Does Therapeutic Massage Ameliorate Chemotherapy-Induced Peripheral Neuropathy?

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INTRODUCTION and CONCEPT

Chemotherapy-induced peripheral neuropathy (CIPN):

- Common, potentially severe, dose-limiting side effect of many 1st and 2nd line chemotherapy regimens.
- Affects ~1/3 of cancer patients who receive chemotherapy , often requiring dose reduction or interruption of treatment.
- Affects feet and often hands as well.
- Long-lasting or permanent in some patients.
- Profound impact on quality of life (QoL).
- Etiology unclear, but causative agents include:
  - Taxanes: e.g. Docetaxel, Paclitaxel, Taxol
  - Platins: e.g. Cisplatin, Carboplatin, Oxaliplatin.

Current Treatment for CIPN:

- No established and acceptable standard of care.
- Standard practice (as for other chronic nerve pain):
  - Steroids, numbing agents, antidepressants, anticonvulsants, opioids/narcotics
  - In long-term these drugs can themselves be toxic.
- During anti-cancer chemotherapy:
  - Reduce chemotherapy dose and/or discontinue it.
- Interest in alternative, non-pharmacologic approaches.

HYPOTHESES

Primary:

Therapeutic massage reduces sensory signs and symptoms of CIPN, and improves quality of life.

Secondary:

Effects are mediated by, or reflected in, improved peripheral blood flow.

METHODS

Non-randomized controlled design (Grade 2 CIPN):

- Treatment Group (n=15):
  - 12 treatments in 5 weeks: 15 minutes per lower extremity
  - Follow for 19 additional weeks
- Monitoring Group (observation only) (n=8):
  - Eligible but cannot accommodate treatment schedule
  - Monitor for 6 weeks.

Assessments

- Neuropathic symptoms (NPS-CIN, CINPAT, EORTC QLQ-CIPN-20): severity, quality, anatomic symptom extension
- Neuropathic signs: monofilament, vibration sensitivity (TNSr)
- Cancer-specific quality of life (EORTC QLQ-30), including impacts on activities of daily living
- Superficial circulation of feet: emitted heat (FLIR camera), localized temperature.

PRELIMINARY RESULTS: TREATMENT GROUP

STUDY POPULATION (N=10)

Grade 2 CIPN:

- Moderate; Limiting instrumental ADL
- secondary to taxane or platin.

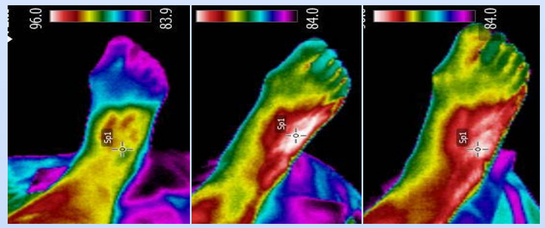
Characteristic	N (%)
Female	8 (80%)
Male	2 (20%)
Age (years)	61.2 ± 11.9 (48 – 82)
CIPN (years)	2.0 ± 3.0 (0.3–7.4)
Diabetes	1 (10%)
Smoker	2 (20%)
Prior anti-CIPN Rx	3 (30%)
Chemotherapy	Platin: 2, Taxane: 7, Both: 1
Primary site	Breast: 6, Colon: 2, Lung: 4

SYMPTOM SEVERITY (CIPNAT SUBSET)

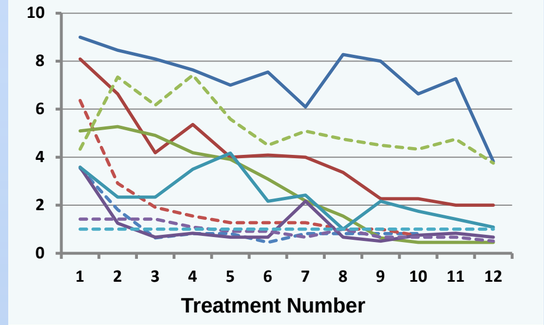
Score (0 – 10)	Mean (Median) Before	After	Change	p-value[1]
Composite	4.6 (4.0)	1.4 (0.8)	-3.2 (-3.0)	0.006*
Numbness	6.5 (5.8)	2.8 (2.7)	-3.6 (-4.0)	0.011*
Cold Sens.	5.8 (7.5)	1.6 (1.0)	-4.1 (-5.0)	0.011*
Tingling	5.4 (5.8)	1.6 (1.0)	-3.8 (-4.2)	0.006*
Aches	3.7 (4.0)	0.6 (0.0)	-3.1 (-3.5)	0.011*
Nerve pain	3.6 (3.8)	0.7 (0.0)	-3.0 (-3.2)	0.011*
Weakness	3.3 (3.5)	0.6 (0.0)	-2.8 (-2.2)	0.011*

[1] Wilcoxon matched-pairs signed-rank test.
N=10 participants. Higher score = more severe.
Subset of CIPNAT (CIPN Assessment Tool elements)

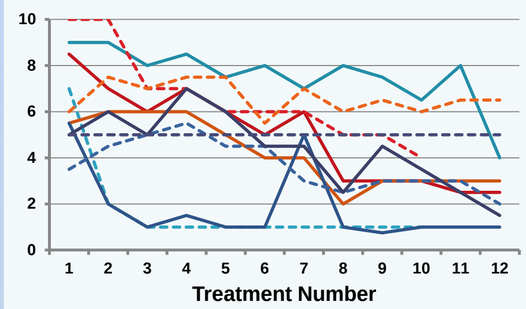
FLIR THERMOGRAPHY: EXAMPLE



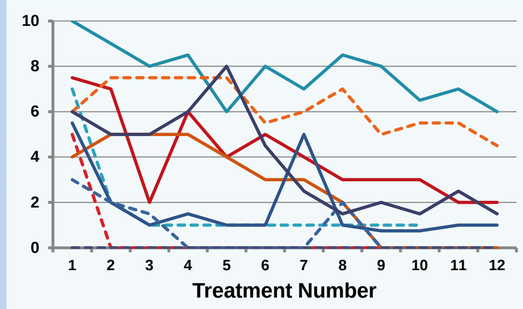
Composite Symptom Severity



Numbness



Tingling



NEUROPATHIC PAIN SCORE (NPS)

Significant reductions (improvement) in 5-point Pain Quality scores using NPS-CIN.

QUALITY OF LIFE (EORTC QLQ)

Significant improvements in Pain, Fatigue, Physical domains, relevant symptoms and ability to be physically active.

PREVIOUS WORK

Cunningham et al. Case Report of a Patient with Chemotherapy-Induced Peripheral Neuropathy Treated with Manual Therapy (Massage). Supportive Care in Cancer. Epub 2011 July 16.

SPECIFIC AIMS

Aim 1

Assess impacts of massage on:
- CIPN signs & symptoms
- QoL

CORRELATE

Aim 2

Assess impacts on measures of superficial circulation

Aim 3

Establish design feasibility:
- Treatment and monitoring schedules
- Assessment tools
- Patient design preferences.

Estimate effect sizes (pre-post treatment effect).
Design future Phase III RCT of efficacy and mechanism.

CONCLUSIONS

Major Findings to Date:

- Improvements in symptoms "As good as expected with drugs"!
- Are additional treatments advisable for patients with worse or more established symptoms?
- Durability: "maintenance treatments"?
- Mechanism: temperature appears to increase after treatment is completed. Analyses are pending.

Issues for Future Consideration:

- Planning randomized clinical trial (RCT):
  - No acceptable standard of care for "control"
  - Impossible to be "blinded".
- Which patients are most likely to benefit?
- Does efficacy vary by chemo agent, total dose?
- Does variability in delivery of treatment elements affect efficacy?

FUTURE RESEARCH PLANS

Address Efficacy and Physiologic Mechanisms:

- RCT in patients with established CIPN.
- RCT for prevention or reduction of CIPN in patients receiving chemotherapy
- Case-control study:
  - Blood circulation in feet of CIPN patients vs non-CIPN cancer controls
- Cohort study:
  - Among patients receiving chemo, do changes in superficial circulation predict risk for, or onset of, symptomatic CIPN?

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