What is the Role of Lasers in Podiatric Practice?

The clinical impact of Lasers’ in day to day podiatric practice using an evidence based clinical review.

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Outline

• Overview of available Laser technology
• Overview of Lasers in Medicine
• Why we need to know the role and effect of Laser technology
• Common uses in the Podiatric Medicine practice. What is the current evidence?
  • Verrucae Pedis
  • Onychomycosis
  • Diabetic Ulceration/Neuropathic Pain
  • Soft Tissue Injuries
Mechanisms and effects of light-tissue interactions
Tissue responses to Laser energy

Thermal
• Most surgical lasers produce thermal effect at the tissue level. This includes the ability of the laser to cut, coagulate, vaporize, and ablate tissues.

Mechanical
• Mechanically disrupt tissues by producing sonic (acoustic) energy, like the breaking apart of kidney stones in the ureter.
  • Shock waves generated in the tissue by mechanisms such as bubble expansion/collapse or plasma formation. The mechanical properties of the tissue govern the propagation of these waves and their biological effect.

Chemical.
• Activating light-sensitive medications to disrupt and change tissue
  • If photon energy is high enough (UV, Excimer laser), direct bond-breaking is possible.
  • Alternatively, the molecule can be raised to an excited state generation of free radicals and reactive oxygen species.
Medical uses of Lasers

• Dermatology
  • Removal of skin tumours, external ulcers and warts. (*Photo-thermal, vaporization, photo-dynamic therapy*)
  • Treatment of port wine stain (naevi flammei), haemangioma. (*Photo-thermal, selective photo-thermolysis*)
  • Hair removal. (*Selective photo-thermolysis*)
  • Tattoo removal. (*Selective photo-thermolysis*)

• Orthopaedics
  • Cartilage and bone ablation. (*Photo-thermal*)

• Ophthalmology, Oncology, Neurosurgery, Angioplasty, Gastroenterology, Ear, Nose and Throat, Dentistry
Lasers commonly used in Dermatology

<table>
<thead>
<tr>
<th>Wavelength (nm)</th>
<th>Laser</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>308 (ultraviolet)</td>
<td>Excimer</td>
<td>Psoriasis, vitiligo, leukoderma</td>
</tr>
<tr>
<td>455; 514 (blue-green)</td>
<td>Argon (continuous)</td>
<td>Telangiectases, thick port wine stains in adults; epidermal pigmented lesions</td>
</tr>
<tr>
<td>504-690 (green-yellowish-red)</td>
<td>Argon-pumped tunable dye (continuous)</td>
<td>Telangiectases, thick port wine stains in adults; epidermal pigmented lesions; photodynamic therapy</td>
</tr>
<tr>
<td>510 (green)</td>
<td>Flashlamp-pumped dye (short-pulsed)</td>
<td>Epidermal pigmented lesions; red tattoos</td>
</tr>
<tr>
<td>511 (green)</td>
<td>Copper vapor / bromide (pseudo-continuous)</td>
<td>Epidermal pigmented lesions</td>
</tr>
<tr>
<td>521; 531 (green)</td>
<td>Krypton (continuous)</td>
<td>Epidermal pigmented lesions</td>
</tr>
<tr>
<td>532 (green)</td>
<td>KTP (pseudo-continuous)</td>
<td>Telangiectases, thick port wine stains in adults; epidermal pigmented lesions</td>
</tr>
<tr>
<td>532 (green)</td>
<td>KTP (long-pulsed)</td>
<td>Telangiectases, thick port wine stains in adults; epidermal pigmented lesions</td>
</tr>
<tr>
<td>532 (green)</td>
<td>Frequency doubled Q-switched Nd:YAG (pulsed)</td>
<td>Epidermal pigmented lesions; red tattoos</td>
</tr>
<tr>
<td>568 (yellow)</td>
<td>Krypton (continuous)</td>
<td>Telangiectases, thick port wine stains in adults</td>
</tr>
<tr>
<td>595-600 (yellow)</td>
<td>Flashlamp-pumped dye (long-pulsed)</td>
<td>Port wine stain, port wine stain in children, telangiectases, warts, hypertrophic scars, striae</td>
</tr>
<tr>
<td>694 (red)</td>
<td>Q-switched ruby (pulsed)</td>
<td>Epidermal and dermal pigmented lesions; blue, black and green tattoos</td>
</tr>
<tr>
<td>755 (infrared)</td>
<td>Q-switched alexandrite (pulsed)</td>
<td>Epidermal and dermal pigmented lesions; blue, black and green tattoos</td>
</tr>
<tr>
<td>755 (infrared)</td>
<td>Alexandrite (long-pulsed)</td>
<td>Hair removal</td>
</tr>
<tr>
<td>810 (infrared)</td>
<td>Diode (long pulsed)</td>
<td>Hair removal</td>
</tr>
<tr>
<td>980 (infrared)</td>
<td>Diode (continuous; pulsed)</td>
<td>Vascular lesions; telangiectasia</td>
</tr>
</tbody>
</table>

ANSI Z136.3-2005, American National Standard for the Safe Use of Lasers in Health Care Facilities
Low-level Laser therapy (class III laser)

High-power Laser therapy (class IV therapeutic laser)

(AKA: LLLT, LILT, Cold laser, Soft Laser)

- **Low energy laser therapy** uses irradiation intensities that induce minimal temperature elevation (not more than 0.1 to 0.5°C), if any.
- Optimum energy density low compared to other forms of laser therapy like ablation, cutting, and thermally coagulating tissue
- **LLLT Power densities** lower than those needed to produce heating of tissue, (less than 100 mW/cm², depending on wavelength and tissue type.)
- **High-power lasers (Class IV therapeutic lasers);** (not class IV surgical lasers) power output of up to 7,500 mW;
  - More power = deeper penetration (up to 10 cm instead of 0.5 to 2.0 cm for class III lasers)
  - Larger surface treatment area (cover up to 77 cm² instead of 0.3 to 5.0 cm² for class III lasers).
Lasers in Podiatric Medicine

- Surgical and LLLT Lasers are not new to Podiatric Medicine
- CO2
- Diode
- Nd:Yag
- Low-level laser (or light) therapy (LLLT), "bio-stimulation" or "photo-biomodulation" is practiced as part of physical therapies in many parts of the world.
- Recent FDA and Health Canada clearance 1064nm Nd:YAG laser for “temporary increase of clear nail in patients with onychomycosis” **Controversial
Why do we need to know the role and effect of Laser technology?

• Ethical, and medico-legal considerations require an evidence based and defensible position when providing any intervention on patients.**

• Reimbursement –
  • 3rd party insurance providers deem many Laser interventions experimental and because there is inadequate evidence.**
  • **This may be the case for many Podiatric intervention's!
"There are three kinds of falsehoods: lies, damned lies, and statistics."

This well-known saying is part of a phrase often attributed to Benjamin Disraeli and popularized in the U.S. by Mark Twain:
• "Aw, people can come up with statistics to prove anything, Kent. Forty percent of all people know that!"
   -----Homer Simpson, The Simpsons ("Homer the Vigilante")

• “People use statistics the way a drunk uses a lamp post — for support, not illumination."
   ---- Baseball announcer Vin Scully

• During World War I, helmets were almost withdrawn from British soldiers.
  • Generals called for their removal as they increased incidences of head wounds twelvefold and doubled total casualties.
  • The reason? If someone gets hit in the head by some shrapnel and lives it's a "head wound" and if they are unable to fight, the person is a "casualty"; if they die from a bullet in the brain, then they are a "fatality" and so don't appear on casualty statistics. Since helmets let more people survive, the number of head wounds soared
  • The real justification "A dead soldier needs a funeral." A wounded soldier gets dragged out of combat by at least one of his buddies, and then provided weeks, months or even years of medical attention.

• Cyclists being treated for head wounds have increased massively since wearing a helmet became more widespread.
  • Of course this is because they previously wouldn't have survived the accident at all.
Verrucae Pedis
• **CO2 lasers** emit infrared light (10,600 nm) absorbed by water.
  - Nonselective thermal tissue destruction.
  - A focused CO2 laser used as a scalpel to excise the wart down to the subcutaneous tissue after which the base of the wart is vaporized by a defocused beam until a clean surgical field.

• **Er:YAG laser** emits a shorter wavelength infrared radiation (2940 nm) that is absorbed 12 to 18 times more efficiently by water-containing superficial cutaneous tissues than the CO2 laser.
  - Laser has a smaller zone of thermal damage, allowing more precise thermal ablation with minimal scarring.

• **Nd:YAG** laser’s principal emission wavelength is at 1064 nm, still in the infrared range.
  - Hyper-thermic treatment with this laser has been reported to cause remission with no recurrence.

• **Pulsed Dye Laser** is through yellow light absorption (585 nm)
  • Selective microvascular destruction of dilated capillaries in the warts from thermal damage occurring upon by oxyhemoglobin. Removal of the blood supply, cell-mediated immune response contribute to wart healing

• **Potassium-Titanyl-Phosphate (KTP) Laser** KTP crystal doubles the frequency of pulsed (Nd:YAG) laser energy to a 532 nm wavelength, which is in the green electromagnetic spectrum (Greenlight-laser)
  • Selectively absorbed by hemoglobin not by water. Utilized in the treatment of recalcitrant cutaneous warts

• **Photodynamic Therapy** Does NOT use endogenous target absorbers
  • Uses light of a wavelength absorbed by specific photosensitizing molecules that are exogenously administered to the target tissue
  • i.e. 5-aminolaevulinic acid (ALA), a prodrug stimulates porphyrin accumulation in the tissue. Porphyrins then act as the photosensitizing agent.
CO2

Nd:YAG
Guidelines for cutaneous warts 2014, British Association of Dermatologists: J.C. Sterling et al

- Treatment protocols (pulse width, fluence, spot size, number of pulses and duration of treatment) vary between studies, making efficacy difficult to evaluate.


- PDL
  - Most warts are pared down before PDL to facilitate absorption of the laser energy.
  - Pre-treatment with SA 30% for 5 days, followed by PDL, led to faster complete clearance
  - 93% clearance
  - 2-5 treatments
  - Complications: Local pain (Generally not severe enough to warrant treatment cessation), haemorrhagic bullae, pigmentary change and scarring.
  - Pulsed dye laser can be considered for treatment of recalcitrant warts, although the effectiveness is unproven.

Reviewing the Literature
• **Pulsed dye laser versus Nd:YAG laser in the treatment of plantar warts: a comparative study**
  Abd El-Shakor et al Lasers in Medical Science May 2014, Volume 29, Issue 3, pp 1111-1116

• Compared pulsed dye laser (PDL) and neodymium yttrium aluminum garnet (Nd:YAG) lasers in the treatment of recalcitrant plantar warts.
  - 46 patients multiple plantar warts. Lesions in each patient, divided into 2 groups: one treated with Nd:YAG (spot size, 7 mm; energy, 100 J/cm²; and pulse duration, 20 ms) the other with PDL (spot size, 7 mm; energy, 8 J/cm²; and pulse duration, 0.5 ms).
  - Applied bi weekly maximum 6 sessions.
  - Cure rate PDL 73.9 % vs. Nd:YAG (78.3 %). Number of sessions PDL (mean, 5.05 ± 0.2) vs. Nd:YAG (mean, 4.65 ± 0.5) NO significant difference.
  - Complications: Hematoma. Relapse 8.7 % Nd:YAG vs. 13 % PDL NO significant difference (p = 0.74).

• Results suggest PDL and Nd:YAG lasers effective in treatment of resistant plantar warts. PDL is safer and less painful but needs more sessions, while Nd:YAG is more painful and shows more complications.
- Guidelines for cutaneous warts 2014, British Association of Dermatologists: J.C. Sterling et al

- CO2 laser, neodymium-doped yttrium aluminium garnet (Nd:YAG), Er:YAG, infrared and potassium titanyl phosphate laser
  - Small number of cohort studies.
  - 5 mm; pulse duration, 20 msec; and fluence, 200 J/cm². NO concomitant topical treatment used
  - Clearance rate 96%
  - Clearance rate of deep palmopantar warts after the first treatment was low (44.1%)
  - Recurrence rate, 3.27%
  - Concluded, long-pulsed Nd:YAG laser is safe and effective for the removal or reduction of warts and is less dependent on patient compliance than are other treatment options.
• **Guidelines for cutaneous warts 2014, British Association of Dermatologists; J.C. Sterling et al**

• **Photo Dynamic Therapy**
  - Difficult to compare efficacy rates in published papers due to variation in regimens,
  - Duration of application of topical photosensitizers,
  - Type of light source used,
  - Fluorescence and the number of treatments.
  - Many studies prepare warts before treatment, with curettage, blunt scraping, scalpel or keratolytic cream to enhance penetration.

• Cohort studies show clearance rates of warts between 58% and 95%.

• PDT can be used in combination with laser;
  - 12 patients with periungual warts treated with CO2 fractional laser followed by methyl-5-aminolaevuninic acid (MAL)-90% of treated warts clearing completely with no recurrence in 6 months.
  - 19 patients with hand and foot warts treated with MAL-PDT plus a PDL light source, cleared 53% of treated warts; hand warts cleared more effectively than plantar warts.
Sample Nd:YAG Laser Settings

- 100-200 Joules/cm²
- 6-20 milliseconds pulse width
- 5-7 mm spot size
- Do not treat tissue beyond wart border, to avoid damage to healthy tissue
- Give one single pulse, assess result; give additional pulse(s) only if needed
- May cause haematoma / ulcer
- May require 2+ treatments
- Wart should change color and fall off within a few weeks
Other things to consider!

• Are you following CPG /Cochrane Reviews? (Cryo./Sal Acid)
• Warts are very vascular, so laser parameters are set to target the blood vessels that feed the wart
• Debride hyperkeratotic tissue prior to laser treatment by planing the wart as thinly as possible but try to avoid bleeding
• Scarring, Hyper/Hypo pigmentation
• May use local anesthesia if necessary for patient tolerance BUT high post complications
• May cause haematoma (esp. - NdYAG)
• Salicylic Acid pre PDL = less treatments
• Laser plume viable HPV particles
Onychomycosis
Laser treatment of Onychomycosis infections

Why?

• Onychomycosis common problem, significant impact on quality of life.
• Oral terbinafine therapy cure rate as high as 46%, still the most effective, proven, long-term treatment for onychomycosis in patients without contraindications
• Current oral treatments, unacceptable side effect profiles, contraindicated in some patient populations
• Lasers have quickly risen to be considered among viable treatments for onychomycosis
  • Premarket Section 5–510(k) Summaries submitted to the FDA, approval of each device has been sought for the limited indication of “temporary increase in clear nail”
• Possible selective photo-thermolysis?

• Laser therapy is intended to exploit the differences in laser energy absorption and thermal conductivity between the fungal infection and the surrounding tissue. The absorption of light energy by the fungi results in the conversion of the energy into heat or mechanical energy.

• Exact mechanism of laser therapy under investigation, may combine direct fungicidal effects of the laser with induced modifications in the immune system or changes in the local microenvironment. Gupta, Skin Therapy Letter. 2012;17(9)

• Laser therapy for onychomycosis is currently being studied in vitro and in vivo.
• Lasers and PDT
  • Administered locally,
  • Avoid systemic side effects. Aside from minimal pain during administration
  • Well tolerated

• Scarcity of QUALITY peer-reviewed literature
• Laser device previously acquired for prior indications,
  • eager to discover additional innovative applications
• Financial incentives may also have a role in widespread adoption
‘The evidence pertaining to the effectiveness of laser treatment of onychomycosis is limited, and of poor methodological quality. Future studies using a randomised controlled trial designs with larger study populations and clear procedures are required to permit a full evaluation of this emerging technology’.

Bristow IR. *J Foot Ankle Res.* 2014 Jul 27;7
<table>
<thead>
<tr>
<th>Laser System</th>
<th>Type of Laser</th>
<th>Wavelength (nm)</th>
<th>Energy Fluence (J/cm²)</th>
<th>Spot Size (mm)</th>
<th>Pulse Length</th>
<th>Pulse Frequency (Hz)</th>
<th>International Approvals for Onychomycosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dualis SP™, Fotona</td>
<td>Long pulse Nd:YAG</td>
<td>1064</td>
<td>35–40</td>
<td>4</td>
<td>35 ms</td>
<td>1</td>
<td>EU</td>
</tr>
<tr>
<td>PinPointe™ FootLaser™, Nuvolase</td>
<td>Short pulse Nd:YAG</td>
<td>1064</td>
<td>25.5</td>
<td>2.5</td>
<td>100–3000 μs</td>
<td>1</td>
<td>US, Canada, EU, Australia</td>
</tr>
<tr>
<td>GenesisPlus™, Cutera</td>
<td>Short pulse Nd:YAG</td>
<td>1064</td>
<td>16</td>
<td>5</td>
<td>300 μs</td>
<td>2</td>
<td>US, Canada, EU</td>
</tr>
<tr>
<td>VARIA™, CoolTouch</td>
<td>Short pulse Nd:YAG</td>
<td>1064</td>
<td>-</td>
<td>-</td>
<td>600 μs</td>
<td>-</td>
<td>US, EU</td>
</tr>
<tr>
<td>LightPod® Neo™, Aerolase</td>
<td>Short pulse Nd:YAG</td>
<td>1064</td>
<td>223</td>
<td>2</td>
<td>650 μs</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>JOULE ClearSense™, Sciton</td>
<td>Short pulse Nd:YAG</td>
<td>1064</td>
<td>13</td>
<td>-</td>
<td>0.3–200 ms</td>
<td>6</td>
<td>US</td>
</tr>
<tr>
<td>CoolTouch CT3 Plus™, CoolTouch</td>
<td>Short pulse Nd:YAG</td>
<td>1320</td>
<td>-</td>
<td>2–10</td>
<td>450 μs</td>
<td>-</td>
<td>EU</td>
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<tr>
<td>Mira® 900, Coherent Laser Group</td>
<td>Modelocked Ti:Sapphire</td>
<td>800</td>
<td>$10^{32}$ to $10^{33}$ m² s⁻¹</td>
<td>0.12–0.45</td>
<td>200 fs</td>
<td>76 MHz</td>
<td>-</td>
</tr>
<tr>
<td>Noveon®, Nomir Medical Technologies</td>
<td>Diode</td>
<td>870, 930</td>
<td>212/424</td>
<td>15</td>
<td>-</td>
<td>-</td>
<td>EU</td>
</tr>
<tr>
<td>V-Raser®, ConBio/Cynosure</td>
<td>Diode</td>
<td>980</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Reviewing the Literature

Studies on laser treatment effectiveness in onycomycosis

in vitro

Vural et al.
Manevitch et al.
Aguilar et al.
Bornstein et al.

in vivo

Harris et al.
Manevitch et al.
Aguilar et al.
Kozarev et Vizintin
Hochmanet al.
Landsman et al.
Weiss
## In vitro studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment Description</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vural et al.</td>
<td>Q-switched Nd:YAG laser 532 nm and 1064 nm wavelengths</td>
<td>Inhibition of fungal colony growth</td>
</tr>
<tr>
<td>Manevitch et al.</td>
<td>Femtosecond infrared titanium sapphire, 800 nm</td>
<td>Complete clearance of T.rubrum infected nail clippings</td>
</tr>
<tr>
<td>Aguilar et al.</td>
<td>Q-switched Nd:YAG laser, 1320 nm by vacuum and thermal shock</td>
<td>Inhibition of T. rubrum colony growth</td>
</tr>
<tr>
<td>Bornstein et al.</td>
<td>Diode, 870/930 nm 4074 – 4500 J/cm²</td>
<td>Complete clearance of T. rubrum and C.albicans</td>
</tr>
</tbody>
</table>

• Evaluated a sub-millisecond Nd:YAG 1,064 nm laser for treating onychomycoses of the toenail.
  • Thirteen subjects (9 female, 4 male) with 37 affected toenails received 1 to 3 treatments 4 and/or 8 weeks apart with a sub-millisecond 1,064 nm Nd:YAG laser.
  • Diagnosis confirmed with microscopy.
  • Average follow-up time was 16 weeks post-final treatment
  • Treatments well tolerated, no adverse events.
  • (81%) had "moderate" to "complete" clearance average of 16 weeks post-final treatment.
  • (51%) were completely clear and all tested negative for fungal infection on direct microscopic analysis
  • (19%) toenails had significant clearance
  • (11%) had moderate clearance

• Results show this treatment modality is safe and effective for the treatment of onychomycosis in the short term. Additional studies are needed to more fully assess the clinical and mycological benefits as well as optimize the treatment protocol and parameters.
Laser used:
1. COOLTOUCH

- Nd:YAG Q switched laser
- 1064 or 1320 nm wavelength
- 6-350 microsec
- 4mm beam diameter
- Fluence 4 J/cm²
- 50 ms pulse envelope

<table>
<thead>
<tr>
<th>Study</th>
<th>In vitro Bornstein et al.</th>
<th>In vivo Landsman et al.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laser system</td>
<td>Noveon, diode, 870/930 nm</td>
<td>Noveon, diode, 870/930 nm</td>
</tr>
<tr>
<td>Power output (W)</td>
<td>11.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Energy fluence (J/cm²)</td>
<td>4500 Over 720 sec</td>
<td>204 + 424 Over 120 + 240 sec</td>
</tr>
<tr>
<td>Total energy used in protocol</td>
<td>7920 J</td>
<td>360 + 750 J</td>
</tr>
<tr>
<td>Outcome</td>
<td>100% Clearance</td>
<td>38% negative cultures after 3 x 6 min Tx</td>
</tr>
</tbody>
</table>

Fotona Dualis Laser Specifications

The 1064 nm Nd:YAG laser was used with:
- 35-45 J/cm² of fluence
- 30-35 msec of pulse duration
- 4 mm of spot size
- 1 Hz of frequency

CONCLUSION:
Effective but...
Study lacks control group, (N=72)

FAILURE TO REPRODUCE RESULTS

- Same methodology and protocol
- Only 37.14% (N=35) negative cultures after 3 months

- Possible causes:
  - 30% of patients had *Scytalidium diminutum* infection
  - 14.3% of patients had dimished peripheral circulation
  - Subungual hyperkeratosis


Wantphalideedscha R. The Efficacy and Safety of 1064 nm Nd:YAG Laser in the Treatment of Onychomycosis – Thai Experiences

www.Fotona.com
GenesisPlus (Cutera) Laser Specifications

The 1064 nm Nd:YAG laser was used with:
- 16 J/cm² fluence
- 0.3 msec of pulse duration
- 5 mm of spot size
- 2 Hz of frequency

Goal for effective treatment is to heat and hold tissue temperature at 43°-46° as indicated by yellow LEDs.

Use 700-800 pulses / 5 toes.

U. Kimura et al. study

The 1064 nm Nd:YAG laser was used with:
- 14 J/cm² fluence
- 0.3 msec of pulse duration
- 5 mm of spot size
- 5 Hz of frequency

CONCLUSION:
Very similar design to previous study
51% of microscopically negative samples
Study lacks control group, (N=13)


GenesisPlus (Cutera) Laser Specifications

The 1064 nm Nd:YAG laser was used with:
- 16 J/cm² fluence
- 0.3 msec of pulse duration
- 5 mm of spot size
- 2 Hz of frequency

CONCLUSION:
70% of improvement in nail condition
Study lacks control group, (N=7)
No cultures post Tx

Weiss D. 3 Month Clinical Results using Sub-millisecond 1064 nm Nd: YAG Laser for the Treatment of Onychomycosis.
OCT
(optical coherence tomography) may be useful in effectiveness studies

OCT: nail fungus

The Nail in OCT

Hematoma

Courtesy PD Dr Messmer, Munich, Germany

Courtesy PD Dr Messmer, Munich, Germany
Conclusions

• Sufficiently powered randomized control trials compared to previously existing therapeutic options are needed before lasers are deemed a standard of onychomycosis treatment.
  • Lack of placebo or standard of care control groups,
  • Limited enrollments
  • Different thresholds for significant clearance of debris from the nail,
  • Head-to-head comparisons between different laser devices -which device is optimum for the various types of onychomycosis and etiologic fungi
  • Insufficiently interrogated safety profiles, hindering a meaningful conclusion of clinical benefit compared to previously existing options.
• Evidence to date has not indicated superior outcomes in long-term end points to standard of care systemic therapy
• Anti-fungal mechanisms remain unverified.
• Difficulty evaluating any therapy for onychomycosis is, distinguishing between reinfection and treatment failure.

• Optimal window for follow up to establish complete clinical and mycologic clearance has not been established.

• Growth rate of toenails suggests testing at 18 months would be reasonable because the nail should have completely grown out by that time.

• Laser therapy may prove to be more attractive than PDT (No lengthy pre-treatment regimens.)

• Decline in clearance rate between 12 and 18 months = PDT does not result in a complete cure. (Slow growth T. rubrum or selective uptake and

• Optimal PDT protocol may yet be undiscovered.


Review Laser Therapy for Onychomycosis: Fact or Fiction? J. Fungi 2015, 1, 44-54. L Liddell , T Rosen
• **Perhaps it is more appropriate to approach onychomycosis as a chronic disease necessitating regular episodes of therapy to prevent**

• Factors such as repetitive nail trauma, dystrophic nails, poor nail hygiene, and diabetes predispose patients to multiple episodes of infection

• Patients more susceptible to reinfection because of dystrophic nails or for other reasons, rather than a discrete episode of infection that can be cured outright.
Lasers & Onychomycosis: What's Next?

- Photodynamic phototherapy
- A standard research protocol
- Chromophore related Laser treatment
- More studies on Laser can be expected to find best wavelength and protocol
  - Laser therapy for onychomycosis in patients with diabetes at risk for foot complications: study protocol for a randomized, double-blind, controlled trial (LASER-1) Leonie Nijenhuis-Rosien1,2*, Nanne Kleefstra3,4, Maurice J Wolfhagen5, Klaas H Groenier1,6, Henk JG Bilo1,3,6 and Gijs WD Landman
- Studies Optical Coherence Tomography (OCT) controlled
Diabetic Foot Ulceration

- Summarised in vitro and in vivo studies done on various cell types and animal models, respectively, using low level laser irradiation (LILI).
- Effects of LLLT in vitro, the underlying mechanisms are being identified.
- Clinical studies in DM limited,
  - Methodological heterogeneity explains varied results.
  - Better designed, well-controlled, randomized, double-blind studies needed Phototherapy important tool in speeding up the healing process as well as alleviating pain and inflammation.
- Need to inform health care providers of the beneficial effects of phototherapy.
Laser light absorbed by chromophores in cell, mitochondria in the case of visible red light.
• Leads to increase in adenosine triphosphate (ATP), reactive oxygen species (ROS), nitric oxide (NO), and intracellular calcium (iCa^{2+}).
• Activation of transcription factors get translocated to the nucleus and activate gene transcription.
• Leads to increased cell survival and wound healing.

Tissue Responses to Postoperative Laser Therapy in Diabetic Rats Submitted to Excisional Wounds  April 24, 2015 DOI: 10.1371/journal.pone.0122042 Cristiano de Loura Santana, et al

- Demonstrated LLLT in immediate postoperative period enhanced tissue repair process in diabetes
  - Modulating inflammatory process,
  - Increasing synthesis of myofibroblasts
  - Enhancing collagen organization.

- Similar effects achieved a single time with an energy density of 4 J/cm² and applied four times with an energy density of 1 J/cm².

- Application in the inflammatory phase was the most important factor to the enhancement of the tissue repair process.

- Further studies should be conducted to determine the role of the red wavelength on the modulation of glycation through biochemical analysis and
Low Level Laser Therapy for the Treatment of Diabetic Foot Ulcers: A Critical Survey Evidence-Based Complementary and Alternative Medicine

Volume (2014), Article ID 626127, Kathrin H. Beckmann, Gesa Meyer-Hamme, and Sven Schröder

• Biometrical and histological analysis “faster lesion contraction showing quicker re-epithelization and reformed connective tissue with more organized collagen fibers”
• Reduced inflammatory reaction,
• Provoked proliferation of myofibroblasts in experimental cutaneous wounds
• Laser energy stimulates molecules & atoms of cells,
• Does not cause significant increase in tissue temperature
• Laser needles not inserted into the skin; optical light fibers are fixed on the acupuncture points in an upright position.
  • High optical density achieved, minimizing light scattering at surface of the skin.
  • Therapeutic effects are of similar dimension to those evoked by manual needle acupuncture
  • Bi-chromatic laser needles combine wavelengths, for example, of red (685 nm) and infrared (785 nm) light. penetration depth in human skin is 2-3 cm. Blue light (405 nm) is supposed to have a bactericidal effect on the tissue surface.
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A Randomized Clinical Trial on the Effect of Low-Level Laser Therapy on Chronic Diabetic Foot Wound Healing: A Preliminary Report  

- Placebo treatment ($n = 10$) or LLLT ($n = 13$) (685 nm, energy density $10 \text{ J/cm}^2$)
- Week 4, the size of ulcers decreased significantly in the LLLT group ($p = 0.04$).
- 20 weeks, LLLT group, 8 patients complete healing; placebo group 3 patients complete wound healing.
- The mean time of complete healing, LLLT patients (11 weeks) less than in placebo patients (14 weeks) **NOT** statistically significant.

**Conclusions:** The study provides evidence that LLLT can accelerate the healing process of chronic diabetic foot ulcers, and it can be presumed that LLLT may shorten the time period needed to achieve complete healing.
Efficacy of Low Level Laser Therapy on Wound Healing in Patients with Chronic Diabetic Foot Ulcers—A Randomised Control Trial  
Indian Journal of Surgery

- Initial ulcer area was 2608.03 mm² in study group and 2747.17 mm² in control group ($p = 0.361$).
- Final ulcer area was 1564.79 mm² in study group and 2424.75 mm² in control group ($p = 0.361$).
- Percentage ulcer area reduction was $40.24 \pm 6.30$ mm² in study group and $11.87 \pm 4.28$ mm² in control group ($p < 0.001, Z = 7.08$).
- Conclusion: Low Level Laser Therapy is beneficial as an adjunct to conventional therapy in the treatment of diabetic foot ulcers (DFU).
Bacterial Wound Burden

• Assessed antimicrobial effect and tolerability of a single dose of a photo-activated gel containing RLP068 in the treatment for infected foot ulcers in subjects with diabetes.

• A randomized, double-blind, parallel series, placebo-controlled phase IIa trial performed with three concentrations of RLP068 (0.10, 0.30, and 0.50 %), measuring total and pathogen microbial load before and 1 h after topical gel application and photo-activation with 689 nm red light), Days 3, 8, and 15, as add-on to systemic treatment with amoxicillin and clavulanic acid.

• A dose-dependent reduction in total microbial load observed immediately after illumination, with progressive fading during follow-up.

• No safety issues emerged. Systemic absorption negligible.

• Photodynamic antimicrobial treatment with RLP068 of infected diabetic foot ulcers well tolerated produces significant reduction in germ load.

• Further clinical trials are needed to verify the efficacy of this approach as add-on to systemic antibiotic

The wound subjected to LLLT with conventional therapy showed decreased infection rate at 10th day of culture as compared to conventional dressing group alone

- Finding was not statistically significant.
- Large scale trials are required to know the anti-infective property of LLLT.
- Multicentre trials are required to know the anti-infective property of LLLT
Peripheral Neuropathy
Develop a scientifically sound and clinically relevant evidence-based guideline for the treatment of painful diabetic neuropathy (PDN).

Performed a systematic review of the literature from 1960 to August 2008

- Classified the studies according to the American Academy of Neurology classification of evidence scheme for a therapeutic article, and recommendations were linked to the strength of the evidence.
- The basic question asked was: “What is the efficacy of a given treatment (pharmacological: anticonvulsants, antidepressants, opioids, others; and non-pharmacological: electrical stimulation, magnetic field treatment, low-intensity laser treatment, Reiki massage, others) to reduce pain and improve physical function and quality of life (QOL) in patients with PDN?”

- Pregabalin (Level A)

- Venlafaxine, duloxetine, amitriptyline, gabapentin, valproate, opioids (morphine sulphate, tramadol, and oxycodone controlled-release), and capsaicin (Level B).

- Other treatments INCLUDING LLLT have less robust evidence or the evidence is negative.
Effects of 660- and 980-nm low-level laser therapy on neuropathic pain relief following chronic constriction injury in rat sciatic nerve. Lasers in Medical Science September 2014, Volume 29, Issue 5, pp 1593-1598 M. Masoumipoor et al

- Chronic constriction injury (CCI) well-known model for neuropathic pain studies.
- Comparison of the mechanical and thermal threshold showed significant difference between the therapeutic effects of the two groups that received LLLT.
- 660-nm wavelength had better therapeutic effects than 980-nm wavelength, so the former one may be used for clinical application in neuropathic cases.
Musculoskeletal Injuries
- **Effects of Low-Level Laser Therapy (LLLT) and Diclofenac (Topical and Intramuscular) as Single and Combined Therapy in Experimental Model of Controlled Muscle Strain in Rats.** 
  Photochemistry and Photobiology Volume 89, Issue 2, pages 508–512, March/April 2013 Rodrigo Leal de Paiva Carvalho et al

- Muscle injuries represent 30% of sports injuries. Most used treatments are nonsteroidal anti-inflammatory drugs (NSAIDs),

- Evaluated the effect of single and combined therapies (LLLT, topical application of diclofenac and intramuscular diclofenac) functional & biochemical aspects in experimental model of controlled muscle strain in rats.

- Muscle strain induced by overloading tibialis anterior muscle of rats. Injured groups received either no treatment, or a single treatment with topical or intramuscular diclofenac (TD and ID), or LLLT (3 J, 810 nm, 100 mW) 1 h after injury.

- Walking track analysis functional outcome, biochemical analyses COX-1 and COX-2 & levels of prostaglandin
  - All treatments significantly decreased COX-1 and COX-2 gene expression compared with injury group (P < 0.05). However, LLLT showed better effects than TD and ID regarding PGE2 levels and walking track analysis (P < 0.05). We can

- Concluded that LLLT has more efficacy than topical and intramuscular diclofenac in treatment of muscle strain injury in acute stage.
• Thirty patients administered LLLT and completed 12 months of follow-up. Patients treated twice a week for 3 weeks for 6 treatments evaluated at baseline, 2 weeks post procedure, and 6 and 12 months post procedure. Visual Analog Scale (VAS) and Foot Function Index (FFI) at study follow-up periods.

• Patients demonstrated a mean improvement in heel pain VAS from 67.8 out of 100 at baseline to 6.9 out of 100 at the 12-month follow-up period.

• Total FFI score improved from a mean of 106.2 at baseline to 32.3 at 12 months post procedure.

• **Conclusion:** Further studies are warranted, study showed that LLLT is a promising treatment of chronic plantar fasciitis.

• Studied low-level laser therapy.

• 69 subjects enrolled placebo-controlled, randomized, double-blind, multicenter study evaluated low-level laser therapy for treatment of unilateral chronic fasciitis.

• Participants treated twice a week for 3 weeks, total 6 treatments
  • Evaluated: before procedure and weeks 1, 2, 3, 6, and 8.
  • Foot Function Index, VAS Pain rating,
    • Doppler ultrasonography on plantar fascia to measure fascial thickness before and after treatment.
  • Intervention demonstrated a mean improvement in heel pain VAS 29.6 ± 24.9 compared with the placebo subjects, 5.4 ± 16.0, a statistically significant difference (p < .001).
  • *Additional studies warranted, data demonstrated that low-level laser therapy is a promising treatment of plantar fasciitis.*

RCT evaluations at baseline and 4, 12, and 52 weeks. Investigated effectiveness of LLLT as an adjunct to a program of eccentric exercises for the treatment of Achilles' tendinopathy.

- Observers were blinded to groupings.
- Mid portion Achilles' tendinopathy assigned randomly, 2 groups. Both groups performed eccentric exercises over 3-month period. Received either active or placebo application of LLLT 3 times per week for the first 4 weeks; dose was 3J per point.
- Outcome Sport Assessment–Achilles' questionnaire (VISA-A); and VAS
- Baseline characteristics no differences between groups. Primary outcome point, no statistical difference in VISA-A scores between groups (P>.05). All other outcome scores showed no significant difference between the groups at any time point.

Conclusions The clinical effectiveness of adding LLLT to eccentric exercises for the treatment of Achilles' tendinopathy has NOT been demonstrated using the parameters in this study.
A strange one to leave you with!

- **Foot Orgasm Syndrome: A Case Report in a Woman**
The Journal of Sexual Medicine Volume 10, Issue 8, pages 1926–1934, August 2013 Marcel D. Waldinger MD, PhD, FECSM et al

- Woman presented undesired orgasmic sensations originating in left foot,
  - interview, physical examination, sensory testing, magnetic resonance imaging (MRI-scan), electromyography (EMG), transcutaneous electrical nerve stimulation (TENS), blockade of the left S1 dorsal root ganglion performed.

- Subtle attenuation of sensory amplitudes of the left suralis, and the left medial and lateral plantar nerve tracts was found at EMG. MRI- no foot abnormalities.

- TENS at the left metatarso-phalangeal joint-III of the left foot elicited an instant orgasmic sensation that radiated from plantar toward the vagina. TENS applied to the left side of the vagina elicited an orgasm that radiated to the left foot.

- Diagnostic blockade left S1 dorsal root ganglion reduced frequency and intensity of orgasmic sensation in the left foot.

- Additional therapeutic blockade of the same ganglion with 0.8 mL bupivacaine 0.50 mg combined with pulsed radiofrequency treatment and LLLT resulted in a complete disappearance of the foot-induced orgasmic sensations.

- Conclusion
  - Foot orgasm syndrome (FOS) is described in a woman. Blockade of the left S1 dorsal root ganglion alleviated FOS. It is hypothesized that FOS, occurring 1.5 years after an intensive care emergency, was caused by partial nerve regeneration (axonotmesis), after which afferent (C-fiber) information from a small reinnervated skin area of the left foot and afferent somatic and autonomous (visceral) information from the vagina on at least S1 spinal level is misinterpreted by the brain as being solely information originating from the vagina.
Thanks!

Questions?