

## Effect of Low-Level Laser Therapy on Osseointegration: A Comprehensive Review

Dr Raghavendra Adaki<sup>1</sup>, Dr Shridevi Adaki<sup>2</sup>, Dr Amol Karagir<sup>3</sup>, Dr Jivanasha Agrawal<sup>4</sup>

1Professor and HOD, Department of Prosthodontics, Bharati Vidyapeeth Deemed to be University, Dental College and Hospital, Sangli, Email: [raghavendra.adaki@bharativedyapeeth.edu](mailto:raghavendra.adaki@bharativedyapeeth.edu)

2Associate Professor, Department of Oral Medicine and Radiology, Bharati Vidyapeeth Deemed to be University, Dental College and Hospital, Sangli, Email: [shridevi.adaki@bharativedyapeeth.edu](mailto:shridevi.adaki@bharativedyapeeth.edu)

3Assistant Professor, Department of Oral Medicine and Radiology, Bharati Vidyapeeth Deemed to be University, Dental College and Hospital, Sangli, Email: [amol.karagir@bharativedyapeeth.edu](mailto:amol.karagir@bharativedyapeeth.edu)

4Professor and HOD, Department of Orthodontics and Dentofacial Orthopedics, Bharati Vidyapeeth Deemed to be University, Dental College and Hospital, Sangli, Email: [jivanasha.agrawal@bharativedyapeeth.edu](mailto:jivanasha.agrawal@bharativedyapeeth.edu)

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### ABSTRACT

Low-Level Laser Therapy (LLLT), also known as photobiomodulation, has garnered attention in the field of implant dentistry for its potential to enhance osseointegration—the direct structural and functional connection between living bone and the surface of a load-bearing implant. This review aims to critically evaluate the current evidence on the efficacy of LLLT in promoting bone regeneration and improving the integration of dental implants with surrounding bone tissue. By analysing both preclinical and clinical studies, we seek to elucidate the underlying mechanisms of LLLT and its practical applications in enhancing implant success rates.

**Keywords:** Laser Therapy, Bone Regeneration, Dental Implants, Photobiomodulation

### 1. INTRODUCTION

The success of dental implants largely depends on effective osseointegration, a process that ensures the stable anchorage of the implant within the bone. Achieving optimal osseointegration is influenced by various factors, including the biological response of bone tissue, implant surface properties, and patient-related conditions such as bone quality and systemic health. Despite advancements in implant design and surgical techniques, challenges persist in enhancing bone healing, particularly in patients with compromised bone conditions.

LLLT has emerged as a non-invasive therapeutic modality purported to stimulate cellular activity and promote tissue repair. The application of LLLT in bone healing and osseointegration has been the subject of numerous studies, with varying outcomes. In vitro and in vivo research suggests that LLLT may enhance osteoblastic activity, increase vascularization, and modulate inflammatory responses, thereby facilitating bone regeneration.<sup>1</sup> However, the clinical efficacy of LLLT in improving implant integration remains a topic of debate.

This review aims to provide a comprehensive analysis of the existing literature on the effects of LLLT on osseointegration. By examining both experimental and clinical studies, we seek to clarify the potential benefits and limitations of LLLT in the context of dental implantology. Understanding the mechanisms by which LLLT influences bone healing processes is crucial for developing standardized treatment protocols and optimizing patient outcomes.

### 2. MECHANISMS OF LOW-LEVEL LASER THERAPY IN BONE HEALING

Low-Level Laser Therapy (LLLT), also known as photobiomodulation, has been extensively studied for its potential to enhance bone healing processes. The mechanisms by which LLLT influences bone repair are multifaceted, involving cellular proliferation, modulation of inflammatory responses, and promotion of angiogenesis.

#### 1. Cellular Proliferation and Differentiation

LLLT has been shown to stimulate the proliferation and differentiation of osteoblasts, the cells responsible for bone formation.<sup>2</sup> This effect is primarily mediated through the absorption of specific wavelengths of light by mitochondrial

chromophores, leading to increased adenosine triphosphate (ATP) production and enhanced cellular activity. The upregulation of reactive oxygen species (ROS) following LLLT exposure also plays a crucial role in osteogenic differentiation, as ROS act as secondary messengers in various signaling pathways that promote bone regeneration.<sup>2</sup>

## 2. Modulation of Inflammatory Responses

The inflammatory phase is a critical initial step in bone healing. LLLT has been observed to modulate this phase by reducing the expression of pro-inflammatory cytokines and increasing anti-inflammatory cytokines.<sup>3</sup> This modulation creates a more favorable environment for tissue repair and regeneration. Studies have demonstrated that LLLT can influence the expression of genes related to inflammation, thereby accelerating the healing process.<sup>3</sup>

LLLT irradiation stimulates [mitochondrial metabolism](#), which results in an increased expression of adenosine triphosphate (ATP), molecular oxygen production<sup>4</sup> and transcription factors.<sup>5</sup> These effects may increase the synthesis of DNA, RNA and cell-cycle regulatory proteins, therefore stimulating [cell proliferation](#).<sup>6, 7</sup> Moreover, LLLT could modulate the expression of some [inflammatory mediators](#) such as [interleukin 1 \$\beta\$](#) , (IL1 $\beta$ ), [interleukin 6](#) (IL6), [interleukin 10](#) (IL10) and [tumor necrosis factor  \$\alpha\$](#)  (TNF $\alpha$ ).<sup>4, 8, 9, 10</sup>

## 3. Promotion of Angiogenesis

Effective bone healing requires the formation of new blood vessels to supply nutrients and oxygen to the regenerating tissue. LLLT has been shown to promote angiogenesis by stimulating endothelial cell proliferation and migration.<sup>2</sup> This process ensures adequate vascularization of the healing bone, which is essential for successful osseointegration and overall bone health.<sup>2</sup>

## 4. Enhancement of Osteogenic Differentiation of Stem Cells

LLLT has been reported to promote the osteogenic differentiation of mesenchymal stem cells (MSCs), which are progenitor cells capable of developing into osteoblasts.<sup>2</sup> This effect is partly due to the increase in ROS levels induced by LLLT, which activate signaling pathways that drive osteogenesis.<sup>2</sup> By enhancing the differentiation of MSCs into bone-forming cells, LLLT contributes to improved bone regeneration and healing.<sup>2</sup>

## 5. Acceleration of Fracture Healing

Clinical and preclinical studies have indicated that LLLT can accelerate the fracture healing process.<sup>11</sup> This acceleration is attributed to the combined effects of enhanced osteoblastic activity, reduced inflammation, and improved angiogenesis. The application of LLLT has been associated with increased callus formation and mineralization, leading to faster bone repair.

## 6. Influence on Gene Expression

LLLT has been shown to affect the expression of genes involved in bone healing. By modulating the expression of specific genes related to inflammation and angiogenesis, LLLT creates a more conducive environment for bone regeneration.<sup>3</sup>

## 3. PRECLINICAL STUDIES

Preclinical research has extensively investigated the effects of Low-Level Laser Therapy (LLLT) on osseointegration using various animal models.<sup>12</sup> These studies have consistently demonstrated that LLLT can enhance bone healing and implant integration. For instance, Oliveira et al. evaluated the osseointegration of implants placed in areas grafted with different osteoconductive bone substitutes and irradiated with infrared LLLT.<sup>12</sup> The study found that LLLT improved osseointegration in grafted sites, suggesting its potential to enhance bone healing in compromised conditions.

Another study investigated the effect of LLLT on the stability of implants placed in the posterior maxilla of rabbits.<sup>13</sup> The results indicated that LLLT promoted better implant stability and bone formation around the implants, highlighting its positive influence on osseointegration.

Additionally, a study assessed the effects of LLLT on the healing and attachment of titanium implants in bone using a rabbit model.<sup>14</sup> The findings demonstrated that LLLT enhanced peri-implant bone formation, as evidenced by resonance frequency analysis and micro-computed tomography.

## 4. CLINICAL STUDIES

Clinical investigations have also explored the efficacy of LLLT in enhancing osseointegration in human subjects. A pilot clinical study<sup>15</sup> evaluated the effect of LLLT on the osseointegration of immediate dental implants in the anterior and premolar regions of the mandible. The study concluded that LLLT improved implant stability and accelerated the osseointegration process, suggesting its potential as an adjunctive therapy in implant dentistry.

Similarly, a clinical trial assessed the effect of LLLT on the osseointegration of immediately loaded implants with a connective tissue graft.<sup>16</sup> The findings demonstrated that LLLT had a positive effect on implant stability and bone healing, supporting its clinical application in enhancing osseointegration.

Furthermore, a study evaluated the influence of postoperative LLLT on the osseointegration of self-tapping implants in the posterior maxilla.<sup>17</sup> The results indicated that LLLT improved implant stability and bone formation, highlighting its potential to enhance osseointegration in clinical settings.

## 5. MECHANISTIC INSIGHTS

Low-Level Laser Therapy (LLLT) has been shown to enhance bone healing and osseointegration through several interconnected biological mechanisms:

1. **Promotion of Angiogenesis:** LLLT stimulates the formation of new blood vessels, ensuring an adequate blood supply essential for bone regeneration.<sup>2</sup> This process is mediated by the upregulation of vascular endothelial growth factor (VEGF), which facilitates the growth of new capillaries within the healing bone tissue.<sup>2</sup>
2. **Stimulation of Osteogenic Differentiation:** LLLT enhances the differentiation of mesenchymal stem cells into osteoblasts, the cells responsible for bone formation.<sup>2</sup> This effect is achieved through the activation of signaling pathways such as the Wnt/ $\beta$ -catenin pathway, leading to increased expression of osteogenic markers like osteocalcin and alkaline phosphatase.<sup>2</sup>
3. **Modulation of Reactive Oxygen Species (ROS):** LLLT induces a transient increase in ROS levels, which act as secondary messengers in cellular signaling pathways.<sup>2</sup> This controlled ROS production promotes osteoblast proliferation and differentiation, contributing to enhanced bone healing.
4. **Coupling of Angiogenesis and Osteogenesis:** By simultaneously promoting blood vessel formation and osteogenic activity, LLLT ensures a synchronized healing process.<sup>2</sup> The enhanced vascularization supplies necessary nutrients and oxygen, supporting the metabolic demands of active osteoblasts during bone regeneration.

## 6. CLINICAL IMPLICATIONS

The mechanistic benefits of LLLT translate into several clinical advantages in the context of osseointegration and implant dentistry:

1. **Enhanced Implant Stability:** Clinical studies have demonstrated that LLLT application can improve the stability of dental implants. For instance, a study<sup>13</sup> evaluating the effect of LLLT on implant stability in the posterior maxilla found that LLLT-treated implants exhibited higher stability values compared to controls.
2. **Accelerated Healing Time:** By promoting angiogenesis and osteogenesis, LLLT can reduce the healing period required for implants to achieve osseointegration.<sup>1</sup> This acceleration allows for earlier loading of implants, improving patient outcomes and satisfaction.
3. **Improved Outcomes in Compromised Conditions:** Patients with conditions that impair bone healing, such as osteoporosis or diabetes, may particularly benefit from LLLT.<sup>18</sup> The therapy's ability to enhance bone regeneration can mitigate the challenges posed by these conditions, leading to more predictable implant success.
4. **Non-Invasive Adjunctive Therapy:** LLLT offers a non-invasive and painless adjunct to conventional implant procedures.<sup>19</sup> Its application does not require additional surgical intervention, making it an attractive option for both clinicians and patients seeking to enhance implant success rates.

## 7. CONCLUSION

Low-Level Laser Therapy (LLLT) has emerged as a promising non-invasive modality for enhancing bone healing and osseointegration. Through its ability to stimulate angiogenesis, promote osteogenic differentiation, modulate reactive oxygen species (ROS), and enhance the coupling of vascular and bone tissue formation, LLLT has demonstrated significant potential in improving implant stability, reducing healing time, and increasing success rates of osseointegration. Preclinical and clinical studies have provided substantial evidence supporting its efficacy, particularly in challenging conditions such as osteoporosis, diabetes, and irradiated bone.

Despite these promising findings, challenges remain in the standardization of LLLT protocols. Variations in wavelength, dosage, exposure time, and frequency across different studies have led to inconsistent outcomes, making it difficult to establish universally accepted guidelines for clinical application. Additionally, while short-term studies indicate positive effects, long-term evaluations on implant success and maintenance of osseointegration are still limited.

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