Vol 4 | Issue 2 | Pages 60-63

Journal of Oral Cancer and Research
ISSN: 2689-8837

Review Article

DOI: 10.36959/915/580

Oral ID® as an Adjunctive Tool for Surgical Margin in patients with oral squamous cell carcinoma: A comparative study

*Yassmin Abdalla Mohamed**

Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, University of Khartoum, Khartoum, Sudan

Abstract

Background: The condition of the resected margin in oral squamous cell carcinoma continues to be an important prognostic factor; the use of optic technology could help surgeons in determining the margin status at real time. This study aims to evaluate Oral ID, a hand held device that uses the principal of auto-fluorescence to determine surgical safe margins in patients with oral squamous cell carcinoma, and to compare the results with those of the conventional 1 cm margin method.

Methodology: This study was descriptive, comparative analytical study carried out at Khartoum Dental Teaching Hospital and Oral Histopathology Diagnostic Laboratory, Faculty of Dentistry, University of Khartoum. A total of 92 margins obtained from 31 patients, 46 margins were taken by Oral ID and the other 46 were taken by the traditional 1cm method. All margins were examined histological with conventional Hematoxylin and Eosin stain.

Results: It was found that all tumors showed fluorescence loss: A significant association was found between the use of Oral ID and obtaining a free margin P (0.02) the sensitivity of Oral ID was found to be 74% the specificity was found to be 89%. Ten out of the 46 margins obtained by fluorescence showed mild dysplasia and two margins showed high grade dysplasia. The 46 margins obtained by the traditional 1cm margin showed different field alterations two were involved, one was close, five showed high grade dysplasia and 14 showed mild dysplasia yielding a specificity of 52.2%.

Conclusion: Using Oral ID for surgical margin assessment increases the accuracy to 74% compared to the conventional method which was found to be 52.2%. The results of the device are comparable to other auto-fluorescence devices of different trademarks. Further development of the device to help overcome its many limitations is strongly advised.

Introduction

Oral cancer is a major public health problem both in the Sudan and worldwide. Of all oral neoplasms squamous cell carcinoma is one of the most frequent tumors affecting the oral cavity. Recent studies have shown that more than 90%of the neoplasms affecting the oral cavity are of squamous cell carcinoma type [1-2]. In addition to the high prevalence of the disease reports from local centers and worldwide indicate an ongoing increase in the incidence of the disease. The use of a local snuff "Toombak "and infection by HPV have shown to be the major causes in the Sudan [3-5]. The gold standard for the treatment of OSCC remains surgical excision with tumor free margins. The importance of obtaining free margins at surgery cannot be overemphasized as this directly affects the prognosis of the patient [6-7] failing to do so will dramatically affect the rates of recurrence and survival [6-9]. It also exposes the patient to the hazards and complications of a second surgery or adjunctive therapy such as radiotherapy and chemotherapy, adding the burden of post therapeutic complications and extra cost on the patient.

A diagnostic aid to help the clinician to delineate surgical margins would be very useful [7-10]. Recent trials on using tissue auto-fluorescence as a sensitive method to detect surgical margins have been described in various tumors such as breast cancer (BC) and have shown accurate results [11-12]. Poh et al in Canada has used a similar device to detect field change around squamous cell carcinoma and found a positive correlation between loss of heterozygosis and fluorescence visualization loss. In this study we intended to investigate the

***Corresponding author:** Yassmin Abdalla Mohamed, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, University of Khartoum, Khartoum, Sudan

Accepted: December 23, 2021

Published online: December 27, 2021

Citation: Mohamed YA (2021) Oral ID® as an Adjunctive Tool for Surgical Margin in patients with oral squamous cell carcinoma: A comparative study. J Oral Cancer Res 4(2):60-63

ability of this method to delineate surgical margins at real time using a new auto-fluorescence device named Oral ID, a relatively cost effective device that detects cancerous and precancerous lesions by the principle of fluorescence [2-13]. Oral ID cancer screening device has gained the US food and drug administration clearance yet no studies on the general population have been carried out to assess the validity of this device. It uses a blue light with a wavelength (435-460nm) it is equipped with eyewear to use with the device [13]. The objective of this study was to investigate the value of Oral ID as an adjunctive tool to help delineate dysplastic changes around cancers and to calculate the sensitivity and specificity of the device in comparison to the traditional 1cm method and to other comparable auto-fluorescence hand held devices.

Materials And Methods

Study sample: Thirty-one patients previously diagnosed with primary oral cancer that presented for treatment in Khartoum Dental Teaching Hospital were accrued to participate in the study eligibility criteria included the presence of primary oral cancer T1-T4 with no previous history of chemotherapy and radiotherapy, an informed consent was obtained from all participants, except one eight-year-old participant, were the consent was obtained from the mother of the patient.

Method: The Tumor surgical site was first assessed under operating room illumination and the lesion was documented using a digital camera (Sony Cyber shot 20.1 megapixels, Model Name: DSC-W830, optical zoom ×8 with filter). The margins of the tumor were demarcated using a surgical marker 1cm away from the tumor by the surgeon. Lights in the operating room were turned off, the surgical site of the tumor and the margin were examined using direct fluorescence visualization. The normal contra lateral side was examined as a control. If the area of the surgical margin showed fluorescence loss the margin was extended into the fluorescence visualization retained area; on the other hand if the margin retained the normal fluorescence, the 1cm margin was considered sufficient. Intensity of the light was divided four degrees: 0 no change, 1 light brown, 2 dark brown 3 black; the intensity of light observed in the patient tumor was observed and recorded. The lights were turned back on and the distance between the conventional 1cm tumor margin and the fluorescence margin was ascertained using a flexible ruler. The tumor was surgically resected according to the furthest margin and fixed in 10% buffered formalin and submitted to the Oral Pathology Lab in Khartoum University.

One biopsy was taken from each margin. The margins obtained by fluorescence were marked with green ink while the margins 1cm away from the tumor was marked with blue ink. The margins were stained with routine H&E stain for histological examination. Each slide was evaluated by two investigators. The second investigator was not aware of the fluorescence status to reduce bias. The margins were treated according to the guidelines issued by the UK Royal College of Pathologists [14].

Results

During a period of two years 31 patients diagnosed with oral squamous cell carcinoma attending Khartoum Dental Teaching Hospital were included in this study. The sample was selected conveniently. A total of 92 margins were obtained from the patient samples: 46 margins were obtained by fluorescence and the remaining 46 margins were obtained by the traditional 1 cm method. The samples were conventionally processed and examined histological by H&E. The mean distance of fluorescence margin in this study was 1.2cm with a standard deviation of 0.2cm with the highest value being 1.5cm and the lowest value being 1cm.

All examined tumors showed fluorescence loss. Thirty-four out of the 46 margins obtained by fluorescence were clear of alteration or tumor, yielding a sensitivity of (74%). No margins were involved and none were close, twelve margins showed dysplasia, only two of them (4%) showed high grade dysplasia. On the other hand, (52%) of the margins obtained by the one centimeter method were free, 2 margins were involved (4.3%) and one margin was close (2.2%). Nineteen out of the 46 margins taken by the conventional method were dysplastic (41.3%), 8 of the dysplastic lesions (17.4%) were high grade dysplasia (Table 2) . In forty-four percent of the cases the fluorescence margin was equal to 1cm. There was a significant association between the use of fluorescence and obtaining a free margin (Z =2.213, P-Value = 0.027).The sensitivity of Oral ID in this study was approximately 74% whereas the specificity for Oral ID was found to be 89% (Table 3).

The device detected five false positives out of the total number margins taken by fluorescence 46, yielding a specificity of 89%. We compared the percentage of high grade lesions (carcinoma, CIS, high grade dysplasia) out of the total amount of involved margins in both the margins obtained by Oral ID and the traditional 1 cm method we found the amount of high grade dysplasia's at the conventional method to be 36.4% compared 16.7% for the Oral ID.

Discussion

Oral ID is a hand held, optical device that detects tissue auto-fluorescence. It was manufactured by Forward Science Technology Company. The device has been recently described as a new method that could help surgeons taking critical decisions at real time. This is very important as the literature states that high grade dysplasia at the mucosal margins correlates positively with secondary tumors and local recurrences[15]. The device was used to evaluate surgical margins and the results were compared to those of the traditional 1 cm method. This study was carried out on a sample of 31 patients all of whom were operated on by a single surgeon to limit confounding factors. A total of 92 margins were obtained from the 31 patients participating in this study. 46 were taken by fluorescence and 46 were taken by the conventional 1 cm method.

The samples were examined using standard H&E stain In the present study, the mean distance of extension of fluorescence loss beyond clinically visible tumors was found

Table 1: Field Alteration At The Margin.

Margin histology		free	involved	close	dysplasia at the margin	Total
Fluorescence margin	Count	34	0	0	12	46
	%	73.9%	0.0%	0.0%	26.1%	100.0%
Traditional 1cm margin	Count	24	1	2	19	46
	%	52.2%	2.2%	4.3%	41.3%	100.0%
Total	Count	58	1	2	31	92
	%	63.0%	1.1%	2.2%	33.7%	100.0%

Table 2: Sensitivity of Oral ID

	Fluorescence	Traditional 1cm
Free Margin No.	34	24
Total No. Of Margins	46	46
Sensitivity	74%	52.2%

Table 3: Ability to discriminate high grade lesions from normal mucosa.

		high grade dysplasia	low grade dysplasia	Total
1cm margin	Count	8	14	22
	%	36.4%	63.6%	100.0%
Oral ID	Count	2	10	12
	%	16.7%	83.3%	100.0%
Total	Count	10	24	34
	%	29.4%	70.6%	100.0%

to be 1.2 cm with a standard deviation of 0.2cm. The study of Poh et al. in 2016 found a mean distance of 1.3cm with a standard deviation of 0.57cm [13]. This finding indicates that the use of the traditional 1 cm method is not sufficient to eradicate disease . The findings of Poh et al. 2016 support this, as they have stated that if the traditional 1cm technique was used in their study; half of the margins would have cancer or dysplasia. In the present study the percentage of free margins obtained by the traditional 1cm method was only 52.2 %**.** All examined tumors showed fluorescence loss. Thirty-four out of the 46 margins obtained by fluorescence were clear of alteration or tumor, yielding a sensitivity of (74%). No margins were involved and none were close, twelve margins showed dysplasia, only two of them (4%) showed high grade dysplasia.

On the other hand, (52%) of the margins obtained by the one centimeter method were free, 2 margins were involved (4.3%) and one margin was close (2.2%). Nineteen out of the 46 margins taken by the conventional method were dysplastic (41.3%), 8 of the dysplastic lesions (17.4%) were high grade dysplasia. (Table 1)**.** In forty four percent of the cases the fluorescence margin was equal to 1cm. These findings are very different from those of Poh et al. where only 1 out of 66 margins obtained by fluorescence showed dysplasia yielding a sensitivity of 98%. [13]. Certainly differences in the results of the two studies can be attributed to the differences in the criteria of inclusion of patients; as Poh et al. restricted their study to T1-T2 lesions only. The literature also states that the penetration depth of auto fluorescence illumination is relatively shallow, and is therefore best used to evaluate superficial margins [16]. Accessibility of the tumor also affects the results as the boundaries of posterior tumors are very difficult to delineate. Fluorescence qualities also differ from site to site, and the best results were obtained when the device was used on the tongue and gingival.

Awan et al. in their study which used a similar device found a sensitivity of 84%and a specificity as low as 15% but Awan et als' study was conducted to evaluate the device as a screening tool which could explain the relatively higher sensitivity very low specificity found in his study [17,18].A meta-analysis on in-vivo optical imaging in the head and neck, 12 different studies were included in their research and the mean sensitivity and specificity for auto fluorescence devices was found to be 72.4% and 63.79%, respectively. The sensitivity of the present study was within the range of study which was found to be from 20% to 100% and the specificity ranged from 15.3% to 100% [16].

The low level of specificity in the meta-analysis can be explained by the fact that most of studies included in the analysis were conducted to evaluate the device as a screening tool. Lane at al. conducted a pilot study on 44 patients using histology as the gold standard, the device achieved a sensitivity of 98% and specificity of 100% when discriminating normal mucosa from severe dysplasia/carcinoma in situ (CIS) or invasive carcinoma [19]. In the present study, the ability of Oral ID to discriminate high grade lesions from normal mucosa was approximately 96%.

A significant association between the use of fluorescence and obtaining a free margin was found in this study, with a P value of (0.02). Poh et al. in 2006 showed that there was a significant association between the areas of (FVL) and (LOH) even in histological clear margins with a P value of (0.04):

From the above findings one can speculate that if molecular studies were performed in this study a significant difference in (LOH) between the fluorescence and conventional one cm margin would have likely been found

The strengths of the study were that it was restricted to a single operator to reduce confounding factors as much as possible. Two operators decided the area of fluorescence loss to reduce subjectivity. To the best of the investigators knowledge no studies have been carried out on Oral ID in particular. The pathologist attended each operation, and the margins were marked in the operating theatre to insure accuracy of margin delineation. Oral ID has given relatively good results as it was able to increase the sensitivity of the traditional 1cm margin from (52.2%) to approximately (74%) achieving a (21.8%) improvement in sensitivity, it also has a high ability in distinguishing high grade lesions and invasive carcinoma from normal mucosa and does not require consumables so no per patient cost; the device itself is of medium cost, which makes it relatively economic (compared to other similar commercial products); it is easily disinfected, portable and allows the detection of a big number of lesions

On the other hand the limitations are; the contrast between normal and abnormal is not always clear, suggesting the need for intensifying screens or adjustment of the wavelength of the light to increase the contrast [16]. Interpreting the fluorescence findings is highly subjective, and depends on the experience of the operator which jeopardizes the reproducibility of the results. Keratin is auto-fluorescent so hyper-keratinized areas may not show loss of fluorescence even in the presence of dysplastic lesion which also serves as a source of decreased accuracy [20] The device only assesses lateral spread of cancer and cannot assess the depth of cancer extension. The study strongly recommends multicenter double blind experimental clinical trials with larger sample size and follow up of the operated patients is also recommended to correctly assess the accuracy of the device. We also recommend molecular studies and IHC staining on low risk margins of both Oral ID and 1cm margins for proper risk assessment.

Conclusion

- Using the principal of fluorescence gave an accuracy of 74% whereas the conventional method gave an accuracy of 52%.
- The device may be useful in taking intraoperative decisions but should not by any means be considered a substitute for traditional histology.
- The results obtained with Oral ID device are comparable to results obtained by other auto-fluorescence devices with different trade names.

References

1. Shin D, Vigneswaran N, Gillenwater A, et al.(2010) advances in fluorescence imaging techniques to detect oral cancer and its precursors. Future Oncol 6: 1143-1154.
2. Saini R. Oral Cancer Screening in Dental Set Up. Int J Biomed adv res. 2015 6: 199-203.
3. Idris AM, Ahmed HM, Malik MOA et al.(1995) Toombak dipping and cancer of the oral cavity in the sudan: a case-control study. int j cancer. 63: 477-480.
4. 85% of oral cancer cases in Sudan caused by chewing tobacco, study shows - Sudan Tribune: Plural news and views on Sudan [Internet] [cited 2016 Apr 10] Available from.
5. Idris AM, Prokopczyk B, Hoffmann D et al. (1994) Toombak: A major risk factor for cancer of the oral cavity in Sudan. Prev Med 23:832-839.
6. Lane P, Poh CF, Durham JS et al.(2011) Fluorescence-guided surgical resection of oral cancer reduces recurrence.
7. Ravi SB, Annavajjula S (2014) Surgical Margins and Its Evaluation in Oral Cancer: A Review. J Clin Diagn Res JCDR 8: ZE01-ZE05.
8. Mondal SB, Gao S, Zhu N et al. (2014) Real-time fluorescence image-guided oncologic surgery. adv cancer res 124:171-211.
9. Swinson B, Jerjes W, El-Maaytah M et al. (2006) Optical techniques in diagnosis of head and neck malignancy. Oral Oncol. Mar 42: 221-228.
10. Analysis of the surgical margins of the oral cancer using in situ and ex vivo fluorescence spectroscopy - zotero
11. Dip FD, Ishizawa T, Kokudo N et al.(2015) fluorescence imaging for surgeons: concepts and applications. springe 357 p.
12. Zhu C, Palmer GM, Breslin TM et al.(2008) Diagnosis of breast cancer using fluorescence and diffuse reflectance spectroscopy: a Monte-Carlo-model-based approach. J Biomed Opt. 13: 34015.
13. Oral cancer initial diagnosis influences final prognosis - Google Search [Internet]. [cited 2016 Apr 15].
14. Dissanayaka WL, Pitiyage G, Kumarasiri PVR et al.(2012) Clinical and histopathologic parameters in survival of oral squamous cell carcinoma. oral surg oral med oral pathol oral radiol. Apr 113: 518-25.
15. El-Naggar A ,Chan JKC, Grandis JR et al.(2017) WHO classification of head and neck tumors.
16. Poh CF, Zhang L, Anderson DW et al.(2006) Fluorescence visualization detection of field alterations in tumor margins of oral cancer patients. clin cancer res off j am assoc cancer res 12: 6716-6722.
17. Chenzhou Wu, John Gleysteen, Nutte Tarn Teraphongphom,et al. (2018) In-vivo optical imaging in head and neck oncology: basic principles, clinical applications and future directions | International Journal of Oral Science Int J Oral Sci 18: 10.
18. Awan KH, Morgan PR, Warnakulasuriya S et al. (2011) Evaluation of an autofluorescence based imaging system (VELscope™) in the detection of oral potentially malignant disorders and benign keratoses. Oral Oncol 47: 274-277.
19. Nomura T, Shibahara T.(2013) Detection of field alterations using useful tools for oral squamous cell carcinoma. Jpn Dent Sci Rev 49: 106-15.
20. Lane PM, Gilhuly T, Whitehead PD et al. (2006) simple device for the direct visualization of oral-cavity tissue fluorescence. j biomed opt. 11: 24006.
21. Xiaobo Luo , Hao Xu, Mingjing He, et al. (2016) Accuracy of auto fluorescence in diagnosing oral squamous cell carcinoma and oral potentially malignant disorders: a comparative study with aero-digestive lesions 16: 29943.