**PhD in Bioengineering and Medical-Surgical Sciences**

**Research Title:** Potential use of optical coherence tomography in patients with oral lichen planus treated with photobiomodulation or standard medication

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**Context of the research activity**

Oral lichen planus (OLP) is a relatively common chronic inflammatory disease (1-2% of the total population), of unknown aetiology, rarely undergoing spontaneous remission and potentially premalignant.

OLP is difficult to palliate and in several cases, most therapies are merely symptomatic; even if the best treatment remains high-potency topical corticosteroids, management is usually empirical, without adequate control groups or corrected study designs.

Low-level laser therapy (LLLT) is an approach increasingly used in medicine, which has potential biostimulating effects also if applied to oral tissues by improving wound healing, enhancing epithelization after periodontal surgery, and preventing or healing induced oral mucositis.

Laser biostimulation can obtain different intracellular biological reactions to stimulate regenerative abilities, without undesired adverse effects, reducing also the pharmacological support and its possible invasiveness. Besides explaining many controversies in the field of low-power laser effects (e.g., the diversity of effects, the variable magnitude or absence of effects in certain studies), the proposed redox-regulation mechanism may be a fundamental explanation for some clinical effects of irradiation, for example the positive results achieved in treating wounds, chronic inflammation, and ischemia, all characterized by acidosis and hypoxia.
A variety of therapeutic effects of LLLT have been reported on a broad range of oral disorders. It has been found amenably practical in dental applications including soft as well as hard tissues of the oral cavity. LLLT has been found to be efficient in acceleration of wound healing, enhanced remodelling and bone repair, regeneration of neural cells following injury, pain attenuation, endorphin release stimulation and modulation of immune system. Clinical studies have demonstrated the effectiveness of LLLT in patients with OLP, or other pre-cancerous conditions of the oral mucosa, which are poorly responsive to topical drug treatments.

A few studies evaluating the structural changes of the oral tissues involved by LLLT; most of these uses of traditional biopsy procedures, which invalidate the therapeutic efficacy of laser biomodulation.

The Optical Coherence Tomography (OCT) could repeat, in real time, an image of architecture of epithelial and sub-epithelial tissues and surrounding structures. A computer transforms the information obtained in a screen image, allowing a sort of histological examination “in vivo” of the oral mucosa without anatomical drawing on the patient. The OCT allow to evaluate the morphological changes of epithelial layers with a depth of tissue penetration of 1-2 mm, more than enough range for the oral mucosa, the latter having a thickness of about 0.2-1 mm.

To date OCT has never been used in oral medicine to detect epithelial changes during different types of treatment.

Some few previous reports have been done to analyse bullous oral diseases in order to evaluate the feasibility to image epithelial architecture of oral mucosae using the in-vivo OCT, seemed to be a valid non-invasive auxiliary diagnostic device able to show in vivo the epithelial layers and basal membrane.

Other findings are present in dermatological studies suggesting that there is a potential for the application of OCT scanning in the acute phase of different skin diseases in order to distinguish them for a faster diagnosis and better management and treatment.

**Objectives**

**Aims and significance:**

The aim of this study will be to evaluate, through the use of OCT, possible morphometric changes of the oral tissues that have performed the LLLT (Group A), compared to usual drug topical corticosteroid therapy (Group A), in a selected population of patients with erosive histologically proven OLP.

This will be a 2-month prospective randomized controlled trial, with one year of follow-up.
In the first year of the project, patients will be recruited. In the second year of the project, trial will start and the 3rd year will be used to make proper conclusions and write thesis (and papers).

This is the first ever-reported project that would analyse the conceivable tissue changes of the oral mucosa (affected by pathological changes) during photobiomodulation (compared to usual drug therapy). It should be possible to ascertain the effectiveness of laser therapy compared to topical medication, both clinically and morphology. We would like to possible validate the use of OCT as a non-invasive diagnostic tool for potentially malignant lesions of the oral mucosa.

**Experimental Design:**

Randomization (n=100 total population).

**Group A:**

a) Selection of patients affected of erosive and painful OLP, in a prospective manner (n=50);

b) Rating histopathological OCT HSL-2100-HW 50 kHz scan rate (Santec);

c) Start of LLLT with "Raffaello diodes laser" 980/645 nm (DMT Liss I) num = 8 sessions (2 times for week for a total of 4 weeks). The device must be used according to the manufacturer’s instructions. A collimated probe, with a diameter of 0.6 cm and a spot size of 0.28 cm², is used. The output power is 300 mW, verified using the calibrating door of the laser device, and the power density is about 1 W/cm². A “spot” technique is used, with a slight overlapping in order to evenly distribute energy covering all the mucosal lesions and also the peri-lesional tissues up to 0.5 cm. Each session has to be performed delivering a fluence of 4 J/cm² per lesion, and the probe was held perpendicularly at a distance of about 2 mm. The time of delivery per point of application is calculated using the formula t (time)=D (dose-fluence) X A (area of the spot)/P (output power).

d) Histological evaluation with OCT;

e) continue, num = 8 sessions (2 times for week for a total of 4 weeks), and new evaluation with OCT;

f) Follow-up to 1, 3, 6, 12 months (after end of the therapy), with assessments respective OCT.
**Group B:**

a) Selection of patients affected of erosive and painful OLP, in a prospective manner (n=50);

b) Rating histopathological OCT HSL-2100-HW 50 kHz scan rate (Santec);

c) Start the “gold-standard” drug therapy with clobetasol dipropionate 0.05% in an aqueous gel of 4% hydroxyethyl cellulose (100 g) in equal parts (50:50): domiciliary applications 2 times/ day for 4 weeks;

d) Histological evaluation with OCT;

e) Complete treatment after other 4 weeks at the same dose and evaluation with OCT;

f) Follow-up to 1, 3, 6, 12 months (after end of the therapy), with assessments respective OCT.

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**Skills and competencies for the development of the activity**

The applicant must have experiences and skills in Oral Medicine and Special Need Patients (documentable in research and hospital activities), possible having already achieved a Master of Science in Oral Medicine. Especially documented activities in LLLT in oral diseases must be provided. She/he will need to work actively in a team to set standards and procedures that achieve an elevated level of quality and productivity. The incumbent would play a significant role in the expansion of the educational and clinical missions of the School in an environment strongly supportive of inter-professional engagement. Duties include and are not limited to overseeing the project proposed, teaching of oral medicine to dental and graduate students, active participation in diagnostic consultation for patients of the School, and engagement in interdisciplinary research.