

## BIBLIOGRAPHY

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7. Margara et al, *Chirurgia*, Vol.21, N.6 – pag 311-314, December 2008
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**A BIOPHYSICAL TREATMENT IN  
PERIPHERAL COMPLICATIONS  
IN DIABETIC PATIENTS.**



# FREMS™: a biophysical treatment in peripheral complications in diabetic patients.

## FREMS™: Scientific Rationale

FREMS™ is a “biocompatible” electrical neurostimulation of recent generation. Thanks to its physical characteristics it enhances vasomotion<sup>1</sup> thus peripheral blood flow<sup>2</sup>, it induces the modulation of angiogenic growth factors (VEGF)<sup>3</sup> and functional recovery of peripheral nervous system<sup>4</sup>.

The clinical outcome is a significant **pain control**, **tissue regeneration** and **functional recovery** of the treated area.

Several clinical studies has demonstrated the actions mechanisms and benefit effects of FREMS™.

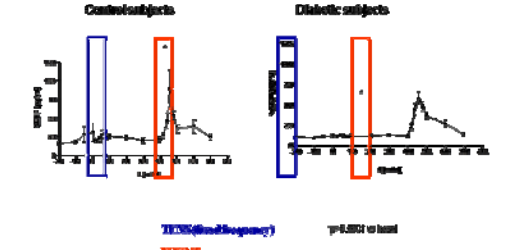
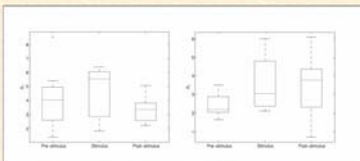
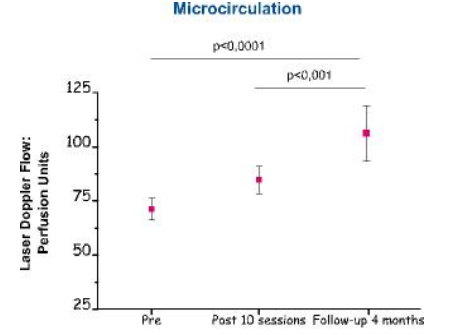
## FREMS™: Technical Rationale

FREMS™ consists in series of biphasic, asymmetric, electrically balanced pulses.

It is characterized by a “multiparametric modulation” of frequency, pulse duration and amplitude of the provided electrical signal.

**FREMS™ is a biophysical treatment dedicated to NEURO-VASCULAR REHABILITATION of legs complications and chronic wounds**

## FREMS™: Action Mechanisms

<p><b>Growth factors release ( VEGF )</b></p> <p>□ “Induction of vascular endothelial growth factor release by transcutaneous frequency modulated neural stimulation in diabetic polyneuropathy”.</p> <p><i>Bevilacqua M. et al. J Endocrinol Invest. 2007</i></p>	 <p>Control subjects      Diabetic subjects</p> <p>VEGF (pg/ml)</p> <p>Time (min)</p> <p>FREMS (blue frequency)</p> <p>p&lt;0.001 vs basal</p>
<p><b>Enhancement of vasomotion activity thus peripheral blood flow increase</b></p> <p>□ “Recovery of 0,1 Hz microvascular skin blood flow in disautonomic diabetic (type 2) neuropathy by using FREMS”.</p> <p><i>L. Bocchi et al [submitted] (10)</i></p>	<p><b>Results</b></p> <p>During the stimulation, there is an increase of the values of the Rv parameter:</p> <ul style="list-style-type: none"> <li>• normal subjects: +12%</li> <li>• pathological cases: +50% (p&lt;0.05).</li> </ul> <p>After the stimulation, the values of the parameter tends to return towards the initial position.</p> <p>•Control group: values of Rv after the stimulation are in the same range as before the stimulation.</p> <p>•Diabetic group: The effect of the stimulation persists after the stimulation itself has ceased (p &lt; 0.05).</p> 
<p>□ “FREMS enhances cutaneous microvascular flow in patients with diabetic neuropathy”.</p> <p><i>Conti M. et al. J Diabetes Complications [December 2008]</i></p>	<p><b>Microcirculation</b></p>  <p>Laser Doppler Flow: Perfusion Units</p> <p>Pre      Post 10 sessions      Follow-up 4 months</p> <p>p&lt;0,0001      p&lt;0,001</p> <p>anova p=0,0002 ; N=40</p>

Specific and different FREMS™ sequences have been investigated in:

### PAINFUL DIABETIC NEUROPATHY

“Effectiveness of frequency-modulated electromagnetic neural stimulation in the treatments of painful diabetic neuropathy” Bosi et al. 2005 Diabetologia<sup>(4)</sup>

#### CONCLUSIONS:

- ✓ FREMS is a safe and effective therapy for neuropathic pain in patients with diabetes and is able to modify some parameters of peripheral nerve function (Increase in sensory tactile perception and motor nerve conduction velocity).
- ✓ Clinical benefits persisted at the 4-month follow-up.
- ✓ No significant side effects were recorded during the study

### PERIPHERAL ARTERIAL DISEASES

“Neuromodulation FREMS in the treatment of diabetic peripheral arterial disease (PAD)”. Da Ros et al. EASD 2006<sup>(5)</sup>

#### CONCLUSIONS:

In diabetic patients with PAD, FREMS seems to achieve considerable effects on:

- ✓ Improvement of oxymetric values at 3 months follow-up;
- ✓ Improvement of pain free walking distance at 3 months follow up;
- ✓ In patients with no indications of revascularization FREMS can lead to amelioration without risks;

### LEG/FOOT DIABETIC ULCERS

“Frequency Rhythmic Electrical Modulation System in the treatment of chronic painful leg ulcers”. Jankovic et al. 2008 Arch Dermatol Res.<sup>(6)</sup>

#### CONCLUSIONS:

- ✓ FREMS significantly facilitates epithelialisation of ulcer cruris and significantly decreases pain level, especially in the first 36-48h without damaging effects.
- ✓ It has cumulative effects which is evidenced 2 months after treatment.

“Frequency Rhythmic Electrical Modulation System in the treatment of diabetic ulcers”. Margara et al. 2008 Chirurgia<sup>(7)</sup>

#### CONCLUSIONS:

- ✓ FREMS accelerate wound healing and reduce pain associated both to ulcers and to diabetic neuropathy. Follow-up at 30 and 45 days.

### DNOAP – CHARCOT’S NEURO-ARTHROPATHY

“Effectiveness of frequency modulated electromagnetic neural stimulation (FREMS) in the treatment of the acute phase of Charcot’s neuro-arthropathy (DNOAP)”. Piaggese et al. DFG 2008<sup>(8)</sup>

#### CONCLUSIONS:

This short-term pilot study showed encouraging results for the application of FREMS in the acute phase of DNOAP, associated to immobilization and weight relief.

### WOUND HEALING

Non-Healing ulcers: Domiciliary assistance including electrical neurostimulation. Clinical outcome and costs reduction. Veneziano et al.<sup>(9)</sup>

#### CONCLUSIONS:

- ✓ FREMS may be a **valid tool for the healing of complex chronic wounds**
- ✓ **Reduction of area and specially of depth** were significant after few weeks of starting FREMS therapy;
- ✓ **Pain control** was as well significant with elimination of this important component of chronic wounds;
- ✓ Effectiveness in healing (time of assistance -58%) and in **costs** (direct management cost -31%);
- ✓ FREMS treatment allowed the improvement of **quality of assistance** and quality of life of patients.