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# Primary malignant melanoma of the oral cavity: assessment of outcome from the clinical records of 35 patients

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*Abstract*. Oral malignant melanoma is extremely rare and carries a poor prognosis. The treatment of choice remains controversial. We retrospectively studied 35 patients with primary malignant melanoma of the oral cavity between 1970 and 2001 to define the clinical features of this disease and evaluate treatment methods. The main variables studied were clinical findings, response to therapy, and outcome. Surgery with complete macroscopic resection was performed at the primary site in 13 patients (surgery group) and radiotherapy was done without surgery in 17 (non-surgery group). The 5-year cumulative survival rate was 15.4% in the surgery group, 35.3% in the non-surgery group, and 21.8% overall. Distant metastasis was present in 64.7% (11/17) of the non-surgery group and 76.9% (10/13) of the surgery group. Improved outcome in oral malignant melanoma requires the development of new therapies and the prevention of distant metastasis.

Key words: oral malignant melanoma; surgery; radiotherapy; distant metastasis.

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Oral malignant melanoma accounts for only 0.5% of all oral malignancies[2], and oral melanoma represents 0.2–8.0% of all melanomas[15]. Owing to the rarity of this tumor, diagnosis and treatment remain a matter of debate. The aggressive biologic behavior of oral malignant melanoma is particularly problematic. The treatment of choice for oral malignant melanoma is wide surgical resection[1,18], and recent advances in surgical techniques have increased the range of resection. However, the outcome of oral malignant melanoma remains poor. Multidisciplinary treatment including modalities such as radiotherapy has received increasing attention[6].

Oral malignant melanoma is more common in Japan[22] than in Caucasian populations[9]. We studied 35 patients with primary oral malignant melanoma between 1970 and 2001. To our knowledge, this to be one of the largest series of oral malignant melanomas in which treatment, clinical course, and outcome were assessed in detail. Our main goals were to define the clinical features of oral melanoma and to evaluate treatment methods.

## Patients and methods

Between 1970 and 2001, 23 patients with primary malignant melanoma arising in the oral region (No. 1–16, 19, 26–29, 34, 35) were treated at Tokyo Medical and Dental University, and 12 (No. 17, 18, 20–25, 30–33) were treated at Sapporo Medical University. At the former institution, located in the center of Japan, oral melanoma was treated mainly by radiotherapy in all but 3 patients (No. 26, 28, 29), while at the latter, located in the northern part of Japan, all but 1 patient (No. 17) underwent surgery. We retrospectively reviewed the medical records of these patients to assess clinical features, treatment, and outcome.

Surgical treatment with complete macroscopic resection was performed at the primary site in 13 patients (surgery

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group), and radiotherapy was done without surgery in 17 (non-surgery group). Of the other 5 patients, 2 received chemotherapy, and 3 remained untreated. Clinical stage was determined according to the 2002 International Union against Cancer (UICC) staging system for cutaneous melanoma. Statistical analysis was performed with the use of SPSS, version 10.0J for Windows. Survival was estimated according to the Kaplan–Meier method, and the statistical significance of differences in survival was assessed by the log-rank test.

## Results

The patients' age ranged from 30 to 92 years (mean, 65.2 years). Twenty-six (74.3%) of the 35 patients were aged between 50 and 80 years. Fourteen were men and 21 women. There was a definite predilection for occurrence in the maxillary gingiva and palate (91.4%, 32 of 35 lesions), with 17 lesions occurring in both the maxillary gingiva and palate, 10 in the palate alone, and 5 in the maxillary gingiva alone. The other 3 lesions arose in the mandibular gingiva or tongue.

In the non-surgery group (Table 1), the primary lesion was controlled in 9 of the 17 patients, with no recurrence. Regional lymph node metastasis was found in 8 patients after treatment of the primary lesion (No. 5, 7, 10, 11, 12, 13, 16, and 17) and in 4 patients at presentation (No. 2, 3, 4, and 6). Five patients (No. 7, 10, 11, 12, and 17) received surgery (No. 7, 10, lymph node resection; No. 11, 12, 17, radical neck dissection) with postoperative radiotherapy, and regional lesions were controlled in 4 (No. 7, 10, 11, and 17), all of whom had no recurrence. In 1 (No. 16) of the 4 patients given radiotherapy for regional lymph node metastasis, lesions subsequently disappeared clinically, but in the other 3 (No. 2, 4, and 6), regional lesions were not completely controlled. The primary and regional lesions were additionally treated by chemotherapy and immunotherapy. The chemotherapeutic regimen used was either 5-fluorouracil orally (300 mg per day) or intra-arterially (250 mg per day; total dose, 1750 mg), dacarbazine (1 course = 500 mg, 1–4 courses) intravenously, cisplatin (100–120 mg) intravenously, or bleomycin (5 mg per day) intravenously. For immunotherapy, Krestin, OK-432, or BCG was used. OK-432 is a biological response modifier consisting of lyophilized powder made from cultures of penicillin-treated, low-virulence, Su-strain human *Streptococcus pyogenes* (Picibanil, Chugai Pharmaceutical Co. Ltd., Tokyo, Japan). Krestin is a biological response modifier with a diverse range of biological activities that is produced from *Coriolus vesicolor*, a fungus belonging to the class Basidomycetes. Distant metastasis was found in 11 of the 17 patients in the non-surgery group. All 11 of these patients died from their tumors. Distant metastasis was found in 7 of the 8 patients whose primary lesions were not controlled by radiotherapy. Four of these 7 patients died from their tumors within 1 year after presentation. Four patients (No. 6, 11, 13, and 16) received radiotherapy for distant metastasis and had prolonged remission. One patient (No. 8) was lost to follow-up 8 years 4 months after presentation. Survival of the 17 patients in the non-surgery group ranged from 3 months to 14 years 3 months, and the 5-year survival rate was 35.3% (Fig. 1). One patient (No. 10) died of general prostration, 1 (No. 14) of enteral disease, and 2 (No. 7, 17) of unknown causes. The histological depth of tumor invasion ranged from 2 to 9 mm (mean, 4.5 mm).

All 13 patients in the surgery group (Table 2) underwent tumor resection, and the primary lesion was controlled in 12. Recurrent lesions were diagnosed in 2 patients after surgery and in one after radiotherapy. All recurrent lesions were controlled by surgery. Postoperative radiotherapy was performed in 3 patients (No. 18, 20, and 26). Preoperative radiotherapy was given to one patient (No. 29). In another (No. 19), the primary lesion did not respond completely to radiotherapy, but was subsequently controlled by surgery. Regional lesions were detected in 3 patients (No. 18, 19, and 21) at presentation and in 3 (No. 25, 27, and 28) after treatment of their primary lesions. Neck dissection was performed in 5 (No. 18, 19, 21, 25, and 27) of these 6 patients. Lesions were controlled in 4 of the 5 patients who underwent neck dissection, including one patient

*Table 1.* Non-surgery group

| | | | | | | | Treatment | | | Final control | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Age | Gender | Location | Size (mm) | Stage | Depth(mm) | Primary lesion | Regional lesion | Distant metastasis | Primary lesion | Regional lesion | Outcome |
| 1 | 45 | F | MGP | 20 × 30 | IV | ? | R(20 Gy) | | Bone | No | | 6M(Dc) |
| 2 | 71 | M | MGP | 38 × 11 | III | 4.5 | R(60 Gy) | (At pr)R(50 Gy) | | No | No | 1Y(Dc) |
| 3 | 75 | F | MGP | 45 × 40 | III | 2 | R(13.3 Gy) → I | (At pr) I | Liver | No | No | 6M(Dc) |
| 4 | 82 | F | MGP | 45 × 46 | III | 6 | R(52 Gy) | (At pr) R(52 Gy) → C | Lung | No | No | 3M(Dc) |
| 5 | 57 | M | MGP | 24 × 14 | III | 3 | R(50 Gy) → I | (Later) C | Lung | No | No | 10M(Dc) |
| 6 | 46 | M | MG | 26 × 32 | III | 5 | R(54.5 Gy) → C → I | (At pr)R(52 Gy) | Lung, etc. | No | No | 8M(Dc) |
| 7 | 65 | M | MGP | 20 × 20 | II | 4 | R(124 Gy) | (Later) S → R(70 Gy) | | Yes | Yes | 14Y3M(DX) |
| 8 | 57 | F | MP | 40 × 35 | II | 9 | R(130 Gy) → I | | | Yes | | 8Y4M(A0) |
| 9 | 60 | F | MGP | 30 × 25 | II | 8.5 | R(92.5 Gy) | | Lung | Yes | | 6Y3M(Dc) |
| 10 | 65 | M | MGP | 35 × 25 | II | 5 | R(80 Gy) | (Later) S → R(45 Gy) | | Yes | Yes | 3Y11M(DO) |
| 11 | 73 | F | MGP | 50 × 25 | II | 3 | R(27.5 Gy) | (Later) S → R(35.5 Gy) | Lung, etc. | Yes | Yes | 3Y1M(Dc) |
| 12 | 72 | M | MP | 34 × 32 | II | 3 | C → R(113 Gy) → C | (Later) S → R(rec)(47.5 Gy) | Lung | Yes | No | 3Y8M(Dc) |
| 13 | 32 | F | MnG | 95 × 11 | II | 3 | R(317 Gy) → I → C | (Later) no therapy | Lung | No | No | 2Y8M(Dc) |
| 14 | 79 | F | MP | 30 × 30 | I | 2 | R(133 Gy) | | | Yes | | 4Y(D0) |
| 15 | 67 | F | MGP | 40 × 50 | I or II | ? | R(124 Gy) → I → C | | Lung | No | | 3Y11M(Dc) |
| 16 | 58 | F | MP | 30 × 26 | I or II | ? | R(83 Gy) → I → C | (Later) R(66 Gy) | Bone | Yes | Yes | 2Y6M(Dc) |
| 17 | 66 | M | MG | 12 × 8 | I or II | ? | R(76 Gy) | (Later) S → R(60 Gy) | | Yes | Yes | 7Y3M(DX) |

S: surgery; R: radiotherapy; C: chemotherapy; I: immunotherapy; MGP: maxillary gingiva and palate; MG: maxillary gingiva; MP: maxillary palate; Mng: mandibular gingiva (Later): regional metastasis developing after the initial treatment; (At pr): regional metastasis at presentation; (rec): recurrence; Dc: dead of cancer (malignant melanoma); D0: dead without malignant melanoma; DX: dead with unknown cause; A0: alive without malignant melanoma.

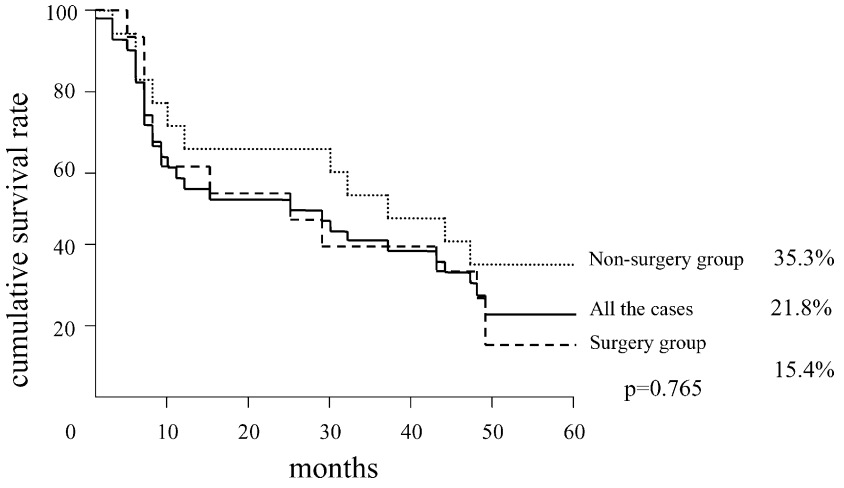


*Fig. 1.* Five-year cumulative survival rate (Kaplan–Meier method).

(No. 21) who received surgery again for a recurrent regional lesion, which was subsequently controlled. In patient 27, the primary lesion was controlled by radiotherapy, but after 11 months regional metastasis was diagnosed in the right cervical region, and radical neck dissection was performed. Fourteen months after the operation, surgery was performed for recurrence of the primary lesion and for regional metastatic lesions in the left cervical region. Ten months after the second operation, a distant metastatic lesion to the lung and a regional lesion in the middle cervical region were found, and the patient died 4 years after presentation. Patient 28 had postoperative metastasis with distant metastasis to the lung; surgery was not feasible. The adjuvant chemotherapy and immunotherapy in the surgery group were similar to those in the non-surgery group. Distant metastasis was detected in 10 of the 13 patients. In 8 of these patients, primary and regional lesions were controlled. Two of the 3 patients without distant metastasis were alive as of this writing. The histological depth of tumor invasion ranged from 0.5 to 10 mm (mean, 3.5 mm). Survival ranged from 5 months to 23 years 7 months, with a 5-year survival rate of 15.4% (Fig. 1).

Five patients received neither radiotherapy nor surgery (Table 3). Two (No. 31 and 33) had distant metastasis at presentation and were given chemotherapy, and 3 (No. 32, 34, and 35) were elderly and refused treatment. The histological depth of invasion ranged from 4 to 8 mm.

The 5-year cumulative survival rate of the 35 patients was 21.8% (Fig. 1).

*Table 2.* Surgery group

| | | | | | | | Treatment | | | Final control | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Age | Gender | Location | Size (mm) | Stage | Depth (mm) | Primary lesion | Regional lesion | Distant metastasis | Primary lesion | Regional lesion | Outcome |
| 18 | 50 | M | MnG | 55 × 10 | III | ? | C → S → R(42 Gy) | (At pr)S → R(42 Gy) | Heart | Yes | Yes | 5M(Dc) |
| 19 | 59 | F | MGP | 46 × 20 | III | 5 | R(80 Gy) → I → C → S → C | (At pr)R(40 Gy) → S | Lung | Yes | Yes | 1Y3M(Dc) |
| 20 | 56 | F | MP | 24 × 12 | II | 3 | S → I → S(rec) → R(60 Gy) | | Lung | Yes | | 3Y7M(Dc) |
| 21 | 71 | F | MGP | 55 × 45 | II | 10 | C → S → I → S(rec) | (At pr)S → S(rec) | Heart | Yes | Yes | 4Y1M(Dc) |
| 22 | 56 | F | MP | 20 × 20 | II | 2.5 | S → I-C | | | Yes | | 23Y7M(A0) |
| 23 | 70 | F | MGP | 25 × 25 | II | 5 | S → C → I | | Lung | Yes | | 9M(Dc) |
| 24 | 55 | M | MP | 18 × 15 | II | 4 | C → S → C | | Lung, etc. | Yes | | 2Y1M(Dc) |
| 25 | 67 | F | MGP | 28 × 35 | II | 5 | S | (Later) S | | Yes | Yes | 6Y9M(A0) |
| 26 | 84 | F | MGP | 30 × 40 | II | 3 | S → R(60 Gy) | | | No | | 2Y5M(Dc) |
| 27 | 64 | M | MGP | 13 × 14 | II | 2.5 | R(70 Gy) → S(rec) | (Later) S → S | Lung | Yes | No | 4Y(Dc) |
| 28 | 30 | F | MGP | 30 × 30 | II | 2.5 | S → C | (Later) no therapy | Lung | Yes | No | 7M(Dc) |
| 29 | 75 | F | MP | 20 × 22 | I | 2 | R(16 Gy) → S | | Systemic | Yes | | 7M(Dc) |
| 30 | 69 | M | MG | 40 × 30 | I | 0.5 | C → S→ I | | Brain | Yes | | 8M(Dc) |

S: surgery; R: radiotherapy; C: chemotherapy; I: immunotherapy; MGP: maxillary gingiva and palate; MG: maxillary gingiva; MP: maxillary palate; Mng: mandibular gingiva; (Later): regional metastasis developing after the initial treatment; (At pr): regional metastasis at presentation; (rec): recurrence; Dc: dead of cancer (malignant melanoma); D0: dead without malignant melanoma; A0: alive without malignant melanoma.

*Table 3.* Other patients

| | | | | | | | Treatment | | Final control | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Age | Gender | Location | Size (mm) | Stage | Depth (mm) | Primary lesion | Regional lesion | Distant metastasis | Primary lesion | Outcome | Others |
| 31 | 62 | F | Tongue | 47 × 47 | IV | 8 | C | | Lung, etc. | No | 7M(Dc) | Inoperable |
| 32 | 89 | M | MP | 48 × 47 | IV | 6 | | | | No | 3M(Dc) | Inoperable |
| 33 | 77 | M | MG | 38 × 12 | III | ? | C | | Systemic | No | 11M(Dc) | Inoperable |
| 34 | 92 | F | MP | 30 × 49 | ? | 3 | | | | No | 6M(Dc) | |
| 35 | 86 | M | MG | ? | ? | 4 | | | | No | 1M(Dc) | Inoperable |

C: chemotherapy; MG: maxillary gingiva; MP: maxillary palate; Dc: dead of cancer (malignant melanoma).

## Discussion

Most previously reported series of oral melanoma have focused on etiology, without adequate follow-up of treatment response[2,7,9,11]. To our knowledge, our study represents the largest series of oral primary malignant melanoma to include the details of treatment and clinical course.

Pandey et al.[13] reported that the treatment policy for malignant mucosal melanoma is unclear. The treatment of most patients is left to the discretion of the individual surgeon. They recommended that data should be pooled from various centers to analyze key determinants of outcome and thereby establish a treatment policy. In accordance with this recommendation, we analyzed the clinical records of 35 patients with oral malignant melanoma treated at 2 university hospitals in Japan.

The primary lesion was controlled in 53% (9/17) of the non-surgery group and 92.3% (12/13) of the surgery group. Traditionally, malignant melanoma has been treated mainly by surgery, with radiotherapy and chemotherapy playing an adjunctive role[2]. In contrast to cutaneous melanoma, oral malignant melanoma can be controlled by radiotherapy provided that disease remains localized[10,17,19,20]. Our results agree with previous findings.

Regional metastases were found in 18 of our 35 patients. Snow et al.[18] reported that after initial treatment lymph node metastasis rarely develops without recurrence. In our series, however, regional metastasis occurred even after local control had been obtained. All surgery in our series was radical. Regional metastasis was not controlled by surgery in only 1 patient (No. 12). Our results support those of Blatchford et al.[3] and Kristian et al.[8], who argue that radical neck dissection should be reserved for confirmed lymph node metastasis and not done prophylactically, despite the propensity for melanoma to metastasize. Shah et al.[16] concluded that regional metastases do not affect the survival of patients with mucosal melanomas of the head and neck. In our study, regional failure was confirmed in 41.2% (7/17) of the non-surgery group and 15.4% (2/13) of the surgery group. In the non-surgery group, regional disease was not controlled by radiotherapy in 3 of 4 patients. Regional disease should therefore be treated by surgery alone or surgery combined with other treatments.

In our study, distant metastasis was recognized in 64.7% (11/17) of the non-surgery group, 76.9% (10/13) of the surgery group, and 65.7% (23/35) overall. Previous studies have reported that the average rate of distant metastasis is 10% at presentation, as compared with 51.5% after treatment in primary mucosal melanoma of the head and neck[9]. The corresponding figures in our study were 8.6 and 60.0%, respectively. Local recurrence might be a harbinger of distant metastasis[3,16,18]; however, in 11 of the 23 patients with distant metastasis, primary and regional lesions had been controlled. There is no effective therapy for distant metastasis. Radiotherapy was associated with prolonged remission. Chemotherapy and immunotherapy might help to prevent distant metastasis, but this remains unclear.

The 5-year cumulative survival rate was 35.3% in the non-surgery group and 15.8% in the surgery group. Most of the patients died of distant metastasis, especially in the surgery group. There was no correlation between outcome and the depth of tumor invasion, consistent with the results of previous studies[11,12,14,21] and contrasting with the correlation found in cutaneous melanoma[4,7]. Ohashi et al.[11] recommended that many stage I cases, especially those with a depth of invasion of less than 2 mm, be studied to determine whether the depth of invasion correlates with outcome. One series of oral malignant melanoma has reported a mean 5-year survival rate of 12.3%[9]. The poor outcome of patients with oral melanoma may result from delayed diagnosis. Cohn-Cedemark et al.[5] attributed decreased mortality from melanoma to improved prevention, because no major improvements have been made in the treatment of primary or advanced melanomas. Others[2] have concluded that early diagnosis and treatment may improve the outcome of oral melanoma. However, the development of new, more effective means of treatment and ways to prevent distant metastasis are urgently needed.

## References


1. Anneroth G, Carlson GO, Eneroth CM, Moberger G. Primary melanoma in the oral mucous membrane. Swed Dent J 1973: **66**: 27–37.
2. Barker BF, Carpenter WM, Daniels TE, Kahn MA, Leider AS, Lozada-Nur F, Lynch DP, et al. Oral mucosal melanoma: the WESTOP Banff workshop proceedings. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997: **83**: 672–679.
3. Blatchford SJ, Koopmann CF, Coulthhard SW. Mucosal melanoma of the head and neck. Larngoscope 1986: **96**: 929–934.
4. Breslow A. Thickness: cross-sectional areas and depth of invasion in the prognosis of cutaneous melanoma. Ann Surg 1970: **172**: 902–908.
5. Cohn-Cedemark G, Mansson-Brahme E, Rutqvist LE, Larsson O, Johansson H, Ringborg U. Trends in mortality from malignant melanoma in Sweden, 1970–1996. Cancer 2000: **89**: 348–355.
6. Gorsky M, Epstein JB. Melanoma arising from the mucosal surfaces of the head and neck. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998: **86**: 715–719.
7. Hicks MJ, Flaitz CM. Oral mucosal melanoma: epidemiology and pathobiology. Oral Oncol 2000: **36**: 152–169.
8. Kristian F, Eilber FR, Morton D, Clark Jr WH. Malignant melanoma of the head and neck. Head Neck 1978: **1**: 123–128.
9. Manolidis S, Donald PJ. Malignant mucosal melanoma of the head and neck review of the literature and reports of 14 patients. Cancer 1997: **80**: 1373–1386.
10. Mimura M, Tanaka N, Eishi Y, Kimijima Y, Amagasa T, Ichinose S, Kinoshita Y, Mizutani N. An ultrastructural study of the influence of radiation against cell line-derived human oral malignant melanoma. Med Electron Microsc 1997: **30**: 81–87.
11. Ohashi K, Kasuga T, Tanaka N, Enomoto S, Horiuchi J, Okada N. Malignant melanomas of the oral cavity: heterogeneity of pathological and clinical features. Virchows Archiv A Pathol Anat 1992: **420**: 43–50.
12. Ostman J, Anneroth G, Gustafasson H, Tavelin B. Malignant oral tumours in Sweden 1960–1989—an epidemiological study. Oral Oncol Eur J Cancer 1995: **31B**: 106–112.
13. Pandey M, Abraham EK, Mathew A, Ahamed IM. Primary malignant melanoma of the upper aero-digestive tract. Int J Oral Maxillofac Surg 1999: **28**: 45–49.
14. Peckitt NS, Wood GA. Malignant melanoma of the oral cavity: a case report. Oral Surg Oral Med Oral Pathol 1990: **70**: 161–164.
15. Pilskin ME, Malignant melanoma of the oral cavity. In: Clark Jr WH, Goldman LI, Mastrangelo MJ, eds: Human Malignant Melanoma. New York: Grune and Stratton 1979: 125–137.
16. Shah JP, Huvos AG, Strong EW. Mucosal melanomas of the head and neck. Am J Surg 1977: **134**: 531–535.
17. Shibuya H, Takeda M, Matsumoto S, Hoshino M, Suzuki S, Takagi M. The efficacy of radiation therapy for a malignant melanoma in the mucosa of the upper jaw. An analytic study. Int J Radiat Oncol Biol Phys 1992: **25**: 35–39.

18. Snow GB, Van Der Esch EP, Van Sloaten EA. Mucosal melanomas of the head and neck. Head Neck 1978: **1**: 24–30.
19. Tanaka N, Amagasa T, Iwaki H, Shioda S, Takeda M, Ohashi K, Reck SF. Oral malignant melanoma in Japan. Oral Surg Oral Med Oral Pathol 1994: **78**: 81–90.
20. Tanaka N, Mimura M, Ichinose S, Odajima T. Malignant melanoma in the oral region: ultrastructural and immunohistochemical studies. Med Electron Microsc 2001: **34**: 198–205.
21. Tanaka N, Nagai I, Hiratsuka H, Kohama G. Oral malignant melanoma: long-term follow up in three patients. Int J Oral Maxillofac Surg 1998: **27**: 111–114.
22. Umeda M, Mishima Y, Teranobu O, Nakanishi K, Shimada K. Heterogeneity of primary malignant melanoma in oral mucosa: an analysis of 43 cases in Japan. Pathology 1988: **20**: 234–241.

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