Topical Compression in Restless Leg Syndrome

Reduces Moderate to Severe Restless Leg Syndrome

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Conflicts and Notices

- Employed by medi USA; Vice President of Business Development; President CircAid Medical
- medi acquired the technology and research January 2015

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In under 12 minutes…

- *What is restless leg syndrome?*
- *What is topical compression?*
- *What are the clinical benefits of topical compression when you have restless leg syndrome?*

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Restless Leg Syndrome
Willis-Ekbom Disease

- *"Restless leg syndrome (RLS) is a neurological disorder that causes a strong **urge to move your legs**. This urge to move often occurs with strange and unpleasant feelings in your legs. Moving your legs relieves the urge and the unpleasant feelings.*

- *The urge to move and unpleasant feelings happen when you're resting and inactive. Thus, they tend to be worse in the evening and at night."*

  - National Institute of Health

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What are the Causes of RLS?

- *Unknown but believed to be;*
  - Genetic Factors (50% have family member w/ RLS)
  - Environmental and Health Factors such as;
    - Sitting for long periods of time
    - Iron deficiency, kidney failure, diabetes, nerve problems, venous disease or pregnancy
    - Taking certain medications such as antihistamines or antidepressants
    - Drinking alcohol or caffeine
    - Smoking or using other tobacco products
    - Lack of sleep

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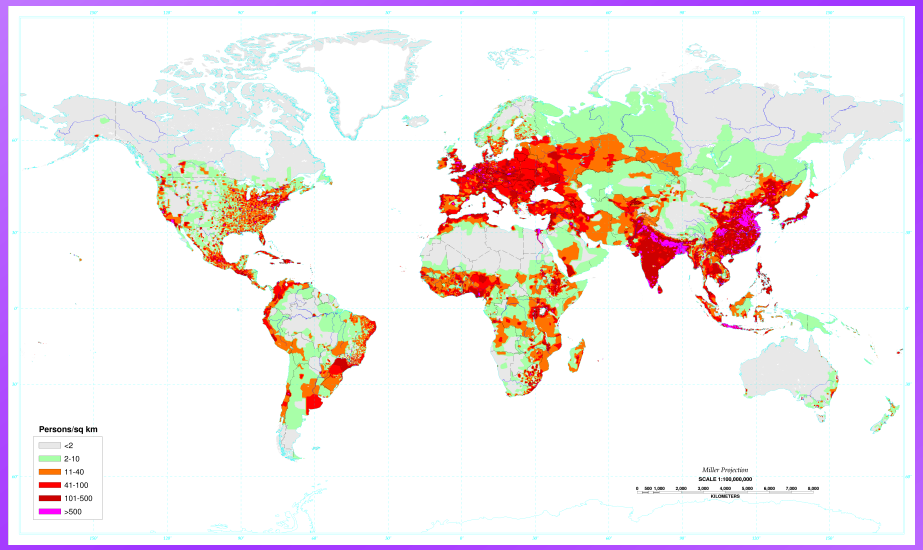
Demographics of RLS

- Approximately 9-10% of the population is affected
- 2-3% of adults suffer from moderate to severe RLS Symptoms
- The incidence of RLS is about twice as high in women versus men



- RLS may begin at any age
- Severely affected with RLS tend to be middle-aged or older
- Symptoms become more frequent and last longer with age

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Current approaches to treatment

- **Pharmaceuticals (e.g., REQUIP®, MIRAPLEX®)**
  - Drugs principally used for the treatment of Parkinson's disease
  - E.g., opioids, central nervous system depressants, or dopamine agonists
  - Costs: $360 - 1,500/yr.

- **Negative side effects:**
  - Nausea, vomiting, dizziness, risk of addiction
  - Pharmaceuticals lose their effect over time, so patients need to increase dosage to maintain benefits
  - Rebound effect: Symptoms get worse after stopping the use of pharmaceuticals

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http://www.nhlbi.nih.gov/health/health-topics/topics/rls

Current approaches to treatment

- **Vibrating Pad – "Relaxis"**
- Counter stimulation provided by a vibrating pad
- $750

- **Homeopathic Remedies**
  - Non-regulated:
  - Limited data/efficacy
  - Not physician recommended
  - Annual costs $360-500/yr.

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Other approaches

- Hot or cold baths
- Massage
- Compression stockings
- Pneumatic compression devices
- Near-infrared light therapy: treatments with a device that uses near-infrared light to help increase the circulation in your legs

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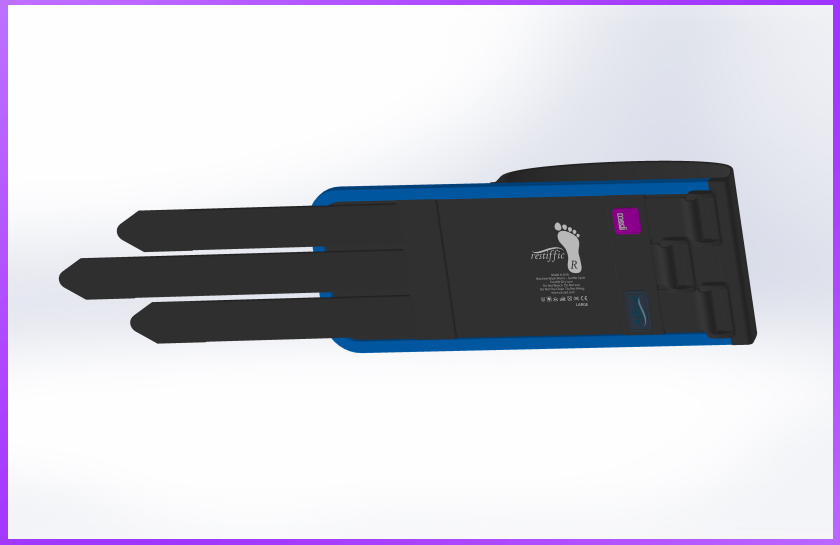
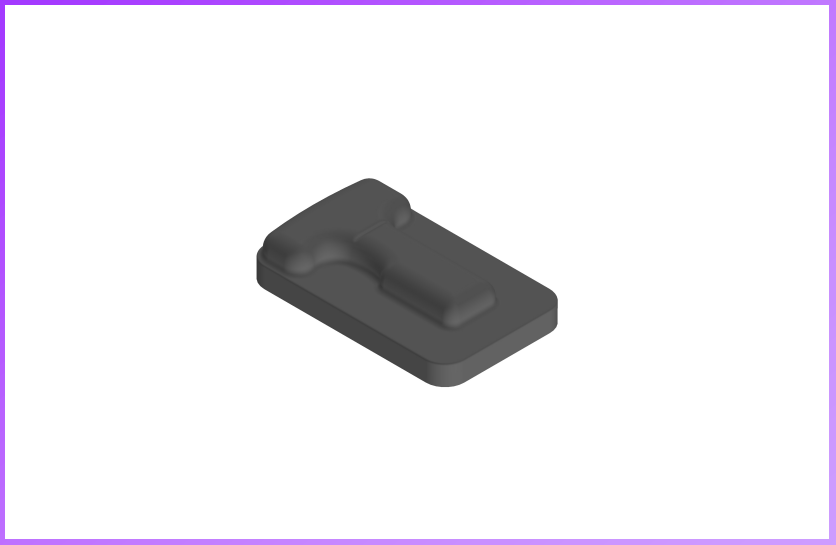
A new treatment for RLS - Topical Compression of the Feet

- The RESTIFFIC Restless Leg device is a foot wrap designed to apply continuous, adjustable squeezing pressure on specific muscles in the feet.
- The device is to be applied before bedtime or while the person is seated or supine.





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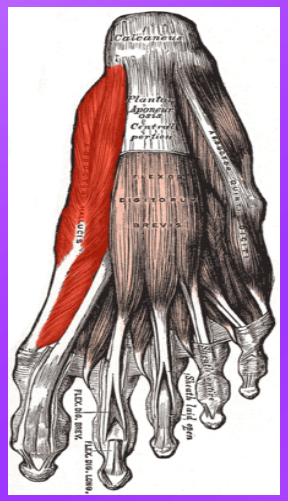
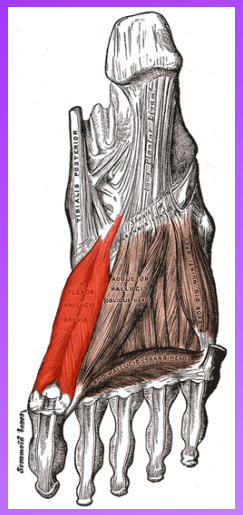
Topical Compression of the Foot

Restiffic devices: apply adjustable topical compression on the *abductor hallucis* and the *flexor hallucis brevis* muscles in the foot.



Abductor hallucis



Flexor hallucis brevis

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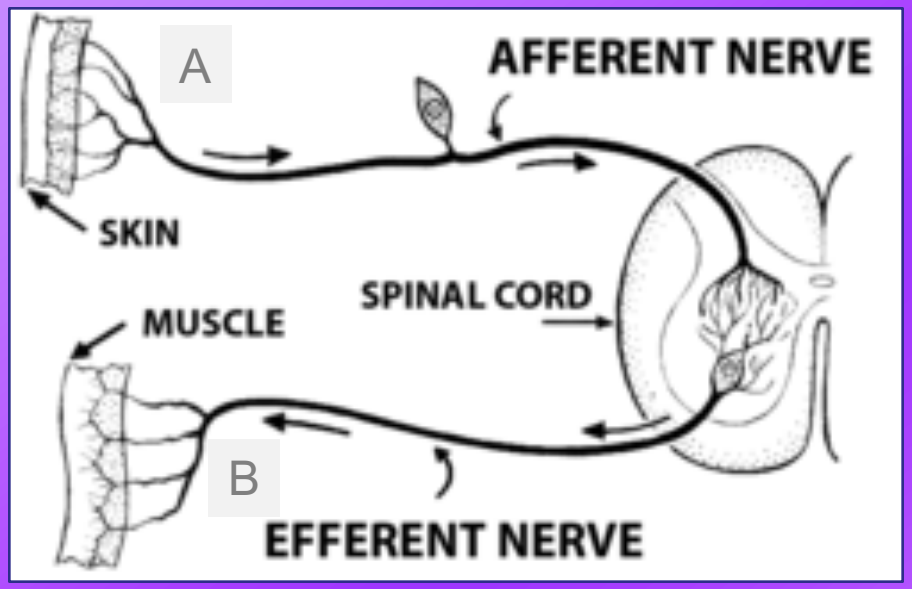
Mechanism of Action

HYPOTHESIS



- restiffic® causes pressure in the nerve endings of the incoming (afferent) nerve in specific muscles in the foot (A).
- A message is sent to the spinal cord, brain stem and brain.
- The brain interprets the message as pressure, not irritation, then sends a message through the outgoing (efferent) nerve to the muscles.
- Leg muscles relax, rather than contract, thus alleviating the symptoms of RLS (B)

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RLS Device - Prototype

Left Foot

Right Foot

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Study Design

- Single-arm, open label clinical trial with repeated measures design
- Study population:
  - 22 women and 8 men
  - Mean age 51.5 years (range 30 to 75 years)
  - Moderate to severe primary RLS (IRLSS > 15)
  - Reported Symptoms 2-3 times weekly for over 6 months
- Patients recorded their symptoms over 8 weeks
  - Week 1: No treatment
  - Week 2-4: Treatment with restiffic®
  - Week 5: No treatment
  - Week 6-8: Treatment with restiffic®

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Study Assessments

- International Restless Legs Syndrome Study Group rating scale (IRLSS) Rating Scale (patient- generated)
- Clinical Global Impression Scale (CGI) Scale (physician-generated)

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IRLSS Survey Administration

A	B	C	D
Without Study Device	With Study Device	Without Study Device	With Study Device
Day 1 Thru 7	Day 8 Thru 28	Day 29 Thru 35	Day 36 Thru 56
SURVEYS	SURVEYS	SURVEYS	SURVEYS
3x	8x	3X	8X

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CGI Survey Administration

Days 1, 29, 36, 57

Severity

Improvement

Efficacy Index

Descriptive statistics used to analyze scores

Number of Responders

(Percent much improved or very much improved

Comparison to historic controls by chi square (α=.05)

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RESULTS - IRLSS SCORES

- Baseline Day 1
  - Average Score 25.1 ± 5.3 (Severe)
- Final Day 57
  - Average Score 7.8 ± 6.5 (Mild)
- Mean difference 17.2 ± 6.2, 95% confidence interval 14.9 through 19.5 ($p \leq .0001$)

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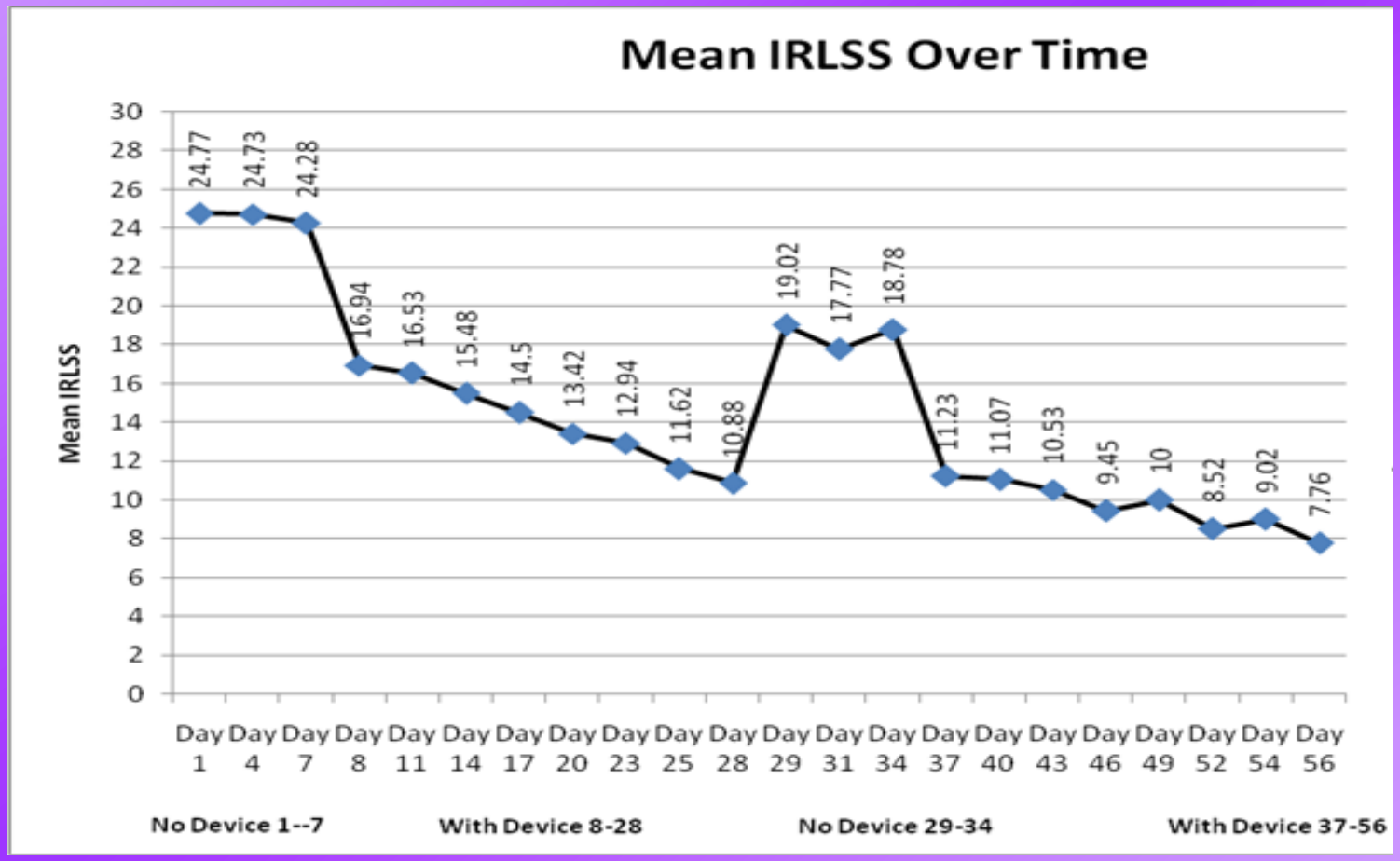
IRLSS Scores *by Time Periods*



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How does this compare?

Ropinirol N=464 Meta analysis*	Ropinirol Placebo N=467 Meta analysis*	RLS Device N=30
12	8.9	17.4

- Trenkwalder 2004 *
- Walters 2004 *
- Bogan 2006 *

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How does this compare?

Adjustable Topical Compression Device

- 1.44 times as effective as ropinirole
- 2 times as effective as ropinirole placebo pill in reducing symptoms of moderate to severe RLS

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Results CGI

- Clinical Global Impression Scale

  - Severity Scale
  - Improvement Scale and
  - Efficacy Index

  (Side effects vs Therapeutic efficacy).

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Severity Scale - (Physician Observation)

- 97% (29/30)experienced a decrease in severity,
- 83% (25/30) experienced two or more levels of decrease in severity

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Improvement Scale - (Physician Observation)

- All patients improved.
- In 90% (27/30), symptoms were “much improved” or “very much improved”

These subjects were designated as “responders”

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Efficacy Index - (Physician Observation) (Side Effect vs. Therapeutic Effect)

- All patients improved, one with minimal side effects that did not interfere with activities.
- 60% (18/30), showed marked improvement and complete or nearly complete remission of all symptoms, with no side effects;
- 86% (26/30) of subjects showed moderate to marked improvement with no side effects

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Clinical Trial Results: CGI- Global Improvement

Global Improvement significantly greater for RESTIFFIC™ compared with REQUIP® ($p < .05$)

Percent Responders*

- RESTIFFIC™ = 90% (27/30)
- REQUIP® = 63% (293/464)
- REQUIP® placebo = 47% (219/467)

- *(much improved or very much improved)

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Adverse Events

AEs definitely related to device occurred in seven subjects. These resolved when the device was loosened.

pain (2);

paresthesia (2);

irritability (3);

spasm (1);

local complication-warm feet (1).

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Follow-up Survey
1.4 ± 0.5 years (range 0.7 to 2.4 years)

- 17 questions (10 from the IRLSS scores and 7 additional questions)
- Conducted by phone and mail-in surveys
- 57% (17/30) patients responded.
- Results from the initial survey were compared to the final survey by *t* test (alpha = .05)

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Long-term Follow-Up Survey

- Mean IRLSS scores decreased from severe to mild.
- Of 65% (11/17) who responded, all reported no problems wearing the device.
- 94% (16/17) would recommend the device.

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Long-term Follow-Up Survey

- Four patients reported complete remission of symptoms; several reported still wearing the device, but less frequently and for a shorter duration.
- 70% (12/17) rated the device either 9 or 10 on a 1 to 10 scale, 10 being the best

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Summary RLS (Restiffic) Device

- 1.44 times as effective as ropinirole and twice as effective as placebo in reducing IRLSS scores.
- Significantly greater percent responders 90% (27/30), vs ropinirole, 63% (293/464) ($p < .05$)
- Produced none of the side effects associated with drug therapy. AEs were minimal, transitory, and relieved by loosening straps.

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restless no more…
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