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THE ROLE OF HIGH FREQUENCY ELECTRICAL STIMULATION IN THE CHEMOTHERAPY INDUCED PERIPHERAL NEUROPATHY POPULATION: A CASE SERIES

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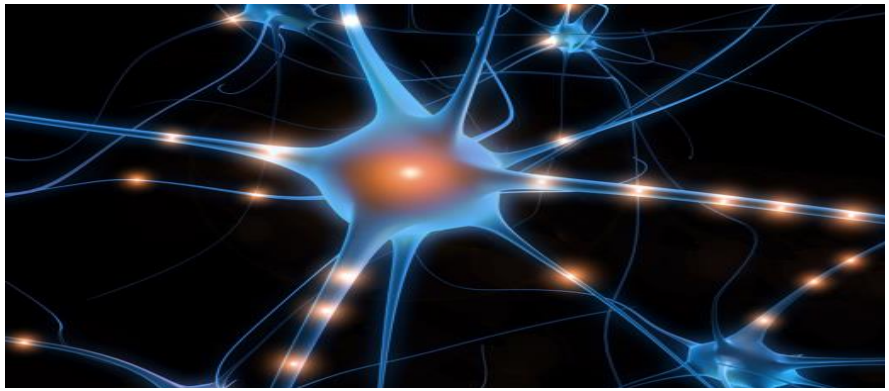

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Background

- Chemotherapy induced peripheral neuropathy (CIPN) is a dose-limiting effect of certain chemotherapy agents most common with Taxanes, Vinca Alkaloids, and Platinum compounds.
- The exact pathology of how CIPN happens is still under investigation.
- It is found that approximately 30-40% of patients can develop CIPN with treatments and is a contributing factor for early termination of chemotherapy (2014).

Previous studies

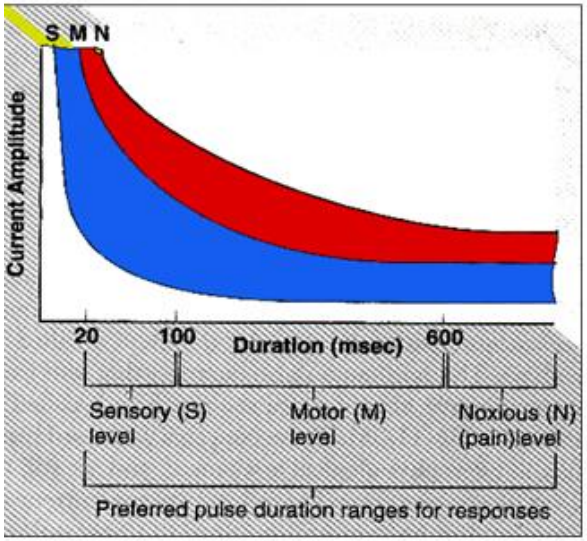
- 2010- case report using low frequency electrical stimulation found a 20% reduction in a numeric pain rating (NPR) in ten days. (2010 Smith, Coyne)
- 2013 - utilized acupuncture with 50 Hz of stimulation at certain points for 15 minutes for eight days, without significant effects when compared to vitamin B and placebo trials. (2013 Rostock).
- With both of these studies, there have been modest improvements in pain levels. Additionally, the use of low frequency electrical stimulation has been reportedly used for decreasing cancer pain and there has been some look at acupuncture for peripheral neuropathy pain with modest improvements.

Case study

- Metastatic gynecological cancer with CIPN
- High frequency stimulation (50Hz) was delivered two times a day for 14 days with the use of a sock and glove attachment to her home ES unit – an EMSI Flex-MT unit
- This patient reduced 30% of the time by 1 point on the NPR within sessions. However, while this is not a minimally clinically important difference, over two weeks, she had a reduction of 2 points on the NPR, which is shown to be above MCID for those with chronic pain (Farrar et al, 2001).
- She also had discharged her narcotic pain medications and utilized OTC pain medication one time in the two-week period.

Putting the pieces together

- Took the results of the initial case study and modified based on:
  - Research on CIPN and neuropathic pain
  - Research into higher frequency electrical stimulation



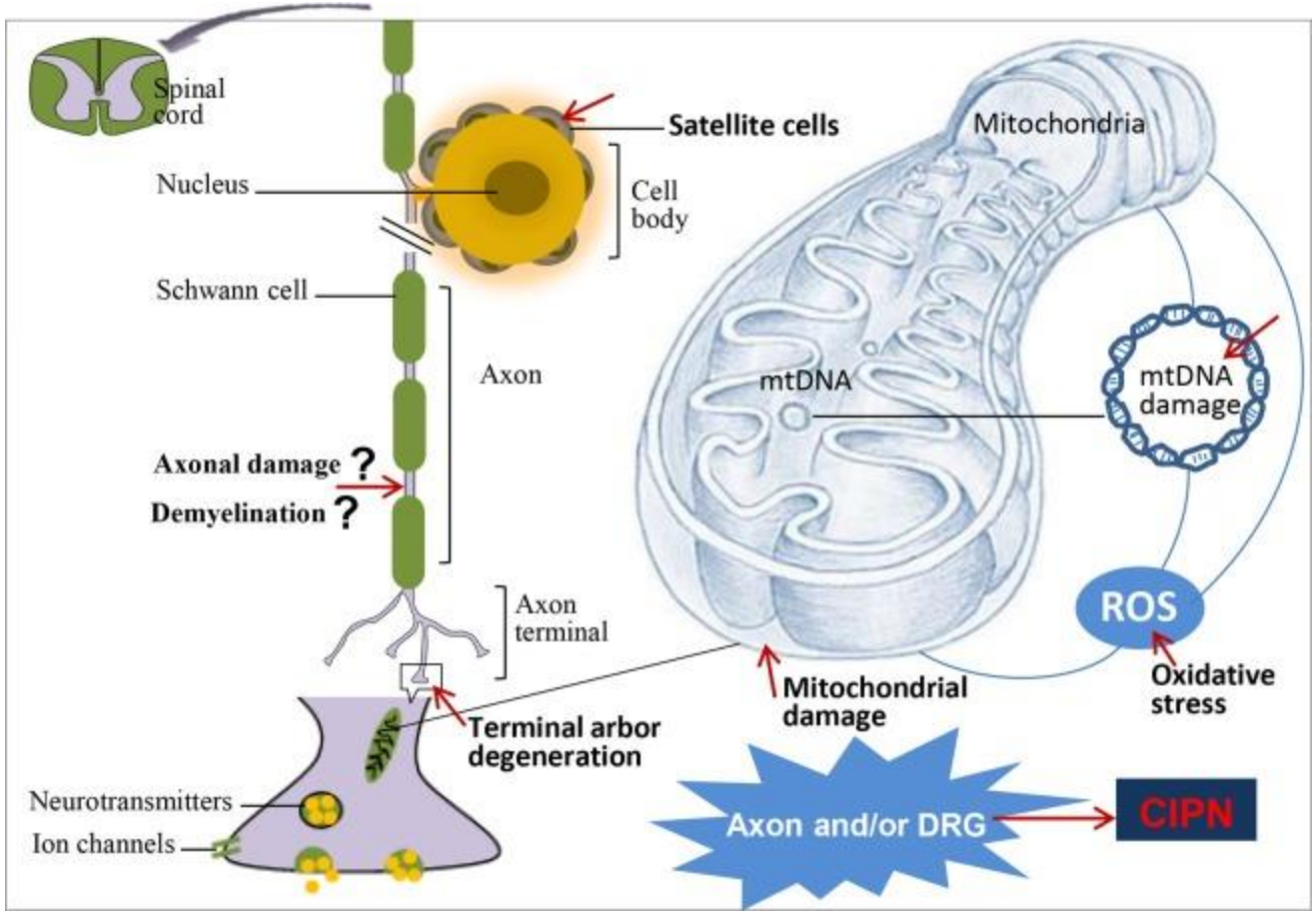
Chemotherapy Induced Peripheral Neuropathies

- There is similarities and doesn't just change sensation. In children, CIPN is noted most often with motor changes first. In adults – do we have motor changes? If so this leads us to other nerve fibers being affected – it may be both motor and sensory nerve fibers.

ES for Modulating Pain

- Selective stimulation of the large diameter afferent A-beta sensory fibers can result in gating noxious afferent input from smaller diameter unmyelinated nociceptive C fibers and small myelinated A-delta fibers at the level of the spinal cord (Michlovitz, Bellew, Nolan, 2012)
- Brief intense TENS suggested which combines both the sensory and motor components since CIPN appears to affect both.
- High frequency TENS will stimulate large diameter fibers and high duration is utilized when there is neurological damage. Small fibers will also be stimulated.

"Thus, peripheral nerve degeneration or small fiber neuropathy is generally accepted as underpinning the development of CIPN (Ling et al., 2010; Boyette-Davis et al., 2011; Burakgazi et al., 2011; Wang et al., 2012)."



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Purpose

The purpose of this study was to investigate the use of high frequency stimulation use at home to reduce patients' pain with a different electrical stimulation settings to determine if there were results similar to that of the previous case study or greater improvements.

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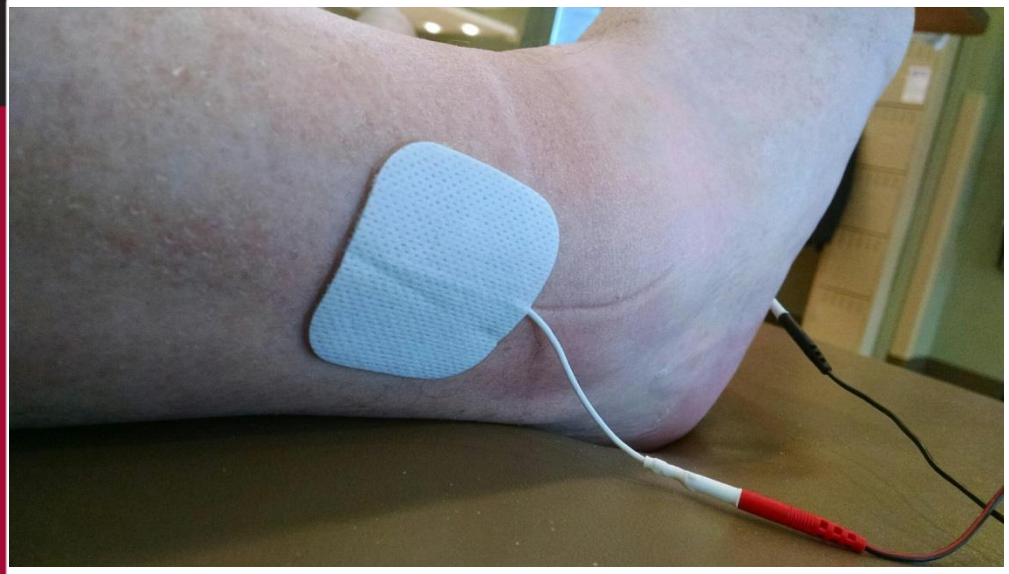
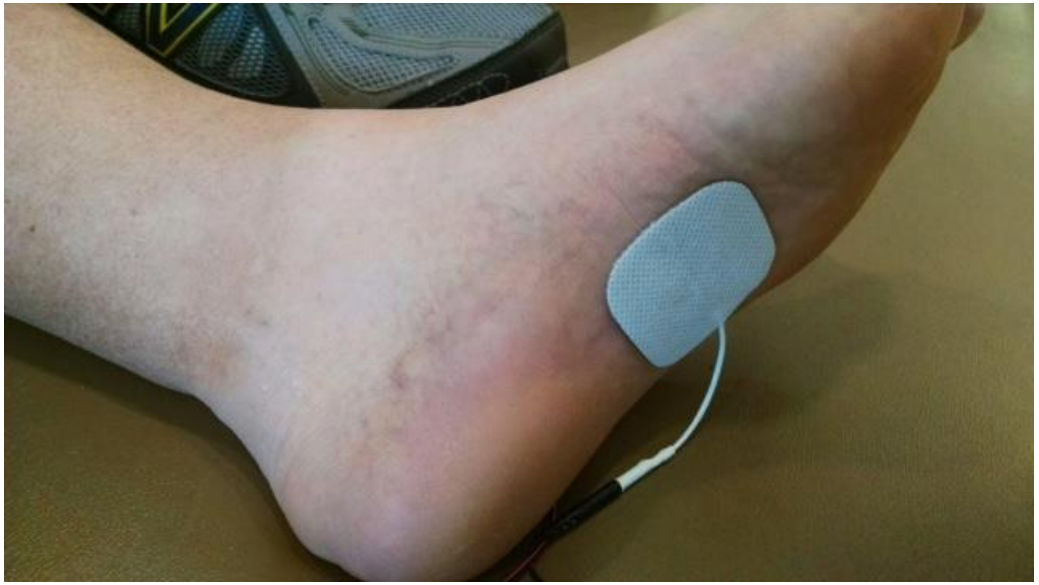
Investigative protocol design

- The participants will be using an FDA approved home electrical stimulation unit set at 80 Hz at 300 microsecond duration placed at the proximal and distal ends of symptom extension, on most affected dermatome pathway, for 20 minutes two times a day.
- Total length of time = 14 days



L4/5 dermatomal pathway most affected; put at the proximal and distal ends



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Exclusion criteria

- Age < 18 years old
- Spinal or brain metastasis (secondary to influence of these mets on pain in the extremities)
- Prior history of spinal surgery (secondary to the influence of previous neuropathy type pain)
- Changes in pain medications during the course of the study (or start of pain medication within two weeks of study)
- Open skin/wound tissue
- Pacemaker
- Diabetes
- Seizure disorder
- History of HIV
- Active coronary artery disease <6 months
- Pregnancy
- Past adverse reaction to ES unit
- Prior history/diagnosis of diabetic peripheral neuropathy or other peripheral neuropathies from vitamin or other disease process prior to their chemotherapy treatments.

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Inclusion criteria

- Age of > 18 years of age
- Diagnosis of of peripheral neuropathy s/p chemotherapy treatments or chemotherapy induced peripheral neuropathy, from either a licensed physician and/or their oncologist
- Undergoing treatment (>1 month) or have been through treatments (cessation <1 year) with any of the CIPN known medications such as Taxanes, Vinca Alkaloids, Bortezomib, or Platinum compounds
- Subjective average daily reports of pain >3/10 on a VAS scale or ADL dysfunction
- Pain experienced >1 month

Outcome measures

- TNSr Items: symptom extension, pin sensibility, vibration sensibility, strength, and tendon reflexes
- NPS-CIN items
- Numeric Pain Rating scale
- FACT-G (Quality of life scale)
- ECOG scale

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NPS-CIN

PLEASE CIRCLE ANSWERS TO THE FOLLOWING QUESTIONS:

	0	1	2	3	4
HOW INTENSE IS YOUR NEUROPATHY PAIN?	NOT AT ALL	MILD	MODERATE	SEVERE	EXCRUTIATING
HOW UNPLEASANT IS YOUR NEUROAPTHY PAIN	NOT AT ALL	MILD	MODERATE	SEVERE	EXCRUTIATING
HOW SHARP DOES YOUR NEUROPATHY PAIN FEEL?	NOT AT ALL	MILD	MODERATE	SEVERE	EXCRUTIATING
HOW DEEP DOES YOUR NEUROPATHY PAIN FEEL?	NOT AT ALL	MILD	MODERATE	SEVERE	EXCRUTIATING
HOW NUMB DOES YOUR NEUROPATHY PAIN FEEL?	NOT AT ALL	MILD	MODERATE	SEVERE	EXCRUTIATING
HOW TINGLY DOES YOUR NEUROPATHY PAIN FEEL?	NOT AT ALL	MILD	MODERATE	SEVERE	EXCRUTIATING

Adapted from Table 1 Modified 5-Item TNSr and NPS-CIN Item Scoring found in Cancer Nurs. 2010 Mar 30. [in print]. The Reliability and Validity of a Modified Trotal Neuoropthy score-Reduced and Neuropathic Pain Severity Items When Used to Measure Chemotherapy-Induced Peripheral Neuropathy in Patients Receiving Taxanes and Platinums. Lavoie Smith EM et al.

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TNSr

SYMPTOM EXTENSION (Description of how far the pain, tingling, numbness goes up the limb):

PIN SENSIBILITY (tested using Semmes Weinstein monofilament):

VIBRATION SENSIBILITY (tested using a 128 Hz tuning fork):

REFLEXES (using a reflex hammer bilaterally at bilateral tricep, brachioradialis, patella, and achilles):

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Patient log

Please complete this log at each session (A and B) each day and bring back with you at your next visit:

Day/Time	Pain Prior* (0 to 10)	Pain After* (0-10)	Activity Level Prior (Increased, Decreased, Same)
1 A			
1 B			
2 A			
2 B			
3 A			
3 B			
4 A			
4 B			
5 A			
5 B			
6 A			
6 B			
7 A			
7 B			
8 A			
8 B			
9 A			
9 B			
10 A			
10 B			
11 A			
11 B			
12 A			
12 B			
13 A			
13 B			
14 A			
14 B			

* 0-10 scale: 0 is no pain/discomfort/symptoms at all and 10 is the worst pain imaginable
Please complete 20 minutes of the stimulation two times daily. You should make sure the settings on your device are set at: 80 Hz and 300 ms pulse duration. The pad placement should be according to the picture given to you.

Should you have any questions or problems before your follow up call, please call Kathleen at 215-721-1871.
Your follow up phone calls will be on:

_____ at _____ _____ at _____
_____ at _____ _____ at _____

Participant 1

- 60 Year old female
- Dx: s/p Ovarian Cancer
- Medication hx**: Carboplatin, Doxcil, Taxol**

Participant 2

- 63 year old female
- Dx: s/p Ovarian Cancer
- Medication hx: **Carboplatin, Taxotere**
- Excluded from study secondary to discharge from medication >1 year
- Patient ended up wanting to continue to trial it at home after traditional therapy concluded – results provide some insights

Participant 3

- 77 year old male
- Dx: Multiple Myeloma
- Medication hx: **Acyclovir**

Participant 4*

- 53 year old female
- s/p Breast Cancer
- Medication Hx: **Herceptin, Carboplatin**

Participant 5

- 41 year old female
- Dx: Cervical CA
- Medication Hx: **Carboplatin**

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Results	Change in Pain	Change 5-Item TNSr	Change NPS-CIN	Total Change		Fact-G
Participant 1	4	9	1	10		5
Participant 3	3	8	6	14		1
Participant 4	3	9	-1	8		-2
Participant 4-b	1.5	3	7	10		4
Participant 5	5	8	8	16		5
MCID	**1-1.7**	**NA**	**NA**	**NA**		**3 to 7**

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	Percent Change Right	Percent Change Left
Hip Flexion	3%	-16%
Knee Flexion	-9%	-7%
Knee Extension	2%	8%
Ankle Dorsiflexion	42%	29%
Ankle Plantarflexion	-41%	-10%
1st Metatarsal Flexion	-2%	222%
1st Metatarsal Extension	-30%	-38%
Toe Flexion	147%	68%
Toe Extension	112%	102%

Participant 3	Percent Right	Percent Left
Hip Flexion	15%	6%
Knee Flexion	6%	30%
Knee Extension	-1%	-12%
Ankle Dorsiflexion	-35%	-34%
Ankle Plantarflexion	-5%	59%
1st Metatarsal Flexion	-8%	-16%
1st Metatarsal Extension	-14%	-21%
Toe Flexion	18%	26%
Toe Extension	7%	17%

Participant 4	Percent Right	Percent Left
Hip Flexion	-23%	-22%
Knee Flexion	-40%	-47%
Knee Extension	29%	-19%
Ankle Dorsiflexion	25%	-2%
Ankle Plantarflexion	45%	-9%
1st Metatarsal Flexion	81%	26%
1st Metatarsal Extension	-44%	-64%
Toe Flexion	96%	67%
Toe Extension	73%	16%

Participant 4B	Percent Right	Percent Left
Hip Flexion	1%	22%
Knee Flexion	23%	40%
Knee Extension	-3%	7%
Ankle Dorsiflexion	-21%	-25%
Ankle Plantarflexion	-1%	-2%
1st Metatarsal Flexion	-45%	-29%
1st Metatarsal Extension	-35%	-52%
Toe Flexion	29%	46%
Toe Extension	14%	5%

Participant 5	Percent Right	Percent Left
Hip Flexion	-13%	37%
Knee Flexion	12%	9%
Knee Extension	-7%	78%
Ankle Dorsiflexion	-38%	-32%
Ankle Plantarflexion	70%	49%
1st Metatarsal Flexion	130%	183%
1st Metatarsal Extension	-59%	-27%
Toe Flexion	93%	29%
Toe Extension	-20%	0%

Highlight indicates greater than minimally detectable change

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Brief Conclusions

- Clinical important changes in strength made in a majority of areas of the LE (>4%)
- FACT – G scores show improvement in 50% of the participants and particularly in the **physical well being area and above MCID**
- Pain change above MCID in all
- Every participant had a clinical important change on the TNSr/NPS-CIN
- Every participant reportedly able to wear shoes again

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Further research modifications

- Longer than 14 days
- Decreasing to 15 minutes
- Adding Biodex testing as an outcome measure
- Study design to do: Estim alone, exercise alone/balance/strengthening, EStim+exercise, no intervention
- Taking population and doing a follow up after 1 month, 3 months, 6 months, and 12 months of cessation of treatment with electrical stimulation