

## Clinical applications of ILIB technique in Dentistry – State of Art

Aplicações clínicas da técnica ILIB na Odontologia – Estado da Arte

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### **Abstract**

Intravascular Laser Irradiation of Blood (ILIB) represents a systemic laser photobiomodulation, where irradiation of a given artery is recommended through the use of laser light with different wavelengths. The technique developed in the 1970s, in the former Soviet Union. The present narrative review aimed to describe current aspects of ILIB therapy and its indications in different areas of health, especially in Dentistry. For the selection, searches were carried out in the PubMed, Google Scholar, Scielo and Cochrane databases, from October 2020 to January 2021. Scientific articles were selected in Portuguese and English, which had the full text available and which were published between 2015 and 2020. Some manuscripts were added for contextualization, totaling 53 studies. It was observed that the systemic effect of ILIB is achieved by irradiating the blood circulation. Increased cellular metabolism, increased production of nitric oxide and stimulated the action of the enzyme CuZn Superoxide Dismutase have been reported, and also had a documented analgesic and anti-inflammatory effect. Studies suggest that ILIB has been indicated in different areas of health and can be applied in the prevention and treatment of systemic and local, chronic and acute conditions. In dentistry, the technique was most suitable for the treatment of inflammatory conditions, such as periodontitis, mucositis, postoperative surgeries and orofacial pain. Thus, the effects of ILIB suggest its use in dental practice. However, further studies are needed, such as randomized clinical trials, to validate the use of ILIB.

**Keywords:** Low-level light therapy; Lasers; Lasers, Semiconductor; Light.

### **Resumo**

A Irradiação Intravascular de Sangue a Laser (ILIB) representa uma modalidade de fotobiomodulação sistêmica, em que a irradiação de uma determinada artéria é realizada através de luz laser com diferentes comprimentos de onda. A técnica foi desenvolvida na década de 1970, na antiga União Soviética. A presente revisão narrativa teve como objetivo descrever os aspectos atuais da terapia ILIB e suas indicações em diferentes áreas da saúde, especialmente na Odontologia. Para a seleção dos artigos, foram realizadas buscas nas bases PubMed, Google Acadêmico, Scielo e Cochrane, no período de outubro/2020 a janeiro/2021. Foram selecionados artigos científicos em português e inglês, com texto completo disponível e publicados entre 2015 e 2020. Alguns manuscritos foram adicionados para contextualização, totalizando 53 estudos. Observou-se que o efeito sistêmico da ILIB é alcançado através da irradiação da circulação sanguínea. Na literatura, há relatos do aumento do metabolismo celular, aumento da produção de óxido nítrico e estímulo da enzima CuZn Superóxido Dismutase, além de promover efeito analgésico e anti-inflamatório. Estudos sugerem que a ILIB tem sido indicada em diferentes áreas da saúde e pode ser aplicada na prevenção e tratamento de condições sistêmicas e locais, crônicas e agudas. Na Odontologia, indica-se para o tratamento de

condições inflamatórias, como periodontite, mucosite, pós-operatório de cirurgias e dores orofaciais. Desta maneira, os efeitos da ILIB sugerem seu uso na prática odontológica. No entanto, mais estudos são necessários, como ensaios clínicos randomizados, para validar o uso desta ferramenta.

**Palavras-chave:** Terapia de luz de baixa intensidade; Lasers; Lasers, Semicondutores; Luz.

### Resumen

La Irradiación Láser Intravascular de la Sangre (ILIB) representa la fotobiomodulación láser sistémica, donde se recomienda la irradiación de determinada arteria con láser con diferentes longitudes de onda. La técnica desarrollada en la década de 1970, en la antigua Unión Soviética. La presente revisión narrativa tuvo como objetivo describir aspectos actuales de la terapia ILIB y sus indicaciones en diferentes áreas de la salud, especialmente en Odontología. Para la selección, se realizaron búsquedas en las bases PubMed, Google Scholar, Scielo y Cochrane, de octubre/2020 a enero/2021. Se seleccionaron artículos científicos en portugués e inglés, que tuvieran disponible el texto completo y que fueron publicados entre 2015 y 2020. Se agregaron algunos manuscritos para contextualización, totalizando 53 estudios. Se observó que el efecto sistémico de ILIB se logra al irradiar la circulación sanguínea. Se ha informado aumento del metabolismo celular, de la producción de óxido nítrico y estimulación de la acción de la enzima CuZn Superóxido Dismutasa. También tuvo un efecto analgésico y antiinflamatorio. Los estudios sugieren que ILIB se ha indicado en diferentes áreas de la salud y se puede aplicar en la prevención y tratamiento de condiciones sistémicas y locales, crónicas y agudas. En Odontología, la técnica es adecuada para el tratamiento de afecciones inflamatorias, como periodontitis, mucositis, cirugías posoperatorias y dolor orofacial. Los efectos de ILIB sugieren su uso en la práctica dental. Sin embargo, se necesitan más estudios, como ensayos clínicos aleatorizados, para validar el uso de ILIB.

**Palabras clave:** Terapia de luz de bajo nivel; láseres; Láseres, Semicondutores; Luz.

## 1. Introduction

The acronym ILIB refers to Intravascular Laser Irradiation of Blood (ILIB) and represents a therapeutic modality of systemic laser photobiomodulation. This technique recommends the irradiation of a certain artery through the use of blue, red or green laser light. Because it is the application of laser light across a reduced spectrum, it has an easier targeting and absorption, which contribute to the induction of its biostimulatory effects (Ansari, 2015; Meneguzzo et al., 2019; Tomé et al., 2020).

Originally, this technique consisted of inserting a catheter, associated with an optical fiber, intravascularly. However, due to its invasive character, this practice has been less used. At present, the therapy has been carried out transcutaneously and consists of the application of a specific type of laser in the anatomical region close to an artery, such as the radial, for example, in order to make light contact with this vessel viable, and this way. To enable the primary effects of laser therapy to reach other tissues through the bloodstream (Lima, 2019; Meneguzzo et al., 2019).

Photobiostimulatory therapies, such as ILIB, have gained increasing popularity among the scientific community as a result of their medicinal therapeutic properties (KazemiKhoo & Ansari, 2015). The recent research suggests that this technique would act on several systemic healing mechanisms in order to control inflammatory processes and induce the production of nitric oxide (NO) with a vasodilating and pro-angiogenic action. This way, it would make it possible to reduce tissue hypoxia and favor tissue oxygenation. ILIB has proven to be a powerful, low-cost tool for the treatment of systemic conditions, such as high blood pressure and type 2 diabetes mellitus (Ansari, 2015; KazemiKhoo & Ansari, 2015).

The therapeutic properties presented by laser photobiomodulation have allowed it to be widely used by several areas of health, among which is Dentistry. The biostimulatory effects promoted by this therapy, in addition to its systemic action, can be observed locally and favor tissue repair, with control of the inflammatory process, analgesia and antimicrobial action. Thus, the use of ILIB in several dental specialties has become more frequent, especially in periodontics and postoperative oral surgical procedures (Lima, 2019; Silva, 2019).

Given the possibilities offered by this therapeutic modality and the scarcity of studies that address its applicability in some areas of health, with emphasis on Dentistry, the present narrative literature review aimed to highlight its possible mechanisms of action and biostimulatory effects, as well as how to check clinical indications in dental practice.

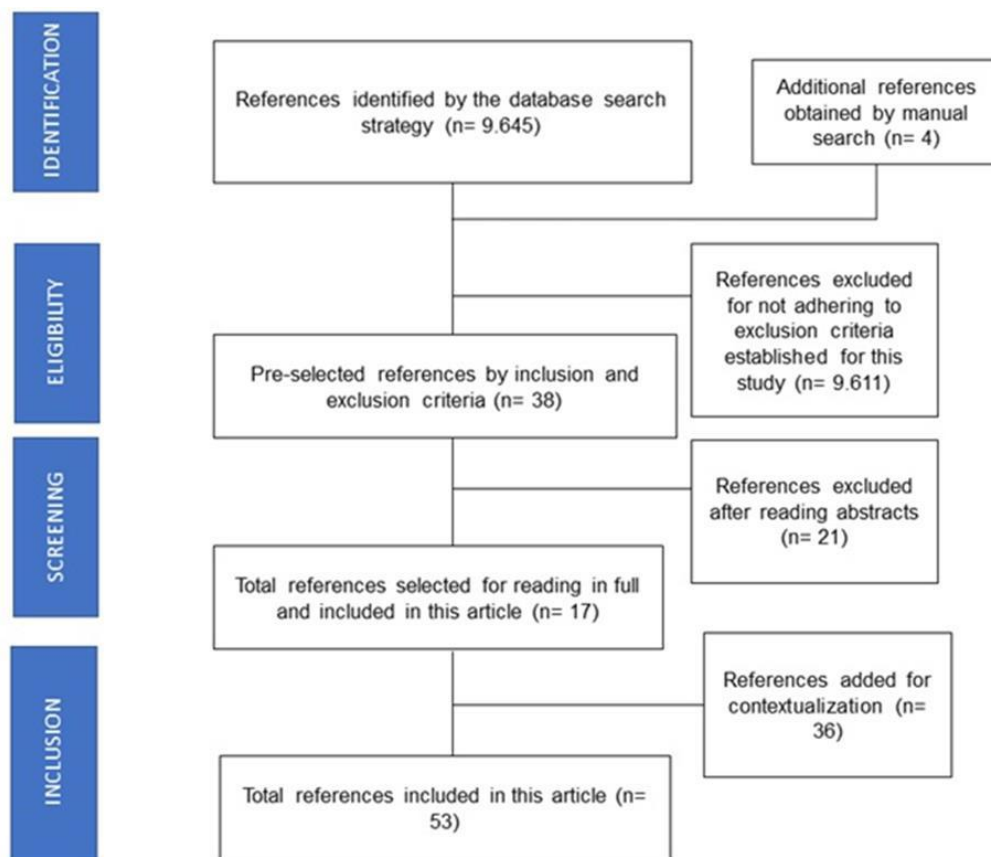
## 2. Methodology

It was a narrative literature review. For the selection of articles on the chosen theme, a bibliographic search was performed in the databases PubMed, Google Scholar, Scielo and Cochrane, from October 2020 to January 2021. The descriptors selected for the research were “ILIB”, “Transcutaneous Laser”, “Intravascular Laser”, “Intravenous Laser”. In order to establish the relationship between the use of this technique and Dentistry, the aforementioned terms associated with the Boolean expression AND were used, with the following combinations “ILIB AND Dentistry”, “Intravascular Laser AND Dentistry”, “Intravascular Laser AND Dentistry”, “Transcutaneous Laser AND Dentistry” and “Transcutaneous Laser AND Dentistry”.

The inclusion criteria for the selection of scientific articles included manuscripts in Portuguese and English, which had the full text available and which were published between 2015 and 2020. Articles that did not approach the proposed theme, that were outside the period, as well as a clinical case report, were excluded. Some articles published prior to the specified period were included to contextualize the theme of this review due to its scientific relevance.

After consulting the databases and applying the search strategies, as well as using the inclusion and exclusion criteria, 6 articles were identified in PubMed, 18 in Google Scholar, 11 in Scielo and 3 in Cochrane, making a total of 38 manuscripts. Three studies were removed because they were duplicated. In addition, 4 articles were added through manual search and consultation of the bibliographic references of the manuscripts included in the review. Subsequently, after reading the abstracts, 17 studies remained, which were selected for full reading of the text and included in the present narrative review since they exclusively addressed the theme ILIB (Figure 1). Additional studies (n = 36) were used to contextualize the clinical indications and cellular and / or molecular mechanisms modulated by the use of ILIB.

**Figure 1** - Articles search strategy, according to the inclusion criteria outlined. Search period: October 2020 to January 2021.



Source: Own authorship.

### 3. State of Art

#### 3.1 History and general aspects of the ILIB technique

The concept of photobiomodulation encompasses techniques that use light in order to promote systemic and local biological effects. Among these techniques, low-intensity laser photobiomodulation can be mentioned, where the ILIB technique is inserted. Traditionally, the use of light for therapeutic purposes is located in the visible light spectrum that covers the bands from red to infrared. However, there is evidence in the literature that blue and green light can also produce biomodulatory effects of a systemic character (Serrage et al., 2019).

ILIB is a non-medicated therapeutic practice, with biostimulatory properties, so that it can have wide applicability in living beings. The word laser is an acronym that translates to Amplification of Light by Stimulated Emission of Radiation or Light Amplification by Stimulated Emission of Radiation, which corresponds to an irradiation of the non-ionizing electromagnetic type. It is believed that specific wavelengths of electromagnetic irradiation (400-1100 nm) can cause photochemical and photo-physical effects, and thus, promote biological repercussions (Lima, 2019; Serrage et al., 2019).

The development of ILIB therapy began in the 1970s, in the former Soviet Union, by Russian scientists Meshalkina and Sergievsky. Initially, the studies were conducted with a HeNe laser (632.8 nm), power from 1 to 3 mW, with an application time of approximately 30 minutes, with the objective of evaluating the primary effects of laser light on the cardiovascular system, through the observation of anatomical sites with signs of ischemia and /or those with increased microcirculation. These initial clinical investigations proposed to elucidate the therapeutic properties of ILIB and the mechanisms involved in this therapy (Lima, 2019; Meneguzzo et al., 2019).

Due to questions of a political nature that date back to the implementation of the ILIB technique, the information obtained from the first observational studies was not widely disseminated in the world scientific community and was more restricted to Russia for a long period. As a consequence, the ILIB has not had major repercussions in the scientific literature and its use has not been encouraged due to the low presence of scientific evidence. However, at the beginning of the 21st century, there was a growing interest in this therapeutic modality and it started to be studied more in several countries, such as Japan, China, Canada and Northern Ireland (Meneguzzo et al., 2019; Moskvina, 2017).

The original technique was characterized by the intravascular insertion of a disposable catheter associated with a 2mm thick optical fiber in veins, which provided blood irradiation directly and continuously (Silva, 2019; Tomé et al., 2020). However, this methodology was discontinued due to its more invasive character (Meneguzzo et al., 2019). At present, the clinical practice consists of an indirect route of administration over an artery through an electrode. Thus, it came to be called modified ILIB.

Currently, two types of ILIB have been described in the literature. The first modality includes intravascular irradiation through the skin in the wrist region, also known as transcutaneous ILIB. In this technique, the optical fiber is positioned over the skin towards the radial artery. The device is kept in position with the aid of an elastic bracelet (Figure 2). It has been described as a safer and more comfortable technique for the patient (Silva, 2019; Wang et al., 2016). Intranasal irradiation, initially known as low intensity intranasal laser therapy (ILILT), consists of inserting the optical fiber into the internal region of the nostril. The protocol suggests that the application occurs between 15 to 30 minutes, using a diode laser (650-660 nm) (Meneguzzo et al., 2019).

**Figure 2** - Application of the ILIB technique ILIB via transcutaneous.



Source: Own autorship.

### 3.2 Biological Effects of ILIB

With the inclusion of laser photobiomodulation in clinical practices and its increasing popularity, it was possible to generate a large number of information about the therapeutic properties of ILIB. This therapeutic resource triggers a systemic effect, achieved through the irradiation of the blood circulation and, thus, affects other tissues. It has been documented a possible modulation of the mitochondrial redox system and, consequently, a reduction in the biological markers of oxidative stress. However, the nature of this mechanism of action is still unknown (KazemiKhoo & Ansari, 2015; Wang et al., 2016; Pin et al., 2018; Dominguéz & Velásquez, 2020).

Among the scientific community, the absorption of photons emitted by the laser by the enzyme cytochrome c oxidase (CCO) is accepted as the source of the benefits obtained by photobiomodulatory therapies. It is a component of the electron transport chain, responsible for converting  $O_2$  molecules into  $H_2O$ . Concomitant, the synthesis of adenosine triphosphate (ATP) occurs. It is believed that CCO is the main photoreceptor of light and, when stimulated, causes a greater breakdown of oxygen molecules in the tissue. Another direct consequence of this mechanism would be the increase in blood oxygen concentration, due to the increased metabolism, culminating in the reduction of tissue hypoxia (Wang et al., 2016; Serrage et al., 2019).

The direct effect of ILIB's action on the mitochondrial redox system consists of controlling the production of reactive oxygen species (ROSs), which originate from the oxidative metabolism of the mitochondria (Tafur & Mills, 2008). It is known that these, when in excess, have a cytotoxic effect that results in cellular and tissue damage and, as a rule, cell death. However, more recent evidence suggests that ROSs can trigger cellular signaling mechanisms and, consequently, regulate tissue metabolism through cell proliferation and death (Menon & Goswami, 2006). In fact, according to Huang et al. (2012), the intravascular application of HeNe laser (632.8nm) results in increased mitochondrial metabolism, by increasing the biosynthesis of ATP and mtDNA molecules, and generation of ROSs.

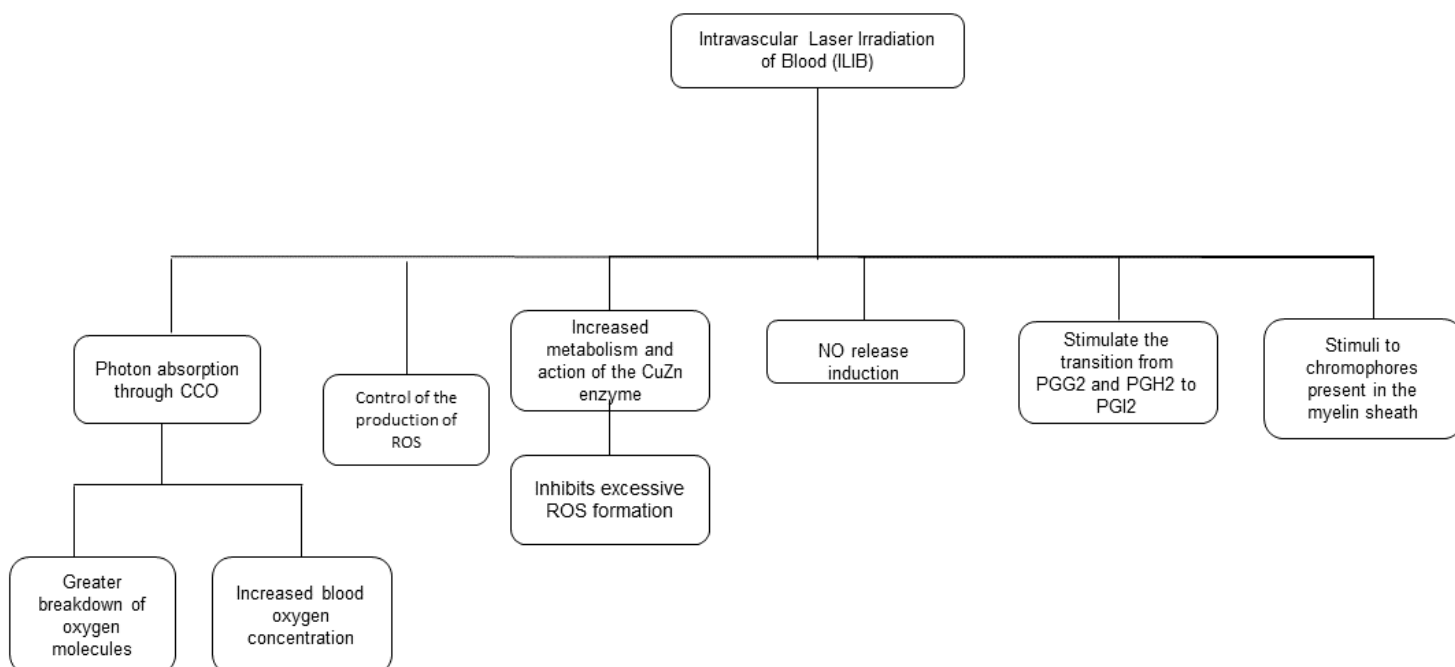
Another possible antioxidant mechanism presented by the ILIB is the increase in the metabolism and action of the enzyme CuZn Superoxide Dismutase (SOD) (Meneguzzo et al., 2019; Dominguéz & Velásquez, 2020). It is a component of the enzymatic antioxidant defense system, responsible for converting  $O_2$  into  $H_2O_2$ . This molecule represents part of the cellular defense mechanism against oxidative stress, composed of the enzymes catalase (CAT) and glutathione oxidase (GPx). Together, these inhibit the excessive formation of ROS, and prevent the spread of cell damage (Menon & Goswami, 2006; Barbosa et al., 2010). As a result of its antioxidant property, blood irradiation with laser would cause a balance of redox potential in the patient's

tissues as a whole, which can culminate in the control of systemic pathological processes, such as coronary artery disease (CAD), atherosclerosis, diabetes mellitus type 2, among others (Meneguzzo et al., 2019).

The antioxidant actions triggered strongly influence the systemic effects obtained as a result of its administration. These can be achieved in several ways. It is believed that ILIB (634nm) is also capable of inducing the release of 97% more nitric oxide (NO) present in human monocytes, according to the study by Lindgård et al. (2006). NO is a simple gas molecule, which acts as a cellular messenger, endogenous vasodilator and a cytotoxic molecule for invading microorganisms (Flora & Zilberstein, 2000; Makela, 2005). Originated in the process of catalyzing L-arginine, especially in endothelial cells and monocytes, NO induces mitochondrial biogenesis, telomerase activity and reduced ROS production (Lindgård et al., 2006).

Some studies indicate that the therapy can induce, by stimulating the chromophores present in the myelin sheath of peripheral nerves, an analgesic effect, in order to contribute to a better quality of life for patients with chronic diseases (Wang et al., 2016; Jang & Lee, 2012). Another possible effect presented by the therapy is its performance in the process of synthesis of prostaglandins. ILIB has been documented to stimulate the transition from prostaglandin G<sub>2</sub> (PGG<sub>2</sub>) and prostaglandin H<sub>2</sub> (PGH<sub>2</sub>) to prostaglandin I<sub>2</sub> (PGI<sub>2</sub>) (Kahraman, 2004). Such chemical mediators, of lipid origin, have a similar function to hormones, in order to act in cellular signaling mechanisms, such as the inflammatory response and pain mechanisms (Seo & Oh, 2017). PGI<sub>2</sub>, or prostacyclin, is a mediator of lipid origin derived from arachidonic acid, which is produced mainly by endothelial cells. It has an important vasodilating and anti-inflammatory effect, and promotes pain reduction and modulation of the inflammatory process (Kelton & Blajchman, 1980; Tam, 1999; Mitchell & Kirkby, 2019). A synthesis of the biological effects triggered by ILIB is shown in Figure 3.

**Figure 3** - Graphical representation of the biological effects generated by the ILIB therapy.



Source: Own authorship.

### 3.3 Clinical indications of ILIB in different health areas

For more than 40 years, ILIB has been applied in the most diverse health areas. The biological effects favor its indication for the treatment of chronic systemic conditions. For example, in individuals with diabetes mellitus who have microangiopathy and peripheral neuropathy, the development of wounds resulting from tissue hypoxia and secondary hypertension can be seen



(Reiber et al., 1992; Houreld et al., 2010; Chapple & Genco, 2013). It is believed that ILIB therapy may be effective in the management of these clinical conditions due to its possible effect on L-arginine and NO, and also by the ability to induce an immediate hypoglycemic effect, due to the influence of these molecules on the glucagon hormones, insulin and growth hormone (GH) (Ansari, 2019; KazemiKhoo et al., 2016; Meneguzzo et al., 2019). It is known that as a result of high blood glucose, diabetic patients may present tissue hypoxia, reduced NO in their tissues and an impaired tissue repair process (Reiber et al., 1992). Thus, due to its antioxidant capacity and controlling the metabolism of ROSs, ILIB can induce the reduction of tissue hypoxia and increase the supply of oxygen to the tissues. Thus, it favors the healing process (Houreld et al., 2010; KazemiKhoo et al., 2016).

It is also believed that some complications caused by diabetes, such as cardiovascular and endothelial dysfunction, have a relationship with the positive regulation of arginase. It is an enzyme responsible for hydrolyzing L-arginine in urea and L-ornithine. The literature indicates that its increase reduces the production of NO, and contributes to the development of tissue and vascular damage already mentioned. Thus, the ability to release NO, presented by ILIB, favors its indication for the prevention and treatment of these diseases (Shemyakin et al., 2012; Kazemi Khoo et al., 2016).

ROSs can induce oxidative stress on tissue components. When generated in high quantities, these species cause damage to biological structures, such as cell membranes and mitochondria (Meneguzzo et al., 2019; Domínguez, Velásquez & David, 2020). It is believed that ILIB therapy, through its control of oxidative stress generated due to oxygen metabolism, can be administered to patients with chronic alterations, such as autoimmune and neuropathic diseases (Huang et al., 2012; Wang et al., 2016; Tomé et al., 2020).

ILIB is used in a multidisciplinary way, being used by professionals from different health areas, such as Speech Therapy, Physiotherapy and Nursing (Mikhaylov, 2015; Gomes & Schapochnik, 2017; Weis, 2018; Xiong et al., 2021). The biomodulatory effects induced by the practice, favor an early intervention and with systemic amplitude, and it has been considered a useful therapeutic option in practices of the so-called Integrative Medicine (IM). It is a health model focused on therapeutic actions and the study of problems associated with lifestyle, through the implementation of Integrative and Complementary Practices (Otani & Barros, 2006). As for IM, photobiomodulatory therapies have gained space in Physiotherapy (Weis, 2018). Their therapeutic properties allow them to be used in treatments for chronic pain, inflammation, allergic rhinitis, musculoskeletal injuries and, also, to favor the healing process (Burduli & Gutnova, 2010; Yıldırım et al., 2013). Therefore, the integration of this technique in the clinical practice of these professionals had a positive impact on the patient's prognosis (Scheerder et al., 2001; Xiao et al., 2003; Babaev et al., 2012; Tomimura et al., 2014). Table 1 describes some studies that evaluated the applicability of ILIB in different clinical conditions.

**Table 1** - Indications of ILIB and its clinical effects documented in the literature.

Clinical condition	Effects	Author (Year)
<i>Vascular diseases</i>	Stimulus to angiogenesis Reduction of spheric areas Elimination of vessel spasms Elimination of blood stasis Hypocoagulant effect Increased blood fibrinolytic activity Reduction in fibrinogen levels Increased fibrinolysis Prothrombin proportion reduction	Mikhaylov, 2015
<i>Myopia</i>	Progression speed reduction Assistance in controlling the axial lengthening of the eye	Xiong et al., 2021
<i>Pancreatitis</i>	Sharp initial rise in ceruloplasmin production	Burduli & Gutnova, 2010
<i>Allergic Rhinitis</i>	Reduction symptom severity	Yildirim et al., 2013
<i>Clinical Intrastent</i>	Avoid proliferation and migration of smooth muscle cells	de Scheerder et al., 2001
<i>Brain Stroke</i>	Increases the level of cAMP in blood cells  Reduces blood viscosity Improves microcirculation Reduces oxidative stress Exacerbated immune response	Xiao et al., 2013
<i>Hepatocellular insufficiency</i>	56% reduction in Bilirubin levels 19.8% reduction in blood urea levels 11% reduction in creatinine levels Reduction in Aspartate Aminotransferase activity Reduction in Alanine Aminotransferase activity Reduction in Lactate Dehydrogenase activity	Babaev et al., 2012
<i>Systemic Arterial Hypertension</i>	Decrease in Heart Rate	Tomimura et al., 2014
<i>Chronic Spinal Cord Injury</i>	Quantitative increase in mtDNA Increased ATP synthesis Significant reduction in Malondialdehyde Control of oxidative stress LDL reduction	Huang et al., 2012

Source: Own autorship.

### 3.4 Clinical indications of ILIB in Dentistry

The biological effects induced by ILIB can favor the clinical practice of dental surgeons and induce positive results during the treatment of certain disorders of the stomatognathic complex. Several illnesses are present in the clinical practice of the dentist, among them, periodontal diseases (PD) stand out, such as periodontitis (Armitage, 1999; Almeida et al., 2006). It is known that chronic systemic diseases, such as diabetes mellitus, can influence the progression of PD and affect its prognosis (Chapple & Genco, 2013; Taylor, Preshaw & Lalla, 2013). It is believed that ILIB, as an adjunct therapy to scaling and root



planing, may favor the control of PD, due to its hypoglycemic and antioxidant action, by reducing oxidative stress (Abdulkabbar et al, 2017; Santos et al., 2019).

Surgical procedures in the area of Dentistry include small and large oral surgeries, as well as surgeries that cover more extensive anatomical sites. In the postoperative period of all types of surgical procedures, ILIB can be indicated due to the inflammatory and painful conditions that affect the tissues involved (Oliveira et al., 2013). The literature indicates that transcutaneous laser therapy is capable of modulating the inflammatory infiltrate and pain in order to reduce these processes. As a consequence, it can decrease the occurrence of trismus, and thus, provide a more positive postoperative experience for the patient (Seo & Oh, 2017).

Antineoplastic therapies, such as radio and/or chemotherapy, have side effects that are often deleterious due to their cytotoxicity, including the stomatognathic system, as in the case of the development of oral mucositis (OM). OM is characterized by the presence of inflammation, which promotes pain, odynodyphagia, dysgeusia and, consequently, malnutrition, which directly affects the patient's quality of life (Kostler et al., 2001). Due to the effects obtained from photophysical and biochemical processes, it is believed that low-level laser therapies, such as ILIB, can assist in the prevention and treatment of OM, since the therapy is able to accelerate the healing process, reduce pain and assist in the treatment of xerostomia, factors associated with its progression (Reolon et al., 2017).

Another very common clinical condition in dental practice is temporomandibular disorder (TMD), which can be defined as a set of clinical problems that affect the masticatory muscles, the temporomandibular joint (TMJ) and its associated structures. TMD can have a negative impact on the quality of life of its patients. As clinical signs and symptoms, pain in the muscles associated with chewing, TMJ pain, joint crackling, headache, muscle tenderness, among others are mentioned (Shukla & Muthusekhar, 2016). There are studies that report the indication of photobiomodulatory therapies for non-invasive treatment of this clinical condition, in order to reduce its main symptom, which is pain, and, consequently, favor the restoration of patients' quality of life (Shukla & Muthusekhar, 2016; Munguia et al., 2018). However, there is a scarcity of studies that have assessed the impact of ILIB as an effective therapeutic approach in the management of TMD. In fact, in dentistry, despite the wide spectrum of use of laser photobiomodulation, ILIB still remains little explored. Table 2 describes some studies that evaluated the applicability of ILIB in dentistry.

#### **4. Final Considerations**

ILIB has been present for over 40 years as a technique capable of causing several biological effects, such as inflammation biomodulation, analgesia, oxidative stress control, among others. These characteristics favor its use in several areas of health, specially in dentistry. However, despite evidence already documented in the literature, ILIB still lacks clinical studies in order to expand knowledge about its biomodulatory effects, especially randomized clinical trials. It is important to highlight that a large part of the published studies on ILIB are available only in the Russian language, a fact that makes it difficult to access the results of investigations in this area.

**Table 2** - Applicability of ILIB in dentistry.

Clinical condition	Effect	Author (Year)
<i>Periodontal Disease (PD)</i>	Favor the control of the PD	Abduljabbar et al., 2017
<i>Postoperative period of surgical procedures</i>	Modulation the inflammatory infiltrate Pain reduction	Oliveira Sierra e al., 2013
<i>Oral Mucositis (OM)</i>	Acceleration of the healing process Reduction in pain Assist in the treatment of xerostomia	Reolon et al., 2017
<i>Temporomandibular disorder (TMD)</i>	Reduction in pain	Assis, Soares & Victor, 2012 Shukla & Muthusekhar, 2016 Munguia et al., 2018

Source: Own authorship.

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