

Calmare®

Scrambler Therapy MC-5A

Treatment of Chronic Neuropathic Pain Caused By
Chemotherapy

Background

- Developed in Rome over a period of more than 16 years
- Professor Giuseppe Marineo, inventor
- FDA Clearance February 2009
- CE Mark Certification 2008
- Competitive Technologies, Inc., sponsor of technology
- Non-invasive modality for chronic neuropathic pain refractory to drugs

Background

- Chronic neuropathic pain is common in cancer and non-cancer patients
- Pain management is mostly unsatisfactory
- Chemotherapy-induced peripheral neuropathy (CIPN) affect 30% to 40% of patients
- Stocking-and-glove pain is the predominant symptom
- Persists for years after treatment
- No standard effective therapy for CIPN

Chemotherapy induced peripheral neuropathy (CIPN)

- 30-70% of patients
- Taxanes, bortezomib, carboplatin/oxaliplatin, x-
alomides, ixabepilone....
- Has become a dose limiting toxicity
- Painful, disabling, persistent.
- Mechanism(s)
 - direct nerve injury and
 - recruitment of neighboring normal neurons
 - “windup” at cord, brain level
 - direct reorganization of nerve fibers (plasticity)
 - sodium/calcium channels, receptors

Things that don't work for taxane or platinum neuropathy...

- In RCTs, nortryptilline, amitryptilline don't work. Vit E might prevent but rescue the cancer. Wolf S, et al. Eur J Cancer 2008
- In RCT, Glutamine does not work. (Jacobson SD, J Supp Oncol 2003)
- In RCT, lamotrigine (Lamictal) also does not work (Rao D, Cancer 2008)
- In RCT, gabapentin (Neurontin) does not work. Rao D, Cancer 2007
- TENS with/without drugs; does not work for cancer pain. Cochrane review.

What is Scrambler therapy?

- Patient-specific *cutaneous* electro-stimulation similar to spinal cord stimulation, but non-invasive.
- Creates "non-pain" information in packets of rapidly varying impulses, given non-invasively using the patient's own nerves.
- 30-45 minute long sessions using EKG-like pads. Above and below pain.
- Stinging, then tingling, then intermittent pulse; adjust to tolerance.
- No side effects reported in over 4000 patients; over 3000 in use in Italy. US FDA Cleared Feb 09.

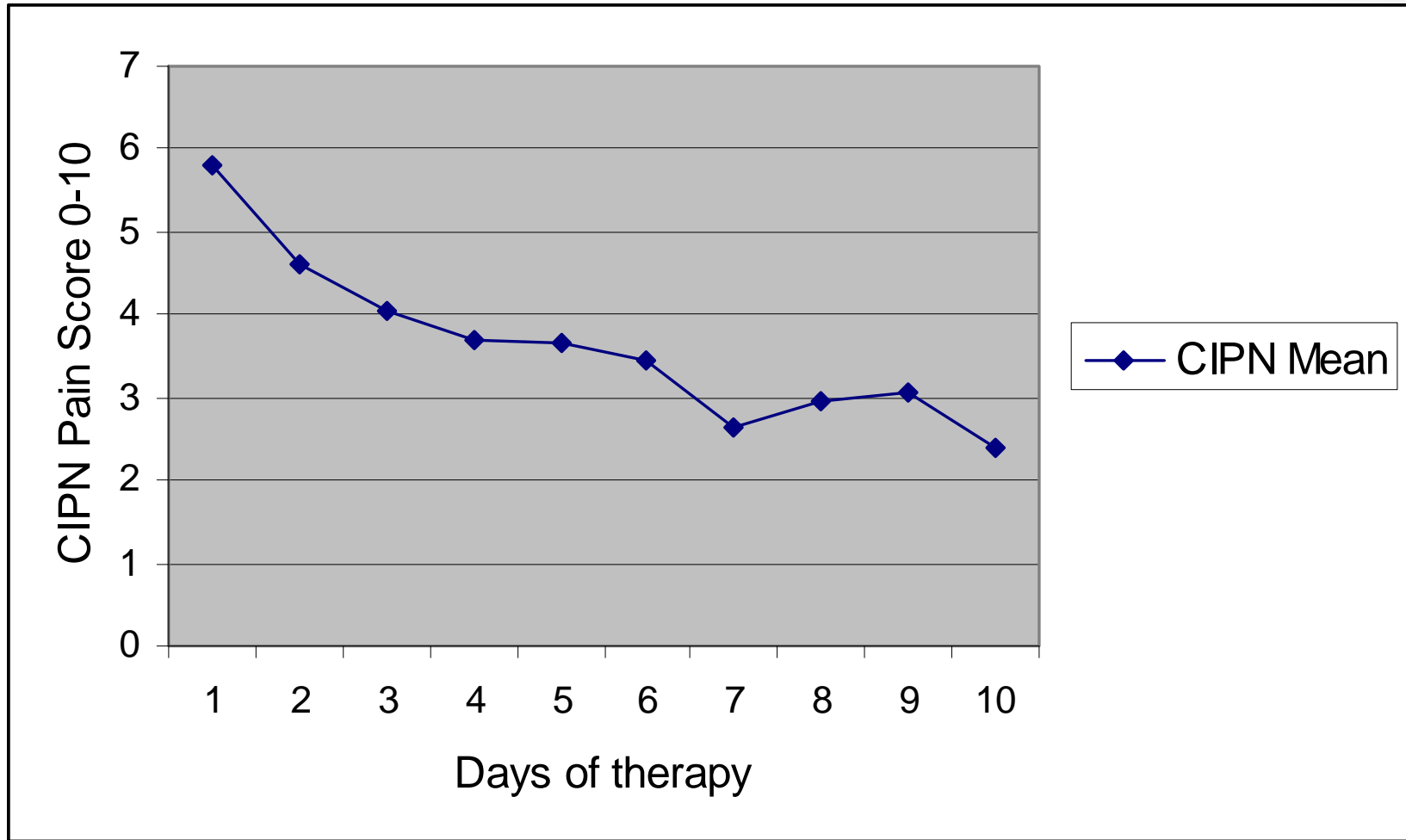


Calmare® Scrambler Therapy MC-5A works for chemotherapy induced neuropathic pain

Table: Effect of Electrocutaneous stimulation with Calmare® MC-5A therapy on Pain Scores¹

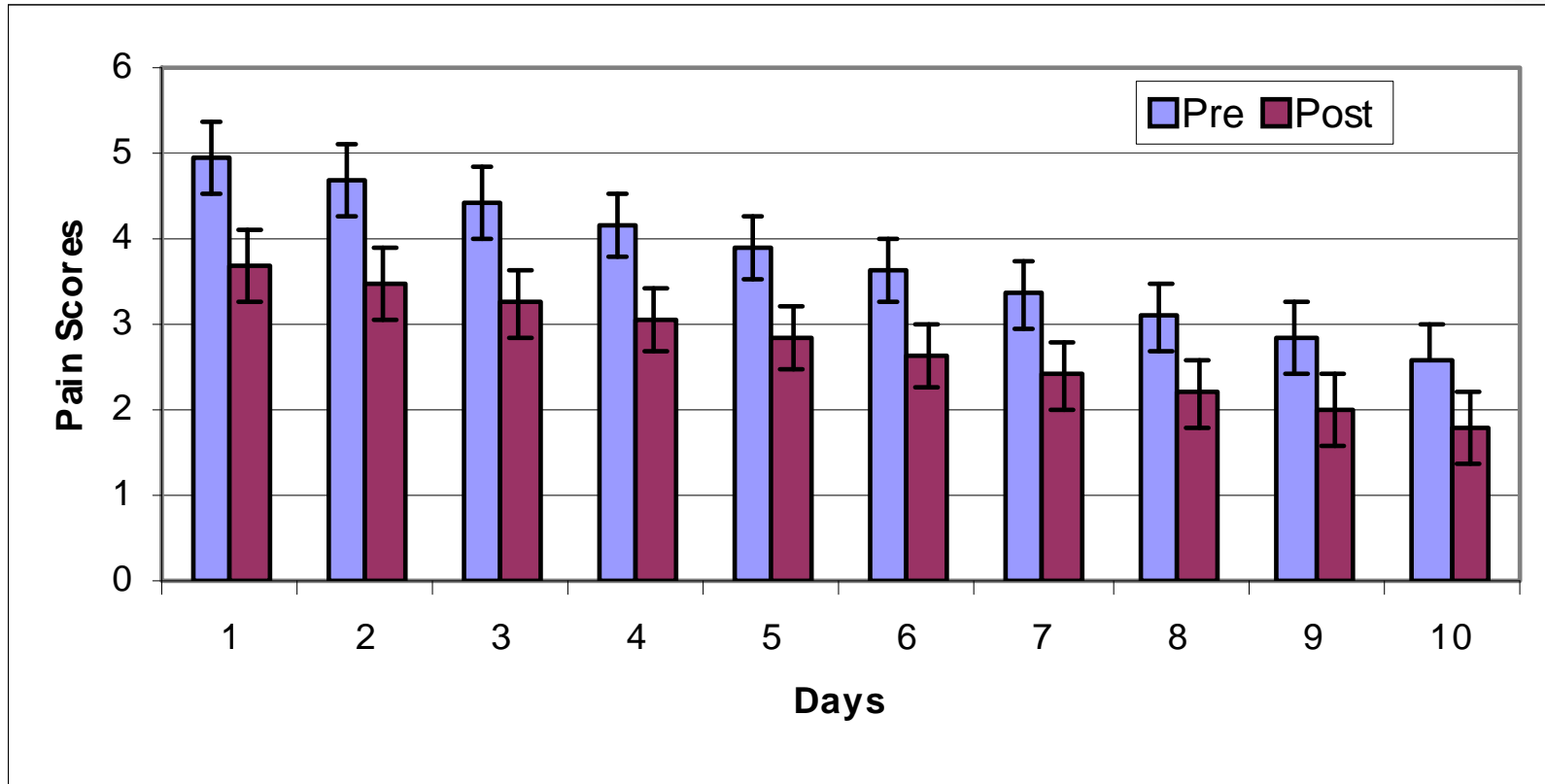
	Before	After	P value, statistical test
Reduction in pain by 20%	0	15 of 16 (94%)	<0.0001, Fischer's exact test
CIPN pain score	5.81±1.11	2.38±1.82 -59%	<0.0001, paired t test
Adjusted pain scores	4.9±0.4	1.8±0.4 -64%	< 0.0001
Daily reduction in pain scores	3.74± 0.38	2.72± 0.38 -1.02, -27%	< 0.001

MC5-A Calmare™ therapy works for chemotherapy induced neuropathic pain



Unadjusted CIPN "pain now" scores¹

MC5-A Calmare™ therapy works for chemotherapy induced neuropathic pain



Adjusted CIPN pain scores, repeated measures analysis¹

Calmare® Scrambler Therapy MC-5A

Interesting observations for CIPN

- Patients' pain go to ZERO and stay there for at least several weeks or months.
- Patients have noted relief of numbness, and return of normal sensation and motor function. Numbness alone does not respond.
- Some patients had pain relief from 6 to 0 in one 30 minute session, with no recurrence
- Protocol treatment is 10 -12 sessions at up to 45 minutes per session
- Retreat with a few sessions.

Scrambler Therapy helps neuropathic pain (post surgical, post herpetic, spinal stenosis)

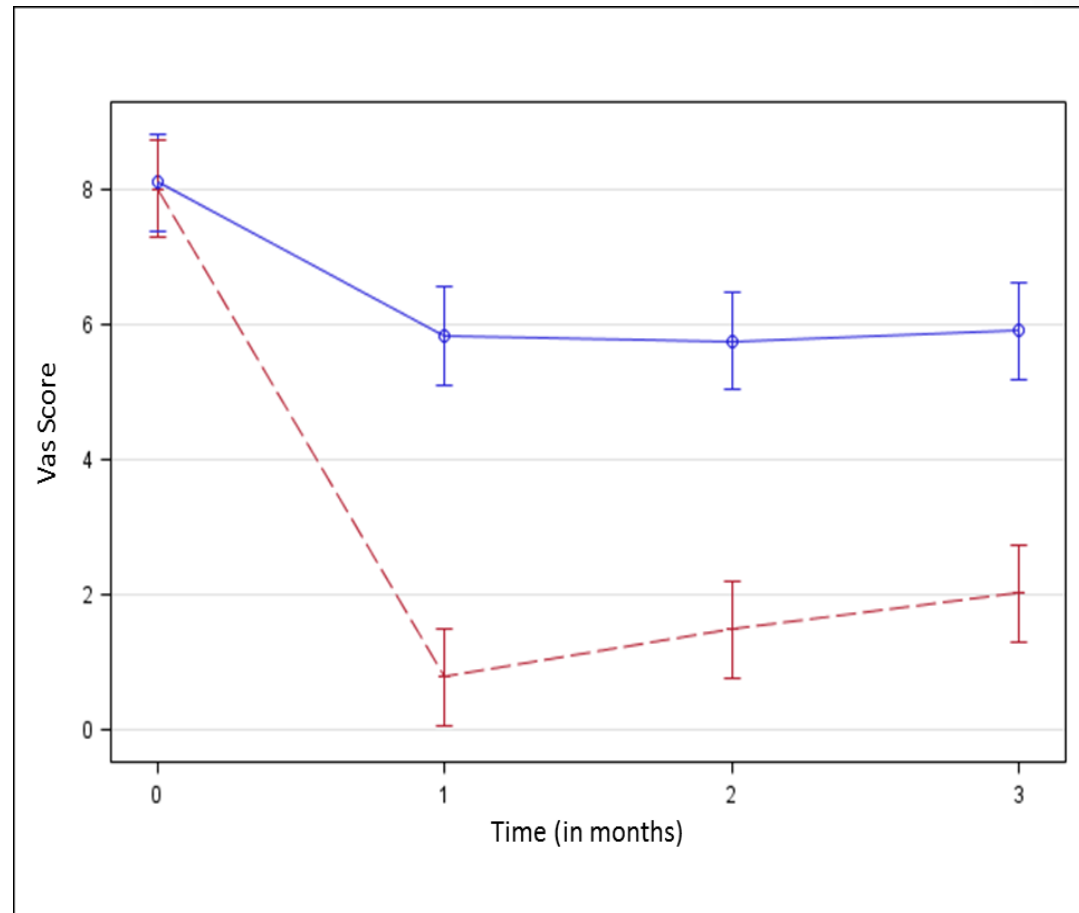
Marineo G, Vittorio I, Cristiano G, Vincenzo M, Smith TJ*. MC5-A Scrambler Therapy Relieves Chronic Neuropathic Pain More Effectively Than Guideline Based Drug Management, in press.

RCT in 52 patients with refractory peripheral neuropathy

26 in each arm, balanced, stratified
-Top: guideline based treatment

-Bottom: Scrambler added to not-working drugs

91% reduction in pain scores with no toxicity.



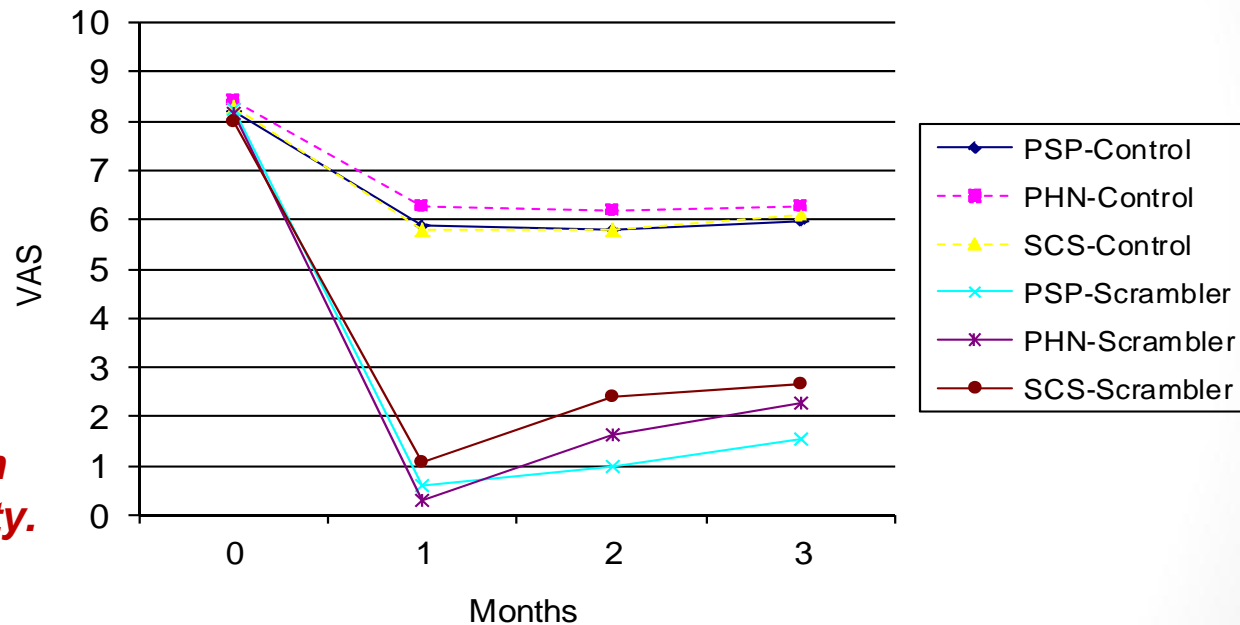
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Figure 3: Effect of treatment by type of pain



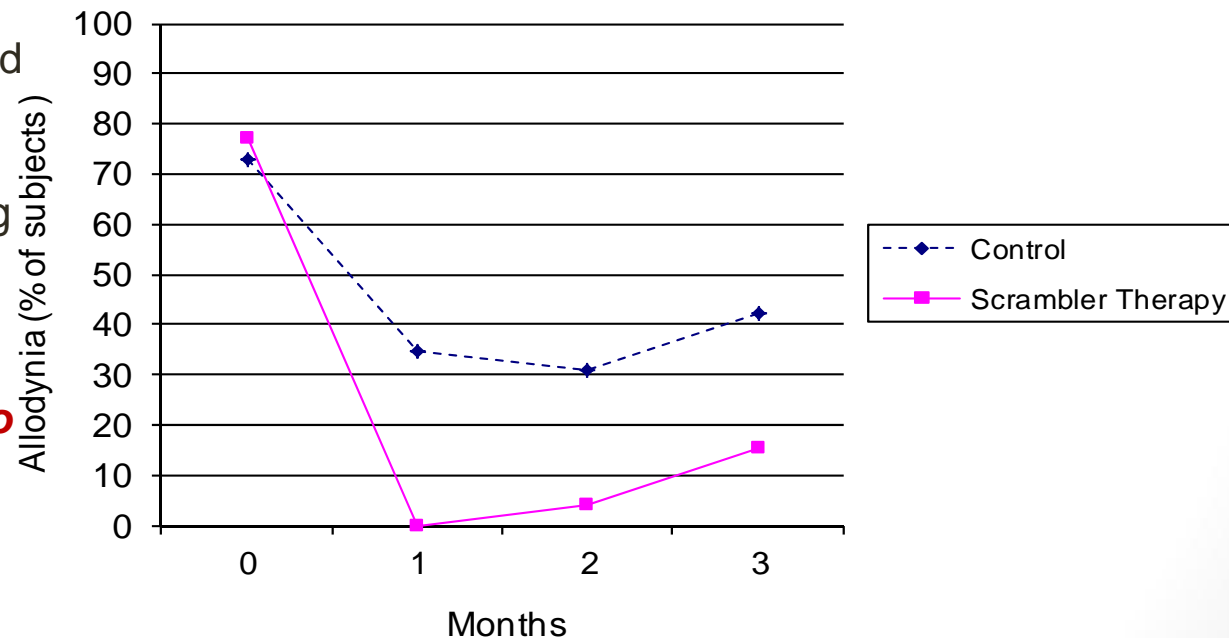
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Figure 4: Effect of treatment on allodynia



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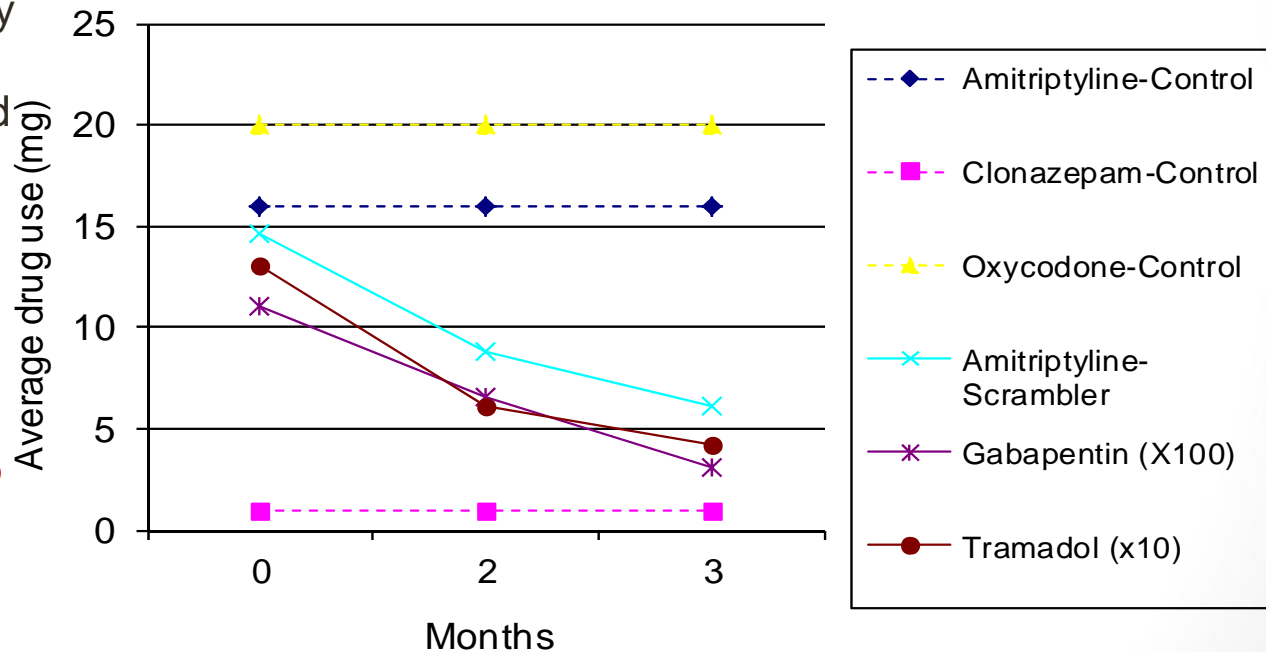
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Figure 5: Effect of treatment on pain medication use



The magnitude of pain reduction is **LARGE** but similar to that of other interventional therapies in RCTs vs. medical management

- Intraspinal bupivacaine + opioid, **VAS pain 7.57 to 3.67 (-52%)**. Smith T, et al, J Clin Onc 2002
- Spinal cord stimulators in neuropathic pain, **7.6 to 3.8 (over 50% reduction)** Kumar K, et al. Pain. 2007;132:179-88.
- Calmare[®], CIPN, **-59%**, Smith T, et al, JPSM 2010;40(6):883-891
- Calmare[®] MC-5A chronic neuropathic pain in RCT, **8 to 0.7 points (-91%)** (Marineo G, et al., in press, JPSM)

Lessons Learned

- Interactive modality between operator and patient
- Learning curve required for complex patient treatment
- Hospital facility environment recommended
 - Where people get Rx
 - Volume, expertise
- Requires trained medical professional (physician/nurse)
- Not a TENS device

Thank you.

Competitive Technologies, Inc.

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