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### A comparative analysis of oral and maxillofacial pathology over a 16-year period, in the North of Portugal.

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#### SUMMARY

**Objectives:** To determine the frequency and spectrum of oral and maxillofacial lesions biopsied in a hospital population in the northern region of Portugal.

**Methods:** We conducted descriptive analysis of pathology reports from biopsies of oral and maxillofacial lesions performed between 1990 and 2006, in Oporto Hospital Center. Information on gender, age, location and the histopathological diagnosis were analysed.

**Results:** The cases revealed that 1520 (47.7%) of the patients were male and 1666 (52.3%) patients were female. They had a mean age of 47.8 years (S.D. $\pm$ 18.6). The site most frequently biopsied was the labial mucosa (17.5%). A non-neoplastic diagnosis was established in 2162 (63.3%) cases, oral potentially malignant disorders in 163 (5.1%) cases, and neoplasms in 886 (27.6%) cases (403 benign and 483 malignant). The most reported diagnosis was fibroepithelial polyp (n=186;15.9%), followed by squamous cell carcinoma (SCC) (n=158;13.6%). SCC was the most frequent lesion found in males (n=279;18.4%) whilst fibroepithelial polyp was the most common diagnosis in females (n=268;16.1%). The most common lesion in patients aged 0 to 17 years-old was a follicular cyst (n=25;12.8%), whereas in patients aged 18 to 64 years it was a fibroepithelial polyp (n=299;13%). SCC was the most frequent lesion found in patients aged 65 or over (n=160;24.6%).

**Conclusion:** This large sample provides useful information about the incidence and distribution of oral biopsies over a period of 16 years allowing valuable comparison with other countries. Non-neoplastic lesions were the most commonly reported, with fibroepithelial polyp being most frequent. SCC was the second more frequent diagnosis.

#### INTRODUCTION

The oral cavity can develop a wide range of lesions, with diverse origins and nature, including either benign or malignant lesions. Carrying out a biopsy is one of most important investigations in oral medicine. A biopsy not only shows the morphological characterisation of the tissue but also is the gold standard for obtaining a definitive diagnosis for many lesions, especially concerning malignant diseases<sup>1</sup>. Oral health professionals, including general dentists, are very familiar with dental and periodontal lesions. However, the diagnosis of some lesions and diseases of the oral soft tissues can be more challenging<sup>2</sup>. In view of this, literature on the frequency and prevalence of oral and maxillofacial lesions, not only increase awareness of disease patterns within populations, but highlight lesions that oral health professionals are most likely to face in their daily practice.

Worldwide there have been few histological-based studies of oral and maxillofacial lesions which include both a comprehensive spectrum of oral lesions and patients of all ages<sup>3-7</sup>. Most of the published reports are designed to analyse only a specific lesion or disease, limited to a certain age group, or based on screenings or clinical surveys, without histological diagnostic confirmation<sup>8-18</sup>.

The aim of this study was to determine the spectrum and the frequency of biopsied oral and maxillofacial lesions, in a North Portugal hospital population, comprising all ages and genders, and then to compare the results with other studies reported worldwide.

#### MATERIAL AND METHODS

We performed a retrospective, 16 year (1990-2006) descriptive analysis of oral and maxillofacial biopsies, at the Pathology Department of the *Hospital de Santo António (HSA)* Oporto Hospitalar Center in Portugal. Patients from the Oporto community were referred by their General Practitioner (GP) to this central based city hospital. The study was reviewed and approved by the institutional review board of the *Hospital de Santo António (HSA)* Oporto Hospitalar Center (Investigation, Formation and Teaching Department – DEFI; 024/CES/03). The study was performed in full accordance with the World Medical Association Declaration of Helsinki. Data regarding histopathological diagnosis and respective clinical information were retrieved from patient hospital records and inserted into a Microsoft<sup>®</sup> Excel database. The data was anonymised prior to analysis. This included information on gender, age, site of the lesion, clinical diagnosis and the histopathological

diagnosis. Exclusion criteria were: biopsies showing normal tissue, repeated biopsies of already diagnosed lesions (e.g., the excisional removal of a lesion that was previously diagnosed with an incisional biopsy), and cases with unclear or missing data, or with an inconclusive diagnosis.

The lesions were classified using a system recommended by the ICD-DA (International Classification of Diseases, Dentistry and Stomatology), and by the WHO classification of tumours (2005). For analysis purposes, we decided to divide the diagnoses into 3 groups: non-neoplastic lesions, oral potentially malignant disorders (OPMD), and neoplastic lesions. These were further subdivided into 9 major subcategories: inflammatory lesions, infective lesions, cystic lesions, reactive lesions, potentially malignant disorders, autoimmune or metabolic diseases, hamartomatous lesions or congenital alterations, benign neoplasms and malignant neoplasms. Patients aged between 0 and 17 years old were considered young patients, with ages 18 to 64 classified as adult patients and patients 65 and over classified as elderly patients <sup>19,20</sup>.

Statistical analysis was carried out using IBM SPSS Statistics version 22.0 software (IBM Corporation, NY, US). The results were presented in absolute and relative frequency. Possible associations between pathological groups (non-neoplastic, OPMD and neoplastic groups) and categorical or continuous variables were evaluated by chi-square test or ANOVA test, respectively. A *P*-value of less than 0.05 was considered significant.

#### RESULTS

From the original data set of 3737 cases, we excluded 136 cases as they revealed a histopathological diagnosis of normal tissue (without cellular or tissue alterations). A further 389 cases were excluded for the following reasons; they were repeated biopsies for the same lesion, had missing data or had an unclear diagnosis. Therefore a final sample of 3212 oral biopsies were included. 1666 (52.3%) of these were from females and 1520 (47.7%) were from male patients (female: male ratio of 1.09). Within the sample, the patient's age ranged from 3 to 100 years old, with a mean age of 47.8 years (S.D.  $\pm$  18.6) and the 6<sup>th</sup> decade being the most common (n=628; 20%). There were 196 (6.2%) cases in the young age group, 2300 (73.1%) in adults and 651 (20.7%) in the elderly group.

The most frequently affected oral site was the labial mucosa (n=561), followed by the buccal mucosa (n=550), tongue (n=519), gingiva (n=349), major salivary glands (n=300), palate (n=182), floor of the mouth (n=75), maxilla (n=357), mandible (n=287), and mouth NOS (not otherwise specified) (n=32).

When classified within pathological diagnostic groups, 2162 (63.3%) lesions corresponded to non-neoplastic diagnoses, 163 (5.1%) were OPMD, and 886 (27.6%) were neoplasms (Table 1). The non-neoplastic biopsies were more likely to be from females than males, this was in contrast to potentially malignant disorders and neoplasms (P < 0.001) which were more commonly from male patients. The mean age of patients with non-neoplastic lesions was lower than those observed in patients with neoplasms or OPMD (P < 0.001). The buccal mucosa was the most affected site in non-neoplastic lesions and OPMD, while the tongue was the most affected site for neoplasms (P < 0.001).

#### Non-neoplastic group

The most common subcategory within non-neoplastic diagnoses was reactive lesions (n=679), followed by cystic lesions (n=647), inflammatory lesions (n=636), autoimmune or metabolic conditions (n=89), hamartomatous or congenital lesions (n=67), and infective lesions (n=45). The most prevalent reactive lesion was the fibroepithelial polyp (n=385). This was more commonly observed in females (n=268), patients affected had a mean age of 48.9 $\pm$ 16 years, and the buccal mucosa was most frequently affected (47%). With regards to cysts and odontogenic tumours, the inflammatory odontogenic cyst was the most frequent lesion (n=264). The mean age of patients affected was 38.4 $\pm$ 15.9, with males being more commonly affected (n=152), and it presenting mainly in the maxilla (69.7%). Other non-neoplastic lesions and their distribution by gender, age and site are presented in Table 2 and Tables S1-S6.

#### **Oral Potentially Malignant Disorders**

Leukoplakia was the most common potentially malignant oral disorder (n=76) with a mean age of  $57.53\pm15.66$ , and predominantly being found in males (n=48). The most affected location was the buccal mucosa (36.8%). Other potentially malignant oral disorders and their distribution by gender, mean age, and predominant location, are presented in Table 3.

#### Neoplasms

From the 886 neoplasms, 403 were benign and 483 were malignant (Table S7-8). The benign pleomorphic adenoma was the most frequent benign neoplasm, affecting mainly the major salivary glands (MSG) (75%) and especially the parotid gland (n=69; 83.1% of MSG), with more cases noted in females (n=69) with a mean age of  $43.38\pm17.7$  years old. If we exclude the major salivary glands the most frequent benign neoplasm was the epithelial cell papilloma (n=96; 34% of all oral cavity locations). The most common malignant neoplasm was

squamous cell carcinoma (n=373). This tumour was more common in males (n=279), the mean age of patients was  $61.55\pm13.5$  and it affected predominantly the tongue (30.8%). Regarding salivary gland malignancies, mucoepidermoid carcinoma (n=13) was the most common salivary gland malignancy, it mostly affected major salivary glands (38.5%) especially the parotid gland (n=5; 100% of MSG). This was followed by adenoid cystic carcinoma (n=10) located most often in the floor of the mouth (30%) and MSG (30%) especially in the submandibular gland (n=2; 66.6%). Table 4 shows the neoplastic lesions distributed by gender, mean age, and the predominant location.

#### The Top 10 distributed by gender and age

We investigated the ten most common diagnoses of the entire sample population (Figure 1). Fibroepithelial polyp (n=385) was the most common lesion, followed by squamous cell carcinoma (n=373). By analysing the distribution of the lesions according to gender, we observed that the fibroepithelial polyp (n=268) was the most frequent lesion found in females, whereas the most common lesion in males was SCC (n=279) (Figure 2). When we analysed the most common diagnoses divided by age group, follicular cyst (n=25) was the predominant lesion in the young age group (0 to 17 year-old), fibroepithelial polyp was the most common in the adult group (18 to 64 years) (n=299), and SCC (n=160) was the most prevalent in the elderly group (+ 65 years) (Figure 3).

#### DISCUSSION

Information on the frequency of oral and maxillofacial lesions is an important aspect of oral health practice and provides epidemiological information on the distribution of the lesions within the populations. From this descriptive retrospective analysis (1990-2006), 3212 oral biopsies were included representing a 16 year study period. This compares with Tay <sup>3</sup> who reviewed oral biopsies from 1993 to 1997, reviewing a total of 2057 reports, of which 1986 separate diagnoses were recorded. Dimba et al. <sup>7</sup> reported a 4-year study of oral biopsies in a pathology laboratory at the University of Nairobi Dental Hospital, in Kenya, which included 548 samples. While, Jones and Franklin <sup>14</sup> studied 44,000 oral and maxillofacial pathological specimens, from adults 17 years and over, submitted for diagnosis to a laboratory over a 30-year period (1973-2002).

The data obtained in our sample showed a slightly increased number of biopsies in females compared with males, consistent with findings reported by others <sup>4,15,16</sup>. This could reflect a

greater female population in the north of Portugal (according to the Census of 2011). By contrast, analysing only the OPMD and neoplasms groups, we observed that these lesions affected males more frequently, as expected and confirmed by other data <sup>5,6</sup>.

All decades of life considered in the study were affected but there was a peak in the  $6^{th}$  decade of life. This pattern was not true for all groups of lesions, as oral potentially malignant disorders and neoplasms showed a higher mean age and were therefore more common in older patients, whereas non-neoplastic lesions were more common in younger patients. This is in accordance with reported studies <sup>15,21-24</sup>.

The reactive lesion group was the most common pathological group. Fibroepithelial polyp was particularly common, representing 12% of the entire sample. It was seen most commonly in the 5<sup>th</sup> decade of life, mainly in females and located most often in the buccal mucosa, which is in accordance with data published in the literature <sup>3,14,16,17,25</sup>. Indeed, fibroepithelial polyp was the most frequent lesion of the whole study. This is not surprising as the oral cavity is a unique organ that is often subjected to multiple traumatic and pathological stimuli such as fractured teeth, maladapted prostheses, malocclusion and other dental problems.

Inflammatory odontogenic cysts were the most common lesions in the cystic and odontogenic tumours group, representing 8.2% of the overall sample. A greater number of cases were seen in the maxilla. By contrast, the second more frequent cyst; the follicular cyst, was more prevalent in the mandible. When the analysis was focused to the young group only, the follicular cyst was the most prevalent, as observed by Ha et al. <sup>18</sup>. Mucoceles were the second most prevalent lesions in this group, most commonly observed in the labial mucosa of males, as reported by others <sup>14,26</sup>.

The most common autoimmune lesion was Sjögren's syndrome (n=18) which demonstrated a higher prevalence in females, in accordance with the literature  $^{25,27}$ . The elevated number of cases located in the labial mucosa for this disease reflects the preferred site for minor salivary gland biopsies.

Regarding oral potentially malignant disorders, leukoplakia (n = 76) was the most prevalent, constituting 2.4% of the total sample, which is in line with several reports  $^{4,11,14}$ . The authors elected to include lichen planus as an OPMD as suggested by Warnalulasuryia et al  $^{21}$ . Although leukoplakia is a clinical term, given the importance of this lesion as a potentially malignant disorder, we chose to include this diagnosis within the OPMD group. This gave us a greater understanding of the frequency of oral potentially malignant disorders in this

population<sup>21</sup>. Following histological diagnosis, we reviewed the clinical history to confirm diagnosis of oral leukoplakia. Nevertheless, we admit, it is possible that some cases of leukoplakia which were absent of clinical information on the pathological report and the clinical history, could therefore be under the designation of epithelial hyperplasia or hyperkeratosis.

The most common benign neoplasm was pleomorphic adenoma, followed by squamous cell papilloma. Indeed, these two benign neoplasms were also the most reported by Jones and Franklin<sup>14</sup>, although they reported squamous papilloma as the more prevalent lesion. Regarding salivary glands only, pleomorphic adenoma was the most common benign tumour, most commonly located in major salivary glands especially the parotid gland, followed by Warthin's tumour, that is consistent with the literature <sup>27,28</sup>.

Malignancy represented 15% of the overall sample, which is similar to that reported by Ali and Sundaram <sup>29</sup>, but higher than that reported by Jones and Franklin <sup>14</sup> and Tay <sup>3</sup>. The most common malignancy was squamous cell carcinoma, which was consistent with several reports <sup>4,6,16,17,29</sup>. We feel this result clearly shows that biopsies are vital for the diagnosis of such a prevalent tumour. There was a predilection for the tongue as this was the most commonly affected site (32.9%) there was also a correlation with male gender and age of 70–79. This is consistent with other reports <sup>4,5,23,24,29</sup>. When we analysed the most frequent lesions distributed by gender and age, interestingly, SCC was the most prevalent lesion in males and in the elderly group. However, we must bear in mind that oral cancer, in both young adults and in females, is rising in several parts of the world including Portugal. In the last decade, an increasing trend for oral cancer in the Portuguese population has been reported, especially in females<sup>30</sup>.

Regarding salivary gland malignant neoplasms, the mucoepidermoid carcinoma and adenoid cystic carcinoma were the most frequent malignant tumours, as observed by Correa et al. <sup>15</sup>. This slight predominance of mucoepidermoid carcinoma over adenoid cystic carcinoma is in accordance with the reports from Jones and Franklin <sup>14</sup> although contrasts with the inverse frequency of these two neoplasms in other studies <sup>17</sup>.

The results of the present study must be interpreted in light of the limitations of this type of retrospective study. We acknowledge the limitations of not subdividing some of the locations of the lesions. Moreover, the selected sample may not represent the Oporto population as it is focused on a hospital based population. Nevertheless, this is a public and central hospital that receives the general population of Oporto city, including patients that were referred to a Stomatology centre, hence giving a large spectrum of diseases. We feel this is evidenced by

the 150 different diagnoses seen in this series. It is important to note that we only evaluated biopsied lesions, therefore oral lesions, that did not undergo any biopsy, will not be included in the results. Nevertheless, a strength of this study is the inclusion of the histological description which proves the accuracy of diagnosis compared with those studies where the diagnosis is only clinical. Moreover, we described the predominant location for each lesion, which we believe is an important contribution towards a better understanding of the various lesions' epidemiology. To the best of our knowledge, this study is the first report from a large scale analysis of oral cavity biopsies in a central hospital, based from a population in northern Portugal.

#### Conclusion

The most common lesions that affected the oral cavity were non-neoplastic, with the fibroepithelial polyp being the most common lesion of the entire studied sample. SCC was the second most frequent diagnosis, which was especially common in males between the ages of 60-69. This large sample therefore provides useful information about the frequency and distribution of oral lesions over a period of 16 years. It also allows a useful comparison to other countries. We believe that the data presented here will be useful in formulating differential diagnoses and this will be of particular interest to pathologists, oral/ maxillofacial surgeons and general dental practitioners.

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#### REFERENCES

1. Lingen MW, Kalmar JR, Karrison T, et al. Critical evaluation of diagnostic aids for the detection of oral cancer. *Oral Oncol* 2008 44: 10-22.

2. Ergun S, Ozel S, Koray M, et al. Dentists' knowledge and opinions about oral mucosal lesions. *Int J Oral Maxillofac Surg* 2009 38: 1283-1288.

3. Tay AB. A 5-year survey of oral biopsies in an oral surgical unit in Singapore: 1993-1997. *Ann Acad Med Singapore* 1999 28: 665-671.

4. Sixto-Requeijo R, Diniz-Freitas M, Torreira-Lorenzo JC, et al. An analysis of oral biopsies extracted from 1995 to 2009, in an oral medicine and surgery unit in Galicia (Spain). *Med Oral Patol Oral Cir Bucal* 2012 17: e16-22.

5. Mendez M, Carrard VC, Haas AN, et al. A 10-year study of specimens submitted to oral pathology laboratory analysis: lesion occurrence and demographic features. *Braz Oral Res* 2012 26: 235-241.

6. Weir JC, Davenport WD, Skinner RL. A diagnostic and epidemiologic survey of 15,783 oral lesions. *J Am Dent Assoc* 1987 115: 439-442.

7. Dimba EA, Gichana J, Limo AK, et al. An audit of oral diseases at a Nairobi centre, 2000-2004. *Int Dent J* 2007 57: 439-444.

8. Pentenero M, Broccoletti R, Carbone M, et al. The prevalence of oral mucosal lesions in adults from the Turin area. *Oral Dis* 2008 14: 356-366.

9. Kovac-Kovacic M,Skaleric U. The prevalence of oral mucosal lesions in a population in Ljubljana, Slovenia. *J Oral Pathol Med* 2000 29: 331-335.

10. Castellanos JL,Diaz-Guzman L. Lesions of the oral mucosa: an epidemiological study of 23785 Mexican patients. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008 105: 79-85.

11. Axell T. A preliminary report on prevalences of oral mucosal lesions in a Swedish population. *Community Dent Oral Epidemiol* 1975 3: 143-145.

12. Rioboo-Crespo Mdel R, Planells-del Pozo P,Rioboo-Garcia R. Epidemiology of the most common oral mucosal diseases in children. *Med Oral Patol Oral Cir Bucal* 2005 10: 376-387.

13. Jones AV, Franklin CD. An analysis of oral and maxillofacial pathology found in children over a 30-year period. *Int J Paediatr Dent* 2006 16: 19-30.

14. Jones AV, Franklin CD. An analysis of oral and maxillofacial pathology found in adults over a 30-year period. *J Oral Pathol Med* 2006 35: 392-401.

15. Correa L, Frigerio ML, Sousa SC, et al. Oral lesions in elderly population: a biopsy survey using 2250 histopathological records. *Gerodontology* 2006 23: 48-54.

16. Carvalho Mde V, Iglesias DP, do Nascimento GJ, et al. Epidemiological study of 534 biopsies of oral mucosal lesions in elderly Brazilian patients. *Gerodontology* 2011 28: 111-115.

17. Kelloway E, Ha WN, Dost F, et al. A retrospective analysis of oral and maxillofacial pathology in an Australian adult population. *Aust Dent J* 2014 59: 215-220.

18. Ha WN, Kelloway E, Dost F, et al. A retrospective analysis of oral and maxillofacial pathology in an Australian paediatric population. *Aust Dent J* 2014 59: 221-225.

19. Scott J,Cheah SB. The prevalence of oral mucosal lesions in the elderly in a surgical biopsy population: a retrospective analysis of 4042 cases. *Gerodontology* 1989 8: 73-78.

20. Al-Khateeb T, Al-Hadi Hamasha A, Almasri NM. Oral and maxillofacial tumours in north Jordanian children and adolescents: a retrospective analysis over 10 years. *Int J Oral Maxillofac Surg* 2003 32: 78-83.

21. Warnakulasuriya S, Kovacevic T, Madden P, et al. Factors predicting malignant transformation in oral potentially malignant disorders among patients accrued over a 10-year period in South East England. *J Oral Pathol Med* 2011 40: 677-683.

22. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. *Oral Oncol* 2009 45: 309-316.

23. Monteiro LS, Amaral JB, Vizcaino JR, et al. A clinical-pathological and survival study of oral squamous cell carcinomas from a population of the North of Portugal. *Med Oral Patol Oral Cir Bucal* 2014 19: e120-126.

24. Albuquerque RP, Lopez-Lopez J, Jane-Salas E, et al. A pioneering epidemiological study investigating the incidence of squamous cell carcinoma of tongue in a Portuguese population. *Med Oral Patol Oral Cir Bucal* 2012 17: e550-554.

25. Al-Khateeb TH. Benign oral masses in a Northern Jordanian population-a retrospective study. *Open Dent J* 2009 3: 147-153.

26. Wang YL, Chang HH, Chang JY, et al. Retrospective survey of biopsied oral lesions in pediatric patients. *J Formos Med Assoc* 2009 108: 862-871.

27. Tian Z, Li L, Wang L, et al. Salivary gland neoplasms in oral and maxillofacial regions: a 23-year retrospective study of 6982 cases in an eastern Chinese population. *Int J Oral Maxillofac Surg* 2010 39: 235-242.

28. Tilakaratne WM, Jayasooriya PR, Tennakoon TM, et al. Epithelial salivary tumors in Sri Lanka: a retrospective study of 713 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009 108: 90-98.

29. Ali M,Sundaram D. Biopsied oral soft tissue lesions in Kuwait: a six-year retrospective analysis. *Med Princ Pract* 2012 21: 569-575.

30. Monteiro LS, Antunes L, Bento MJ, et al. Incidence rates and trends of lip, oral and oropharyngeal cancers in Portugal. *J Oral Pathol Med* 2013 42: 345-351.

#### **Figures legends:**

Figure 1. The 10 most common histological diagnoses (1990-2006).

**Figure 2**. The 10 most common histological diagnoses distributed by gender (1990-2006). A, Males; B, Females.

**Figure 3**. The 10 most common histological diagnoses distributed by age groups (1990-2006). A, Young patients (0 to 17 years-old); B, adult patients (18 to 64 years); and C, elderly patients (65+ years).

#### **Table legends:**

**Table 1.** Number of lesions in diagnostic groups distributed by gender, age and predominant location.

**Table 2.** Number of non-neoplastic diagnoses by diagnostic category (including the 5 most prevalent lesions in each category) distributed by gender, age and predominant site.

 Table 3. Number of potentially malignant disorders distributed by gender, age and predominant site.

**Table 4.** Number of neoplastic diagnoses by diagnostic category (including the 5 most prevalent in each category and tissue origin) distributed by gender, age and predominant site.

#### **Supplementary tables**

**Table S1.** Number of Inflammatory lesions/ diagnoses distributed by gender, age and predominant site.

**Table S2.** Number of Infective lesions/ diagnoses distributed by gender, age and predominant site.

**Table S3.** Number of Cystic lesions/ diagnoses distributed by gender, age and predominant site.

Table S4. Number of reactive lesions/ diagnoses distributed by gender, age and predominant site.

**Table S5.** Number of Autoimmune or metabolic lesions/ diagnoses distributed by gender, age and predominant site.

**Table S6.** Number of Congenital or development disorders/ diagnoses distributed by gender, age and predominant site.

Table S7. Number benign neoplasms/ diagnoses distributed by gender, age and predominant site.

**Table S8.** Number of malignant neoplasms/ diagnoses distributed by gender, age and predominant site.

#### **TABLES**

			Gender <sup>a</sup>			Age <sup>a</sup>		Site	
	n	n %		Male	<i>P</i> -value <sup>b</sup>	Mean ±S.D.	<i>P</i> -value <sup>c</sup>	Predominant site (%)	<i>P</i> -value <sup>b</sup>
a) Diagnostic Group									
Non-neoplastic	2162	63.3	1239	909		45.06±18.34		BM (17)	<0.001
OPMD	163	5.1	73	90	-0.001	56.14±14.9	-0.001	BM (45.4)	
Neoplasms	886	27.6	354	521	< 0.001	$52.8 \pm 18.2$	< 0.001	TNG (23.8)	
Total	3212	100	1666	1520		47.8±18.6		LAM (17.5)	

Legends: OPMD – Oral Potentially Malignant Disorders; LAM – Labial Mucosa; BM – Buccal Mucosa; TNG – Tongue <sup>a</sup> In some patients the variable is unknown <sup>b</sup> *P*-value for the differences were calculated using *chi-square test*. <sup>c</sup> *P*-value for the differences were calculated using *Anova test*.

Diagnostic Category		0/	Gend	ler <sup>a</sup>	Age <sup>a</sup>	Site	
	n	%	Female	Male	Mean ±S.D.	Predominant (%)	
Inflammatory lesions	636	29.4	363	265	48.37±18.39	GEN (23.1%)	
Non-specific ulcer	96	4.4	53	42	51.6±18.6	TNG (40.6)	
Chronic sialadenitis	91	4.2	49	40	$46.68 \pm 14.2$	MSG (85.7)	
Pyogenic / pregnancy granuloma	89	4.1	57	31	46.61±20.1	GEN (36)	
Chronic inflammation	83	3.8	48	34	51.38±17.5	LAM (30.1)	
Peripheral giant-cell granuloma	49	2.3	27	22	45.14±23.8	GEN (71.4)	
Infective lesions	45	2	31	14	47.59±19.48	MAN (20)	
Actinomycosis	11	0.5	9	2	57±18.6	GEN (66.7)	
Warts	9	0.4	6	3	38.89±20.6	LAM (66.7)	
Tuberculosis	7	0.3	6	1	53.57±24	PAL (100)	
Abscess / Fistulae	5	0.2	3	2	36.2±11.9	MNOS (40)+ MAX (40)	
Syphilis ulcer	3	0.1	0	3	55±4.6	TNG (66.7)	
Cystic lesions	647	29.9	273	372	35.9±17.4	MAX(47.6)	
Inflammatory odontogenic cyst	264	12.2	112	152	38.37±15.9	MAX (69.7)	
Follicular cyst	97	4.4	40	57	32.90±17.5	MAN (50.5)	
Mucocele/retention cyst	91	4.2	31	59	33.56±18.7	LAM (79.1)	
Keratocyst	46	2.1	29	17	36.52±19.2	MAN (87)	
Ameloblastoma	16	0.7	4	12	40.56±17.9	MAN (81.3)	
Reactive lesions	679	31.4	457	218	$50 \pm 16.1$	BM (37.4)	
Fibroepithelial polyp	385	17.8	268	114	48.98±16.2	BM (47)	
Epulis fissuratum	71	3.3	61	10	55.24±11.4	GEN (52.1)	
Fibroepithelial epulis	66	3	44	22	47.91±15.7	GEN (100)	
Keratosis	57	2.6	27	30	52.95±14.8	TNG (47.4)	
Epithelial hyperplasia	51	2.3	28	22	54.48±17.6	TNG (31.4)	
Auto-immune or metabolic lesions	89	4.1	72	17	49.97±15.49	LAM (62.9)	
Sjögren's Syndrome	48	2.2	47	1	50.83±12.8	LAM (93.8)	
Pemphigus	13	0.6	8	5	53.54±13.6	BM (84.6)	
Amyloidosis/amyloid substance	7	0.3	2	5	61.86±16.8	LAM (57.1)	
Pemphigoid	4	0.2	4	0	63.5±19.8	GEN (50)	
Erythema multiform	4	0.2	3	1	35.5±18.1	LAM (50)	
Congenital or development disorders	67	3	43	23	43.3±18.6	LAM (41.8)	
Vascular anomalies	37	1.7	22	14	49.9±17.9	LAM (48.6)	
Exostosis	8	0.4	6	2	$46.38{\pm}15.9$	MAN (62.5)	
Melanocytic nevus	6	0.3	2	4	32.17±16.9	LAM (100)	
Lentigo	4	0.2	4	0	30±13.3	LAM (75)	
White spongy nevus	3	0.1	1	2	33±26.1	BM (66.7)	
Total	2162	100	1239	909	45.06±18.34	<b>BM</b> (17)	

<b>Table 2.</b> Number of non-neoplastic diagnoses by diagnostic category (including the 5 most prevalent
lesions in each category) distributed by gender, age and predominant site.

Legends: LAM – Labial Mucosa; BM – Buccal Mucosa; GEN – Gingiva; TNG – Tongue; FOM – Floor Of the Mouth; PAL – Palate; MSG – Major Salivary Glands; MAX – Maxilla; MAN – Mandible; MNOS – Mouth NOS (non-otherwise specified). <sup>a</sup> In some patients the variable is unknown

Table 3. Number of oral potentially malignant disorders distributed by gender, age and predominant site.

Diagnostia Catagory			%	Gender		Age	Location	
Diagnostic Category		n	70	Female	Male	Mean ±S.D.	Predominant (%)	
Leukoplakia *		76	46.6	28	48	57.53±15.66	BM (36.8)	
Lichen planus		61	37.4	32	29	50.9±14.42	BM (70.5)	
Actinic cheilitis		18	11.04	9	9	64.94±8.2	LAM (100)	
Epithelial dysplasia**		7	4.3	3	4	62.29±10.83	BM (42.9)	
Erythroplasia		1	0.61	1	0	70	FOM (100)	
	Total	163	100	73	90	56.14±14.9	BM (45.4)	

Legends: LAM – Labial Mucosa; BM – Buccal Mucosal; FOM – Floor Of the Mouth. \* Including cases with hyperkeratosis or epithelial hyperplasia (without dysplasia) with a clinical diagnosis of leukoplakia. \*\* Including leukoplakias with dysplasia

	n	% -	Gender <sup>a</sup>		Age <sup>a</sup>	Location	
Diagnostic Category			Female	Male	Mean ±S.D.	Predominant (%)	
Benign neoplasms	403	12.5	225	173	44.8±18.2	MSG (30.8)	
Epithelial origin							
Pleomorphic adenoma	112	12.6	69	43	43.38±17.7	MSG (75)	
Squamous cell papilloma	96	10.8	57	38	43.46±17.9	TNG (39.6)	
Warthin's tumour	25	2.8	2	23	54.50±12.8	MSG (96)	
Basal-cell adenoma	7	0.8	5	2	56.43±11.3	MSG (71.4)	
Adenoma NOS	6	0.7	6	0	57.3±8.8	BM+PAL (66)	
Mesenchymal origin or others							
Haemangioma	55	6.2	34	21	49.31±17	LAM (52.7)	
Lipoma	23	2.6	6	15	54.81±16.5	BM(26.1)	
Fibroma	22	2.5	14	7	43.95±16.7	BM (50)	
Lymphangioma	12	1.4	7	5	41.25±19.6	TNG (58.3)	
Granular cell tumour	6	0.7	4	2	34.6±7	TNG (100)	
Malignant neoplasms	483	15	129	348	59.7±15.2	TNG (26.3)	
Epithelial origin							
Squamous cell carcinoma	373	42.1	91	279	61.55±13.5	TNG (30.8)	
Mucoepidermoid carcinoma	13	2.7	7	6	$47.25 \pm 17.8$	MSG (38.5)	
Adenoid cystic carcinoma	10	1.1	3	6	53.22±13.6	FOM+MSG (60)	
Carcinoma in situ	6	0.7	1	5	$62.83{\pm}16.8$	LAM (50)	
Verrucous carcinoma	5	0.6	2	3	70.60±9.4	GEN (40)	
Undifferentiated carcinoma	5	0.6	1	4	52±20.9	GEN (40)	
Mesenchymal origin and other's							
Lymphoma	25	2.8	13	12	51.12±21.7	MSG (24)	
Kaposi's Sarcoma	9	1	0	9	$36.78 \pm 5.2$	PAL (55.6)	
Metastasis	8	0.9	2	6	67.38±12.3	LAM+TNG+MSG (75	
Sarcoma NOS	2	0.2	1	1	22	GEN (100)	
Plasmocytoma	2	0.2	1	1	42.50±16.3	GEN+MAN (100)	
Total	886	100	354	521	52.8±18.2	<b>TNG (23.8)</b>	

**Table 4.** Number of neoplastic diagnoses by diagnostic category (including the 5 most prevalent in each category and tissue origin) distributed by gender, age and predominant site.

Legends: NOS – Non Otherwise Specified; LAM – Labial Mucosa; BM – Buccal Mucosa; GEN – Gingiva; TNG – Tongue; FOM – Floor Of the Mouth; PAL – Palate; MSG – Major Salivary Glands; MAN – Mandible. <sup>a</sup> In some patients the variable is unknown