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# Effectiveness of 808 nm Near Infrared (NIR) Laser Photobiomodulation for Accelerating Postoperative Wound Healing

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**Abstract**

**Introduction:** Inadequate wound treatment can lead to complications like methicillin-resistant *Staphylococcus aureus* (MRSA) infections, increased medical risks, and skin ulcers. Antimicrobial resistance is a global health threat, and Indonesia's injury prevalence has increased. Laser photobiomodulation therapy, using near-infrared (NIR) wavelengths, has shown potential in accelerating wound healing by stimulating cellular energy, enhancing blood flow, reducing inflammation, and promoting cell proliferation and collagen synthesis.

**Methods:** Each treatment sample received NIR therapy for 15 minutes per session on days 0, 1, 2, 3, and 5. Wound measurements were recorded, and blood samples were collected for laboratory testing to assess the effectiveness of laser therapy in postoperative wound healing. Meanwhile, the control group did not receive therapy but underwent wound measurements and blood sample collection. The data obtained were analyzed using the SPSS non-parametric Friedman test to compare the mean values of TNF-α, IL-1β, and TGF-β1 expression between the control and therapy groups. The Mann-Whitney test followed this to determine whether there were significant differences between the groups. A significance level of $P<0.05$ was used.

**Results:** The use of NIR laser therapy in the treatment group resulted in a 35% reduction in wound length and a 46% reduction in wound width. In the control group, wound length decreased by 30%, while wound width decreased by 26%. These results indicate that NIR therapy is effective in tissue regeneration, as evidenced by the reduction in wound size due to granulation formation and re-epithelialization. Statistical analysis of laboratory assessments showed significant differences in IL-1β and TGF-β1 cytokine expression ($P<0.05$) in the treatment group, while TNF-α expression did not show a significant difference ($P>0.05$) between the two groups.

**Conclusion:** Clinical assessment shows that NIR has an effect on the formation of better wound tissue and shows good wound quality.

**Keywords:** Photobiomodulation, Infrared diode laser, Wound healing, Inflammatory cytokines

## Introduction

The presence of disturbances in wounds, such as infections, not only hampers work productivity but can also lead to serious complications.[1] Various factors can contribute to poor wound healing, including the cause of the wound itself, underlying health conditions, as well as environmental and socioeconomic factors. One of the primary reasons wounds fail to heal and become chronic is untreated infections,[2] such as those caused by methicillin-resistant *Staphylococcus aureus* (MRSA). Wound infections can lead to further inflammation and increased pain, potentially resulting in skin ulcers, especially in individuals with certain medical conditions.[3] These complications may require additional medical treatment, which inevitably increases healthcare costs.[4] Open wounds, where skin integrity is compromised, expose underlying tissue to contamination. Post-surgical wounds require specialized care for optimal healing and preventing microbial infections.[5]

Based on basic health research (Riskesdas) data, the prevalence of injuries in Indonesia has increased each year, from 7.5% in 2007 to 8.2% in 2013 and 9.2% in 2018.[6] The long-term use of antibiotics can lead to microbial resistance, making wound healing more difficult. Meanwhile, antiseptic use also has drawbacks, such as causing skin irritation.[7] The World Health Organization

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(WHO) ranked antimicrobial resistance among the top 10 global health threats in 2019, prompting the search for effective, selective methods for wound healing.[8] Photobiomodulation therapy (PBMT), a near-infrared (NIR) light therapy, is widely recognized for its role in wound healing.[9,10] Light emitted within this wavelength range has been shown to stimulate healing, reduce pain, and promote cell proliferation in wounds.[11]

PBMT, also known as low-level laser therapy (LLLT), utilizes low-intensity radiation within the visible or NIR light spectrum to stimulate various biological processes.[12,13] The first law of photobiology states that low-intensity light photons can affect living biological systems by absorbing chromophores' electronic absorption bands, with optimal tissue penetration occurring at 650 nm-1200 nm.[14,15]

Research indicates that wavelengths in the NIR region, with energy doses below 5 J/cm², are most effective for tissue regeneration, accelerating wound healing, and enhancing mitochondrial energy metabolism.[16] This therapy utilizes deep infrared light penetration to improve tissue oxygenation.[17] The process involves targeting mitochondrial enzymes like cytochrome C oxidase, which activate key molecules like ATP, ROS, NO, and $Ca^{2+}$ ions, accelerating cellular signaling pathways for wound healing.[18]

Clinical monitoring is a crucial method for wound assessment, evaluating various stages of healing to provide a comprehensive picture of the wound's response to laser therapy.[19] Skin injury progresses through coagulation, inflammation, proliferation, and remodeling, involving various cell types and extracellular matrix components.[20] The process begins with blood aggregation, platelet aggregation, and inflammatory cell migration. The transition from the inflammatory to proliferative phase involves migration, proliferation, and remodeling.[21]

This study focuses on post-surgical wound healing for perianal fistula, abscess, and haemorrhoids, addressing a gap in research. Global and national epidemiological data show that haemorrhoids affect 4.4% of the population, perianal fistulas account for 8.6%-10% of anorectal cases, and perianal abscesses are linked to fistulas in 40%-50% of cases. The increasing prevalence of these conditions in Indonesia emphasizes the need for effective postoperative management. The study evaluates the efficacy of NIR PBMT in promoting wound healing.

This research demonstrates the effectiveness of NIR therapy in two main phases of wound healing: the inflammatory phase and the proliferation phase. These phases are characterized by the formation of granulation tissue and the re-epithelialization process, which contribute to the reduction of wound margins. Additionally, this study provides novel insights into the role of NIR photobiomodulation in modulating inflammatory cytokine expression, particularly highlighting its differential effects on IL-1β, TGF-β1, and TNF-α in the wound healing process. Unlike previous studies that focused on general wound size reduction, this research integrates cytokine profiling to reveal mechanistic evidence of how PBMT influences pro-inflammatory and pro-regenerative signaling pathways. Additionally, the study validates a short-duration NIR exposure protocol (15 minutes per session) as an efficient, non-invasive therapeutic strategy, optimizing energy delivery while ensuring minimal tissue disruption.

## Materials and Methods

### *Subjects*

This clinical study, approved by the Ethics Committee of Airlangga University Hospital, involved men and women aged 16-60 with cases of perianal fistula, abscess, and hemorrhoids. Participants were selected based on inclusion criteria, including post-operative subjects, surgical categories, and informed consent. The study excluded individuals with certain conditions, including vasculitis, autoimmune disorders, malnutrition, vulnerable groups, and those using retinoic acid creams for over a month. The participants were observed and subsequently analyzed for wound healing therapy effectiveness.

### *Study Design and Treatment Protocol*

The study involved patients who underwent surgery and received therapy using an NIR diode laser. The treatment was evaluated on days 0, 3, and 5 after surgery. The wound was measured for size, VAS score, and granulation formation. Laboratory tests measured pro-inflammatory cytokines concentration. The VAS score was used to determine pain levels and wound healing. Clinical evaluations were conducted on days 0, 3, and 5 using a 10-point VAS scale.[22] Figure S1 shows procedures and mechanisms of NIR therapy in wound healing.

### *Participants and Inclusion Criteria*

Participants were recruited from Airlangga Hospital. The inclusion criteria were: (1) patients aged 18–65 years, (2) patients diagnosed with perianal fistula, abscess, or hemorrhoids requiring surgical intervention, and (3) patients with no history of immunosuppressive conditions or severe comorbidities. Patients with active infections unrelated to the surgical site or those on long-term steroid therapy were excluded.

### *Intervention: Near-Infrared Therapy*

The intervention group received NIR therapy using a LightStim for Pain device, manufactured by LightStim, emitting at a wavelength of 808 nm. The power density was set at 100 mW/cm², and each session lasted 15 minutes. Therapy was administered daily for 5 days. The control group received standard wound care, including regular dressing changes and pain management, without NIR exposure.

Wound healing progression was evaluated using digital caliper measurements on days 1, 3, and 5, a standardized scoring system, clinical examination, photographic comparison, and visual analog scale (VAS) scores recorded at each follow-up visit.

### *Statistical Analysis*

The study used IBM SPSS to analyze wound measurements and ELISA test results for cytokine parameters. The Friedman test evaluated changes in wound length and width measurements between treatment and control groups, with a decision-making hypothesis based on the significance value. The Mann-Whitney U test was used to compare treatment and control groups at a single time point, with a significance value of $P < 0.05$ indicating a significant difference.[23]

## Results

### *Clinical Assessment*

A study on perianal fistula cases showed that NIR therapy significantly reduced wound width in the treatment group, while the control group showed a greater reduction in length. Granulation tissue appeared by day 3 (H3), marking the proliferation phase. VAS scores dropped significantly by day 5 (H5), indicating less pain. H0: 5-6 refers to moderate pain on day 0 (VAS range). Table S1 shows wound healing progress. "+" means the healing marker is present; "–" means it is absent.

There were 10 samples registered for abscess cases, five in the therapy group and five in the control group, showing significant differences in the healing process. The treatment group experienced a consistent reduction in wound size, faster granulation formation, and optimal healing, with active granulation visible from day 3 to day 5, but sample 4 showed fluctuating data.

Table S2 shows the progress of wound healing in abscess cases. NIR therapy significantly accelerated tissue regeneration in the treatment group, leading to faster and better healing, reduced wound length and width, and a significant reduction in pain levels.

This hemorrhoid research involved 10 samples divided into two groups: the treatment group (5 samples) and the control group (5 samples), with varying levels of hemorrhoid severity, namely grade III (4 individuals) and grade IV (6 individuals). Visual evaluation of postoperative wounds was challenging, primarily due to the presence of residual blood vessels and variations in hemorrhoid severity.

The study found that NIR therapy significantly accelerated wound healing compared to the control group, resulting in an average reduction in wound length and width by up to 52%. The treatment group also showed a significant reduction in pain levels and faster progress in granulation tissue formation and re-epithelialization, making it a superior method for accelerating hemorrhoidal wound healing. Table S3 illustrates Progress in wound healing in hemorrhoid cases.

The statistical test results showed a significant difference in the average wound length and width across the three measurement intervals (days 0, 3, and 5) in both groups based on the Friedman test ($P < 0.05$). However, the Mann-Whitney test indicated that a significant difference was only found in wound length between the two groups on day 0 ($P < 0.05$). In contrast, no significant differences were observed in wound length on days 3 and 5 or in wound width throughout the measurement intervals ($P > 0.05$). The study found significant progress in wound healing in the treatment group compared to the control group, with a cumulative reduction in wound size, as indicated by the statistical results from Friedman test wound measurement data and Mann-Whitney U test wound measurement data. Table S4 shows the statistical results Friedman test wound measurement data and statistical results of Mann-Whitney U test wound measurement data.

### *Laboratory Assessment*

The transition from the inflammatory phase to the proliferative phase in wound healing involves decreased inflammatory mediators like TGF-β1, which reduces inflammation and initiates tissue repair and regeneration. This reduces nerve stimulation, pain, and inflammation. In non-healing wounds, pro-inflammatory cytokines are higher, while TGF-β1 is lower. As healing progresses, pro-inflammatory cytokines decrease, while growth factors increase, indicating the transition from inflammation to tissue repair.[24] Table S5 shows the Friedman test results of TNF-α cytokine parameters and Mann-Whitney U test results of TNF-α cytokine parameters. Figure 1 shows the comparison of Average TNF-α Levels between the therapy and control groups.

Table S6 shows the Friedman test results of IL-1

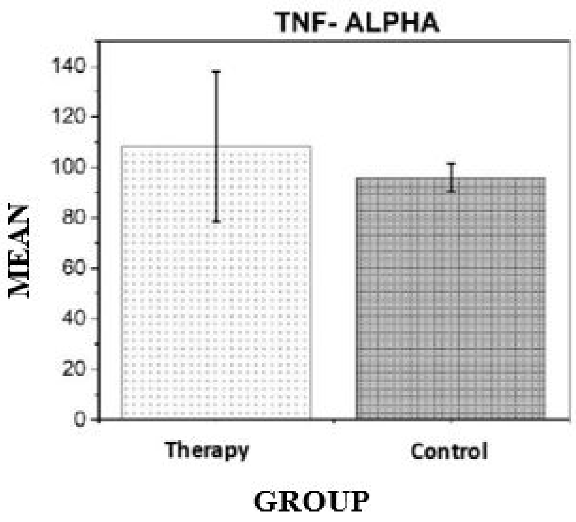


**Figure 1.** Comparison of Average TNF-α Levels Between the Therapy and Control Groups

cytokine parameters and the Mann-Whitney U test results of IL-1 cytokine parameters. Figure 2 shows the comparison of average IL1-β Levels between the therapy and control groups.

TNF-α levels showed no significant changes within or between the groups ($P>0.05$, Table S6). IL-1β levels significantly decreased in the therapy group ($P=0.006$), while the control group showed no change ($P=0.638$). L-1β levels differed significantly between the groups on day 5 ($P=0.048$), while the difference on day 3 showed a trend toward significance ($P=0.055$), suggesting possible therapeutic effects. Figure 2 shows the comparison of average IL1-β levels between the therapy and control groups.

Table S7 shows the Friedman test results of TGF-β1 cytokine parameters and the Mann-Whitney U test results of TGF-β1 cytokine parameters. Figure 3 shows the comparison of average TGF-β1 levels between the therapy and control groups.

The study found no significant differences in TNF-α and IL-1β parameters between the treatment and control groups, but a significant increase in concentration in the treatment group. However, time interval tests showed no significant changes. Factors influencing the results include high data variations, short observation intervals, and uncontrolled external factors. High data variations and large standard deviations may obscure true effects, while short observation intervals may not allow sufficient time to observe full effects.[25]

## Discussion

### *Cellular Mechanisms of Near Infrared Therapy on Wound Tissue*

PBMT uses infrared light to enhance tissue oxygenation, targeting mitochondrial enzymes like cytochrome C oxidase. This process activates cellular signaling, supporting wound healing. PBMT reduces inflammation, promotes immunomodulation, and increases fibroblast activity. It regulates macrophage activity, reduces pro-inflammatory cytokines, and increases blood circulation.[26] Figure S2 shows the schematic diagram and illustrates the mechanism of photobiomodulation by near infrared light at a wavelength of 630-1000 nm.

PBMT, using a NIR laser, improves wound healing by shifting cytokine balance, reducing oxidative stress, and improving immune response.[27] It accelerates wound healing by killing pathogenic cells and increasing fibroblast activity. This therapy stimulates collagen synthesis, extracellular matrix production, and re-epithelialization formation, thereby supporting overall wound healing and improving healing outcomes through better molecular and cellular regulation.[28]

### *Wound Healing Factors and the Role of Inflammatory Cytokines*

The body's natural response to injury involves three phases: inflammation, proliferation, and remodeling/maturation. Inflammation triggers vasoconstriction, forming a blood clot, and inflammation allows immune cells to migrate to the wound site. Proliferation begins with new blood vessels, forming angiogenesis and granulation tissue.[29]

TGF-β1 is crucial in the transition from the inflammatory phase to the proliferative phase, promoting fibroblast differentiation and collagen production.[30] Monitoring and regulating these cytokines during wound healing are essential to prevent chronic wounds.[31] The transition reduces inflammation, allowing tissue repair and regeneration. In non-healing wounds, pro-inflammatory cytokines like IL-1 and TNF-α are higher, while TGF-β1 is lower. Over time, these cytokines decrease, while growth factors increase, indicating a shift from the inflammatory phase to the proliferation and remodeling phase.[32] Research

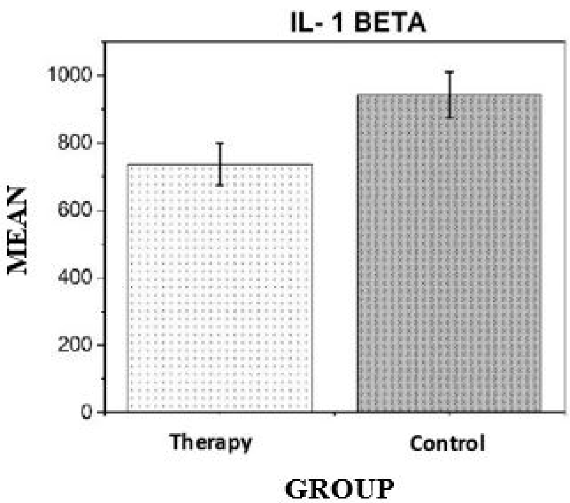


**Figure 2.** Comparison of Average IL1-β Levels Between the Therapy and Control Groups

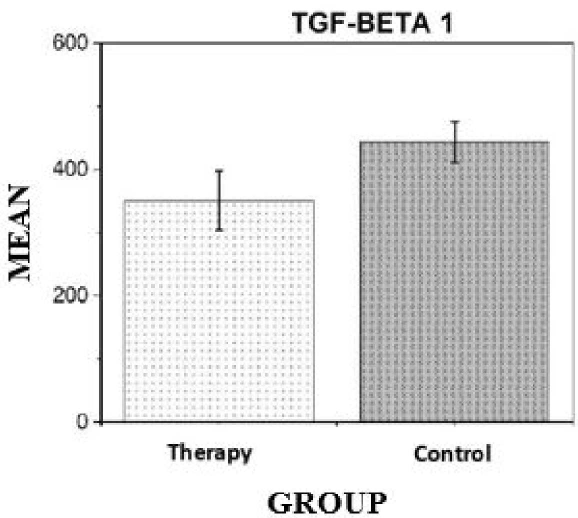


**Figure 3.** Comparison of Average TGF-β1 Levels Between the Therapy and Control Groups

by Yadav et al, who also used NIR in their experiments, showed a synergistic reduction in inflammation and pain and an increase in cell adhesion and migration. This was evidenced by a significant decrease in the expression of TNF-α, NF-κB, IL-1β, COX-2, and substance-P receptor proteins, as well as an increase in fibronectin regulation compared with other groups.[33]

Cytochrome C Oxidase activation leads to increased ATP, cAMP, reactive oxygen species (ROS), and intracellular calcium, stimulating downstream pathways involved in anti-inflammatory effects, repair, proliferation, and cellular migration. TGF-β1 acts as a marker for transitioning from the inflammatory to the proliferative phase. NIR significantly reduces TNF-α, NF-κB, IL-1β, COX-2, and substance-P receptor proteins, while increasing fibronectin expression and enhancing cell adhesion and migration. NIR improves swelling and redness through nitric oxide-mediated vasodilation and suppression of VEGF expression. Although re-epithelialization rates were similar between the groups, the treatment group showed better tissue quality. TGF-β1 expression in the treatment group increased, supporting the transition from inflammation to proliferation, unlike in the control group.[20]

### *The Role of Near Infrared on the Quality of Wound Healing*

The study focused on three signs of inflammation: tumor swelling, rubor (redness), and function laksa (loss of function).[34] Results showed that tumor swelling and rubor subsided significantly in both groups by day 3. The treatment group showed a significant decrease in pain and swelling levels, while the control group did not show significant changes.[35]

NIR has been shown to accelerate healing, reduce inflammation, and restore tissue function, particularly after surgery. It enhances blood circulation by promoting nitric oxide release, which leads to vasodilation, improved oxygen delivery, and a reduction in inflammatory mediators. This suppresses pro-inflammatory cytokines, reducing swelling and redness.[36] NIR also stimulates mitochondria, accelerates cell regeneration, and activates signaling pathways for tissue repair. It reduces swelling and redness, accelerates inflammation resolution, and suppresses VEGF expression. Its analgesic effect reduces inflammation-related pain, accelerating tissue recovery and overall healing.[37]

### *Effectiveness of Using Near Infrared in Postoperative Wound Healing*

The study found that NIR therapy accelerates the healing process by stimulating cells involved in tissue regeneration, inflammation reduction, and wound microenvironment optimization. The treatment group showed better granulation tissue formation and effective re-epithelialization, indicating the effectiveness of the intervention. However, the number of samples showing re-epithelialization in both groups was not significantly different, suggesting the benefits of the treatment are primarily in terms of new tissue quality or regeneration efficiency.[38]

Wound length and width were measured instead of area due to the practicality and accuracy of linear measurements in small animal models. Area calculation can be challenging due to irregular shapes and movement. The use of length and width provides reliable, reproducible data on wound closure. The control group's greater reduction in wound length may seem contradictory to the conclusion supporting NIR efficacy. However, wound length is more influenced by passive contraction, while width reduction reflects active healing, such as cellular migration and tissue remodeling. NIR treatment likely enhances these processes, explaining the superior width reduction in the treated group. Data were only collected until day 5 to focus on the early inflammatory and proliferative phases of wound healing, where NIR therapy is most active in modulating immune response and initiating tissue regeneration. During each session, the NIR diode laser probe was held at a fixed distance of approximately 1–2 cm from the wound surface to ensure uniform light distribution and optimal energy absorption without direct contact. This time frame captures critical molecular and cellular changes, particularly the shifts in cytokine expression and fibroblast activity. However, future studies should include later time points (e.g., days 7 and 14) to evaluate the sustained effects of therapy and tissue remodeling outcomes.

LLLT, also known as PBMT, is a treatment method that uses lasers to stimulate tissues through photoelectric, photo-energetic, and photochemical reactions, resulting in beneficial responses.[39,40] Photobiomodulation, on the other hand, employs a 650 nm-wavelength diode laser to accelerate the healing process, while also reducing pain and inflammation by activating the cells' response to light. PBMT is a treatment technique that uses low-level infrared light spectrum lasers to stimulate tissue.[41] It works by absorbing photons through molecular photoacceptors or chromophores.[42,43] Effective tissue penetration occurs within the range of 650 to 1200 nm, with absorption and scattering being more pronounced in the blue region [44]. Most LLLT treatments for animals and patients utilize red and NIR light.[45-47] Wound healing consists of fibrosis and regeneration, where fibrosis replaces damaged tissue with connective tissue.[48,49] PBMT is a powerful method that accelerates wound healing in body tissues, as injured tissues often experience structural and functional impairments. To accelerate recovery, external stimulation is required to prompt cells into the regeneration phase, making PBMT a vital tool.

## Conclusion

Based on the research results, visual wound measurements (length and width) and subjective assessment of the wound showed a decrease in size in the treatment group compared to the control group. Significant differences were found in the qualitative assessment, indicating that the use of NIR therapy positively affected post-operative wounds. However, when related to the results of the cytokine parameter test, the body's immune response did not show a significant difference across the three parameters. The laboratory testing results of cytokine and growth factor expression did not show clinically linear results. These findings confirm that infrared laser therapy can accelerate the inflammatory phase and tissue regeneration, supporting the wound healing process based on clinical assessment. Further evaluation and monitoring are needed to understand the role of infrared laser therapy in wound healing, especially in different clinical conditions.

### Authors' Contribution

**Conceptualization:** Waode Erimelga Nurfitri, Suryani Dyah Astuti, Prihartini Widiyanti, Ricky Wibowo, Deny Arifianto, Winarno, Ahmad Khalil Yaqubi, Muhammad Nurdin, Nasrul Anuar Abd Razak, Hery Wibowo.
**Formal analysis:** Waode Erimelga Nurfitri, Winarno.
**Funding acquisition:** Suryani Dyah Astuti.
**Methodology:** Waode Erimelga Nurfitri, Suryani Dyah Astuti, Ricky Wibowo, Winarno, Nasrul Anuar Abd Razak.
**Supervision:** Suryani Dyah Astuti, Prihartini Widiyanti.
**Validation:** Suryani Dyah Astuti, Prihartini Widiyanti, Ricky Wibowo, Deny Arifianto, Winarno, Ahmad Khalil Yaqubi, Muhammad Nurdin, Nasrul Anuar Abd Razak.
**Writing–original draft:** Waode Erimelga Nurfitri, Prihartini Widiyanti, Deny Arifianto.
**Writing–review & editing:** Suryani Dyah Astuti, Ahmad Khalil Yaqubi, Muhammad Nurdin.

### Competing Interests

The authors declare no conflict of interest.

### Ethical Approval

This clinical study has been approved by the Ethics Committee of Airlangga University Hospital (No. 130/KEP/2023) in accordance with the Indonesian Government's clinical trial guidelines.

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### Supplementary Files

Supplementary file 1 contains Tables S1-S7 and Figures S1-S2.

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