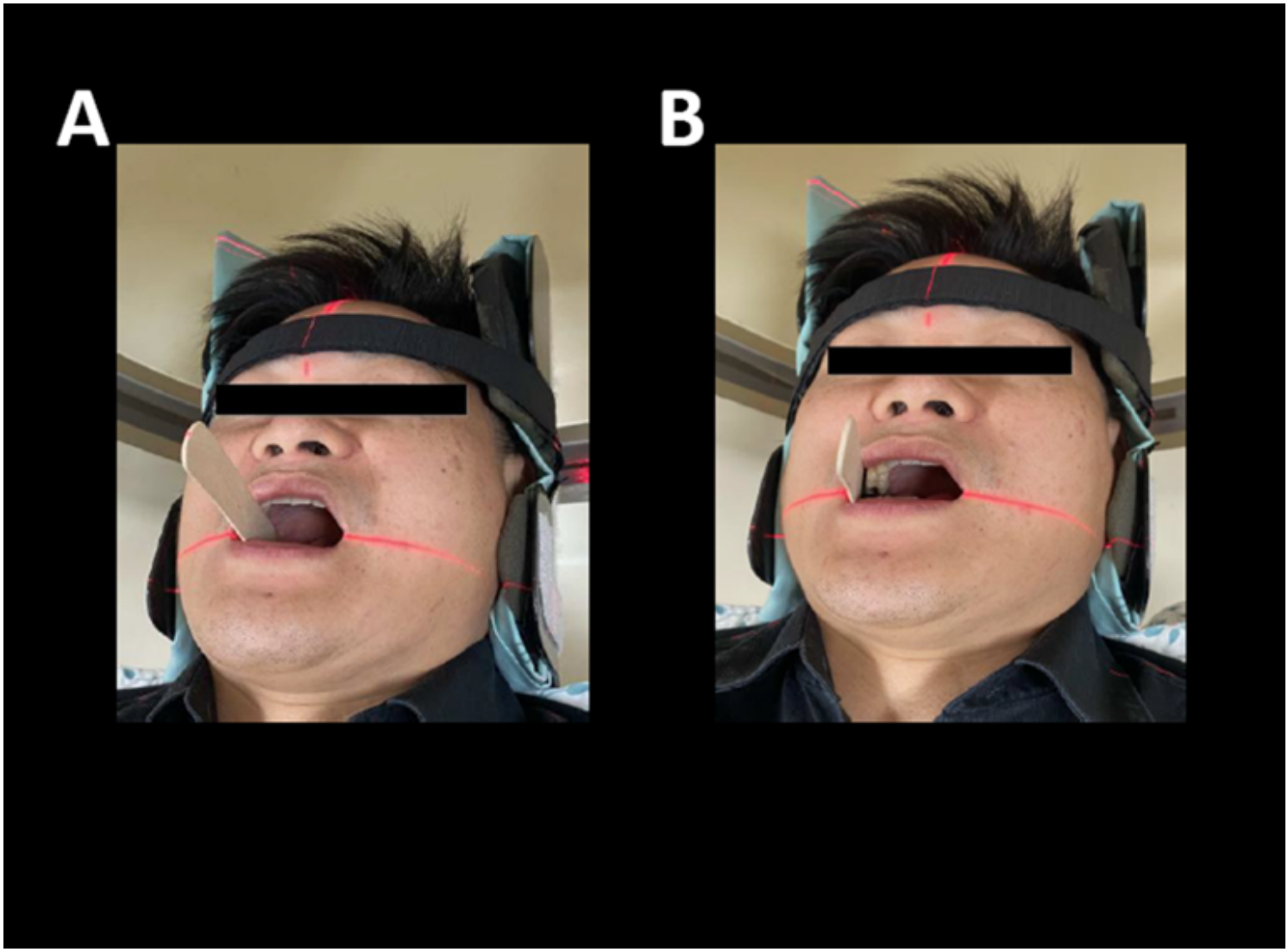

Figure 1

TD positioning for the TD-assisted method. **A.** With tongue depressor placed between the tongue border and the teeth. **B.** With tongue depressor placed between the buccal mucosa and the teeth.

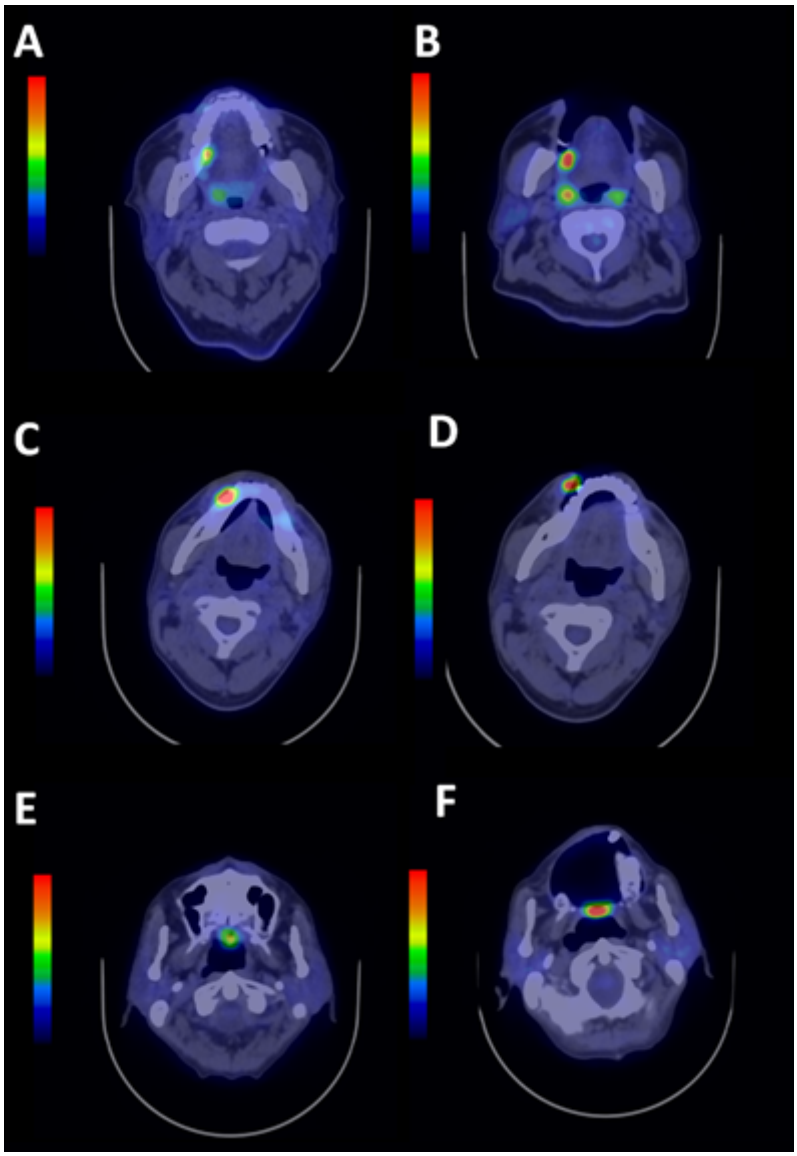

Figure 2

An example of images without TD placed (**A,C.E**) and with TD placed (**B,D,F**) in group 1-3. **A.** The FDG-avid lesion at the right-side tongue border was consistent with tongue cancer in a 43-year-old male patient. The tumor was very close to the teeth and was hard to fine the demarcation on images without TD placed. **B.** After tongue depressor placed between the tongue border and the teeth, the images revealed the tumor with a clear gap from the adjacent tissue. The tongue tumor was clearly separated from the teeth, mouth floor and inner gum sulcus. **C.** An FDG-avid lesion at the right buccal mucosa was consistent with buccal cancer in a 46-year-old male patient. The tumor was abutting the teeth without gap on images without TD placed. **D.** After tongue depressor placed between the buccal mucosa and the teeth, the images revealed the buccal tumor with a clear gap from the teeth. The buccal mucosa tumor was clearly separated from tooth and outer gum sulcus. **E, F.** An FDG-avid lesion at the palate region was consistent with palate cancer in a 58-year-old male patient. The tumor can be distinguish on both images without TD and with TD placed.