# Low Level Laser Therapy

# B-Cure Laser Pro for Treatment of Diabetic Foot Ulcers

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***Sponsored by B-Cure Laser***

# Introduction | Low Level Laser Therapy

## Mechanism of Action:

- Production of ATP
- Accelerates blood flow to the wound, the synthesis of collagen and elastin
- Stimulates the macrophages cells
- Increases the number of mast cells which help to heal the wounds
- Accelerates the proliferation of keratinocytes

  (comprise the main component of the epidermis)

# Introduction | Low Level Laser Therapy

## Medical Uses:

- Pain therapy
- Musculoskeletal conditions
- Wound healing
- Anti inflammatory

# Clinical Studies | LLLT - Introduction

1967- Endre Mester first described accelerated healing of burn wounds in mice, using low-level laser therapy (LLLT)

# Clinical Studies | LLLT – Wound Healing

In vitro & in vivo studies have shown that LLLT affects almost every molecular aspect of wound healing:

- Increasing ATP levels

(Karu 1999; Pastore et al. 1996)

- Promotion of proliferation and migration of keratinocytes*, endothelial cells** and fibroblasts***

(Fushimi et al. 2012; Grossman et al. 1998)*
(Chen, Hung, and Hsu 2008; Kipshidze et al. 2001; Schindl et al. 2003)**
(Hawkins and Abrahamse 2006; Houreld and Abrahamse 2007)***

# Clinical Studies | LLLT – Wound Healing

- Increasing collagen synthesis

(Labbe et al. 1990; Prabhu et al. 2012; Saperia et al. 1986)

- Enhancing phagocytic and bactericidal activities of inflammatory cells

(Duan et al. 2001; Hemvani, Chitnis, and Bhagwanani 2005; Kupin et al. 1982)

- Modulation of expression and secretion of relevant chemokines and cytokines

(Peplow et al. 2011a)

Although the experimental evidence is sound, the efficacy of LLLT in the clinical setting is still controversial, showing mixed results

# Study Design | Double Blind Clinical Trial

**Experimental:** Standard of care + Active B-Cure Laser Pro
**Control:** Standard of care + **Placebo** B-Cure Laser Pro

## LLLT Treatments:

- Once every day, for 12 weeks
  (6 times a week except Saturdays)
- 8 minutes for every 4.5cm² wound area

## Standard of Care:

- Rinsing the ulcer
- Pads
- Advanced dressing

# Materials | LLLT (B-Cure Laser Pro)

- **Type of laser** - solid-state Laser diode GaAlAs
- **Laser wavelength** - 808nM (infrared)
- **Maximum power** - 250 mW
- **Laser Pulse frequency** - 13 kHz
- **Energy** - appx. 1.2 J/cm2/minute
- **Total energy** - appx 5 Joules per minute
- **Laser beam** - one coherent beam of: 45mm longX10mm wide=4.5cm²

# Study Design | Criteria

## Inclusion Criteria:

- Diabetes
- Chronic foot ulcer, which has been present for at least 6 weeks
- Wound size 4-30 $cm^2$
- ABI > 0.6

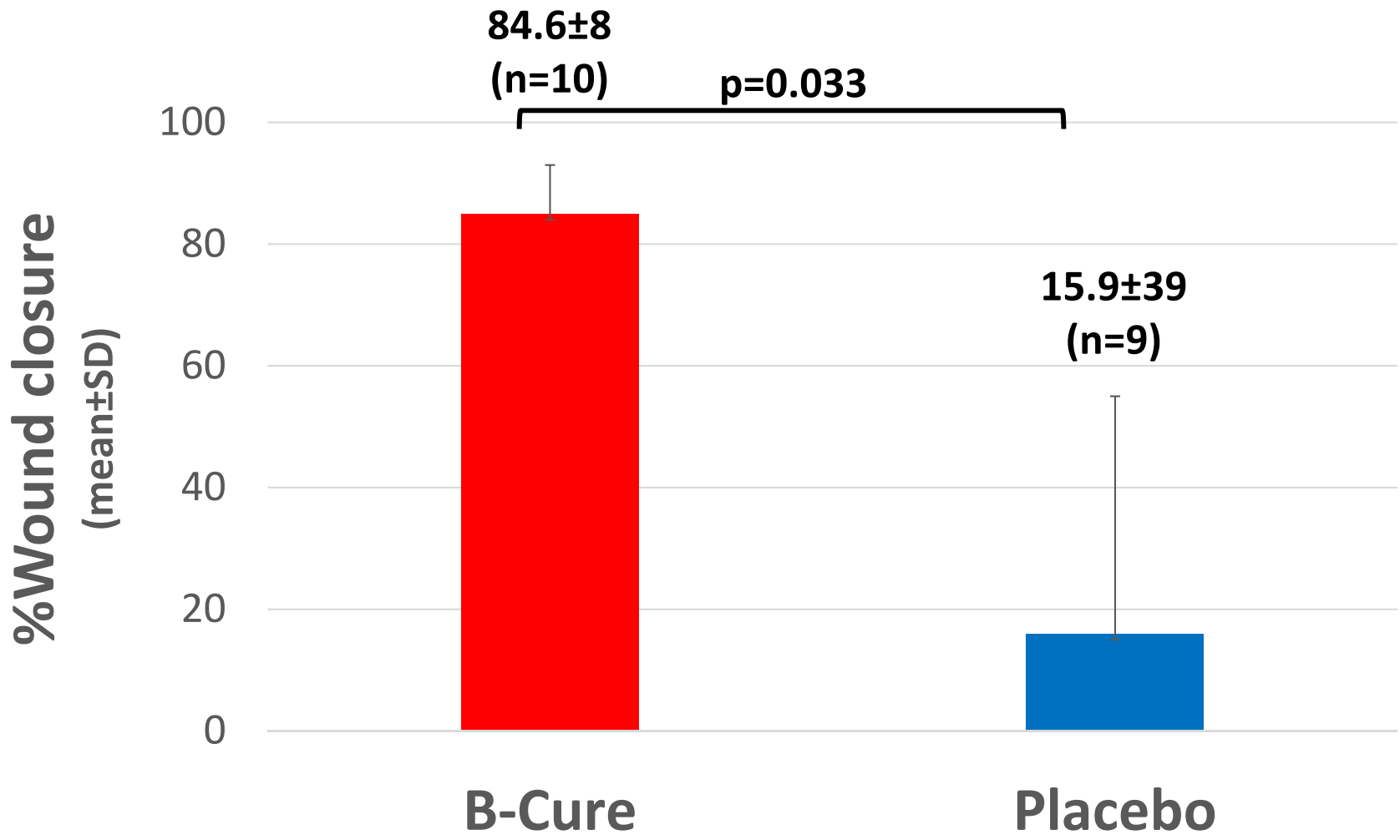
## Exclusion Criteria:

- Pregnancy
- Active malignant disease

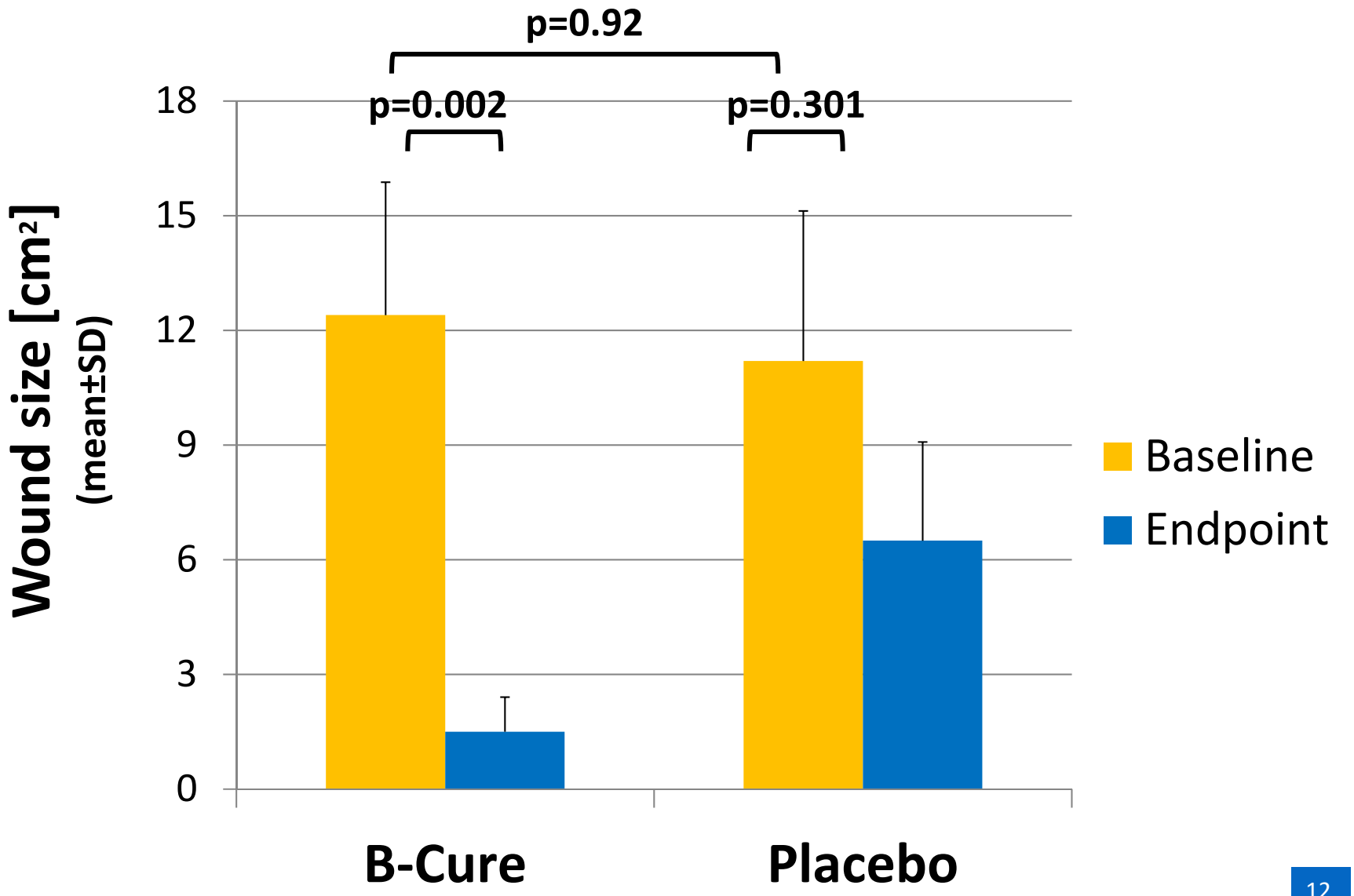
# Study Design | Patients Characteristics

| | Active | Placebo |
|---|---|---|
| Number of patients | 10 | 9 |
| Male / Female | 6/4 | 6/3 |
| Average Age | 64.6 ± 11.3 | 57.4 ± 10.2 |
| Hemodialysis | 3 | 2 |

# Results | Comparison of % Wound Closure



# Results | Comparison of Mean Wound Size ($cm^2$)



# Results | Original Data

| PN | Group | Area at baseline [$cm^2$] | Area at termination [$cm^2$] | Absolute change [$cm^2$] | %Closure | Time [weeks] |
|---|---|---|---|---|---|---|
| **1** | Active | 3 | 0 | -3 | 100 | . |
| **3** | Active | 24 | 0 | -24 | 100 | . |
| **4** | Active | 3 | 0.6 | -2.4 | 80 | 8 |
| **7** | Active | 6 | 0.3 | -5.7 | 95 | 10 |
| **8** | Active | 25 | 0.1 | -24.9 | 99.6 | 12 |
| **11** | Active | 8 | 5.5 | -2.5 | 31.3 | 12 |
| **13** | Active | 14.3 | 0 | -14.3 | 100 | 8 |
| **14** | Active | 3.8 | 0 | -3.8 | 100 | 10 |
| **16** | Active | 25 | 2.4 | -22.6 | 90.4 | 12 |
| **19** | Active | 12 | 6 | -6 | 50 | . |
| **5** | Placebo | 4 | 3.8 | -0.3 | 6.3 | 4 |
| **6** | Placebo | 4.5 | 0 | -4.5 | 100 | 10 |
| **9** | Placebo | 4 | 15 | 11 | -275 | 8 |
| **10** | Placebo | 4 | 1.2 | -2.8 | 70 | 12 |
| **12** | Placebo | 11.3 | 1.2 | -10.1 | 89.3 | 12 |
| **15** | Placebo | 16 | 21 | 5 | -31.3 | 8 |
| **17** | Placebo | 37.5 | 5.5 | -32 | 85.3 | 12 |
| **18** | Placebo | 16 | 9.3 | -6.7 | 41.6 | 12 |
| **20** | Placebo | 3.8 | 1.6 | -2.1 | 57.3 | . |

# Results | Wound Size

| | Placebo (n=9) | | | | Active (n=10) | | | |
|---|---|---|---|---|---|---|---|---|
| | Baseline | Endpt. | Change | %Closure | Baseline | Endpt. | Change | %Closure |
| **Mean ±SD** | 11.2±11.1 | 6.5±7.3 | -4.7±12.0 | 16±117 | 12.4±9.2 | 1.5±2.4 | -10.9±9.6 | 84.6±24.4 |
| **Median [IQR]** | 4.5 [12.0] | 3.8 [9.6] | -2.8 [8.6] | 57.3 [89.5] | 10 [20.3] | 0.2 [2.4] | -5.8 [19.6] | 97.3 [20.0] |
| **Min** | 3.8 | 0.0 | -32 | -275 | 3.0 | 0.0 | -24.9 | 31.3 |
| **Max** | 37.5 | 21 | 11 | 100 | 25 | 6.0 | -2.4 | 100 |
| **Lower 95%CI** | 2.7 | 0.9 | -13.9 | -74.0 | 5.8 | -0.2 | -17.8 | 67.1 |
| **Upper 95% CI** | 19.8 | 12.0 | 4.5 | 67.1 | 19.0 | 3.2 | -4.1 | 102.1 |

**No adverse effects in the experimental group**

# Results | Pictures From the active Group

Patient A




Patient B



Patient C


# Results | Improvement > 90%

| Improvement | Placebo | Active | Total |
|---|---|---|---|
| **Less than 90%** | 8 (42.1%) | 3 (15.8%) | 11 (57.9%) |
| **More than 90%** | 1 (5.3%) | 7 (36.8%) | 8 (42.1%) |
| **Total** | 9 (47.4%) | 10 (52.6%) | 19 (100%) |

p=0.019

## Limitations:

- Small cohorts
- Ended before the planned number of recruits achieved

# Results | summary

- No difference in baseline values of placebo vs active (p=0.92)
- A statistically significant reduction in ulcer size over baseline was observed in the active group (p=0.002) but not in the placebo group (p=0.301)
- Direct comparison in the % wound closure showed a statistical significant difference between the study groups (p=0.033)
- Percent of wound closure was categorized using cut-off 90%: closure ≤90% or >90%. was statistically significant between groups (p=0.019)

# Conclusions

- B-cure laser Pro is a safe treatment
- B-cure laser Pro seems to improve and facilitate diabetic wound healing



# Thank You