ERCHONIA® HLS™

A Pilot Evaluation of the effect of the Erchonia® HLS™ for the relief of tinnitus symptoms

ERCHONIA CORPORATION

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TABLE OF CONTENTS

STUDY INFORMATION

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PURPOSE OF STUDY
The purpose of this pilot study is to determine the effectiveness of the Erchonia® HLS™, manufactured by Erchonia Corporation (the Company), in providing temporary relief of tinnitus symptoms in adults 18 years and older.

STUDY DURATION
The estimated total duration of the study is about two months.

EXPECTED RESULTS
Following completion of the study procedure administration protocol with the Erchonia® HLS™, it is anticipated that compared with baseline, subjects will show a reduction in tinnitus symptoms at study endpoint evaluation.

HISTORY OF THE CLINICAL STUDY

WIRB PRO NUM: 20182570**:** A double-blind, placebo-controlled randomized evaluation of the effect of the Erchonia® FX-635™on the relief of tinnitus symptoms

DEVICE DESCRIPTION

The Erchonia® HLS Laser will be self-administered by the subject at home, for a total of 56 treatment administrations: Daily administration for 8 consecutive weeks. Each HLS administration will last a total of 10 minutes.

The Erchonia HLS Laser is a hand-held single diode, variable hertz laser that is portable, self-contained, lightweight, and battery operated.

The Erchonia HLS Laser emits a 640 nanometer (nm) wavelength with a tolerance of ±10 nanometer. The diode is classified by the Center for Devices and Radiological HHLSth (CDRH) as Class II laser diode in accordance with IEC 60825-1, compliant to 21CFR1040 via Laser Notice#50.

An internal battery that is recharged using an external inductive charging base powers the laser. The internal battery powers the specially created and patented electronic diode that emits a <10mW red laser beam.

The HLS Laser has the following specifications:

Power	7.5 mW ± 1.00 mW
Wavelength	640 nm ± 10 nm
Waveform	Variable Hertz
Joules	4.5 Joules per treatment administration
Energy Source	Single electronic diode, with patented optics

Power Supply	100-240 V ac; 50-60 Hz electrical outlet, lithium-ion Polymer battery
Duty Cycle	50%
Energy Delivery	Handheld treatment probe
Treatment Time	10 minutes
Target Size	Line pattern, manually scanned over area of treatment

DEVICE SPECIFICATIONS

Figure 1 below contains an image of the Erchonia HLS Laser, and a description of the system components follows.

Figure 1: The Erchonia HLS Laser

#1 POWER BUTTON (ON/OFF)

The Power Button allows you to turn the device ON "|" or OFF "O". To turn the device ON, press and hold this button until the green (#3 Power On Light) turns on. To turn off the device it is recommended to use the **"Power Down"** icon on the **"Function Screen".** Refer to the Powering Down section. In the unlikely event that your device stops responding to touches, by pressing and holding the power button for 10 seconds will force shut down the device. This is only recommended if the device cannot be turned off from the **"Power Down"** screen.

#2 LASERS ON LIGHT
The Lasers ON is an LED indicator light that will light up when the Laser is ON and shut off when the laser is OFF.

#3 POWER ON LIGHT
The Power On LED indicator will display a constant green light when the device is powered on.

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

#5 PIVOTING LASER MOUNT
The Pivoting Laser Mount allows the user to adjust the laser angle based on user preference.

#6 LASER DIODE
The device consists of a single electronic laser diode, with patented optics. The laser diode when activated by the internal power source generates laser energy thereby emitting a red beam. This is a specially designed and patented unit created to ensure the laser beam is focused and directed for the most optimal use.

CHARGER BASE AND POWER SUPPLY

The Erchonia HLS Laser contains a unique battery system designed by specification to provide the end user with a constant and consistent power, capable of intense use for extended periods, while yet being lightweight for portability. The battery system encompasses the internal battery component, the inductive charger base, and the external power supply. The internal battery is sHLSed by the vendor and then encased within the device housing and can only be replaced by the manufacturer. The battery component is refreshed by the use of an external power supply used with the charger base. The power supply is an IEC 60601 3rd Ed. certified unit, compliant to CE/CB standards.

Figure 2 below contains an image of the Erchonia HLS Laser charger base and power supply, and a description of the system components follows.

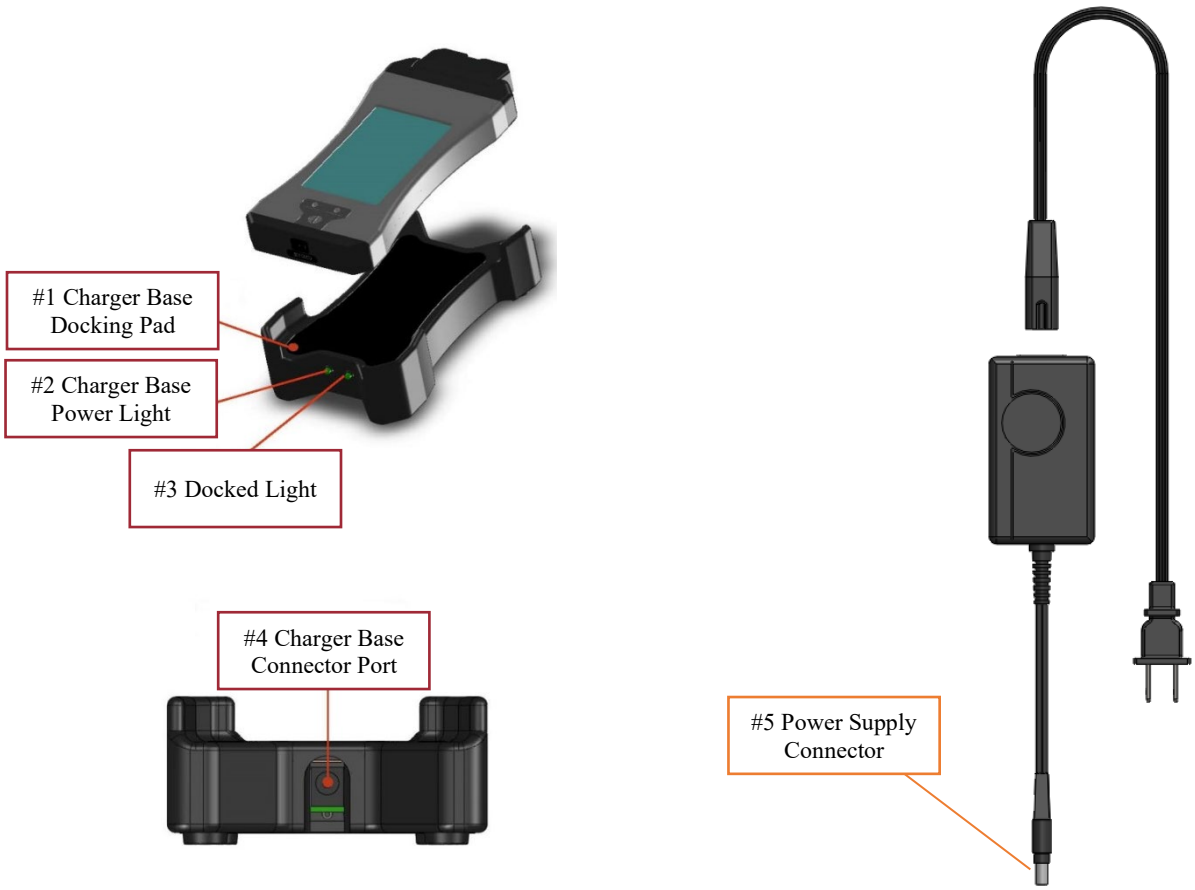


Figure 2: The Erchonia HLS Laser Charger Base and Power Supply

#1 CHARGER BASE DOCKING PAD

The Charger Base Docking Pad is a custom based system specifically designed to charge the laser device. It is an inductive charging system that charges the device wirelessly.

#2 CHARGER BASE POWER LIGHT

The Charger Base Power Light is an LED power indicator that will light up when the Power Supply connector is plugged into the Charger Base Docking Pad.

#3 DOCKED LIGHT

The Docked light is an LED indicator light that will light up to indicate when the device is correctly docked in the charger base docking pad. The LED will flash ON and OFF when correctly in place and turn off when removed from the charger base docking pad.

#4 CHARGER BASE CONNECTOR PORT

The Charger Base Connector Port is the location where the Power Supply Connector is plugged into for charging.

#5 POWER SUPPLY CONNECTOR

The Power Supply Connector plugs into the Inductive Charger Base Connector Port to provide power to charger base.

DEVICE LABELING

The Erchonia HLS Laser is manufactured in accordance to the Good Manufacturing Procedures consistent with national regulatory agencies; such as FDA, EU, HC, TGA, and Anvisa. Per ISO and FDA standards the device and laser are classified as Class II.

Each of these governing agencies requires specific labeling. All required labels are affixed according to the relevant codes, as shown in Figure 3 below.

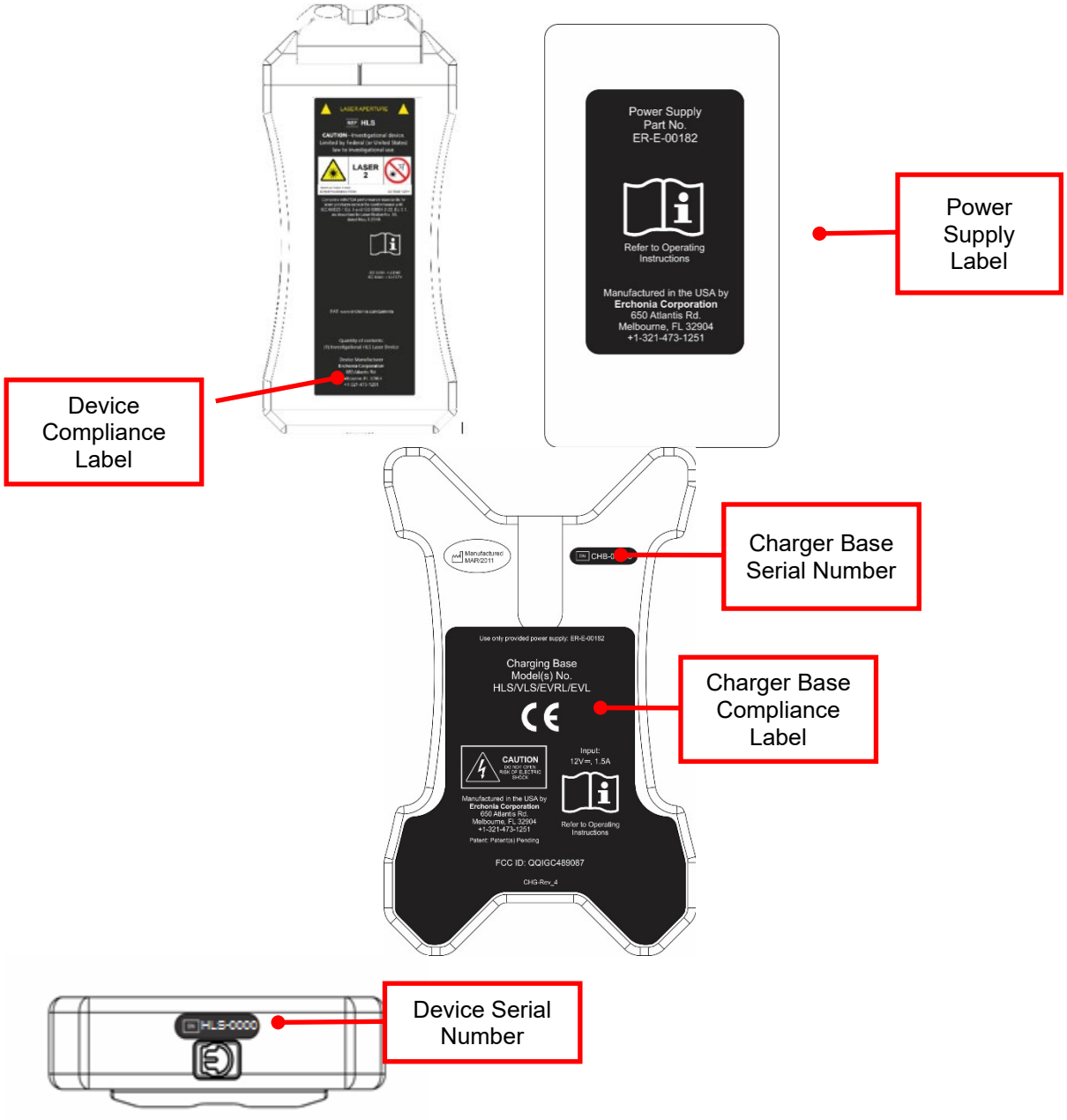


Figure 3: Erchonia HLS Laser **L**abeling

DEVICE SAFETY

RISK AND PREVENTION OF EYE INJURY

The Erchonia® HLS Laser Device 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 patient. 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 will be implemented for the subject receiving the laser procedure administrations.

Subject Safety Goggles

These safety glasses are KenTek Corporation KenTek KGOG Medium Goggles Filter#6101 light blue safety goggles. These safety goggles are completely enclosing of the eyes and surrounding area such that no light may permeate the sHLS to reach the eye. The KenTek KGOG Medium Goggles Filter#6101 has the following specifications:

- *Filter#6101 specifications:*
  - ✓ OD 2.30 @ 635nm
  - ✓ VLT 60%
  - ✓ 635D LB2
  - ✓ KTK CE 2056

- *Frame specifications*
  - ✓ Goggle fit-over with foam comfort pads and elastic strap
  - ✓ Curved lens
  - ✓ IdHLS for smaller faces and Rx lenses
  - ✓ *Size:* Medium Fit-Over
  - ✓ *Dimensions***:** Lens: Width 63mm, Height 40mm; Bridge: 18mm ; Inside Front: 153mm

The KenTek Corporation KenTek KGOG Medium Goggles safety goggles are shown in Figure 5 below.

Figure 5: KenTek Corporation KenTek KGOG Medium Goggles Safety Goggles

COMPLIANCE APPLICABLE CODES

The Erchonia HLS is compliant with the following applicable codes:

FDA
21CFR 820 – Quality System Regulations
21CFR 1040.10 and 1040.11 by laser Notice 50

ISO
13485 – Medical Device Quality
14971 – Risk Management

EMC 2004/108/EC
LVD 2006/95/EC
IEC 60601-1-2 EMC
IEC 60601-1- Safety
IEC 60825-1 – Laser Safety
CB Certified

FOOD AND DRUG ADMINISTRATION (FDA) DETERMINATION OF NON-SIGNIFICANT RISK (NSR) STATUS

(i) Regulatory Clearances**:** The Food and Drug Administration (FDA) has determined the family of Erchonia® low level laser 635 red diode devices to be non-significant risk (NSR) through numerous **510(k) clearances**, as follows.

1. **K180197:** *Erchonia® FX-635™ Laser*: is indicated for the following two indications:

   a. as an adjunct to provide relief of minor chronic low back pain of musculoskeletal origin.
   b. as an adjunct to reducing chronic heel pain arising from plantar fasciitis.

2. **K132940:** *Erchonia® Allay™:* is indicated as an adjunct to reducing chronic heel pain arising from plantar fasciitis.

3. **K072206:** *Erchonia® EML Laser:* is indicated for the temporary reduction in post-surgery pain at 24 hours after surgery following bilateral breast augmentation surgery.

4. **K050672:** *Erchonia® EVRL Laser*: The Erchonia EVRL Laser is generally indicated:

   a. while using the red diode, for adjunctive use in providing temporary relief of minor chronic neck and shoulder pain of musculoskeletal origin, and
   b. while using the blue diode, to treat dermatological conditions, and specifically indicated to treat moderate inflammatory Acne Vulgaris.

5. **K041139:** *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.

6. **K100509 & K130741:** *Erchonia® THL1 Laser & Erchonia® PL5000*: is indicated for adjunctive use in providing temporary relief of minor chronic neck and shoulder pain of musculoskeletal origin.

7. **K130996:** *Erchonia® XLR8™*: The Erchonia XLR8™ is indicated for the following three indications:

   a. adjunctive use in providing temporary relief of minor chronic neck and shoulder pain of musculoskeletal origin
   b. as an adjunct to liposuction procedures of the thighs, hips and stomach for reduction of pain associated with the recovery process
   c. temporary reduction in post-surgery pain at 24 hours after surgery following bilateral breast augmentation surgery

8. **K123237 & K133718:** *Erchonia® Zerona™ 2.0 Laser & Zerona®-Z6*: is indicated for use as a non-invasive dermatological aesthetic treatment as an adjunct for individuals intending to undergo liposuction procedures for the reduction of circumference of hips, waist, and thighs.

9. **K121695 & K082609:** *Erchonia® ML Scanner (MLS) & Erchonia® Zerona:* is indicated for use as a non-invasive dermatological aesthetic treatment as an adjunct for individuals intending to undergo liposuction procedures for the reduction of circumference of hips, waist, and thighs.

10. K21690 & K120257: *Erchonia® MLS, Zerona, Zerona-AD*: is indicated for use as a non-invasive dermatological aesthetic treatment as an adjunct for individuals intending to undergo liposuction procedures for the reduction of circumference of the upper arms.

11. K082609: *Erchonia® ML Scanner (MLS)*: is indicated for use as a non-invasive dermatological aesthetic treatment for the reduction of circumference of hips, waist and thighs.

(ii) Pre-IDE Reviews**:** FDA has previously reviewed numerous clinical study protocols employing various Erchonia® Corporation 635 nm red diode low level laser devices, including each of the clinical studies conducted in support of the above 510(k). For each of the FDA's pre-IDE reviews of Erchonia 635 nm red diode low level laser clinical study protocols, there was concurrence from FDA that the clinical study protocols and application of the Erchonia laser devices therein were considered non-significant risk (NSR).

INSTITUTIONAL REVIEW BOARD (IRB) DETERMINATION OF NON-SIGNIFICANT RISK (NSR) STATUS

Erchonia® Corporation 635 nm red diode low level laser devices have been determined to be non-significant risk (NSR) when applied in various clinical studies through several IRBs, as follows:

- Western Institutional Review Board (WIRB®) has previously determined Erchonia low level laser devices to be non-significant risk (NSR) when applied in the following clinical studies:

  1. **WIRB PRO NUM: 20131165:** Erchonia® ZERONA 6 Headed Scanner (EZ6): An evaluation of the effect of the Erchonia® ZERONA 6 Headed Scanner (EZ6) six-week treatment protocol on circumference reduction of the waist, hips, highs and upper abdomen clinical study

  2. **WIRB PRO NUM: 20130851:** Erchonia® ML Scanner (MLS): An evaluation of the effect of the Erchonia® ML Scanner (MLS) laser on increasing blood circulation in individuals with chronic heel pain clinical study

  3. **WIRB PRO NUM: 20130488:** Erchonia® TMJ laser: A pilot evaluation of the effect of the Erchonia® TMJ Laser on reducing jaw pain and improving jaw function for individuals with temporomandibular joint (TMJ) disorder

  4. **WIRB PRO NUM: 20121548:** Erchonia® MLS: A double-blind, placebo-controlled randomized evaluation of the effect of the Erchonia® ML Scanner (MLS) laser on reducing pain associated with degenerative arthritis (osteoarthritis) of the midfoot clinical study protocol

  5. **WIRB PRO NUM: 20120787:** Erchonia® MLS: A double-blind, placebo-controlled randomized evaluation of the effect of the Erchonia® ML Scanner (MLS) on low back pain clinical study protocol

  6. **WIRB PRO NUM: 20111793:** Erchonia® MLS: A double-blind, placebo-controlled randomized evaluation of the effect of the Erchonia® ML Scanner (MLS) laser on chronic heel pain clinical study protocol

  7. **WIRB PRO NUM: 20110331:** Erchonia® MLS: An evaluation of the effectiveness of the Erchonia® ML Scanner (MLS) as a non-invasive dermatological aesthetic treatment for the reduction of circumference of the upper arms clinical study protocol

8. **WIRB PRO NUM: 20120911:** Erchonia® MLS: A double-blind, placebo-controlled randomized evaluation of the effect of the Erchonia® ML Scanner (MLS) on body contouring of the waist, hips and thighs five-day treatment protocol clinical study protocol

9. **WIRB PRO NUM: 20110758**: Erchonia® MLS: A pilot evaluation of the effect of the Erchonia® ML Scanner (MLS) laser device on enhancing body weight loss, fat loss and circumference reduction of the waist, hips and thighs clinical study protocol

10. **WIRB PRO NUM: 20121330:** Erchonia LUNULA™**:** An Evaluation of the Effect of the Erchonia LUNULA™ on Treating Toenail Onychomycosis Clinical Study Protocol; Version 6.0 August 7, 2012

11. **WIRB PRO NUM: 20110461:** Erchonia FX-405™**:** An Evaluation of the Effect of the Erchonia FX-405™ on Treating Toenail Onychomycosis Clinical Study Protocol; Version 3.0 March 19, 2011

12. **WIRB PRO NUM: 20120489:** Erchonia® MLS: A double-blind, placebo-controlled randomized evaluation of the effect of the Erchonia® ML Scanner (MLS) on lipid panel levels clinical study protocol

OTHER POTENTIAL RISKS

Other potential risks and their mitigation include:

(i) Electric shock: operator risk only: mitigated through electrical safety testing.
(ii) Electromagnetic interference: mitigated through EMC/EMI testing.
(iii) User error: mitigated through instructions for use documentation.

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

STUDY INDICATION: TINNITUS

DEFINITION AND DESCRIPTION

The study indication to be evaluated in this study is the temporary relief of tinnitus symptoms.

Tinnitus involves hearing sound when no external sound is present. The type of noise may include one or more of ringing, buzzing, roaring, clicking or hissing. It may vary in pitch from a low roar to a high squeal and may be heard in one or both ears. Tinnitus may be present all the time, or it may come and go. If persistent and intolerable or sufficiently bothersome, tinnitus can cause functional impairment in thought processing, emotions, hearing, sleep, and concentration, all of which can substantially negatively affect quality of life.

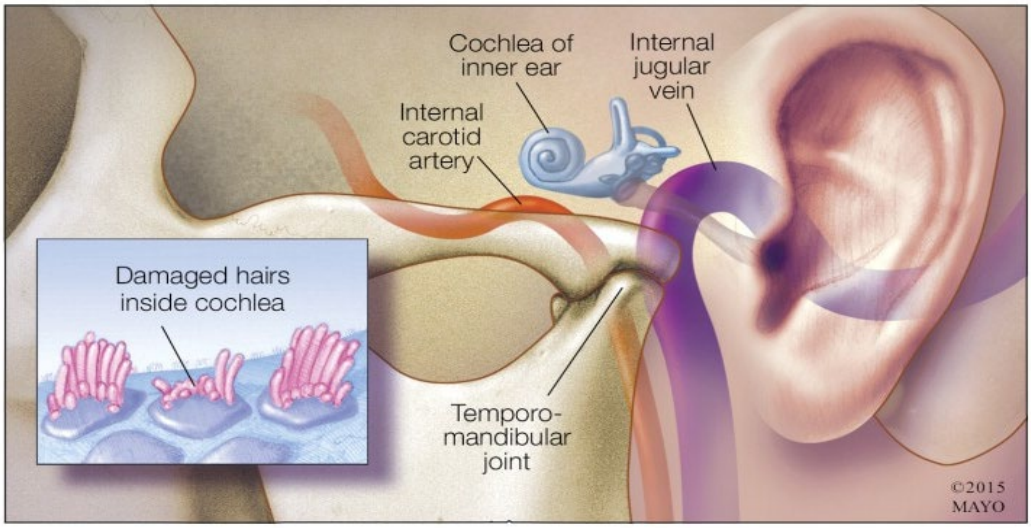
There are two types of tinnitus:

- *Subjective tinnitus* is tinnitus that is only heard by the affected individual. It is the most common type of tinnitus and can be caused by problems in the outer, middle or inner ear, or by damage to auditory nerves or pathways.
- *Objective tinnitus* is tinnitus that can be heard by both the affected individual and other people. It is much rarer than subjective tinnitus and may be caused by a blood vessel problem, a middle ear bone condition or muscle contractions.

This clinical study will focus on evaluation of subjective tinnitus only.

CAUSES AND ETIOLOGIES

Tinnitus is most commonly the result of damage to the cilia in the inner ear. Cilia are tiny hairs in the inner ear that move in response to the pressure of sound waves which subsequently triggers ear cells to release an electrical signal through the auditory nerve to the brain where the signals are interpreted as sound. Damage to the cilia can send random electrical impulses to the brain, causing tinnitus.



Damage to the cilia resulting in tinnitus is most commonly a result of one of the following:

- *Presbycusis: age-related hearing loss:* Presbycusis is commonly associated with aging, usually starting around age 60.
- *Exposure to loud noise:* Loud noises, constant or impact, such as those from heavy equipment, chain saws and firearms, are common sources of noise-related hearing loss. Tinnitus caused by short-term exposure, such as attending a loud concert, usually goes away; long-term exposure to loud sound can cause permanent damage.
- *Earwax blockage:* Earwax protects the ear canal by trapping dirt and slowing the growth of bacteria. Excessive earwax accumulation typically hardens and causes blockage of the ear canal, which can lead to hearing loss or irritation of the eardrum, which in turn can lead to tinnitus.
- *Otosclerosis:* Stiffening of the bones in the middle ear can affect hearing and cause tinnitus.

Other causes of tinnitus include hyperactivity (increased firing rate) and hyper-excitability in structures of the auditory system. Research has demonstrated that increased spontaneous neural firing rate and hyperexcitability in structures of the auditory nervous system can be caused by exposure to loud noise.

Less common causes of tinnitus include:

- *Meniere's disease:* an inner ear disorder that may be caused by abnormal inner ear fluid pressure. In addition to tinnitus, dizziness is a common symptom of Meniere's disease.
- *Temporomandibular Joint (TMJ) disorders*
- *Head or neck injuries:* can affect the inner ear, auditory nerves or auditory pathways and processing linked to hearing. Such injuries generally cause tinnitus in only one ear.
- *Acoustic neuroma:* a benign tumor that develops on the cranial nerve that runs from the brain to the inner ear and controls balance and hearing. This condition generally causes tinnitus in only one ear.
- *Blood vessel disorders:* Certain types of blood vessel disorders may on occasion cause pulsatile tinnitus, such as atherosclerosis, head and neck tumors, hypertension, turbulent blood flow and malformation of capillaries.

Medications that can cause or worsen tinnitus include certain antibiotics, cancer medications, diuretics, quinine medications, antidepressants and excessive aspirin use. Generally, the higher the medication dose, the worse the tinnitus. Often the tinnitus will stop when the medication use ceases.

RISK FACTORS

- Loud noise exposure
- Advanced age
- Male gender
- Smoking
- Cardiovascular problems

COMPLICATIONS

Tinnitus can significantly affect quality of life, and may elicit additional symptoms of:
- Fatigue
- Stress

- Sleep problems
- Trouble concentrating
- Memory problems
- Depression
- Anxiety and irritability

STATISTICS

About 10% of all adults in the U.S. report experiencing bothersome tinnitus.

Of tinnitus sufferers in the U.S. about:
- *40% report constant or near constant symptoms.*
- *27% report symptom duration exceeding 15 years.*
- *10% report their tinnitus as being a "big" or "very big" problem.*
- *30% report their tinnitus as interfering with sleep.*

The most commonly physician-prescribed treatments include medications (45.5%); hearing aids (9.2%), masking devices (4.9%), and cognitive-behavioral therapy (0.2%).

ASSESSMENT AND DIAGNOSIS

Assessment and diagnosis of tinnitus may include one or more of the following.

- *Case History:* including evaluation of existing available test results (e.g., lab work, cranial nerve assessment); patient description of tinnitus; medical history; medication use; work environment; history of noise exposure and trauma; other ear problems such as hearing loss and vertigo.
- *Audiologic Evaluation:* otologic and audiologic assessment, as applicable.
- *Tinnitus Pitch Matching:* comparing the pitch of the tinnitus to external tones of varying frequencies for tonal-sounding tinnitus.
- *Tinnitus Loudness Matching:* comparing an external tone or broadband noise to the patient's perception of the loudness level of their tinnitus.
- *Minimum Masking Level:* determining the level of broadband or narrowband noise required to mask or alleviate the tinnitus.
- *Evaluation for Presence of Residual Inhibition:* temporary result of tinnitus suppression wherein the effect lasts from a few seconds onwards after masking.
- *Subjective Patient Questionnaires:* to address different elements of tinnitus impact on severity, disability, functional impact, psychological factors, quality of life), etc.

TREATMENT AND MANAGEMENT OPTIONS

In general, there is no cure for tinnitus, unless it is associated with an underlying medical condition that can be rectified or medication whose use can be ceased. Tinnitus management may include one or more of the following options.

- *Treating an underlying health condition:* certain medical conditions may cause or exacerbate tinnitus. Treatment of such conditions, if existing, can help alleviate tinnitus; for example, removal of excessive ear wax, treatment of an underlying vascular condition, changes to medication use.

- *Noise Suppression/Sound Therapy:* Noise may help suppress the perception of tinnitus. Noise suppression options include:

- ✓ White Noise Machines/Sources producing simulated environmental sounds such as falling rain or ocean waves, or even fans, humidifiers, dehumidifiers and air conditioners may help alleviate tinnitus, particularly useful for tinnitus that is bothersome at night.
- ✓ Hearing Aids, where applicable, can alleviate tinnitus through amplification and/or masking effects.
- ✓ Wearable Masking Devices are worn in the ear similarly to hearing aids and produce a continuous, low-level white noise that suppresses tinnitus symptoms.
- ✓ Tinnitus retraining, involving use of a wearable device to deliver individually programmed tonal music to mask the specific frequencies of the patient's tinnitus, usually in combination with patient counseling.

- *Informational and Educational Counseling*
  - ✓ Cognitive behavioral therapy (CBT) is a specific form of therapy focusing on modification of problem emotions, thoughts, and behaviors. In patients with tinnitus, CBT can help reduce negative responses and improve quality of life.
  - ✓ Counseling can help with both learning coping techniques to lessen the perception of tinnitus and with management of other related problems such as anxiety and depression.
  - ✓ Support groups
  - ✓ Education Understanding tinnitus and means of alleviating symptoms can help.

- *Tinnitus-Specific Management Programs*
  - ✓ Tinnitus Retraining Therapy (TRT) is a habituation-based intervention that includes a combination of directive counseling and sound therapy customized to the specifics of the patient's tinnitus.
  - ✓ Progressive Tinnitus Management (PTM) focuses on teaching the patient to self-manage negative reactions to tinnitus.
  - ✓ Tinnitus Activities Treatment (TAT) is an intervention using individualized counseling focused on thoughts and emotions, hearing and communication, sleep, and concentration, as well as low-level partial masking sound therapy.

- *Alternative Therapies* include biofeedback training; hypnotherapy; acupuncture and myofascial trigger point therapy; neuromodulation; psychotherapy (e.g. mindfulness training and relaxation training); transcranial magnetic stimulation; vagus nerve stimulation; and herbal supplements such as ginkgo biloba, zinc supplements and B vitamins.

- *Medications:* There are no medications to specifically treat tinnitus, but certain medications may be prescribed to treat associated symptoms such as anxiety and depression, including tricyclic antidepressants (such as amitriptyline and nortriptyline); and alprazolam (Niravam, Xanax).

THEORY OF MECHANISM OF OPERATION OF APPLICATION OF LOW LEVEL LASER LIGHT (LLLT) USING THE ERCHONIA® HLS™ TO RELIEVE TINNITUS SYMPTOMS

The neurophysiological model of tinnitus proposes that tinnitus results from the abnormal processing of a signal generated in the auditory system that occurs before the signal is perceived centrally. This then results in 'feedback', whereby the annoyance created by the tinnitus causes the individual to focus increasingly on the noise, which in turn exacerbates the annoyance and so a vicious cycle develops. Therefore, in this model, tinnitus is hypothesized to result from continuous firing of cochlear fibers to the brain, from hyperactivity of cochlear hair cells or from permanent damage to these cells being translated neuronally into a 'phantom' sound-like signal that the brain perceives it is hearing.

Low level laser therapy (LLLT) induces a photochemical reaction in the cell, called biostimulation or photobiomodulation. It is an irradiation technique that can induce biological processes using photon energy. Most evidence of efficacy of LLLT is based on the increase in energy state and the activation of mitochondrial pathways. It has been reasonably well established that mitochondria are a principal intracellular target of red and near infrared light. Cytochrome C oxidase (unit IV of the mitochondrial respiratory chain) is a chromophore that absorbs infrared light up to 1000 nm.

Several hypotheses have been proposed for the mechanism of action of LLLT as applied to tinnitus. It is predominantly believed that the respiratory chain plays a central role in the effect induced by laser therapy. Laser energy in the red and near infrared light spectrum is capable of penetrating tissue to stimulate mitochondria in the cells to produce energy through the production of adenosine triphosphate (ATP). Mitochondria are the power supplies of all cells that metabolize fuel and produce energy for the cell in the form of ATP. LLLT irradiation has been demonstrated to increase the production of ATP. Increased ATP production is believed to enhance cell metabolism, promoting the damage recovery process, returning cells to a healthy state and reversing many degenerative conditions.

Regarding tinnitus, LLLT has been reported to alter the collagen organization within the cochlea, especially within the basilar membrane to increase the stiffness of the basilar membrane. Furthermore, LLLT has a beneficial effect on the recovery of damaged cochlear hair cells (cilia) through increasing cell proliferation; synthesis of ATP and collagen; releasing growth factors (including nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), glial cell line-derived neurotrophic factor (GDNF) and ciliary neurotrophic factor (CNTF); promoting local blood flow in the inner ear associated with suppression of the sympathetic nerve action potential; and activating repair mechanisms in the inner ear through photochemical stimulation of the hair cell mitochondria. LLLT leads to activation of related cortical areas in healthy subjects.

Additionally, studies have shown red laser plays a direct role on vagus nerve to recover parasympathetic/sympathetic nervous system balance. The descending fibers of the vagus nerve supply parasympathetic control to the heart and organs in the abdomen. The afferent vagus nerve fibers target cells in the nucleus of the solitary tract (NST), which send axons to many different parts of the brain. Of importance to the treatment of tinnitus is the fact that these axons can activate cells in the nucleus of Meynert and thereby facilitate plastic changes

SUPPORTING MATERALS

Treatment of Chronic Tinnitus with Low Level Laser Therapy
Int.J. PharmTech Res. 2016,9(3), pp 37-45
Rokaia A. M. Toson1, Mohamed M. Khalaf1, Ahmed M. A. Seleim2, Maha A. Hassan1

Tinnitus causes disability associated with concentration deficits, insomnia, hypersensitivity to sounds, anxiety and depression. Often a combination of several complaints leads to a diminished quality of life. The purpose of the study was to determine the effect of the Low-Level Laser Therapy (LLLT) in the treatment of chronic tinnitus. Sixty patients with chronic subjective tinnitus were included in this study and were randomly divided into two equal groups: (study group and control group). Study group received Low Level Laser Therapy, 3 times per week for 1 month while control group received placebo laser, 3 times per week for 1 month. The clinical findings of the patients were analyzed before and after the treatment via the Visual Analogue Scale (VAS) and Tinnitus Severity Index (TSI) Questionnaire. All sixty patients completed the study. There were no adverse effects observed. The Visual Analog Scale (VAS) score difference before and after the treatment was statistically significant ($p = 0.0001$). Also, statistical difference was found before and after the treatment in the Tinnitus Severity Index (TSI) Questionnaire score ($p = 0.0001$). In relation to the VAS and TSI Questionnaire scores, the study revealed that the results obtained in the study group were superior to that of control group. The present study for treatment of tinnitus resulted in subjective tinnitus improvement in55.55% in study group while only 11.75% in control group measured via the VAS. Comparison between groups post treatment revealed a significant decrease in VAS and TSI in study group compared to control group ($p < 0.05$). **It was concluded that Low Level Laser Therapy (LLLT) was considered an effective treatment modality for the treatment of chronic subjective tinnitus.**

Low level laser effect in treatment of patients with intractable tinnitus due to sensorineural hearing loss.
J Lasers Med Sci. 2014 Spring;5(2):71-4.
Mirvakili A[1], Mehrparvar A[2], Mostaghaci M[2], Mollasadeghi A[2], Mirvakili M[1], Baradaranfar M[1], Dadgarnia M[1], Davari M[1].

INTRODUCTION: Tinnitus is defined as a perception of sound without an external acoustic stimulus. Due to large number of causes and limited knowledge of its pathophysiology, tinnitus remains an obscure symptom.

METHODS: This was a cross-sectional study on 120 patients with tinnitus and sensorineural hearing loss who were randomly divided into two groups; one group received low-level laser and the second group used the same instrument but off, for 20 sessions of 20 minutes. A tinnitus handicap inventory (THI) and Visual Analog Scale (VAS) were used to evaluate the severity of patients' symptoms. Severity and frequency of tinnitus were also determined using Audiometric tests.

RESULTS: The average age of the 120 patients in the two groups of study were not statistically significantly different. **The mean difference of severity of tinnitus between the two groups was statistically significant at the end of the study and 3 months after completion of treatment**. The VAS and THI mean differences after the treatment were statistically significant between the two groups but not statistically significant after 3 months of completion the study.

CONCLUSION: Low level laser radiation is effective for short-term treatment of Tinnitus caused by sensorineural hearing loss and its impact may be reduced over the time.

Low-level laser therapy in patients with complaints of tinnitus: a clinical study.
ISRN Otolaryngol. 2012 Apr 9; 2012:132060.
Salahaldin AH[1], Abdulhadi K, Najjar N, Bener A.

OBJECTIVE: The objective of the study was to investigate the effectiveness of low-level laser therapy (LLLT) in treating patients who were suffering from long-term complaints of tinnitus with well-understood etiology and who were not responding to conventional therapy.

DESIGN: This is a prospective clinical study conducted during the period from May 2010 and February 2011.

SETTING: Audiology Clinic, Outpatient Department, Hamad General Hospital.

SUBJECTS AND METHODS: The study included 65 patients aged 15-76 years with chronic unilateral or bilateral tinnitus with a minimum duration of illness of one year. The investigation included 101 ears of 65 patients. A 5mW laser with a wavelength of 650 nm was applied transmeatally for 20 minutes once daily for 3 months. The study was based on a face-to-face interview with a designed questionnaire that recorded the diagnosis of patients, clinical evaluation and audiometric test results, and side effects of low-level laser therapy (LLLT) and scored their symptoms loudness on five-point scale every two weeks. A decrease of one scale point regarding the loudness duration and degree of annoyance of tinnitus was accepted to represent an improvement; at the same time, a pure tone audiometric test was carried out and the results recorded. In addition, a record of the side effect was taken.

RESULTS: Over half of the patients (56.9%) had some form of improvement in their tinnitus symptoms. Mild improvement was reported in 33.8% of patients, moderate improvement was reported in 16.9%, and full improvement was reported in 6.15%. Of the patients who reported dizzy spells as a symptom of their tinnitus condition, 27.7% reported mild improvement and 16.9% reported full improvement. Common side effects of LLLT were noted among 20% of patients; however, all of them were mild and disappeared within a few days.

CONCLUSION: **Low-level laser therapy was found to be useful for treatment of chronic tinnitus**.

Low-level laser for treatment of tinnitus: a self-controlled clinical trial.
J Res Med Sci. 2011 Jan;16(1):33-8.
Okhovat A[1], Berjis N, Okhovat H, Malekpour A, Abtahi H.

BACKGROUND: Despite the high prevalence and morbidity, tinnitus remains an obscure symptom. We assessed the efficacy of low-level laser for treatment of tinnitus.

METHODS: It was a self-controlled clinical trial study on 61 outpatients with subjective tinnitus. The patients were irradiated with a 650nm, 5mW soft laser for twenty days and twenty minutes per day. The sensation of tinnitus was measured on a Visual Analog Scale (VAS) before and two weeks after treatment, and they were compared by means of Wilcoxon signed rank test.

RESULTS: Thirty-eight (62.3%) patients were men and twenty-three (37.7%) were women. Fourteen patients (31.8%) worked in a noisy environment. The VAS mean difference before and after the treatment was statistically significant ($p < 0.0001$). The best treatment effect was in the youngest group and there were significant differences between this group and the middle age and older groups ($p = 0.018$ and 0.001, respectively). The mean VAS score reduction was not statistically significant between male and female patients ($p = 0.23$). Also, the treatment outcome according to the noise level in patient's workplaces was not significantly different in women ($p = 0.693$), but it was significant in men ($p = 0.029$).

CONCLUSIONS: **Transmeatal low-level laser irradiation is effective for the treatment of tinnitus** and some variables like age and job can affect the treatment outcome.

Effect of low-level laser therapy on cochlear hair cell recovery after gentamicin-induced ototoxicity.
Lasers Med Sci. 2011 Dec 4.
Rhee CK, et. Al.

There is increasing use of laser for the treatment of many hearing disorders, especially ringing in the ears, called tinnitus. The cochlear hair cells in the ear are the sensory receptors of the auditory system. It is well established that antibiotic drugs can damage hair cells and cause hearing loss. Although many studies have indicated a positive effect of laser therapy on neural cell survival, there has been no study on the effects of laser therapy on cochlear hair cells. This study clearly showed that the number of hair cells was significantly larger in the laser treated group. This is the first study in the literature that has demonstrated the beneficial effect of laser therapy on the recovery of cochlear hair cells and should help us understand how we can prevent some of the harmful side effects of antibiotic treatment.

Effectiveness of combined counseling and low-level laser stimulation in the treatment of disturbing chronic tinnitus.
Int Tinnitus J. 2008;14(2):175-80.
Cuda D[1], De Caria A.

We recruited 46 adult patients affected by disturbing tinnitus lasting for at least 3 years. All were treated with a combined counseling protocol constituting hypnotherapeutic and muscle relaxation techniques. We randomly assigned 26 patients to the group receiving low-level laser stimulation treatment and 20 to the placebo group. The laser power was 5 mV and the wavelength 650 nm. The irradiation lasted 20 minutes daily for 3 months. The Tinnitus Handicap Inventory (THI) questionnaire was submitted at the beginning and at the end of treatment. The THI scores improved in the entire sample after treatment but more significantly in the group receiving low-level laser stimulation. From the point of view of clinical classification, **approximately 61% of irradiated patients had tinnitus severity decreased by one class, in comparison to 35% of the placebo group.**

Laser irradiation of the guinea pig basilar membrane.
Lasers Surg Med. 2004;35(3):174-80.
Wenzel GI, Pikkula B, Choi CH, Anvari B, Oghalai JS.
Bobby R. Alford Department of Otorhinolaryngology & Communicative Sciences, Baylor College of Medicine, Houston, Texas 77030, USA.

BACKGROUND AND OBJECTIVES: The cochlea is the part of the inner ear that transduces sound waves into neural signals. The basilar membrane, a connective tissue sheet within the cochlea, is tonotopically tuned based on the spatial variation of its mass, stiffness, and damping. These biophysical properties are mainly defined by its constituent collagen fibers. We sought to assess the effect of laser irradiation on collagen within the basilar membrane using histological analysis.

STUDY DESIGN/ MATERIALS AND METHODS: Four excised guinea pig cochleae were stained with trypan blue. From these, two were irradiated with a 600 nm pulsed dye laser and two were used as controls. Collagen organization was visualized using polarization microscopy.

RESULTS: Laser irradiation reduced the birefringence within the basilar membrane as well as within other stained collagen-containing structures. Larger reductions in birefringence were measured when more laser pulses were given. The effects were similar across all turns of each cochlea.

CONCLUSIONS: **Laser irradiation causes immediate alterations in collagen organization within the cochlea that can be visualized with polarization microscopy. These alterations may affect cochlear tuning.** Ongoing research is aimed at analyzing the effect of laser irradiation on cochlear function. It is conceivable that this technique may have therapeutic benefits for patients with high-frequency sensorineural hearing loss.

Assessing The Autonomic Effect Of Vagal Nerve Stimulation With Low Level Lasers By Heart Rate Variability
Journal of Neurology. 21. 1-6. 10.5580/IJN.54164.

Machado, Calixto & Machado, Y & Chinchilla, Mauricio & Foyaca-Sibat, Humberto. (2019).
Vagus nerve stimulation (VNS) has been approved to treat refractory epilepsy, and for other conditions. The invasive nature of the electrical stimulus, which requires surgical implantation of electrodes around the cervical vagus nerve, is a technical limitation. The low-level laser therapy (LLLT) is actually considered a non-invasive technique, and has been increasingly used in diverse areas of medical practice. We developed a pilot study using LLLT for VNS in normal subjects, and assessing its effect on the autonomic nervous system (ANS) by the heart rate variability (HRV) methodology. Fifteen normal participants from 22 to 46 years, divided in three groups of 5 subjects each, paired in age and gender, were studied applying VNS using LLLT by lasers of different frequencies: RED Laser (in 5 subjects); VIOLET Laser (5 subjects); and RED/VIOLET Laser (5 subjects). The study included three experimental conditions: Basal record (10 minutes), VNS (10 minutes), and Post-VNS (10 minutes). The LF/HF ratio was considered, because it provides a measurement of the parasympathetic/sympathetic balance. When the RED laser was used for VNS there was a predominance of the parasympathetic activity. On the contrary, the stimulus with VIOLET laser provoked a sympathetic prevalence. Similarly, to the stimulus with the RED laser, when the RED/VIOLET laser was applied there was a predominance of the parasympathetic activity. **As a conclusion, this study showed that VNS using LLLT is a non-invasive and safe method, and should be considered for future protocols to recover parasympathetic/sympathetic nervous system balance in different conditions.**

Transmeatal cochlear laser (TCL) treatment of cochlear dysfunction: a feasibility study for chronic tinnitus.
Lasers Med Sci. 2003;18(3):154-61.
Tauber S, Schorn K, Beyer W, Baumgartner R.

Low-level-laser-therapy (LLLT) targeting the inner ear has been discussed as a therapeutic procedure for cochlear dysfunction such as chronic cochlear tinnitus or sensorineural hearing loss. Former studies demonstrate dose-dependent biological and physiological effects of LLLT such as enhanced recovery of peripheral nerve injuries, which could be of therapeutic interest in cochlear dysfunction. To date, in patients with chronic tinnitus mastoidal and transmeatal irradiation has been performed without systematic dosimetric assessment. However, light-dosimetric studies on human temporal bones demonstrated that controlled application of laser light to the human cochlea depends on defined radiator position within the external auditory meatus. This feasibility study first presents a laser application system enabling dose-controlled transmeatal cochlear laser-irradiation (TCL), as well as preliminary clinical results in patients with chronic cochlear tinnitus. The novel laser TCL-system, consisting of four diode lasers (lambda=635 nm-830 nm) and a new specific head-set applicator, was developed on the basis of dosimetric data from a former light-dosimetric study. In a preliminary clinical study, the TCL-system was applied to 35 patients with chronic tinnitus and sensorineural hearing loss. The chronic symptoms persisted after standard therapeutic procedures for at least six months, while retrocochlear or middle-ear pathologies have been ruled out. The patients were randomized and received five single diode laser treatments (lambda=635 nm, 7.8 mW cw, n=17 and lambda=830 nm, 20 mW cw, n=18) with a space irradiation of 4 J/cm2 site of maximal cochlear injury. For evaluation of laser-induced effects complete otolaryngologic examinations with audiometry, tinnitus masking and matching, and a tinnitus-self-assessment were performed before, during and after the laser-irradiation. **The first clinical use of the TCL-system has been well tolerated without side-effects and produced no observable damage to the external, middle or inner ear. Changes of tinnitus loudness and tinnitus matching have been described. After a follow-up period of six months tinnitus loudness was attenuated in 13 of 35 irradiated patients, while two of 35 patients reported their tinnitus as totally absent. Hearing threshold levels and middle ear function remained unchanged.** Further investigations by large double-blind placebo-controlled studies are mandatory for clinical evaluation of the presented TCL-system and its therapeutic effectiveness in acute and chronic cochlear dysfunction.

JUSTIFICATION FOR THE CURRENT CLINICAL STUDY

Tinnitus is a chronic problem affecting about one in every ten Americans. The persistent perception of sound is not only annoying and bothersome, but can affect multiple aspects of an individual's life, disrupting communication and sleep, and causing emotional and social disturbances such as anxiety and depression. At present, there is no cure for tinnitus and most treatment or management options are of limited short-term benefit restricted to the time of application. Low level laser therapy, such as through application of the Erchonia HLS™ Laser, has been shown through numerous prior trials and FDA clearances to effect positive change in numerous areas, including symptom perception arising from neurocognitive disruptions through its inflammatory reduction and neuromodulation properties. Therefore, it follows that application of Erchonia LLLT may help to alleviate the severity of tinnitus symptoms, providing a simple, non-invasive, safe, effective and side-effect free alternative therapy to reducing the severity of symptoms of tinnitus in affected individuals.

STUDY DESIGN

This pilot study is a non-blinded, two-group evaluation of the effect of the Erchonia® HLS™ on providing relief from the symptoms of tinnitus.

SUBJECT GROUPS

There will be two subject groups (Group A and Group B) in this pilot study. All subjects in both groups will be test subjects; that is, all study subjects will receive the active Erchonia® HLS laser device. The only difference between subject groups will be the anatomical area(s) where the Erchonia® HLS laser device is applied.

NON-BLINDED DESIGN

This pilot study will be non-blinded, such that both subjects and the investigator(s) will be aware that they are receiving the study procedures with active (true) Erchonia® HLS laser device.

NON-RANDOMIZED

As this pilot study wherein, all subjects receive the active procedure administrations, this is a non-randomized study design. The Investigator will assign 5 subjects to Group A and 5 subjects to Group B.

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 the symptoms of tinnitus, or from response to the following recruitment materials.

a) Flyer

WANTED

ADULTS WITH TINNITUS ONGOING OVER THE LAST 6 MONTHS FOR A CLINICAL STUDY OF THE EFFECTS OF LOW LEVEL LASER LIGHT ON REDUCING TINNITUS SYMPTOMS

THIS STUDY INVOLVES 8 WEEKS OF SELF-ADMINSTERED LASER LIGHT PROCEDURES WITH THE ERCHONIA® HLS™ LASER AT YOUR HOME

FOR MORE INFORMATION PLEASE CONTACT:

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

b) Newspaper Ad

Tinnitus Research Study

This study is to see if the Erchonia® HLS™, a non-invasive, investigational device that uses low-level laser light, can help to relieve tinnitus that has been ongoing for at least 6 months.

The study involves 8 weeks of self-administered at home treatments.

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

Compensation
A subject will not receive financial compensation for his or her participation in this clinical study.

A subject will not be charged for the cost of the study procedures with the Erchonia® HLS™ 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 10 qualified subjects enrolled in this pilot study, all receiving active procedures. 5 subjects will be assigned to Group A and 5 subjects to Group B.

STUDY PROCEDURE

STUDY TEST BATTERY

The following is a list and description of the study 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.

BASELINE VARIABLES

A. Tinnitus Variables

- Diagnosed etiology of tinnitus, if known. *Responses:* presbyacusis, noise-induced, unknown.
- Number of months/years since tinnitus onset.
- Location of tinnitus. *Responses*: unilateral - right ear, unilateral - left ear, bilateral - both ears, nonspecific (generally inside the head).

B. Medication and Treatment

- *Prior treatment approaches for tinnitus reduction:* Record all prior treatments, whether conventional or alternative, tried by the subject for tinnitus reduction.
- *Concomitant Medication and Therapy Use:* Record all over-the-counter and prescription medications currently used for any indication (other than the management of tinnitus symptoms)

***C. Subject Demographics*:** Subject age, gender and ethnicity are recorded.

OUTCOME ASSESSMENT TOOLS

PRIMARY OUTCOME MEASURE:

Tinnitus Handicap Inventory (THI)

The Tinnitus Handicap Inventory (THI) (Newman et al, 1996, Newman et al, 1998) is a 25-item self-report questionnaire that has Functional, Emotional and Catastrophic subscales. It has excellent convergent validity, construct validity and test-retest reliability. The THI takes 10 minutes to complete.

The individual responses to each of the 25 items are recorded as follows:

- ✓ Yes: 4
- ✓ Sometimes: 2
- ✓ No: 0

Individual scores for each question are added for the total THI score ranging from 0 to 100.

Another way of looking at the results of the THI is by Grade determination, as follows:

- *Grade 1 - slight - (THI 0-16)* – Tinnitus only heard in quiet environment, very easily masked. No interference with sleep or daily activities; generally pertains to individuals who are experiencing but are not troubled by tinnitus.
- *Grade 2 - mild - (THI 18-36)* – Tinnitus easily masked by environmental sounds and easily forgotten with activities. May occasionally interfere with sleep but not daily activities.

- *Grade 3 - moderate - (THI 38-56)* – Tinnitus may be noticed even in the presence of background or environmental noise although daily activities may still be performed. Less noticeable when concentrating. Not infrequently interferes with sleep and quiet activities.
- *Grade 4 - severe - (THI 58-76)* – Tinnitus almost always heard, rarely if ever masked. Leads to disturbed sleep pattern and can interfere with ability to carry out normal daily activities. Quiet activities adversely affected. Hearing loss is likely present, but its presence is not essential.
- *Grade 5 - catastrophic - (THI 78-100)* - All tinnitus symptoms at level of severe or worse. Should be documented evidence of medical consultation. Hearing loss is likely present, but its presence is not essential. Associated psychological pathology is likely to be found in hospital or general practitioner records. Given the epidemiological data, grading in this group should be extremely rare.

SECONDARY OUTCOME MEASURES:

Numerical Rating Scale (NRS)

The Numerical Rating Scale (NRS) will be used to capture the self-reported daily impact of Tinnitus Annoyance and Tinnitus Loudness. Zero represents 'no impact at all' whereas the upper limit represents 'the worst impact ever possible'.

NUMERICAL SCALE: TINNITUS ANNOYANCE

How does the subject rate his or her tinnitus annoyance on a scale of 1 to 100? With 1 being “No Annoyance” and 100 being “Worst possible Annoyance”.

TINNITUS ANNOYANCE SCORE: _____/100_

NUMERICAL SCALE: TINNITUS LOUDNESS

How does the subject rate his or her tinnitus loudness on a scale of 1 to 100? With 1 being “No Loudness” and 100 being “Worst possible Loudness”.

TINNITUS LOUDNESS SCORE: _____/100

Subject Satisfaction with Study Outcome

The subject is asked to rate how satisfied he or she is with any change in his or her overall tinnitus 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 your tinnitus following the study procedures with the study laser device?”

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

STUDY PROCEDURE PROTOCOL

PRE-PROCEDURE ACTIVITIES
Pre-procedure activities will be conducted remotely over videoconference or telemedicine.

STUDY QUALIFICATION

SIGNING OF INFORMED CONSENT FORM
The participant will be sent an electronic version of the Informed Consent Form. The PI will remotely video conference with the prospective research participant, presenting and reviewing in detail the items in the informed consent form with the individual and answering any questions he or she may have. When finished, the researcher and participant will electronically sign the consent form and print or download the signed document for archiving.

ASSIGNMENT OF SUBJECT IDENTIFICATION NUMBER
The subject is 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.

- Subjective tinnitus
- Tonal tinnitus.
- Constant tinnitus on-going at least half the time over at least the past 6 months.
- Willing to abstain from other tinnitus-related treatments except prior hearing aid use throughout the study duration.
- Willing and able to refrain from activities or work involving excessive noise exposure without the use of effective hearing protection throughout study participation.
- 18 years of age or older
- Primary language is English

EXCLUSION CRITERIA

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

- Objective tinnitus
- Atonal, pulsatile, intermittent, or occasional tinnitus
- Severe or profound hearing loss in one or both ears
- Current or prior surgically removed acoustic neuroma
- Consistent use of any of the following drugs known to cause or increase tinnitus (primarily ototoxins) within the past 30 days:
  - ✓ NSAIDS (motrin, naproxen, relafen, etc)
  - ✓ aspirin (exceeding 300mg per day) and other salicylates
  - ✓ Lasix and other "loop" diuretics
  - ✓ "mycin" antibiotics such as vancomycin
  - ✓ quinine and related drugs
  - ✓ Chemotherapy agents such as cis-platin
- Acute or chronic vertigo/dizziness
- Ménière's disease
- Prior stapendectomy
- Prior mastoidectomy
- Auditory nerve tumor (acoustic neuroma), current or surgically removed in the past
- Active infection/wound/external trauma to the areas to be treated with the laser
- Medical, physical or other contraindications for, or sensitivity to, light therapy
- Pregnant, breast feeding, or planning pregnancy prior to the end of study participation
- 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

INCLUSION CRITERIA PART 2

- Total THI score is **38 (Grade 3) or greater.**
- Numerical Rating Scale (NRS): Tinnitus Annoyance is **40 out of 100 or greater.**
- Numerical Rating Scale (NRS): Tinnitus Loudness is **40 out of 100 or greater.**

SUBJECT GROUP ASSIGNMENT

A fully qualified subject is assigned by the investigator to Procedure Group A or to Procedure Group B.

PRE-PROCEDURE EVALUATION PHASE

The pre-procedure evaluation phase commences following successful study qualification, on the same day or another day. During pre-procedure evaluation, the following is recorded over videoconference or telemedicine:

BASELINE VARIABLES

- Tinnitus Variables
- Medication and Treatment

- Subject Demographic

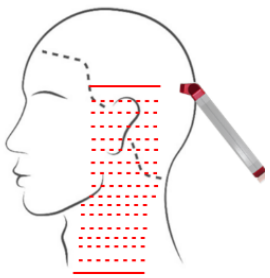
PROCEDURE ADMINISTRATION PHASE

The qualified subject will be shipped a Erchonia® HLS™ device, that is preset and cannot be altered by the end user. Additionally, the subject will be shipped Erchonia® HLS™ Operation Manual and Treatment Log Form that corresponds to the subject's assigned treatment group (A or B). The procedure administration phase lasts 8 weeks and comprises 56 procedure administrations with the Erchonia® HLS™ administered by the subject at home: daily procedure administrations for 8 weeks.

PROCEDURE ADMINISTRATION PROTOCOL

- The procedure administration phase of the study commences following completion of the pre-procedure phase, on the same day or up to 15 days later.
- The procedure administration phase extends over 8 consecutive weeks.
- Each subject receives 56 total procedures with the Erchonia® HLS™: daily procedure administrations for 8 weeks.
- Each procedure administration lasts 10 minutes.
- Each procedure administration is competed at the subject's home.
- Each subject will be provided an at home "Operation Manual" that details the laser use and treatment administration.
- Each subject will be provided at home "Treatment Log Forms" to document each time the treatment is administered.

- **Group A: Procedure administration protocol is as follows:**
  1. The subject is correctly fitted with the provided safety goggles.
  2. The Erchonia® HLS laser is held at approximately 4 inches from the skin throughout the entire treatment.
  3. The Erchonia® HLS™ is then activated for 5 minutes.
  4. The laser treatment begins approximately 1 inch above the right ear and applied in a slow continuous sweeping motion down the right side of the neck and then proceed back to top of ear. This back and forth sweeping motion is performed for 5 continuous minutes.



  5. Step 4 is then repeated over the left side of head and left side of neck. Both the right and left side will receive 5-minute treatment each.

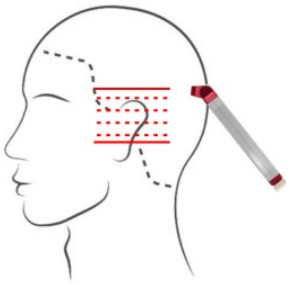
  6. The subject's protective eyewear is then removed, and the session is over.

- **<u>Group B:</u> Procedure administration protocol is as follows:**
  - This is an alternating treatment protocol, such as the subject will apply the laser treatment to the head on days 1 and 2, and on day 3 the laser is applied to the midsection. This 3-day rotation is followed throughout the 8 weeks and is detailed in the subjects "Treatment Log Forms".

1. The subject is correctly fitted with the provided safety goggles.
2. The Erchonia® HLS laser is held at a distance of approximately 4 inches from the skin throughout the entire treatment.
3. The Erchonia® HLS™ is then activated for 5 minutes.

Group B, Head Treatment is applied as follows:

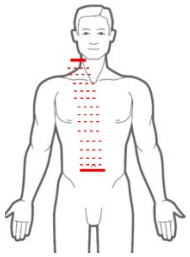
4. The laser treatment begins approximately 1 inch above the right ear and applied in a slow continuous sweeping motion down to the center of the ear and then proceed back to top of ear. This back and forth sweeping motion is performed for 5 continuous minutes.



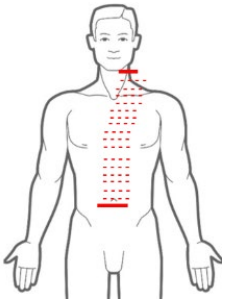
5. Step 4 is then repeated over the left side of head and ear. Both the right and left side will receive 5-minute treatment each.
6. The subject's protective eyewear is then removed, and the session is over.

Group B, Mid-Section Treatment is applied as follows:

7. The laser treatment begins above the umbilicus and applied in a slow continuous sweeping motion up the right side of the neck (vagus nerve) and then proceed back to umbilicus. This back and forth sweeping motion performed for 5 continuous minutes.



8. Step 4 is then repeated over the left side of midsection. Both the right and left side will receive 5-minute treatment each.



9. The subject's protective eyewear is then removed, and the session is over.

PROCEDURE ADMINISTRATION PHASE MEASURES

2 WEEK EVALUATION

Following 2 weeks of study procedure administrations with the Erchonia® HLS™, the following will be recorded over videoconference or telemedicine with the site investigator and subject:

- Numerical Rating Scale (NRS): Tinnitus Loudness
- Numerical Rating Scale (NRS): Tinnitus Annoyance
- Tinnitus Handicap Inventory (THI)
- Adverse Events Evaluation

4 WEEK EVALUATION

Following 4 weeks of study procedure administrations with the Erchonia® HLS™, the following will be recorded over videoconference or telemedicine with the site investigator and subject:

- Numerical Rating Scale (NRS): Tinnitus Loudness
- Numerical Rating Scale (NRS): Tinnitus Annoyance
- Tinnitus Handicap Inventory (THI)
- Adverse Events Evaluation

8 WEEK EVALUATION: STUDY ENDPOINT

Following 8 weeks of study procedure administrations with the Erchonia® HLS™, the following will be recorded over videoconference or telemedicine with the site investigator and subject as outlined in the STUDY TEST BATTERY section above. These recordings will form the study endpoint data set from which change from baseline will be evaluated with respect to assessing study outcome.

- Tinnitus Handicap Inventory (THI)
- Numerical Rating Scale (NRS): Tinnitus Loudness
- Numerical Rating Scale (NRS): Tinnitus Annoyance
- Subject Satisfaction With Study Outcome
- Adverse Events Evaluation

ADVERSE EVENTS

At any time throughout the duration of the clinical trial that is necessary, any and all potential adverse events reported by a subject will be reported to the investigator and 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® HLS™ include, but are not necessarily limited to: skin irritation, discoloring, rash, indentations and infection.

PRIVACY AND CONFIDENTIALITY

Records for each subject in this clinical study will be maintained in separate files in a locked filing cabinet at the respective test site. The investigator at the test site will be responsible for ensuring that all records for a subject pertaining to his or her participation in the clinical study are maintained in the subject's file at all times other than when information is being recorded on them.

Copies of all subject case report forms will be made and supplied to Regulatory Insight, Inc. and Erchonia Corporation. Regulatory Insight, Inc. and Erchonia Corporation will maintain these copies in a separate clinical study file that is kept in a locked filing cabinet on their respective premises. The original records will be maintained at the respective test sites.

Subjects' identities will be kept confidential by assigning each subject a subject ID upon acceptance into the study. The subject ID will comprise the investigator's two initials (first and last name initials) and a three-digit number that will be based upon the subject's order of entry into the clinical study. For example, with Principal Investigator John Black would have a subject ID of JB101-JB110. Neither the study Sponsor nor Regulatory Insight, Inc. will receive any additional identifying information about a subject and will therefore have no way of linking a subject ID to a particular subject and his or her results.

MONITORING OF THE CLINICAL STUDY

Prior to commencement of the study, the trained study Monitor(s) will provide formalized and documented training to the conduct of clinical studies in general, to the specifics of the current clinical study protocol, to the identification and reporting of adverse events and protocol deviations and to the correct set-up, operation and treatment application of the Erchonia® HLS to the study population for all study staff involved parties. A formalized Clinical Trial Monitoring Plan will be in place for real time, remote and on-site monitoring, as applicable, that will be strictly followed to ensure on-going compliance and accuracy of procedures at the test site(s).

STATISTICAL ANALYSIS

As this is an observational pilot study only, there are no pre-established primary or secondary outcome measures and no pre-established individual subject or study success criteria; rather it is the goal of this study to explore the potential benefits of low level laser therapy administration with the Erchonia HLS™ in reducing symptoms related to tinnitus, the results of which may be used to assist in developing a controlled clinical study to formally evaluate the study goal in the future.

Outcomes Evaluated
The following outcomes will be evaluated as recorded across study duration:

- Tinnitus Handicap Inventory (THI)
- Numerical Rating Scale (NRS): Tinnitus Loudness
- Numerical Rating Scale (NRS): Tinnitus Annoyance
- Satisfaction Rating

Co-Variate Evaluation
Consideration will be given to the role of demographic variables and procedure group assignment.

Evaluation Time Points
Evaluation time points are baseline (pre-treatment), two weeks, four weeks, and 8 weeks study endpoint.

Statistical Procedures
Outcome data will be presented descriptively and through trending. One-way ANCOVA analysis to evaluate the change in measurements across evaluation points may be applied, as applicable.

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: A pilot evaluation of the effect of the Erchonia HLS for the relief of tinnitus symptoms.

PROTOCOL NO.: R-EAR-PILOT
WIRB® Protocol #

SPONSOR: Erchonia Corporation

INVESTIGATOR: Kathleen L. Amos, AuD
205 Lennon Lane
Suite 201
Walnut Creek, California 94598
United States

STUDY-RELATED PHONE NUMBER(S): Kathleen L. Amos, AuD
(925) 954-8095 (24 hours)

This consent form is being sent to you electronically and may be discussed with family or friends before making your decision. This consent form may contain words that you do not understand. Please ask the study doctor or the study staff during the videoconference to explain any words or information that you do not clearly understand.

SUMMARY

You are being asked to be in a research study. The purpose of this consent form is to help you decide if you want to be in the research study. Please read this form carefully. To be in a research study you must give your informed consent. “Informed consent” includes:

- Reading this consent form,
- Having the study doctor or staff explain the research study to you,
- Asking questions about anything that is not clear.
- .

You should not join this research study until all of your questions are answered.

Things to know before deciding to take part in a research study:

- The main goal of a research study is to learn things to help patients in the future.
- The main goal of regular medical care is to help each patient.
- No one can promise that a research study will help you.
- Taking part in a research study is entirely voluntary. No one can make you take part.
- If you decide to take part, you can change your mind later on and withdraw from the research study.
- The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

- This study involves experimental (investigational) device procedures that are being tested for a certain condition or illness. An investigational device is one that has not been approved by the U.S. Food & Drug Administration (FDA).

After reading and discussing the information in this consent form you should know:

- Why this research study is being done;
- What will happen during the research;
- What device and procedures will be used;
- Any possible benefits to you;
- The possible risks to you;
- The other medical procedures, drugs or devices that could be used instead of being in this research study; and
- How problems will be treated during the study and after the study is over.

If you take part in this research study, you will be given a copy of this electronically signed and dated consent form.

PURPOSE OF THE STUDY

In this study, the Sponsor, Erchonia Corporation, and investigators are studying the use of a device called the Erchonia® HLS™ that gives off low level laser light. This study is to see if using the Erchonia® HLS™ can help to relieve the symptoms of tinnitus. The Erchonia® HLS™ is cleared for marketing by the U.S. Food and Drug Administration (FDA) to provide relief of minor chronic neck and shoulder pain of musculoskeletal origin. However, its use in this study is investigational, as the HLS™ has not been cleared for market by the FDA for relieving symptoms of tinnitus.

PROCEDURES

- If you agree to take part in this study, you will be one of about 10 people taking part.
- This is a test group only study. This means that if you choose to take part in this study, you will get the active (true) study treatments.

To take part in this study, you must agree to not try any other treatments to help with your tinnitus symptoms, until your part in the study is over. You may continue to wear hearing aids that you are already wearing.

- The study takes about two months to complete.
- The study process is as follows:

Screening

If you are interested in taking part in this research study, we will conduct a video conference screening in order to:

- Get information about your tinnitus and about treatments you may have tried to relieve your tinnitus symptoms.
- Get information about your other medical history, including information about other current medical conditions you may have and medications you may be taking.
- Ask you to complete a questionnaire about how your tinnitus impacts your everyday life.
- Ask you to rate how annoying your tinnitus is to you on a scale from 0 to 100, where ‘0’ means ‘not annoying at all’ and ‘100’ means ‘unbearably annoying.’

- Ask you to rate the how loud your tinnitus is to you on a scale from 0 to 100, where '0' means 'no tinnitus noise at all' and '100' means 'unbearably loud'.
- Get information about your age, gender and ethnicity.

The screening call lasts about 30 to 40 minutes.

At-Home Treatment Phase (8 Weeks)
The treatment phase will start once you have successfully completed the screening.

- You will be shipped a Erchonia HLS Laser and Operation manual.
- You will be responsible for self-administering the laser light treatments once daily over an 8 week period, for a total of 56 treatments.
- Each treatment session takes 10 minutes.
- Right after each treatment with the Erchonia® HLS™ laser, you will document the date of applied treatment in a provided treatment log form.
- You cannot try any other treatments to help with your tinnitus until your part in the study is over. You may continue to wear hearing aids that you are already wearing.

Treatment Evaluations(Week 2, Week 4 and Week 8)
The treatment Phase includes 3 required videoconference calls with a site investigator.

A video conference call will be scheduled at 2 and 4 weeks after starting the at-home treatment phase; during the video conference we will:

- Ask you to complete a questionnaire about how your tinnitus impacts your everyday life.
- Ask you to rate how annoying your tinnitus is to you on a scale from 0 to 100, where '0' means 'not annoying at all' and '100' means 'unbearably annoying.'
- Ask you to rate the how loud your tinnitus is to you on a scale from 0 to 100, where '0' means 'no tinnitus noise at all' and '100' means 'unbearably loud'.

The evaluation call takes about 15 to 20 minutes.

A final video conference call will be scheduled following the 8 weeks of at-home treatments; during this video conference call we will:

- Provide return shipping instructions for the Erchonia HLS Laser, and the completed at home treatment log.
- Ask you to complete a questionnaire about how your tinnitus impacts your everyday life.
- Ask you to rate how annoying your tinnitus is to you on a scale from 0 to 100, where '0' means 'not annoying at all' and '100' means 'unbearably annoying.'
- Ask you to rate the how loud your tinnitus is to you on a scale from 0 to 100, where '0' means 'no tinnitus noise at all' and '100' means 'unbearably loud'.
- Ask you to rate how satisfied you are with the outcome of the treatment administration with the Erchonia® HLS™ Laser on a five-point scale.

This evaluation visit takes about 15 to 20 minutes.

RISKS AND DISCOMFORTS
The complete risk profile or anticipated risks with the use of the Erchonia® HLS™ laser device is not known. However, there may be risks to using the device with this study procedure such as skin irritation, itching, discoloring, rash, indentations, pain/discomfort and infection.

It is possible that you will not get any improvement in your tinnitus symptoms or that they may even worsen.

Women who are pregnant or nursing a child may not take part in this study.

NEW INFORMATION
You will be told about any new information that might change your decision to be in this study. You may be asked to sign a new consent form if this occurs.

BENEFITS
Your tinnitus symptoms may lessen while you are in this study; however, this cannot be promised. The results of this study may help people to relieve tinnitus symptoms in the future.

COSTS
It will not cost you anything to be part of the study. Erchonia Corporation, the sponsor of this research will provide use of the Erchonia® HLS™ laser device to do the study treatment free of charge during this study. The cost for all study related procedures and measurements will also be covered by Erchonia Corporation. Nothing will be billed to you or to your insurance company.

PAYMENT FOR PARTICIPATION
You will not be paid for your part in this research study.

ALTERNATIVE TREATMENT
If you decide not to enter this study, there is other care available to you, such as treating an underlying health condition; noise suppression or sound therapy; informational and educational counseling; tinnitus-specific management programs; alternative therapies such as biofeedback training, hypnotherapy, acupuncture, myofascial trigger point therapy, neuromodulation, psychotherapy, transcranial magnetic stimulation, vagus nerve stimulation and herbal supplements; and medications to treat associated symptoms of tinnitus such as anxiety and depression. The study doctor will discuss these with you. You do not have to be in this study to be treated for your tinnitus.

COMPENSATION FOR INJURY
If you are injured or get sick from being in this study, call the study doctor immediately. The study doctor will provide emergency medical treatment. Your insurance will be billed for this treatment. The sponsor will pay any charges that your insurance does not cover. No other payment is routinely available from the study doctor or sponsor.

VOLUNTARY PARTICIPATION AND WITHDRAWAL
Your participation in this study is voluntary. You may decide not to participate, or you may leave the study, at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any of the following reasons:

- if it is in your best interest;
- you do not consent to continue in the study after being told of changes in the research that may affect you;
- or for any other reason.

SOURCE OF FUNDING FOR THE STUDY
The sponsor, Erchonia Corporation, will pay for this research study.

QUESTIONS
Contact Kathleen L. Amos, AuD at (925) 954-8095 (24 hours) for any of the following reasons:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study treatment, or
- if you have questions, concerns or complaints about the research

If you have questions about your rights as a research subject or if you have questions, concerns or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com.

WIRB is a group of people who independently review research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have gotten satisfactory answers.

If you agree to be in this study, you will receive a signed and dated copy of this consent form for your records.

CONSENT
I have read this consent form (or it has been read to me). All my questions about the study and my part in it have been answered. I freely consent to be in this research study.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

By signing this consent form, I have not given up any of my legal rights.

_____
Subject Name (printed)

CONSENT SIGNATURE:

Signature of Subject (18 years and older)	Date
Signature of Person Conducting Informed Consent Discussion	Date

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?

The study doctor will get your personal and medical information. For example:

- Research records
- Records about your study visits.

Who may use and give out information about you?

The study doctor and the study staff.

Who might get this information?

The sponsor of this research. "Sponsor" means any persons or companies that are:

- working for or with the sponsor, or
- owned by the sponsor.

Your information may be given to:

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- Institutional Review Board (IRB)
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to see if the research was done right.

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
This permission will be good until December 31, 2060.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
There is a risk that your information will be given to others without your permission.

_____
Subject Name (printed)

CONSENT SIGNATURE:

_____ _____
Signature of Subject (18 years and older) Date

_____ _____
Signature of Person Conducting Informed Consent Discussion Date