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Fluorescence spectroscopy for the detection of potentially malignant disorders and squamous cell carcinoma of the oral cavity

Ana Lucia Noronha Francisco PhD[a], Wagner Rafael Correr[b], Luciane Hiramatsu Azevedo PhD[c], Vivian Galletta Kern PhD[c], Clóvis Antônio Lopes Pinto PhD[d], Luiz Paulo Kowalski PhD[e,*], Cristina Kurachi PhD[b,]**

[a] *Department of Oral Diagnosis, School of Dentistry of Piracicaba, University of Campinas (UNICAMP), Av. Limeira 901, Piracicaba 13414-018, São Paulo, Brazil*
[b] *Department of Physics and Materials Science, Physics Institute of São Carlos, University of São Paulo (USP), Av. Trabalhador São-Carlense 400, São Carlos 13566-590, São Paulo, Brazil*
[c] *Special Laboratory of Laser in Dentistry, School of Dentistry of São Paulo, University of São Paulo (USP), Av. Professor Lineu Prestes, Cidade Universitária, São Paulo 05508-000, São Paulo, Brazil*
[d] *Department of Pathology, A.C. Camargo Cancer Center, Rua Prof. Antonio Prudente 211, São Paulo 01509-900, São Paulo, Brazil*
[e] *Department of Head and Neck Surgery and Otorhinolaryngology, A.C. Camargo Cancer Center and the National Institute of Science and Technology in Oncogenomics (INCITO), Rua Prof. Antonio Prudente 211, São Paulo 01509-900, São Paulo, Brazil*

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Early diagnosis;
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Summary Oral cancer is a public health problem with relevant incidence in the world population. The affected patient usually presents advanced stage disease and the consequence of this delay is a reduction in survival rates. Given this, it is essential to detect oral cancer at early stages. Fluorescence spectroscopy is a non-invasive diagnostic tool that can improve cancer detection in real time. It is a fast and accurate technique, relatively simple, which evaluates the biochemical composition and structure using the tissue fluorescence spectrum as interrogation data. Several studies have positive data regarding the tools for differentiating between normal mucosa and cancer, but the difference between cancer and potentially malignant disorders is not clear.

The aim of this study was to evaluate the efficacy of fluorescence spectroscopy in the discrimination of normal oral mucosa, oral cancer, and potentially malignant disorders.

* Corresponding author.
** Corresponding author at: Physics Institute of São Carlos, University of São Paulo, Avenida Trabalhador São-Carlense 400, São Carlos 13566-590, Brazil. Tel.: +55 16 33739810; fax: +55 16 33739811.
E-mail addresses: lp.kowalski@uol.com.br (L.P. Kowalski), cristina@ifsc.usp.br (C. Kurachi).

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The fluorescence spectroscopy was evaluated in 115 individuals, of whom 55 patients presented oral squamous cell carcinoma, 30 volunteers showing normal oral mucosa, and 30 patients having potentially malignant disorders. The spectra were classified and compared to histopathology to evaluate the efficiency in diagnostic discrimination employing fluorescence. In order to classify the spectra, a decision tree algorithm (C4.5) was applied. Despite of the high variance observed in spectral data, the specificity and sensitivity obtained were 93.8% and 88.5%, respectively at 406 nm excitation. These results point to the potential use of fluorescence spectroscopy as an important tool for oral cancer diagnosis and potentially malignant disorders.

Introduction

Annually, about 10 million malignant tumors are diagnosed worldwide, and cancer of the oral cavity represents 6% of all cases [1,2]. Different tumors may affect the oral cavity, and oral squamous cell carcinoma (OSCC) is the most frequent one, representing 90% of all cases [2—5]. Unfortunately, in most cases, the patients present for treatment with advanced stage disease, with consequent decrease in survival rates [1,6]. The treatment of these patients is usually aggressive and may be mutilating [7]. Despite the recent advances in the treatment of OSCC, there has been only a small increase in the survival rate [8].

Disease local and regional control and rehabilitation of patients with advanced oral carcinoma are extremely difficult. On the other hand, initial lesions are more easily removed with less patient mutilation and better prognosis [9,10].

Some OSCC lesions come from pre-existing potentially malignant disorders [6,11] with the annual malignant transformation rate of approximately 1% [11,12]. Patients with previous history of oral cancer, especially those that had been heavy smokers, present an altered oral mucosa (cancerization field). Although oral lesions are common, to predict the biological behavior of them remains a challenge. The standard methodology for the diagnosis of these lesions is clinical examination and histopathological analysis. Most oral potentially malignant disorders (PMD) are clinically present as leukoplakia or erythroplakia, but histologically they can show a wide variety of phenotypes, such as hyperkeratosis, dysplasia or even carcinoma [13].

Currently, there is great interest in optical techniques that use fluorescence to evaluate lesions using a non-invasive procedure. Based on the tissue optical properties and diagnostic sensitivity to capture the fluorescence emitted by native fluorophores, these optical techniques have been indicated to differentiate endogenous tissue variations [14—16]. The fluorescence spectroscopy has become an important tool in detecting potentially malignant and malignant lesions in the oral mucosa [17,18]. The biochemical composition and tissue architecture can be assessed by the emitted fluorescence spectrum, which will be modified in the presence of tissue alterations [19]. Mathematical algorithms can then be developed and optimized to classify the respective tissues in histological categories based on their spectral characteristics [20—23].

The aim of this study was to determine the ability of fluorescence spectroscopy to discriminate normal and abnormal oral mucosa, potentially malignant and/or malignant oral lesions.

Patients and methods

This prospective study was performed at the Department of Head and Neck Surgery and Otorhinolaryngology, A.C. Camargo Cancer Center and LELO-USP (Special Laboratory of Laser Dentistry), São Paulo, Brazil. The clinical research protocol was approved by the Ethical Committee of the participant institutions, and all recruited patients that agreed to participate as volunteers signed an informed consent form.

The fluorescence spectroscopy system is composed of an excitation light source, an interrogation probe, a portable spectrophotometer USB 2000 (Ocean Optics, USA) and a laptop. Two solid state lasers, a diode emitting at 406 nm and a doubled-frequency neodymium: YAG at 532 nm, were used as excitation light sources. The interrogation probe is a Y-type fiberoptic probe, where one tip is connected to the spectrophotometer and the other one to the excitation laser. Two optical fibers of 600 μm in diameter are positioned side by side. One conducts the excitation light and the other collects the re-emitted light by the tissue. The outer diameter of the interrogation tip is 1.6 mm and the total diameter of the area that is placed in contact with the tissue surface is 3.2 mm. The spectroscopic data was acquired using the software OOIBase32 (Ocean Optics, USA).

All subjects were interviewed and the data filled in a standardized interview form containing information regarding the habits (including tobacco and alcohol consumption), family history, etc. Clinical examination was performed and examiner clinical impression was recorded. In patients with cancer (C) and PMD, clinical characteristics, including lesion dimensions, color, and site were evaluated. In vivo fluorescence spectroscopy measurements were performed under both excitation wavelengths, collecting as many points needed to cover the whole lesion surface, at least one hour after the last meal. In the case of identification of superficial clinical heterogeneities, as leukoplakia or erythroplakia, fluorescence spectra were taken and identified to correlate with distinct clinical patterns. Tissue research was not taken from area of necrosis, usually present at the center of ulcerated lesions. In each chosen area, five spectroscopic measurements under each wavelength were taken. The patient evaluation was performed at the surgical theater at A.C. Camargo Hospital, after induction of general anesthesia, and at outpatient clinics at LELO, before the biopsy procedure or surgical resection of the lesions.

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