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RESEARCH ARTICLE

Measurement Variations Between Computed Tomography Derived Depth of Invasion and Histological Depth of Invasion in Oral Squamous Cell Carcinoma

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Abstract

Background: In treatment planning of oral squamous cell carcinoma the extent of local growth, regional and distant spread which is evaluated by tumor node metastasis (TNM) classification is needed. Clinically found depth of invasion from computed tomography may vary from histopathological depth of invasion. Accurate clinical measurement is essential for preoperative patient counseling, treatment planning and prognosis. So, it is essential to find out between two variations of depth of invasion in oral squamous cell carcinoma.

Objective: To determine variations in computed tomography derived depth of invasion with histopathological depth of invasion in oral squamous cell carcinoma.

Method: Twenty-four patients who fulfilled the criteria of the study were selected by purposive sampling. Cross sectional study had done.

Results: Most (37.5%) of the patients were aged ≥60 years followed by 29.2% were aged between 50 to 59 years, 16.7% were 40 to 49 years and 16.7% were 30 to 39 years of age. Among all the patients, 66.7% were female and 33.33% were male. Buccal mucosa (75%) was commonest site of cancer. Among the patients, exophytic growth was found in 70.8% cases followed by 16.7% was endophytic growth and 12.5% was ulcerative growth. Majority (70.8%) had Depth of invasion of cancer was above 10 mm followed by 20.8% had 5 to 10 mm and 8.3% had below 5mm both radiologically and histopathological assessment. CT scan derived DOI has a significant, positive and strong correlation coefficient with the histopathological DOI. CT derived DOI was higher in exophytic growth of tumor and lower in endophytic and ulcerative type of growth than histological DOI and that was also statistically significant.

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Conclusion: CT scan can be a good guide to assess preoperative depth of invasion as a part of TNM staging.

Key words: Oral Squamous Cell Carcinoma (OSCC), Depth of Invasion (DOI), Computed Tomography (CT), Radiological vs Histological DOI.

1. Introduction

Detecting oral cancer at an early stage is believed to be the most effective means of reducing rates of death[1]. Oral squamous cell carcinoma (OSCC) is the most frequently encountered neoplasm of the oral cavity, accounting for 80.05% of all oral cancers[2]. The extent of disease is the prime indicator of prognosis for most cancer patients and provides the main criterion for the selection of therapy. Tumor size, nodal involvement, metastasis classification (TNM) is the most widely used system for recording the extent of local growth and regional and distant spread of cancer[3]. Oral cancer treatment based on staging of oral cancer. In oral squamous cell carcinoma (OSCC), depth of invasion (DOI) is an important predictive, prognostic, and staging parameter[4]. Depth Of invasion is measured during histopathological examination as par 6th edition AJCC guideline. In newer cancer staging by 8th edition of AJCC depth of invasion is included which means histopathological penetrating length of cancer cell present from the basal membrane of the normal mucosa perpendicularly to the deepest portion of invasion[5]. The length should be assessed preoperatively which will modify treatment plan as well as reconstruction option. Depth of invasion larger than 4 mm is a strong predictor of node metastasis, high local recurrence and 5 years overall survival rate and neck dissection is recommended for those[6]. Option of measurement in our hand is image-based technique like contrast CT scan, MRI, ultrasonography as we use these tools mostly[7]. As a preoperative cancer staging tool CT scan is a superior to assess the radiological depth of invasion[6]. CT has the best correlation coefficient with histopathological depth of invasion[4]. The aim of the study is to assess the accuracy of imaging-based (CT scan) estimation of depth of invasion in relation with the histopathological depth of invasion. This information will guide proper assessment preoperatively as well as treatment planning and planning for radiotherapy and or chemotherapy.

2. Materials and Methods

2.1 Study Design

Cross sectional study.

2.2 Place of Study

Department of Oral and Maxillofacial Surgery, Dhaka Dental College Hospital, Mirpur-14, Dhaka, Bangladesh.

2.3 Period of Study

1st February 2021 to 31st January 2022 (12 months).

2.4 Study Population

Those patients who fulfil the inclusion and exclusion criteria in the Department of Oral and Maxillofacial Surgery, Dhaka Dental College Hospital, Mirpur-14, Dhaka.

2.5 Sampling Method

Purposive sampling. All available patients meeting the selection criteria were selected until required sample was achieved.

2.6 Statistical Analysis

SPSS Version 26.

2.7 Sample Size

24.

2.7.1 Sample size calculation

Sample size has been calculated with the formula

$N= z^2pq/d^2$

Here,

N= sample size

Z = 1.96 (z = 1.96 at 95% confidence interval, which is constant.).

P = 0.065 (Incidence rate of OSCC was 6.5%) (Barma et al., 2020).

q = 1-0.065= 0.935

d = margin of error 10%.

=0.1

e = 0.2 (acceptable error in the estimate of e is set at 20% of pt.)

Using above formula, the expected sample size

$$N = \frac{(1.96)\ 2 * .065 * .935}{x(0.1)^{\ 2}}$$

$$= \frac{.2334}{.01}$$

= 23.34

Estimated sample size is 24.

2.8 Study Procedure

Twenty-four patients with nonrecurrent oral squamous cell carcinoma who were undergoing surgery and willing to participate in this study were selected. Clinical depth of invasion was measured by Computed Tomography (CT scan). After operation the resected specimens were sent for histopathological examination and according to the histopathology report pathological DOI was done. All the patients were observed by the same group of oral and maxillofacial surgeons, radiologist, pathologist & prosthodontists.

2.9 Data Management and Data Analysis Procedures

After collection of data, it was checked for any discrepancy, incompleteness & prepared by using SPSS for windows version 26.0.

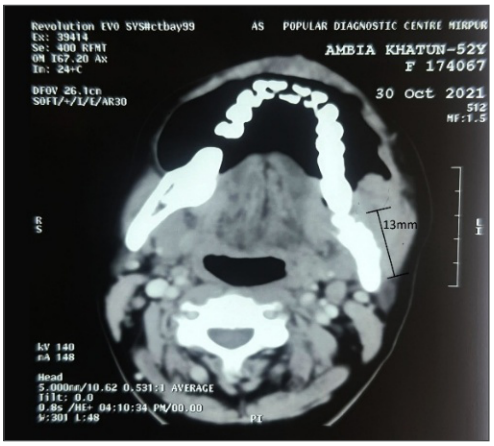

Figure 1. *Depth of invasion Measured from CT scan.*

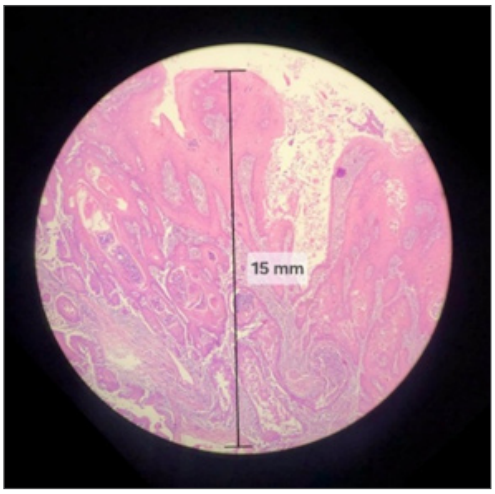

Figure 2. *Depth of invasion measured histopathologically.*

3. Results

Table 1. *Distribution of the patients by Age group (n=24)*

Age group (Years)	Frequency (n)	Percentage (%)
≤ 39	4	16.7
40 to 49	4	16.7
50 to 59	7	29.2
above 60	9	37.5
Mean ± SD (Range)	51.5±11.2 (31-70)	
Total	24	100

Table 1 shows that majority (37.5%) of the patients were aged ≥60 years followed by 29.2% were aged between 50 to 59 years, 16.7% were 40 to 49 years and 16.7% were below 39 years of age. Mean age of the patients was 51.5±11.2 years.

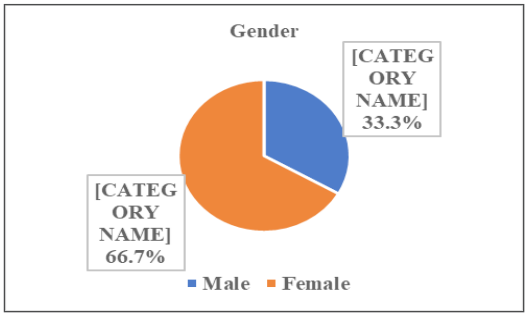

Figure 3. *Gender distribution of study patients (n=24) shows that among all the patients, 66.7% were female and 33.33% were male.*

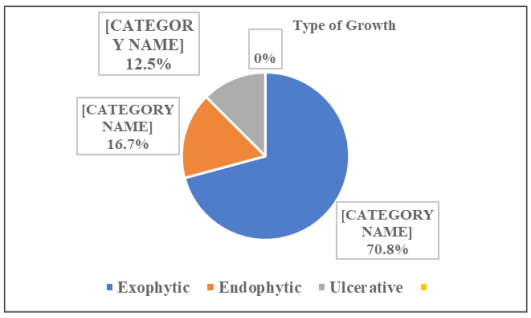

Figure 4. *Distribution of the patients by type of growth (n=24) shows that among the patients, exophytic growth was found in 70.8% cases followed by 16.7% was endophytic growth and 12.5% was ulcerative growth.*

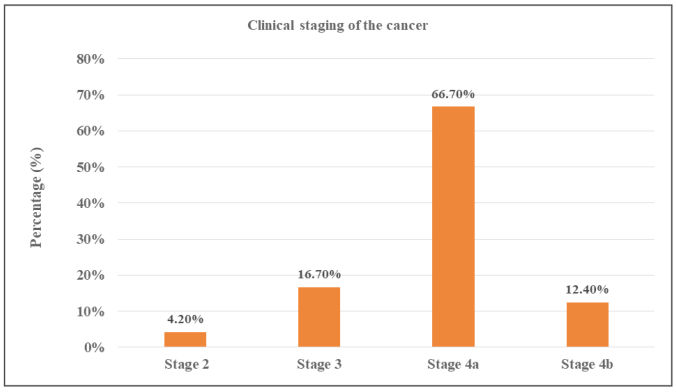

Figure 5. *Distribution of the patients according to the clinical stages of the cancer (n=24) reveals that among all, majority (66.7%) had clinically cancer stage 4a followed by 16.7% had stage 3, 12.4% had stage 4b and 4.2% had stage 2.*

Table 2. *Distribution of the study patients according to site of cancer (n=24)*

Site of cancer	Frequency (n)	Percentage (%)
Buccal mucosa	19	83.4
LGBS	13	54.2
RMT	6	25
UGBS	2	8.3
Tongue	2	8.3
Palate	2	8.3

**Multiple answer considered, LGBS= Lower gingivobuccal sulcus, UGBS= Upper gingivobuccal sulcus, RMT= Retromolar trigon*

Table 2 shows buccal mucosa (83.4%) was commonest site of cancer among the patients followed by LGBS (54.2%), RMT (25%) UGBS (8.3%), tongue (8.3%) and palate (8.3%).

Table 3. *Clinical tumor size and lymph node classification of the patients (n=24)*

Classification	Frequency (n)	Percentage (%)
T classification		
T2	2	8.3

T3	7	29.2
T4a	13	54.2
T4b	2	8.3
N classification		
N0	6	25
N1	12	50
N2a	1	4.2
N2b	5	20.8

Table 3 shows clinically majority (54.2%) of the patients was in T4a stage followed by 29.2% in T3, 8.2% in T2 and 8.3% in T4b stage. Besides, 50% was in N1 stage, followed by 20.8% was in N2b, 4.2% was in N2a stage and 25% of the patients was in N0 stage.

Table 4. *Histopathological tumor size and lymph node classification of the patients (n=24)*

Classification	Frequency (n)	Percentage (%)
T classification		
T2	3	12.5
T3	8	33.3
T4a	13	54.2
N classification		
N0	16	66.7
N1	2	8.3
N2a	2	8.3
N2b	2	8.3
N3a	1	4.2
N3b	1	4.2

Table 4 shows majority (54.2%) of the patients was in T4a stage followed by 33.3% in T3 and 12.5% in T2 stage. Besides, 66.7% of the patients was in N0 stage followed by 8.3% was in N1 stage, 8.3% was in N2a, 8.3% was in N2a stage, 4.2% was in N3a stage and 4.2% was in N3b stage.

Table 5. *Comparison of clinical and histopathological logical classification of tumor size (n=24)*

		Clinical stage of Tumor size				P value*
		T2	**T3**	**T4a**	**T4b**	
Histological stage of tumor size		n (%)	n (%)	n (%)	n (%)	
	T2	0 (0)	2 (28.6)	1 (7.7)	0 (0)	
	T3	1 (50)	4 (57.1)	1 (7.7)	2 (100)	0.004
	T4a	1 (50)	1 (14.3)	11 (84.6)	0 (0)	

**p value was determined by Fisher Exact test.*

Table 5 shows among all the cases, 9 patients showed different tumor size and histopathological classification than clinical findings and that was statistically significant.

Table 6. *Distribution of the patients by histopathological depth of invasion (DOI) of cancer (n=24)*

Histopathological DOI	Frequency (n)	Percentage (%)
<5mm	2	8.3
5 to 10 mm	5	20.8
>10	17	70.8
Mean±SD (Range)	12.2±4.7 (4-20)	
Total	24	100

Table 6 shows majority (70.8%) had DOI of cancer was above 10 mm followed by 20.8% had 5 to 10 mm and 8.3% had below 5mm. Mean DOI of the patients was 12.2±4.7.

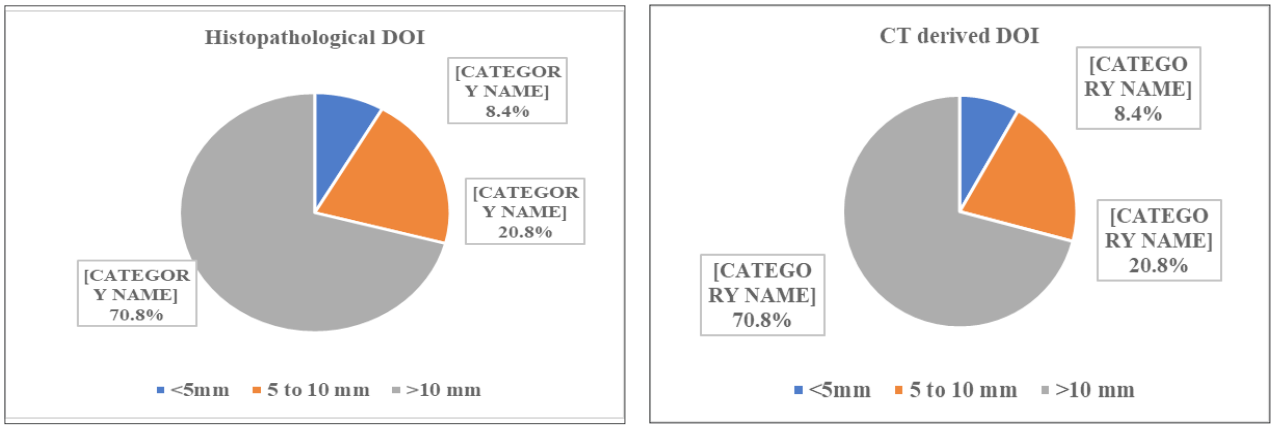

Figure 6. *Histopathological DOI and CT derived DOI among the cancer patients (n=24) reveals that in both histopathology and CT showed that majority of the cancer had DOI >10mm (70.8%), followed by 20.8% was 5 to 10 mm and 8.4% had <5mm.*

Table 7. *Comparison of histopathological DOI and CT derived DOI of the cancer (n=24)*

		CT derived DOI of the cancer			P value*
		Concordant	upstaged	Downstage	
		n (%)	n (%)	n (%)	
	<5mm	0 (0)	2 (18.2)	0 (0)	
Histopathological DOI of cancer	5 to 10 mm	2 (50)	2 (18.2)	1(11.1)	0.306
	>10 mm	2 (50)	7 (63.6)	8 (88.9)	

**p value was determined by Fisher Exact test, DOI= Depth of invasion*

Table 7 shows no significant difference found between histopathological DOI and CT derived DOI of the cancer.

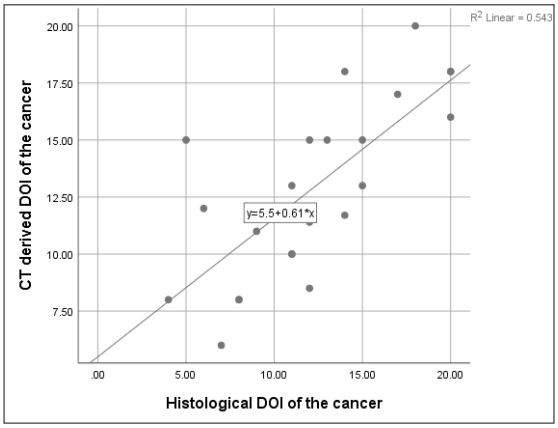

Figure 7. *Scattered plot showing the correlation between histopathological DOI and the CT derived DOI of the cancer (n=24)*

In figure 7 scattered plot shows positive correlation was found between histopathological DOI and CT derived DOI of the cancer and that was statistically significant.

Table 8. *Correlation of the histopathological DOI with the CT derived DOI of the cancer (n=24)*

	Correlation coefficient (r)	P value*
Histological DOI of cancer vs CT derived DOI of the cancer	0.737	<0.001

**p value was determined by Pearson correlation test, DOI= Depth of invasion*

Table 8 shows CT estimated depth of invasion correlated significantly with histopathological depth of invasion of the cancer.

Table 9. *Cross-tabulation of histopathological DOI and CT derived DOI of the cancer (n=24)*

CT derived DOI	Histological DOI			
	<5mm	5 to 10mm	>10mm	Total
5 to 10 mm	1	3	3	**7**
>10 mm	1	2	14	17
Total	**2**	**5**	**17**	**24**

Table 9 shows cross tabulation of comparison to histopathological DOI, CT derived DOI 5 to 10 mm could truly detect 3 cases among 5 and CT derived DOI >10 mm could truly detect 14 cases. Diagnostic accuracy of CT derived DOI showed 50% sensitivity, 77.78% specificity, 42.85% PPV, 82.35% NPV and 70.83% accuracy.

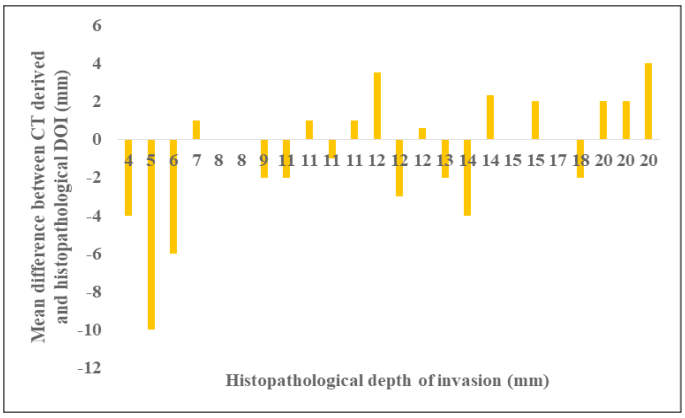

Figure 8. *Water plot comparing the mean difference between the CT derived DOI and the histopathological DOI (n=24)*

Figure 8 shows that mean difference between CT derived and histopathological depth of invasion was 4 to -10mm.

Table 10. *Mean difference between histopathological DOI and CT derived DOI in different types of growth (n=24)*

Types of growth	Histopathological DOI	CT derived DOI	Mean difference	P value*
	Mean±SD (Range)	Mean±SD (Range)	Mean±SD (Range)	
Exophytic	11.7±4.7 (4 to 20)	13.3±3.7 (6 to 20)	-1.6±3.3 (-10 to 4)	0.002
Endophytic	13.5±4.3 (11 to 20)	11.6±4.3 (8.5 to18)	1.9±1.2 (1 to 3.5)	0.037
Ulcerative	13.3±6.1 (8 to 20)	12.5±5.1 (8 to 18)	0.9±1 (0 to 2)	0.005

**P value was determined by paired sample t test, DOI= Depth of invasion*

Table 10 shows that CT derived DOI was higher in exophytic growth of tumor and lower in endophytic and ulcerative type of growth than histopathological DOI.

Table 11. *Histopathological DOI and CT derived DOI in different site of cancer (n=24)*

Site of cancer	Histological DOI	CT derived DOI	P value*
	Mean±SD (Range)	Mean±SD (Range)	
Buccal mucosa	12±4.5 (4-20)	12.6±4 (6-20)	0.414
RMT	13.2±6.4 (8-20)	13.1±4.6 (8-18)	0.961
LGBS	12.6±3.8 (6-20)	13.4±4 (6-20)	0.321
UGBS	15.5±6.4 (11-20)	14±2.8 (12-16)	0.656
Tongue	10±2.8 (8-12)	11.5±4.9 (8-15)	0.500
Palate	17.5±3.5 (15-20)	14.5±2.1 (13-16)	0.205

**p-value was determined by paired sample t test, LGBS= Lower gingivobuccal sulcus, UGBS= Upper gingivobuccal sulcus, RMT= Retromolar trigon*

Table 11 shows No significant difference found between histopathological DOI and CT derived DOI regarding different site of cancer.

4. Discussion

24 patients with oral squamous cell carcinoma were included in the study which was conducted in Dhaka Dental College Hospital. The mean age of the patients was 51.5±11.2 years with the majority was female (66.7%). All the patients were habitually betel quid and areca nut chewer. Clinically majority (54.2%) of the patients were in T4 a stage followed by 29.2% in T3, 8.3% in T2, and 8.3% in T4b stage. Besides, 50% was in N1 stage, f ollowed by 20.8% was in N2b, 4.2% was in N2a stage and 25% of the patients were in N0 stage. Waech et al. also fo und the majority had early tumor size in the T3-T4 stage but 63.6% nodal involvement was in N0 stage[4]. Chin et al. found the majority of the tumor size was in T2 stage and nodal involvement was in N0 stage[8]. In the study of Baba et al. T staging categories ranged from T1 to T3, and T2 lesions were most prevalent (52%), followed by T3 lesions (43%)[6]. The current study observed that majority (70.8%) had DOI of

cancer was above 10 mm followed by 20.8% who had 5 to 10 mm and 8.3% had below 5mm. The mean DOI of the patients was 12.2±4.7. The current study compares the depth of invasion measured by CT with a histological depth of invasion of oral squamous cell cancer patients. It was observed that CT estimated depth of invasion correlated (r=0.737) significantly with a histopathological depth of invasion. Which denotes positive and strong correlation between Ct derived DOI and histopathological DOI. Study also revealed the correlation coefficient between CT-DOI and histopathological DOI was greater and CT-DOI correlated strongly with pathological DOI, (correlation coefficient = 0.74, $p < 0.001$)[6]. On another study also found a better correlation coefficient (r=0.718) for CT[4]. The mean difference between CT derived and histopathological depth of invasion was found between 4mm to -10mm among the patients. A small inconsistency between histological depth of invasion and imaging-based depth of invasion is inherent to their nature, as they are similar but not the same[9]. Due to several specimen cutting guides, some degree of variations of the histopathological depth of invasion will always be apparent. Moreover, only a small part of the whole tissue specimen is visualized on histology, potentially missing the deepest infiltration. On the other hand, imaging-based estimated depth of invasion is assessed from the mucosal surface perpendicularly to the deepest point of the tumor. As it contains a three-dimensional stack, it facilitates the identification of the deepest point[10]. The current study revealed that CT-derived DOI was higher in exophytic growth of a tumor and lower in an endophytic and ulcerative type of growth than histological DOI and that was statistically significant. The mean difference in exophytic, endophytic, and ulcerative growth of tumor from histological DOI was 1.6±3.3, 1.9±1.2, and 0.9±1 mm accordingly. Previous studies unveiled that the discrepancy shall be greater between exophytic, well differentiated tumors, meanwhile, ulcerative, endophytic tumors might be dangerously underestimated by the imaging-based depth of invasion. It has recently been shown that the difference in imaging-based and histological depth of invasion was greater for endophytic ulcerative tumors[11,12]. Baba et al. compared both CT and MRI DOI with the histological DOI and observed that the absolute value of the difference between pathological DOI and CT-DOI was smaller than that of the difference between pathological DOI and MRI DOI and declared that CT-DOI can be useful to estimate the pathological DOI in OSCC[6]. Locatello et al. suggested that with a standardized imaging protocol patients could be better classified according to CT-derived DOI[10]. The current study observed that in buccal mucosa mean hDOI12 mm mean, rDOI 12.6 mm. In Retromolar trigon area mean hDOI 13.2mm, meanr DOI 13.1mm. Tongue mean hDOI 10mm mean rDOI 11.5mm. Palate mean hDOI 17.5mm, mean rDOI 14.5mm.Previous study shown that Retromolar trigon mean value of hDOI 5.43mm mean value of rDOI 6.56mm. Hard palate, mean hDOI was 4.75 mm, mean rDOI was 5.44 mm.Buccal mucosa of the cheek mean values of hDOI 4.75mm and rDOI is 7.79 mm[10]. In comparison to histological DOI, CT derived DOI 5 to 10 mm could truly detect 4 cases among 5 and CT derived DOI >10 mm could truly detect 14 cases. Diagnostic accuracy of CT derived DOI showed 50% sensitivity, 77.78% specificity, 42.85% PPV, 82.35% NPV and 70.83% accuracy. Study reveals that sensitivity values of CT scan 33%-100% and specificity values of 57.1%-100%, another study detection of mandibular bone tissue invasion by SCC, with sensitivity values of 83% (CT), and specificity values of 100% (CT). This because as CT scan can interpret bone more precisely and additionally low number of sample sensitivity is reduced in current study[13-16]. According to the current study CT measurements of DOI in OSCC lead to an overestimation of histological DOI, especially in tumors with DOI<5 mm. Above 5 mm up to 10 mm and 10 mm above up and down staging is observe. This also corelate with the previous study. Overall, the depth of invasion was overestimated by imaging by about 10%, the explanation for general overestimation is explained by the shrinkage and distortion of the specimen from the in-situ measurement by the surgeon to final pathologic evaluation which was reported to be up to 30%. Shrinkage of specimen and CT has poor soft tissue measurement study found that CT has less over estimation than MRI and ultrasound[8,17,18,19]. CT scan can be a better option for preoperative assessment of DOI.

5. Conclusion

According to the study Buccal mucosa was most commonly affected site of squamous cell carcinoma and majority was exophytic growth. Preoperative CT measurements of depth of invasion in oral cancer led to an overestimation of histopathological depth of invasion, especially in thin tumors with depth of invasion<5 mm. Positive and strong correlation was found between histopathological DOI and CT derived DOI. In comparison to histopathology diagnostic accuracy of CT showed sensitivity, specificity, PPV,

NPV and accuracy was 50%, 77.78%, 42.85%, 82.35% and 70.83% accordingly. On an average CT scan can be a good guide to measure radiological depth of invasion.

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