
# CRYOCOMPRESSION vs CONTINUOUS-FLOW COOLING: OPTIMAL METHOD TO DELIVER LIMB HYPOTHERMIA IN PREVENTING CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY

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National University of Singapore; National University Hospital, Singapore

NUS National University of Singapore

NUHS National University Health System

National University Cancer Institute, Singapore (NCIS)

HAEMATOLOGY ONCOLOGY RESEARCH GROUP

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# Faculty Disclosure

| | |
|---|---|
| ✓ | No, nothing to disclose |
| | Yes, please specify: |

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# Unmet clinical need

## Chemotherapy-induced peripheral neuropathy

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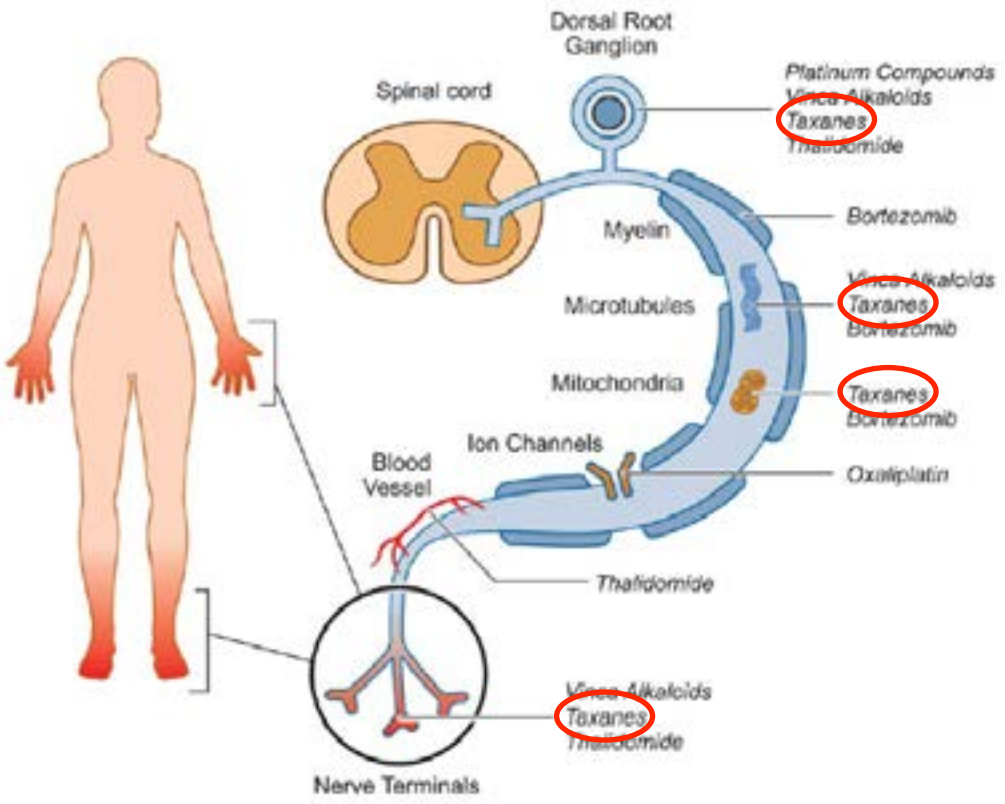


***"Glove-and-Stocking" distribution of CIPN symptoms***

- Damage to peripheral nerves due to **neurotoxic chemotherapeutic agent**
- Occurs in **57-83%** of patients treated with taxane and platinum chemotherapy
- Only symptomatic treatment – pain killers/ **Dose limitation** and reduction


**AJ Windebank *et al.*, *J Perip Nerv Syst*, 2008.**

**SB Park *et al.*, *CA Cancer J Clin*, 2013.**

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# Background

## Limb hypothermia for preventing CIPN

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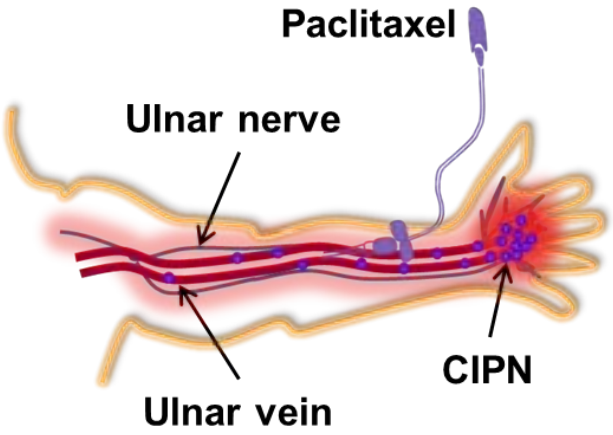
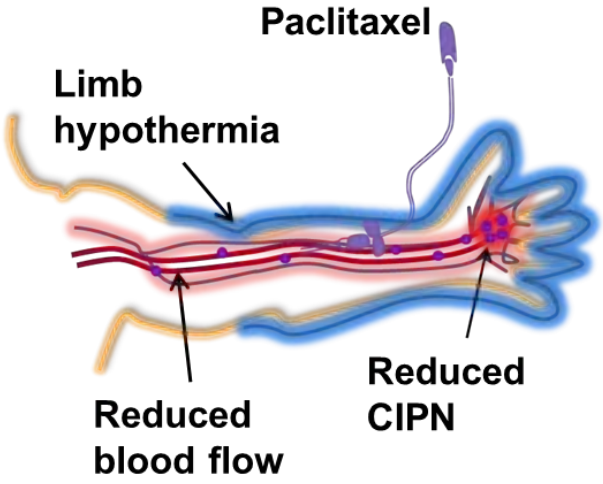
**Chemotherapy**




**Limb hypothermia**




US Patent Application No.: 14/761,239
A. Bandla *et al.*, *Acta. Oncol.*, 2015.
R. Sundar, A.Bandla *et al.*, *Front. Oncol.*, 2017.

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# Background

## Temperature-dependent hemodynamics

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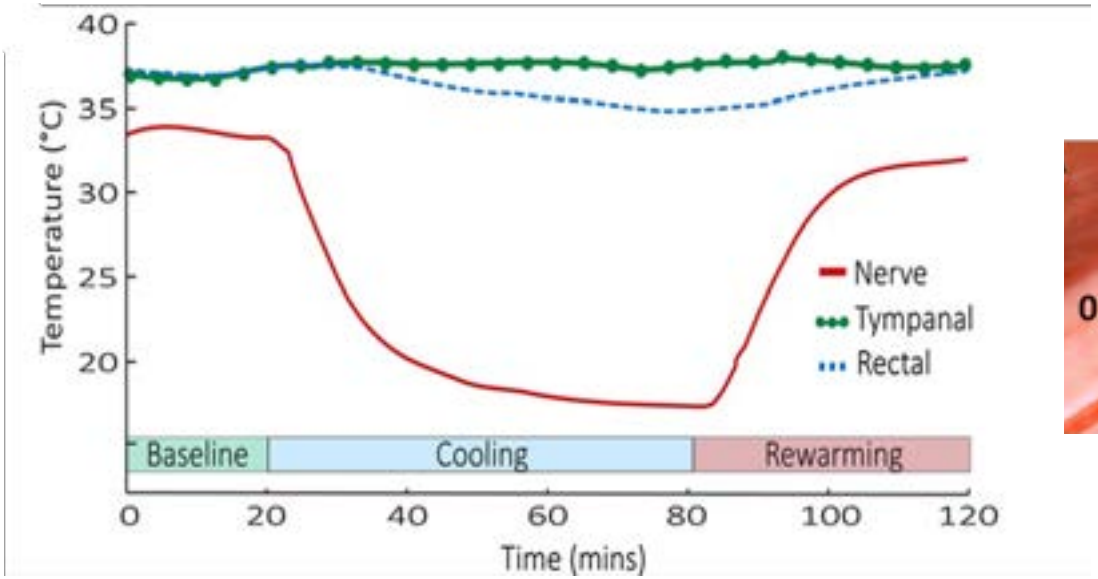


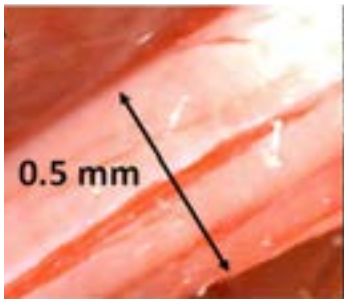


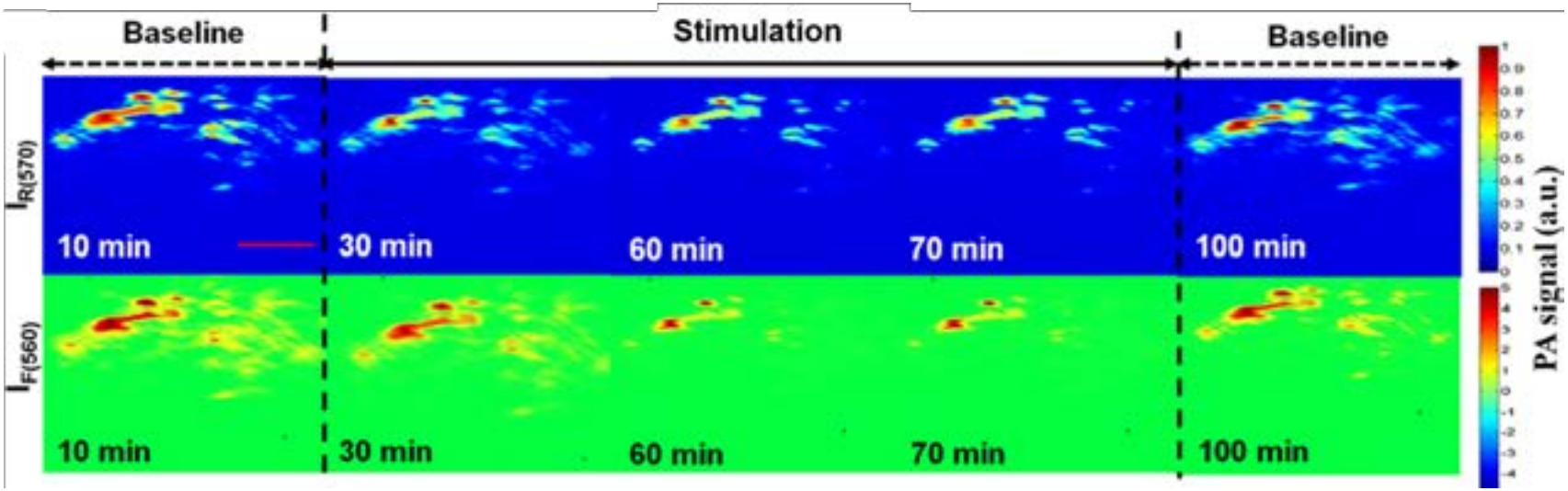




LD Liao *et al.*, *Biomed Eng Online*, 2013.

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# Background

## Modes of limb hypothermia for preventing CIPN

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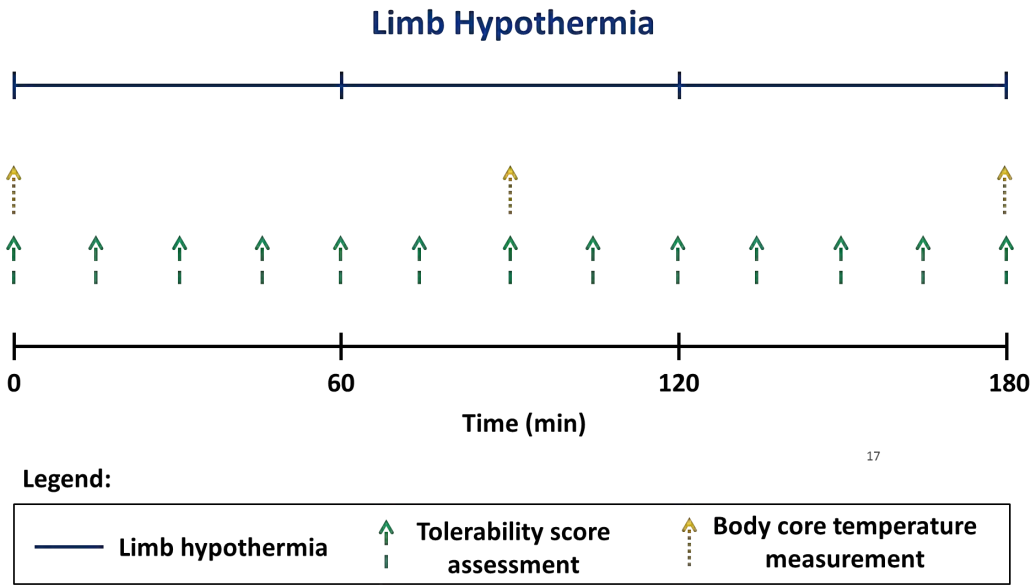
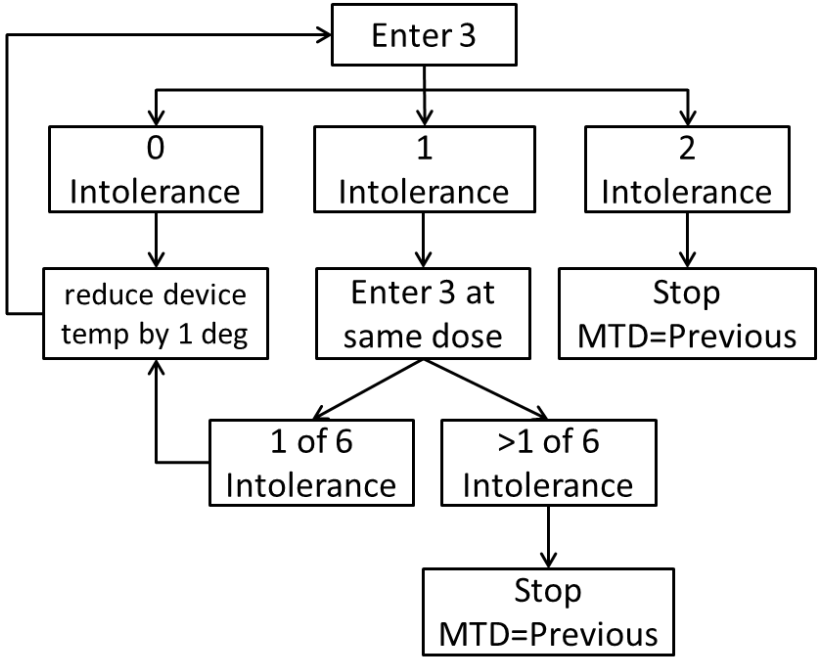
http://pioneerintrees.com/tag/cryotherapy/
US Patent Application No.: 14/761,239
https://www.huffingtonpost.co.uk/laura-price/my-chemotherapy-diary-part-iii_b_2130557.html

# Experiment set-up

## Limb hypothermia in healthy volunteers

- **Healthy volunteers** were recruited for study
- Limb hypothermia with continuous, multi-channel temperature monitoring





A. Bandla *et al.*, *Acta. Oncol.*, 2015.
R. Sundar, A.Bandla *et al.*, *Front. Oncol.*, 2017.

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# Results

## Safety and tolerability of limb hypothermia in healthy volunteers

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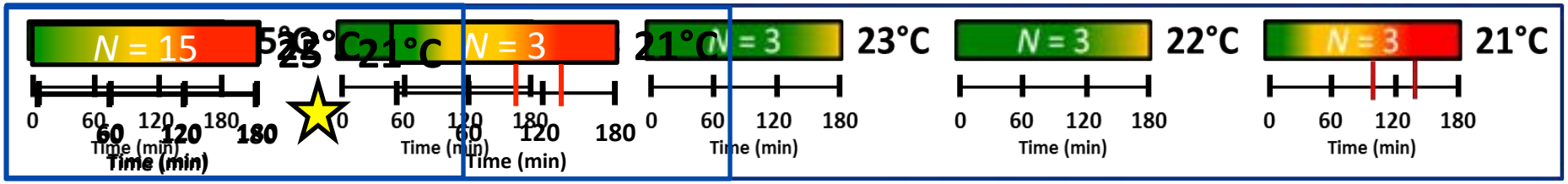
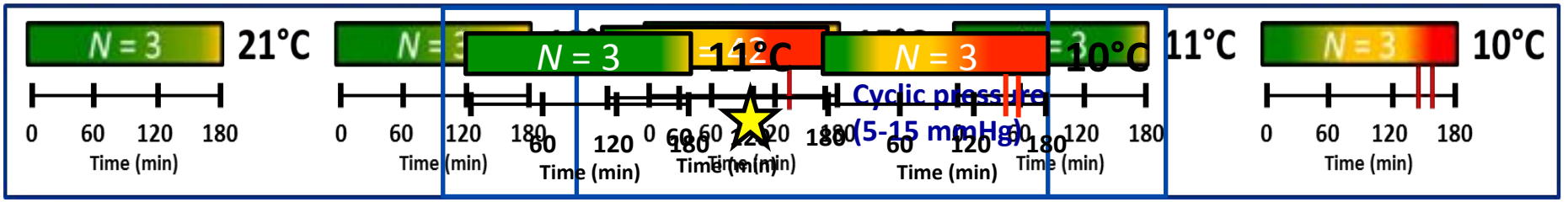
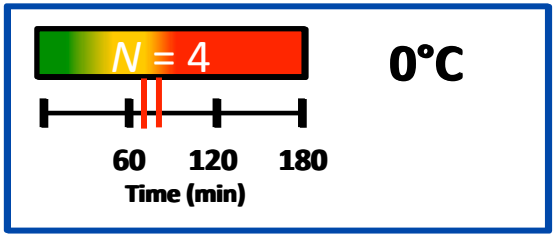
### Continuous-flow cooling
(cooling without pressure)




### Cryocompression
(cooling + pressure)




### Frozen gloves





A. Bandla *et al.*, *Acta. Oncol.*, 2015.
R. Sundar, A.Bandla *et al.*, *Front. Oncol.*, 2017.

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# Results

## Safety and tolerability of limb hypothermia in cancer patients

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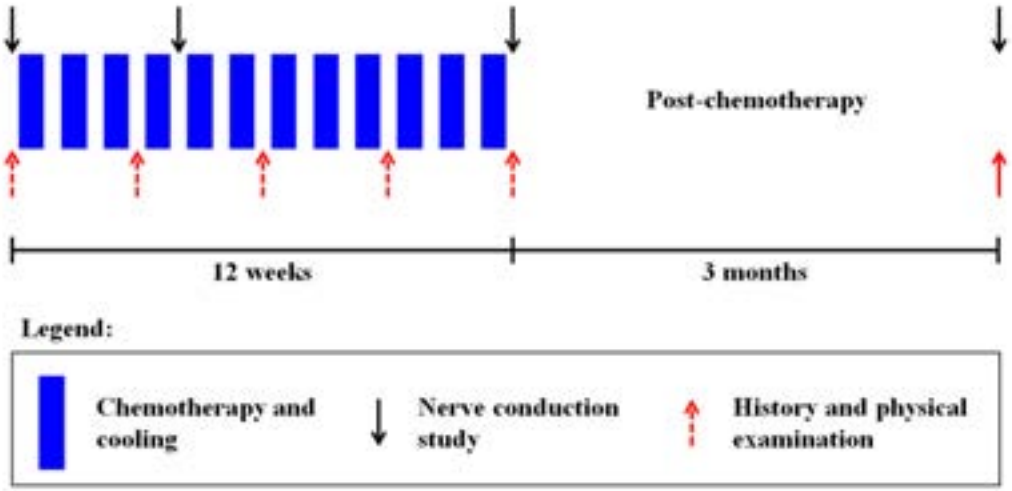
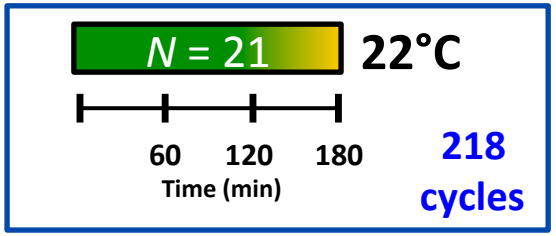
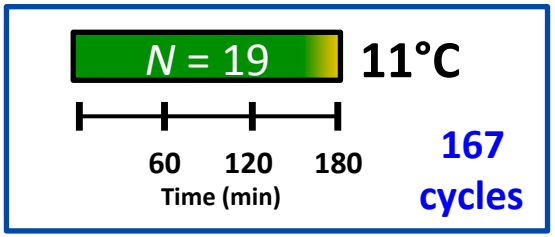



### Continuous-flow cooling
(cooling without pressure)




### Cryocompression
(cooling + pressure)




R. Sundar, A.Bandla *et al.*, *Front. Oncol.*, 2017.
R. Sundar, A.Bandla et al., ASCO, 2018.

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# Results

## Skin temperature changes in healthy volunteers

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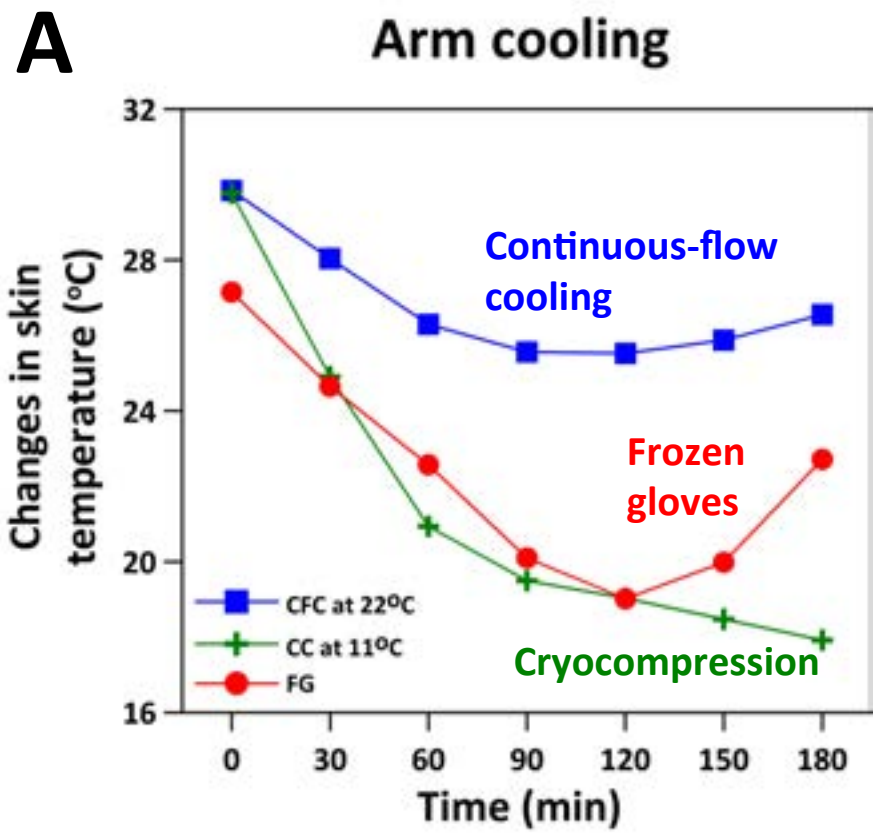


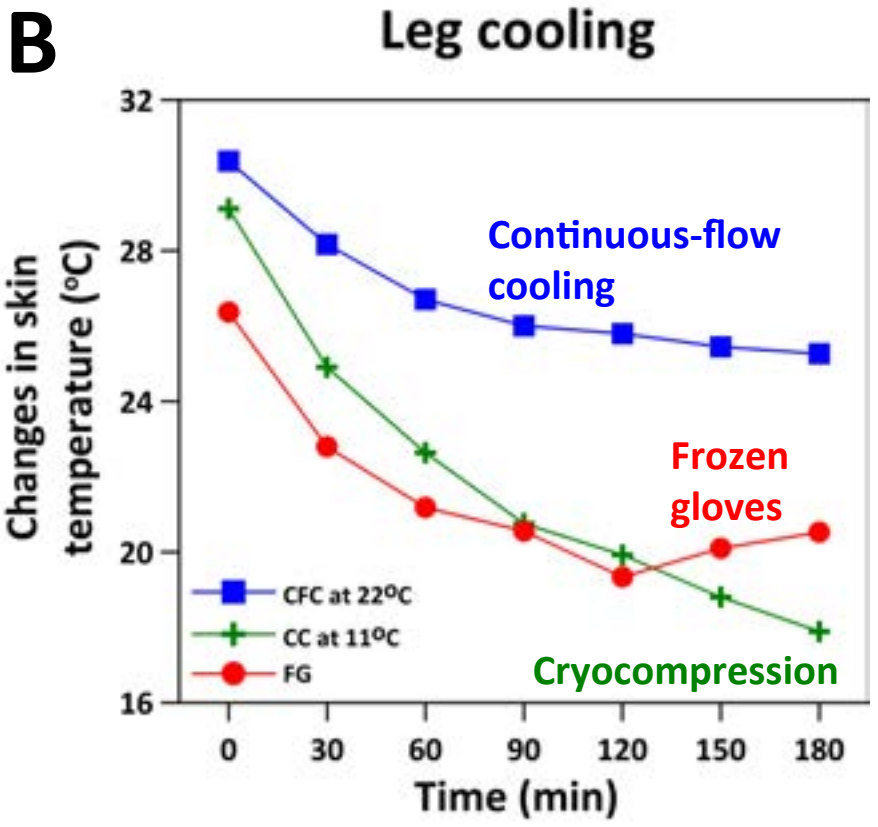



A. Bandla *et al.*, *Acta. Oncol.*, 2015.
R. Sundar, A.Bandla *et al.*, *Front. Oncol.*, 2017.

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# Conclusions

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- **Continuous-flow cooling and Cryocompression are safe and well tolerated by healthy volunteers for a duration of 3 hours.**
- **Frozen gloves were minimally/not tolerated for a duration of 3 hours.**
- **Cryocompression allows for limb hypothermia at lower temperatures than continuous-flow cooling, with similar safety profile.**
- **Cryocompression may provide greater efficacy in preventing CIPN in cancer patients, with clinical trials currently ongoing (NCT03248193).**

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# Acknowledgements

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**We sincerely thank:**

- **All volunteers and patients who participated in our trials.**
- **SINAPSE and Haematology Oncology Research Group team.**
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# Acknowledgements

## PreChIN Team @ NUHS

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# Thank You!

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# Experiment set-up

## Measures of tolerability

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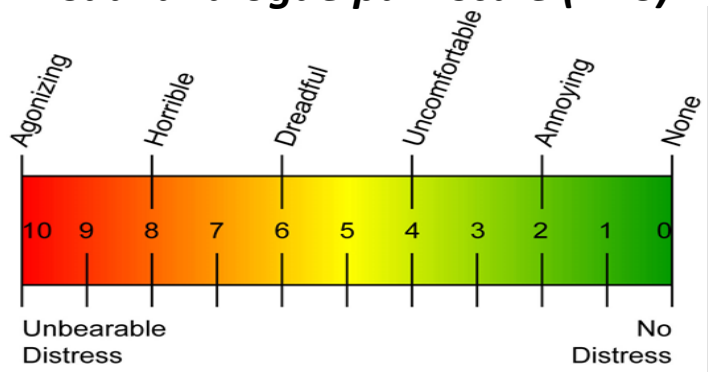
### *Visual analogue pain scale (VAS)*




### *Shivering assessment scale (SAS)*

0 – none
1 – mild
2 – moderate
3 – severe

### *Subjective tolerance scale (STS)*

0= tolerated
1 = no problem maintaining
2=tolerating cooling, but not without discomfort
3= only barely tolerated
4= intolerable

### *Composite Tolerability Score (CTS)*

**Intolerable**
>7 on VAS **OR** > 2 on SAS **OR** > 3 on STS
**OR**
>6 on VAS **AND** >1 on SAS **AND** >1 on STS


**A Bandla *et al.*, *Acta. Oncol.*, 2015.**
**R. Sundar, A.Bandla *et al.*, *Front. Oncol.*, 2017.**

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Acta Oncologica

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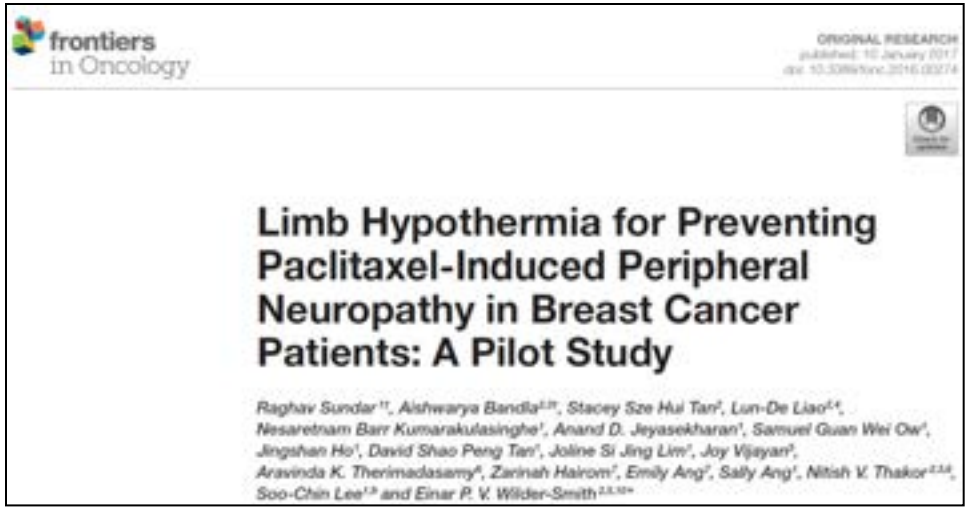
## Hypothermia for preventing chemotherapy-induced neuropathy – a pilot study on safety and tolerability in healthy controls

Aishwarya Bandla, Raghav Sundar, Lun-De Liao, Stacey Sze Hui Tan, Soo-Chin Lee, Nitish V. Thakor & Einar P. V. Wilder-Smith



frontiers in Oncology

ORIGINAL RESEARCH

## Limb Hypothermia for Preventing Paclitaxel-Induced Peripheral Neuropathy in Breast Cancer Patients: A Pilot Study

*Raghav Sundar[1†], Aishwarya Bandla[2,3†], Stacey Sze Hui Tan[2], Lun-De Liao[2,4], Nesaretnam Barr Kumarakulasinghe[1], Anand D. Jeyasekharan[1], Samuel Guan Wei Ow[1], Jingshan Ho[1], David Shao Peng Tan[1], Joline Si Jing Lim[1], Joy Vijayan[5], Aravinda K. Therimadasamy[6], Zarinah Hairom[7], Emily Ang[2], Sally Ang[1], Nitish V. Thakor[2,3,8], Soo-Chin Lee[1,9] and Einar P. V. Wilder-Smith[2,3,10]**

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PATIENT AND SURVIVOR CARE

## Cryocompression for enhanced limb hypothermia in preventing paclitaxel-induced peripheral neuropathy.

Raghav Sundar, Aishwarya Bandla, Stacey Tan, Nesaretnam Barr Kumarakulasinghe, Yiqing Huang, Sally Ang.

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Abstract Disclosures

Abstract

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southwest technologies inc.

December 28, 2017

# URGENT: MEDICAL DEVICE RECALL NOTICE
# Hypothermia Caps, Mittens and Slippers

Southwest Technologies, Inc is voluntarily recalling all Hypothermia products including Caps, Mittens and Slippers for the intended use of reduction of chemotherapy induced alopecia, onycholysis and skin toxicity. **Serious injuries have occurred or could occur due to the failure mode associated with this recall. We have reports of two (2) serious injuries.**

**Reason for the Voluntary Recall:**
Products (hypothermia mitts, hypothermia slippers and hypothermia caps) entered into the market are misbranded for use during Chemotherapy treatments. In addition Southwest Technologies, Inc. has been informed that two (2) instances of frostbite to digits have occurred in the last year while using the hypothermia mitts.

**Risk to Health:**
The device has not passed FDA clearance for the intended use and may cause frostbite to digits on patients with but not limited to diabetic neuropathy, Raynaud's disease, Distal metastasis, Distal arteriopathy, and cold intolerance.

**How to recognize that the device may fail.** If patients are using the above products, they may feel pain in digits prior to the frostbite occurring. Discontinue use immediately at the first indication of pain.

**Actions to be taken by the Customer/User:**

**DISCONTINUE USE OF PRODUCT IMMEDIATELY!** You the customer/distributor may do one of three actions to aid Southwest Technologies, Inc. in this recall.

1). **DISCONTINUE** use of the product **IMMEDIATELY** and **Return** the attached **Medical Device Recall Return Response** within **30 days** of receipt of this notice.
2). **DISCARD** any remaining product in your possession **IMMEDIATELY** and **Return** the attached **Medical Device Recall Return Response** within **30 days** of receipt of this notice.
3). **RETURN** any product to Southwest Technologies, Inc. and **Return** the attached **Medical Device Recall Return Response** within **30 days** of receipt of this notice.