

Synergism between platelet-rich fibrin with superpulsed laser and pulsed magnetic field in the treatment of disc herniations: A therapeutic protocol

Palmerindo Antônio Tavares de Mendonça Néto ^{1,*}, Douglas Scott Johnson ², Dana York ³, Dirceu Moraes Junior ⁴, Carlos Stéfano Hoffmann Brito ⁵, Daniel Ramos Gonçalves Lopes ⁶ and Mayara Magda Dantas Tavares de Mendonça ¹

¹ *Regenera Dor Institute, Juazeiro do Norte, Ce, Brazil.*

² *Senior Visiting Fellow, Laboratory of Phototherapy and Innovative Technologies; São Paulo, Sp, Brazil.*

³ *European Medical Laser Association; New York, Ny, EUA.*

⁴ *Clinical Lumius; Joinville, Sc, Brazil.*

⁵ *Carlos Stéfano Institute; Belo Horizonte, Mg, Brazil.*

⁶ *Gaio and Lopes Specialty Medicine; Rio de Janeiro, Rj, Brazil.*

World Journal of Advanced Research and Reviews, 2025, 25(02), 593-608

Publication history: Received on 28 December 2024; revised on 02 February 2025; accepted on 05 February 2025

Article DOI: <https://doi.org/10.30574/wjarr.2025.25.2.0415>

Abstract

Herniated discs affect about 1% to 5% of the general population and are more common in adults between the ages of 30 and 50 years, the peak of productive age. Among the risk factors are obesity, sedentary lifestyle and activities that involve weightlifting. This condition often results in chronic pain, depression, work disability, and reduced daily functional capacity. Clinically, patients present with localized pain with or without irradiation, muscle weakness, tingling, and, in more severe cases, loss of sensation. The definitive diagnosis is obtained through imaging tests, such as CT scans or MRIs, which allow confirmation of the extent and location of the hernia. Therapeutic options range from conservative approaches, including physical therapy and analgesic and anti-inflammatory medications, to surgical interventions for cases where there is significant neurological impairment. Recently, innovative therapies such as superpulsed laser, pulsed magnetic field, and Orthobiological, such as injectable platelet-rich fibrin, have shown promising results. The combination of orthobiologicals with superpulsed laser and pulsed magnetic field offers an integrated approach to modulate the inflammatory response and promote tissue regeneration. This therapeutic synergy can provide effective symptomatic relief, injured tissue repair, and accelerated recovery. The regenerative approach to herniated discs, which combines orthobiological, superpulsed laser, and pulsed magnetic field, has the potential to revolutionize treatment by offering a minimally invasive, safe, and effective option for patients. Additional studies are needed to evaluate the statistical effectiveness and side effects of this innovative approach.

Keywords: Disc hernia; Non-surgical treatment; Minimally invasive treatment; Regenerative medicine; Orthobiological; Superpulsed laser treatment; Pulsed magnetic field

1. Introduction

Disc herniation is a statistically relevant condition, affecting about 1% to 5% of the general population, with a higher incidence in adults between 30 and 50 years of age, the peak of the productive period ^[1-5] and is the leading cause of spine surgery in adults ^[3]. Risk factors include obesity, sedentary lifestyle, and activities that require weightlifting. ^[6, 7]

* Corresponding author: Palmerindo Antônio Tavares de Mendonça Néto

The condition significantly impacts quality of life, leading to chronic pain often associated with depression, work incapacity, and loss of the ability to perform daily activities without assistance. Studies indicate that herniated discs are one of the main causes of absenteeism at work and high health costs. [8, 9, 10]

A herniated disc pain crisis occurs when the nucleus pulposus, the soft, gelatinous inner part of the intervertebral disc, leaks through a fissure or tear in the annulus fibrosus, the outer, resistant, fibroelastic layer of the disc. [11, 12] This extrusion can generate a local inflammatory process associated or not with compression of adjacent nerve structures, including the spinal cord or nerve roots, leading to varied neurological symptoms. [13] Herniated discs are most often found in the lower back, although they can occur in any segment of the spine. [14, 15, 16; 17]

Intervertebral discs play a crucial role in absorbing impact and maintaining the flexibility and mobility of the spine. However, due to aging, mechanical wear or trauma, the annulus fibrosus may weaken or fissure, allowing the nucleus pulposus to protrude. [18]. Underlying causes of herniated discs include disc degeneration, overexertion, jerky or repetitive movements, and genetic predispositions. [3,4, 19, 20]

The treatment of disc herniations has traditionally been dominated by conservative approaches, such as physiotherapy and medication, or by surgical intervention when symptoms persist or worsen. However, between these two treatment extremes, there lies an emerging and promising field of minimally invasive interventions and regenerative medicine technologies. These intermediate approaches not only aim to alleviate pain and restore functionality but also minimize the risks and recovery time associated with traditional surgeries. Techniques such as epidural injections, nucleoplasty, and stem cell therapies represent the future of disc herniation treatment, offering new hope for patients seeking effective and less invasive alternatives. [18]

This article seeks to perform a literature review on disc herniations and to seek therapeutic synergism between different therapeutic options to set up a feasible, minimally invasive and reproducible protocol for the treatment of disc herniations.

2. Material and methods

2.1. Clinical Presentation of herniated discs

Clinically, herniated discs can manifest with localized and/or radiating pain (such as sciatica in the case of lumbar hernias), acute or progressive loss of strength, tingling, paresthesia and, in more severe cases, loss of sensitivity in the affected dermatome. [3, 4, 21]

Diagnostic evaluation usually involves imaging tests, such as CT scans or magnetic resonance imaging, which confirm the extent and location of the herniated disc. [3, 22]

Symptoms may vary according to the location of the hernia. In lumbar hernia, patients often report low back pain radiating to the legs, muscle weakness, and tingling. Cervical hernia, on the other hand, can cause neck pain radiating to the upper limbs, often being confused with angina. [3, 12, 19, 23]

2.2. Impact of the inflammatory response on the etiopathogenesis of disc herniation

Metainflammation and oxidative stress are closely related to the etiopathogenesis of lumbar disc herniations. Several studies have shown that chronic inflammation contributes to the degeneration of the intervertebral discs, weakening the fibrous ring and increasing the risk of developing hernias. For example, research by Freemont (2009) highlights the importance of inflammation in the pathogenesis of disc degeneration.

Oxidative stress, caused by the imbalance between the production of reactive oxygen species (ROS) and the antioxidant capacity of the body, in addition to being associated with cellular senescence, is also associated with disc degeneration, accelerating the deterioration of the structural components of the intervertebral discs, leading to herniation. [24]

The metabolic changes generated by the combination of these factors can exacerbate the degeneration process, compromising the structural integrity of the discs and increasing the risk of developing herniated discs. [9]

Thus, the approach to metainflammation and oxidative stress can be crucial in planning a treatment plan for lumbar disc protrusions and herniations. It is essential that the instituted therapeutic plan modulates the inflammatory response and reduces oxidative stress to improve clinical outcomes in patients with herniated discs. [7]

2.3. Therapeutic options

Treatment can range from conservative approaches, such as physical therapy, analgesic and anti-inflammatory medications, to surgical interventions in cases where there is significant impairment of neurological functions or failure in conservative treatment. [25]

Innovative therapies such as superpulsed laser, pulsed magnetic field, and orthobiological, among which we can highlight injectable platelet-rich fibrin (iPRF), have shown promising results in recent studies. [26-28]

2.3.1. Conservative treatment

This approach should be thought of for cases of milder symptoms and in initial stages before thinking about invasive treatments. Physiotherapy is one of the main therapeutic modalities used in this stage of treatment, with protocols that include muscle strengthening exercises, mobilization, and stretching techniques. These protocols can act to reduce pain and improve the functionality of patients. [3, 4, 19, 29]

In addition to physical therapy, the use of nonsteroidal anti-inflammatory drugs (NSAIDs) is common in conservative treatment. NSAIDs act by reducing the inflammatory response and, consequently, the perception of pain, providing symptomatic relief and being relatively effective in the symptomatic control of herniated discs. [3, 19]

Another option in conservative treatment is corticosteroids, also used to reduce the inflammatory response generated by herniated tissue and relieve pain. Corticosteroid therapy may be beneficial in cases of herniated discs with exacerbated inflammatory response, although its use should be carefully monitored due to possible side effects and the risk that corticosteroids may impede the natural course of resorption of the hernial process. [24, 30]

Another option often used in conservative treatment is opioids, which can also be used in cases of severe pain that do not respond to other treatments. However, its use should be restricted to the short term and under strict medical supervision, due to the risk of addiction and other side effects. [31]

2.3.2. Surgical treatment

Considered in cases where conservative methods fail, and the patient's quality of life is compromised. [32]

Conventional discectomy is the traditional technique, where the herniated disc is excised through an incision in the surrounding tissue. This surgery can be done by a posterior, lateral or anterior access route, depending on the location of the hernia. Microdiscectomy, on the other hand, is a variant that stands out for the use of the surgical microscope to obtain a clearer visualization of the anatomical structures. This technique reduces the incision and, consequently, the muscle injury, resulting in less postoperative pain, shorter hospitalization time, and reduced recovery time. [2, 33]

The minimally invasive approach has brought new perspectives for the treatment of herniated discs. This technique includes endoscopy, where surgeons access the herniated disc through small insertions, using an endoscope to guide the removal of disc material. [26] Another technique is percutaneous discectomy, which uses special needles to remove the herniated disc, making it ideal for patients with smaller hernias. [34] These approaches have been shown to be successful in reducing the length of hospital stay, recovery time, and the immediate complication rates inherent to the procedure.

Although surgical treatment of herniated discs often has a good immediate evolution, there are risks and complications associated with any surgical intervention. Among the most common complications are infection, bleeding and nerve damage. Discectomy, even in its minimally invasive form, can present risks of damage to the adjacent nerve root, which can cause neurological deficits. [10, 35-37] Another significant risk is the possibility of disc herniation recurrence. Studies have shown recurrence rates ranging from 5 to 15%, depending on the technique used and the patient's profile. [30, 36, 38] In addition, disc failure syndrome is a condition in which the patient continues to have symptoms after the surgical procedure, which can result from multiple factors, such as the presence of pain unrelated to the herniation. [2]

The surgical treatment of herniated discs has been evolving with the introduction of minimally invasive approaches that offer advantages in terms of recovery and reduction of complications. However, careful patient selection and the choice of the appropriate surgical technique are essential to optimize results and minimize risks. Continuous innovation and refinement of surgical techniques, coupled with proper patient assessment, are essential to achieve positive therapeutic outcomes and improve the quality of life of individuals affected by herniated discs. [36, 39, 40, 41]

2.3.3. Transcutaneous laser nucleoplasty

Herniated discs can also be treated with transcutaneous laser application, also known as percutaneous laser nucleoplasty, a minimally invasive technique used to treat herniated discs.

This procedure consists of introducing a needle through the skin to the center of the intervertebral disc, through which an optical fiber will be passed and transmit the laser energy vaporizing from the nucleus pulposus, reducing intradiscal pressure and relieving compression on adjacent nerve roots. [28]

As it is a minimally invasive procedure, it can be performed with local anesthesia and light sedation, minimizing the risk of complications such as bleeding and infections, generating important pain relief soon after the procedure and allowing patients to return more quickly to their daily activities. [42]

Although percutaneous laser nucleoplasty is effective for many patients, it is indicated for milder cases, without major compressive effects or caudal migration of the hernia.

This technique works by reducing the mechanical effect of the hernia, not modulating the local inflammatory response, not being a regenerative procedure and not replacing conventional surgery in more severe or complex cases.

2.3.4. Orthobiologicals

Failure in the conservative approach, a better understanding of the etiopathogenesis of disc degeneration with evolution to the formation of herniated discs, risk of sequelae, high cost and the desire of patients to live without pain while not wanting to undergo surgical procedures have led several medical specialists to seek alternative methods capable of inducing the regeneration of the herniated disc without the risk of additional problems.

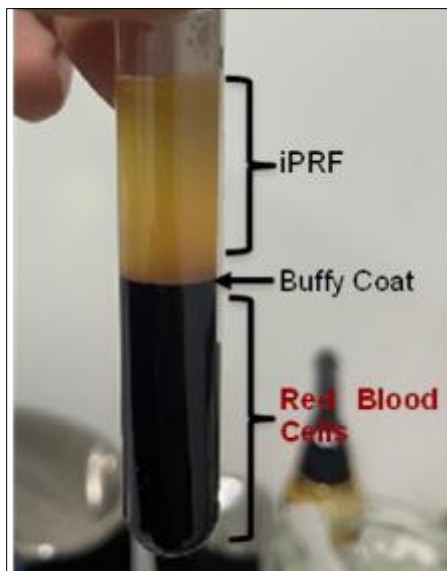


Figure 1 iPRF is an autologous product, without anticoagulant, minimally processed and capable of being prepared on an outpatient basis in a closed system, without the need for specialized orthobiological preparation centers. Its processing technique does not require expensive inputs, being an easily reproducible technique and capable of being applied in any center with trained professionals around the world

Among these alternatives, the use of orthobiologicals has been the subject of extensive debate and articles in the scientific literature regarding their applicability as a therapeutic option in musculoskeletal regenerative medicine [25, 43, 44; 45] Several orthobiologicals have been reported in the treatment of herniated discs, such as bone marrow aspirate (BMA), bone marrow aspirate concentrate (BMAC), expanded and laboratory-cultured mesenchymal cells, platelet-rich plasma, and platelet lysate, among other orthobiologicals. Each product has advantages and disadvantages, such as the presence of mesenchymal cells, the amount of growth factors, cytokines, and the ability to modulate the inflammatory response in various diseases that affect bones, cartilage, muscles, and tendons, demonstrating its ability to broaden the therapeutic spectrum in the most varied pathologies. [44-49]

Due to the ease of obtaining and preparation, without the need for specialized orthobiological processing centers, it was chosen in this work to use an autologous orthobiological product, not expanded, minimally manipulated and that does not require complex biological safety laboratories, making the technique can be replicated in several centers and can positively impact the largest number of people. [50]

Platelet- and leukocytes-rich fibrin (L-PRF) is an autologous matrix composed of fibrin, platelets, and leukocytes, extraordinarily rich in growth factors. This composition has been shown to be effective in optimizing the tissue repair process in various applications. L-PRF, by forming a clot, creates a fibrin mesh with nanometer-sized fibers, which function as a scaffold for cell migration, proliferation, and differentiation. In addition, this matrix causes the stimulation of growth factors of this orthobiological to be done gradually and to be maintained for about three weeks, the time necessary to induce neoangiogenesis and tissue repair, thus inducing the regeneration of the injured tissue. [50-55]

In 2014, the liquid (injectable) form of platelet-rich fibrin (i-PRF) was developed from changes in the configuration and processing of the biological material. By centrifuging the blood collected at low rotation speeds, it is possible to separate the blood components without activating the platelets, generating a concentrate of leukocytes, fibrin and platelets in liquid form that will later form a clot. This form of processing allows the material to be prepared without anticoagulants, reducing the handling of the material and enhancing its response when applied [45, 50, 56].



Figure 2 IPRF collection and preparation technique: venipuncture + vacuum aspiration of peripheral blood (A); centrifugation at low G-force to avoid platelet activation (B and D); aspiration of the iPRF while keeping the system closed(C). (C) Mixing of the iPRF with the medications that will be used in the application

For the preparation of the i-PRF, a kit consisting of four plastic collection tubes without additives is used. Centrifugation is conducted for six minutes at 80g at room temperature. After centrifugation, two components are obtained in the tube: a packed red blood cell at the bottom (red) and a supernatant that constitutes the i-PRF (orange). It is crucial to avoid mixing these two phases. The i-PRF is collected with the help of a syringe with a needle directly on the tube, not exposing the system to ambient air and contaminants.

The i-PRF was designed to achieve the same goals as its precursor (PRF), but in liquid form. Like PRF, i-PRF contains most white blood cells, including leukocytes (monocytes, neutrophils, lymphocytes) and platelets. One of the main characteristics of i-PRF, in addition to being in liquid form, is that it coagulates within five to ten minutes after its production, enabling its immediate application in a minimally invasive way by needles in procedures. [50, 57, 58]

Regarding the route of application of iPRF, the article by Singh et al. (2017) compared the efficacy of caudal epidural steroid injections and selective nerve root blocks (SNRB) in the management of pain and disability associated with lumbar disc herniation.

This prospective, randomized, blinded study enrolled eighty patients with lumbar disc herniation at one level, divided equally into two groups to receive caudal injections or SNRB. The results showed that the group that received the caudal epidural injections had a significant reduction in pain and functional disability with sustained beneficial effects up to one year after treatment. Patients treated with caudal epidural injections experienced a more than 50% reduction in pain for up to one year, while patients in the SNRB group experienced a similar reduction for up to six months.



Figure 3 Caudal epidural infiltration, performed in the sacral hiatus. A) Sonovisualization of the sacral hiatus in the transverse plane. Although caudal epidural block can be performed under radioscopy, it is possible to perform it safely with the transducer positioning shown in B). In the transverse plane, the needle is easily visualized throughout the path as in C), but this positioning requires the use of larger needles and is made difficult by the sacral inclination or size of the buttocks. We chose to perform the off-plane block as in D). As the needle is inserted out of plane, the power doppler resource is used to make sure that the application is being performed in the correct place, as observed in E) [59]

In addition, the improvement in disability, as measured by the Oswestry Disability Index (ODI), was more pronounced and sustained in the caudal injection group, with a reduction of 65.4% at 12 months compared to 46.7% in the SNRB group.

Based on the findings of Singh et al. (2017), the combination of caudal epidural injections with facet block may provide superior and long-lasting pain relief and improve function in patients with lumbar disc herniation. Caudal epidural injections are effective in reducing inflammation and nerve compression, while facet blocks directly address facet joint pain, which can be a significant co-contributor to low back pain. Thus, the combination of these two therapeutic approaches offers a comprehensive strategy to manage chronic low back pain, optimizing clinical outcomes and improving patients' quality of life.

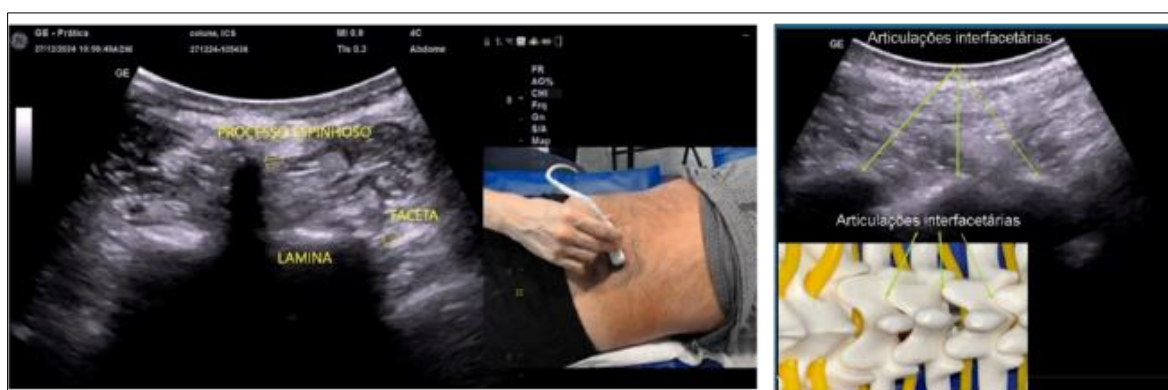


Figure 4 Ultrasound positioning to locate the lumbar facets and perform sonoguided facet block. Also previously described as a block performed under radioscopy, ultrasound allows dynamic visualization, with the monitoring of the passage of the needle until it reaches the therapeutic target while being able to visualize muscles, blood vessels and nerves, giving more safety to the application and allowing the technique to be performed on an outpatient basis. The application can be done with a transverse sonoimage, where the spinous process, lamina, and facet of the vertebra approached can be observed, as observed in A), or with a sagittal sonoimage, which will allow the visualization of multiple facets at multiple levels, as observed in B), being a preferential approach when more than one level of facet needs to be approached for symptomatic control of the patient. [60, 61]

2.3.5. Laser therapy

The use of laser has shown promise in the treatment of pain and various pathologies, including herniated discs, especially due to its ability to promote tissue regeneration and modulate the inflammatory response. [62]

Laser therapy utilizes specific wavelengths such as 660nm, 875nm, 905nm, and 1064nm to cover the entire therapeutic spectrum of the light window, allowing for deeper penetration and enhanced light absorption.

Lasers work with three emission modes: continuous, pulsed and superpulsed, each with specific characteristics and distinct applications [63, 64]. The continuous laser offers a constant beam, ideal for procedures that require the photothermal effect such as ablations and cauterizations, while the pulsed laser emits light at regular intervals, allowing a more exact control of the energy applied [63, 64]. The superpulsed laser combines the benefits of continuous and pulsed modes, emitting high-intensity pulses at extremely short intervals, which results in high photon delivery without tissue heating, being especially effective in regenerative medicine, as it promotes photobiomodulation without adverse photothermal effects and has a lower risk of tissue damage. [65-67]

In a study on neuropathic pain in rats, Hsieh et al performed cutaneous application of light in the range of 660 nm (red) on the area of a compressive lesion of the sciatic nerve in rats. This therapy not only decreased the pain process, but also considerably decreased the expression of TNF- α , IL1- β , and hypoxia-inducible factor 1 α (HIF-1 α) when compared to sham controls. If the inflammatory response is closely related to the genesis of sciatica, a non-invasive therapy capable of chemically modulating the inflammatory process and containing the pain process in a non-pharmacological way should be routinely used in symptomatologic control. [62, 68]

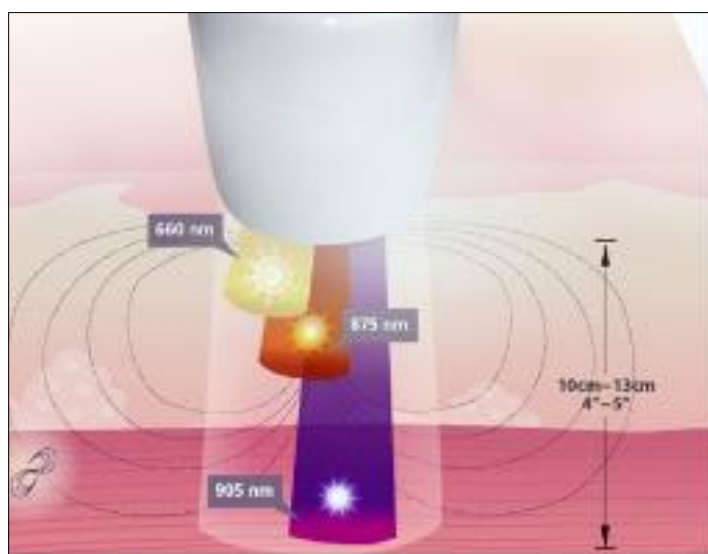


Figure 5 Multi-wavelength laser therapy activating distinct chromophores and maximizing biological response. [67]

Laser therapy also acts by modulating the inflammatory response through the polarization of macrophages when subjected to light in the 905nm (infrared) range. These cells of the white blood lineage can be activated for an M1 phenotype, which will generate an inflammatory response (through the cytokines TNF- α , IL1- β , IL-6), or an M2 phenotype generating a regenerative response (through the cytokines TGF- β , IL-10) contributing not only to the improvement of symptoms, but also inducing tissue repair in the treated area. [62, 69]

This approach results in significant bio stimulant effects. The superpulsed application provides billionths of a second pulses, combined with up to 50,000 mW of peak power, allowing for a higher concentration of light energy (photons) that penetrates deeper into the target tissue without risk of overheating and tissue damage secondary to the application. [62]

Rocha et al. (2006) point out that high-level laser therapy can reduce inflammation by reducing the presence of inflammatory chemical mediators and cytokines, in addition to reducing edema and migration of inflammatory cells. These effects are crucial for speeding up the healing process and preventing complications associated with chronic

inflammation. In addition to modulating inflammation, high-intensity laser stimulates the production of new cells and fibroblast proliferation, promoting collagen formation and neovascularization.



Figure 6 Application of superpulsed laser at levels previously defined by ultrasonography. Predefined protocols are used as described in the text

Studies, such as the one by Barcellos et al. (2023), demonstrate that high-level laser therapy can significantly accelerate wound healing and improve nerve function around the herniated disc. This combined approach of bio stimulant and anti-inflammatory effects makes high intensity superpulsed laser an effective and safe option in the management of herniated discs [70]. In literature reviews, no side effects were observed in the use of superpulsed laser in the management of patients with pain. [62]

2.3.6. Pulsed magnetic field.

Finally, the pulsed magnetic field (CMP) is a therapeutic option that uses high-frequency magnetic fields to treat various diseases, among which we can mention herniated discs due to its ability to promote blood circulation and reduce pain and inflammation. [72-77]

Clinical studies demonstrate that the application of CMP can relieve pain and improve motor function in patients with lumbar disc herniation, providing an effective and non-invasive alternative to conventional treatment. [72; 73, 74; 78] CMP works by inducing electrical currents in tissues, stimulating the production of growth factors and improving cell regeneration. [75, 79]



Figure 7 Application of the pulsed magnetic field for low back pain secondary to herniated discs: a non-invasive, painless technique that can be applied over clothing and immobilizations used by the patient and acts by modulating pain processes and inducing tissue repair

The physicochemical mechanisms involved in the therapeutic effect of CMP include inhibiting the expression of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF- α), contributing to the decrease in inflammation and pain [73, 78] and the modulation of gene expression and the activation of cell signaling pathways [75, 79]. Exposure to CMP will increase the production of growth factors such as platelet-derived growth factor (PDGF) and transforming growth factor beta (TGF- β), which are essential for tissue repair and regeneration of intervertebral discs.

In addition to modulating inflammation, CMP stimulates the production of new cells and fibroblastic proliferation, inducing collagen formation and neovascularization. These processes are essential for efficient healing and tissue regeneration. CMP therapy can speed up wound healing and improve neuromuscular function around the herniated disc. [80, 81]

The efficacy of CMP in the treatment of pain secondary to lumbar disc herniations has been demonstrated in several clinical studies. For example, randomized controlled trials have shown that patients treated with CMP had a significant reduction in pain intensity and functional disability compared to the control group [72, 73, 82]. Another study noted that combining CMP with physical therapy resulted in improved clinical outcomes, including improved mobility and quality of life for patients. [83]

In summary, the pulsed magnetic field is a promising therapy for the treatment of pain secondary to lumbar disc herniations, offering an effective and safe approach to relieve pain and promote tissue regeneration [78, 84, 85]. The application of CMP can activate physicochemical mechanisms that favor the production of growth factors and the reduction of inflammation, contributing to the recovery of patients. [86-89]

3. Results and discussion

The results obtained with the combination of injectable platelet-rich fibrin (iPRF) with superpulsed laser and pulsed magnetic field (CMP) for the treatment of disc herniations demonstrate promising potential for minimally invasive regenerative therapy. The proposed approach aims to bridge the gap between conservative treatments and surgical interventions, providing an effective and safe option for patients seeking symptomatic relief and tissue recovery without the risks inherent in surgery.

The literature suggests that chronic inflammation and oxidative stress are determining factors in the pathophysiology of herniated discs [7, 9, 12, 24, 90]. The use of iPRF stands out for its ability to modulate the inflammatory response and promote angiogenesis and cell proliferation, favoring the recovery of the injured intervertebral disc. Previous studies indicate that the sustained release of growth factors present in iPRF may contribute to pain reduction and long-term functional improvement [43-58, 91].

The intervertebral disc is recognized as an organ with immune privilege due to its avascular nature and the presence of anatomical barriers that limit the exposure of the immune system to its internal components (Alves, 2018). However, when a herniated disc occurs, these barriers are broken, exposing the nucleus pulposus to the immune system and triggering an inflammatory response. Studies indicate that this response can lead to spontaneous resorption of herniated material through immunological mechanisms. [30, 90]

The superpulsed laser, in turn, acts on the photobiomodulation of tissues, reducing the release of pro-inflammatory cytokines and stimulating mitochondrial activity in cells involved in tissue repair. Experimental evidence demonstrates that this therapy aids in nerve regeneration and disc tissue remodeling, contributing to the improvement of radicular pain symptoms and spinal functionality. [40, 67-71]

The CMP completes this therapeutic protocol by acting directly on pain modulation and stimulation of cell repair. The pulsed magnetic field has been widely studied for its ability to influence gene expression and collagen synthesis, promoting the recovery of connective and cartilage tissues [72-79]. In addition, its non-invasive and painless application represents a viable alternative for patients who do not tolerate or have contraindications to conventional pharmacological treatments.

The continuous modulation of the inflammatory response generated by the growth factors released by the iPRF fibrinolysis process results in a continuous modulation in the inflammatory process of the disc herniation, facilitating the progression of disc tissue repair.

The benefits of a minimally invasive and regenerative treatment compared to surgical and conservative treatment are evident in several aspects. First, this type of approach significantly reduces work absenteeism, since the recovery time is shorter, and the patient can resume his daily activities more quickly [93]. In addition, pain improvement is achieved in a progressive and sustained way, without the need for more aggressive interventions. Quality of life is also positively impacted, as the therapy promotes the patient's functional recovery without the risks and complications associated with surgical procedures.

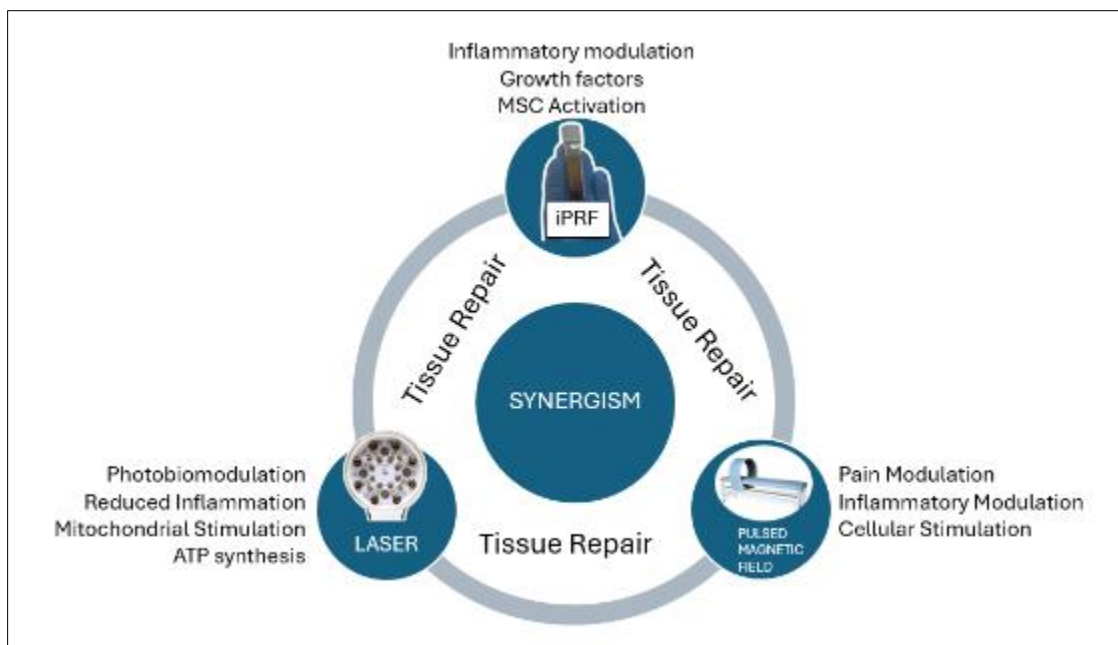


Figure 8 The three approaches interconnect and enhance the regenerative and anti-inflammatory effects, creating a favorable environment for the recovery of herniated discs

Another fundamental aspect is the cost reduction associated with the reduction in the indication of surgical interventions for the treatment of herniated discs [93]. Minimally invasive procedures require shorter hospital stays, reduce the need for prolonged rehabilitation, and minimize postoperative complications, reducing overall costs for public and private health systems. In addition, by avoiding prolonged absences from work and reducing dependence on chronic analgesia, the economic and social impact becomes even more significant.

The findings of this study are in line with recent research, such as the study published by Souza et al. (2018), which discusses the benefits of regenerative therapies in the treatment of herniated discs and their applicability in clinical practice. This study reinforces the efficacy of minimally invasive approaches in reducing pain, improving functionality, and reducing the need for surgical interventions, corroborating the data presented in this study.

Although the initial results are encouraging, it is essential to conduct randomized controlled trials with larger sample sizes to validate the statistical efficacy and safety of this approach. In addition, the standardization of application protocols and the determination of the optimal dose for each therapy are fundamental aspects for its large-scale clinical implementation.

The association between orthobiological therapies and regenerative technologies represents a new frontier in regenerative medicine, promoting a holistic and personalized approach to the treatment of herniated discs. This strategy has the potential to revolutionize clinical practice, reducing the need for invasive surgical procedures and improving the quality of life of patients, while reducing the socioeconomic impact of this injury on society.

4. Conclusion

Classically, lumbar disc herniation is the main diagnostic cause of lumbar spine pain, affecting 1 to 5% of the general population. The typical clinical picture includes low back pain, followed by low back pain and sciatica. Initial treatment is conservative, using drug management, physical therapy, and percutaneous root blocks. Surgical intervention is indicated in cases of failure to control pain, significant motor deficit, radicular pain with foraminal bone stenosis, or cauda equina syndrome. Refined surgical techniques, which preserve the ligamentum flavum and remove only the extruded fragment, have shown superior results in resolving sciatica symptoms and reducing long-term recurrence.

Despite advances in surgical techniques, conservative treatment remains the first line of approach, with microdiscectomy being preferable in surgical cases due to its balance between invasiveness and efficacy. Revision

surgery to treat fibrosis is challenging and often results in a poor prognosis. The prevention of epidural fibrosis is therefore one of the main objectives of modern surgical interventions for lumbar disc herniation.

Recurrence of symptoms and lack of favorable evolution in surgical results may be associated with metainflammation and oxidative stress, important metabolic alterations in the development of lumbar disc herniations, and their control may be essential to prevent and treat this condition. Deyo et al. (2015) highlight the need for therapeutic approaches that aim to reduce these processes to improve patients' quality of life.

The associated treatment between orthobiologics and regenerative technologies such as superpulsed laser and pulsed magnetic field emerges as a middle ground between the conservative and surgical approach in the treatment of herniated discs, gradually presenting increasingly better results in relation to conservative treatment and without the complications inherent to surgical treatment.

Classically, regenerative medicine is based on three pillars: Scaffold, mesenchymal cells and bioactive molecules, but in view of the exponential growth of regenerative medicine as a medical specialty, it is necessary that this concept be expanded with the use of regenerative technologies, so that tissue regeneration has not three, but 4 pillars: the physical modulation of the biological response is a reality that can no longer be ignored by the scientific community.

We must move from the stage in which we evaluate the affectivity of orthobiologics in the treatment of lesions and start the search for synergistic mechanisms between therapies to optimize the clinical result of the treatments implemented in our patients.

By understanding the mechanism of action of these three therapeutic approaches, we can infer that the treatment of herniated discs can be optimized by combining the application of injectable platelet-rich fibrin with superpulsed laser and pulsed magnetic field (CMP). Because each of these techniques contributes to the modulation of the inflammatory response and promotion of tissue regeneration, the combination of these three therapies offers an integrated approach that maximizes the benefits of inflammatory modulation and tissue regeneration in the treatment of herniated discs.

This therapeutic synergy can provide more effective symptomatic relief, in addition to inducing the repair of injured tissue and accelerating the recovery of patients, significantly improving their quality of life in a safe, minimally invasive way and at a lower cost than the surgical approach.

Although more studies with a large volume of patients are needed to evaluate the statistical efficacy of this technique and side effects, the regenerative approach in the treatment of herniated discs may revolutionize the treatment of herniated discs. Performing minimally invasive procedures, in a safe and echo-guided way using autologous, minimally manipulated orthobiologics associated with superpulsed laser and pulsed magnetic field can treat the painful symptomatology of patients, induce disc regeneration, effectively healing the lesion without the risks inherent to the surgical procedure.

Within the use of orthobiologics, standardization is fundamental, and there is a need for further studies comparing the effectiveness of the association of other orthobiologics with superpulsed laser and pulsed magnetic field in the treatment of disc herniation.

Compliance with ethical standards

Disclosure of conflict of interest

Author Douglas Scott Johnson presents as a conflict of interest to serve as Senior Vice President of Clinical and Scientific Affairs at Multi Radiance Medical and Chief Scientific Officer at PhotoOpTx. The other authors have no conflicts of interest.

References

- [1] Deyo, R. A., et al. (2015). Trends, major medical complications, and charges associated with surgery for lumbar disc herniation in the United States. *Journal of Bone and Joint Surgery*, 97(3), 203-210.
- [2] Loh, K., et al. (2019). Percutaneous endoscopic discectomy in lumbar disc herniation: Efficacy and complications. *Global Spine Journal*, 9(5), 491-496.

- [3] Vialle, L. R., Vialle, E. N., Suárez Henao, J. E., & Giraldo, G. (2010). Lumbar disc herniation. *Brazilian Journal of Orthopedics*, 45(1), 17-22. <https://doi.org/10.1590/S0102-36162010000100004>.
- [4] Perfeito, R. S.; MARTINS, E. (2021) Lumbar disc herniation: etiology, diagnosis and most commonly used treatments. *Perspective Magazine: Science and Health*, v. 11, n. 21, p. 45-60, 2023. Available at: <<https://cientifica.cnec.br/index.php/revista-perspectiva/article/view/124>>
- [5] Manchikanti, L., et al. (2014). Epidemiology of low back pain in the United States. *Pain Physician*, 17(3), E1-E9.
- [6] Kato, T., et al. (2018). Clinical outcomes of conservative treatment for cervical disc herniation. *Spine Surgery and Related Research*, 2(3), 205-210.
- [7] Choi, J. H., et al. (2018). Risk factors for lumbar disc herniation: a systematic review. *Journal of Orthopaedic Surgery and Research*, 13(1), 1-9.
- [8] Buchbinder, R., et al. (2018). Surgery for lumbar disc herniation: a systematic review and meta-analysis. (Comparison of interventions for lumbar disc herniation: a systematic ...) *The Lancet*, 391(10134), 2089-2099.
- [9] Atlas, S. J., et al. (2006). The effect of magnetic resonance imaging on the management of patients with low back pain. *The New England Journal of Medicine*, 354(24), 2638-2645.
- [10] Tache-Codreanu D-L, Trăistaru MRelement. The effectiveness of high-intensity laser in improving motor deficits in patients with lumbar disc herniation. *Life*. 2024; 14(10):1302. <https://doi.org/10.3390/life14101302>
- [11] Adams, M. A., & Roughley, P. J. (2006). What is intervertebral disc degeneration, and what causes it? *European Spine Journal*, 15(Suppl 3), S1-S2.
- [12] Freemont, A. J. (2009). The cellular and molecular pathology of intervertebral disc degeneration. *The Journal of Pathology*, 217(3), 282-292.
- [13] Brinjikji, W., Luetmer, P. H., Comstock, B., Bresnahan, B. W., Chen, L. E., Deyo, R. A., & Jarvik, J. G. (2015). Systematic literature review of imaging features of spinal degeneration in asymptomatic populations. *AJNR American Journal of Neuroradiology*, 36(4), 811-816.
- [14] Jensen, M. C., Brant-Zawadzki, M. N., Obuchowski, N., Modic, M. T., Malkasian, D., & Ross, J. S. (1994). Magnetic resonance imaging of the lumbar spine in people without back pain. *New England Journal of Medicine*, 331(2), 69-73.
- [15] Leite, R., Silva, P., & Santos, A. (2021). Prevalence of Lumbar Disc Herniation in Brazil. *Brazilian Journal of Orthopedics*, 56(4), 234-241. <https://doi.org/10.1590/S0102-36162021000400011>
- [16] Costa, M., & Rodrigues, F. (2022). Lumbar disc herniation: Etiology, diagnosis and treatment. *Medical Journal of Pernambuco*, 11(2), 45-53. <https://doi.org/10.5007/1312-5286.2022v11n2p45>
- [17] Almeida, D., & Oliveira, J. (2023). Advances in the diagnosis and treatment of lumbar disc herniation: A systematic review. *Journal of Health Sciences*, 19(1), 28-37. <https://doi.org/10.18256/2317-8051.2023v19n1p28>
- [18] Bogduk, N. (2012). *Clinical Anatomy of the Lumbar Spine and Sacrum*. Elsevier Health Sciences.
- [19] Sussela, A. O., Bittencourt, A. B., Raymondi, K. G., Tergolina, S. B., & Ziegler, M. S. (2017). Herniated disc: epidemiology, pathophysiology, diagnosis and treatment. *Acta Orthopaedica Belgium*, 79(6), 726-730. Available at *Acta Orthopaedica Belgium*.
- [20] Botelho, R.; Canto, F.; Carvalho, M.; Daniel, J.; Defino, H.; Façanha, Filho, F.; Meves, R.; Moraes, O.; Mudo, M.; Pimenta Junior, W.; Ribeiro, C.; Tarico, M.; Zylbersztejn, S.; Assis, M. Lumbar disc herniation in adults, *Brazilian Society of Orthopedics and Traumatology, Brazilian Society of Neurosurgery. Clinical guidelines in complementary health*, 2011.
- [21] Deyo, R. A., et al. (2009). Low back pain. *The New England Journal of Medicine*, 360(21), 2192-2199.
- [22] Modic, M. T., & Ross, J. S. (2005). Lumbar degenerative disk disease. *Radiology*, 245(1), 43-61.
- [23] Carvalho, M. E. I. de; Carvalho Junior, R. M. de; Carvalho, R. A.; Paula Junior, A. R. de. (2010). Functional limitation in patients with lombar disk herniation and the impact on working life. *Rev. Ter. Man*, 8(38), 320-324. Available at LILACS, ID: lil-606221. Responsible library: BR512.1
- [24] Kumar, S., et al. (2019). Efficacy of laser therapy in the management of herniated discs: A systematic review. *Pain Physician*, 22(1), 1-10.

- [25] Atlas, S. J., Deyo, R. A., Keller, R. B., Chapin, A. M., Patrick, D. L., Long, J. M., & Singer, D. E. (2001). ("Functional outcome of surgical treatment for multilevel lumbar spinal ...") "The Maine Lumbar Spine Study, part II: 1-year outcomes of surgical and nonsurgical management of sciatica." ("August 1, 1996 - Volume 21 - Issue 15: Spine") *Spine*, 26(10), 1179-1187.
- [26] Koes, B. W., et al. (2010). Diagnosis and treatment of low back pain. *BMJ*, 340, c1035.
- [27] Lee, J. H., et al. (2019). Efficacy of platelet-rich plasma in the treatment of lumbar disc herniation: A systematic review. *Journal of Orthopaedic Surgery and Research*, 14(1), 1-7.
- [28] Singh, V., Manchikanti, L., Calodney, A. K., & Staats, P. S. (2003). Percutaneous lumbar laser disc decompression: a systematic review of current evidence. *Pain Physician*, 6(4), 463-482.
- [29] Lopes, T.K. (2009) Conservative treatment for lumbar disc herniation: physical therapy protocols. *Lage*.
- [30] Xie, L., Dong, C., Fang, H., Cui, M., Zhao, K., Yang, C., & Wu, X. (2024). Prevalence, clinical predictors and mechanisms of resorption in lumbar disc herniation: a systematic review. *Orthopedic Revisions*, 16. <https://doi.org/10.52965/001c.121399>
- [31] Sousa, L. S., Pinheiro, M. S. C., & Rodrigues, J. L. G. (2021). Indiscriminate use of opioids and their consequences. *PubSaúde*, 6, a190. <https://dx.doi.org/10.31533/pubsaude6.a190>
- [32] Lang, K., et al. (2021). "Endoscopic vs. Microdiscectomy for Lumbar Disc Herniation: A Systematic Review and Meta-Analysis." *Spine*, 46(3), 170-178.
- [33] Huang, Y., et al. (2022). "Microdiscectomy for lumbar disc herniation: A meta-analysis of outcomes." *European Spine Journal*, 31(5), 1042-1052.
- [34] Lee, J. H., et al. (2020). The effectiveness of magnetotherapy for pain relief in patients with lumbar disc herniation: A meta-analysis. *Pain Medicine*, 21(1), 1-10.
- [35] Choi, D. J., et al. (2021). Surgical management of lumbar disc herniation: A comprehensive review of techniques, risks, and outcomes. *Journal of Neurosurgery: Spine*, 35(3), 345-357.
- [36] Mensah, E.O.; Chalif, J.I.; Padeiro, J.G.; Chalif, E.; Oliveira, J.; Groff, M.W. Challenges in Contemporary Spine Surgery: A Comprehensive Review of Surgical, Technological, and Patient-Specific Issues. *J. Clin. Med* **2024**, *13*, 5460. <https://doi.org/10.3390/jcm13185460>
- [37] Aljawadi A, Sethi G, Islam A, Elmajee M, Pillai A. Sciatica Presentations and predictors of poor outcomes after surgical decompression of lumbar disc herniation: a review article. *Cureus*. November 21, 2020; 12(11):e11605. DOI: 10.7759/cureus.11605. PMID: 33240732; PMCID: PMC7681772.
- [38] Khan, M. A., et al. (2023). "Recurrence of herniated lumbar disc after discectomy: a systematic review and meta-analysis." *Spine Journal*, 23(1), 19-28.
- [39] Alves Filho, A. C.; Gonçalves, A. L. F.; Barbosa, A. de M. (2021) Conservative versus surgical treatment in patients with lumbar disc herniation. *BrJP*, São Paulo, v. 4, n. 4, p. 357-361. DOI: 10.5935/2595-0118.20210067.
- [40] Negrelli, W. F., (2001). Herniated disc: treatment procedures. *Acta ortop bras.*:39–45. Available from: <https://doi.org/10.1590/S1413-78522001000400005>
- [41] Lyro, A. S., Carvalho Filho, P. B. (1985). Lumbar disc herniation, surgical treatment: considerations on 62 cases. *ECMAL*, v. 3, n. 1, p. 14-16, 1st sem. 1985. Available at: <https://pesquisa.bvsalud.org/portal/resource/pt/lil-28017>.
- [42] Davis, R. J., et al. (2017). Clinical presentation of lumbar disc herniation. *Journal of Neurosurgery: Spine*, 26(4), 482-490.
- [43] Chang, Y., Yang, M., Ke, S., Zhang, Y., Xu, G., & Li, Z. (2020). Effect of platelet-rich plasma on intervertebral disc degeneration in vivo and in vitro: A critical review. *Oxidative Medicine and Cellular Longevity*, 2020. <https://doi.org/10.1155/2020/8893819>
- [44] Machado, E.S.; Oliveira, F.P.; Vianna de Abreu, E.; de Souza, T.A.d.C.; Meves, R.; Grohs, H.; Ambach, MA; Oliveira, A.; de Castro, R.B.; Pozza, D.H.; et al. (2023) Systematic Review of Platelet-Rich Plasma for Low Back Pain. *Biomedicamentos*, 11, 2404. <https://doi.org/10.3390/biomedicines11092404>
- [45] Lana J.F., Purita J., Everts P.A., De Mendonça Neto P.A.T. *et al.* (2023) Platelet-Rich Plasma Power-Mix Gel (PMP)—An Orthobiologic Optimization Protocol Rich In Growth Factors And Fibrin. *Gels*; 9(7): 553

- [46] Purita J., Lana J.F., Kolber M., Rodrigues B.L., Mosaner T., et al. (2020) Bone Marrow-Derived Products: A Classification Proposal–Bone Marrow Aspirate, Bone Marrow Aspirate Concentrate or Hybrid? *World J Stem Cells*; 12(4):241.
- [47] Dhillon, M. Dhillon M.S., Behera P., Patel S., Shetty V., (2014) Orthobiologics and Platelet Rich Plasma. *Indian J Orthop*; 48:1-9.
- [48] Huddleston H.P., Maheshwer B., Wong S.E., Chahla J., Cole B.J. *et al.* (2020) An Update on The Use of Orthobiologics: Use of Biologics for Osteoarthritis. *Oper Tech Sports Med*; 28(3):150759.
- [49] Lana J.F., da Fonseca L.F., Mosaner T., Tieppo C.E., Azzini G.O., *et al.* (2020) Bone Marrow Aspirate Clot: A Feasible Orthobiologic. *J Clin Orthop Trauma*; 11: S789-S794.
- [50] Anitua E., Sanchez M., Nurden A.T., Nurden P., Orive G. *et al.* (2006). New Insights into and Novel Applications for Platelet-Rich Fibrin Therapies. *Trends Biotechnol*; 24(5):227-34.
- [51] Zochodne, D. W. The challenges and beauty of peripheral nerve growth. *Journal of the Peripheral Nervous System*, Wiley Online Library, 2012. DOI: 10.1111/j.1529-8027.2012.00378. x. Available at: <<https://onlinelibrary.wiley.com/doi/10.1111/j.1529-8027.2012.00378.x>>.
- [52] Saluja H., Dehane V., Mahindra U. (2011). Platelet-Rich Fibrin: A Second-Generation Platelet Concentrate and A New Friend of Oral and Maxillofacial Surgeons. *Ann Maxillofac Surg*, 1(1):53-57.
- [53] Dohan D.M., Choukroun J., Diss A., Dohan S.L., Dohan A.J., et al. (2006a). Platelet-Rich Fibrin (PRF): A Second-Generation Platelet Concentrate. Part I: Technological Concepts and Evolution. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 101(3):e37-e44.
- [54] Choukroun, J.; Diss, A.; Simonpieri, A.; Girard, M.-O.; Schoeffler, C.; Dohan, S.L.; Dohan, A.J.J.; Mouhyi, J.; Dohan, D.M. Platelet-Rich Fibrin (PRF): A Second-Generation Platelet Concentrate. Part IV: Clinical Effects on Tissue Healing. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* 2006, 101, e56–e60.
- [55] Kardos D., Hornyák I., Simon M., Hinsenkamp A., Marschall B., *et al.* (2018). Biological And Mechanical Properties of Platelet-Rich Fibrin Membranes After Thermal Manipulation and Preparation in A Single-Syringe Closed System. *Int J Mol Sci*; 19(11):3433.
- [56] Miron R.J., Fujioka-Kobayashi M., Hernandez M., Kandalam U., Zhang Y., *et al.* (2017). Injectable Platelet Rich Fibrin (I-PRF): Opportunities in Regenerative Dentistry? *Clin Oral Investig*; 21:2619-2627.
- [57] Pavlovic V, Ciric M, Jovanovic V, Trandafilovic M, Stojanovic P. (2021). Platelet-Rich Fibrin: Basics of Biological Actions and Protocol Modifications. *Open Medicine*; 16(1):446-454.
- [58] Kang YH, Jeon SH, Park JY, Chung JH, Choung YH, et al. (2011). Platelet-Rich Fibrin is a Bioscaffold and Reservoir of Growth Factors for Tissue Regeneration. *Tissue Engineering Part A*; 17(3-4):349-359.
- [59] Najman, I. E., Frederico, T. N., Segurado, A. V. R., & Kimachi, P. P. (2011). Caudal epidural block: anesthetic technique for exclusive use in children? Is it possible to perform it in adults? What is the role of ultrasound in this context? *Brazilian Journal of Anesthesiology*, 61(1), 102–109. <https://doi.org/10.1590/S0034-70942011000100011>
- [60] Gofeld, Michael. (2008). Ultrasonography in Pain Medicine: A Critical Review. *Pain practice: the official journal of World Institute of Pain*. 8. 226-40. 10.1111/j.1533-2500.2008.00215. x.
- [61] Gofeld, Michael. (2011) *Advanced Ultrasound Imaging in Pain Medicine*.
- [62] Cheng, K., Martin, L. F., Slepian, M. J., Patwardhan, A. M., Ibrahim, M. M., Mechanisms and Pathways of Pain Photobiomodulation: A Narrative Review, *The Journal of Pain*, Volume 22, Issue 7, 2021, Pages 763-777, ISSN 1526-5900, <https://doi.org/10.1016/j.jpain.2021.02.005>.
- [63] Hobbs, E. R.; Bailin, P. L.; Wheeland, R. G.; Ratz, J. L.. Superpulsed lasers: minimizing thermal damage with high irradiance, short-duration pulses. *The Journal of Dermatologic Surgery and Oncology* 13(9):p 955-964, September de 1987.
- [64] Lanzafame, R.J., Naim, J.O., Rogers, D.W., and Hinshaw, J.R. (1988), Comparison of continuous-wave, chop-wave, and superpulse laser wounds. *Lasers Surg. Med.*, 8: 119-124.
- [65] Grandinetti, V. dos S., Miranda, E. F., Johnson, D. S., Paiva, P. R. V. de, Tomazoni, S. S., Vanin, A. A., Albuquerque Pontes, G. M., Frigo, L., Marcos, R. L., Carvalho, P. de T. C. de, & Leal-Junior, E. C. P. (2015). The thermal impact of

phototherapy with concurrent super-pulsed lasers and red and infrared LEDs on human skin. *Lasers in Medical Science*, 30(5), 1575-1581.

- [66] Chung, H., Dai, T., Sharma, S.K. et al. The nuts and bolts of low-level laser (light) therapy. *Ann Biomed Eng* 40, 516–533 (2012).
- [67] Leal-Junior, E. C. P., & Tomazoni, S. S. (2019). Synergistic effects of combination of three wavelengths and different light sources in cytochrome c oxidase activity in intact skeletal muscle of rats. In *Medical Laser Applications and Laser-Tissue Interactions IX* (Vol. 11079, 110791E). SPIE. <https://doi.org/10.1117/12.2526834>
- [68] Hsieh, Y.-L., Chou, L.-W., Chang, P.-L., Yang, C.-C., Kao, M.-J. e Hong, C.-Z. (2012), Low-level laser therapy relieves neuropathic pain and promotes recovery of function in rats with chronic constriction injury: Possible involvement in hypoxia-inducible factor 1 α (HIF-1 α). *J. Comp. Neurol.*, 520: 2903-2916. <https://doi.org/10.1002/cne.23072>
- [69] Ketz, A. K., Byrnes, K. R., Grunberg, N.E., Kasper, C. E., Osborne, L., Pryor, B., Tosini, N. L., Wu, X., Anders, J. J. (2017). Characterization of macrophage/microglia activation and effect of photobiomodulation on the neuropathic pain-spared nerve injury model. *Pain Med*, 18, pp. 932-946
- [70] Henriques, Á. C. G., Cazal, C., & Castro, J. F. L. de. (2010). Action of laser therapy on the process of cell proliferation and differentiation: a review of the literature. *Journal of the Brazilian College of Surgeons*, 37(4), 295–302. <https://doi.org/10.1590/S0100-69912010000400011>
- [71] Barcellos, G. D. M., Barbosa, G. V., Diniz, I. V. V., de Souza Barbosa, L., Ferrugine, R. P. D. S., & da Silva Freitas, V. (2023). The effect of laser therapy on tissue healing. *Health Praxis*, 1(1), 01-19.
- [72] Arneja, A. S., Kotowich, A., Staley, D., Summers, R., & Tappia, P. S. (2016). Electromagnetic fields in the treatment of chronic low back pain in patients with degenerative disc disease. *Science of the Future OA*, 2(1).
- [73] Beljan, I., & Švraka, E. (2023). Effectiveness of magnetotherapy in the treatment of patients with lumbar syndrome. *Health Bulletin*, 9(1), 74-85.
- [74] Paolucci T., Pezzi L., Centra A.M., Giannandrea N., Bellomo R.G., Saggini R. Electromagnetic field therapy: a rehabilitation perspective in the treatment of musculoskeletal pain - a systematic review. *J Pain Res*. 2020 12 de junho;13:1385-1400.
- [75] Mayer Y., Shibli J.A., Saada H.A., Melo M., Gabay E., Barak S, et al.. Pulsed Electromagnetic Therapy: Literature Review and Current Update. *Braz Dent J* [Internet]. 2024;35:e24–6109.
- [76] Rajalekshmi R., Agrawal D.K.. Energizing Healing with Electromagnetic Field Therapy in Musculoskeletal Disorders. *J Orthop Sports Med*. 2024; 6(2):89-106.
- [77] Ross, C. L., Teli, T., & Harrison, B. S. (2016). Electromagnetic field devices and their effects on nociception and peripheral inflammatory mechanisms of pain. *Alternative therapies in health and medicine*, 22(3), 52-64.
- [78] Seppia, C. D., Ghione, S., Luschi, P., Ossenkopp, K., Choleris, E., Kavaliers, M. (2007) Pain perception and electromagnetic fields, *Neuroscience & Biobehavioral Reviews*, Volume 31, Issue 4, Pages 619-642, ISSN 0149-7634, <https://doi.org/10.1016/j.neubiorev.2007.01.003>.
- [79] Maziarz, A., Kocan, B., Bester, M., Budzik, S., Cholewa, M., Ochiya, T., & Banas, A. (2016). How electromagnetic fields can influence adult stem cells: positive and negative impacts. *Stem cell research & therapy*, 7(1), 54.
- [80] Almeida, N., & Silva, M. F. (2021). Effects and Applications of High Intensity Electromagnetic Field (PEMF) in Health and Aesthetics. *Journal of Sustainable Development*, 18(10), 217-224. Available at: <https://rsdjournal.org/index.php/rsd/article/download/21724/19291/261101>.
- [81] Oliveira, R. S., & Araújo, J. R. (2022). Pulsed and Moderate Electric Fields for the Stimulation of Bacteria and Yeasts in Biotechnological Processes. *Brazilian Journal of Biotechnological Processes*, 12(8), 182-195. Available at: <https://lume.ufrgs.br/bitstream/handle/10183/252211/001136680.pdf?sequence=1>.
- [82] Park, W.-H. et al. (2014) Effect of Pulsed Electromagnetic Field Treatment on the Relief of Lumbar Myalgia; A Single-center, Randomized, Double-Blind, Sham-Controlled Pilot Trial Study, *Journal of Magnetism*. The Korean Society of Magnetism.
- [83] Cristiano, L., Pratellesi, T. (2020). Mechanisms of Action And Effects of Pulsed Electromagnetic Fields (PEMF) in Medicine. 1. 33. 10.52916/jmrs204033.

- [84] Esposito, M., Lucariello, A., Riccio, I., Riccio, V., Esposito, V., & Riccardi, G. (2012). Differentiation of human osteoprogenitor cells increases after treatment with pulsed electromagnetic fields. *In vivo (Athens, Greece)*, 26(2), 299-304.
- [85] Saggini, R., Bellomo, R.G., Saggini, A., Iodice, P. e Toniato, E. (2009) Rehabilitation treatment for low back pain with external pulsed electromagnetic fields. *International Journal of Immunopathology and Pharmacology* 2009 22:3_suppl, 25-28
- [86] Dan-bo Su, Zi-xu Zhao, Da-chuan Yin, Ya-jing Ye. (2024) Promising application of pulsed electromagnetic fields on tissue repair and regeneration, *Progress in Biophysics and Molecular Biology*, Volume 187, 2024, Pages 36-50, ISSN 0079-6107, <https://doi.org/10.1016/j.pbiomolbio.2024.01.003>.
- [87] Mansourian M, Shanei A. (2021) Evaluation of the effects of the pulsed electromagnetic field: a systematic review and meta-analysis on the highlights of two decades of research in in vitro studies. *Biomed Res Int.* 2021 July 29, 2021:6647497. DOI: 10.1155/2021/6647497. PMID: 34368353; PMCID: PMC8342182.
- [88] Levada, J. S., & Souza, M. R. (2024). Herniated Disc: Review of Modern Therapeutic Approaches. *Brazilian Journal of Integrated Health and Humanization*, 1-15. Available at <https://bjih.emnuvens.com.br/bjih/article/download/3047/3268/6801>.
- [89] Kull, P., Keilani, M., Remer, F. *et al.* (2023) Efficacy of pulsed electromagnetic field therapy on pain and physical function in patients with nonspecific low back pain: a systematic review. *Wien Med Wochenschr* <https://doi.org/10.1007/s10354-023-01025-5>
- [90] Alves, B. M. K. O. (2018). Immunological mechanisms in the spontaneous resorption of intervertebral disc herniations. *Portuguese Journal of Orthopedics and Traumatology*, 26(3), 228-235.
- [91] Castro, A. B., Herrero, P., & Pires, F. R. (2018). Platelet-rich fibrin: preparation, definition of quality, clinical use. *Health Surveillance in Debate: Society, Science & Technology*, 6(4), 61-68.
- [92] Souza, I. M. B., Sakaguchi, T. F., Yuan, S. L. K., Matsutani, L. A., do Espírito-Santo, A. S., Pereira, C. A. M., & Marques, A. P. (2018). Herniated disc: epidemiology, pathophysiology, diagnosis and treatment. *Physiotherapy and Research*, 25(1), 125-137.
- [93] Almeida, D. B., & Prandini, M. N. (2018). Lumbar disc herniation. *Brazilian Journal of Orthopedics*, 53(1), 100-106.