Stomatologija, Baltic Dental and Maxillofacial Journal, 15: 78-83, 2013

# Oral cancer calibration and diagnosis among professionals from the public health in São Paulo, Brazil José Carlos Alves, Renato Pereira da Silva, Karine Laura Cortellazzi, Fabiana de Lima Vazquez,

José Carlos Alves, Renato Pereira da Silva, Karine Laura Cortellazzi, Fabiana de Lima Vazquez, Regina Auxiliadora de Amorim Marques, Antonio Carlos Pereira, Marcelo de Castro Meneghim, Fábio Luiz Mialhe

# SUMMARY

Oral cancer is a public health problem responsible for 13% of deaths worldwide in 2008 and screening programs can be useful to detect individuals more vulnerable to the disease, improving its prognosis.

*Objectives.* The aim of the present study was to evaluate oral cancer calibration (*in lux* and *in vivo* methodologies) and diagnosis processes performed by dental surgeons (DSs) of the public health system in São Paulo, Brazil.

*Material and methods.* Thirty-three oral cancer photographs were examined during *in lux* calibration, while 560 individuals were examined during *in vivo* calibration. Oral conditions were coded as "0 – sound tissues", "1 – buccal lesions without malignant potential" and "2 – buccal lesions with malignant potential". The final sample for oral cancer screening was composed of 336 individuals, age-range 40 years or older.

*Results*. Kappa values for interexaminer agreement were 0.67 and 0.45 for *in lux* and *in vivo* respectively. The accuracy of both methodologies was over 80%. Oral cancer screening revealed 48 healthy individuals, 273 oral lesions coded as "1" and 12 oral lesions coded as "2".

*Conclusion.* In spite of the low reproducibility, the validity of the visual examination in oral cancer screening was satisfactory, showing its importance as part of preventive oral cancer programs and public health system campaigns.

Key words: oral cancer, oral diagnosis, calibration.

# INTRODUCTION

Nowadays the cancer is a worldwide public health problem. Cancer was responsible for around 13% of all deaths in the world in 2008. For the year 2015, around 15 million new cases of cancer are

<sup>1</sup>Health Municipal Secretariat from São Paulo city, Brazil <sup>2</sup>Department of Nutrition and Health, Federal University of Viçosa, Brazil

<sup>3</sup>Department of Social Dentistry, Piracicaba Dental School, University of Campinas, Brazil

<sup>4</sup>Department of Community Dentistry, University from São Paulo (UNIP), São Paulo, Brazil

José Carlos Alves<sup>1</sup> – D.D.S., MSc Renato Pereira da Silva<sup>2</sup> – D.D.S., MSc, PhD, prof. Karine Laura Cortellazzi<sup>3</sup> – D.D.S., MSc, PhD, collaborator prof. Fabiana de Lima Vazquez<sup>3</sup> – D.D.S., MSc, PhD student Regina Auxiliadora de Amorim Marques<sup>1,4</sup> – D.D.S., MSc, PhD, prof. Antonio Carlos Pereira<sup>3</sup> – D.D.S., MSc, PhD, prof. Marcelo de Castro Meneghim<sup>3</sup> – D.D.S., MSc, PhD, prof. Fábio Luiz Mialhe<sup>3</sup> – D.D.S., MSc, PhD, prof.

Address correspondence to Dr. Renato Pereira da Silva Department of Nutrition and Health (DNS), Federal University of Viçosa (UFV) Zip code 36570-000, Viçosa, MG, Brazil E-mail address: renatop.silva@ufv.br expected. The estimated number of cancer deaths, for 2015, will be around 9 million (1).

In Brazil, cancer is one of the main causes of death in the entire nation. Around 518,510 new cases of cancer (men – 257,870; women – 260,640) are expected in 2012. For the year 2012, the 5 most incident cancers expected among men are non-melanoma skin (63,000 new cases), prostate (60,000 new cases), lung (17,000 new cases), colon and rectal (14,000 new cases) and stomach (13,000 new cases) cancer. Among women, the 5 most incident cancers expected for the same year are non-melanoma skin (71,000 new cases), breast (53,000 new cases), uterine (18,000 new cases), colon and rectal (16,000 new cases) and lung (10,000 new cases) cancer (2).

In Brazil, there is growing concern about oral cancer. The population in the age-range of 30 years or older, who are tobacco-users, heavy drinkers, men, of low socio-economic status and with compromised health status is at the highest risk of developing this disease (8). For the year 2012, 14,170 new cases of oral cancer are expected in Brazil (men - 9,990; women - 4,180). Approximately 4,430 (men - 3170; women - 1260) and 1,330 (men - 970; women - 360) new cases of oral cancer are expected for the year 2012 in the state and the city of São Paulo, respectively (2).

The Brazilian strategies for oral cancer prevention consist of health programs that target tobacco and alcohol users. These programs are conducted by multidisciplinary Primary Health Care (PHC) teams of the Brazilian National Health Service (SUS), seeking integral health promotion (3, 4). A secondary strategy for oral cancer prevention, also conducted by PHC includes meticulous visual examination of the oral cavity seeking to identify precancerous lesions and asymptomatic tumors. The prognosis of oral cancer depends directly on its early detection (3, 5).

When oral cancer is diagnosed, death occurs within 12 months after the diagnosis in 50% of the subjects with this condition in North, Central and South America and the Caribbean region. Another 10% to 20% of the 5-year survivors will die prematurely from cancer. So cancer prevention and its early diagnosis are strategies widely used to control the burden of this disease (2, 6).

In the public health system of São Paulo, one of the largest cities in Latin America, cancer diagnosis has recently been routinely performed. In the period between 1998 and 2000, the Social Organization Santa Marcelina (SOSM) was the pioneer in the development of oral health promotion, prevention and recovery activities based on oral disease screening, in association with the Secretary of Health of the State of São Paulo, in the eastern area of the city of São Paulo (7).

Although oral cancer screening can be considered a positive strategy for its early diagnosis and treatment in populations, the personnel who perform oral examinations for screening programs need to be properly trained and calibrated (5).

According to Biggar et al. (8) there are few international studies with large cohorts conducted on oral cancer screening and "a comprehensive comparison of these programs examining the techniques used and the screening results would be beneficial in providing a more practical approach to strategy development and implementation of an oral cancer screening".

Therefore, the aim of the present study was to evaluate the oral cancer calibration process and diagnosis performed by dental surgeons (DSs) from the Basic Health Units of the Family Health Care Program (FBHU)

# MATERIAL AND METHODS

This study was conducted in accordance with Resolution No. 196/96 of the National Health Council of the Brazilian Ministry of Health, and No. 179/93 of the Dental Professional Ethical Code of the Brazilian Dental Council, after being approved by the Research Ethics Committee of the Secretary of Health of the city of São Paulo, Protocol No. 417/2009.

The participants were 39 DSs who worked in 18 FBHU of SOSM, in the eastern zone of the city of São Paulo. These DSs were experienced in oral cancer screening, as they had been doing this work since 2004, when the city of São Paulo started its programs for training professionals in oral cancer diagnosis. However none of them were calibrated, and no evaluation of the agreement reached by these professionals had been performed up to that time (9).

The present study was composed of 3 stages: *in lux* and *in vivo* calibration and oral cancer screening in the population. A gold standard examiner (GSE), specialist in Semiology and with vast experience in oral cancer diagnosis, led the *in lux* and *in vivo* calibration stages.

# In lux calibration

This calibration was accomplished by 39 DSs, who examined photographs of 33 oral cancer lesions in different stages of development, for 1 minute each (10).

The total time of this stage, including training, discussions about clinical cases and the examiners' calibration, conducted by a gold standard examiner, lasted 4 hours. Cohen's Kappa ( $\kappa$ ) was used to determine the interexaminer agreement. The validity of this stage (sensitivity, specificity, positive and negative predictive values and accuracy tests), was established by confronting the examiners' diagnoses against the GSE's diagnoses.

#### In vivo calibration process

Twenty-seven DSs participated in this stage. Twelve DSs from the previous stage, who attained the lowest interexaminer agreement were excluded at this stage. A convenience sample of 560 individuals in the age-range of 40 years and older, from 6 FBHU that were invited to participate in the activity, was examined by the DSs and also by the GSE by means of meticulous visual inspection of the oral cavity (labial and buccal mucosa, retromolar area, gingival, tongue, floor of mouth and hard palate), using a wooden spatula to withdrawn soft tissues carefully, under natural lighting.

Individuals with lesions suggestive of oral cancer, detected in this stage were referred to Dental Specialties Centers (DSC) in the city of São Paulo, where the cancer diagnosis was confirmed or refuted by biopsies. True positive cases, confirmed by histopathological examinations, were promptly sent to the head and neck cancer services of the city of São Paulo.

For study purposes the clinical conditions were coded as "0 - sound tissues"; "1 - oral lesions without malignant potential"; "2 - oral lesions with malignant potential".

As in the previous stage, reproducibility and validity were obtained.

# **Oral cancer screening**

Oral cancer screening was performed by the 27 DSs from the previous stage at the 18 FBHU in 95.361 individuals (men = 42.404; women = 52.957) in the age-range of 40 years or older, examined between November of 2009 and December of 2010 using an opportunistic and invitational approach (8). This screening was conducted in accordance with the World Health Organization's recommendations and criteria to determine its validity (11).

At the FBHU, the DSs performed an initial clinical examination, which is cheaper and non-invasive. Individuals in whom lesions suggestive of oral cancer were detected at this examination, were referred to the Secondary Dental Care unit, where they were re-examined by professionals specialized in Semiology, who used histopathological examination to confirm the DSs' diagnosis. True positive cases of oral diseases were promptly sent to the head and neck cancer service of the municipality of São Paulo.

#### RESULTS

The reproducibility and validity of the *in lux* and *in vivo* calibration stages are presented below.

The *in lux* calibration reproducibility and validity values were slightly higher than the values obtained in the *in vivo* calibration, showing the growing degree of difficulty of the second method, in comparison with the first calibration method. However, the Kappa values were below 0.80 (80%) for both calibration methods (Table 1).

A total of 95.361 individuals were examined at the oral cancer screening centers of the 18 FBHUs, from November 2009, through to December 2010. This examination detected oral lesions in 653 individuals, who were referred to the DSC. However, 315 (48.2%) of these individuals did not present at the DSC, and were excluded from the study. Two individuals classified under clinical condition "0 – sound tissues" did not meet the inclusion criterion for this study, and were also excluded. Thus, the final sample was composed of 336 individuals classified by the DSs, as code "1 – oral lesions without malignant potential" or code "2 – oral lesions with malignant potential". The detailed diagnosis of the final sample is presented in Table 2.

Table 2 shows some discrepancy between the DSs diagnosis and the GSE/Histopathological diagnosis. Of the 332 individuals coded as "1" by the DSs, 48 individuals were confirmed as code "0" by the GS; 273 individuals were confirmed as code "1" and 11 individuals were confirmed as code "2". Of the 4 individuals coded as "2" by the DSs, only one was confirmed with this code by the GSE. The other 3 individuals were confirmed as code "1" by the GSE (Table 2).

The 288 oral lesions confirmed by GSE and/or histopathological examination expressed in Table 2 are detailed in Table 3.

All the traumatic keratosis lesions detected by the visual examination performed by the GSE were confirmed by the histopathological examination (Table 3).

# DISCUSSION

In spite of the technological advancements in oral cancer diagnosis, visual examination continues to be an important diagnostic tool when examining a population at high risk for this disease. Its low financial cost, low potential to produce discomfort to the individual examined, simple and easy-toperform technique are desirable characteristics in oral cancer screenings accomplished around the

Table 1. In lux and in vivo calibration reproducibility and validity

	Kappa	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
In lux calibration*	0.67	93.72	77.56	86.54	87.90	87.43
In vivo calibration**	0.45	52.14	90.44	61.42	86.61	81.78

\* accomplished by 39 DSs in the year 2010; \*\* accomplished by 27 DSs in the year 2009.

world. However there is no scientific evidence to support the effectiveness of oral cancer screenings in reducing mortality rates (3, 5, 12-15).

The visual examination of the oral cavity is highly influenced by the examiners' subjectivity, experience and physical-emotional state. Therefore,

**Table 2.** DSs X GSE/Histopathological oral cancer diagnosis, 2009/2010

Clinical condition	DSs	GSE/Histopathological
0	0	48
1	332	273
		3
2	4	11
		1
Total	336	

GSE - gold standard examiner; DSs - dental surgeons.

Table 3. Distribution of	confirmed	oral lesions
--------------------------	-----------	--------------

Clinical condition	Oral lesion	Diagnosis	
		GSE	Histopatho- logical
Code 1: oral lesions with-	Hemangioma	6	-
out malignity potential	Anatomical hyperplasia	1	_
	Burning mouth syndrome	2	_
	Fibroma	3	_
	Nodule	1	_
	Mucocele	1	_
	Candidosis	6	_
	Traumatic keratosis	11	11
	Traumatic ulcer	1	_
	Lymphomegaly	1	_
	Cheilitis	2	_
	Fibrous scar	_	1
	Lipoma	1	2
	Papilloma	1	4
	Bacterial Colony	_	1
	Inflammatory process	_	21
	Giant cell granuloma	_	1
	Prosthesis trauma	33	_
	Cyst	3	_
	Adenoma	_	2
	Mucositis	_	2
	Inflammatory fibrous hyperplasia	99	_
	Other lesions	58	
Code 2: oral lesions with	Actinic Cheilitis	2	_
malignity potential	Erosive lichen planus	2	1
	Oral cancer	-	7
	Total	234	54

the goal of previously calibrating these examiners is to reduce clinical disagreements among them (15, 16).

The low Kappa values for *in lux* ( $\kappa$ =0.67) and *in vivo* ( $\kappa$ =0.45) calibration in this study may reflect the need to realize more training and calibration sessions for examiners involved in oral cancer screenings. In addition, these results may reflect methodological flaws in constituting the sample for the calibration process. The slightly higher value of the interexaminer agreement *in lux* in comparison with *in vivo* calibration is partially due to the intrinsic characteristic of each calibration method. Thus, the low Kappa values may not reflect the real interexaminer agreement. Another factor to consider is that whereas part of the individuals' clinical history is lost in the *in lux calibration*, direct observation of the clinical conditions is easier. In the *in vivo* 

> calibration the situation is reversed; anamnesis is realized, however, it is more difficult to see clinical details in the oral cavity during the visual examination, because of the saliva and soft tissues having to be withdrawn. The absence of the intraexaminer agreement calculation was a limitation to be overcome in future oral cancer screenings (3, 17). Thus the reproducibility found for both calibration methods shows the need to implement methodological measures to achieve values of at least 80% (18).

> The validity of visual examination is equally important to the results of oral cancer screening. In the present study, the validity was obtained at the in lux and in vivo calibration stages, showing satisfactory accuracy values, 87.43% and 81.78%, respectively. Again the constitution of the sample examined, especially the prevalence of the disease in the population, may have played an important role in the sensitivity, specificity, positive and negative predictive test values. In general, while under ideal examination conditions,

during *in lux* calibration, high sensitivity values are obtained to the detriment of the specificity test; whereas under real conditions, during *in vivo* calibration, the opposite occurs.

An additional limitation of this study was that reproducibility and validity tests were not performed at the stage of oral cancer screening. The reproducibility and validity values of the visual examination are evidence of the need to reinforce frequent training and continued health education programs for professionals working in the public health system (5, 19).

Although there is no strong scientific evidence to support or refute the use of visual examination or another diagnostic method (e.g. toluidine blue, fluorescence imaging, brush biopsy) as an effective method for oral cancer screening to reduce mortality rates in the high-risk group (tobacco and/or alcohol users), the prevention and early diagnosis of oral cancer must be encouraged and accomplished by National Health Systems (5, 14, 15, 21).

In addition to the methodological issues involved in the diagnostic methods in oral cancer screening programs, rigorous planning of the actions, an integrated and effective health system, as well an efficient information system are needed in order for these programs to achieve some impact on the local nosological status (5).

The high abstention rates, such as those found in this study (48.4%), and the low adhesion of the

# REFERENCES

- GLOBOCAN Project. Online analysis. Prediction. [Accessed 2011 may 20]. Available in: <a href="http://globocan.iarc.fr/">http://globocan.iarc.fr/</a>
- 2. National Cancer Institute (INCA). Estimativa 2012: incidência de câncer no Brasil (Estimate/2012 - Cancer Incidence in Brazil). Rio de Janeiro: INCA; 2011.
- Rodrigues VC, Moss SM, Tuomainen H. Oral cancer in The U.K.: to screen or not to screen. *Oral Oncol* 1998;34:454-65.
- 4. Petersen PE. The World Oral Health Report 2003: continuous improvement of oral health in the 21st century - the approach of the WHO Global Oral Health Programme. *Community Dent Oral Epidemiol* 2003;31(suppl.1):3-23.
- Antunes JLF, Toporcov TN, Wünsch-Filho V. Resolutividade da campanha de prevenção e diagnóstico precoce do câncer bucal em São Paulo, Brasil [The effectiveness of the oral cancer prevention and early diagnosis program in São Paulo, Brazil]. *Rev Panan Saude Publica* 2007;21:30-6.
- 6. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. *Oral Oncol* 2009; 45:309-16.
- Vasconcelos EM. Comportamento dos cirurgiõesdentistas das unidades básicas de saúde do município de São Paulo quanto à prevenção e ao diagnóstico precoce do câncer bucal. [Dentists' behavior from basic health units of the city of São Paulo related to oral cancer prevention and early diagnosis] [dissertation]. São Paulo: USP/FO; 2006.

population to these health programs must also be considered when planning oral cancer screenings (12). Biggar et al. (8) affirmed that compliance with referrals after screening is a variable that depends on the way participants are recruited and that high risk subjects (men, heavy drinkers, smokers, the elderly) are less likely to participate in invitational studies. Therefore, a feasible solution to these problems is to adopt a common risk approach, and the implementation of active search strategies by primary health care professionals to identify new cases of oral cancer (3, 4, 22). To include oral cancer screenings in other health programs or campaigns is also an opportune and cost-effective intervention (23).

A reproducible and valid visual examination allied to the factors listed above produces relevant information about oral cancer in a local population, and the findings of this study point in this direction.

### CONCLUSION

In spite of its low reproducibility, the validity of the visual examination in oral cancer screening was satisfactory, showing its importance as part of preventive oral cancer programs and campaigns in public health of the municipality of São Paulo, Brazil. However additional studies measuring the real impact of oral health screenings on the reduction of mortality rates are necessary.

- 8. Biggar H, Forrest A, Poh CF. Global oral cancer screening programs: review and recommendations. *Can J Dent Hygiene* 2007;41:138-46.
- São Paulo. Health Municipal Secretariat. Oral health technical area. Relatório final da campanha de prevenção e diagnóstico do câncer bucal, 2010 (Final report of the prevention campaign and diagnosis of oral cancer, 2010.) [accessed 2011 May 20]. Available in: <a href="http://www.pre-feitura.sp.gov.br/cidade/secretarias/saude/saude\_bucal/>">http://www.pre-feitura.sp.gov.br/cidade/secretarias/saude/saude\_bucal/></a>.
- 10. Brazil. Health Ministry. Health Attention Secretariat. Basic Attention Department. National Oral Health Coordination. SB Brasil 2010: Pesquisa Nacional de Saúde Bucal (SB Brasil 2010: National oral health research). Technical project. Brasília, 2009.
- 11. World Health Organization (WHO). Principles and practice of screening for disease. Geneva: WHO; 1968.
- 12. Patton LL. The effectiveness of community-based visual screening and utility of adjunctive diagnostic aids in the early detection of oral cancer. *Oral Oncol* 2003;39:708-23.
- Downer MC, Moles DR, Palmer S, Speight PM. A systematic review of measures of effectiveness in screening for oral cancer and precancerous. *Oral Oncol* 2006;42:551-60.
- 14. Brocklehurst P, Kujan O, Glenny AM, Oliver R, Sloan P, Ogden G, et al. Screening programmes for the earlyv detection and prevention of oral cancer. Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.:

CD004150. DOI:10.1002/14651858.CD004150.pub3. Available in: < http://www.thecochranelibrary.com>.

- 15. Fedele S. Diagnostic aids in the screening of oral cancer. Head Neck Oncol 2009;1:5 doi:10.1186/1758-3284.
- 16. World Health Organization (WHO). Oral health surveys: basic methods. 4th ed. Geneva, 1997.
- Bader JD, Shugars DA, McClure FE. Comparison of restorative treatment recommendations based on patients and patient simulations. *Oper Dent* 1994; 19:20-5.
- Zain AT. Training examiners for a national epidemiological survey of oral mucosal lesion. Int Dent J 1996;46:536-42.
- 19. Patton LL, Ashe TE, Elter JR, Southerland JH, Strauss RP. Adequacy of training in oral cancer prevention and screening as self-assessed by physicians, nurse practitioners, and dental health professionals. *Oral Surg Oral*

Med Oral Pathol Oral Radiol Endod 2006;102:758-64.

- 20. Petersen PE. Oral cancer prevention and control the approach of the World Health Organization. *Oral Oncol* 2009;45:454-60.
- 21. Sankaranarayanan R, Ramada K, Thomas G, Muwonge R, Thara S, Mathew B, et al. Effect of screening on oral cancer mortality in Kerala, India: a cluster-randomized controlled trial. *Lancet* 2005;365:1927-33.
- 22. Sartori LC. Rastreamento do câncer bucal: aplicações no Programa Saúde da Família [Oral cancer screening: an application in Health Family Program][dissertation]. São Paulo: USP/FSP; 2004.
- 23. Speight PM, Palmer S, Moles DR, Downer MC, Smith DH, Henriksson M, et al. The cost-effectiveness of screening for oral cancer in primary care. *Health Technol Assess* 2006;10:1-144.

Received: 28 08 2012 Accepted for publishing: 23 09 2013