

## Correlation between glucose transporter type-1 expression and $^{18}\text{F}$ -FDG uptake on PET in oral cancer

Chul-Hwan Kim, Moon-Young Kim

Department of Oral and Maxillofacial Surgery, College of Dentistry, Dankook University, Cheonan, Korea

**Abstract** (J Korean Assoc Oral Maxillofac Surg 2012;38:212-20)

**Objectives:** Fluorine-18 fluorodeoxyglucose positron emission tomography ( $^{18}\text{F}$ -FDG PET) is a non-invasive diagnostic tool for many human cancers wherein glucose uptake transporter-1 (GLUT-1) acts as a main transporter in the uptake of  $^{18}\text{F}$ -FDG in cancer cells. Increased expression of glucose transporter-1 has been reported in many human cancers. In this study, we investigated the correlation between  $^{18}\text{F}$ -FDG accumulation and expression of GLUT-1 in oral cancer.

**Materials and Methods:** We evaluated 42 patients diagnosed with oral squamous cell carcinoma (OSCC) and malignant salivary gland tumor as confirmed by histology. 42 patients underwent pre-operative  $^{18}\text{F}$ -FDG PET, with the maximum standardized uptake value ( $\text{SUV}_{\text{max}}$ ) measured in each case. Immunohistochemical staining was done for each histological specimen, and results were evaluated post-operatively according to the percentage (%) of positive area, intensity, and staining score.

**Results:** For OSCC,  $\text{SUV}_{\text{max}}$  significantly increased as T stage of tumor classification increased. For malignant salivary gland tumor,  $\text{SUV}_{\text{max}}$  significantly increased as T stage of tumor classification increased. For OSCC, GLUT-1 was expressed in all 36 cases. GLUT-1 staining score (GSS) increased as T stage of tumor classification increased, with the difference statistically significant. For malignant salivary gland tumor, GLUT-1 expression was observed in all 6 cases; average GSS was significantly higher in patients with cervical lymph node metastasis than that in patients without cervical lymph node metastasis. Average GSS was higher in OSCC ( $11.11 \pm 1.75$ ) than in malignant salivary gland tumor ( $5.33 \pm 3.50$ ). No statistically significant correlation between GSS and  $\text{SUV}_{\text{max}}$  was observed in OSCC or in malignant salivary gland tumor.

**Conclusion:** We found no statistically significant correlation between GSS and  $\text{SUV}_{\text{max}}$  in OSCC or in malignant salivary gland tumor. Studies on the various uses of GLUT during  $^{18}\text{F}$ -FDG uptake and SUV and GLUT as tumor prognosis factor need to be conducted through further investigation with large samples.

**Key words:** Mouth neoplasms, Positron-emission tomography, Glucose transporter-1, Standardized uptake value

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### I. Introduction

Patients diagnosed with oral cancer around the world number more than 500,000 every year<sup>1</sup>. According to the American Cancer Society, oral cancer was the 8th most frequently found malignant tumor in the USA in 2007, accounting for 2.4% of overall cancer diagnosis and having

5-year survival rate of 50%<sup>2</sup>. Most oral cancers can be detected at the early stage through simple ocular inspection or palpation, but it is important to determine the stage of the cancer precisely since the complete elimination of the primary tumor and cervical lymphatic metastasis are essential for successful treatment considering the long-term survival rate and the prognosis of the patient.  $^{18}\text{F}$ -Fluorodeoxyglucose positron emission tomography ( $^{18}\text{F}$ -FDG PET) is a non-invasive method capable of diagnosing the primary tumor in the early stage as well as lymphatic metastasis and remote metastasis and evaluating the prognosis of the patient. Furthermore, it allows tracking observation for the treatment process and recurrence of cancer. Thus, it is widely used for the evaluation of various cancers. In fact, its usefulness for oral diseases is receiving growing attention. Glucose

**Chul-Hwan Kim**

Department of Oral and Maxillofacial Surgery, College of Dentistry, Dankook University, 119, Dan-daero, Dongnam-gu, Cheonan 330-714, Korea  
TEL: +82-41-550-1996 FAX: +82-41-551-8988  
E-mail: kimchoms@dankook.ac.kr

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and glycogen as its stored form are the energy source for the aerobic metabolism of the cell. A malignant tumor cell expresses high glucose uptake rate and demand compared with normal cells due to the increase of glucose uptake transporter (GLUT) and enhancement of glycolytic activity<sup>3</sup>. Widely used as the marker substance for PET,  $^{18}\text{F}$ -FDG is an analogue of the glucose flown into the cell competitively with the glucose<sup>4</sup>; here, glucose and  $^{18}\text{F}$ -FDG are flown into the cell through GLUT, which has 6 subtypes: GLUT-

1, GLUT-2, GLUT-3, GLUT-4, GLUT-5, and GLUT-7. The type and degree of their expressions vary according to the different regions and tissues of the body<sup>5</sup>. Currently, the overall expression of GLUT-1 is known to be increasing in various cancer cells such as esophageal cancer, colon cancer, pancreas cancer, non-small cell lung cancer, and brain tumor; this is related to the clinical stage, invasiveness of tumor, remote metastasis, and unfavorable prognosis<sup>6-9</sup>. This study sought to measure the degree of expression of GLUT-1 in

**Table 1.** Characteristics of patients and results of  $^{18}\text{F}$ -FDG PET imaging and GLUT-1 immunostaining

Case No.	Sex (M/F)	Age (yr)	Site	Diagnosis	T classification	N classification	SUV <sub>max</sub>	GLUT-1 proportion	GLUT-1 intensity
1	M	70	Cheek	SCC WD	3	0	4.6	3	3
2	M	73	Oral floor	SCC WD	2	0	6.2	4	3
3	F	71	Gingiva	SCC WD	1	0	4.4	4	3
4	M	53	Gingiva	SCC MD	2	0	9.3	4	3
5	F	69	Gingiva	SCC WD	2	2b	2.7	4	3
6	M	78	Tongue	SCC WD	1	1	4.0	4	3
7	M	61	Cheek	SCC WD	3	1	5.2	3	3
8	F	73	Palate	SCC WD	2	2c	14.7	4	3
9	F	75	Palate	SCC WD	1	0	7.1	4	3
10	M	67	Oral floor	SCC WD	1	0	6.7	4	3
11	F	69	Gingiva	SCC WD	2	0	8.2	3	3
12	M	67	Palate	SCC WD	2	1	3.0	4	3
13	F	53	Gingiva	SCC WD	2	1	5.4	4	3
14	M	67	Tongue	SCC WD	2	1	10.4	4	3
15	F	61	Gingiva	SCC WD	3	2c	23.8	4	3
16	M	76	Gingiva	SCC MD	4a	x	21.6	3	3
17	M	73	Palate	SCC WD	1	0	3.4	4	3
18	F	76	Cheek	SCC WD	1	0	3.0	3	3
19	F	57	Tongue	SCC MD	1	0	8.4	4	3
20	F	46	Gingiva	SCC MD	4a	2a	6.2	2	2
21	M	64	Palate	SCC WD	2	0	10.2	4	3
22	M	68	Palate	SCC WD	1	0	4.4	3	3
23	M	77	Gingiva	SCC WD	2	0	11.7	4	3
24	F	57	Tongue	SCC WD	2	0	8.4	4	3
25	M	75	Palate	SCC WD	3	1	8.6	4	3
26	F	86	Tongue	SCC WD	4a	0	12.6	4	3
27	M	32	Oral floor	SCC MD	2	0	11.0	4	3
28	M	63	Gingiva	SCC MD	1	0	5.9	4	3
29	M	67	Gingiva	SCC WD	2	0	5.3	4	3
30	M	71	Oral floor	SCC MD	4	1	11.4	3	3
31	M	29	Tongue	SCC WD	1	0	3.0	4	3
32	F	58	Oral floor	SCC WD	1	0	3.0	4	3
33	M	29	Gingiva	SCC WD	1	0	3.0	3	3
34	F	81	Tongue	SCC WD	2	1	7.5	4	3
35	M	59	Palate	SCC WD	2	1	7.3	4	3
36	M	33	Tongue	SCC WD	2	0	10.7	4	3
37	F	43	Palate	MEDC	2	0	3.2	2	2
38	F	90	Palate	METC	3	0	9.8	2	2
39	F	78	Tongue	ACC	2	0	5.2	1	2
40	F	65	Palate	ADC	3	2c	8.9	3	2
41	M	45	Palate	CCC	2	1	4.7	4	3
42	M	29	Cheek	ACCC	2	0	5.3	2	2

( $^{18}\text{F}$ -FDG PET: fluorine-18 fluorodeoxyglucose positron emission tomography, GLUT-1: glucose uptake transporter-1, M: male, F: female, SCC WD: squamous cell carcinoma well-differentiated type, SCC MD: squamous cell carcinoma moderately differentiated type, MEDC: mucoepidermoid carcinoma, METC: myoepithelial carcinoma, ACC: adenoid cystic carcinoma, ADC: adenocarcinoma, CCC: clear cell carcinoma, ACCC: acinic cell carcinoma, SUV<sub>max</sub>: maximum standardized uptake value)

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patients with oral squamous cell carcinoma and patients with malignant salivary gland tumor, analyze the relationship with  $^{18}\text{F}$ -FDG PET results to determine the correlation, and evaluate its usefulness in the diagnosis.

## II. Materials and Methods

### 1. Object of the study

A retrospective study was conducted on 42 patients who were diagnosed with oral squamous cell carcinoma and malignant salivary gland tumor and who underwent operations from May 2006 to July 2011. All operations were performed by 1 oral and maxillofacial surgeon, and GLUT-1 in the removed tumor tissues was immunohistochemically stained. The study targeted patients who received PET-computed tomography (CT) before the surgery to check the degree of  $^{18}\text{F}$ -FDG uptake by the tumor inside the oral cavity. No patients received anticancer chemotherapy or anticancer radiation treatments before the surgery, and patients with insulin-dependent diabetes were excluded. At least 24 out of 42 patients were male and 18 were female, with average age of 63.

Tissue samples of 42 patients were collected from the following regions: 12 from gingiva, 12 from palate, 9 from tongue, 5 from oral floor, and 4 from cheek.

Among 42 patients, 29 had well-differentiated type of oral

squamous cell carcinoma, 7 had moderately differentiated type of oral squamous cell carcinoma, 1 had mucoepidermoid carcinoma, 1 had myoepithelial carcinoma, 1 had adenoid cystic carcinoma, 1 had adenocarcinoma, 1 had clear cell carcinoma, and 1 had acinic cell carcinoma.(Table 1) Typical cases are shown in Figs. 1-3.

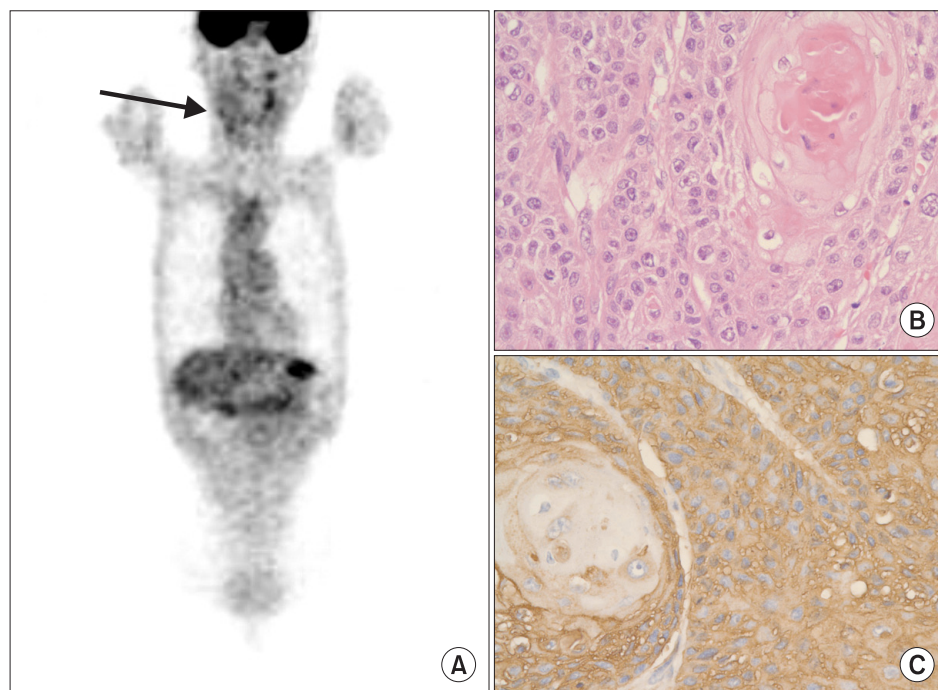
### 2. Method

#### 1) $^{18}\text{F}$ -FDG PET and results

$^{18}\text{F}$ -FDG PET was performed on 42 patients before the surgery. For PET scan, patients fasted for 8 hours before scanning, their weight and blood sugar were measured, and they were scanned when blood sugar level was 80-120 mg/dL. Each patient was given 0.15 mCi/kg of  $^{18}\text{F}$ -FDG through intravenous injection, and scan was formed with PET/CT system (Gemini GXL-6; Philips International B.V., Amsterdam, the Netherlands). Later, maximum standardized uptake value ( $\text{SUV}_{\text{max}}$ ) of the primary tumor region was measured from PET image. One nuclear medicine specialist identified the highest FDG uptake region to determine the  $\text{SUV}_{\text{max}}$ .

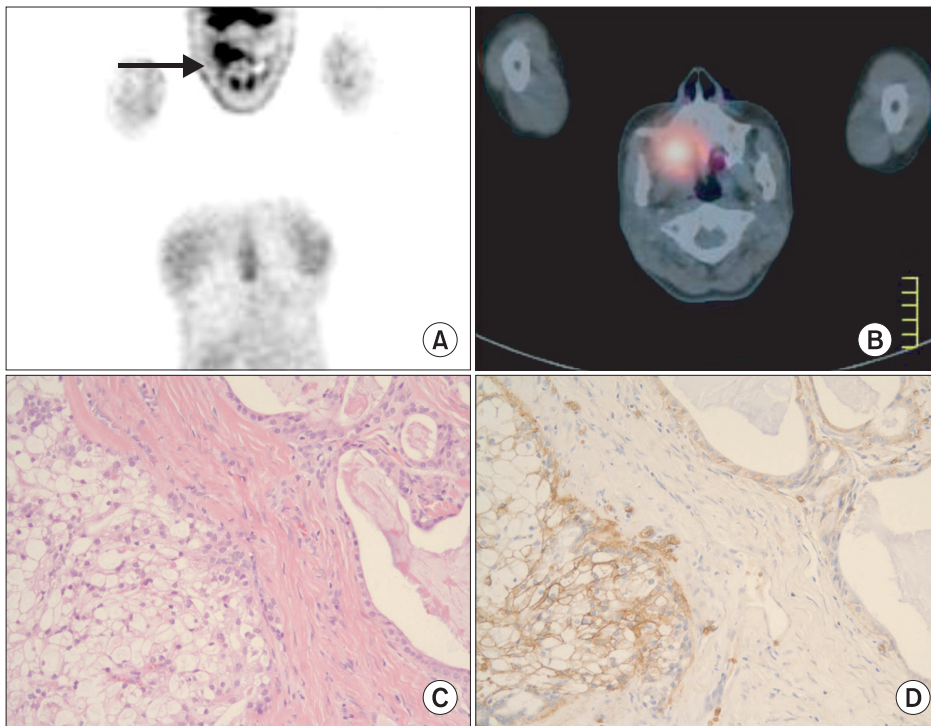
#### 2) Immunohistochemical examination of GLUT-1

Immunohistochemical staining was done on the paraffin block produced by fixing tumor tissues in formalin. The pathological tissue slide stained with hematoxylin-eosin



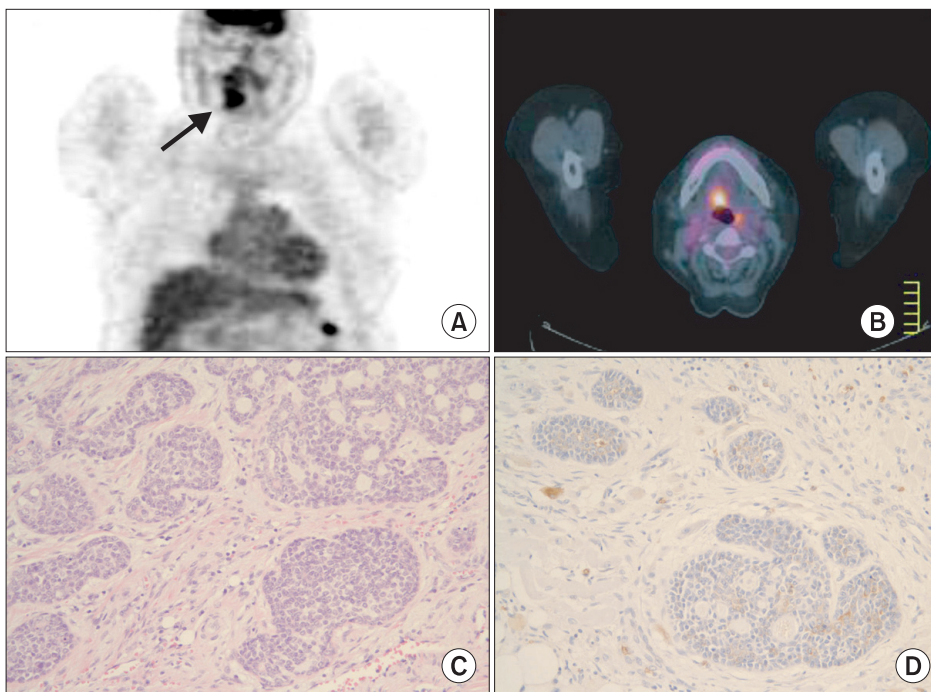
**Fig. 1.** Well-differentiated squamous cell carcinoma in the oral floor of a 73-year-old man (case No. 2). A. Positron emission tomography. Coronal maximum intensity projection image with increased fluorodeoxyglucose accumulation in the right floor of mouth (arrow). B. Well-differentiated squamous cell carcinoma confirmed on H&E staining ( $\times 400$ ). C. Immunohistochemical staining score for glucose uptake transporter-1 in tumor cells was 12 (strong intensity and more than 75% of positive area) ( $\times 400$ ).

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**Fig. 2.** Mucoepidermoid carcinoma in the right maxilla of a 43-year-old woman (case No. 37). A. Positron emission tomography (PET). Coronal maximum intensity projection image with increased fluorodeoxyglucose accumulation in the right floor of mouth (arrow). B. Fused PET and computed tomography images. A tumor shows maximum standardized uptake value of 3.2. C. Mucoepidermoid carcinoma confirmed on H&E staining ( $\times 200$ ). D. Immunohistochemical staining score for glucose uptake transporter-1 in tumor cells was 4 (moderate intensity and 25-50% of positive area) ( $\times 200$ ).

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**Fig. 3.** Adenoid cystic carcinoma in the right maxilla of a 78-year-old woman (case No. 39). A. Positron emission tomography (PET). Coronal maximum intensity projection image with increased fluorodeoxyglucose accumulation in the right floor of mouth (arrow). B. Fused PET and computed tomography images. A tumor shows maximum standardized uptake value of 5.2. C. Adenoid cystic carcinoma confirmed on H&E staining ( $\times 200$ ). D. Immunohistochemical staining score for glucose uptake transporter-1 in tumor cells was 2 (weak intensity and 25-50% of positive area) ( $\times 200$ ).

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was reexamined, and typical paraffin blocks for the tumor of each patient were selected. The paraffin block was sliced into 4  $\mu\text{m}$  thick pieces and deparaffined and hydrated. All immunohistochemical staining processes were automated with the Bond Polymer Refine Detection (Leica Biosystems, Newcastle, UK) system. The antigen retrieval process was skipped, and anti-GLUT-1 rabbit monoclonal antibody

(Epitomic, Burlingame, CA, USA) was diluted at the ratio of 1 : 1,000 and used as the primary antibody.

For the interpretation of the immunohistochemical staining of GLUT-1 antibody, the case wherein it was stained along the cell membrane of the tumor cell was considered positive. Staining was divided into 4 grades according to intensity (0=negative, 1=low, 2=medium, 3=high) and analyzed

separately in 4 grades (1=0-25%, 2=25-50%, 3=50-75%, 4=75-100%) according to the percentage of positively stained tumor cell. The result of multiplication of two variables (GLUT-1 staining score) was used as GLUT-1 staining score (GSS). Pathological slides were read by one pathologist without providing the clinical information of patients.(Table 2)

### 3. Statistical method

The T, N stage and  $SUV_{max}$  of tumor and GLUT-1 expression score in tumor cell were expressed in the form of average $\pm$ standard deviation. SPSS version 12.0 (SPSS Inc., Chicago, IL, USA) was used as the statistical program for the comparative analysis of the measurements; ANOVA was used for the comparison of average between groups, and Pearson's correlation test, for the correlation between  $SUV_{max}$  and GSS. Results were considered statistically significant when  $P$ -value was less than 0.05.

**Table 2.** Immunohistochemical staining results

Characteristic	No. of patients
GLUT-1	
% positive area	
<25%	1
25-50%	4
50-75%	9
>75%	28
Intensity	
Weak	0
Moderate	6
Strong	36

(GLUT-1: glucose uptake transporter-1)

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**Table 3.** Correlation between  $SUV_{max}$  and histological differentiation, T, N stage in oral squamous cell carcinoma

	n	$SUV_{max}$	
		Mean $SUV_{max}$	$P$ -value
All	36	7.84 $\pm$ 4.83	
Differentiation			
Well	29	7.19 $\pm$ 4.57	
Moderate	7	10.54 $\pm$ 5.31	0.1
Poor	0		
T grade			
T1, T2	28	6.73 $\pm$ 3.24	
T3, T4	8	11.75 $\pm$ 7.35	0.007
N stage			
N0	24	7.33 $\pm$ 4.29	
N+	12	8.85 $\pm$ 5.84	0.384

( $SUV_{max}$ : maximum standardized uptake value)

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## III. Results

### 1. Correlation between $SUV_{max}$ and histological differentiation, T, N stage in oral squamous cell carcinoma

The average  $SUV_{max}$  of a total of 36 samples was 7.84 $\pm$ 4.83.  $SUV_{max}$  according to histological differentiation did not have statistical significance ( $P=0.1$ ), tending to have higher statistical significance with higher T stage ( $P=0.007$ ). Note, however, that  $SUV_{max}$  did not have correlation with cervical lymphatic metastasis ( $P=0.384$ ). (Table 3)

### 2. Correlation between $SUV_{max}$ and T, N stage in malignant salivary gland tumor

The average  $SUV_{max}$  of a total of 6 samples was 6.18 $\pm$ 2.58.  $SUV_{max}$  tended to have higher statistical significance with higher T stage ( $P=0.004$ ) but no correlation with cervical lymphatic metastasis ( $P=0.726$ ). (Table 4)

**Table 4.** Correlation between  $SUV_{max}$  and T, N stage in malignant salivary gland tumor

	n	$SUV_{max}$	
		Mean $SUV_{max}$	$P$ -value
All	6	6.18 $\pm$ 2.58	
T grade			
T1, T2	5	6.48 $\pm$ 2.76	
T3, T4	1	4.70 $\pm$ 0.00	0.004
N stage			
N0	4	5.87 $\pm$ 2.78	
N+	2	6.80 $\pm$ 2.97	0.726

( $SUV_{max}$ : maximum standardized uptake value)

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**Table 5.** Correlation between Glut-1 staining score and histological differentiation, T, N stage in oral squamous cell carcinoma

	n	Glut-1	
		Mean GSS	$P$ -value
All	36	11.11 $\pm$ 1.75	
Differentiation			
Well	29	11.38 $\pm$ 1.24	
Moderate	7	10.00 $\pm$ 3.00	0.176
Poor	0		
T grade			
T1, T2	28	11.57 $\pm$ 1.07	
T3, T4	8	9.50 $\pm$ 2.67	0.017
N stage			
N0	24	11.25 $\pm$ 1.32	
N+	12	10.83 $\pm$ 2.44	0.509

(Glut-1: glucose uptake transporter-1, GSS: Glut-1 staining score)

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**Table 6.** Correlation between Glut-1 staining score and T, N stage in malignant salivary gland tumor

	n	Glut-1	
		Mean GSS	P-value
All	6	5.33±3.50	0.89
T grade			
T1, T2	5	4.00±1.41	
T3, T4	1	12.00±0.00	0.049
N stage			
N0	4	3.50±1.00	
N+	2	9.00±4.24	

(Glut-1: glucose uptake transporter-1, GSS: Glut-1 staining score)

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### 3. Correlation between GSS and histological differentiation, T, N stage in oral squamous cell carcinoma

GLUT-1 expression was observed in all 36 samples, and average GSS was measured to be 11.11±1.75. GSS according to histological differentiation did not have statistical significance ( $P=0.176$ ), tending to have higher statistical significance with higher T stage ( $P=0.017$ ) but no correlation with cervical lymphatic metastasis ( $P=0.509$ ). (Table 5)

### 4. Correlation between GSS and T, N stage in malignant salivary gland tumor

GLUT-1 expression was observed in all 6 samples, and average GSS was measured to be 5.33±3.50. GSS according to T stage did not have statistical significance ( $P=0.89$ ). Note, however, that GSS in patients with cervical lymphatic metastasis showed higher statistical significance compared with that in patients without cervical lymphatic metastasis ( $P=0.049$ ). (Table 6)

### 5. Correlation between $\text{SUV}_{\text{max}}$ and GSS in oral squamous cell carcinoma

There was positive correlation between GSS and  $\text{SUV}_{\text{max}}$ , but such was not statistically significant ( $r=0.058$ ,  $P=0.738$ ). (Table 7)

### 6. Correlation between $\text{SUV}_{\text{max}}$ and GSS in malignant salivary gland tumor

There was no significant correlation between GSS and  $\text{SUV}_{\text{max}}$  ( $r=-0.099$ ,  $P=0.852$ ). (Table 8)

**Table 7.** Correlation between  $\text{SUV}_{\text{max}}$  and Glut-1 staining score in oral squamous cell carcinoma

	OSCC	r (P)
$\text{SUV}_{\text{max}}$	7.84±4.83	0.058 (0.738)
GSS	11.11±1.75	

(SUV<sub>max</sub>: maximum standardized uptake value, Glut-1: glucose uptake transporter-1, OSCC: oral squamous cell carcinoma, GSS: Glut-1 staining score)

Values are r (correlation coefficient), with P (probability value) enclosed in parentheses.

Chul-Hwan Kim et al: Correlation between glucose transporter type-1 expression and  $^{18}\text{F}$ -FDG uptake on PET in oral cancer. J Korean Assoc Oral Maxillofac Surg 2012**Table 8.** Correlation between  $\text{SUV}_{\text{max}}$  and Glut-1 staining score in malignant salivary gland tumor

	SGC	r (P)
$\text{SUV}_{\text{max}}$	6.18±2.58	-0.099 (0.852)
GSS	5.33±3.50	

(SUV<sub>max</sub>: maximum standardized uptake value, Glut-1: glucose uptake transporter-1, SGC: salivary gland cancer, GSS: Glut-1 staining score)

Values are r (correlation coefficient), with P (probability value) enclosed in parentheses.

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## IV. Discussion

$^{18}\text{F}$ -FDG PET is a test method that facilitates the discovery of malignant tumor cells. Used as the marker substance,  $^{18}\text{F}$ -FDG has the advantage of finding the location of the primary tumor and the metastatic lesions non-invasively since it is taken in by cells with abnormally increased metabolism such as cancer cells. SUV measured after  $^{18}\text{F}$ -FDG PET scan is the relative ratio that semi-quantitatively expresses  $^{18}\text{F}$ -FDG intake by abnormal tissue in comparison with proximate normal tissues based on the principle that  $^{18}\text{F}$ -FDG is distributed evenly throughout the body when it is administered, enabling comparison between patients. Normal tissue has the same  $^{18}\text{F}$ -FDG distribution, i.e., SUV is close to 1, but abnormal tissues such as cancer increase uptake unlike their proximate tissues; thus enabling the calculation of relative uptake increase rate compared with normal tissues<sup>4</sup>. This is used for the discrimination of malignant tumor and benign tumor, carrying great significance in evaluating the response after tumor treatment and determining the prognosis of tumor<sup>10-12</sup>. Thus, despite the high cost, the application scope of PET is gradually broadening.

A variety of studies were conducted on the correlation between the prognosis of head and neck cancer patients and SUV. Minn et al.<sup>13</sup> reported that the prognosis was more unfavorable when SUV was high in the case of 37 head

and neck squamous cell carcinoma patients. According to Torizuka et al.<sup>14</sup>, more aggressive treatment must be considered when FDG uptake is higher, based on their examination of 50 head and neck squamous cell carcinoma patients. Kunkel et al.<sup>15</sup> stated that the group with below-average SUV showed significant increase of survival rate compared with the group with above-average SUV.

A few possibilities are suggested as to the reason for having more unfavorable prognosis when SUV is higher in PET. First, the size of cancer is large in patients wherein the tumor has progressed; thus, the number of cells in the tumor is reflected on SUV. In fact, the study on lung cancer showed that SUV as well as the size of cancer can be used as prognosis-estimating factor<sup>16</sup>. Second, patients whose cancer is progressing exhibit deterioration of overall health and abnormal glucose metabolism, with <sup>18</sup>F-FDG uptake increasing in proportion to the speed of cell division and proliferation of cancer<sup>13</sup>. Third, there are studies reporting low histological differentiation given high SUV, weakening the effect of anticancer chemotherapy or radiation treatment. As such, PET was cited as a factor in estimating prognosis independently for head and neck cancer<sup>17</sup>.

According to recent studies, SUV showed significant correlation with the T stage of the tumor and histological differentiation in squamous cell carcinoma in the head and neck<sup>18-21</sup>. In this study, T stage was higher when SUV<sub>max</sub> was high in oral squamous cell carcinoma, showing statistically significant result but no significant correlation between SUV<sub>max</sub> and histological differentiation of tumor. The malignant salivary gland tumor also showed statistically significant result since T stage was high when SUV<sub>max</sub> was high.

PET has limits in showing the anatomical structure compared with CT or magnetic resonance imaging. Moreover, since it reflects the tissue with high glucose metabolism, the uptake of marker substance can increase in organs with active glucose metabolism such as brain, tonsil tissue, and salivary gland as well as inflammatory tissues and in organs excreting the marker substance such as kidney and bladder; thus displaying less discrimination capacity for organs<sup>4,7</sup>. For this, studies are being conducted from various viewpoints to find the elements that increase <sup>18</sup>F-FDG uptake by malignant tumor and influence diagnostic sensitivity in the discrimination and diagnosis with benign tissues. Studies are currently conducted as well with regard to the correlation between <sup>18</sup>F-FDG uptake and expression of GLUT-1 in relation to the increase of glucose metabolism of cancer cell,

increase of hexokinase activity, proliferation speed of cancer cells, distribution of macrophagocytes, and size of cancer<sup>22,23</sup>. Among these elements, the high expression of GLUT-1 was reportedly unfavorable to the prognosis of tumor, lowering the survival rate<sup>15</sup>. GLUT was found to express tissue specifically, with GLUT-1 mostly detected in red blood cell and vascular tissue and GLUT-3 mainly expressed in cerebral tissues and inflammatory cells<sup>24</sup>. In particular, the overexpression of GLUT in head and neck squamous cell carcinoma was reported to be common, and GLUT-1 and 3 were frequently expressed in patients with lymphatic metastasis<sup>25,26</sup>. In this study, GLUT-1 in oral squamous cell carcinoma did not have statistical significance in relation to cervical lymphatic metastasis. Note, however, that GLUT-1 was expressed actively in patients with malignant salivary gland tumor and lymphatic metastasis, with the correlation statistically significant.

According to recent studies, the expression of squamous cell carcinoma, which occurs in the head and neck region, shows close relationship with the T stage of the tumor and histological differentiation<sup>18-21</sup>. Tian et al.<sup>27</sup> reported that the degree of GLUT-1 expression had low correlation with SUV since SUV was high, but the expression of GLUT-1 was low when the ratio of inflammatory cell increased relatively, and that both SUV and GLUT-1 were high when the ratio of tumor cell increased relatively since the ratio of tumor cells and inflammatory cells in cancer varied according to the region of body and GLUT-1 was expressed more in the tumor cell than the inflammatory tissue. Similarly, positive correlation was noted between GSS and SUV in oral squamous cell carcinoma in this study. Thus, the type and degree of GLUT-1 were deduced to form part of the factors influencing SUV<sub>max</sub>, but they did not have statistically significant correlation. This could be explained by the fact that GLUT-1 was expressed intensively in all oral squamous cell carcinomas, but the difference between the degrees of expression was not statistically significant; in fact, it was difficult to find changes in SUV<sub>max</sub> in PET scan. Furthermore, it would be difficult to ignore the influence of the local volume effect occurring during the measurement of SUV and error due to the uptake period of the radiotracer. There were differences in the degree of expression of GLUT-1 according to the ratio of inflammatory cell within the tumor; the subtype of GLUT may exist in great diversity according to each tumor, including the effect of different paths related to glucose uptake such as the hexokinase enzyme system on different tumors. The correlation between SUV and GLUT-

1 seemed to be weakened by these effects. Note, however, that there was correlation between the expression of GLUT-1 and  $^{18}\text{F}$ -FDG uptake in non-small cancer cells in the lung, colon cancer, and sarcoma<sup>9,18,28</sup>. A few previous studies also reported clinical correlation between glucose metabolism and PET image<sup>13,15,29</sup>. An in-depth study of the role of GLUT-1 related to  $^{18}\text{F}$ -FDG uptake and the correlation with SUV is expected to yield meaningful outcomes.

## V. Conclusion

This study investigated the correlation between T, N stage, histological differentiation of tumor, and total expression score related to the rate and intensity of GLUT-1 expression and  $\text{SUV}_{\text{max}}$  among 42 patients who were diagnosed with oral squamous cell carcinoma and malignant salivary gland tumor and who had surgery after receiving PET-CT scan at the Department of Oral and Maxillofacial Surgery, School of Dentistry, Dankook University from May 2006 to July 2011. As a result, the following conclusions were drawn:

1. Higher  $\text{SUV}_{\text{max}}$  was obtained with higher T stage in oral squamous cell carcinoma, indicating high statistical significance ( $P=0.007$ ).
2. Higher  $\text{SUV}_{\text{max}}$  was obtained with higher T stage in malignant salivary gland tumor, indicating high statistical significance ( $P=0.004$ ).
3. Glut-1 expression was observed in all 36 samples of oral squamous cell carcinoma, and higher GSS was obtained with higher T. The difference was statistically significant ( $P=0.017$ ).
4. Glut-1 expression was observed in all 6 samples of malignant salivary gland tumor, with the average GSS among patients with cervical lymphatic metastasis showing higher statistical significance compared with that among patients without cervical lymphatic metastasis ( $P=0.049$ ).
5. The average GSS ( $11.11 \pm 1.75$ ) of oral squamous cell carcinoma was higher than the average GSS ( $5.33 \pm 3.50$ ) of malignant salivary gland tumor.
6. No significant correlation was found between GSS and  $\text{SUV}_{\text{max}}$  in oral squamous cell carcinoma ( $r=0.058$ ,  $P=0.738$ ) or in malignant salivary gland tumor ( $r=-0.099$ ,  $P=0.852$ ).

According to the findings above, studies on the use of various types of GLUT related to  $^{18}\text{F}$ -FDG uptake and on SUV and GLUT as prognostic factors of the tumor with a large number of samples are additionally needed in the future.

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