Photobiomodulation therapy prevents severe acute radiodermatitis: a randomized, placebo-controlled trial in breast cancer patients

**Presenting author:** Jolien ROBIJNS, PhD student, Hasselt University, Hasselt, Belgium

**Co-authors:** Sandrine Censabella, PhD, Stefan Claes, BSc, Luc Pannekoeke, BSc, Lore Bussé, MSc, Iris Kaminksi, BSc, Dora Colson, BSc, Annelies Maes, MD, Paul Bulens, MD, Leen Noé, MD, Marc Brosens, MD, An Timmermans, MD, Ivo Lambriechts, MD, PhD, Veerle Somers, PhD, Jeroen Mebis, MD, PhD

**MASCC/ISOO 2018 Annual Meeting**
Parallel Session 4: Young Investigator Awards
28/06/2018
# Faculty Disclosure

<table>
<thead>
<tr>
<th>Company Name</th>
<th>Honoraria / Expenses</th>
<th>Consulting / Advisory Board</th>
<th>Funded Research</th>
<th>Royalties / Patent</th>
<th>Stock Options</th>
<th>Ownership / Equity Position</th>
<th>Employee</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limburg Clinical Research Program</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limburgs Kankerfonds</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASA srl</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kom op Tegen Kanker</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MASC C Young Investigator Award</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
</tbody>
</table>
Introduction
Acute radiodermatitis (ARD)

- **What?** Inflammatory skin reaction at the irradiated area
- **Incidence?** Affects 90-95% of radiotherapy (RT) patients
- **Associated with?**
  - Itchiness
  - Pain
  - Quality of life impairment
- **Consequences for the patient?**
  - Dose reductions
  - In rare cases, treatment interruptions
- **Prevention and treatment?**
  - General skin care advice
  - Topical steroids/creams
  - Wound dressings

Wong et al. Support Care Cancer (2013) 21:2933-2948
# Introduction

**ARD – Skin assessment**

<table>
<thead>
<tr>
<th>RTOG Grade 1</th>
<th>RTOG Grade 2</th>
<th>RTOG Grade 3</th>
<th>RTOG Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute follicular erythema/depilation / dry peeling / decreased sweating</td>
<td>Bright erythema / moist desquamation in the skin folds/moderate oedema</td>
<td>Confluent moist areas of peeling outside the folds / pitting oedema</td>
<td>Ulceration, bleeding, necrosis (rarely seen)</td>
</tr>
</tbody>
</table>

---

Introduction
Photobiomodulation therapy (PBMT)

- **What?**
  - Light therapy based on visible and/or (near)-infrared light (600-1000 nm)

- **Light sources?**
  - Laser or Light-Emitting diodes (LEDs)

- **Biological effects?**
  - Anti-inflammatory
  - Pain reduction
  - Stimulates wound healing
  - **BIOSTIMULATION**

- **Indications in oncology?**
  - Oral mucositis
  - Lymphedema
  - Osteonecrosis
  - Acute radiodermatitis
  - ...
## Introduction

**PBMT and acute RD**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PBMT type</strong></td>
<td><strong>Patient type</strong></td>
<td><strong>PBMT set up</strong></td>
<td><strong>Control group</strong></td>
<td><strong>Results</strong></td>
</tr>
<tr>
<td>Laser diode</td>
<td>Breast cancer</td>
<td>Daily, after the RT session</td>
<td>/</td>
<td>Accelerated wound healing</td>
</tr>
<tr>
<td>632.8 nm</td>
<td></td>
<td>3x/week until complete healing</td>
<td>Retrospective</td>
<td>Significantly reduced incidence of RD grade ≥ 2</td>
</tr>
<tr>
<td>30 J/cm(^2)</td>
<td></td>
<td></td>
<td>Placebo</td>
<td>No significant effects</td>
</tr>
<tr>
<td>3 mW/cm(^2)</td>
<td></td>
<td></td>
<td>Institutional skin care</td>
<td>Significantly reduced incidence of RD grade ≥ 2</td>
</tr>
<tr>
<td>LED</td>
<td></td>
<td>Daily, before + after the RT session</td>
<td>Institutional skin care</td>
<td>Significantly reduced incidence of RD grade ≥ 2</td>
</tr>
<tr>
<td>590 nm</td>
<td></td>
<td>2x/week starting at a RT dose of 40 Gy, after the RT session</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.15 J/cm(^2)</td>
<td></td>
<td>2x/week starting at first day of RT, before the RT session</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not specified</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laser diode</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>808 + 905 nm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 J/cm(^2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>168 mW/cm(^2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LED</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>660 + 850 nm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.15 J/cm(^2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>44.6 mW/cm(^2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

*Schindl et. al. Photodermatol Photoimmunol Photomed 2000; 16: 34–37*
*DeLand et.al. Lasers in Surgery and Medicine, 2007. 39:164–168*
*Strahlenther Onkol. 2017 Jun;193(6):491-498,*
*Censabella et.al. Support Care Cancer (2016) 24:3925–3933*
Material and Methods

AIM
Investigate the efficacy of PBMT in the prevention of ARD in breast cancer patients undergoing RT

Study design: Prospective, randomized placebo-controlled trial (TRANSDERMIS trial)

EGILIBILITY CRITERIA

Inclusion criteria
- Female
- Breast cancer
- Lumpectomy
- Standard fraction RT regime: 66 Gy in 25 x 2Gy to whole breast + 8 x 2 Gy to the tumor bed
- Signed informed consent

Exclusion criteria
- Mastectomy
- Previous irradiation to the same breast
- Metastatic disease
- Concurrent chemotherapy
- Use of bolus material during RT
- Brachytherapy boost

Stratification on breast volume (i.e. planned target volume, PTV):
- Small: <450 cc
- Medium: 450-800 cc
- Large: >800 cc

Randomization 1:1

Placebo group (n=60)
- Standard skin care
- Sham laser (2x/week, from the first until the last day of RT)

PBMT group (n=60)
- Standard skin care
- PBMT (2x/week, from the first until the last day of RT)
Material and Methods

• Outcome measures
  – What?
    • RTOG criteria
    • Objective skin measures
  – When?
    - Erythema
    - Melanin
    - Transepidermal water loss (TEWL)
    - Hydration
    - Baseline
    - RT dose 40 Gy
    - End RT (66 Gy)
Results
RTOG criteria

Control group (n=60)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Percentage</th>
<th>PBMT group (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 0</td>
<td>92%</td>
<td>70%</td>
</tr>
<tr>
<td>Grade 1</td>
<td>7%</td>
<td>27%</td>
</tr>
<tr>
<td>Grade 2</td>
<td>3%</td>
<td>5%</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0%</td>
<td>7%</td>
</tr>
</tbody>
</table>

* *p< 0.05 (chi-square test, two-tailed)
Results

Objective skin measures

*\( p < 0.05 \) (Wilcoxon-Mann-Whitney test, two-tailed)
Conclusion

• Preventive PBMT significantly reduces the incidence of moist desquamation

• First RCT that shows by both a clinical and objective approach that PBMT is able to prevent aggravation of ARD in breast cancer patients

• Future RCTs are necessary to further investigate the effectiveness, feasibility, and safety of PBMT in the management of ARD in all cancer patients
This research is part of the Limburg Clinical Research Program UHasselt-ZOL-Jessa, supported by:
Acknowledgments

• **Promotor**: Prof. Dr. Jeroen Mebis

• **Co-promoters**: Prof. Dr. Veerle Somers, Prof. Dr. Ivo Lambrichts, Prof. Dr. Niels Hellings

• **Radiotherapists of the LOC**: Dr. Paul Bulens, Dr. Annelies Maes, Dr. Marc Brosens, Dr. Leen Noé

• **Dermatologist**: Dr. An Timmermans

• **Clinical psychologist**: Dr. Sandrine Censabella

• **RT nurses**: Luc Pannekoke, Stefan Claes, Leen Van Bever

• **Doctors, nurses and secretaries of the radiotherapy department of the Limburg Oncology Centre, Jessa Hospital**

• **TRANSDERMIS study participants and their families**

• **Internship students**: Lore Bussé, Iris Kaminski, Dora Colson