ERCHONIA® FX-635™

A double-blind, placebo-controlled randomized evaluation of the effect of the Erchonia® FX-635™on low back pain clinical study protocol

ERCHONIA CORPORATION

Version 4.2
January 7, 2017

STUDY INFORMATION

PURPOSE OF STUDY

The purpose of this clinical study is to determine the effectiveness of the Erchonia® FX-635™, manufactured by Erchonia Corporation (the Company), in providing temporary acute relief of minor episodic chronic low back pain of musculoskeletal origin.

STUDY DURATION

The estimated total duration of the study is four to five months.

INDICATION FOR USE

The indication (claim) being sought through support of the results of this clinical study is: "The Erchonia® FX-635™ is indicated for adjunctive use in providing temporary acute relief of minor episodic chronic low back pain of musculoskeletal origin."

It is intended that the results of this clinical study be used to support a 510(k) submission to FDA for clearance to market the device for the intended indication.

EXPECTED RESULTS

Following completion of the study procedure administration protocol with the Erchonia® FX-635™, it is anticipated that compared with baseline, a significantly greater proportion of subjects in the test group than in the placebo group will show a 30% or greater reduction in self-reported low back pain VAS rating at study endpoint evaluation.

DEVICE INFORMATION: ERCHONIA® FX-635™

DEVICE DESCRIPTION & DETAILS

The Erchonia® FX-635™ used in this study is made up of 3 independent 17 mW, 635 nm red laser diodes mounted in scanner devices with flexible arms positioned equidistant from each other.

The Erchonia® FX-635™ is a variable hertz device. The variable hertz feature of the Erchonia® FX-635™ is a pulsed wave, defined as containing a selected series of breaks, variances that are preprogrammed.

The Erchonia® FX-635™ utilizes internal mechanics that collects the light emitted from each of the laser diodes and processes each through a proprietary patented lens which redirects the beam with a line refractor. The refracted light is then bent into a spiraling circle pattern that is totally random and independent of the other diodes.

The Erchonia® FX-635™ has the following specifications:

- ✓ Configuration: Class 2 Line Generated Laser Diode Modules
- ✓ Wavelength: 635 nm
- ✓ Power Output (Mean): 17 mW
- ✓ Modulation: Pulsed Wave (50% duty Cycle)
- ✓ Display: Full Color TFT Touch Screen Control Center
- ✓ Adjustments:
  - 44” Vertical Arm Height Adjustment.
  - Three Independent Adjustable Arms
- ✓ Power Source: 100-240 VAC 50-60 Hz
- ✓ Chassis:
  - Metal Frame Powder Coated for Ease of Cleaning
  - 4 Anti-Static Casters (4 Locking)
- ✓ Housing: Black Carbon Fiber Finish Thermoformed from Non-Allergen Material/Plastic
- ✓ Weight: 70 lbs.

Dosage calculations for the Erchonia® FX-635™

Equations:
1) Intensity = W/cm2
2) Dosage = (J/cm2)=(W/cm2) x τ(s)
3) Oval Surface area = π x (r1/2) x (r2/2)
MW = miliwatts
W= Watts

Intensity:
Intensity ÷ oval surface area = intensity at tissue
1) 17.5 mW / 1000 = 0.0175 W (Intensity conversion from mW to W)
2) π x (9cm/2) x (9.5cm/2) = 21.375 cm2 (surface area of treated region at single diode at 3.5” above the skin surface.
3) 0.0175 / 21.375 cm2 = 8.2 x10-4 W/cm2 (intensity for single diode at skin)
4) 8.2 x 10-4 W/cm2 x (3 diodes) = 2.46 x10-3 W/cm2 (intensity for all 3 diodes combined at the skin)

Dosage delivered to the skin:
Intensity x τ(s) = dosage at specific area
1) 2.46 x 10-3 W/cm2 x (900 seconds) = **.0865 J/cm2** (total dosage delivered to the skin)

The Erchonia® FX-635™ used in this study is shown in Figures 1 and 2 below.

Figure 1: Erchonia® FX-635™

Figure 2: Erchonia® FX-635™

The Erchonia® FX-635™ System Components is shown in Figures 3 and 4 below.

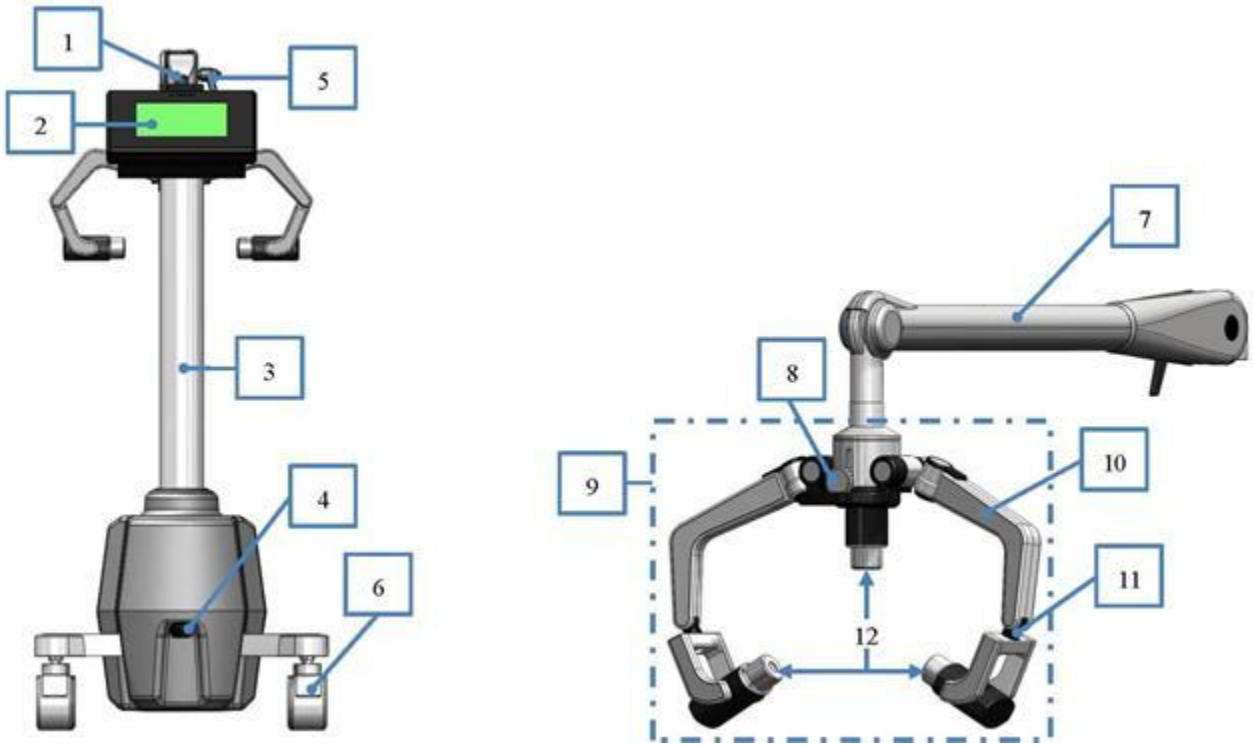


Figure 3: Erchonia® FX-635™ System Components

1. Power Safety Lockout Key
2. Touch Screen
3. Main Upright of Base
4. Power Inlet/Fuse Holder
5. Arm Lock (Fig. 2)
6. Wheel Lock
7. Boom Arm
8. Center Head Adjustment Knob
9. Laser Head Assembly
10. Upper Arms
11. Upper/Lower Pivots
12. Laser Output Heads
13. Locking Knob – not shown
14. Power Cord – not shown
15. Electrical Connector – not shown

POWER SAFETY LOCKOUT KEY (1)
The Power Safety Lockout Key is the outwardly visible portion of an internal locking mechanism on top of the touch screen [2] that comes with an external key. Together they allow the end user to turn the device ON or OFF. (“O” = OFF and “|” = ON) In the OFF position the device is locked.

TOUCH SCREEN (2)
The touch screen functions as a display screen and an input panel, providing information to the user and a means to operate the device by touching the appropriate icon.

MAIN UPRIGHT OF BASE (3)
The main upright of base supports the boom arm and contains the electrical connector (See Setup) and the Locking Knob [13].

POWER INLET/FUSE HOLDER (4)
The device contains an appliance coupler (power inlet) and a flexible detachable power cord [14]. This is the location on the device where the power cord is connected.

ARM LOCK (5)
The Arm Lock is the black lever attached to the side of the Boom Arm. This is a secondary locking mechanism for the boom arm. The arm tension can be adjusted or locked into position with the arm lock lever.

WHEEL LOCKS (6)
The device includes four antistatic wheels that enable ease for maneuverability. Once the device is transported to the desired location the wheel locks can be engaged to eliminate excessive movement of the device.

BOOM ARM (7)
The Boom Arm serves to position the Laser Head Assembly [9] vertically only. It is designed to adjust by intentional force from the end user. This allows the end user to lower and raise the Laser Output Heads for proper positioning to patient for accurate treatment distance.

CENTER HEAD ADJUSTMENT KNOB (8)
The Center Head Adjustment Knob [8] serves to adjust the treatment height of the center head. This also acts as the locking mechanism for the center head.

LASER HEAD ASSEMBLY (9)
This three-head assembly located on the end of the laser arm (boom arm) accommodates the laser output heads, pivots, arms and center head adjustment knob. This assembly can be rotated 120 degrees for proper positioning to patient for accurate treatment.

UPPER ARMS (10)
The upper arms serve as a positioning support for Laser Output Heads [12]. It is designed to adjust by intentional force from the end user. This allows the end user to lower and raise the Laser Output Heads for proper positioning to patient for accurate treatment distance.

UPPER/LOWER PIVOTS (11)
The upper and lower pivots serve as a positioning support for Laser Output Heads [12]. It is designed to adjust by intentional force from the end user. This allows the end user to move the laser output heads in and out, as well as side to side for proper positioning to patient for accurate treatment distance.

LASER OUTPUT HEADS (12)
The three plastic housings located on the end of the Lower Pivots [11] as well as the center of laser head assembly [9], accommodates the lens, laser diodes, motors, and their associated electronics. The side heads are designed to adjust by intentional force from the end user; this allows the end user to change the angle of the laser output heads for proper positioning to patient for accurate treatment distance. The center head is designed to be adjusted by center head adjustment knob [8].

LOCKING KNOB (13)
The locking Knob is utilized to secure the two-piece assembly [3 & 7], also preventing the boom arm assembly from unwanted rotation during use.

POWER CORD (14)
The device contains a flexible detachable power cord.

ELECTRICAL CONNECTOR (15)
The electrical connector is a two-piece assembly. The electrical connector connects the main head assembly to the base assembly in order to transfer data and power.

This pictorial shows the simple 2-piece assembly of the scanner. This assembly is best done with 2 people.

The 2 major components are the arm [7] and base [3].

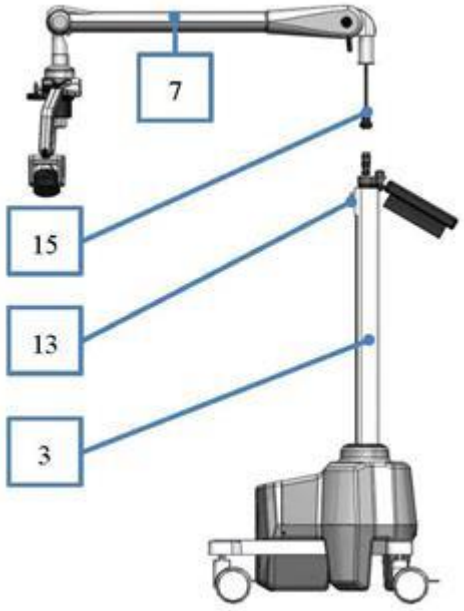


Figure 4: Erchonia® FX-635™ Assembly

DEVICE SAFETY

RISK AND PREVENTION OF EYE INJURY

The Erchonia® FX-635™ is classified by the FDA/IEC as a Class 2 laser device. This designation represents a current standard for use in order to ensure the safety of the subject. A Class 2 laser is determined to have a chronic viewing hazard. Pointing the laser beam directly into the eye and maintaining it there for an extended period of time could prove to be damaging.

To ensure there is no possible instance of residual effect, eye protection is implemented for both the investigator administering the study procedures with the Erchonia® FX-635™ Laser and for the subject receiving the laser procedure administrations.

A pair of specialty safety glasses is provided for use during all procedure applications. These safety glasses are Laser Safety Industries PN: 100-40-240 light blue safety glasses. These safety glasses have the following specifications:

- ✓ OD 4+ @ 630-690 nm
- ✓ OD 7+ @ 690-970 nm
- ✓ OD 5+ @ 970-1100 nm
- ✓ VLT 36%

The Laser Safety Industries PN: 100-40-240 light blue safety glasses are shown in Figures 5 & 6 below.

Figures 5 & 6: Laser Safety Industries PN: 100-40-240 Safety Glasses*
*The block out glasses is specifically for the clinical trial

STUDY INDICATION, THEORY OF MECHANISM OF OPERATION, & SUPPORTING MATERIALS

STUDY INDICATION: MINOR EPISODIC CHRONIC LOW BACK PAIN OF MUSCULOSKELETAL ORIGIN

The study indication to be evaluated in this study is the temporary acute relief of minor episodic chronic low back pain of musculoskeletal origin.

STATISTICS

Around $50 billion is spent in the U.S. each year on low back pain, the most common cause of job-related disability and a leading contributor to missed work. Back pain is the second most common neurological ailment in the United States, second only to headache.

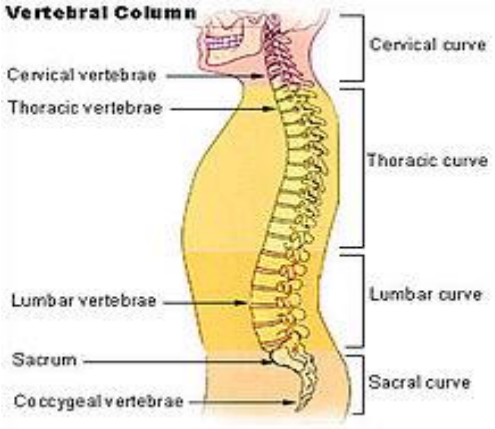
Over a lifetime, 80% of people have lower back pain, with 26% of American adults reporting pain of at least one day in duration every three months. 41% of adults aged between 26 and 44 years reported having back pain in the previous 6 months. Men and women are equally affected. It occurs most frequently between ages 30 and 50, due in part to the aging process but also as a result of sedentary life styles with too little (sometimes punctuated by too much) exercise.

DESCRIPTION & DEFINITION

Low back pain is a common musculoskeletal disorder affecting 80% of people at some point in their lives.

➢ Anatomy of the back

The lumbar region (lower back region) is comprised of five vertebrae (L1-L5). In between these vertebrae lie fibrocartilage discs (intervertebral discs), which act as cushions, preventing the vertebrae from rubbing together while at the same time protecting the spinal cord. Nerves stem from the spinal cord through foramina within the vertebrae, providing muscles with snsations and motor associated messages. Stability of the spine is provided through ligaments and muscles of the back, lower back and abdomen. Small joints which prevent, as well as direct, motion of the spine are called facet joints (zygapophysial joints).



➢ Etiologies of low back pain

The vast majority of low back pain (with many estimates as high as 99% incidence) stems from benign musculoskeletal problems, referred to as **non-specific low back pain** (meaning that the precise cause can be difficult to determine) – the etiology being evaluated in this study. It is caused by **lumbar sprain or strain** a stretch injury to the ligaments, tendons, and/or muscles of the low back. The stretching incident results in microscopic tears of varying degrees in the soft tissues of the lower back. The injury can occur because of overuse, improper use or trauma. A diagnosis of nonspecific low back pain occurs in the absence of any serious underlying pathology or nerve root compromise.

Other etiologies of low back pain that are not being evaluated in this study include the following:

✓ Mechanical: Apophyseal osteoarthritis; diffuse idiopathic skeletal hyperostosis; degenerative discs; Scheuermann's kyphosis; s ("slipped disc"); thoracic or lumbar spinal stenosis;

spondylolisthesis and other congenital abnormalities; fractures; leg length difference; restricted hip motion; misaligned pelvis - pelvic obliquity; anteversion or retroversion; and abnormal foot pronation
- ✓ Inflammatory: Seronegative spondylarthritides (e.g. ankylosing spondylitis); rheumatoid arthritis; infection - epidural abscess or osteomyelitis
- ✓ Neoplastic: bone tumors (primary or metastatic); and intradural spinal tumors
- ✓ Metabolic: osteoporotic fractures; osteomalacia; ochronosis; and chondrocalcinosis.
- ✓ Psychosomatic: Tension myositis syndrome
- ✓ Paget's disease
- ✓ Referred pain: Pelvic/abdominal disease; prostate cancer; and posture
- ✓ Depression
- ✓ Oxygen deprivation

➢ Classification of low back pain

- ✓ Acute low back pain generally lasts from a few days to less than 4 weeks.
- ✓ Sub-acute low back pain lasts 4-12 weeks
- ✓ Chronic low back pain is defined as pain in the lower back region that persists for more than 3 months. It is often progressive, and the cause is typically mechanical or non-specific in nature; that is, the cause can be difficult to determine.

➢ Presentation of low back pain

Lumbar sprain strain is characterized by localized discomfort in the low back area with onset after an event that mechanically stressed the lumbar tissues. The severity of the injury can range from mild to severe, depending on the degree of strain and resulting spasm of the muscles of the low back.

➢ Diagnosis

Diagnosis of low back pain

Medical history and physical exam can usually identify any dangerous conditions or family history that may be associated with the low back pain. Factors such as the onset, site, and severity of the pain; duration of symptoms and any limitations in movement; and history of previous episodes or any health conditions that might be related to the pain are considered. The physician will examine the back and conduct neurologic tests to determine the cause of pain and appropriate treatment. Blood tests and imaging tests may be performed to rule out more serious sources of the pain such as tumors.

Diagnostic methods available to confirm the cause of low back pain include:
- ✓ *X-ray imaging* to look for broken bones or an injured vertebra. Tissue masses such as injured muscles and ligaments or painful conditions such as a bulging disc are not visible on conventional x-rays.
- ✓ *Computerized tomography (CT)* is used when disc rupture, spinal stenosis, or damage to vertebrae is suspected as a cause of low back pain.
- ✓ *Magnetic resonance imaging (MRI)* is used to evaluate the lumbar region for bone degeneration or injury or disease in tissues and nerves, muscles, ligaments, and blood vessels.
- ✓ *Electrodiagnostic procedures* include electromyography (EMG), nerve conduction studies, and evoked potential (EP) studies to assess the electrical activity in a nerve to detect if muscle weakness results from injury or a problem with the nerves that control the muscles.

CURRENT THERAPEUTIC APPROACHES TO THE MANAGEMENT OF EPISODIC CHRONIC LOW BACK PAIN OF MUSCULOSKELETAL ORIGIN

The treatment of lumbar sprain strain centers about reducing pain and inflammation and consists of:

- ✓ *resting* the back to avoid reinjury,
- ✓ *medications* to relieve pain and muscle spasm such as o*ver-the-counter analgesics*, including NSAIDs (aspirin, naproxen, and ibuprofen) to reduce stiffness, swelling, and inflammation and to ease mild to moderate low back pain; c*ounter-irritants* applied topically to the skin as a cream or spray stimulate the nerve endings in the skin to provide feelings of warmth or cold and dull the sense of pain, and to reduce inflammation and stimulate blood flow; a*nticonvulsants* which may be useful in treating certain types of nerve pain; some *antidepressants*, particularly tricyclic antidepressants such as amitriptyline and desipramine; o*pioids* such as codeine, oxycodone, hydrocodone, and morphine
- ✓ *local heat* applications
- ✓ *massage*, and
- ✓ *reconditioning exercises* to strengthen the low back and abdominal muscles after healing.
- ✓ Spinal manipulation

When back pain does not respond to more conventional approaches, alternative options are available, such as:

- ✓ *Acupuncture*. It is believed this process triggers the release of naturally occurring painkilling molecules called peptides and keeps the body's normal flow of energy unblocked.
- ✓ *Biofeedback* is used to help the patient learn to effect a change in his or her response to pain, for example, by using relaxation techniques.
- ✓ *Traction* involves the use of weights to apply constant or intermittent force to gradually "pull" the skeletal structure into better alignment.
- ✓ *Transcutaneous electrical nerve stimulation (TENS):* TENS may also help stimulate the brain's production of endorphins (chemicals that have pain-relieving properties).
- ✓ *Ultrasound* is used to warm the body's internal tissues, causing the muscles to relax. Sound waves pass through the skin and into the injured muscles and other soft tissues.

Alternative therapies for managing chronic low back pain are growing in popularity as they are less invasive and without side-effects compared with traditional treatments, especially medications.

Surgical procedures are also a treatment option for low back pain. However, the outcomes are often poor and not lasting; yet still, back operations are the 3rd most common form of surgery in the United States, with about 300,000 back surgeries performed annually in the U.S.

THEORY OF MECHANISM OF OPERATION OF THE APPLICATION OF LOW LEVEL LASER LIGHT USING THE ERCHONIA® FX-635™ TO PROVIDE TEMPORARY ACUTE RELIEF OF MINOR EPISODIC CHRONIC LOW BACK PAIN OF MUSCULOSKELETAL ORIGIN

The scientific principle underlying laser physics was first developed by Albert Einstein in 1916. The biological effects of low-level laser therapy (LLLT) have been studied for forty years all around the globe, and no unwanted side effects have been noted anywhere. The safety record is strong.

All the cells in the body have receptors on their cell membranes that are able to read different frequencies of energy contained in the electromagnetic spectrum. This spectrum includes ultraviolet, infrared, and visible light. Soft (low-level) lasers produce visible and infrared light. The different frequencies of light communicate information to the cells that is understood by the receptors on the membrane of the cell and on the membrane of the cell's mitochondrion (the enzymatic engine of the cell). This energetic information eventually reaches the cell's DNA, which directly controls cell function.

When the cells are able to receive better information, they work better. When cells function better so do the tissues that they comprise, like bones, cartilage, tendons, ligaments, etc. In this way, LLLT promotes the healing and regeneration of damaged tissues. The energy from soft lasers is able to affect every tissue and system in the body. Scientists have shown that soft laser light is able to penetrate into the body; research has demonstrated that it has both local effects on tissue function and also systemic effects that are carried throughout the body by the blood and possibly also by acupuncture meridians.

The key basic physiological effects of low level laser light include:

1) increased cell membrane polarization and permeability
2) increased ATP production and respiratory chain activity
3) increased enzyme activity
4) increased collagen and epithelial production
5) increased capillary formation
6) increased macrophage (immune) activity
7) analgesic effects due to elevated endorphin production, electrolytic nerve blockage, and improved blood and lymph flow
8) anti-inflammatory effect due to improved circulation and accelerated tissue regeneration; and 9) increased production of antioxidants.

Of additional benefit is that light energy from low level lasers will only be absorbed by those cells and tissues that are not functioning normally and that need it. Soft laser light has no effect on healthy cells.

SUPPORTING MATERALS

- **Comparison of the effect of laser and magnetic therapy for pain level and the range of motion of the spine of people with osteoarthritis lower back].**

Zdrodowska B, Leszczyńska-Filus M, Leszczyński R, Błaszczyk J.
Pol Merkur Lekarski. 2015 Jan;38(223):26-31

Increased expression of degenerative disease of the lumbar spine is an onerous task, which reduces the efficiency of the activity and life of many populations. It is the most common cause of medical visits. In 95% of cases the cause of complaints is a destructive process in the course of degenerative intervertebral disc called a lumbar disc herniation. Protrusion of the nucleus pulposus causes severe pain and impaired muscle tone, often more chronic and difficult to master. Successful treatment of lumbar disc herniation constitutes a serious interdisciplinary problem. It is important to properly planned and carried out physiotherapy. Based on the number of non-invasive methods, to reduce muscle tension, mute pain and alleviation of inflammation. It is the treatment safe, effective, and at the same time, which is their big advantage, readily available and cheap. It is worth noting that not every method has the same efficiency. The question that the methods are effective in relieving pain and helping to effectively increase the range of motion led to a comparison of two methods - Low Level Laser Therapy (LLLT) and pulsating magnetic field therapy.

AIM: The aim of the study was to compare the efficacy of LLLT and pulsating magnetic field therapy in combating pain and increase range of motion of the spine of people with degenerative spine disease of the lower back.

MATERIALS AND METHODS: 120 patients with diagnose lumbar disc herniation whit no nerve roots symptoms. Patients were divided into two Groups: A and B. Group A of 60 patients were subjected to laser therapy (λ=820nm, P=400mW, Ed=6-12 J/cm²) and the second Group B of 60 patients too, to pulsating magnetic fields procedures (5mT, 30 Hz, 15 minutes). Every patient before rehabilitation started and right after it has finished has undergone examination. Subjective pain assessment was carried out using a modified Laitinen questionnaire and Visual Analogue Scale of Pain intensity. Spine mobility was evaluated whit the Schober test and the Fingertip-to-floor-test. The obtained results were subjects to statistical analysis.

RESULTS: Research shows that both low energy laser and pulsating magnetic field physical attributes are effective methods for the treatment of pain and restricted mobility of the spine caused by disc herniation. Careful analysis emphasizes greater efficiency laser for pain. In contrast, a statistically greater improvement in global mobility of the spine, as well as flexion and extension of the lumbar recorded in group B, where the applied pulsating magnetic field.

CONCLUSIONS**: Both laser and magnet therapies reduce pain and improves mobility of the spine of people with degenerative spine disease of the lower back.** Comparison of the effectiveness of both methods showed a **greater analgesic effect of laser treatment**, and greater mobility of the spine was observed under the influence of pulsating magnetic field therapy.
PMID: 25763584

- **Tri-length laser therapy associated to tecar therapy in the treatment of low-back pain in adults: a preliminary report of a prospective case series.**

Osti R, Pari C, Salvatori G, Massari L.
Lasers Med Sci. 2015 Jan;30(1):407-12.

Low-back pain is very frequent, especially in active adult population. There are several different orthopaedic condition that can cause low-back pain, and the pain worsen the quality of life significantly. The treatments vary from drugs, physical therapies, kinesiology, local infiltrations, and so on.Laser therapy has an important role in the treatment of the inflammatory causes of pain, with several studies that demonstrate the efficacy of low and high energy laser therapy in the treatment of low-back pain. Sixty-six consecutive patients with low-back pain with or without leg pain were treated using a combination of Tri-length laser I-Triax® (Mectronic Medicale, Bergamo, Italy) and Pharon® tecar therapy (Mectronic Medicale, Bergamo, Italy). The patients were treated three times a week, every other day, for a total of 10 sessions. Clinical results were evaluated using visual analogic scale for individual pain (0 to 10) and the Oswestry disability scale (ODS). Tests started before the beginning of therapies and 8 weeks after the end of the therapies. Visual analogic scale (VAS) score significantly improved from an average value of 8.1 ± 1.58 pre-treatment to an average value 8-weeks post-treatment of 2.63 ± 2.74 ($P < .01$). ODS values start from a pre-treatment average value of 53.0 ± 13.0 to a post-treatment average value of 23.5 ± 19.8 ($P < .01$). A higher improvement both in VAS and in ODS was denoted in the group of patient with low-back pain and leg pain (respectively, VAS from 8.66 ± 1.58 to 2.86 ± 2.94 and ODS from 57.8 ± 15.5 to 23.7 ± 19.5). Low-back pain, associated or not with leg pain, is a very common clinical situation. The treatments of this condition are different, and an important role can be given to the laser therapy. The conclusion of this study is that **the association between laser therapy iLux-Triax® and tecar therapy Pharon® in the treatment of low-back pain, with or without leg pain, can significantly reduce pain and improve the quality of life in patients with degenerative and inflammatory problems.**
PMID: 25376670

- **Effect of diode laser in the treatment of patients with nonspecific chronic low back pain: a randomized controlled trial.**

Vallone F, Benedicenti S, Sorrenti E, Schiavetti I, Angiero F.
Photomed Laser Surg. 2014 Sep;32(9):490-4.

BACKGROUND DATA**:** Low back pain is a common, highly debilitating condition, whose severity is variable. This study evaluated the efficacy of treatment with Ga-Al-As diode laser (980 nm) with a large diameter spot (32 cm(2)), in association with exercise therapy, in reducing pain.

OBJECTIVE: The present study aimed to evaluate the pain reduction efficacy of treatment with the Ga-Al-As diode laser (980 nm) in combination with exercise therapy, in patients with chronic low back pain (CLBP).

METHODS: This study evaluated 100 patients with CLBP (mean age 60 years) who were randomly assigned to two groups. The laser plus exercises group (Laser+EX: 50 patients) received low-level laser therapy (LLLT) with a diode laser, 980 nm, with a specific handpiece [32 cm(2) irradiation spot size, power 20 W in continuous wave (CW), fluence 37.5J/cm(2), total energy per point 1200 J] thrice weekly, and followed a daily exercise schedule for 3 weeks (5 days/week). The exercises group (EX: 50 patients) received placebo laser therapy plus daily exercises. The outcome was evaluated on the visual analogue pain scale (VAS), before and after treatment.
RESULTS: **At the end of the 3 week period, the Laser+EX group showed a significantly greater decrease in pain than did the EX group.** There was a significant difference between the

two groups, with average Δ VAS scores of 3.96 (Laser+EX group) and 2.23 (EX group). The Student's t test demonstrated a statistically significant difference between the two groups, at p<0.001.

CONCLUSIONS: This study demonstrated that **the use of diode laser (980 nm) with large diameter spot size, in association with exercise therapy, appears to be effective**. Such treatment might be considered a valid therapeutic option within rehabilitation programs for nonspecific CLBP.
PMID: 25141218

- **Short-term therapeutic effects of 890-nanometer light therapy for chronic low back pain: a double-blind randomized placebo-controlled study.**

Hsieh RL, Lee WC.
Lasers Med Sci. 2014 Mar;29(2):671-9.

We conducted a double-blind randomized placebo-controlled study to investigate the effects of short-term 890-nm light therapy in patients with chronic low back pain in a rehabilitation clinic. Thirty-eight women and 22 men with chronic low back pain (mean age, 60.3 years; range, 32-80 years) received 40-min sessions of hot-pack therapy combined with active or placebo 890-nm light therapy (wavelength = 890 nm, radiant power output = 6.24 W, power density = 34.7 mW/cm(2) for 40 min, total energy = 83.2 J/cm(2)) over the lower back three times weekly for 2 weeks. Participants were assessed before and after treatment by using a range of motion measurements, a visual analog scale evaluation of pain, the Multidimensional Fatigue Inventory, the Biodex Stability System, the Fear-Avoidance Beliefs Questionnaire, repeated chair-rising times, the Frenchay Activity Index, the Oswestry Disability Questionnaire (ODQ), and the Osteoarthritis Quality of Life Questionnaire. The severity of disability based on the ODQ score was used as the primary clinical outcome measurement. Compared to the baseline measurements, participants in the treatment group reported significant reductions in fear-avoidance beliefs regarding physical activity (P = 0.040) and work (P = 0.007) and in the severity of disability (P = 0.021). **Treatment with hot-pack therapy and 890-nm light therapy was associated with reductions in the severity of disability and fear avoidance beliefs in patients with chronic low back pain**.
PMID: 23820974

- **Low level laser therapy for patients with cervical disk hernia.**

Takahashi H, Okuni I, Ushigome N, Harada T, Tsuruoka H, Ohshiro T, Sekiguchi M, Musya Y.
Laser Ther. 2012 Sep 30;21(3):193-7.

BACKGROUND AND AIMS: In previous studies we have reported the benefits of low level laser therapy (LLLT) for chronic shoulder joint pain, elbow, hand and finger pain, and low back pain. The present study is a report on the effects of LLLT for chronic neck pain.

MATERIALS AND METHODS**:** Over a 3 year period, 26 rehabilitation department outpatients with chronic neck pain, diagnosed as being caused by cervical disk hernia, underwent treatment applied to the painful area with a 1000 mW semi-conductor laser device delivering at 830 nm in continuous wave, 20.1 J/cm(2)/point, and three shots were given per session (1 treatment) with twice a week for 4 weeks.
RESULTS: 1. A visual analogue scale (VAS) was used to determine the effects of LLLT for chronic pain and after the end of the treatment regimen a significant improvement was observed (p<0.001). 2. After treatment, no significant differences in cervical spine range of motion were

observed. 3. Discussions with the patients revealed that in order to receive continued benefits from treatment, it was important for them to be taught how to avoid postures that would cause them neck pain in everyday life.

CONCLUSION: The present study demonstrates that **LLLT was an effective form of treatment for neck and back pain caused by cervical disk hernia, reinforced by postural training**.
PMID: 24511189

- **Low power laser in the treatment of the acute low back pain**

Mandić M, Rancié N.
Vojnosanit Pregl. 2011 Jan;68(1):57-61.

BACKGROUND/AIM: Acute low back pain (ALBP) is one of the most frequent painful conditions in the human population. The objective of the paper was to compare the efficacy of the low power laser (LPL) in the pain and the muscular spasm reduction with conservative methods of physical medicine.

METHOD: The prospective cohort study involved 70 patients, men and women, from 25 to 64 years of age with the diagnosis of ALBP. There were two groups: 40 patients in the first group were treated with the LPL with frequency of 73 Hz. The second group was the control group, and it consisted of 30 patients treated with conservative methods of physical medicine (electrotherapy: diadynamic currents CP +/- 3 and CP +/- 3, interferent currents--90 Hz for 15 min; electrophoresis with novocaine). The ALBP were diagnosed by clinical examination and by nuclear magnetic resonance imaging (NMRI). The low power laser--Gallium Arsenide (GaAs) was used. The laser device consisted of 4 laser diodes, each powered of 15 mW, wavelength 904 nm and with frequency 73 Hz. The total period of time for each treatment was 10 minutes and the total dose per treatment was 15 J. The intensity of acute low back pain was assessed by Roland's scale. The degree of the spasm was assessed in the relaxed position and during movements.

RESULTS: The average score in the first group before the onset of rehabilitation was 3.3 +/- 1.1 (Me = 3.0), and in the control group, it was 3.43 +/- 0.89 (Me = 3.0). After five treatments, in patients who were treated with LPL, the average Roland's scale score decreased (1.12 +/- 1.3, Me = 2.0) while there was no change for scores in the control group. After 10 treatments with the LPL, the analgesic effect was obtained in 82.5% of patients from the test group and in 20% of patients in the control group. The analgesic effect in patients of the test group was obtained after 7.5 +/- 2.1 treatments and in the second group after 17.9 +/- 3.2 treatments. The difference was statistically significant ($t = 15.652173$, $p < 0.001$). The spasm disappeared in 92.5% of patients in the test group and in 20% of patients in the control group after 7.02 +/- 2.2 and 17.9 +/- 3.2 treatments respectively. The difference was statistically significant ($t = 15.652173$, $p < 0.001$).

CONCLUSION: **Pain and spasm reduction were obtained in the greater number of patients by usage of the LPL than by usage of conservative methods of physical medicine.**

- **Efficacy of low power laser therapy and exercise on pain and functions in chronic low back pain**

Gur A, Karakoc M, Cevik R, Nas K, Sarac AJ, Karakoc M.
Lasers Surg Med. 2003;32(3):233-8.

BACKGROUND AND OBJECTIVES: The aim of this study was to determine whether low power laser therapy (Gallium-Arsenide) is useful or not for the therapy of chronic low back pain (LBP).

STUDY DESIGN/MATERIALS AND METHODS: This study included 75 patients (laser + exercise-25, laser alone-25, and exercise alone-25) with LBP. Visual analogue scale (VAS), Schober test, flexion and lateral flexion measures, Roland Disability Questionnaire (RDQ) and Modified Oswestry Disability Questionnaire (MODQ) were used in the clinical and functional evaluations pre and post therapeutically. A physician, who was not aware of the therapy undertaken, evaluated the patients.

RESULTS: Significant improvements were noted in all groups with respect to all outcome parameters, except lateral flexion ($P < 0.05$).

CONCLUSIONS: **Low power laser therapy seemed to be an effective method in reducing pain and functional disability in the therapy of chronic LBP**.

- **In chronic low back pain, low level laser therapy combined with exercise is more beneficial than exercise alone in the long term: a randomized trial.**

Djavid GE, Mehrdad R, Ghasemi M, Hasan-Zadeh H, Sotoodeh-Manesh A, Pouryaghoub G.
Aust J Physiother. 2007;53(3):155-60.

QUESTION: Is low level laser therapy an effective adjuvant intervention for chronic low back pain.

DESIGN: Randomized trial with concealed allocation, blinded assessors and intent-to-treat analysis.

PARTICIPANTS: Sixty-one patients who had low back pain for at least 12 weeks.

INTERVENTION: One group received laser therapy alone, one received laser therapy and exercise, and the third group received placebo laser therapy and exercise. Laser therapy was performed twice a week for 6 weeks.

OUTCOME MEASURES: Outcomes were pain severity measured using a 10-cm VAS, lumbar range of motion measured by the Schober Test and maximum active flexion, extension and lateral flexion, and disability measured with the Oswestry Disability Index on admission to the study, after 6 weeks of intervention, and after another 6 weeks of no intervention.

RESULTS: In the laser therapy + exercise group, pain decreased by 1.8 cm (95% CI 0.1 to 3.3, $p = 0.03$), lumbar range of movement increased by 0.9 cm (95% CI 0.2 to 1.8, $p < 0.01$) on the Schober Test and by 15 deg (95% CI 5 to 25, $p < 0.01$) of active flexion, and disability reduced by 9.4 points (95% CI 2.7 to 16.0, $p = 0.03$) more than in the exercise group at 12 weeks.

CONCLUSION**: In chronic low back pain low level laser therapy combined with exercise is more beneficial than exercise alone in the long term.**

- **Acute Low Back Pain with Radiculopathy: A Double-Blind, Randomized, Placebo-Controlled Study.**

Konstantinovic LM, Kanjuh ZM, Milovanovic AN, Cutovic MR, Djurovic AG, Savic VG, Dragin AS, Milovanovic ND.
Photomed Laser Surg.

OBJECTIVE: The aim of this study was to investigate the clinical effects of low-level laser therapy (LLLT) in patients with acute low back pain (LBP) with radiculopathy.

BACKGROUND DATA: Acute LBP with radiculopathy is associated with pain and disability and the important pathogenic role of inflammation. LLLT has shown significant anti-inflammatory effects in many studies.

MATERIALS & METHODS: A randomized, double-blind, placebo-controlled trial was performed on 546 patients. Group A (182 patients) was treated with nimesulide 200 mg/day and additionally with active LLLT; group B (182 patients) was treated only with nimesulide; and group C (182 patients) was treated with nimesulide and placebo LLLT. LLLT was applied behind the involved spine segment using a stationary skin-contact method. Patients were treated 5 times weekly, for a total of 15 treatments, with the following parameters: wavelength 904 nm; frequency 5000 Hz; 100-mW average diode power; power density of 20 mW/cm(2) and dose of 3 J/cm(2); treatment time 150 sec at whole doses of 12 J/cm(2). The outcomes were pain intensity measured with a visual analog scale (VAS); lumbar movement, with a modified Schober test; pain disability, with Oswestry disability score; and quality of life, with a 12-item short-form health survey questionnaire (SF-12). Subjects were evaluated before and after treatment. Statistical analyses were done with SPSS 11.5.

RESULTS: Statistically significant differences were found in all outcomes measured ($p < 0.001$), but were larger in group A than in B ($p < 0.0005$) and C ($p < 0.0005$). The results in group C were better than in group B ($p < 0.0005$). Conclusions: **The results of this study show better improvement in acute LBP treated with LLLT used as additional therapy.**

- **Promising results of Laser for Low Back Pain pilot study presented at ACBSP meeting in Chicago Class IV Laser Therapy; Effective for Back and Neck/Shoulder Pain**

June 25, 2010

BACKGROUND: Class IV laser therapy is a recent modality used to treat pain and promote healing of muscular tissue. The procedure is minimally invasive and easily performed. Laser therapy was added to conventional chiropractic treatment of spinal manipulation and an exercise program for treating patients with back pain. The objective of this investigation was to assess efficacy and safety of the combination and generate preliminary results for a randomized controlled trial.

METHODS: Between 9/2009 and 2/2010, a total of 55 patients with non-surgical lower back pain (sciatica) presented to my office and gave consent for treatment. Twenty-four patients with back pain received spinal Class IV laser therapy in addition to manipulation for back pain. Twenty-one patients (historical controls) received spinal manipulation without Class IV laser therapy. All patients completed VAS scales before treatment (VAS0), at one week (VAS1), and at four weeks (VAS4). Regardless of treatment group, all patients received a personalized regimen of spinal manipulation, manual therapy, and exercise, under the direction of the principal investigator (LDM). Percent difference between VAS0 and VAS4 was compared between groups.

RESULTS: Demographics were similar for both groups (Table 1). Patients in the manipulation + laser group reported pain relief after 2-3 sessions of laser therapy (clinical observation). No adverse events were noted following laser therapy.

Table 1 – Patient demographics and dependent variables

	N	Age	VAS 0	VAS 4	% Difference
Laser + Manipulation	24	54.2 ± 11.1	6.5 ±1.9	1.75 ± 1.6	71.7 ± 22.0
Manipulation Only	21	51.0 ± 12.7	5.5 ± 1.4	3.5 ± 2.1	50.5 ± 28.4

A positive-valued percent differences of VAS between pretreatment and 4wk points; indicate that a quantitative reduction in pain by both treatment groups. Statistical comparison of the groups using an unpaired t-test indicated that the manipulation + laser offers greater pain reduction when compared to manipulation only (p=0.007). Interval estimates indicate a 21.18 larger reduction in VAS (95% Confidence Interval: 6.00, 36.35) in the manipulation + laser group.

Conclusions: These results indicate that both treatments successfully reduced the VAS by the fourth week of treatment, and that a higher reduction in VAS occurred in the group treated by manipulation + laser at week four.

In summary, **Class IV laser therapy is a safe and effective modality for treating low back pain when added to conventional treatment of manipulation and exercise**.

- **Experiences of Acupuncture in the Treatment of Chronic Low Back Pain.** Kertesz Agnes, Hegyi Gabriella. Albert Szent-Gyorgyi Medical University, Szeged, Hungary

INTRODUCTION: Conventional and complimentary medicine offer numerous possibilities for reduction or elimination of chronic pain. In a large majority of cases, conventional therapy affords a satisfactory result. In a significant number of subjects however, the improvement is not appropriate. The present work has the aim of demonstrating the opportunities provided by one of the main branches of complimentary medicine, acupuncture. This report summarizes the results attained by treating chronic low back pain by means of laser-therapy. **METHODS:** 90 patients with chronic pain in the low back took part in the study. They received laser-acupuncture treatment administrated to acupuncture points in the ear and in the body that corresponded to the principles of traditional Chinese medicine. The instrumental parameters, applied: Seirin laser pen Ga A, As diode, 780nm laser category 3B, 5mW, 10Hz. **RESULTS and CONCLUSIONS:** Prior to the acupuncture treatment, these 90 patients had participated in conventional therapy without any essential improvement. **In response to 3-5 laser-acupuncture therapy sessions, complete remission of pain was achieved in 72 cases**. In patients who exhibited only a temporary improvement even after the fifth session, CT and MRI recordings confirmed the suspicion on discus hernia, and these patients underwent surgery. **Even after a period of 3 years, the 72 patients have not observed recurrence of the pain.** These results demonstrate that lasting freedom from pain can be attained in cases, which do not respond to conventional therapy. At the same time, it draws attention to the necessity of the application of modern imaging procedures in order to make an accurate diagnosis in those subjects who do not improve satisfactorily."

- **Low energy laser in the treatment of low back pain**. S. Nikolic, Z. Trojacanec, I.J. Milankovic Address Institute of ME Physiology, Faculty of Medicine, Skopje, F.Y.R.O.M

"The aim of the study was to explore the pain-alleviating effect of low energy laser in low back pain.Thirty-five patients with low back pain have been treated with helium-neon laser type "Bistra" with wavelength 630 nm, average output 15 mW and an irradiance of 250 mW/cm2. The laser was locally applied to 11 sites on and around the low back. After scanning, each point was treated for 30 seconds, five times weekly for a total of ten treatments. The statistical analysis showed that the laser treated patients had a significant faster pain-alleviating effect compared with the 30 patients treated with medicaments only. Subjective responses have been achieved after the first three treatments. **Irradia laser treatment may be a valuable therapy in low back pain and low energy laser can be employed as a pain relieving method."**

- **Low Energy Laser Therapy with Trigger Points Technique**
  Z. Simunovic,
  American Society for Laser Medicine and Surgery Abstracts

"There are also very promising 'trigger points", i.e. myofacial zones of particular sensibility and of highest projection of pain focal points, due to ischaemic conditions. The effect of LLLT and the results obtained after clinical treatment of more than 200 patients (headaches, facial pain, skeletal muscular ailments, myogenic neck pain, shoulder arm pain, epicondylitis humary, tenosynovitis, **low back and radicular pain**, Achilles tendonitis) to whom "trigger points" were applied turned out to be better than we have ever expected. According to clinical parameters, it has been observed that the rigidity decreases, the mobility is restored and that also the spontaneous or induced pain decreases or even disappears. LLLT improves microcirculation and it can also improve oxygen supply. **Results** measured according to VAS/VRS/PTM: **acute pain diminished by 72% and chronic pain by 66%.**"

THERAPEUTIC LASER FOR CHRONIC LOW BACK PAIN

Laser therapy offers a safe and effective treatment modality as either primary or adjunctive therapy.

By William J. Kneebone, CRNA, DC, CNC, DIHom, FIAMA, DIACT

Low back pain will affect 75-85% of all Americans at some point during their lifetime. Approximately 50% of them will have a recurrence within a year. Approximately 90% improve without surgery.[1] Low back pain is the number 2 reason that Americans see their doctor—second only to colds and flu. Approximately 7.4% of patients with low back pain account for 75% of the money spent on low back pain.[2] The vast majority of acute low back pain is the result of injury such as sprain or strain, while the cause of chronic low back pain is multifactorial.[3] Chronic low back pain is defined as pain of more than three months duration. It occurs in 2-8% of those who experience low back pain.[3]

The five most common pain producing structures of low back pain are:

1. Posterior longitudinal ligament
2. Interspinous ligament
3. Spinal nerve root
4. Facet joints
5. Deep muscles.

These structures do not fully account for the pain experienced by many chronic low back pain sufferers. The exact mechanisms of the causes of chronic low back pain continue to be a mystery. Recent scientific studies have implicated a number of chemical mediators as possible contributors to the production of chronic low back pain. These include:

- The peptide somatostatin
- Pro-inflammatory cytokines such as IL-1, IL-6, IL-10, and TNF-alpha
- PGE2
- Nitric oxide.[4]

Patients with chronic low back pain may also have emotional factors such as depression with a four times higher incidence of clinical depression than those without chronic low back pain. Studies have shown that 62% of the patients treated at pain clinics for low back pain have some type of depression.[5]

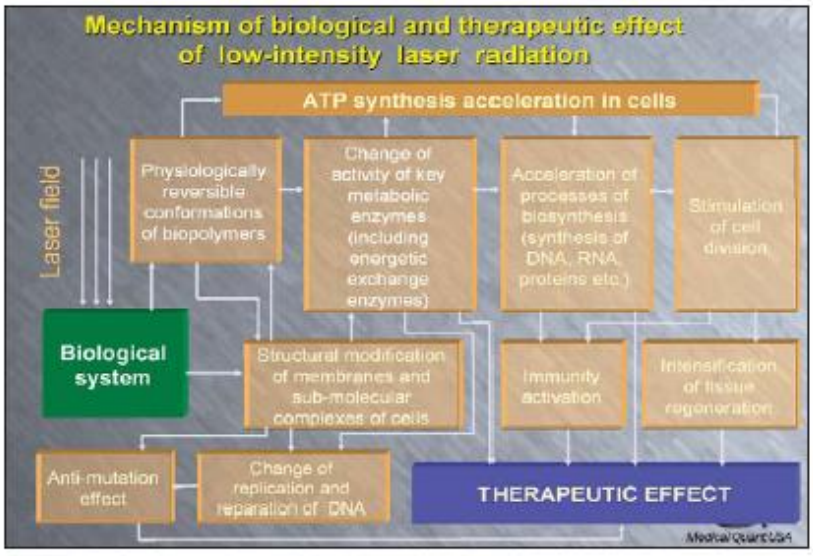


FIGURE 1. *Flowchart of some of the most commonly observed biochemical effects of therapeutic lasers. (Courtesy of MedicalQuant)*

Biochemical Effects

In a prior article, this author discussed a number of biochemical effects that have been observed with laser therapy/phototherapy in a prior article in this journal.[6] Several of these effects directly relate

to the management of the patient with chronic low back pain. Three of the most prevalent features of patients suffering from chronic low back pain are: inflammation, pain, and edema.[6] Injured cells and tissues generate enzymes that encourage the receipt of photons more readily than healthy cells and tissues. Primary photoacceptors, which are activated by light, are thought to be flavins, cytochromes, and porphorins.[7,8]

These photoacceptors are located in the mitochondria and can convert light energy into electro-chemical energy. Chromophores, in the form of porphyrins have been shown to play an important role. Small amounts of singlet oxygen have been shown to accumulate in tissues irradiated with laser light.[9] Singlet oxygen affects the formation of ATP in the mitochondria.[10]

Laser-related research has demonstrated a number of interesting bio-chemical responses that can have a positive clinical effect the chronic low back pain patient. These effects include:

- Stabilization of the cell membrane[11]
- Enhancement of ATP synthesis[12]
- Stimulated vasodilation along with increased histamine, NO and serotonin[13]
- acceleration of leukocyte activity
- Increased Prostaglandin synthesis[14]
- Reduction in Interleukin-1 levels[15]
- Increased angiogenesis[16]
- Enhanced superoxide dismutase[17]
- Decreased C-reactive protein and neopterin levels[18]

Research in laser and light therapy has documented that red and near infrared light reduces pain by a combination of these responses (see Figure 1):

- Increases in b-Endorphins
- Blocked depolarization of C-fiber afferent nerves[19]
- Axonal sprouting and nerve cell regeneration[20]
- Decreased Bradikynin levels
- Ion channel normalization[21]

Tissue Penetration and Saturation

Chronic low back pain is a complex clinical condition which involves many different tissue levels from subcutaneous and muscle tissues to the deeper tendons and ligaments, including the inter-vertebral disc. Laser therapy, if it is to be effective, must be applied in a way that will effectively produce significant biochemical changes in the superficial, medium, and deep tissues. One may recall from the previous article that red light will affect the skin and subcutaneous tissue to an approximate depth of 1 cm. Infrared light will effect deeper tissue structures from 1 -5 cm depth.[22] Comprehensive laser/light therapy for treating chronic low back pain must therefore include the use of both red and infrared wavelengths (See Figure 2).

Laser therapy produces primary, secondary and tertiary effects in the body as I previously discussed in the author's last article.[23] All three of these effects are desirable in the treatment of low back pain. A GaAs superpulsed infrared laser, or high output GaAlAs infrared laser, is necessary to obtain the deep tissue penetration needed to effectively treat the deeper structures of the back. Gruszka, using a GaAs superpulsed laser, found that 9 Joules/cm^2 of energy applied to appropriate points were effective at ameliorating pain in patients with herniated lumbar discs and radiculopathy.[24] Most modern diode lasers utilize pre-programmed treatment settings that help insure adequate numbers of Joules of light energy will be irradiated into the patient's tissues. Tasaki found that relief was obtained in low back pain patients using a GaAlAs laser in the 30–80 mW output range.[25] Reductions in the size of lumbar disc herniations have been demonstrated by Gruszka,[26] Tatsuhide,[27] and others. Tertiary effects by treating acupuncture points have been shown to be effective at decreasing low back pain. Nikolic found that treating acupoints with a 630 nm red laser was most effective.[28]

The results from the application of laser therapy will be maximized by combining several laser techniques together. Clinicians have found that tissue saturation of the effected area of the low back to be the best place to begin. Stimulation of acupoints and/or reflex points is also valuable. The irradiation of lymphatic structures is beneficial, especially when edema is present. Pulse frequency is of some importance, especially when using a GaAs superpulsed laser.[28] Pain relief is best achieved in the frequency range of 1-100 Hz. Inflammation responded well to the 3000-5000 Hz range. Edema responds well to1000 Hz (see Figure 3).

The amount of time it takes to adequately treat an area of involvement (therapeutic levels of Joules of photon energy) in the low back depends on the size of the area and the power output of the laser/light therapy device. This is known as photon or power density (see Figure 4). You can use Figure 5 as a general guide for average duration of treatment at different penetration depths versus laser power output.[29]

Treatment Modality

A typical treatment approach for a patient with chronic low back pain would involve the following:

1. History of condition, physical exam-

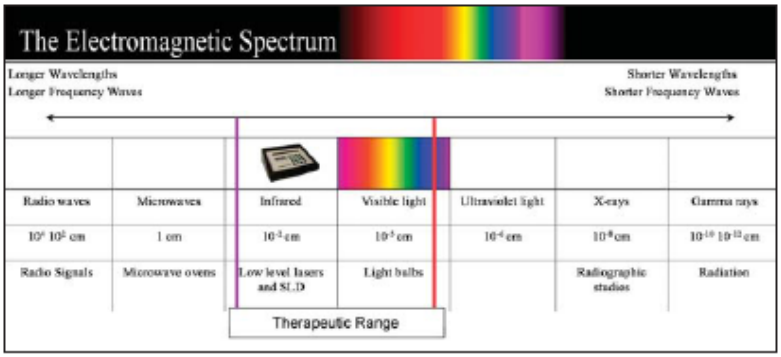


FIGURE 2. *Therapeutic range within the electromagnetic spectrum. (Courtesy Doug Johnson, ATC, CLS)*

Pulse Frequency Settings[36]

Diagnosis	Frequency Range
Pain, neuralgia	1-100 Hz
General stimulation	700 Hz
Edema, swelling	1,000 Hz
General stimulation	2,500 Hz
Inflammation	5,000 Hz
Infection	10,000Hz

FIGURE 3. *(Courtesy Doug Johnson, ATC, CLS)*

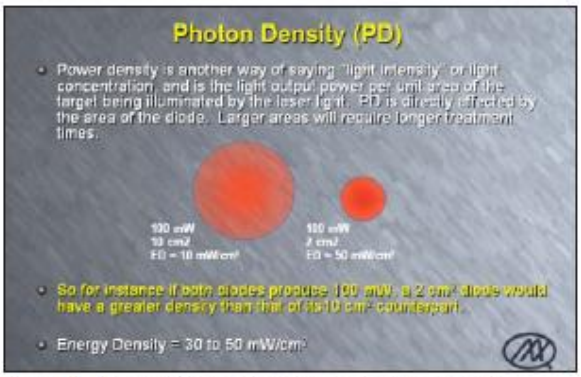


FIGURE 4. *Photon (Power Density) (Courtesy MedicalQuant-West)*

Treatment Time for 50cm² Surface Area with a GaAs Laser

Depth	10mW	25mW	50mW	100mW	200mW
.5 cm	2.5 min	1 min	30 sec	15 sec	10 sec
1 cm	5 min	2 min	1 min	30 sec	15 sec
2 cm	10 min	4 min	2 min	1 min	30 sec
3 cm	15 min	6 min	3 min	1.5 min	45 sec
4 cm	20 min	8 min	4 min	2 min	1 min

The output powers are average powers. Treatment should be done with skin contact.

FIGURE 5. *Note: A surface area of 50 cm2 is roughly equivalent the surface area of an average sized apple sliced in half horizontally. (Courtesy Doug Johnson, ATC CLS)*

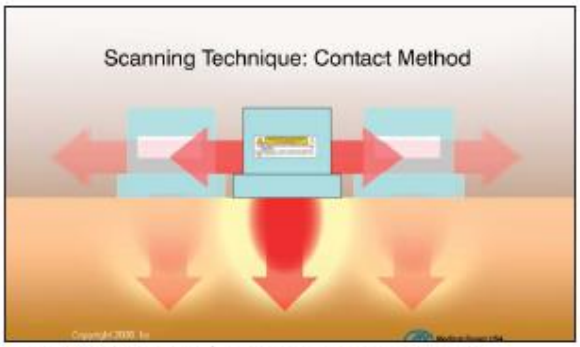


FIGURE 6. *Scanning Technique (Courtesy MedicalQuant-West)*

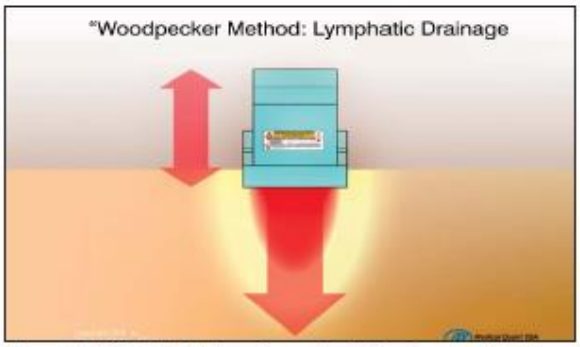


FIGURE 7. *"Woodpecker" pumping method of treating over lymph nodes. (Courtesy MedicalQuant)*

ination of the low back paying particular attention to the level of abnormal muscle, nerve and joint function, as well as pain level. This would include lumbar and pelvic range of motion, lumbar and pelvic orthopedic tests, lower extremity deep tendon reflexes, and Visual Analog Scale.

2. The initial treatment aim is to saturate the primary area of involvement. A good choice would be to use 3000-5000 Hz for 5-10 minutes with a GaAs laser in order to help reduce inflammation. A scanning contact is utilized for this technique in order to maximize the tertiary or systemic effects (see Figure 6). Note that treating the lymph nodes proximal to the area of involvement with 3000 Hz laser emitter utilizing a pumping action—prior to treating the area of involvement—will enhance the reduction of edema (see Figure 7).

3. The secondary treatment aim is to reduce pain and stimulate healing in the deeper tissue of the Right low back. A GaAs superpulsed laser at 5-50 Hz for 5-10 minutes is the best choice in order to get the deepest penetration.[30] This is performed with a stationary contact with the emitter. Note that patients with chronic low back pain can become exacerbated after the initiation of laser therapy so it is advisable to use one half of the above dose during the first treatment, until the individual patient's response can be determined on the first follow-up visit (see Figure 8).

4. A third technique often applied during a treatment session is stimulation of acupoints with the laser emitter. The exact points used are dependant on the clinician's training and experience with acupuncture or acupressure. Treatment involves stimulation of each acupoint for 1 minute at 1000 Hz. See Figures 9 and 10.

Laser therapy treatment times are usually 10–20 minutes per session. Chronic low back pain patients will usually respond best to 3-4 treatments per week. Maximum effect is often reached in 3-4 weeks but several months of care may be necessary in extremely complex cases. It is important to allow for delayed effects and cumulative effects which commonly occur in patients receiving laser therapy. Treating a patient too frequently can actually slow down the recovery process and increase symptoms.[31] While laser therapies can often produce results as a stand alone therapy, they also work very well adjunctively with other therapies such as: physical therapy, manipulation, exercise and stretching. The wound healing effects of therapeutic lasers are well documented in laser related literature suggesting it is also a valuable adjunct during post operative recovery.[32] Laser therapy is extremely safe has few contra-indications as described in Figure 11.

Conclusion

Therapeutic lasers and other phototherapy devices offer a safe, often effective, easily utilized primary or adjunctive therapy that is relatively cost effective to both the clinician and patient. Laser therapy can be a viable part of the multi-faceted approach often needed to bring relief to the millions of chronic low back pain sufferers that present in offices, clinics, and hospitals. The future is promising as research continues to increase understanding of this new healing modality. ■

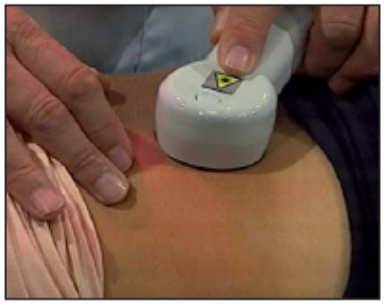


FIGURE 8. *Stationary contact to the Left LA area. (Courtesy MedicalQuant-West)*

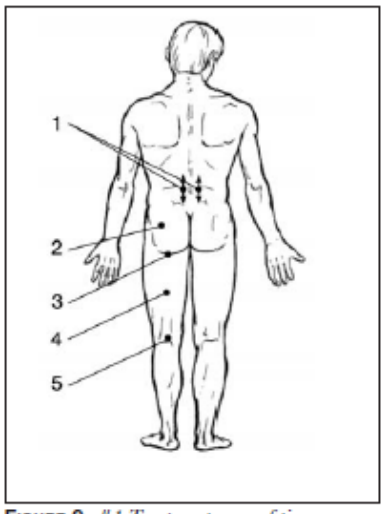


FIGURE 9. *#1 Treatment area of tissue; #2-5Acupoints for LBP*

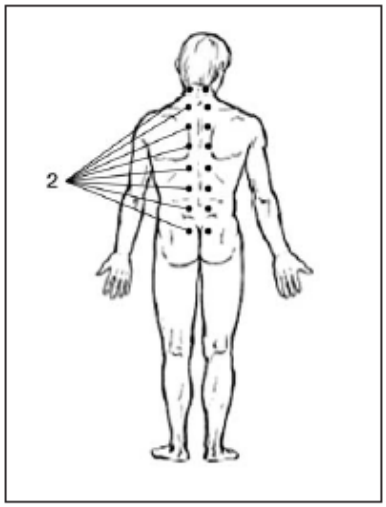


FIGURE 10. *Acupoints for the entire techniques for the low back.*

CONTRAINDICATIONS

Absolute Contraindications

- Cancer (tumors or cancerous areas)
- Direct irradiation of eyes
- Photosensitivities

Relative Contraindications

- Irradiation of the fetus or treatment over the pregnant uterus
- Over areas recently injected with corticosteroids
- Over the thyroid gland

FIGURE 11. *Contra-indications as recommended by NAALT (Courtesy MedicalQuant-West)*

Dr. Kneebone studied nursing at Cook County Hospital in Chicago graduating as an RN in 1972. He completed an anesthesia program at St. Francis Hospital in La Crosse, Wisconsin in 1974. Dr. Kneebone practiced anesthesia until he graduated from Palmer College of Chiropractic in 1978. He has been in a complementary medicine practice in the San Francisco Bay area since 1978. He has post graduate certification in nutrition and homeopathy. He is also a Fellow of the International Academy of Medical Acupuncture and a Diplomate of the International Academy of Clinical Thermology. Dr. Kneebone has been using therapeutic lasers in his practice for over 7 years and has been teaching laser seminars for the past four years. He is scheduled to teach 25 to 30 Cutting Edge Laser Seminars™ next year around the US. He can be contacted at drknee@pacbell.net

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Low Level Laser Therapy (LLLT) for Chronic Low Back Pain (LBP)

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Abstract

Background: LBP is a major health problem with enormous economic and social costs. The toll that bears on individuals, families and society make the successful management of this is common. Despite its widespread use, the effectiveness of LLLT (low level laser therapy) is still controversial. Traditional treatments include drugs, physical treatment, back exercises and education, but they are not always completely helpful. Many people seek alternative treatments, such as LLLT. Therefore main goal of this study is determine the effect of LLLT on the intensity of chronic LBP.
Method: This randomized clinical trial (RCT) has been done at medical laser center of Pastor-no hospital in Tehran. 30 patients with chronic LBP (because of lumbago) in rhea range of 30-60 years old were randomly divided to the laser treatment group and laser placebo group. Both of two groups went under treatment for 3 times in a week for 4 weeks. Applied laser in laser treatment group was continuous red light laser and pulse infrared with Mustang system with 890nm wavelength and 4-6 J/cm2 dose (energy), and was irradiated on the mentioned vertebral bodies and spinouts processes. Treatment in laser placebo group was done with off laser. Efficacies of treatment were evaluated with pain questionnaire and thermograph. Data was analyzed with chi-square ($\chi 2$) and t-student statistical tests.

Results: The laser treatment group patients have significant symptomatic relief without any side effect. Due to the pain questionnaire and thermograph, in first and second week, there was significant difference between two groups ($P<0.05$) before and after the third week, in regard to the pain questionnaire and thermograph a significant difference between two groups was found ($P<0.05$).
Conclusion: Based on the findings, if low level laser is irradiated on the mentioned area with appropriate dose, wavelength and exposure time, it will be a suitable and less aggressive method without side effect on the LBP.

Keywords: Low back pain, low level laser therapy (LLLT)

Introduction

Sixty to eighty percent of people suffer from back pain at some time in their lifetime. Of those who develop acute LBP, up to 30% probably developed chronic LBP. LBP is a major health problem with enormous economic and social costs. The toll on individuals, families and society makes the successful management of this common, but benign condition is an important point. LBP affects a large proportion of the population. LLLT is alternative therapy to pharmacological treatments for chronic pain. Despite its widespread use, the effectiveness of LLLT is still controversial. Traditional treatments include drugs, physical treatment, back exercises and education, but they do not always help. Many people seek alternative treatments, such as LLLT. We found three systematic reviews and five additional RCTs of LLLT for LBP. This is one of the most common problem related to the musculoskeletal system and is recognized to be the second most common reason for the patients to visit a doctor in the modern societies [1,2]. In a methodological research related to chronic LBP studies, it was estimated that the incidence and the annual average incidence were 19.2% and 82.7%, respectively. [2, 3] Chronic LBP is the most common expensive occupational disability in younger patients than 45 years old and two thirds (67%) of adult patients mostly in their 4^{th} and 5^{th} decades of life suffer from the disease [4]. Studies show that the causes of this pain might be referred to the ligaments, joints, vertebral, muscles, Para vertebral, blood vessels and spinal nerve roots or inter vertebral disc degeneration [4].Chronic LBP may be associated with psychological, physical, economical and social difficulty in 17% of the cases[16]. As a result, treatment of such patients seems quite challenging and the practitioner needs to employ multiple approaches in order to bring the disorder under control. Many different models of treatment such as exercise, massage, drugs, TENS, surgery and laser therapies are used to treat LBP. Laser was used in various surgeries in the 20^{th} century, but not routine for musculoskeletal disorders [7]. Low and medium energy lasers such as GaAs or HeNe with wavelengths of 600-980nm are used for various methods of physical therapy. It is shown that low level lasers can affect many cellular and sub cellular processes. There are many patients suffering from chronic pain such as those with rheumatoid arthritis and osteoarthritis whom are treated with such lasers [7-10]. On the other hand, there are some reports in the literature, which do not show such effects on the muscle and bone pathologies [11-13]. The present study has been conducted to estimate the efficacy of low level laser on chronic LBP.

Material and Methods

This study included with 15 patients to laser and 15 patients to placebo laser. Including and excluding criteria for selecting patients include of these issues: suffering from LBP more than 6 months, Age between 30-60 years, haven't pregnant, haven't any previous spine surgery history, haven't known neurological defects, haven't systemic or psychological disorder.

The patient's selection was based on their history and medical exams. The patients with definite radiographic pathology were excluded and only the patients with LBP due to lumbago were included. At first, demographic data such as age and sex and subsequently pain and functional specifications

were assessed and documented. Pain functional assessments were based on Visual Analogue Scale (VAS), pain questionnaire, Roland Disability Questionnaire (RDQ) and Modified Oswestry Disability Questionnaire (MODQ). The patients were examined with Schober test and flexion and lateral flexion examinations in order to measure the range of lumbar motion. The patients were examined by a physician blind to the treatment procedures. RDQ was used for functional assessment in patients during their daily activities. Twenty four questions with answer yes or no defined scores were asked. A score of 14 or more was considered as poor result. MODQ scale including 10 items expresses different aspects of human body functions. Each item has 0-5 scores and the higher the score, the more disable the patient. The final score was multiplied by 2 and expressed as percentage. This scale has a total of 50 questions. We used Schober test to examine the status of spinal flexion. GaAs is one of the known low level lasers that can penetrate and have its effect on tissue in the depth of 1-5cm. In this study, patients of laser treatment group were treated with laser at 3 times per week for 4 weeks. The lasers used for treatment were continuous red and pulsed infrared light with wavelengths of 890nm. The energy density of 2-4J/cm^2 was used to irradiate the tender points of the vertebrae L4, L5 and S1 and the fasciae, sacral ligaments and Ileum and gastronomies muscles. The exposure time was 2 minutes per point for red and 30 seconds for infrared lights. The total exposure time was 30 minutes. The trigger and acupuncture points were irradiated 1-2 J/cm^2. The power of the red and IR light were 10mW and 80W, produced by Russian diode laser device "Mustang". In the placebo laser group, the procedure included 3 times per week for 4 weeks with the laser machine was turned off on the lumbar, knee and the muscles of glottal and spinal regions were treated. Statistical analysis performed by using chi-square (χ^2), t-test with $P<0.05$ significant.

Results

The patients' specifications taking part in this study are listed in table 1. There was no statistical difference in age, sex, duration of LBP, activities and education status of the patients in the two groups. Results were analyzed as weighted mean differences (VSA) with 95% confidence intervals (CI). The causes of LBP including strain, sport injuries, sudden movements, falling, accidents, stress or idiopathic causes are shown in diagram 1.

According to chi-square test, we not found significant difference in causes ($P>0.05$). Based on thermo graphic and VAS scores a significant difference between the two groups in pain was achieved ($P<0.05$).

When the results were pooled from different pain scales used in this trial, a statistically significant difference in favor of laser treatment was found with a MODQ of - 0.28. This study also measured pain during movement and found a statistically significant difference in favor of laser treatment with a VSA of -1.16. Then found a statistically significant difference in favor of laser treatment for patient-assessed global disease activity with laser compared to placebo (RR 1.70, CI: 1.1 to 2.63). this trial evaluated the effectiveness of laser treatment in vertebrae L4, L5 and S1 and the fasciae, sacral ligaments and Ilium and astronomies muscles and found a statistically significant difference RDQ (38.69, 95% CI: 29.25 to 48.13) using the change in VAS score to measure pain.

This study found a statistically significant difference in favor of laser treatment at the end of treatment and at 3 and 4 weeks post-treatment for morning stiffness. Other outcome measures of joint tenderness and strength did not yield significant differences.

Discussion

The results of this study support the use of LLLT in the treatment of chronic LBP. Clinicians and researchers should consistently report the characteristics of the LLLT device and the application techniques used. New trial on LLLT should make use of standardized outcome measures. This analysis

lacked data on how LLLT effectiveness is affected by four important factors: 1-type of applications, 2-site of application, 3-treatment duration of LLLT, 4-optimal frequencies and 5-intensities.

This trial included showed a statistically significant difference favoring laser treatment when compared to placebo for at least one outcome measure. This may be dose not report beneficial effects. The varying results of this trial may be due to the method of laser application and/or other features of LLLT application. There is clearly a need to investigate the effects of different dosages on LLLT effectiveness for chronic LBP in future randomized, controlled clinical trials. Also, more studies should be done to investigate the anti-inflammatory action of laser as well as the appropriate parameters needed to achieve an anti-inflammatory effect. The biologic effects of such lasers are not completely known, but they can be effective on some pathobiologic processes like increasing vascularization, stimulating fibroblasts and increasing collagen synthesis, improving microcirculation and perfusion and healing the connective and neural tissues. These are observed in vitro and there are less convincing reports in human body studies [14, 15].

The advantages of using lasers are their simple application, low expense, availability and experience [14]. Most of the laser treatments are experimental and there are fewer consensuses on the details. One of the difficulties in using LLLT is the arbitrary and optional methods used by the physicians particularly in wavelength, power, and frequency and radiation time. Some authors have reported the better result of LLLT in rheumatic disease, joints disease and myofacial syndromes in comparison to drugs [7, 12].

This may be due to various ways of LLLT application in bone and joint diseases. The positive effect of LLLT in diminishing LBP may be the result of increased chondrite and matrix components [3, 8]. Skinner and et al reported that GaAs laser has great effect on fibroblast function and increases the healing of connective tissue. They assume that these changes are due to bio-stimulative effect of laser at the cellular level [14].In his opinion, LLLT can activate cytoplasmic enzymes, increase O_2 consumption, produces more ATP, nucleic acids and proteins. Furthermore, LLLT can decrease prostaglandin and inflammation as well. Due to inhibiting effect on prostacyclin, it can inhibit the exacerbation of inflammation and pain in arthritis and bone disease [14]. In the present study, chronic LBP was diminished in the 3rd and 4th week after treatment according to thermograph and VAS scales. But, we observed no change in the 1st or 2nd week. This may be due to the complexity of the bone and joint diseases. It may be necessary to change the parameters of the treatment (table 1).

In a study complete by Kelin and his colleagues, they postulated that there was significant difference in results for pain treatment in the two groups treated by laser or placebo laser [16].

Also, Basford and et al demonstrated that LLLT can decrease LBP soon after treatment, but has less effect for longer durations [17].

As mentioned in the results section, we did achieve significant differences in RDQ and MODQ scales and schober tests between the groups. These may be the result of few problems such as examiner faults or exhaustion of the patients. This resembles the results reported by Basford and Kelin [16, 17]. Finally, there remain many other questions demanding answers, necessitating further studies. Some of the questions may be cited as:

1) What is the main mechanism of LLLT in improving the pain?
2) What are the suitable wavelengths, exposure points and dosage in treating LBP?
3) What is the best scale to evaluate LBP?

Anyhow, it was shown in this study that choosing appropriate area, wavelength and dosage in LLLT may be effective in decreasing LBP.

Table 1: Baseline characteristics of all subjects with chronic LBP.

Variables	Laser treatment group	Laser placebo group
Age(year), mean±SD	(30-60) 34±7.58	(30-60) 36±6.83
Sex(%)	(59) woman (41) man	(55) woman (45) man
Married (%)	(28) unmarried (72) married	(32) unmarried (68) married
Duration of LBP, Months	17.8±10.5	15.3±9.58
Occupational activity(%)	Hovewives (32) Not working or retived (8) Student (4) At desk mainly (16) At desk and movement (28) Physical labor (12)	Hovewives (30) Not working or retived (8) Student (6) At desk mainly (14) At desk and movement (24) Physical labor (18)
Educational level (%)	Elementury (48) High School (38) University (14)	Elementury (44) High School (40) University (16)

Table 2: Comparison mean results and thermograph number before and after treatment laser group

Criteria	Pre Therapy	First week Therapy	Second week Therapy	Third week Therapy	Forth week Therapy	One month after Therapy
VAS (Pain)	6+2	5/5+1/8	4+1/8	2/1+1/5	1/7+1/4	2+1/3
RDQ	14+4/5	13/5+4	10+3/2	5/3+2/8	6+2/4	6/5+3
MODQ	30+10/6	30+10	25+9/8	25+9	17+8	17+7/6
Schober (CM)	15+2	15/3+1/7	16/5+1/5	18+1/5	18+3/1	18+2/8
Ant Pos-Flox(CM)	27+14	27+15	24+15/3	15+5/6	19+4/5	18+5/1
Lat Flex (CM) (Right)	28+15	28/5+15/7	29+15/8	29+15/7	31+15	30+13
Lat FlexCM) (Left)	26+15	27+15/3	27/5+16/7	26/8+16/2	27/5+15/3	26+14/8
Thermograph	0	2	4	10	10	7

Table 3: Comparison means results and thermograph number before and after laser placebo group

Criteria	Pre Therapy	First week Therapy	Second week Therapy	Third week Therapy	Forth week Therapy	One month after Therapy
VAS (Pain)	6/5+2/1	6/4+1/4	4/2+1/5	4+1/3	3/1+6/1	4/5+1/8
RDQ	15+4/9	14+5	17/8+3/5	13+4	12+3/9	15+3/8
MODQ	30/5+10/5	28/5+10/8	32+10/2	27+10	27+11/2	31+10/8
Scho- ber (CM)	17+1/8	17+1	15/3+2/1	18+1/2	16+1/5	18+1/3
Ant Pos-Flox (CM)	32/5+15/8	30+15	19+4/6	18+5	16+5/1	18+5/3
Lat -Flex (CM) (Right)	29+14	30+15/2	30+13/8	29+15	29/5+15/2	27+14/3
Lat -Flex (CM) (Left)	27+16/6	26+15/3	27+15	27+16/9	27+15/5	26/5+15

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STUDY DESIGN

This clinical study is a double-blind, placebo-controlled randomized parallel group design multi-site evaluation of the effect of the Erchonia® FX-635™ on providing temporary relief of minor episodic chronic low back pain of musculoskeletal origin.

SUBJECT GROUPS

Each subject will be randomized to the test procedure group or to the placebo procedure group, as follows:

Test procedure group: Subjects randomized to the test procedure group will receive the study procedures with the active (true) Erchonia® FX-635™ laser.

Control procedure group: Subjects randomized to the control procedure group will receive the study procedures with a 'fake' (placebo) Erchonia® FX-635™ laser.

The 'fake' (placebo) laser device will appear to the subject to be an active device, but will not produce any therapeutic light output. The placebo laser device is designed to have the same physical appearance as the actual (active test) laser device, including the appearance of any **visible** light output. Therefore, both the test and control devices emit light when activated that is indistinguishable to the subject. As the laser light does not put out any notable degree of heat or noise, these are not distinguishing factors for subjects between the active and control devices.

Apart from the distinction of whether or not the subject receives the study procedures with the actual or the fake laser device, all subjects and investigative parties will adhere to all phases of the entire protocol design.

DOUBLE BLIND DESIGN

This clinical study will be a double-blind design, such that neither the subject nor the investigator will be aware of whether a subject is receiving the study treatments with the active (test procedure group assignment) or the 'fake' (placebo procedure group assignment) Erchonia® FX-635™ until after the study is completed.

Maintenance of study double-blind throughout the entire course of the study will be achieved through the following means:

1) Each subject will be randomly assigned to Procedure Group A or to Procedure Group B by the independent study Monitor. Subjects assigned to Procedure Group A will be treated with the Erchonia® FX-635™ A and subjects assigned to Procedure Group B will be treated with Erchonia® FX-635™ B. Only the study Sponsor will know which label ('A' or 'B') corresponds to the actual (test) FX-635™ device and which label corresponds to the 'fake' device until the final study data analysis is complete. The Sponsor will ensure that this information is stored and maintained confidentially at the Sponsor's work site. This knowledge will not be shared with the investigators, the subjects, or the study Monitor until the final data analysis is complete.

2) The fake (placebo) Erchonia® FX-635™ is designed to have the same physical appearance as the actual Erchonia® FX-635™, including the appearance of any **visible** light output. Therefore, both the test and sham devices emit light when activated that is indistinguishable to both the subject and to the investigator. As the laser light does not put out any notable degree of heat or noise, these are not distinguishing factors for subjects between the two groups.

3) There will be two independent investigators interacting with subjects:

   (i) *Administration Investigator*: who will be responsible for administrating the study treatments to the subject; and
   (ii) *Assessment Investigator*: who will be responsible for recording the study outcome measures. Only the administration investigator will be aware of whether a subject is assigned to Procedure Group A or B, although he or she will not be made aware of whether A or B corresponds to the true or fake laser. Neither the assessment investigator nor the subject will be aware of the subject's A/B Group assignment. In this way, the assessment investigator will not be able to form an association between A/B Procedure Group and active/sham device over the course of the study if a treatment effect is observed.

4) During the laser procedures, both the subject and the administration investigator will wear NiOR LaserShields® MLA glasses that filter out the laser light spectrum.

RANDOMIZATION

Subject allocation to procedure group will be via variable block randomization with varying block sizes of two, four and six used at random to minimize the likelihood of predicting the next procedure group assignment. In addition, randomization will be stratified by test site.

Randomization will be attained using computer generation sequence methodology, insuring that the randomization methodology and the generated allocation sequence is concealed from the investigator and subjects.

Concealment will be insured as follows:

(ii) Each computer-generated randomization sequence is unique and will therefore not be able to be replicated.
(iii) Randomization will occur to either 'Procedure Group A' or to 'Procedure Group B' rather than to a test or placebo group, and only the study Sponsor will know which assignment (A or B) corresponds to the active device and which corresponds to the fake device. The Sponsor will not reveal this information to any source (investigators, subjects, or study Monitor) until the final study data analysis is complete.

Once a subject has qualified for and been enrolled in the study, the Principal Investigator will contact the study Monitor who will act as the central source for providing sequential subject procedure group assignment.

SUBJECTS

Recruitment

Subjects will be recruited from among the Principal Investigator's/test site's pool of patients who are currently being treated for, or who are seeking treatment for, diagnosed minor episodic chronic low back pain of musculoskeletal origin, or from response to the following recruitment materials.

a) Flyer

WANTED

ADULTS WITH LOW BACK PAIN ONGOING
OVER THE LAST 3 MONTHS FOR A
CLINICAL STUDY OF THE EFFECTS OF
LOW LEVEL LASER LIGHT ON
REDUCING LOW BACK PAIN

THIS STUDY INVOLVES EIGHT
LASER LIGHT PROCEDURES
WITH THE ERCHONIA® FX-635™ LASER
OVER 4 WEEKS AT THE TEST SITE.

THERE ARE TWO MORE VISITS TO THE TEST SITE
ONE MONTH AND TWO MONTHS AFTER
THE LAST LASER LIGHT PROCEDURE.

COMPENSATION OF $300
FOR QUALIFIED PARTICIPANTS

FOR MORE INFORMATION PLEASE CONTACT:

<PI name>
<test site name & location>
<phone # and/or e-mail>

b) Newspaper Ad

Low Back Pain Research Study

This study is to see if the Erchonia® FX-635™, a non-invasive, investigational device that uses low-level laser light, can help to relieve minor low back pain that has been ongoing for at least 3 months.

The study involves eleven visits to a test site and recording some information at home.

Compensation up to $300
For qualified participants

Please contact <PI name> at <test site name & location> at <phone and/or e-mail> for details.

Compensation

A subject who completes his or her participation in this clinical study through to the final post-procedure administration visit will receive financial compensation of $300.

A subject will not be charged for the cost of the study procedures with the Erchonia® FX-635™ Laser or for the cost of any other directly-related evaluations or measurements that occur as part of his or her participation in the study.

Sample size

There will be 64 qualified subjects enrolled in this clinical study:

- 32 subjects in the active procedure group
- 32 subjects in the control procedure group

Rationale for sample size

In the determination of sample size, the following parameters have been established for the purposes of assessing efficacy of the Erchonia® FX-635™ in this clinical study:

- Individual subject success criteria defined as a 30% or greater reduction in self-reported Degree of Pain rating on the 0-100 VAS from baseline to study endpoint evaluation.
- Overall study success criteria defined as a minimum 35% difference between the test device group and the placebo device group in the proportion of individual successes.
- It is anticipated that about 55% of subjects in the test device group and about 20% of subjects in the placebo device group will meet the individual success criteria, and
- Intended application of a two-tailed test with an alpha value of 0.05 and Power of 0.8

The **clinical relevance** of a 30% change in VAS score and a 35% difference in the proportion of individual successes between procedure groups has been well previously established over the past 8 years by FDA's Division of Surgical, Orthopedic and Restorative Devices through numerous pre-IDE reviews, the results of said studies that were subsequently used to successfully support various pain-reduction related indications for various Erchonia Corporation light therapy devices under Product Code NHN for the 510(k)s as listed below:

1. **K101430**; 06/22/10: "The FX-635™-AC DermaScanner™ is indicated, while using the red diodes, for adjunctive use in providing temporary relief of minor chronic neck and shoulder pain of musculoskeletal origin."
2. **K100509**; 06/08/10: "The Erchonia THL1 is indicated for use in providing temporary relief of minor chronic neck and shoulder pain of musculoskeletal origin."
3. **K072206**; 04/24/08: "The Erchonia EML Laser is indicated for the temporary reduction in post - surgery pain at 24 hours after surgery following breast augmentation surgery."
4. **K050672**; 06/02/05: "The Erchonia EVRL Laser is generally indicated while using the red diode for adjunctive use in providing temporary relief of minor chronic neck and shoulder pain of musculoskeletal origin."
5. **K041139**; 09/30/04: "The Erchonia EML Laser is indicated as an adjunct to liposuction procedures of the thighs, hips and stomach for reduction of pain associated with the recovery process."

In consideration of the above parameters established for the purposes of sample size calculation, the sample size of 29 subjects per procedure group (test group and placebo group, separately) has been determined using the following reference calculator: *Hypothesis Testing: Categorical Data - Estimation of Sample Size and Power for Comparing Two Binomial Proportions* in Bernard Rosner's *Fundamentals of Biostatistics.*

It is anticipated that about one-twentieth of subjects overall may withdraw from the study prior to completion for various reasons. Therefore, the following formula is used to determine the final needed starting sample size for each group:

Final sample size = sample size X 1/(1-d); where d = # expected dropouts/# subjects enrolled.
Final sample size = 29 X 1/(1-0.083)
Final sample size = 29 X 1/0.917 = 29 X 1.0905 = 31.62, rounded to 32 subjects per group.

Therefore, a minimum starting sample size of 32 subjects in each procedure group is needed to ensure that a sufficient number remains at the end of the trial (29 subjects per group) for any significant differences found between groups to be considered statistically valid and representative of the general population being sampled. This results in a total of 64 subjects being enrolled in this study across both study procedure groups.

STUDY PROCEDURE

STUDY TEST BATTERY

The following is a listing and description of the study measurement and assessment tools to be used and the variables to be recorded in this clinical study. At each evaluation point, the precise tools and variables from this list that will be employed will be specified.

QUALIFICATION EVALUATION TOOLS

THE SIMPLIFIED CALCULATED OSTEOPOROSIS RISK ESTIMATION (SCORE)

The Simplified Calculated Osteoporosis Risk Estimation (SCORE) questionnaire, developed by Lydick et al., is a screening tool used to determine if a woman should be evaluated for osteoporosis by bone densitometry.

SCORE performed well when compared to other prediction rules. Performance characteristics for SCORE are:

T-score	Sensitivity	Specificity
< -2	98%	28%
< -1	91%	31%

SCORE is comprised of the following 6 questions:

(1) age
(2) race
(3) body weight in pounds
(4) history of rheumatoid arthritis
(5) history of estrogen therapy
(6) types of nontraumatic fractures after the age of 45

Scoring and Total SCORE calculation is as follows:

Question	Finding	Points
race	if patient is not Black	5
	if patient is Black	0
rheumatoid arthritis	if the patient has rheumatoid arthritis	4
	if the patient does not have rheumatoid arthritis	0
history of fractures		((number of nontraumatic fracture types after age 45) * 4) maximum 12
age		3 * (INTEGER ((age) / 10))
estrogen therapy	if the patient has a history of estrogen therapy	-1
	if the patient has never received estrogen therapy	1
weight		(-1) * (INTEGER ((weight in pounds) / 10))

where
• The fracture types are wrist rib and hip; the maximum number is 3.
simplified calculated osteoporosis risk estimation (SCORE) =
= SUM (points for the 6 questions)

Interpretation of SUM SCORE:

• Threshold value: 6
• If SCORE > 6 then bone densitometry evaluation should be conducted.

References: Lydick E Cook K et al. Development and validation of a simple questionnaire to facilitate identification of women likely to have low bone density. Am J Managed Care. 1998; 4: 37-48.

DUAL-ENERGY X-RAY ABSORPTIOMETRY (DEXA)

DEXA is the most accurate means of bone mineral density measurement. A bone density test measures the density of minerals (such as calcium) in the bones using a special X-ray, the results of which are used to estimate bone strength. DEXA uses two different X-ray beams to estimate bone density in the spine and hip. Strong, dense bones allow less of the X-ray beam to pass through them. The amounts of each X-ray beam that are blocked by bone and soft tissue are compared to each other. DEXA can measure as little as 2% of bone loss per year. It is fast and uses very low doses of radiation.

DEXA assessment generates a T-score which represent the individual's bone density compared with the norm for other healthy young adults of the same gender. The T-score is the number of units, or standard deviations, that the individual's bone density is above or below the average.

T-score ranges and associated interpretations is shown below.

T-score	Interpretation
-1 and above	Normal bone density.
Between -1 and -2.5	A sign of osteopenia, a condition in which bone density is below normal and may lead to osteoporosis.
-2.5 and below	Indicative of likely osteoporosis.

The World Health Organization (WHO) criteria will be applied in this study, such that a DEXA T-score of ≤2.5 will be considered likely to have osteoporosis.

BASELINE VARIABLES

BASELINE LOW BACK PAIN VARIABLES: The following is recorded at baseline evaluation:
(i) Location of low back pain: right side only; left side only; across all lower back
(ii) Duration of low back pain: months/years since onset of first episode

PRIOR TREATMENT APPROACHES: Any and all prior treatments that the subject has tried to manage his or her low back pain and associated symptoms (such as reduced ROM), including:
(i) Over-the-counter (OTC) medications
(ii) Prescription medications
(iii) Traditional therapies such as physical therapy, occupational therapy
(iv) Alternative therapies such as herbal supplements, chiropractic manipulation, acupuncture, massage

Noting, for each medication/therapy tried:
(i) Date(s) of use/application
(ii) Duration of use/application
(iii) Perceived effectiveness

BASELINE CONCOMITANT MEDICATION AND THERAPY USE: The following is recorded at baseline evaluation:

(i) Over-the-counter and prescription medications currently used by the subject specifically to relieve his or her low back pain, including dosage and typical frequency of use information.
(ii) Non-drug treatments/therapies (conventional, alternative and experimental) currently used by the subject specifically to relieve his or her low back pain, including information on frequency or duration of use and other pertinent application information.
(iii) Over-the-counter and prescription medications currently used, and therapies currently engaged in by the subject for any non-pain relief indication, including dosages and frequency/duration of use.

SUBJECT DEMOGRAPHICS: The subject's age, gender and ethnicity are recorded.

RESCUE PAIN MEDICATION USE

For the purpose of standardization and comparability of outcome assessment across the study subject population, this clinical study will incorporate the use of rescue pain medication for subject as-needed management of low back pain throughout study participation duration.

The rescue pain medication to be used in this study will be over-the-counter Regular Strength Tylenol® tablets. Each subject will be instructed to take a dosage of Tylenol as needed to control any low back pain he or she may be experiencing, ensuring that the directions for use on the labeling are followed.

The subject will be instructed to record in the Subject Daily Diary each time he or she takes a dose of the study rescue pain medication at any time during the entire course of his or her study participation from study enrollment through to the final post-procedure administration visit.

The subject will be instructed to not take a dose of any other over-the-counter or prescription medications for the indication of pain relief, including NSAIDs other than the specified study rescue pain medication, across the entire course of his or her study participation from study enrollment through to the final post-procedure administration visit.

The subject will be instructed not to record a VAS pain rating (whenever indicated) any sooner than six hours after taking a dosage of the study pain relief rescue medication to ensure that the effect of the pain relief rescue medication does not influence the recorded effect of the study procedures with the Erchonia® FX-635™ device. That is, a VAS rating is only to be recorded once the effect of any previously-consumed rescue pain medication has dissipated. The subject will be able to take another dosage of the study pain relief rescue medication immediately after recording the VAS rating, if needed to manage his or her low back pain.

Throughout the course of his or her study participation, a subject can continue to take any other over-the-counter and/or prescription medication(s) that he or she usually takes for any other (non-pain relief) indication(s), as he or she usually takes them, as reported at Baseline evaluation and approved by the study investigator. Subjects will be required to record each time he or she takes a dose of any non-pain relief indicated medication in the Subject Daily Diary across study participation duration.

OUTCOME ASSESSMENT TOOLS

VISUAL ANALOG SCALE (VAS) DEGREE OF PAIN RATING

Subjects will be asked to rate the overall degree of pain experienced in the lower back region on the following 0-100 mm (0 -10 cm) Visual Analog Pain Scale, by responding to the following question:

"Using the scale below, please mark with a cross (X) the spot along the 0 to 100 line below that best shows how much **pain you feel in your lower back** right now. '0' means you feel no pain at all and '100' means you feel the worst pain imaginable. Please mark only one spot."

The Visual Analog Pain Scale (VAS) is one of the three most commonly used scales for assessing chronic pain. It is a simple scale that consists of a line anchored at one end by a label such as "NO PAIN" and at the other end "WORST POSSIBLE PAIN". The subject marks on the line the spot for the pain intensity, which is then measured.

Standard guidelines for effective use of the VAS that are followed in this clinical study are:

i. The line should be 10, 15 or 20cm long, as other lengths are less reliable.
ii. There should be a small vertical mark at each end, with numbers 0 and 100, and a verbal description.
iii. The verbal description must be in absolute terms (e.g. worst pain imaginable);
iv. The line itself should be clear of any markings and should be horizontal rather than vertical, for more reliable measurements.

Used in the above way, it has been shown that the VAS is a proper ratio scale. Like a thermometer, this means that its two ends are rooted, and a doubling of the score does accurately reflect a doubling of the pain. Consequently, sensitive t-tests and ANOVA methods can be used in the analysis, so that significant differences can be identified with relatively small sample sizes or small differences between groups.
Source: Measuring Pain by Adrian White, Acupuncture in Medicine, November 1998 – Vol 16 No. 2

The subject is instructed to refrain from consuming any pain relief medication within 6 hours of recording a required VAS Degree of Pain Rating to ensure that the effect of the pain relief medication does not influence any potential treatment effect of the study procedure with the Erchonia® FX-635™ evidenced through the VAS ratings. The subject may take a dosage of his or her study rescue pain relief medication immediately after recording a VAS rating, if needed.

THE OSWESTRY DISABILITY INDEX (ODI)/OSWESTRY LOW BACK PAIN QUESTIONNAIRE

The Oswestry Disability Index (ODI) is an index derived from the Oswestry Low Back Pain Questionnaire used by clinicians and researchers to quantify disability for acute or chronic low back pain. The ODI is currently considered the gold standard of low back functional outcome tools for measuring degree of disability and estimating quality of life in a person with low back pain.

The validated questionnaire was first published by Jeremy Fairbank et al. in Physiotherapy in 1980. The current version was published in the journal Spine in 2000. The self-completed questionnaire evaluates the patient’s perceived level of disability in 10 everyday activities of daily living concerning intensity of pain, lifting, ability to care for oneself, ability to walk, ability to sit, sexual function, ability to stand, social life, sleep quality, and ability to travel.

Each topic category is followed by 6 statements describing different potential scenarios in the patient's life relating to the topic. The patient then checks the statement which most closely resembles their situation.

Scoring
Each question is scored on a scale of 0-5, with the first statement being zero and indicating the least amount of disability and the last statement scored 5 indicating most severe disability. If more than one box is marked in each section, the highest score is used to calculate the ODI.

The ODI is expressed as a percentage and calculated by dividing the summed score of each question answered by the total possible score (that is dependent on how many questions are answered) and multiplying by 100.

Zero is equated with no disability and 100 is the maximum disability possible.

Minimum detectable change (90% confidence) is 10% points

Scoring Interpretation
0 to 20: minimal disability
- 21-40: moderate disability
- 41-60: severe disability
- 61-80: crippling back pain
- 81-100: these patients are either bed-bound or have an exaggeration of their symptoms.

References

- Fairbank J, Couper J, Davies J, O'Brian J. The Oswestry low backpain questionnaire, Physiotherapy 1980; 66:271-3. (*Version 1.0*)
- Fairbank J, Pynsent P. The Oswestry disablility index. Spine 2000;25: 2490-53. (*Version 2.0*)
- Roland M, Fairbank J. The Roland-Morris Disability Questionnaire and the Oswestry Disability Questionnaire. Spine 2000;25:3115-3124 (*Version 2.1*)

The Oswestry Low Back Pain Questionnaire is contained in **Appendix D.**

RANGE OF MOTION (ROM)

The subject's ROM measurements for flexion, extension, left lateral flexion and right lateral flexion will be taken using a goniometer and following the American Medical Association Guides (2nd and 4th editions) recommendation using measurements of thoracolumbar and lumbar range of movement, respectively, to estimate the percentage of impairment in patients with chronic low back pain. These measurements evaluate the mobility of the lumbar spine from both an articular and a muscular standpoint.

The table below shows the normal measurement values in degrees for each ROM location.

Measurement	Normal
Flexion	60 degs.
Extension	25 degs.
Left Lateral Flexion	25 degs.
Right Lateral Flexion	25 degs.

SUBJECT DAILY DIARY

Throughout the duration of a subject's participation in this clinical study, from study entry through to the final post-procedure administration visit, inclusive, the subject is required to maintain a Subject Daily Diary. On each day of the study, the subject will record the following information in the Subject Daily Diary, as is applicable:

- ✓ ***Rescue Pain Medication Use*:** The subject will record each time a dose of the study rescue pain medication is taken as needed to manage low back pain.
- ✓ ***Other Pain Medication Use:*** The subject will record each time a dose of pain medication other than the study rescue pain medication is taken to manage low back pain. The subject, will,

however, have been instructed to take only the study rescue medication for low back pain relief during the duration of study participation, but deviations are to be recorded.

- ✓ ***Other Pain Management Use:*** The subject will record each time any treatment, therapy or other means of low back management that is not an OTC or a prescription medication is applied to manage his or her low back pain. The subject, will, however, have been instructed to not engage in any other therapeutic applications for low back pain relief other than the study rescue medication for low back pain relief during the duration of study participation, but deviations are to be recorded.
- ✓ ***Other Non-Pain Relief Medication and Therapy Use:*** The subject will record each time any OTC or prescription medication is taken and/or any treatment or therapy is applied for any indication other than to relieve low back pain. These medications and treatments/ therapies will be recorded independent of whether or not it was report as a concomitant medication.tt/therapy at baseline evaluation.
- ✓ ***Adverse Events*** recording: The subject will record each day whether or not he or she believes an adverse event was experienced that day. The subject will be instructed as to potential adverse events from the laser applications as well as how to identify a potential adverse event in general. The subject will be instructed to contact the study investigator right away if he or she believes an adverse event may have occurred for immediate evaluation.

SUBJECT SATISFACTION WITH STUDY OUTCOME

The subject is asked to rate how satisfied he or she is with any change in low back pain following completion of the laser administration procedures with the Erchonia® FX-635™ by using the 5-point Likert scale presented below to respond to the following question: “Overall, how satisfied or dissatisfied are you with any change in the pain in your lower back following the study procedures with the study laser device?”

- Very Satisfied
- Somewhat Satisfied
- Neither Satisfied nor Dissatisfied
- Not Very Satisfied
- Not at All Satisfied

BLINDING EFFICACY EVALUATION TOOLS

SUBJECT PERCEIVED GROUP ALLOCATION AND RATIONALE

The subject records whether he or she believes to have received the study procedures with the true or fake Erchonia® FX-635™ and records verbatim his or her reasoning or rationale for this perceived determination.

ASSESSMENT INVESTIGATOR PERCEIVED SUBJECT GROUP ALLOCATION AND RATIONALE

The Assessment Investigator records whether he or she believes the subject to have received the study procedures with the true or fake Erchonia® FX-635™ and records verbatim his or her reasoning or rationale for this perceived determination.

STUDY PROCEDURE PROTOCOL

PRE-PROCEDURE ACTIVITIES

The pre-procedure activities will be conducted at the test site prior to administration of the initial study procedure with the Erchonia® FX-635™.

STUDY QUALIFICATION

SIGNING OF INFORMED CONSENT FORM

The PI will commence by presenting and reviewing in detail the items in the informed consent form with the individual and answer any questions he or she may have. To proceed, the individual must willingly sign the informed consent form.

ASSIGNMENT OF SUBJECT IDENTIFICATION NUMBER

The subject will be assigned a unique subject identification number based upon his or her order of entry into the study.

Additional information about the informed consent and subject ID number assignment is contained in a later section of the protocol titled, "SAFETY AND CONFIDENTIALITY ISSUES."

STUDY QUALIFICATION EVALUATION: INCLUSION/EXCLUSION CRITERIA

INCLUSION CRITERIA

To be eligible for study participation, a subject must satisfy each of the following criteria.

- The subject's presenting primary pain must be located in the region of the lower back, right and/or left side(s), with the 'lower back' region defined as the area between the boundaries of the lowest rib and the crease of the buttocks
- Subject's low back pain is of musculoskeletal origin, defined as low back pain stemming from benign musculoskeletal problems wherein the etiology is lumbar sprain or strain - a stretch injury to the ligaments, tendons, and/or muscles of the low back - that occurs in the absence of any serious underlying pathology or nerve root compromise

  Diagnosis is based on the following subject profile information:

  a) Patient History:
  (i) Initial onset of low back pain occurred after one or more of the following:

  - ✓ known injury, such as an accident or fall
  - ✓ overexertion of a muscle, such as after unusual amounts of exercise or unaccustomed activity, or sustained positioning (typically indicative of a strain injury)
  - ✓ sudden force or movement exerted upon ligaments, such as unusual turning or twisting (typically indicative of a sprain injury)

  (ii) At least two of the following five are reported:

  - ✓ Complaints of pain and/or loss of function such as inability to turn, twist or bend normally
  - ✓ Pain located along lower back and upper buttocks; may radiate into surrounding tissue
  - ✓ Pain worsens with activity

- ✓ Painful muscle spasms that can worsen with activity or at night while asleep
- ✓ History of prior back injury

(iii) Otherwise in general good health

b) Physical Examination:
At least three of the following six are reported:

- ✓ Inability/difficulty straightening into normal posture while standing
- ✓ Particular activities, such as sitting, standing, walking, driving, are limited, difficult or impossible
- ✓ While lying in prone position, palpation of muscles in lower lumbar area reveals local tenderness and muscle spasm
- ✓ Change in sensation and/or motor function of knees and ankles
- ✓ Raising straight leg from supine position produces sciatica
- ✓ Upon observation, there is no notable posture, spinal alignment or other back deformities

c) Medication Use History: History of taking muscle relaxants or anti-inflammatory medications, either over-the-counter and/or prescription medications.

d) Records and Diagnostic Testing:
Where available, review of prior relevant medical records from the subject's primary treating physician and review of confirmatory prior diagnostic testing, such as x-ray, MRI or CAT scan reports will be conducted.

If the applicable medical records and diagnostic testing listed above are not available or have not been conducted, the study investigator will record and evaluate all applicable information and perform an x-ray, the results of which will then be reviewed and verified as consistent with the study condition before confirming study qualification.

If following the above review, a definitive diagnosis of low back pain stemming from benign musculoskeletal problems wherein the etiology is lumbar sprain or strain - a stretch injury to the ligaments, tendons, and/or muscles of the low back - that occurs in the absence of any serious underlying pathology or nerve root compromise cannot be made, or other possible etiologies of the low back pain are identified or cannot be satisfactorily ruled out, the subject will not qualify for participation in the clinical study.

- ➢ The subject's presenting low back pain is episodic chronic, defined as:

  - ongoing lower back pain having occurred over at least the preceding three months, with lower back pain having occurred on at least 15 days of each of the preceding 3 months, *and*
  - each individual episode of lower back pain over the preceding 3 months having lasted for a period of at least 24 hours followed by a subsequent period of at least 24 hours without pain

- ➢ The subject's self-reported Degree of Pain rating on the 0-100 VAS pain scale is 40 or greater
- ➢ Subject is willing and able to refrain from consuming any over-the-counter and/or prescription medication and/or herbal supplements intended for the relief of pain and/or inflammation, including muscle relaxants throughout the course of study participation, except for the specified study pain relief medication
- ➢ Subject is willing and able to refrain from engaging in any non-study procedure therapies for the management of his or her low back pain throughout the course of study participation, including

conventional therapies such as physical therapy, occupational therapy and hot or cold packs, as well as alternative therapies such as chiropractic care and acupuncture
- Subject agrees and is able to complete the Subject Daily Diary, as applicable, throughout the course of his or her participation in the study
- 18 years of age or older
- Male or female
- Subject's primary language is English

EXCLUSION CRITERIA

A subject who satisfies any of the following criteria will be excluded from study participation:

- The subject's presenting primary pain is located outside or in addition to the region of the lower back, right and/or left side(s); that is, on the region of the back above the lowest rib and/or below the crease of the buttocks
- Subject's low back pain is undiagnosed, or has been diagnosed by a qualified medical professional as being other than that of benign musculoskeletal origin wherein the etiology is lumbar sprain or strain - a stretch injury to the ligaments, tendons, and/or muscles of the low back - that occurs in the absence of any serious underlying pathology or nerve root compromise
- Subject's low back pain has been diagnosed by a qualified medical professional as being in whole or in part due to one or more of the following origins, or any one or more of the following etiologies of the subject's low back pain cannot be satisfactorily ruled out:
  - ✓ *Mechanical*: such as apophyseal osteoarthritis; diffuse idiopathic skeletal hyperostosis; degenerative discs; Scheuermann's kyphosis; s ("slipped disc"); thoracic or lumbar spinal stenosis; spondylolisthesis and other congenital abnormalities; fractures; leg length difference; restricted hip motion; misaligned pelvis - pelvic obliquity; anteversion or retroversion; and abnormal foot pronation
  - ✓ *Inflammatory*: seronegative spondylarthritides (e.g. ankylosing spondylitis); rheumatoid arthritis; infection - epidural abscess or osteomyelitis
  - ✓ *Neoplastic*: bone tumors (primary or metastatic); and intradural spinal tumors
  - ✓ *Metabolic*: osteoporotic fractures; osteomalacia; ochronosis; and chondrocalcinosis.
  - ✓ *Psychosomatic*: Tension myositis syndrome

- Non-organic pain, defined as demonstration of positive findings for three or more of the five signs in the 'Waddell's Signs of Inorganic Behavior' list indicating a non-organic or psychological component to chronic low back pain, as follows:

  - ✓ Tenderness that is superficial and widespread and/or nonanatomic tenderness (skin discomfort on light palpation or tenderness crossing over non-anatomical boundaries)
  - ✓ Simulation of pain with sham maneuvers; i.e. with axial loading and simulated rotation (eliciting pain when pressing down on the top of the patient's head or rotating the shoulders and pelvis together should not be painful).
  - ✓ Distraction, such that less pain is reported for previously positive pain tests when attention is diverted, such as when performing a distracted straight leg raise test. For example, distraction is demonstrated if the subject complains of pain on straight leg raise, but not if the examiner extends the knee with the patient seated at another time during the evaluation
  - ✓ Regional disturbances: regional weakness or non-atomic sensory changes which deviate from accepted neuroanatomy (such as sensory loss in an entire extremity or side of the body or weakness that is non consistent and jerky; i.e. 'cogwheeling')

- ✓ Overreaction, defined as exaggerated or 'disproportionate' painful response to a stimulus that is not reproduced when the same stimulus is given later; subjective signs regarding the subject's demeanor and reaction to testing

- Known herniated disc injury
- Known osteoporosis with compression fractures
- Osteoporosis defined as both of the following:
  - ✓ a Total SCORE on the Simple Calculated Osteoporosis Risk Estimation (SCORE) screening questionnaire of > 6, and
  - ✓ DEXA T-score ≤ -2.5

  If total SCORE is ≤ 6, then DEXA bone density scanning will not be performed as osteoporosis is not indicated and the subject will remain eligible based on this criteria to continue with study qualification evaluation.

- Congenital deformity of spine
- Current, active chronic pain disease: chronic fatigue syndrome, fibromyalgia, endometriosis, inflammatory bowel disease, interstitial cystitis.
- Cancer or treatment for cancer in the past 6 months, including tumors of the spinal cord
- Subject's presenting low back pain is not episodic chronic, defined as one or more of the following being present:

  - ✓ lower back pain has not been ongoing over at least the preceding three months or has been ongoing for less than the preceding 3 months
  - ✓ lower back pain has occurred on less than 15 days of each of the preceding 3 months
  - ✓ each individual episode of lower back pain over the preceding 3 months has lasted for a period of less than 24 hours
  - ✓ period of time between individual episodes of lower back pain over the preceding 3 months has been less than 24 hours

- Subject's self-reported Degree of Pain rating on the VAS pain scale is less than 40
- Use of any one or more of the following <u>analgesics</u>, or an equivalent, <u>within 7 days</u> prior to commencement of administration of the study procedure protocol with the Erchonia® FX-635™:
  - ✓ paracetamol
  - ✓ Compound analgesics
  - ✓ Topical analgesics: patches, creams and lotions

  N.B.: If any of the above analgesics have been taken within 7 days prior to commencement of administration of the study procedure protocol, the subject will remain eligible for study participation if he or she agrees to refrain from use of the analgesic(s) for 7 days prior to commencement of study procedure administration.

- Use of the following <u>muscle relaxants</u> within the <u>prior 30 days</u>:
  - ✓ cyclobenzaprine (Lexeril, Fexmid)
  - ✓ diazepam (Valium)
  - ✓ meprobamate (Miltown®, Equinil®, Equagesic®, Meprospan®)

  N.B.: If any of the above muscle relaxants have been taken within 30 days prior to commencement of administration of the study procedure protocol, the subject will remain eligible for study participation if he or she agrees to refrain from use of the muscle relaxant(s)

until 30 days of non-use prior to commencement of study procedure administration has been attained.

- Use of any of the following muscle relaxants within 7 days prior to commencement of administration of the study procedure protocol with the Erchonia® FX-635™:
  - ✓ Carisoprodal (Soma®, Sodol®, Soprodol®, Soridol®)
  - ✓ Metaxalone (Skelaxin, Robaxin)

  N.B.: If any of the above muscle relaxants have been taken within 7 days prior to commencement of administration of the study procedure protocol, the subject will remain eligible for study participation if he or she agrees to refrain from use of the muscle relaxant(s) until 7 days of non-use prior to commencement of study procedure administration has been attained

- Use of any of the following antidepressants that has been initiated within 30 days prior to commencement of administration of the study procedure protocol with the Erchonia® FX-635™:
  - ✓ duloxetine (Cymbalta®, Effexor)
  - ✓ amitriptyline
  - ✓ imipramine (Tofranil)
  - ✓ clomipramine (Anafranil)
  - ✓ nortriptyline (Pamelor)
  - ✓ desipramine (Norpramin)
  - ✓ SSRIs (selective serotonin reuptake inhibitors) e.g. Paxil, paroxetine, fluoxetine (Prozac)

- Subject is not willing, or is unable to refrain from engaging in any non-study procedure OTC and prescription medications and treatments and therapies for the management of his or her low back pain throughout study participation, including conventional therapies such as physical therapy, occupational therapy and hot or cold packs, as well as alternative therapies such as chiropractic care and acupuncture
- Subject does not agree or is unable to complete the Subject Daily Diary, as applicable, throughout the duration of his or her study participation
- Systemic corticosteroid therapy or narcotics have been consumed within 30 days (inhaled and topical corticosteroids are permitted) prior to commencement of study procedure administration
- Local or epidural injection of corticosteroids, as well as injections of corticosteroids in the back within 3 months prior to commencement of study procedure administration
- Botulinum toxin (Botox®) injection for chronic low back pain within 4 months prior to commencement of study procedure administration
- Active infection, wound or other external trauma to the areas to be treated with the laser
- Prior surgery to the back or spine
- Medical, physical or other contraindications for or sensitivity to light therapy
- Pregnant, breast feeding, or planning pregnancy prior to the end of study participation
- Serious known mental health illness such as dementia or schizophrenia; psychiatric hospitalization in past two years
- Mental illness/incompetence defined according to the following Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V) definition and criteria: A mental disorder is a syndrome characterized by each of the following:

  - ✓ A clinically significant disturbance in an individual's cognition, emotion regulation, or behavior that reflects a dysfunction in the psychological, biological, or developmental processes underlying mental functioning in the individual

- ✓ The consequences of the mental disorder are usually associated with clinically significant distress in social, occupational, or other important activities, or with disability
- ✓ The dysfunctional cognitions and/or behaviors and significant distresses are not merely an expectable response to a common stressor or loss (e.g. death of a loved one) or a culturally sanctioned response to a particular event (e.g. trance states in religious rituals).
- ✓ The dysfunctional cognitions and/or behaviors and significant distresses are no primarily a results of socially deviant behavior (e.g., political, religious, or sexual) or conflicts that are primarily between the individual and society

- Current and/or prior history of alcohol and/or other substance abuse, defined according to the following Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V) definition and criteria that collectively defines alcohol and substance abuse as a "substance use disorder": a problematic pattern of using alcohol or another substance that results in impairment in daily life or noticeable distress. Diagnosis of substance use disorder according to the DSM-5 requires satisfaction of a minimum of 2 of the following 11 symptoms within a 12-month period:

  1. Consuming more alcohol or other substance (larger amounts or for longer periods) than originally planned
  2. Worrying about stopping or consistently failed efforts to control one's use of a substance
  3. Spending a large amount of time using and/or recovering from use of a substance, or doing whatever is needed to obtain a substance
  4. Use of a substance results in failure to 'fulfill major role obligations' such as those at home, work or school.
  5. 'Cravings' or urges to use a substance
  6. Continuing the use of a substance despite health problems caused or worsened by it, including mental health problems (such as depressed mood, sleep disturbance, anxiety, or "blackouts") or physical health.
  7. Continuing or repeated use of a substance despite its having negative effects on relationships with others.
  8. Continuing or repeated use of the substance in a dangerous situation (e.g., when operating heavy machinery or driving a car)
  9. Giving up or reducing important social, occupational or recreational activities because of the substance use
  10. Building up a tolerance to the alcohol or drug. Tolerance is defined by the DSM-5 as "either needing to use noticeably larger amounts over time to get the desired effect or noticing less of an effect over time after repeated use of the same amount."
  11. Experiencing withdrawal symptoms after stopping use of a substance that can be relieved by taking more of the substance. According to the DSM-V definition and criteria, key 'withdrawal symptoms' include: 'anxiety, irritability, fatigue, nausea/vomiting, hand tremor or seizure in the case of alcohol.'

  Evaluation for satisfaction of the DSM-V 'substance use disorder' criteria will be conducted both with respect to the preceding 12 month period (current abusers) and with respect to any 12-month period in the past (history of prior abuse).

- Developmental disability or cognitive impairment that in the opinion of the investigator would preclude adequate comprehension of the informed consent form and/or ability to record the necessary study measurements
- Involvement in litigation and/or receiving disability benefits related in any way to the parameters of the study

- Subject is less than 18 years of age
- Participation in a clinical study or other type of research in the past 30 days
- Subject's primary language is other than English

WASHOUT PHASE: 48 HOURS PRIOR TO COMMENCEMENT OF THE PRE-PROCEDURE EVALUATION PHASE

The pre-procedure washout phase comprises the 48-hour period immediately preceding the pre-procedure evaluation phase, beginning upon waking on the first 24-hour period.

At the start of the pre-procedure washout phase, the subject commences his or her required abstinence from use of non-study related medications and therapies for the relief of his or her low back pain and also commences the as-needed consumption of the study rescue medication for his or her low back pain that will continue through to the end of the post-procedure evaluation phase.

WASHOUT PHASE MEASURES

On each day of the two-day pre-procedure Washout Phase, the subject records the following measures, as outlined in the STUDY TEST BATTERY section above.

- Subject Daily Diary (all applicable measures)
- Visual Analog Scale (VAS) Degree of Pain Rating: recorded upon waking on each morning of the two-day pre-procedure Washout Phase

CONFIRMATION OF CONTINUED SUBJECT STUDY ELIGIBILITY

Prior to the subject commencing the pre-procedure evaluation phase of the study, the investigator reviews the information recorded in the pre-procedure Washout Phase Subject Daily Diary and determines the average of the 2 low back pain VAS degree of pain ratings recorded by the subject during the Washout Phase. **The calculated 2-day washout phase average VAS pain rating will become the subject's Baseline VAS pain rating for the purpose of study success evaluation.**

In order for the subject to remain qualified for study participation, the following two criteria must be satisfied:

(i) There is no information recorded in the Subject Daily Diary that would render a subject ineligible for continued study participation, such as use of unapproved medications; and
(ii) The subject's 2-day Washout Phase average VAS score must be upheld at 40 or greater. If it is less than 40, the subject's participation in the study ends at this time.

SUBJECT RANDOMIZATION TO PROCEDURE GROUP

A fully qualified subject is randomly assigned to Procedure Group A or to Procedure Group B, following the methodology outlined above in the STUDY DESIGN section of the protocol.

PRE-PROCEDURE EVALUATION PHASE

The pre-procedure evaluation phase commences on the day following successful completion of the two-day pre-procedure Washout Phase and following confirmation of continued subject study eligibility. During the pre-procedure evaluation phase, the following is recorded as outlined in the STUDY TEST BATTERY section above.

BASELINE VARIABLES

- Baseline Low Back Pain Variables
- Prior Treatment Approaches
- Baseline Concomitant Medication and Therapy Use
- Subject Demographics

PRE-PROCEDURE OUTCOME ASSESSMENTS

- Range of Motion (ROM)
- Visual Analog Scale (VAS) Degree of Pain Rating
- Oswestry Disability Index (ODI)/Oswestry Low Back Pain Questionnaire

PROCEDURE ADMINISTRATION PHASE

The procedure administration phase is of 4 weeks duration and comprises 8 test site visits evenly spaced across the 4 weeks for procedure administrations.

PROCEDURE ADMINISTRATION PROTOCOL

- The procedure administration phase of the study will commence within one hour subsequent to completion of the pre-procedure phase.
- The procedure administration phase will extend over 4 consecutive weeks.
- Each subject will receive 8 total procedures with the Erchonia® FX-635™ across the consecutive 4-week procedure administration phase: 2 procedure administrations per week, each procedure administration approximately evenly spaced (3 to 4 days apart).
- Each procedure administration lasts a total of 20 minutes
- Each procedure administration with the Erchonia® FX-635™ will be administered at the investigator's test site.
- The procedure administration protocol for each session is as follows:

1. The subject enters the procedure room and lies comfortably on his or her stomach on the table such that the back area of the subject's body is facing upwards.
2. The subject is correctly fitted with the NoIR protective eyewear.
3. The center diode of the Erchonia® FX-635™ is positioned at a distance of 6 inches above the subject's back, centered on the lower back, with the other 2 diodes centered one each on each of the 2 hip flexors.
4. The Erchonia® FX-635™ is activated for 20 minutes. Each scanner emits to the subject a laser beam of approximately 17 mW with a wavelength of 635 nm, and creates a spiraling circle pattern totally random and independent from the others. These patterns overlap each other to guarantee total coverage within the target area. The target area is approximately 8 x 10 inches or 80 square inches (approx. 516 square centimeters).
5. The subject's protective eyewear is removed and the session is over.

Justification for the Procedure Administration Protocol

In the prior clinical study evaluating efficacy of Erchonia LLLT on the reduction of low back pain, the procedure administration protocol implemented comprised six 15-minute procedure administrations over 3 weeks; 2 procedure administrations per week.

While the results of this study demonstrated statistically significant efficacy of Erchonia active laser treatment over placebo, the effect (the clinically meaningful pain reduction outcome) appeared to develop at a slower rate over a longer period of time than that which had been demonstrated in prior Erchonia Corporation clinical studies for pain reduction indications such as for neck and shoulder pain (K100509) and for chronic heel (plantar fasciitis) pain (K132940), indicating that the condition of chronic low back pain is a more resistant to therapy than the other chronic pain conditions previously evaluated and therefore necessitates a slightly enhanced procedure administration protocol that does not increase the risk to the subject nor compromise subject safety in any way in its implementation.

Therefore, it was decided that slight increments in and modifications to each of the procedure administration outputs variables was warranted to attain a comparable treatment effect for the reduction of chronic low back pain as had been attained in prior Erchonia Corporation pain reduction clinical trials, as shown in the comparative table below:

Treatment Parameter	Initial Trial Treatment Parameter	Modified Current Output Treatment Parameter
Number of Treatments	6	8
Duration of Treatment Administration	3 weeks	4 weeks
Frequency of Treatment Administration	2 times per week	2 times per week
Duration of Each Procedure Administration	15 minutes	20 minutes

PROCEDURE ADMINISTRATION PHASE MEASURES

DAILY MEASURES

Commencing on the same day as the first study procedure administration with the Erchonia® FX-635™, the subject begins to record all of the required information in the Subject Daily Diary, as applicable, at home, and continues to satisfactorily complete the Subject Daily Diary through each day of the procedure administration phase.

The rescue pain medication (OTC Tylenol) use count on day one of the procedure administration phase will serve as the subject's initial (baseline) pain medication count for the purpose of subsequent evaluation of change in utilization of pain relief medication throughout study participation.

FOLLOWING EACH PROCEDURE ADMINISTRATION

Within 10 minutes following administration of each of the 8 study procedure administrations with the Erchonia® FX-635™, the following will be recorded at the test site as outlined in the STUDY TEST BATTERY section above.

- Visual Analog Scale (VAS) Degree of Pain Rating
- Assessment Investigator's Adverse Events Evaluation

FOLLOWING THE FINAL PROCEDURE ADMINISTRATION

In addition to the VAS pain rating recordings and the adverse events evaluation, within ten minutes of completion of the 8th and final procedure administration of the 4-week procedure administration phase of the study, the following will be recorded at the test site as outlined in the STUDY TEST BATTERY section above.

ASSESSMENT AND EVALUATION TOOLS
- Oswestry Disability Index (ODI)/Oswestry Low Back Pain Questionnaire
- Range of Motion (ROM)
- Subject Satisfaction With Study Outcome

BLINDING EFFICACY EVALUATION
- Subject Perceived Group Allocation and Rationale
- Assessment investigator Perceived Subject Group Allocation and Rationale

POST-PROCEDURE ACTIVITIES

POST-PROCEDURE EVALUATION PHASE

The post-procedure administration evaluation phase of this study will commence immediately following completion of the procedure administration phase, and will last 2 months (8 weeks).

POST-PROCEDURE EVALUATION TEST SITE VISITS AND MEASURES

There will be 2 post-procedure evaluation visits at the test site.

ONE MONTH POST-PROCEDURE EVALUATION

One month after completion of the procedure administration phase, the subject returns for a test site visit to record the following measures as per the STUDY TEST BATTERY section above.

- Visual Analog Scale (VAS) Degree of Pain Rating
- Oswestry Disability Index (ODI)/Oswestry Low Back Pain Questionnaire
- Range of Motion (ROM)
- Assessment Investigator's Adverse Events Evaluation

STUDY ENDPOINT EVALUATION: TWO MONTHS POST-PROCEDURE EVALUATION

Two months after completion of the procedure administration phase, the subject returns for a final test site evaluation visit. The two-month post-procedure evaluation visit will serve as the study endpoint evaluation visit, the evaluation point at which study success will be evaluated relative to baseline. At this visit, the following measures will be recorded as per the STUDY TEST BATTERY section above.

ASSESSMENT AND EVALUATION TOOLS

- Visual Analog Scale (VAS) Degree of Pain Rating
- Oswestry Disability Index (ODI)/Oswestry Low Back Pain Questionnaire
- Range of Motion (ROM)
- Subject Satisfaction With Study Outcome
- Assessment Investigator's Adverse Events Evaluation

BLINDING EFFICACY EVALUATION

- Subject Perceived Group Allocation and Rationale
- Assessment investigator Perceived Subject Group Allocation and Rationale

AT-HOME POST-PROCEDURE EVALUATION PHASE MEASURES

DAILY MEASURES

The subject will continue to record all of the required information in the Subject Daily Diary, as applicable, at home, on each day of the two-month post-procedure administration phase.

WEEKLY MEASURES

At the end of each of post-procedure evaluation weeks 1, 2, 3, 5, 6, and 7, the subject will record the following in his or her home upon waking each morning, as outlined in the STUDY TEST BATTERY section above. These measures are already being recorded at the end of post-procedure weeks 4 and 8 as part of the scheduled test site visits.

- Visual Analog Scale (VAS) Degree of Pain Rating
- Oswestry Disability Index (ODI)/Oswestry Low Back Pain Questionnaire

TABLE OF SUBJECT EVENTS

The following table provides a progressive summary of subject events throughout this study.

PRE-PROCEDURE ACTIVITIES

STUDY QUALIFICATION

1) A potentially well-suited and interested candidate for participation in the study attends the investigator's office.
2) The investigator reviews the informed consent form with the candidate.
3) If the candidate continues to be interested and voluntarily signs the informed consent form, the study qualification evaluation phase of the study is performed.

WASHOUT PHASE

4) A qualified subject enters the 48-hour washout phase and partakes in the following:
   - ✓ Commencement of rescue pain medication only use
   - ✓ Completion of Subject Daily Diary
   - ✓ Daily VAS Degree of Pain recordings
5) A subject whose continued study eligibility post-washout is confirmed is randomly assigned to procedure group.

PRE-PROCEDURE MEASURES & VARIABLES

- Baseline Low Back Pain Variables
- Prior Treatment Approaches
- Baseline Concomitant Medication and Therapy Use
- Subject Demographics
- VAS Degree of Pain Rating
- Oswestry Disability Index (ODI)/Oswestry Low Back Pain Questionnaire
- Range of Motion (ROM)

PROCEDURE ADMINISTRATION PROTOCOL

Eight 20-minute study procedure administrations with the Erchonia® FX-635™ over 4 consecutive weeks, 2 treatment administrations per week, administered at the test site.

PROCEDURE ADMINISTRATION PHASE MEASURES

DAILY MEASURES

- Subject Daily Diary

FOLLOWING EACH PROCEDURE ADMINISTRATION

- VAS Degree of Pain Rating
- Assessment Investigator's Adverse Events Evaluation

FOLLOWING THE FINAL PROCEDURE ADMINISTRATION

- Oswestry Disability Index (ODI)/Oswestry Low Back Pain Questionnaire
- Range of Motion (ROM)
- Subject Satisfaction With Study outcome
- Subject Perceived Group Allocation and Rationale
- Assessment Investigator Perceived Subject Group Allocation and Rationale

POST-PROCEDURE ACTIVITIES

AT-HOME MEASURES

DAILY
- Subject Daily Diary

WEEKLY: At the end of each of weeks 1, 2, 3, 5, 6, & 7 of the post-procedure administration phase:
- VAS Degree of Pain Rating
- Oswestry Disability Index (ODI)/Oswestry Low Back Pain Questionnaire

TEST SITE EVALUATION VISITS

ONE MONTH POST-PROCEDURE EVALUATION

- VAS Degree of Pain Rating
- Oswestry Disability Index (ODI)/Oswestry Low Back Pain Questionnaire
- Range of Motion (ROM)
- Assessment Investigators' Adverse Events Evaluation

STUDY ENDPOINT EVALUATION: TWO MONTHS POST-PROCEDURE EVALUATION

- VAS Degree of Pain Rating
- Oswestry Disability Index (ODI)/Oswestry Low Back Pain Questionnaire
- Range of Motion (ROM)
- Subject Satisfaction With Study Outcome
- Subject Perceived Group Allocation and Rationale
- Assessment Investigator's Perceived Subject Group Allocation and Rationale
- Assessment Investigators' Adverse Events Evaluation

ADVERSE EVENTS

At each evaluation and procedure administration test site visit throughout the clinical study, and at any other time throughout the duration of the clinical trial that is necessary, any and all potential adverse events reported by a subject or observed by an investigator will be recorded on the case report form, and subsequently evaluated by a suitably qualified independent reviewer for determination of relationship to the study treatment and whether or not any corrective action needs to be taken. All potential adverse events recorded will be appropriately reported to the governing IRB, as applicable.

It is unlikely and not expected that any adverse events will result from implementation of this clinical study protocol. Prior clinical trials using low level laser light have not typically yielded any adverse events or reactions. However, potential adverse events that may feasibly occur from application of the Erchonia® FX-635™ include, but are not necessarily limited to: skin irritation, discoloring, rash, indentations and infection.

STATISTICAL ANALYSIS

PRIMARY EFFICACY OUTCOME MEASURE: CHANGE IN SUBJECT SELF-REPORTED VAS PAIN RATING FROM BASELINE TO STUDY ENDPOINT

Primary efficacy outcome measure for this clinical study will be a statistically significant difference in the proportion of subjects between test and control groups who achieve a clinically meaningful and statistically significant decrease in self-reported VAS pain rating from baseline to study endpoint.

Subjects meeting Individual Success Criteria
The individual subject success criteria is defined as a 30% or greater decrease in self-reported VAS pain rating at study endpoint relative to baseline.

Overall Study Success Criteria.
Overall study success criteria is defined as at least a 35% difference between procedure groups, comparing the proportion of individual successes in each group. It is anticipated that about 55% of subjects in the test group will meet the individual success criteria and about 20% of subjects in the control group will meet the individual success criteria.

The clinical relevance of a 30% change in VAS score has been well previously established by FDA's Division of Surgical, Orthopedic and Restorative Devices through numerous pre-IDE reviews, the results of said studies that were subsequently used to successfully support various pain-reduction related indications for various Erchonia Corporation light therapy devices under Product Code NHN for the 510(k)s listed below over the past 8 years:

1. K101430; 06/22/10: "The MLS-AC DermaScanner™ is indicated, while using the red diodes, for adjunctive use in providing temporary relief of minor chronic neck and shoulder pain of musculoskeletal origin."

2. K100509; 06/08/10: "The Erchonia THL1 is indicated for use in providing temporary relief of minor chronic neck and shoulder pain of musculoskeletal origin."

3. K072206; 04/24/08: "The Erchonia EML Laser is indicated for the temporary reduction in post - surgery pain at 24 hours after surgery following breast augmentation surgery."

4. K050672; 06/02/05: "The Erchonia EVRL Laser is generally indicated while using the red diode for adjunctive use in providing temporary relief of minor chronic neck and shoulder pain of musculoskeletal origin."

5. K041139; 09/30/04: "The Erchonia EML Laser is indicated as an adjunct to liposuction procedures of the thighs, hips and stomach for reduction of pain associated with the recovery process."

Evaluation Time Point

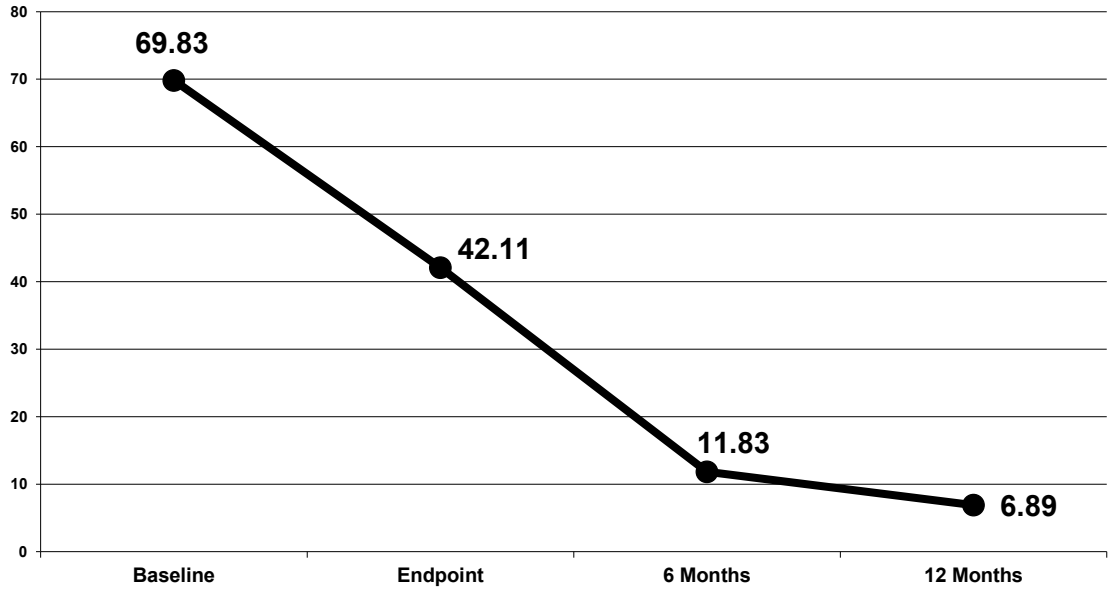
The study end evaluation time point at which study success will be analyzed is at two months post-procedure evaluation relative to baseline evaluation.

The rationale and validation for the timing of the study endpoint is based a combination of factors, as follows:

- The long-term follow-up results of the following Erchonia Corporation clinical trial that successfully supported the following FDA 510(k) clearance for market, demonstrated that while a clinically meaningful and statistically significant reduction in pain did occur over the course of the treatment administration period, the therapeutic effects prevailed, extended and intensified over the longer term, and the difference in efficacy results between active and control groups widened for chronic pain conditions.

  Device: Erchonia® Allay™
  510(k)#: K132940
  Manufacturer: Erchonia Corporation
  Device Class: Class II
  Product Code: NHN
  Clearance Date: 04/14/14
  Indication for Use: The Erchonia® Allay™ laser is indicated as an adjunct to reducing chronic heel pain arising from plantar fasciitis.

  The chart below shows the average VAS heel pain ratings for 23 subjects in the above clinical trial who had been assigned to the active device group and were followed through to 12 months post-procedure. It can be seen that while at study endpoint evaluation (2 weeks post-procedure), a statistically significant and clinically meaningful decrease in mean VAS ratings occurred, this effect prevailed through to 12 months post-procedure follow up to almost negligible recordable pain levels.



We believe this phenomenon occurs for two primary reasons:

(i) It is hypothesized from the understanding of the general mechanism of operation of LLLT to pain reduction (as explained in detail in the clinical study protocol), that the increase in the production of ATP and activate enzymes in the underlying targeted cells of the tissue that cultivate a growth factor response within the cells and promote tissue healing, and new, healthier cell and tissue growth to strengthen and support muscles and tendons, to restore strength and flexibility and to protect against further damage, together with the anti-inflammatory properties of low level lasers that reduce nerve irritation and inflammation to provide pain relief, neither ends nor peaks at completion of treatment administration, but rather the therapeutic properties of the LLLT continue to take effect and to intensify over the prevailing weeks and months.

(ii) Inherent in individuals with chronic pain conditions is the hope in finding a means of substantial and durable pain relief, which is observable in the typical early onset high placebo effect attained in studies evaluating therapeutic pain relief modalities. Therefore, the need for a longer-term evaluation period in order for subjects to distinguish true and enduring pain relief from that of wishful pain relief, and for the true active therapeutic effect versus placebo to prevail is evident.

The above referenced clinical study evaluating the efficacy of Erchonia LLLT in reducing chronic heel pain arising from plantar fasciitis successfully supported the following FDA 510(k) clearance for market:

Device: Erchonia® Allay™
510(k)#: K132940
Manufacturer: Erchonia Corporation
Device Class: Class II
Product Code: NHN
Clearance Date: 04/14/14
Indication for Use: The Erchonia® Allay™ laser is indicated as an adjunct to reducing chronic heel pain arising from plantar fasciitis.

- The findings of this study are consistent with and supported by anecdotal reports by investigators in this study and of other medical professionals who regularly apply Erchonia LLLT in their practices. Many of these practitioners have reported to Erchonia Corporation that patients treated with the Erchonia laser for neck and shoulder pain and heel pain have reported anecdotally at follow-up visits many months after treatment end that their pain has continued to lessen over time.

- Further support comes from prior clinical trials by other Sponsors whose results have been successfully applied to supporting 510(k) market clearances for LLLT devices to the reduction of pain associated with chronic pain conditions. Most notable of these is the MicroLight 830 LLLT study whose results were used to support the indication of the reduction of pain associated with the musculoskeletal condition of carpal tunnel syndrome (K010175). In this study, the study evaluation endpoint was 12 weeks (3 months) post-procedure.

It is for all of the above reasons that it was decided that in the present clinical study, a longer post-procedure endpoint evaluation is warranted to attain a more accurate representation of optimal treatment effect of LLLT application with the Erchonia® FX-635™ laser device to the chronic pain condition of low back pain of musculoskeletal origin.

Hypotheses

- ***Null Hypothesis***: There will be no statistically significant difference in the proportion of individual successes, as defined, between the test and control groups.
- ***Alternative Hypothesis***: There will be a statistically significant difference in the proportion of individual successes, as defined, between the test and control groups, to the effect of 35% or greater.

PRIMARY EFFICACY OUTCOME STATISTICAL EVALUATION METHODS

- **Intent to Treat (ITT) Principle**: Primary efficacy analysis will be according to the intent to treat (ITT) principle; wherein subjects will be included in the analysis if they were randomized to study procedure group, had a valid baseline (pre-procedure) visit including the required low back pain VAS recording; and received at least the first study procedure administration.

- **Missing data** will be handled through *Last Observation Carried Forward (LOCF)*: by carrying forward the last recorded observation to fill in the subsequent missing value.

- **Per-Protocol Analysis** will also be performed for the set of all subjects who were randomized to procedure group and completed the study according to the full protocol.

- **Primary analysis of efficacy** will be according to intent to treat (ITT) analysis through the application of:

  1) **Fisher's exact test** to compare the proportion of success between the test and the control groups, considering that randomization has been diligently conducted and important covariates between the two groups are well balanced.

  2) **Parametric ANCOVA model** analysis with the mean change from baseline to study endpoint in low back pain rating on the VAS as the dependent variable, procedure group as the independent variable of interest and baseline low back pain VAS rating as a covariate. A two-tailed significance level of 5% will be considered to be statistically significant.

- **Covariates:** The following potential covariate baseline variables will be adjusted, as applicable, through application of an ANCOVA analysis for the continuous variables and linear regression analysis for categorical variables.

  - ✓ Baseline Oswestry Disability Index (ODI) score
  - ✓ Age

SUPPORTIVE SECONDARY OUTCOME MEASURE: OSWESTRY DISABILITY INDEX (ODI) SCORE

ODI scores will be considered a secondary endpoint to support the primary pain evaluation outcome measure of subject self-reported degree of low back pain levels recorded on the 0-100 Visual Analog Scale (VAS).

The ODI score will be evaluated as follows:

- Change in ODI score from study baseline to endpoint evaluation will be calculated, with a clinically meaningful change determined to be 10% decrease in points, based on the established minimum detectable change (90% confidence) of 10% points. Statistical significance of the change will be evaluated through parametric t-test and ANCOVA analysis, with a two-way significance level of 5% considered to be statistically significant.
- Correlation analysis will be performed to evaluate the strength of the relationship between the change in VAS ratings and the corresponding change in ODI scores from baseline to study endpoint evaluation.

ADDITIONAL SUPPORTIVE OUTCOME MEASURES EVALUATION

The following additional supportive outcome measures will also be evaluated as exploratory qualitative trending of the following, without claims of statistical significance:

a) mean changes in low back pain VAS ratings across and between all study evaluation time points, within and between procedure groups
b) mean changes in ODI scores across and between all study evaluation time points, within and between procedure groups
c) Mean changes in each of the range of motion measurements across and between all evaluation points, within and between procedure groups
d) Differences in satisfaction with Study Outcome Ratings between procedure groups at both evaluated time points, and change between

EVALUATION OF RESCUE PAIN MEDICATION USE

The impact of rescue pain medication use during the study will be evaluated using descriptive statistics and qualitative comparisons.

BLINDING EFFICACY EVALUATION

Blinding efficacy evaluation will be conducted through analysis of findings from the Subject and the Assessment Investigator Perceived Subject Group Allocation and Rationale responses, recorded at completion of the four-week procedure administration phase and again at study endpoint evaluation at 2 months post-procedure administration.

Statistical evaluation of blinding efficacy will be performed as follows:

(i) The percentage of subjects who correctly perceived their procedure group assignment and the percentage of subjects who did not correctly perceive their procedure group assignment will be calculated.

(ii) The percentage of times the assessment investigators correctly perceived subjects' procedure group assignment and the percentage of times the assessment investigators did not correctly perceive subjects' procedure group assignment will be calculated.
(iii) The **Fischer's Exact categorical analysis technique** for comparison of proportion of successes (accurate procedure group assignment determination) and failures (inaccurate procedure group assignment determination) between subject groups will be performed for each of the subject and assessment investigator determinations.
(iv) **Qualitative analysis confirmation:** Evaluation of the comments provided by the subject and assessment investigators in the rationale section to explain the guess at group assignment will be evaluated and interpreted as follows to either support or negate the numerical findings:

- *Positive blinding efficacy* will be supported through qualitative assessment of comments provided to support perceived group assignment that pertain to the determination being made based on treatment efficacy or lack thereof; e.g.: 'I can bend down and walk around more easily and with less pain than before, so I believe I got the real treatment' or 'I haven't noticed any change in my low back pain, so I believe I got the fake treatment.'

- *Blinding will be determined to have failed* if comments provided to support perceived group assignment pertain to factors such as sensation/visual clues, such as 'I saw/didn't see a light go on', or other factors that pertain to blinding having been compromised such as 'I overheard the doctor saying I wasn't getting the real treatment.'

SAFETY ANALYSES

Safety analyses will be based on all subjects who were randomized to the test or to the placebo procedure group. Safety will be assessed by evaluating and comparing frequency and incidence of observed and/or reported adverse events between test and placebo procedure groups. A chi-square test with a continuity correction will be performed to compare the percentage of subjects who had adverse events between test and placebo group subjects.

Analysis of results will be performed by individual test site and pooled across test sites. Application of a balanced test-control group study design incorporating a varied block by test site randomization procedure will contribute to statistical justification of pooling data across the different test sites.

END OF DOCUMENT