

**Treatment outcome of Photofrin-based photodynamic therapy for T1 and T2 oral squamous cell carcinoma and dysplasia**

Hisazumi IKEDA, DDS, PhD<sup>1</sup>, Takayoshi TOBITA, DDS, PhD<sup>1</sup>, Seigo OHBA, DDS, PhD<sup>2</sup>,

Masataka UEHARA, DDS PhD<sup>3</sup>, Izumi ASAHINA, DDS PhD<sup>1</sup>

Department of Regenerative Oral Surgery, Unit of Translational Medicine, Nagasaki University

Graduate School of Biomedical Sciences<sup>1</sup>

Chief and Chairman: Prof. Izumi ASAHINA, DDS, PhD<sup>1</sup>.

Division of Dentistry and Oral Surgery, Department of Sensory and Locomotor Medicine,

Faculty of Medical Sciences, University of Fukui<sup>2</sup>.

Department of Science of Physical Functions, Division of Maxillofacial Surgery, Kyushu

Dental College<sup>3</sup>

Key words: photodynamic therapy (PDT), Photofrin, squamous cell carcinoma dysplasia

Running title: Photofrin based-photodynamic therapy treatment outcome in the oral cavity

Corresponding author: Hisazumi IKEDA, DDS PhD

Department of Regenerative Oral Surgery, Unit of Translational Medicine

Nagasaki University Graduate School of Biomedical Sciences

1-7-1 Sakamoto, Nagasaki 852-8501, Japan

Tel: +81 95-819-7703; Fax: +81 95-819-7705

E-mail: [hisazumi@nagasaki-u.ac.jp](mailto:hisazumi@nagasaki-u.ac.jp)

## Abstract

**Background:** Photodynamic therapy (PDT) is a minimally invasive treatment modality for early and superficial malignancy or premalignancy in the head and neck regions. However, few studies have examined the use of Photofrin-mediated PDT to manage early carcinoma and dysplasia in the oral cavity.

**Methods:** Between January 2004 and November 2008, 25 T1 to T2 patients with N0 oral squamous cell carcinoma and mucosal dysplasia in the oral cavity were treated by Porfimer sodium (Photofrin®)-mediated PDT at Nagasaki University Hospital. Clinical responses were evaluated according to the guidelines of the Response Evaluation Criteria in Solid Tumors (RECIST). After the PDT and a 2-year follow-up period, disease specific survival rates were then calculated.

**Results:** A total of 30 regions in 25 patients (18 with squamous cell carcinoma and 7 with epithelial dysplasia with hyperkeratosis in the oral cavity) were treated by PDT. Complete response was achieved in 24 of the 25 patients (96%), with a partial response found in the remaining patient. For the three patients who exhibited recurrence at 4, 5, and 15 months after PDT, salvage surgery or a second PDT was performed. Of these three patients, one died due to another disease, while one died due to local lymphatic metastasis that occurred during the follow-up period. Overall, the disease specific survival rate was 95.8%. Treatment-related

edema and pain emerged within 24 hours after irradiation. Pain control using non-steroid anti-inflammatory drugs and opiates was required for 3 to 4 weeks in all patients. Complete healing was attained at 4 to 6 weeks after the treatment. No persistent problems related to functional or esthetic outcomes were noted.

Conclusion: Current results demonstrate the efficacy of Photofrin-mediated PDT on early superficial squamous cell carcinoma and epithelial dysplasia in the oral cavity.

1 Introduction

2 The preferred treatment modalities for early-stage carcinomas and mucosal dysplasia in the  
3 oral cavity are surgery and radiotherapy. While both treatment modalities have good cure rates  
4 during the early stages<sup>1, 2)</sup>, these treatments can lead to functional impairments. Radiotherapy  
5 often has irreversible side effects such as endarteritis, xerostomia, and mucositis, along with an  
6 added risk for osteoradionecrosis. Similarly, surgery can also have unintended side effects, with  
7 both functional and esthetic losses occurring to some degree in other healthy tissues. When  
8 present in the oral cavity, there is a potential for mucosal dysplasia to progress to cancer. A  
9 previous study has reported that the risk of progression to cancer varies from 6% to 36%.<sup>3)</sup> The  
10 management of patients with oral dysplasia presents a considerable problem for surgeons, as  
11 radiotherapy is not always feasible since it can only be administered once. In addition, this  
12 therapy is associated with significant local morbidity. Thus, an optimal treatment for moderate  
13 to severe dysplasia of the oral cavity needs to be safe, effective, repeatable, minimally invasive,  
14 and devoid of permanent sequelae. Photodynamic therapy (PDT) is a photochemical reaction  
15 that is based on the use of a drug, light, and oxygen, with the photochemical reaction leading to  
16 a selective destruction of tumor cells. As compared to the other conventional modalities, there  
17 are several advantages associated with using the PDT methodology. These include: (1) the  
18 treatment is a minimally invasive technique that lacks systemic toxicity; (2) there is selective

1 tumor destruction along with normal tissue preservation; (3) the treatment can be repeated  
2 without any cumulative tissue toxicity; (4) there is little effect on the underlying functional  
3 structures and there is an excellent esthetic outcome; and (5) the treatment can be applied before  
4 or after any conventional treatment modality. PDT has been approved worldwide for use as a  
5 clinical treatment with various photosensitizers.<sup>4,5)</sup> Porfimer sodium (Photofrin®)<sup>6)</sup> is a first  
6 generation photosensitizer with a long history of use that has shown it to be both reliable and  
7 safe.<sup>7)</sup> Photofrin has been licensed for use in esophageal, lung, stomach, and cervix cancer in the  
8 United States, Canada, European Union, Russia, and Japan.<sup>8)</sup> However, Photofrin-based PDT  
9 for carcinoma and dysplasia in the oral cavity has yet to be approved in Japan. Photofrin is  
10 activated at 630 nm, which is a wavelength that can penetrate tissues to a depth of 10 mm<sup>9)</sup>.  
11 Even though Photofrin-based PDT has been shown to be ineffective against deeper tumors, it is  
12 effective for the treatment of superficial malignancies. Since almost all lesions in the oral cavity  
13 can be observed macroscopically, light irradiation treatments can be carried out without having  
14 to use special devices such as endoscopes. Thus, superficial malignancies and mucosal  
15 dysplasia in the oral cavity are good targets for Photofrin-mediated PDT. However, few studies  
16 have specifically examined using Photofrin-mediated PDT to manage carcinoma and dysplasia  
17 in the oral cavity. In this study, we report the clinical outcomes and complications for 25 cases  
18 at 30 sites of oral squamous cell carcinoma and epithelial dysplasia after treatment with

1 Photofrin-mediated PDT in the Department of Oral and Maxillofacial Surgery, Nagasaki  
2 University Hospital from 2004 to 2008.

### 3 Materials and Methods

4 This retrospective study attempted to determine the effects of Photofrin-mediated PDT on oral  
5 squamous cell carcinoma (SCC) and dysplasia. Between January 2004 and November 2008, this  
6 48-month study examined patients seen at the Oral and Maxillofacial Surgery Unit of Nagasaki  
7 University Hospital. All procedures were performed according to the specific protocol approved  
8 by the Institutional Review Board of Nagasaki University Hospital (Approval No. 17). Informed  
9 consent was obtained from all patients prior to their enrollment in the study. To prevent any  
10 photosensitivity side effects, all patients were hospitalized during their treatments. Inclusion  
11 criteria for this study were as follows: (1) biopsy-proven SCC in the oral cavity; (2)  
12 biopsy-proven moderate to severe oral mucosal dysplasia, as per the WHO classification  
13 criteria<sup>9</sup>; (3) tumor diameter less than 4 cm (T1 to T2) without any lymph-node or distant  
14 metastases (N0, M0); (4) tumor depth less than 5 mm, as measured by magnetic resonance  
15 imaging and ultrasound imaging; (5) patients with severe complications who could not tolerate  
16 conventional therapy; and (6) patients who refused conventional therapy or who had previous  
17 failed treatments. Patients were excluded if they had Porphyria or exhibited hypersensitivity for

1 porphyrin. Photofrin (Wyeth-Takeda, Tokyo, Japan) was dissolved in a 5% glucose solution and  
2 administered intravenously 48 hours prior to laser irradiation at a dose of 2 mg/Kg within  
3 10-minute. After PDT administration, all patients avoided direct sunlight. The excitation light  
4 source used in the study was an Excimer dye laser (PDT-EDL1: Hamamatsu Photonics K.K.,  
5 Hamamatsu, Japan). The wavelength was 630 nm, irradiation output was 4 mJ/pulse/cm<sup>2</sup>, and  
6 the repetition rate was 40 Hz. Light was delivered to the tumor via a 400 μm flat-tipped quartz  
7 fiber. Irradiation was performed with the tip of the fiber placed approximately 1.0 cm from the  
8 lesion to make 1cm<sup>2</sup> irradiation spot. Light doses consisted of 100 J/cm<sup>2</sup> <sup>11)</sup>. Irradiation times  
9 needed about 11 minutes for 100 J/cm<sup>2</sup>. The lesion plus an additional 5 mm margin of the  
10 normal mucosa were illuminated. Surrounding normal tissues were covered by wet gauze in  
11 order to protect them from the laser light. Topical or local anesthesia was not required during  
12 any of the treatments in all patients. Treatment times varied from 30 to 150 minutes in  
13 accordance with the lesion size. Postoperative care included an intravenous Betamethasone  
14 4mg/body administration once a day for 3 days in order to relieve any swelling. Intravenous or  
15 orally administered antibiotics were then administered for 1 week to prevent infection. Oral  
16 non-steroid anti-inflammatory drugs (NSAIDs) and opiates were used as needed to control any  
17 postoperative pain. Biopsies were performed 4 to 6 weeks after the PDT. Clinical responses  
18 were evaluated as a complete response (CR), partial response (PR), stable disease, or



1 progressive disease in accordance with the guidelines for the Response Evaluation Criteria in  
2 Solid Tumors (RECIST) <sup>12)</sup>. Follow-ups were performed at 1, 2, 4, 8, 16, 24, 36, 52 weeks and  
3 2 years after the PDT. After completion of 2 years of follow-up, we have continued to follow  
4 the patients where possible.

## 5 Results

### 6 Patients

7 Twenty-five patients were treated by Photofrin-mediated PDT from January 2004 to  
8 December 2008. Table 1 lists the demographic and histopathological characteristics of the  
9 lesions in 25 patients who were treated by Photofrin-mediated PDT. The group included 12  
10 males and 13 females, ranging in age from 29 to 85, with an average age of 70.8 years. A total  
11 of 18 had SCC while 7 were diagnosed as epithelial dysplasia with hyperkeratosis. Out of the 25  
12 patients, 5 had recurrent disease (with 4 undergoing surgery and 1 receiving radiation therapy),  
13 while 20 had primary disease.

### 14 Site and classification

15 A total of 30 regions were treated by PDT in the 25 patients. Locations treated included the  
16 tongue (n=14), gingiva (n=6), palate (n=5), buccal mucosa (n=4) and the floor of the mouth

1 (n=1). In accordance with the WHO histological grading guidelines, 5 out of 7 of the epithelial  
2 dysplasia patients were moderate, while 2 were classified as severe dysplasia with  
3 hyperkeratosis. For the histological grading of the SCC, 17 were classified as well differentiated  
4 while 1 was moderately differentiated. According to the T size classification, 9 were T1 and 10  
5 were T2 (Table 1).

#### 6 Treatment responses

7 Follow-up information was available for all patients. Based on the physical and histological  
8 examinations, 24 out of 25 patients (96%) achieved CR, with the remaining patient classified as  
9 PR. A CR was achieved by 17 out of 18 patients (94.4%) in the SCC group and in 7 out of 7  
10 patients (100%) in the epithelial dysplasia group. As seen in Table 1, the T1 palatal SCC patient  
11 who only achieved PR subsequently underwent surgical resection. As of 2010, this patient has  
12 remained disease-free.

#### 13 Disease-free interval and disease-specific survival rate

14 Recurrences occurred in 3 patients (3/25: 12%) after PDT. In the SCC group, 2 out of the 18  
15 patients had recurrences at 4 and 15 months. Both of these patients underwent surgical resection  
16 and have remained disease-free during the subsequent follow-up periods. In the epithelial  
17 dysplasia group, 1 out of 7 patients had a recurrence at 5 months after the PDT. This patient has

1 been disease-free after undergoing a second Photofrin-mediated PDT procedure. Two SCC  
2 patients died during the follow-up period even though they initially achieved CR. A T2 palate  
3 SCC patient died 4 months after the PDT due to neck metastasis, while a T2 buccal mucosa  
4 SCC patient died at 24 months after PDT due to hepatic cirrhosis. Overall, the total disease  
5 specific survival rate in this study was 95.8%.

#### 6 Postoperative courses

7 Within 24 hours after the irradiation, swelling and edema were observed at the site and  
8 continued for approximately 1 week. Severe swelling was noted more often in patients who had  
9 irradiation of the tongue or buccal mucosa versus the gingiva or palate. While slight dyspnea  
10 that lasted 2 to 3 days was observed in some patients who had irradiation of their tongue, none  
11 of these patients required airway intervention as a result of the treatment. Postoperative pain  
12 occurred 1 to 2 days after PDT, with contact and swallowing pain being the major symptom  
13 seen in all patients. Systemic intraoral administration of NSAIDs was required for 3 to 4 weeks  
14 post-irradiation. Some patients needed oral administration of opiates in addition to the NSAIDs.  
15 Transient odynophagia made it necessary for all patients to continue on a liquid diet for 7 to 10  
16 days after the treatment. Treated areas underwent surface necrosis 2 to 3 days after the  
17 irradiation, with the necrosis lasting for 10 to 14 days. Complete healing occurred 4 to 6 weeks

1 after PDT with little scar formation (Fig 1~4). Direct sunlight caused a phototoxic reaction of  
2 the facial edema in 2 patients. After oral administration of steroids, this reaction resolved within  
3 1 week. All patients had slight skin coloration changes, although no symptoms were noted on  
4 either the face or hands. This change completely disappeared within 1 year in all patients. There  
5 were no persistent problems related to functional or esthetic outcomes in any of the patients.

6

7

8

9

10

11

12

13

14

1 Discussion

2 The main advantage of PDT for oral early carcinoma and dysplasia is the ability to preserve  
3 normal tissue and the oral function. In the oral cavity, almost all of the lesions can be observed  
4 macroscopically. Since light irradiation can be performed without the need for special devices  
5 such as endoscopes, the oral cavity may be an appropriate region for PDT. Over the past 30 years,  
6 the first generation photosensitizer, Porfimer sodium (Photofrin®) <sup>6)</sup>, has been widely utilized  
7 and shown to have a high level of safety.<sup>7)</sup> However, few studies have investigated the  
8 Photofrin-mediated PDT treatment outcomes for SCC and dysplasia in just the oral cavity<sup>13-17)</sup>  
9 In previous studies, treatment outcomes for oral cavity carcinoma and epithelial dysplasia have  
10 been reported to vary from 83.3% to 100% <sup>13-17)</sup>. In the current study, 25 patients with SCC or  
11 epithelial dysplasia in the oral cavity were treated using Photofrin-mediated PDT. A single PDT  
12 treatment resulted in a complete response in 24 out of 25 patients (96%). During the 24-month  
13 follow-up period, recurrence occurred in 3 patients within 15 months. This result demonstrate  
14 the efficacy of Photofrin-mediated PDT for both SCC and epithelial dysplasia in the oral cavity.  
15 The major side effect associated with Photofrin use is its photosensitivity, which can last for up to  
16 4 weeks.<sup>5,11)</sup> In the current study, two patients exhibited photosensitivity after discharge. Upon  
17 further examination, this photosensitivity appeared to be caused by the patients wearing improper  
18 clothing. In addition, although all of the patients exhibited slight pigmentation after the PDT

1 treatment, this completely disappeared without any additional persistent esthetic problems  
2 within 1 year. These findings indicate that photosensitivity was not a major complication in the  
3 current study. One other problem encountered during the treatment period was related to  
4 postoperative swelling and pain. Postoperative swelling was observed within 24 hours after the  
5 original light irradiation, with resolution occurring within 1 week. If the lesions are located at the  
6 base of the tongue or on the posterior portion of the oral floor, the airways could potentially be  
7 compromised. The possibility of airway obstruction needs to be taken into consideration prior to  
8 treatment. Post operative pain was severe and continued to be a problem for a long time. Pain  
9 relief in the current study was obtained by a 3 to 4 week systemic administration of NSAIDs  
10 along with opiates, when necessary. However, the pain duration observed in the current study  
11 was substantially longer than has been previously reported<sup>18)</sup>. Light penetration depth, tumor bed  
12 homogeneity, and the irradiation times have all been reported to have a major influence on  
13 therapeutic effects<sup>18,19)</sup>. Although human tissue transmits light most effectively in the red part of  
14 the visible spectrum, Photofrin only has moderate activity in the tissue because the excitation  
15 wavelength (630 nm) can only penetrate tissue to a depth of 10 mm.<sup>9)</sup> In the SCC group, we  
16 observed a residual tumor on the floor of the mouth in one patient, along with recurrence on the  
17 palate of another patient. The palate and the floor of the mouth have complex structures within  
18 the oral cavity, with both sites having an irregular surface that makes it difficult to accurately

1 illuminate nonhomogenous structures. Therefore, an insufficient light penetration depth  
2 combined with the complex structure may be responsible for the presence of residual tumor  
3 cells. One patient with dysplasia of the tongue had recurrence 5 months after PDT. In this case,  
4 the irradiation areas were 60×20 mm. the irradiation times this patient required over 120 min.  
5 When large irradiation fields require irradiation times that are longer than 120 min, this can  
6 result in a significant source of treatment error due to either patient or light source motion.<sup>20)</sup>  
7 Likewise, the reason for recurrence in patients may be due to an inaccurate light delivery that  
8 occurs as a direct result of the longer required treatment times. It should be noted that patients  
9 with SCC and dysplasia in the oral cavity appear to be amenable to PDT treatments. In contrast,  
10 it is difficult to treat these tumors and premalignancies when using conventional therapies.  
11 When employing PDT, the superficial affected areas can be easily treated without damaging the  
12 surrounding normal tissues. Photofrin is a useful and reliable photosensitizer that has a long  
13 history of administration worldwide. In the current study, Photofrin-mediated PDT for  
14 superficial SCC and dysplasia in the oral cavity resulted in excellent outcomes. Even so, these  
15 promising findings are somewhat tempered by the photosensitivity and weak tissue penetration  
16 problems associated with Photofrin treatments. However, second generation photosensitizers  
17 such as mTHPC<sup>21)</sup> and mono-L-aspartylchlorin-e6<sup>22)</sup> have been shown to not only be rapidly  
18 eliminated in the body but also to have longer excitation wavelengths as compared to Photofrin.

1 Thus, use of these second-generation photosensitizers for PDT may very well to lead to better

2 results when treating early-stage SCC and dysplasia in the oral cavity.

3



1   References

- 2    1: Fein DA, Mendenhall WM, Parsons JT, McCarty PJ, Stringer SP, Million RR, et al.  
3        Carcinoma of the oral tongue: a comparison of results and complications of treatment with  
4        radiotherapy and/or surgery   Head Neck   1994; 16 (4): 358-65.
- 5    2: Gomez D, Faucher A, Picot V, Siberchicot F, Renaud-Salis JL, Bussièrès E, et al.  
6        Outcome of squamous cell carcinoma of the gingiva: a follow-up study of 83 cases  
7        J Craniomaxillofac Surg   2000; 28 (6): 331-335.
- 8    3: Reibel J. Prognosis of oral pre-malignant lesions: significance of clinical, histopathological  
9        and molecular biological characteristics   Crit Rev Oral Biol Med   2003; 14: 47–62.
- 10   4: Hopper C. Photodynamic therapy: a clinical reality in the treatment cancer  
11        Lancet oncol   2000; 1: 219-212.
- 12   5: Dougherty TJ, Gomer CJ, Henderson BW, Jori G, Kessel D, Korbélik M, et al.  
13        Photodynamic therapy   J Natl Cancer Inst   1998; 90(12) : 889-905.
- 14   6: Lui H. Photodynamic therapy in dermatology with Porfimer sodium and benzoporphyrin

- 1 derivative: an update Semin Oncol 1994; 6(15): 11-4.
- 2 7: Calzavara-Pinton PG, Venturini M, Sala R. Photodynamic therapy: update 2006. Part 1:  
3 Photochemistry and photobiology J Eur Acad Dermatol Venereol 2007;21(3):293-302.
- 4 8: Jerjes W, Upile T, Betz CS, El Maaytah M, Abbas S, Wright A, et al. The application of  
5 photodynamic therapy in the head and neck Dent Update 2007; 34:478-480, 483-4, 486 .
- 6 9: T.S. Mang, M. Sullivan, M. Cooper, T. Loree, N. Rigual. The use of photodynamic therapy  
7 using 630 nm laser light and porfimer sodium for the treatment of oral squamous cell  
8 carcinoma Photodiagnosis and Photodynamic Therapy 2006; 3; 272-275
- 9 10: Barnes L, Eveson JW, Reichart PA, Sidransky D. World Health Organization classification  
10 of tumours. Pathology and genetics. Head and neck tumours. World Health Organization:  
11 United Nations; 2005.
- 12 11: Nyst HJ, Tan IB, Stewart FA, Balm AJ. Is photodynamic therapy a good alternative to  
13 surgery and radiotherapy in the treatment of head and neck cancer?  
14 Photodiagnosis Photodyn Ther 2009; 6(1):3-11.
- 15 12: Eisenhauer EA, Therasse P, Bogaerts J, Schwartz L, Sargent D, Ford R, Dancey J, et al.

- 1 New response evaluation criteria in solid tumours: revised ECIST guideline (version 1.1)  
2 Eur J Cancer 2009; 45,228–247.
- 3 13: Grant WE, Hopper C, MacRobert AJ, Bown SG, Photodynamic therapy of malignant and  
4 premalignant lesions in patients with ‘ field cancerization’ of the oral cavity The Journal  
5 of Larygology and Otology 1993; 107: 1140-1145.
- 6 14: Schweitzer VG, Somers ML. PHOTOFRIN-mediated photodynamic therapy for treatment of  
7 early stage (Tis-T2N0M0) SqCCa of oral cavity and oropharynx Lasers Surg Med 2010;  
8 42:1-8.
- 9 15: Rigual NR, Thankappan K, Cooper M, Sullivan MA, Dougherty T, Popat SR, et  
10 al. Photodynamic therapy for head and neck dysplasia and cancer  
11 Arch Otolaryngol Head Neck Surg 2009; 135(8):784-788.
- 12 16: Biel M. Advances in photodynamic therapy for the treatment of head and neck cancers  
13 Lasers Surg Med 2006; 38:349-355.
- 14 17: Gluckman JL. Hematoporphyrin photodynamic therapy: is there truly a future in head and  
15 neck oncology? Reflections on a 5-year experience Laryngoscope 1991; 101(1 Pt1):36-42.

- 1 18: Müller S, Walt H, Dobler-Girdziunaite D, Fiedler D, Haller U. Enhanced photodynamic  
2 effects using fractionated laser light J Photochem Photobiol B 1998; 42(1) : 67-70.
- 3 19: Kubler AC, Haase T, Staff C, Kahle B, Rheinwald M, Mühling J. Photodynamic therapy  
4 of primary nonmelanomatous skin tumours of the head and neck Lasers Surg Med  
5 1999; 25: 60-68.
- 6 20: Allison RR, Cuenca RE, Downie GH, Camnitz P, Brodish B, Sibata CH. Clinical  
7 photodynamic therapy of head and neck cancers – A review of applications and outcomes.  
8 Photodiagnosis and Photodynamic Therapy 2005; 2: 205-222.
- 9 21: Copper MP, Tan IB, Oppelaar H, Ruevekamp MC, Stewart FA. Meta-tetra (hydroxyphenyl)  
10 chlorin photodynamic therapy in early-stage squamous cell carcinoma of the head and neck  
11 Arch Otolaryngol Head Neck Surg 2003; 129:709-711.
- 12 22: Yoshida T, Tokashiki R, Ito H, Shimizu A, Nakamura K, Hiramatsu H, et al. Therapeutic  
13 effects of a new photosensitizer for photodynamic therapy of early head and neck cancer in  
14 relation to tissue concentration Auris Nasus Larynx 2008; 35:545-551.
- 15

Table 1. Photofrin-based photodynamic therapy for T1 and T2 oral squamous cell carcinoma and dysplasia (2004–2008).

Case	Gender	Age	Site	Diagnosis	Histological grading	T classification	Previous treatment	Response	Prognosis
1	F	55	tongue	SCC	well	I		CR	CR
2	F	69	buccal mucosa tongue gingival crest	SCC	well	II		CR	CR
3	F	66	tongue	dysplasia	severe			CR	CR
4	M	61	palate(both side)	dysplasia	moderate			CR	CR
5	F	70	tongue(both side)	dysplasia	severe			CR	CR
6	F	79	tongue	dysplasia	moderate			CR	CR
7	F	70	tongue gingival crest	SCC	well	I		CR	CR
8	F	80	buccal mucosa	SCC	well	I	surgery	CR	CR
9	F	85	gingival crest	SCC	well	II		CR	CR
10	M	83	palate	SCC	moderate	I		CR	recurrence after 15 months
11	M	70	floor of mouth	SCC	well	I		CR	recurrence after 4 months
12	M	75	buccal mucosa	SCC	well	II	radiation	CR	CR
13	M	73	tongue	dysplasia	moderate		surgery	CR	CR
14	F	29	tongue	dysplasia	moderate			CR	CR
15	F	84	gingival crest	SCC	well	I		CR	CR
16	M	76	tongue	SCC	well	I		CR	CR
17	M	71	palate	SCC	well	I		PR	conventional surgery
18	M	70	buccal mucosa	SCC	well	II		CR	CR
19	F	76	gingival crest	SCC	well	I	surgery	CR	CR
20	M	67	tongue	dysplasia	moderate			CR	recurrence after 5 months
21	F	66	gingival crest	SCC	well	II		CR	CR
22	M	75	tongue	SCC	well	II		CR	CR
23	M	80	tongue	SCC	well	II	surgery	CR	CR
24	F	73	palate	SCC	well	II		CR	CR
25	M	68	tongue	SCC	well	II		CR	Dead regional neck metastasis after 4 months

SCC, squamous cell carcinoma; well, well differentiated; moderate, moderate differentiated or moderate dysplasia; CR, complete remission and PR, partial remission.

Figure legends

Fig 1-a. Squamous cell carcinoma at left buccal mucosa (Case No 8)

Before PDT treatment

Fig 1-b. During PDT treatment (Case No 8).

Fig 1-c. After PDT treatment. Tumor disappeared at irradiation site (Case No 8).

Fig 2-a. Squamous cell carcinoma at left buccal mucosa (Case No 9)

Before PDT treatment

Fig 2-b. During PDT treatment (Case No 9)

Fig 2-c. After PDT treatment. First,second premolar and first molar teeth dropped

after treatment(Case No 9).

Fig 3-a.Moderate epithelial dysplasia both side of the palate (Case No 4)

BeforeDuring PDT treatment

Fig 3-b. Moderate epithelial dysplasia both side of the palate (Case No 4)

During PDT treatment

Fig 3-c. After PDT treatment (Case No 4).

Epithelial dysplasia was complete disappeared.

Fig 4-a. Moderate epithelial dysplasia both side of the palate (Case No 20)

Before PDT treatment

Fig 4-b. During PDT treatment(Case No 20)

Necrosis was seen at irradiation site

Fig 4-c. Five month after PDT treatment(Case No 20).

Recurrence was noticed at irradiation site

Fig. 1

a.



b.





Fig. 1

c.

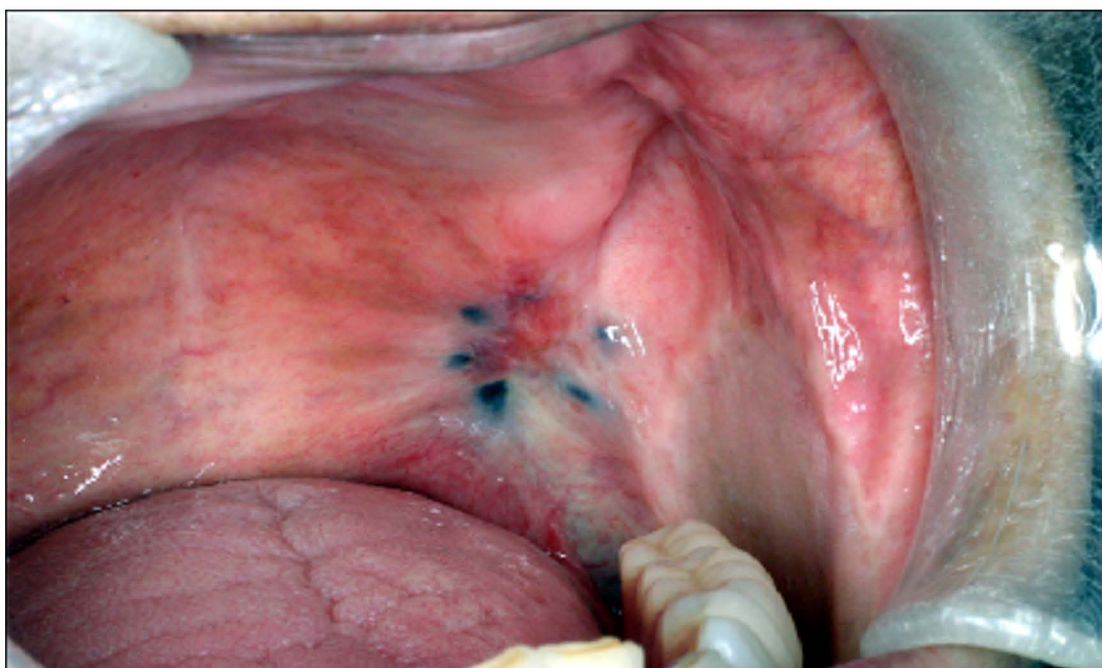


Fig. 2

a.



b.



Fig. 2

c.



Fig. 3

a.



b.



Fig. 3

c.



Fig. 4

a.



b.



Fig. 4

c.

