

Photo Biomodulation for Symptom Management and Supportive Care in Oral Cancer: A Review

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Abstract

Oral cancer management involves surgery, radiotherapy, chemotherapy, or combined chemoradiotherapy. Although these modalities improve survival, they frequently produce oral toxicities that impair function, comfort and treatment compliance. Oral mucositis is the most common and debilitating complication, often accompanied by xerostomia, dysgeusia, dysphagia, hyposalivation, trismus and opportunistic infections. Severe mucositis causes intense pain, nutritional compromise, increased healthcare costs and may necessitate treatment interruptions. Current management is largely symptomatic and fails to prevent tissue injury. Photo biomodulation (PBM) therapy is a non-pharmacological supportive treatment using low intensity red or near infrared lasers. It stimulates mitochondrial activity and adenosine triphosphate production, thus reduces inflammation, enhances wound healing and provides analgesia. Randomized trials and meta-analyses demonstrate significant reductions in mucositis incidence, severity, duration and associated pain. MASCC/ISOO guidelines recommend PBM when applied with appropriate parameters. This review summarizes mechanisms, clinical evidence and guideline-based use, highlighting PBM as an effective safe and patient centred strategy for optimizing supportive care in oral cancer. Standardization of protocols, multidisciplinary approach, and future research like large scale randomized controlled trials (RCTs) are essential for effective and globally applicable healthcare delivery. Such integrated strategy is likely to improve not only patient's quality of life but also supports oncologic treatment for diverse populations.



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Introduction

Oral cancers are commonly managed using surgery, radiotherapy (RT), chemotherapy (CT), or combined chemoradiotherapy (CRT).^{1,2} Although multimodal treatment approaches such as surgery, radiotherapy, chemotherapy and chemoradiotherapy have significantly improved survival outcomes in patients with head and neck cancers, they are often associated with a broad range of treatment-related toxicities. These adverse effects primarily result from inflammatory damage to adjacent normal tissues and are generally considered an inevitable consequence of cancer therapy.³

Early complications typically develop during or shortly after treatment and predominantly affect the oral cavity, manifesting as oral mucositis, dysgeusia, dysphagia, hyposalivation, xerostomia, trismus, and an increased susceptibility to opportunistic infections such as oral candidiasis. In contrast, late complications may arise months to years following therapy and include radiation-induced dental caries, osteoradionecrosis, and medication-related osteonecrosis of the jaw, which can significantly impair oral function and overall quality of life.

Among these, oral mucositis remains the most common and clinically significant complication, affecting nearly all patients undergoing chemoradiotherapy for oral cancer. Clinically, it presents along a spectrum ranging from mild erythema to severe ulcerative lesions with submucosal involvement, often leading to intense pain, impaired speech, dysphagia and compromised nutritional intake. These complications frequently necessitate treatment interruptions or dose modifications, ultimately impacting therapeutic outcomes and increasing healthcare burden due to prolonged hospitalization and the need for supportive pharmacological management.⁴

Photo biomodulation (PBM) is a rapidly advancing, non-invasive therapeutic approach widely used as supportive therapy for oral cancer patients. Formerly known as low-level laser therapy, it involves the application of red (620–700 nm) and near-infrared (600–1000 nm) lasers to stimulate cellular activity. PBM exerts immunomodulatory, anti-inflammatory, analgesic, effects by enhancing mitochondrial function and promoting cellular repair processes. Unlike high-power lasers, it does not generate significant heat or cause structural tissue damage,

making it a safe and effective modality for managing conditions such as wound healing, oral mucositis, and pain-related disorders.

Areas Covered

This review includes effect of photo biomodulation as supportive care in oral cancer which is prevalent issue globally. PubMed and google scholar were searched. A literature search conducted between 2021 and 2025 and relevant scientific studies were also included. The following keywords was used to search relevant data: photo biomodulation OR low-level laser therapy in oral cancer, oral mucositis OR photobiomodulation, infrared & red laser photobiomodulation. We also reviewed systemic reviews, review papers and case reports related to this which gave significant data required. Case reports was reviewed for any biological effects of PBM while systemic reviews and review papers was used to extract data for protocols and dosimetry parameters and analysing available data.

Body

According to Jablonski *et al.*,⁵ the pathogenesis of oral mucositis is multifactorial, involving a complex sequence of biological events. Current understanding, based on both preclinical and clinical models, describes a five-phase process initiated by cytotoxic injury to the epithelial and submucosal tissues. This initial damage results in excessive production of reactive oxygen species (ROS) and activation of nuclear factor kappa B (NF- κ B), which subsequently promotes the release of pro-inflammatory cytokines and chemokines. Progressive microvascular injury, alterations in the extracellular matrix, interactions with the host microbiome, and impaired epithelial regeneration further contribute to mucosal ulceration and delayed tissue healing.⁵

The use of epidermal growth factor receptor (EGFR) inhibitors and tyrosine kinase inhibitors (TKIs), either as monotherapy or in combination with chemoradiotherapy, may further exacerbate mucosal damage and intensify associated clinical symptoms. Additionally, despite advancements in radiation delivery techniques such as intensity-modulated radiotherapy (IMRT), the incidence of oral mucositis remains high, primarily due to the unavoidable exposure of oral mucosal tissues during treatment.⁵

El Mobadder *et al.*,³ reported that conventional management of OM and other oral toxicities remains largely supportive and symptomatic. Current approaches include topical anaesthetics, saline or bicarbonate mouth rinses, mucosal coating agents, antifungal medications, systemic analgesics and nutritional interventions. However, these measures do not adequately address the underlying biological mechanisms responsible for mucosal injury and inflammation. Pain control is often insufficient and opioid use is frequently required in severe cases, introducing additional risks such as sedation, gastrointestinal disturbances and dependency. Importantly, no pharmacological or non-pharmacological intervention has been shown to completely prevent the development of OM, highlighting a critical unmet need in supportive oncology care.³

Mechanism of Action

According to Epstein JB *et al.*,² Photo biomodulation (PBM) therapy has emerged as a promising supportive modality for managing treatment-related complications in cancer care. It involves the application of visible red and near-infrared laser that is absorbed by endogenous cellular chromophores, producing non-thermal photochemical and photophysical effects that elicit beneficial biological responses. Previously referred to as low-level laser therapy, PBM differs from surgical laser applications in that it employs low-intensity light to modulate cellular function without inducing tissue ablation. The therapeutic effects of PBM are largely mediated through its interaction with cytochrome c oxidase within the mitochondrial respiratory chain, leading to enhanced electron transport, stabilization of the transmembrane proton gradient and increased adenosine triphosphate (ATP) synthesis. This promotes cellular metabolism, tissue repair and wound healing by regulating inflammatory responses, stimulating cell proliferation, improving local microcirculation and facilitating tissue remodelling. Additionally, PBM has been shown to reduce oxidative stress, inhibit the release of pro-inflammatory cytokines such as tumour necrosis factor- α and interleukins and provide analgesic effects through neural modulation.^{2,1}

Biological Effects

The biological effects of photo biomodulation (PBM) on exposed tissues are influenced by several

interacting factors, including cellular characteristics such as cell type, spatial location within the irradiation field and the molecular & redox status of the cells. Tissue-specific factors, particularly the local microenvironment, also significantly affect the therapeutic response to PBM. Moreover, treatment parameters such as wavelength, power density (irradiance), mode of delivery (pulsed or continuous), spot size, and duration of exposure are critical determinants of clinical outcomes. PBM is known to demonstrate a biphasic dose–response relationship in accordance with the Arndt–Schulz law, indicating that an optimal tissue-specific irradiation dose is necessary to achieve therapeutic benefits. Suboptimal doses may lead to minimal clinical effects, whereas excessive doses may provide no benefit or potentially induce adverse outcomes. This biphasic response, consistently reported in the literature, contributes to variability in treatment outcomes and may partly explain the differences observed in the effectiveness of PBM therapy in managing cancer-related complications, as reported by Robijns J *et al.*⁶

A growing and robust body of clinical evidence supports the efficacy of photo biomodulation (PBM) in the prevention and management of oral mucositis. Multiple systematic reviews and meta-analyses of randomized controlled trials have demonstrated that PBM significantly reduces the incidence, severity and duration of oral mucositis, as well as associated pain, in patients undergoing radiotherapy or chemoradiotherapy for head and neck cancers. Clinical benefits have been reported with both red (630–670 nm) and near-infrared (780–830 nm) wavelengths, although optimal dosimetry parameters may vary according to the wavelength applied. Beyond mucositis control, PBM has also been shown to improve other treatment-related complications, including xerostomia, hyposalivation, dysgeusia, trismus and overall therapy-associated discomfort. These findings support its role as a comprehensive supportive care modality rather than an intervention limited to a single clinical manifestation, as highlighted by Robijns J *et al.*⁶

Clinical Application Parameters

The Multinational Association of Supportive Care in Cancer and the International Society for Oral Oncology (MASCC/ISOO) have incorporated PBM into their clinical practice guidelines, assigning it

level I evidence for the prevention of oral mucositis in specific oncology settings. These guidelines emphasize that clinical efficacy is highly dependent on appropriate selection of treatment parameters.⁷ Recommended parameters are as follows:

Light Source Used:

1. Low-level lasers (LLLT)
2. Light-emitting diodes (LEDs)

Wavelength Range:

1. Red and near-infrared (NIR) spectrum
2. 600 nm - 1,000 nm

Power Density (Irradiance):

Ranges from 5 mW/cm² to 150 mW/cm²

Duration of Application:

1. Commonly 30–60 seconds per point
2. Shorter durations (2–10 seconds per point) have also been used
3. Shorter exposures may rely on cumulative dose effects through multiple application points.

Therapeutic Dosage:

1. Expressed as energy density (J/cm²)
2. Typically ranges from 0.1 to 12 J/cm²
3. Dose selection depends on tissue type and clinical indication

Types of Low-Level Laser Systems Used:

1. Helium-neon (HeNe) laser
2. Neodymium-doped yttrium aluminium garnet (Nd: YAG) laser
3. Gallium aluminium arsenide (GaAlAs) diode laser
4. Indium gallium aluminium phosphide (InGaAlP) laser
5. Non-thermal, non-ablative carbon dioxide (CO₂) laser

From a safety perspective, PBM is a minimally invasive modality with an excellent tolerability profile. When applied according to established guidelines, PBM does not stimulate tumour growth and should not be administered directly over active tumour sites as presented by Zadik *et al.*⁷

Table 1: Summarised recommended treatment parameters for OM and other symptoms.⁶

Sr. no.	Symptom	Wavelength (nm)	Power density (mW/cm ₂)	Application time (sec/per point)
1.	Oral mucositis	630-680	30-150	30-60
2.	Acute dysphagia	810	30-150	30
3.	Xerostomia and hyposalivation	400-1100	10-150	30
4.	Voice and speech alternations	800-1100	10-150	30

Article Highlights

This article highlights about the conventional therapies available for oral cancer treatment and side effects associated with these modalities. It also reviews the recent advances in supportive care such as photo biomodulation using lasers or LEDs. Following are the key highlights:

- Prevalence of oral mucositis
- Effect of photo biomodulation as supportive care
- Lasers and LEDs
- Dosimetry parameters given by MASCC/ISOO
- Supportive therapy

Results

According to Gisela Cristina *et al.*¹⁸, from week 3 to 3 months follow up, the mean pain score was lower while it was confirmed that not receiving PBM in first week of radiotherapy increased oral mucositis. Various studies confirmed that biological effects of PBM at different wavelength and power values varies yet wavelength of 600 to 1000 is most effective for optimum biological effects. A recent review by Zadik *et al.*⁸, gave two effective PBMT protocol; for red and infrared light for patients undergoing OM prevention post radiotherapy. Preventive use of laser before or after radiotherapy on entire mucous membrane

reduces duration and chances of advanced oral mucositis, as given by Jablonski *et al.*⁵

Discussion

Head and neck cancer is expected to rise substantially in the coming decades, with projections from the Global Cancer Observatory estimating a 61.6% increase in new cases worldwide by 2050. Management of these cancers is typically multimodal, involving surgery, radiotherapy, chemotherapy, or combined chemoradiotherapy. While these approaches have improved survival, they frequently cause significant treatment-related toxicities due to inflammatory damage in normal tissues. Among these complications, oral mucositis (OM) is one of the most common and debilitating, particularly in patients receiving chemoradiotherapy. It can range from mild redness to severe ulcerations, leading to intense pain, difficulty in speaking and swallowing, nutritional compromise and even interruptions in cancer therapy. Other acute and late oral effects include xerostomia, dysgeusia, trismus, infections, radiation-induced caries and osteonecrosis, all of which negatively affect long-term oral health and quality of life. Current management remains largely supportive and symptomatic, with no intervention capable of completely preventing OM. Photo biomodulation (PBM) therapy has emerged as a promising supportive care modality. Using low-intensity red or near-infrared light, PBM stimulates cellular processes without causing thermal damage. By enhancing mitochondrial activity, increasing ATP production, modulating inflammation, reducing oxidative stress and promoting tissue repair, PBM supports mucosal healing and pain control. Its effects depend on appropriate treatment parameters and follow a biphasic dose response, meaning that optimal dosing is crucial for therapeutic benefit. Strong clinical evidence, including systematic reviews and MASCC/ISOO guidelines, supports PBM for the prevention of oral mucositis.

Conclusion

With a favourable safety profile and high patient acceptance, PBM represents an effective, non-pharmacological adjunct that improves quality of life and helps maintain continuity of cancer treatment.

Overall, PBM is effective treatment modality which further needs to be validated(due to lack of standardised PBM parameters and available data) by long term RCTs and evaluating more cases and their results.

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This research does not involve human participants, animal subjects, or any material that requires ethical approval.

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This research does not involve any clinical trials.

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- **Sakshi Dhage:** Review and Editing.
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