Minor salivary gland tumors in a South American population

Adna Conceição Barros[1], Clarissa Araújo Silva Gurgel[2], Mário Caymmi Gomes[3], Ivan Marcelo Gonçalves Agra[4], Leonardo de Souza Kruschewsky[4], Jean Nunes dos Santos[5]

Arch Oncol 2010;18(3):56-9.
UDC: 611.43-006.616-036.22(292.8 JužnaAmerika)"1976/2007"
DOI: 10.2298/A001003056C

[1]Laboratory of Oral Surgical Pathology of School of Dentistry, Federal University of Bahia, Salvador – Bahia, Brazil, [2]Laboratory of Oral Surgical Pathology of School of Dentistry, Federal University of Bahia, Salvador – Bahia, Brazil, [3]Department of Pathology, Aristides Maltez Hospital, Salvador – Bahia, Brazil, [4]Department of Head and Neck Surgery, Aristides Maltez Hospital, Salvador – Bahia, Brazil, [5]Laboratory of Oral Surgical Pathology, School of Dentistry, Federal University of Bahia, Salvador – Bahia, Brazil

Correspondence to:
Jean Nunes dos Santos, Av. Araújo Pinho, 62, Canela, Salvador-BA, Brazil, 40110150

jeanunes@ufba.br

Received: 16.08.2010
Provisionally accepted: 31.08.2010
Accepted: 15.09.2010

SUMMARY

Background: *Salivary gland tumors are uncommon. This study aimed to investigate both clinical and epidemiological aspects of minor salivary gland tumors in a Brazilian population.*

Methods: *From 1976 to 2007, data obtained from clinical records and histological diagnoses were reviewed according to the WHO.*

Results: *A total of 217 MSGTs were identified. Pleomorphic adenomas (83%) and adenoid cystic carcinomas (28.8%) were the most frequent ones. The mean age of patients with benign and malignant tumors was 54.7 and 44.7 years, respectively. There was a female predominance and the palate was the most affected location. Surgery was the treatment of choice, but adjuvant radiotherapy and/or chemotherapy were also used. Recurrence rate of benign and malignant tumors was respectively 11.2% and 20.4%.*

Conclusion: *this population showed a relatively higher proportion of malignant tumors, and these tumors were associated with a higher rate of recurrence when compared to benign tumors. However, the overall recurrence of 16.2% was also within the reported range for these tumors. In addition, despite the results of this study are similar to previous series found in the literature, it provides an important insight into the epidemiology of patients presenting minor salivary gland tumors.*

Key words: *Salivary Glands, Minor; Salivary Gland Neoplasms; Epidemiology; Brazil; Mouth Neoplasms*

INTRODUCTION

Salivary gland tumors represent an important group of neoplasms occurring in the mouth being more frequently seen in major salivary glands. Minor salivary gland tumors (MSGTs) correspond from 9% to 23% of all salivary gland tumors (1-4). Despite their low frequency and distinct biological behavior, MSGTs attract special attention due to their morphological diversity, a fact that renders their complex diagnosis (5).

Several series of salivary gland tumors have been published worldwide and they have demonstrated geographic and ethnic variations in their frequency and distribution (1-5). In the English literature, studies about surveys of minor salivary gland tumors in South America are scarce and only three reports investigating this subject are available, being the last one reported in 1999 (6). The aim of the present study was to review the clinical-epidemiological profile of MSGTs diagnosed in a South American population. In addition, data obtained were compared to the findings of similar studies.

MATERIALS AND METHODS

Following the approval of the Ethics Committee, the archives of the Department of Pathological Anatomy, Hospital Aristides Maltez (Liga Baiana de Combate ao Câncer), Salvador, Bahia, Brazil, comprising a period of 31 years (1976 to 2007) were reviewed. The patients' examinations were retrospectively reviewed to obtain data on variables such as age, gender, anatomical location, and size of the tumors, clinical symptoms, histopathological diagnosis, types of treatment, and recurrence rate. All cases diagnosed as MSGTs were stained with hematoxylin-eosin and reviewed according to the criteria adopted by the World Health Organization (WHO) (7). The data were statistically analyzed using the Mann-Whitney test, Fisher's test, and binomial test. All statistical calculations were performed with BIOESTAT 3.0 software (Sociedade Civil Mamirauá, MCT, CNPq, Conservation International, Brazil, 2003). The level of significance was set at 5%.

RESULTS

A total of 217 cases of MSGTs were analyzed, 99 (45.6%) being benign and 118 (54.4%) malignant tumors (Table 1). In the group of benign tumors, patients' age ranged from 13 to 90 years, with a peak of occurrence in the 3rd decade of life. In the group of malignant tumors, patient age ranged from 17 to 100 years, with a higher frequency in the 6th and the 7th decades of life. Patients with malignant tumors were on average 10 years older than those with benign tumors (54.7 ± 17.9 years versus 44.7 ± 20.6 years). However, the difference in the mean age between the benign and malignant tumor groups was not significant (p >0.05, Mann-Whitney test).

Table 1. Distribution of minor salivary gland tumors according to the histological types

Diagnosis	n	% of group	% of all tumors
Benign	99	-	45.6
Pleomorphic adenoma	82	83.0	37.8
Myoepithelioma	10	10.0	4.6
Basal cell adenoma	4	4.0	1.8
Cystadenoma	2	2.0	0.9
Canalicular adenoma	1	1.0	0.5
Malignant	118	-	54.4
Adenoid cystic carcinoma	34	28.8	15.6
Mucoepidermoid carcinoma	29	24.6	13.4
Adenocarcinoma NOS[a]	28	23.7	12.9
Polymorphous low-grade adenocarcinoma	15	12.7	6.9
Acinic cell carcinoma	8	6.8	3.7
Clear cell carcinoma	3	2.5	1.4
Basal cell adenocarcinoma	1	0.9	0.5

[a]NOS: Not Otherwise Specified

Regarding gender distribution, 137 (63.1%) were female patients and 80 (36.9%) were male patients, the proportion being 1.7:1. In the group of benign tumors, women and men were affected in the 3rd and the 7th decades

of life, respectively (Figure 1). In the group of malignant tumors, the peak of occurrence of the tumor was observed in the 6th decade of life for male patients and in the 7th and the 8th decades for female patients (Figure 2). A significant difference of the mean age between genders was observed in the group of benign tumors ($p<0.05$, Mann-Whitney test), but not in the group of malignant tumors ($p> 0.05$, Mann-Whitney test).

The hard palate was most affected site by benign and malignant tumors (55.8%), followed by the soft palate (13.4%), the buccal mucosa (7.8%), and the lips (7%). Separate analysis of each site showed that tumors in the soft palate, buccal mucosa, tongue, floor of the mouth, alveolar mucosa, and retromolar region were predominantly malignant. On the other hand, tumors affecting the hard palate and upper lip were benign in most cases. Higher frequency of benign tumors was observed in the upper lip, whereas malignant tumors were more frequent in the tongue. This association was statistically significant ($p< 0.05$ and $p< 0.05$, respectively; binomial test).

With respect to possible risk factors for the development of MSGTs, 22% of the patients with malignant tumors were smokers, 13% were alcoholics, and 5% had a family history of cancer. Fifty-eight of 217 patients with MSGTs wore dentures.

Regarding the time of evolution of the tumor, malignant lesions presented a quicker clinical progression when compared to benign ones. Benign tumors presented a time of evolution of less than 12 months in 35.3% of cases, whereas the duration of malignant tumors, until the time of diagnosis, was less than six months in 22.9%. Comparison of benign and malignant tumors with a time of evolution of less than six months showed a significantly longer duration for benign tumors ($p<0.05$, Fisher's test). This also occurred with a time of duration longer than one year.

The mean size of both benign and malignant MSGTs, considering their maximum diameter, was 2.78 cm (range: 0.4 to 6 cm) and 2.27 cm (range: 0.4 to 9.5 cm), respectively.

The presence of a nodule (62.2%) was the main clinical feature of the MSGTs studied. Pain was reported by 20.3% of patients and ulceration detected in 9.2% of them. However, the presence of pain (27.1%) and ulceration (12.2%) was more frequent among malignant tumors when compared to benign ones.

Pleomorphic adenomas (37.8%) and adenoid cystic carcinomas (15.6%) were the most frequent tumors among the MSGTs studied. Pleomorphic adenoma was the most common benign tumor, accounting for 83% of all benign tumors, followed by myoepithelioma, which was observed in 10% of cases. In addition, adenoid cystic carcinoma was the most common malignant tumor (28.8%), followed by mucoepidermoid carcinoma (13.4%) and non-specified adenocarcinoma (12.9%).

With respect to treatment, all benign tumors were surgically removed. In the group of malignant tumors, surgery was the treatment of choice in 65.2% of cases, surgery combined with radiotherapy was applied in 31.4% of cases, and surgery combined with radiotherapy and chemotherapy was carried out in four lesions.

Among the 217 MSGTs treated, the recurrence rate was 16.2%, including 11.2% of benign tumors and 20.4% of malignant tumors. Among malignant tumors, adenoid cystic carcinomas and mucoepidermoid carcinomas were the most frequent recurrent ones. With respect to the type of previous treatment of the recurrent malignant tumors, it was significantly more frequent

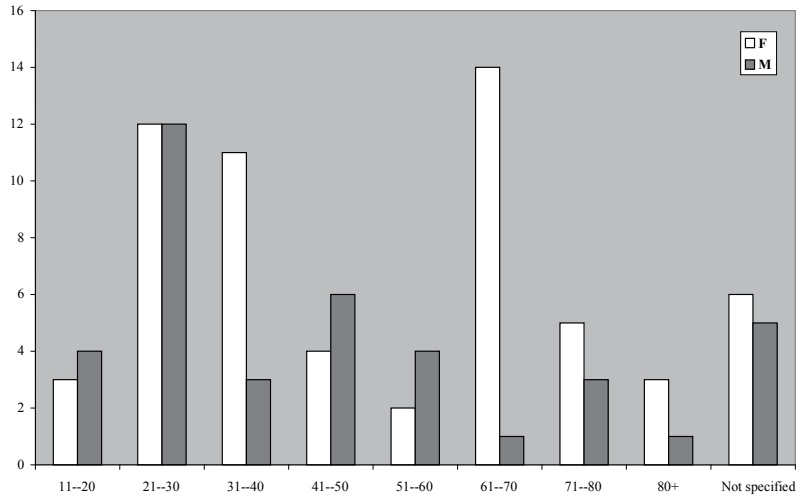

Figure 1. Age distribution by sex of total benign minor salivary gland tumors

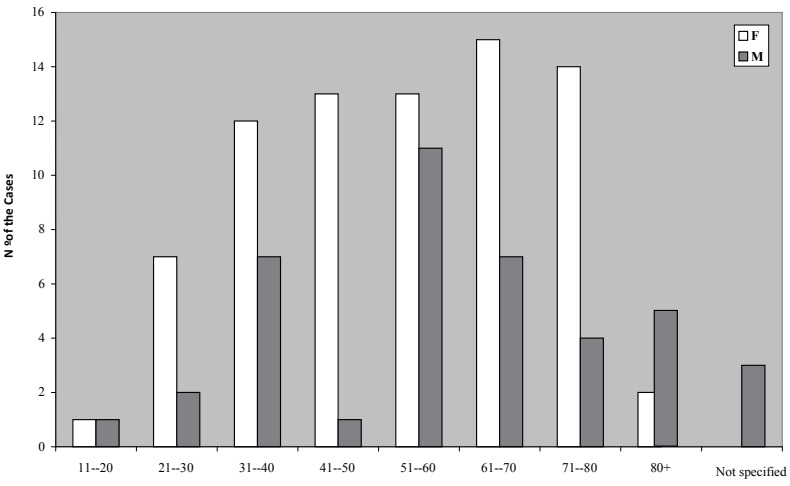

Figure 2. Age distribution by sex of total malignant minor salivary gland tumors

in patients treated by surgery in combination with radiotherapy or chemotherapy than in those submitted to surgery only ($p<0.05$, Fisher's test).

DISCUSSION

Our results showed that the malignant tumors were the most commonly lesions diagnosed among MSGTs, being adenoid cystic carcinoma the most prevalent malignant tumor. High frequency of adenoid cystic carcinomas was consistent with the data previously presented (1, 8-10). It is possible that high percentage of malignant tumors observed in the present study might be related to the fact that the institution where this study was carried out is a referral center for the treatment of cancer. However, there is still lack of agreement regarding the most frequent type of malignant MSGT. In studies carried out in India, Libya, The United Kingdom, Venezuela, and The United States of America (11-15), the mucoepidermoid carcinoma was the most prevalent lesion. With respect to benign tumors, pleomorphic adenoma comprised 37,8 % of all MSGTs, which indicates a frequency comparable to other series (9, 13-15).

Patients with malignant tumors were, on average, 10 years older than those with benign tumors. In contrast, Jansisyanont et al. (16) observed that patients with malignant tumors were six years younger than those

Table 2. Comparison of different distributions of intra-oral minor salivary gland tumors from various countries

Author	Year	Country	Total number of cases	Benign Malignant	Mean Age	F:M	Major Location
Isacsom, Shear[17]	1983	South Africa	201	2.58:1	45	1.4:1	Palate
Eveson, Cawson[1]	1985	Kingdom	336	1.16:1	52.5	1.2:1	Palate
Waldron et al.[2]	1988	United States	426	1.35:1	51.8	1.59:1	Palate
Auclair et al. [3]	1991	United States	3355	1.05:1	46.5	1.56:1	Palate
Loyola et al.[18]	1995	Brazil	164	1.6:1	41.5	1.3:1	Palate
Rivera-Bastidas et al.[14]	1996	Venezuela	62	1,21:1	38.0	1.9:1	Palate
Lopes et al.[6]	1999	Brazil	196	1:1.9	46.3	1:1	Palate
Jansisyanont et al.[16]	2002	United States	80	1:3.2	54.5	1.6:1	Palate
Toida et al.[8]	2005	Japan	82	2.03:1	51.4	1.9:1	Palate
Yih et al.[5]	2005	United States	213	1.15:1	44.7	2.1:1	Palate
Jaber [12]	2006	Libya	75	1:1.6	44.2	1:0.7	Palate
Buchner et al.[15]	2007	United States	380	1.43:1	57.7	2.27:1	Palate
Wang et al.[9]	2007	China	737	1:1.2	45.0	1:1.1	Palate
Pires et al.[20]	2007	United States	546	1.26:1	60.2	1.61:1	Palate
Present study	2008	Brazil	217	1:1.2	51.2	1.7:1	Palate

presenting benign tumors. In general, female patients were more affected, which is in line to previous studies (1, 8, 12, 14, 15, 17, 18), although some authors report that malignant tumors are more common in men (6, 10, 19). MGSTs are common in the palate, mainly in the hard palate, followed by the soft palate, buccal mucosa and lips (8, 14-18, 20). In our study, the hard palate was more involved than the soft palate, and surprisingly, 55% of the tumors located in this site were malignant. Furthermore, in agreement with other authors (5), our study showed that the upper lip was more frequently affected by benign tumors.

Some histological types of salivary gland tumors have shown a marked preference for specific anatomical sites. Loyola et al. (18) reported that cystadenomas are preponderantly encountered in the palate and lips whereas Pires et al. (20) found that these lesions occur more frequently in the lower lip. In addition, Yih et al. (5) observed that 64% of canalicular adenomas are located in the upper lip. In agreement with Buchner et al. (15) in the present study, cystadenomas were located in the buccal mucosa and tongue, and the only case of canalicular adenoma affected the upper lip. Interestingly, we identified that all tumors located in the floor of the mouth, and retromolar area were malignant lesions (9,12).

In the present series, most benign tumors presented a time of duration of more than one year, whereas the time of duration of malignant tumors, until the time of diagnosis, was less than six months, with this difference being significant. These findings agree with those reported by Jansisyanont et al. (16) who observed that malignant tumors progressed faster than benign tumors, and by Lopes et al. (6) who found that the mean time of duration of malignant tumors was half that of benign ones. Other authors as Loyola et al. (18) reported a long mean duration of symptoms: 91.7 months for benign tumors and 28.6 months for malignant tumors. However, these findings differ from those reported by Jaber (12) who observed no significant differences in time of duration between benign and malignant tumors. On the other hand, Otoh et al. (21) showed a longer duration of malignant tumors, with a mean of 72.4 months.

This study showed that the mean diameter of the lesions studied was 2.78 cm (SD=1.6) for benign tumors and 2.27 cm (SD=1.87) for malignant tumors. Similar findings were reported by Perez et al. (22) who observed a larger diameter for benign tumors (3.4 cm) compared to malignant ones (2.9 cm). However, our results differ from the series of Loyola et al. (18) and Yih et al.(5) who found a more marked growth for malignant neoplasms.

According to the literature, we showed that clinical symptoms as a nodule, was frequent in more than 60% of cases (6, 12, 16). Other features as pain and ulceration were more frequently reported by patients with malignant tumors, which is in agreement with previous reports (12, 18).

In the present series, all benign tumors were treated surgically, whereas in the group of malignant tumors, 34.8% were submitted to adjuvant post-operative radiotherapy. Similar results were reported by Lopes et al. (6), in which 55.6% of 196 patients with MSGTs only underwent surgery and 30.2% were submitted to surgery followed by radiotherapy. Postoperative radiotherapy improves local control and the survival rate of patients with tumors that present a high degree of malignancy, compromised surgical margins or perineural invasion. However, radiotherapy should be indicated with caution, taking into account prognostic factors such as location of the tumor, clinical stage, histological type and the presence of compromised surgical margins (23, 24). According to Mucke et al. (25), radiation should be used for patients with higher stage tumors or bad prognostic factors, and as a therapy for patients showing recurrence.

With respect to chemotherapy, its role in the treatment of salivary gland tumors remains uncertain (26).

In the present study, recurrence was observed in 16.2% of the 217 MSGTs, with 11.2% of benign tumors and 20.4% of malignant ones. Furthermore, we observed that patients with recurrent malignant tumors treated by surgery combined with radiotherapy and/or chemotherapy relapsed more frequently than those submitted to surgery only, with this difference being significant. It is possible that the recurrence rate observed in patients submitted to adjuvant radiotherapy and/or chemotherapy might be intrinsically related to prognostic factors of these tumors and does not necessarily predict failures in the treatment method.

Finally, despite discrete variations in the distribution and frequency of some of the tumors studied when compared to other series, the results of our investigation are similar to those reported in other retrospective studies (Table 2). In this respect, some authors suggest that the frequency and

distribution of salivary gland tumors are susceptible to ethnic and geographic variations (3,16,19). Therefore, to the best of our knowledge, this study involves the largest series of MSGTs described in the South American population. The age range and the gender ratio were similar to the ones reported in other series, and the overall recurrence of 16.2% was within the reported range. However, this population showed a relatively higher proportion of malignant tumors, and these tumors were associated with a higher rate of recurrence when compared to benign tumors.

Acknowledgements

The authors wish to thank FAPESB by grants 0122/2007 and Dr. Iguaracyra Araújo, Dr. Heleniemarie Barbosa, Dr. João Carlos Filho, Dr. Silene Roters and Dr. Roberta Carvalho from Department of Pathology, Hospital Aristides Maltez. Salvador-Bahia, Brazil. We thank also Edson, Conceição, Ivanildes, Wendel, Miriam and Maria de Lourdes S. Santos for their excellent technical assistance and Dr. Alberto Valença. Dr. Antônio Luis B. Pinheiro reviewed this manuscript.

Conflict of interest

We declare no conflicts of interest.

REFERENCES

1 Eveson JW, Cawson RA. Tumors of the minor (oropharyngeal) salivary glands: a demographic study of 336 cases. *Oral Pathol.* 1985;14:500-9.
2 Waldron CA, El-Mofty K, Gnepp DR. Tumors of the intraoral minor salivary glands: A demographic and histologic study of 426 cases. *Oral Pathol.* 1988;66:323-33.
3 Auclair PL, Elis GL, Gnep DR, Wenig BM, Janney CG. Salivary gland neoplasms: general considerations. In: Ellis GL, Auclair PL, Gnepp DR, editors. Surgical pathology of the salivary glands. Philadelphia: Saunders; 1991. p. 135-63.
4 Ito FA, Vargas PA, Almeida OP, Lopes MA. Salivary gland tumors in a Brazilian population: a retrospective study of 496 cases. *Int J Oral Maxillofac Surg.* 2005;34:533-6.
5 Yih WY, Kratochvil F, Sewart JC. Intraoral minor salivary gland neoplasms: review of 213 cases. *Int J Oral Maxillofac Surg.* 2005;63:805-10.
6 Lopes MA, Kowalski LP, Santos GC, Almeida OP. A clinicopathologic study of 196 intraoral minor salivary gland tumours. *J Oral Pathol Med.* 1999;28:264-7.
7 Barnes L, Eveson JW, Reichart PA, Sidransky D, editors. The World Health Organization's histological classification of tumors. Pathology and genetics of head and neck tumours. Lyon: IARC Press; 2005. p. 209-81.
8 Toida M, Shimokawa K, Makita H, Kato K, Kobayashi A, Kusonoki Y, et al. Intraoral minor salivary gland tumors: a clinicopathological study of 82 cases. *Int J Oral Maxillofac Surg.* 2005;34:528-32.
9 Wang D, Li Y, He H, Liu L, Wu L, He Z. Intraoral minor salivary gland tumors in a Chinese population: a retrospective study on 737 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2007;104:94-100.
10 Copelli C, Bianchi B, Ferrari S, Ferrari A, Sessena E. Malignant tumors of intraoral minor salivary glands. *Oral Oncol.* 2008;44:658-63.
11 Pandey M, Thomas S, Mathew A, Nair MK. Malignant Tumours of the minor salivary glands: a survival analysis of 17 years from a tertiary referral Cancer Center. *J Postgrad Med.* 2003;49:25-8.
12 Jaber MA. Intraoral minor salivary gland tumors: a review of 75 cases in a Libyan population. *Int J Oral Maxillofac Surg.* 2006;35:150-4.
13 Jones AV, Craig GT, Speight PM, Franklin CD. The range and demographics of salivary gland tumors diagnosed in the UK population. *Oral Oncol.* 2008;44:407-17.
14 Rivera-Bastidas H, Ocanto RA, Acevedo AM. Intraoral minor salivary gland tumors: a retrospective study of 62 cases in a Venezuelan population. *J Oral Pathol Med.* 1996;25:1-4.
15 Buchner A, Merrell PW, Carpenter WM. Relative frequency of intra-oral minor salivary gland tumors: a study of 380 cases from northern California and comparison to reports from other parts of the world. *J Oral Pathol Med.* 2007;36:207-14.
16 Jansisyanont P, Blancheart RH Jr., Ord RA. Intraoral minor salivary gland neoplasm: a single institution experience of 80 cases. *Int J Oral Maxillofac Surg.* 2002;31:257-61.
17 Isacsson G, Shear M. Intraoral salivary gland tumors: a retrospective study of 201 cases. *Oral Pathol.* 1983;12:57-62.
18 Loyola AM, Araújo VC, Sousa SOM, Araújo NS. Minor Salivary Gland Tumours. A Retrospective Study of 164 cases in a Brazilian Population. *Oral Oncol Eur J Cancer.* 1995;31:197-201.
19 Van Heerden WFP, Raubenheimer EJ. Intraoral salivary gland neoplasms: a retrospective study of seventy cases in an African population. *Oral Surg Oral Med Oral Pathol.* 1991;71:579-82.
20 Pires FR, Pringle GA, Almeida OP, Chen SY. Intra-oral minor salivary gland tumors: A clinicopathological study of 546 cases. *Oral Oncol.* 2007;43:463-70.
21 Otoh EC, Johnson NW, Olasoji H, Danfillo IS, Adeleke OA. Salivary gland neoplasms in Maiduguri, north-eastern Nigeria. *Oral Diseases.* 2005;11:386-91.
22 Perez DEC, Pires RP, Alves FA, Almeida OP, Kowalski LP. Salivary gland tumors in children and adolescents: a clinicopahologic and immunohistochemical study of fifty-three cases. *Int J Pediatr Otorhinolaryngol.* 2004;68:895-902.
23 Parsons JT, Mendenhall WM, Stringer SP, Cassisi NJ, Million RR. Management of minor salivary gland carcinomas. *Int J Radiat Oncol Biol Phys.* 1996;35:443-54.
24 Hosokawa Y, Shirato H, Kagei K, Hashimoto S, Nishioka T, Tei K, et al. Role of radiotherapy for mucoepidermoid carcinoma of salivary gland. *Oral Oncol.* 1999;35:105-11.
25 Mucke T, Tannapfel A, Kesting MR, Wagenpfeil S, Robitzky LK, Wolff KD, et al. Adenoid cystic carcinomas of minor salivary glands. *Auris Nasus Larynx.* 2010;37:615-20.
26 Millano A, Longo F, Basile M, Laffaioli RV, Caponigro F. Recent advances in the treatment of salivary gland cancers: emphasis on molecular targeted therapy. *Oral Oncol.* 2007;43:729-34.