LIMBURGS ONCOLOGISCH CENTRUM vzw

PBMT for mucositis and radiodermatitis

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UHASSELT

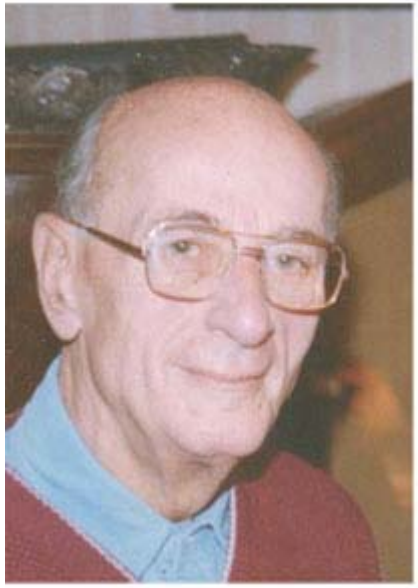
Post-MASCC 2018
23/11/2018
Parker Hotel Brussels Airport, Diegem

Outline part 1

- What is PBMT?
- PBMT for mucositis: update
- Safety issues?

Low-level laser

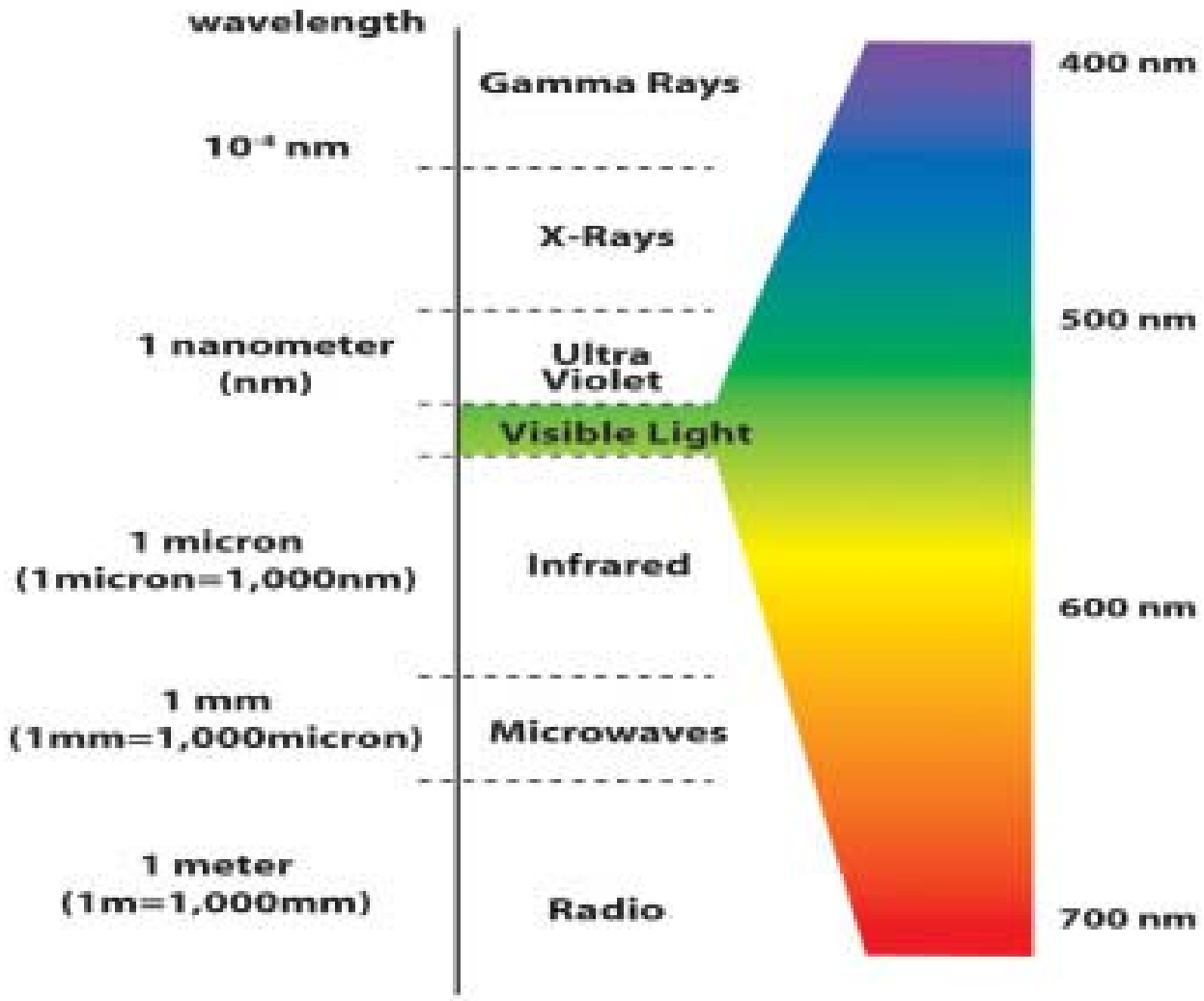
- 1967
- Endre Mester, Budapest
- "effects of laser on skin cancer"



→ Laser biostimulation

Hamblin, M. et al. Low-Level Light Therapy: Photobiomodulation. SPIE press, 2018.

Electromagnetic spectrum



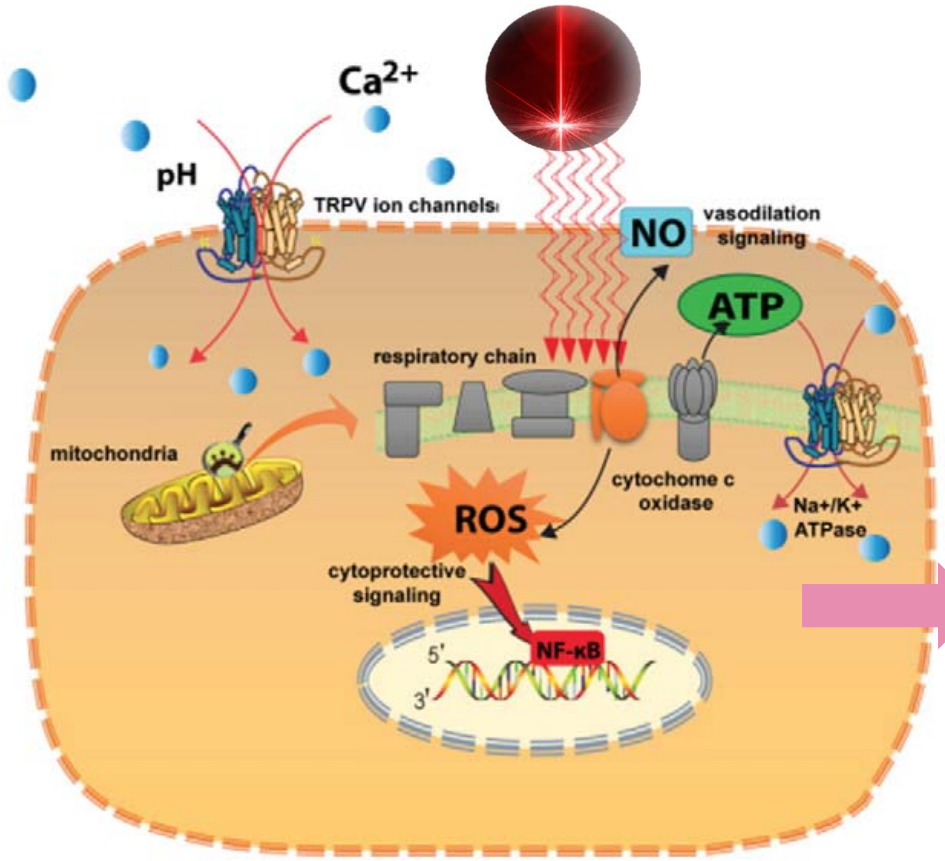
Hamblin, M. et al. Low-Level Light Therapy: Photobiomodulation. SPIE press, 2018.

High vs Low-level lasers

High	Low
Surgical lasers	Medical lasers
Hard lasers	Soft lasers
Thermal	Energy 1-500 mW
Energy : 3000-10000mW	600-1000 nm light

Hamblin, M. et al. Low-Level Light Therapy: Photobiomodulation. SPIE press, 2018.

Biological effects



- Cell proliferation + migration
- Production of growth factors + cytokines
- Increased tissue oxygenation
- Extracellular matrix deposition
- Anti-apoptotic + pro-survival

- **Wound healing**
- **Anti-inflammatory**
- **Pain reduction**

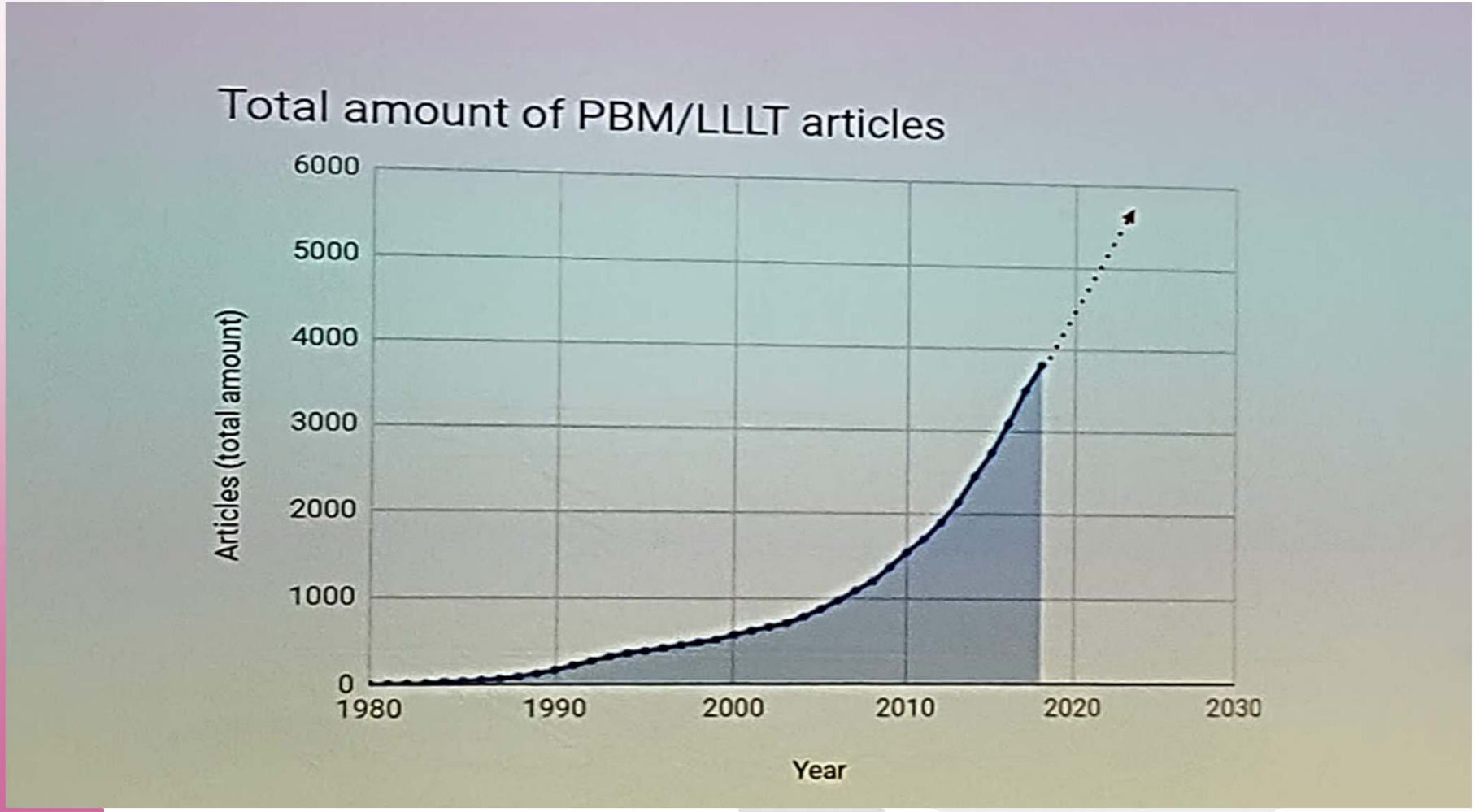
Hamblin, M. et al. Low-Level Light Therapy: Photobiomodulation. SPIE press, 2018.
Robijns, J. et al. BELG J MED ONCOL 2017

Research

- Since 1967: >400 double blind, RND trials
- first clin application: wound healing
- Experiences from lab and clinic:
  - Reduction inflammation
  - Prevention fibrosis
  - Reduces pain
  - Neuroprotective

Bensadoun RJ, Cur Opinion Oncol 2018;30:226-232

Research


Total amount of PBM/LLLT articles
Articles (total amount)
6000
5000
4000
3000
2000
1000
0
1980
1990
2000
2010
2020
2030
Year

Our own experience

- **LLLT in breast cancer patients: retrospective analysis**

Table 1. Patients' status at the start and the end of Low Level Laser Therapy (LLLT)

Outcome	Start LLLT	End LLLT	N improved
Mean number of treated areas	3.89	2.16*	66 (71%)
Mean OM score	6.60	2.78*	75 (80.6%)
Mean pain score[a]	5.14	1.64*	20 (90.9%)
N (%) WHO grade 1	11 (11.8%)	60 (64.5%)*	60 (64.5%)

[a] Pain scores were available for 22 (of the 93) patients. * $p < 0.0001$ (t-test or chi-square, as appropriate).

J.Mebis, S. Censabella, A. Maes, L. Noé, P. Bulens. Cancer Res May 1, 2015 75:P5-15-05

Our own experience

- **LLLT in cancers other than head and neck cancer.**

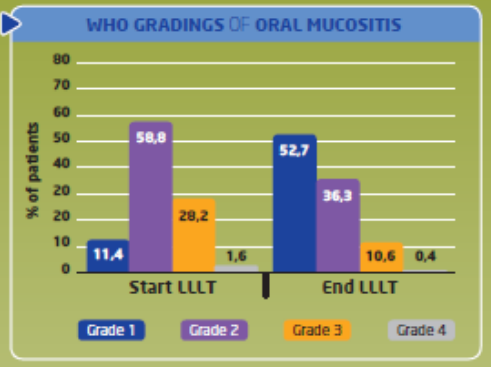
1. POPULATION

PATIENTS' CHARACTERISTICS (N = 245)

Age (years)		**Tumour Stage**	**N (%)**
Mean (M)	59.56	0	4 (1.63)
Standard deviation (SD)	11.80	1	17 (6.94)
Tumour Location	**N (%)**	2	61 (24.90)
Brain	3 (1.22)	3	59 (24.08)
Breast	100 (40.82)	4	51 (20.82)
Colorectal	31 (12.65)	Unknown	53 (21.63)
Gastro-Intestinal	19 (7.76)		
Gynaecologic	13 (5.31)	**Cancer therapy**	**N (%)**
Hematologic	10 (4.08)	Chemotherapy	183 (74.69)
Lung	17 (6.94)	Chemo-radiotherapy	27 (11.02)
Neuroendocrine	5 (2.04)	Radiotherapy	22 (8.98)
Skin	4 (1.63)	Other	9 (3.67)
Urogenital	26 (10.61)	Unknown	4 (1.63)
Unknown	17 (6.94)		
Number of LLLT sessions received		**Time since start cancer therapy (days)**	
M	6.11	M	55.38
SD	5.89	SD	69.13

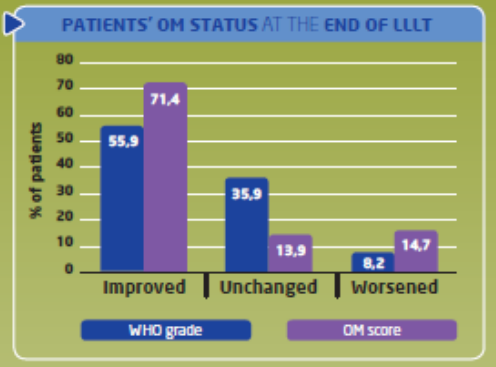
2. OM GRADINGS

At the end of LLLT, there was a **significant improvement** of OM ($p < .0001$), with an increased proportion of patients with OM grade 1 (and a decrease of OM ≥ grade 2).



3. OM SCORES

- OM scores **significantly decreased** ($M = 3.66$ at the end vs 6.67 at the start of LLLT, $p < .0001$)
- At the end of LLLT, patients were categorised according to their status (OM worsened, unchanged, or improved), based on their (highest) WHO grades and OM scores:



Annals of Oncology (2014) 25 (suppl_4): iv517-iv541. 10.1093/annonc/mdu356

Review 2011

11 RCT

Table 1 Trial characteristics

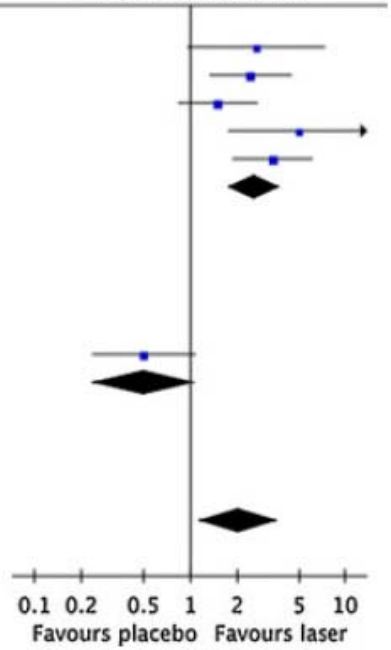
First author (year)	Patient numbers (cancer therapy)	Wavelength (nm)	Laser output (mW)	Spot size (cm2)	Dose (J)	Irradiation time (s)	Outcomes and effect (+/−)
Cowen 1997	30 (chemo/radio)	633	30	0.5	3.5	105	Days+/OMI+
Bensadoun 1999	30 (radiation)	633	60	0.5	2	33	Pain+/OMI+
Arun Maiya 2006	50 (radiation)	633	10	1.0	4	600	Pain+/OMI+
Schubert 2007	70 (transplant)	650/780	40/60	0.04	2	33–50	655 nm only pain+/OMI+
Cruz 2007	60 (chemo/child)	633	50	0.04	0.18	3	n.s.
Kuhn 2007	34 (chemo)	830	100	0.06	6	54	Days+/OMI+
Antunes 2007	38 (transplant)	660	47	0.2	4	17	Pain+/WHO+
Genot-Klastersky 2008	36 (chemo)	650	100	0.45	5	33	Days+/OMI+
Kuhn 2009	21 (chemo/child)	830	100	0.06	6	56	Days+/OMI+
Abramoff 2009	22 (chemo)	685	35	0.5	3	54	Days+/OMI+
Chor 2009	24 (chemo)	660	50	?	2	40	Days+/others−

First column identifies trial by first author's last name and the publication year. Other columns represent: sample size (type of cancer therapy), laser wavelength in nm, laser output in mW, spot size in cm^2, dose in Joules, irradiation time per point, outcomes reported including mucositis severity scales (WHO or OMI), pain and duration of OM in days and dichotomized overall results given by: (+) significantly in favour of LLLT or (−) non-significant between LLLT and placebo

Bjordal JM, Supp Care cancer, 2011

Review 2011

Study or Subgroup	Placebo Events	Total	Laser therapy Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.4.1 Subgroup doses > 1 Joules						
Abramoff 2007	8	11	3	11	13.7%	2.67 [0.95, 7.47]
Antunes 2007	17	19	7	19	18.6%	2.43 [1.32, 4.46]
Chor 2009	12	17	8	17	18.8%	1.50 [0.83, 2.71]
Genot-Klastersky 2008	15	18	3	18	13.5%	5.00 [1.74, 14.34]
Maiya 2006	25	25	7	25	18.6%	3.40 [1.85, 6.23]
Subtotal (95% CI)		90		90	83.3%	2.56 [1.73, 3.79]
Total events	77		28			
Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 5.84$, df = 4 (P = 0.21); $I^2 = 32\%$						
Test for overall effect: Z = 4.70 (P < 0.00001)						
1.4.2 Subgroup doses < 1 Joules						
Cruz 2007	7	31	13	29	16.7%	0.50 [0.23, 1.08]
Subtotal (95% CI)		31		29	16.7%	0.50 [0.23, 1.08]
Total events	7		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.75 (P = 0.08)						
Total (95% CI)		121		119	100.0%	2.03 [1.11, 3.69]
Total events	84		41			
Heterogeneity: $Tau^2 = 0.41$; $Chi^2 = 19.88$, df = 5 (P = 0.001); $I^2 = 75\%$						
Test for overall effect: Z = 2.31 (P = 0.02)						



Doses 1-6J

Reduction of OM prevalence, severity, duration and pain.

Bjordal JM, Supp Care cancer, 2011

Review 2014

- RCT 18

Study or Subgroup	Laser therapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Antunes 2007	1	19	13	19	6.1%	0.08 [0.01, 0.53]
Antunes 2013	3	47	19	47	10.5%	0.16 [0.05, 0.50]
Arbabi Kalati 2013	0	24	10	24	3.6%	0.05 [0.00, 0.77]
Chor 2010	4	17	7	17	11.3%	0.57 [0.20, 1.60]
Gautam (a) 2012	26	111	77	110	16.0%	0.33 [0.23, 0.48]
Gautam (b) 2012	16	55	49	55	15.7%	0.33 [0.21, 0.50]
Hodgson (a) 2012	12	20	9	20	14.5%	1.33 [0.73, 2.44]
Hodgson (b) 2012	12	20	11	20	15.0%	1.09 [0.64, 1.86]
Khouri 2009	0	12	5	10	3.6%	0.08 [0.00, 1.24]
Silva 2011	0	21	6	21	3.6%	0.08 [0.00, 1.28]
Total (95% CI)		**346**		**343**	**100.0%**	**0.37 [0.20, 0.67]**
Total events	74		206			

Heterogeneity: $Tau^2 = 0.55$; $Chi^2 = 44.46$, df = 9 ($P < 0.00001$); $I^2 = 80\%$
Test for overall effect: $Z = 3.29$ ($P = 0.0010$)

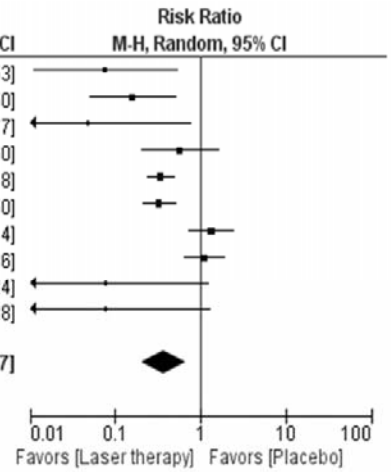


Figure 2. Forest plot of overall incidence of severe (grade 3 or 4) mucositis. Squares to the left of the vertical line indicate that low level laser therapy reduces mucositis. Horizontal lines through the squares represent 95% confidence intervals (CIs). The size of the squares reflects each study's relative weight, and the diamond represents the aggregate risk ratio and 95% CI.
doi:10.1371/journal.pone.0107418.g002

Oberoi S, PLoS ONE9: 2014

Review 2014

Table 2. Summary of outcomes of low level laser therapy as compared to placebo/no treatment.

Outcome	Number Studies	Number Patients	Effect	95% CI[¥]	I^2	*P*
Overall incidence of severe (grade 3 or 4) mucositis	10	689	RR 0.37	0.20 to 0.67	80%	0.001
Incidence of severe (grade 3 or 4) mucositis at anticipated time of maximal mucositis*	6	546	RR 0.34	0.20 to 0.59	62%	0.0001
Overall mean grade of mucositis	8	603	SMD −1.49	−2.02 to −0.95	86%	<0.0001
Duration of severe (grade 3 or 4) mucositis	3	361	WMD −5.32	−9.45 to −1.19	94%	0.01
Incidence of any pain	7	591	RR 0.89	0.76 to 1.04	96%	0.15
Incidence of severe pain**	2	331	RR 0.26	0.18 to 0.37	0%	<0.0001
Overall mean pain scores	5	222	WMD −2.46	−4.41 to −0.77	97%	0.004
Number of patients requiring opioid analgesia	5	530	RR 0.47	0.37 to 0.60	0%	<0.0001
Unplanned radiotherapy interruption due to mucositis in head and neck cancer patients	5	560	RR 0.23	0.12 to 0.44	0%	<0.0001

Abbreviations: RR - risk ratio; SMD - standardized mean difference; WMD – weighted mean difference; CI – confidence interval;
*Maximum anticipated mucositis was week 6±1 in head and neck cancer radiotherapy/chemo-radiotherapy trials and day 10±4 in chemotherapy and hematopoietic stem cell transplantation trials (from date of chemotherapy initiation and stem cell infusion respectively).
** Severe pain defined as a visual analogue scale score >7.
[¥]All analyses used a random-effect model. A risk ratio <1 and a standardized mean difference or weighted mean difference <0 with 95% CIs that do not include 1 or 0 respectively, suggest that low level laser is better than placebo/no therapy.
doi:10.1371/journal.pone.0107418.t002

Oberoi S, PLoS ONE9: 2014

Review 2014

Table 3. Effect of low level laser therapy as compared to placebo/no therapy on overall incidence of severe (grade 3 or 4) mucositis stratified by patient, laser and risk of bias characteristics.

Subgroup	Number Studies	Number patients	RR	95% CI[¥]	*P* for interaction
Population Age					0.90
Adult	8	607	0.33	0.18 to 0.59	
Pediatric or both adult/pediatric	2	82	0.41	0.02 to 10.87	
Underlying Condition					0.85
Chemotherapy or HSCT	7	264	0.35	0.13 to 0.98	
Head and neck cancer radiotherapy/chemo-radiotherapy	3	425	0.32	0.24 to 0.42	
Type of Laser Delivery					<0.0001
Intraoral	8	609	0.29	0.19 to 0.42	
Extraoral	2	80	1.19	0.80 to 1.78	
Energy Density of Laser					0.06
≤4 J/cm2	8	619	0.43	0.23 to 0.78	
>4 J/cm2	2	70	0.06	0.01 to 0.43	
Participants, Personnel and Assessors Blinded					0.11
Yes	8	625	0.42	0.23 to 0.76	
No or unclear	2	64	0.08	0.01 to 0.56	
Allocation Concealment Adequate					0.03
Yes	4	411	0.61	0.30 to 1.25	
No or unclear	6	278	0.16	0.07 to 0.41	

Abbreviations: RR – risk ratio; CI – confidence interval; HSCT – hematopoietic stem cell transplantation.
[¥]All analyses used a random-effect model. A risk ratio <1 with 95% CIs that do not include 1, suggests that low level laser is better than placebo/no therapy.
doi:10.1371/journal.pone.0107418.t003

Oberoi S, PLoS ONE9: 2014

TABLE 2. Summary of reviews with meta-analysis investigating the use of PBMT for the prevention and management of OM in cancer patients.

First author (ref.)	Year	Publication type	Type + number of studies included	Sample size	Wavelength (nm)	Power (mW)	Energy density (J/cm²)	Laser schedule	Results
Bjordal[15]	2011	Systematic review with meta-analysis	11 placebo-controlled RCTs	415	- Red (633–685) - Infrared (780–830)	-Red (10-60) -Infrared (50-100)	1-6 J/point	Minimum 3 sessions/week	Reduced OM prevalence, severity, duration, and associated pain.
Migliorati[17]	2012	Systematic review with meta-analysis	24 clinical trials	NA	400-1200	10-500	2-70	NA	**Recommendation:** - Prevention of OM in adult patients receiving HSCT (650 nm, 40 mW, and 2 J/cm²). **Suggestion:** - Prevention of OM in HNC patients undergoing RT without CTx(632.8 nm).
Oberoi[16]	2014	Systematic review with meta-analysis	18 RCTs and quasi-RCTs	1144	632.8-780	10-100	1.5-6.3	5 sessions/week - daily	Prophylactic PBMT reduced severe OM and pain in patients with cancer and HSCT recipients.

Partially adapted from Robijns et al. (2017)[5]

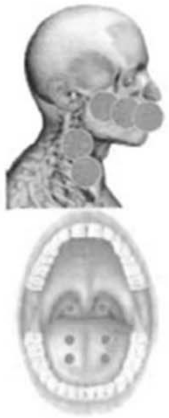
Abbreviations: OM, oral mucositis; CTx, chemotherapy; HNC, head and neck cancer; HSCT, hematopoietic stem cell transplantation; RCT, randomised controlled trial; NA, not available; ref, reference; PBMT, photobiomodulation therapy.

Robijns, Lasers Med Science, 2017; 32:229-242

Guidelines

- MASCC/ISOO
  - Recommendation for prevention of OM in HDSCT +- TBI
  - Recommendation for prevention of OM in HeN RT
  - Recommendation for prevention of OM in HeN RT + CT
- ESMO
- NCCN

Guidelines

Complication	Treatment protocol	Treatment area	PBM device characteristics and application	Therapeutic PBM dose	Optional target tissues
Oral Mucositis	*Prophylactic*: *Chemotherapy*: Protocols vary. Start PBM treatment at first day of CT or prior to therapy and continue during all courses of chemotherapy *Radiotherapy*: Start PBM treatment the first day of RT or prior to RT and continue during all days of RT (no requirement regarding the timing of PBM sessions, before or after RT session) *Therapeutic*: Continue treatment at least 3 times a week until symptoms improve Daily treatment is recommended in case of severe mucositis		*Extra-oral*: IR LED cluster or mixed red and IR LED cluster 20–80 mW cm^{-2} *Intra-oral*: 630–830 nm 20–80 mW	*Extra-oral*: 3 J cm^{-2} IR LED cluster *Intra-oral*: *Prophylactic*: 2 J per point *Therapeutic*: 4 J per point until the whole area involved is covered (2 J for prophylactic use)	*Extra-oral*: Lips, cutaneous surface corresponding to the buccal mucosae, bilateral cervical lymphatic chain *Intra-oral*: *Prophylactic*: treat each of the at risk mucosal surfaces *Therapeutic*: sites vary, depending upon the site of mucositis

Bensadoun RJ, Cur Opinion Oncol 2018;30:226-232

Safety: in vitro

- PBM has been shown to promote cell proliferation, angiogenesis, analgesia/pain control
- Mechanisms: Cytochrome C Oxidase, electron transport ↑ATP, NO
- ↑growth factors, anti-inflammatory cytokines, HSP, MMP, ROS
- Are cell-cultures sufficient?

Safety: in vitro

- PBM therapy with visible and near-infrared sources are **safe** (non-genotoxic, non-mutagenic)
- PBM treatments have differential effects on cells of discrete lineages
- PBM treatments evoke different responses in normal and cancer stem cells

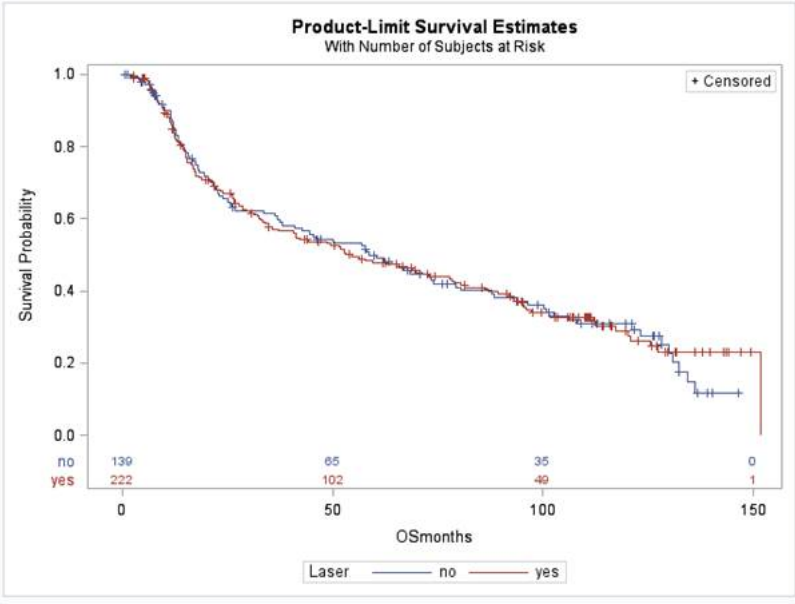
Safety: in vivo

- Retrospective analysis of potential stimulation of tumor growth by PBM used for management of therapy-induced mucositis in head and neck cancer patients.

MT Genot-Klastersky et al. IJB; WALT Congress, 2018

Safety: in vivo

- 361 pts
  - 139 (39%) without LLLT
  - 222 (62%) with LLLT



Overall survival (OS) is defined as time from diagnosis till date of death. Patients alive at last follow-up are censored at the date of last follow-up ➔ 232 OS events

There is no statistical evidence for a difference in overall survival between patients with and without low level laser (LLL): P-value 0.86 (logrank test).
5-year OS
•in patients without LLL: 50%
•in patients with LLL: 48%
Hazard ratio (laser vs not): 0.98 (95% CI, 0.75 to 1.27)

courtesy of MT Genot-Klastersky et al. IJB; WALT Congress, 2018

Safety: in vivo

Supportive Care in Cancer (2018) 26:2417–2423
https://doi.org/10.1007/s00520-018-4046-z

ORIGINAL ARTICLE

CrossMark

Locally advanced oral squamous cell carcinoma patients treated with photobiomodulation for prevention of oral mucositis: retrospective outcomes and safety analyses

Thaís Bianca Brandão[1,2] · Karina Morais-Faria[1,2] · Ana Carolina Prado Ribeiro[1,2,3] · César Rivera[2] · João Victor Salvajoli[4] · Marcio Ajudarte Lopes[2] · Joel B. Epstein[5,6] · Praveen R. Arany[7] · Gilberto de Castro Jr[8] · Cesar Augusto Migliorati[9] · Alan Roger Santos-Silva[1,2]

- Retrospective analysis, 152 advanced OSCC pts, prophylactic OM, 1/2009-12/2014
- 12,5% St III, 87,5% st IV
- 34,2% HK ; RT
- 61,8% CRT
- 4% ICT; HK+RT

Safety: in vivo

Supportive Care in Cancer (2018) 26:2417–2423
https://doi.org/10.1007/s00520-018-4046-z

ORIGINAL ARTICLE

Locally advanced oral squamous cell carcinoma patients treated with photobiomodulation for prevention of oral mucositis: retrospective outcomes and safety analyses

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Table 3 Summary of results reported in the literature from randomized controlled trials including treatment outcomes and survival rates of patients with oral squamous cell carcinoma treated with multimodal therapy. *OS* overall survival, *DFS* disease-free survival, *CT* chemotherapy, *y* year

Author	Year	No. patients	Stage	OS%	DFS%	Local-regional relapse	Distant relapse	Second primaries
Licitra et al. 2003 [13]	1989–1999	195	II–IV	57% (5 y)	–	31%	6.1%	8.2%
Including CT				68.2% (2 y)	63.6% (2 y)	30.5%	8.7%	–
Excluding CT								
Zhong et al. 2013 [14]	2008–2010	256	III or IVA					
Including CT				68.8% (2 y)	62.2% (2 y)	31.3%	5.5%	–
Excluding CT				68.2% (2 y)	63.6% (2 y)	30.5%	8.7%	–
Bossi et al. 2014 [15]	–	198	II–IV					
Including CT				46.5% (10 y)	48.5% (10 y)	29.6% (10 y)	4.1% (10 y)	10.6%
Excluding CT				37.7% (10 y)	36% (10 y)	32% (10 y)	9.3% (10 y)	22.1%
Zhong et al. 2015 [16]	2008–2015	256	III or IVA					
Including CT				61.1% (5 y)	52.7% (5 y)	31.3%	7%	3.1%
Excluding CT				61.1% (5 y)	52.7% (5 y)	39.1%	10.9%	7%
Current series	2009–2014	152	III–IV	46.7% (3.4 y)	51.8% (3.4 y)	29.6%	6.57%	12.5%

Safety: in vivo

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

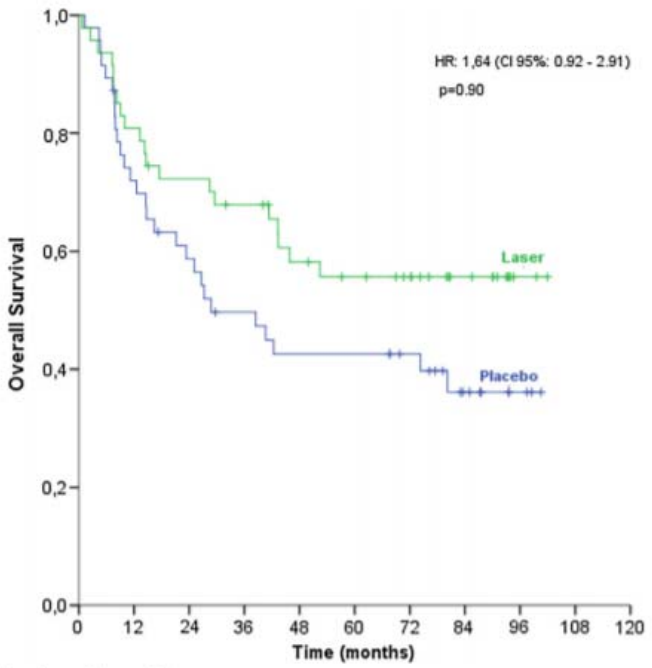
Long-term survival of a randomized phase III trial of head and neck cancer patients receiving concurrent chemoradiation therapy with or without low-level laser therapy (LLLT) to prevent oral mucositis

Héliton S. Antunes [a,*], Daniel Herchenhorn [b], Isabele A. Small [a], Carlos M.M. Araújo [c], Celia Maria Pais Viégas [c], Gabriela de Assis Ramos [a], Fernando L. Dias [d], Carlos G. Ferreira [e]

[a] Clinical Research Division, Instituto Nacional de Câncer (INCA), Rio de Janeiro, Brazil

- 94 pts with oro, naso and hypopharynxca in phase III trial
- Evaluation from 2007-2015
- CRT (HD CDDP)
- LLLT (660nm-100mW-1J-4J/cm2)
- Med FU 41,3 months

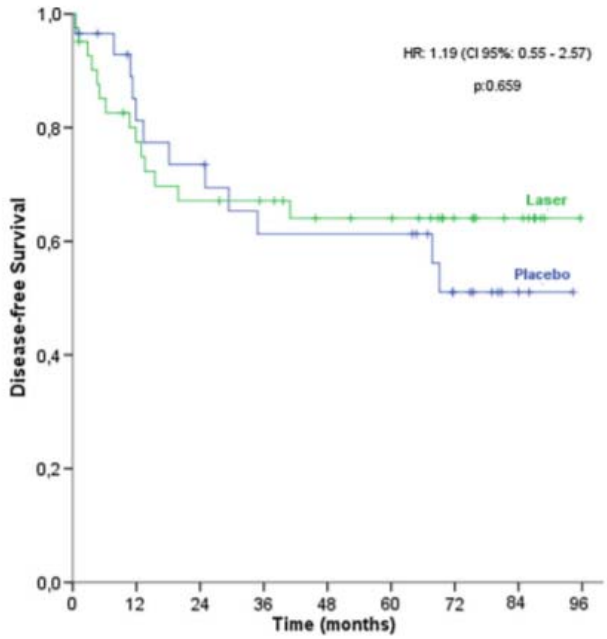
Antunes et al. Oral Oncology, 71 (2017), 11-15



Number of remaining cases

	12	24	36	48	60	72	84	96	108
Laser	38	33	30	24	21	17	11	2	0
Placebo	33	26	21	18	18	15	8	3	0

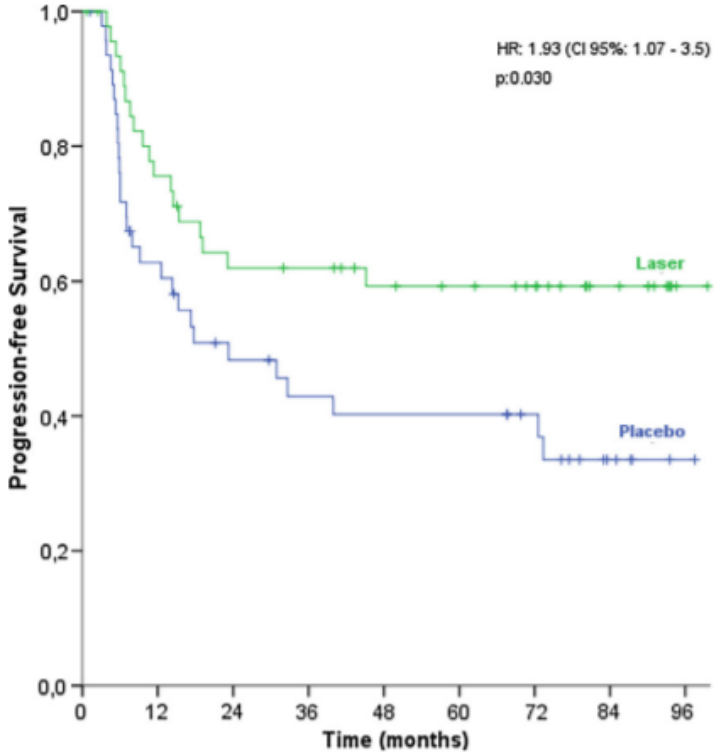
Fig. 1. Overall survival.



Number of remaining cases

	12	24	36	48	60	72	84	96	108
Laser	30	26	24	20	18	12	8	0	0
Placebo	21	19	15	15	15	8	2	0	0

Fig. 2. Disease-free survival.



Number of remaining cases

	12	24	36	48	60	72	84	96	108
Laser	34	27	26	22	20	15	10	1	0
Placebo	27	19	16	16	16	12	5	1	0

Fig. 3. Progression-free survival.

Antunes et al. Oral Oncology, 71 (2017), 11-15

Newer approaches

- Treatment of radiation fibrosis in Head and neck cancer patients
- Treatment of GVHD

Conclusion part 1

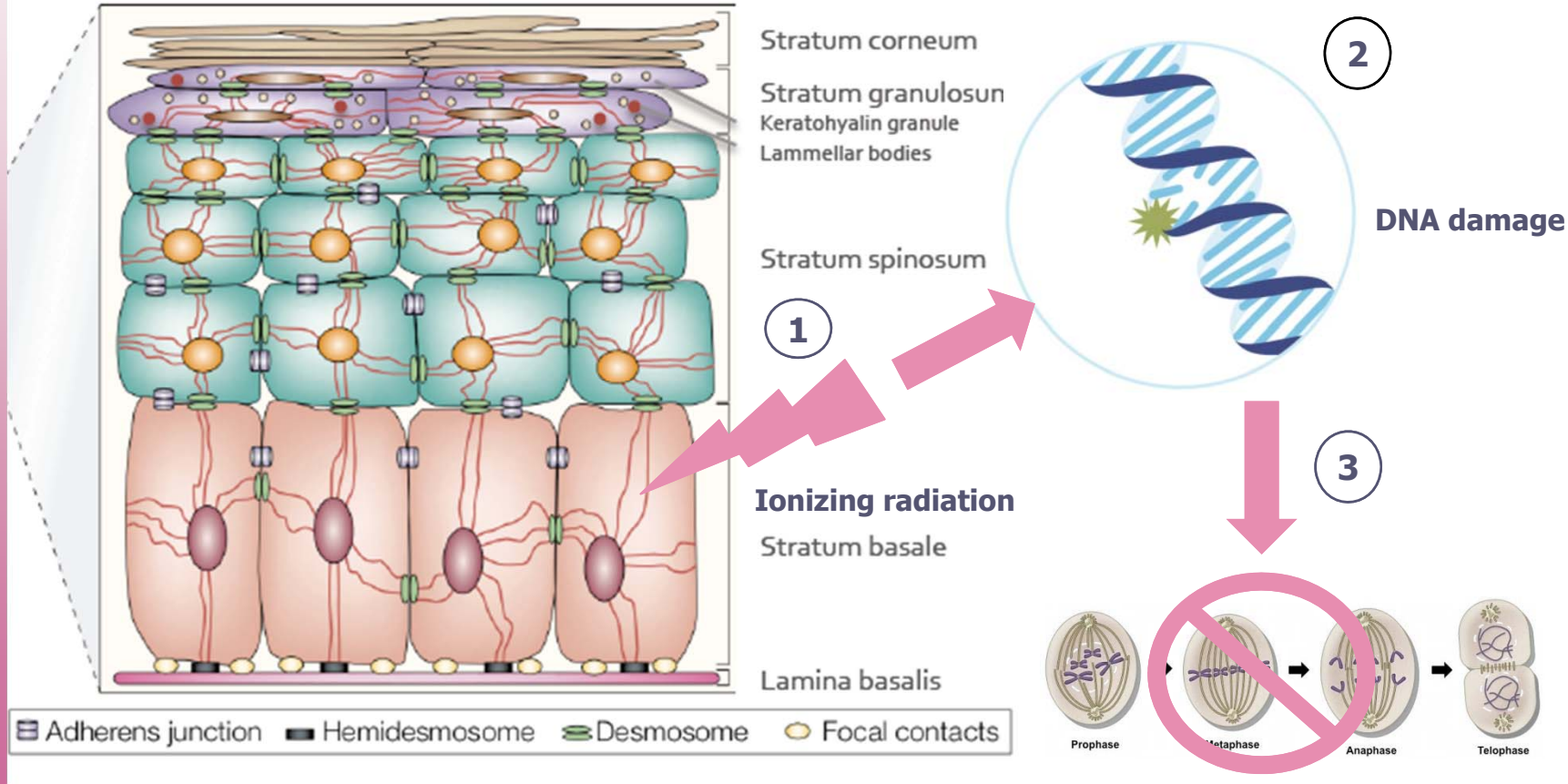
- PBM recommended in OM treatment in most guidelines
- Safety seems reconfirming in vitro and in vivo in appropriate doses
  - Preclinical in-vivo models needed
  - Short and long term cancer outcomes
  - Consistency of PBM parameters

Outline part 2

- Radiodermatitis
- PBMT and radiodermatitis
  - Previous research
  - Our own experience
- Conclusion
- Future perspective

Acute radiodermatitis (RD)

- **What?** Inflammatory skin reaction at the irradiated area



Wells, M. and S. MacBride, Radiation skin reactions, 2003.
Robijns et al. JEWDS, 2018.

Acute radiodermatitis (RD)

Patient experience

- Pain
- Burning sensation
- Itching

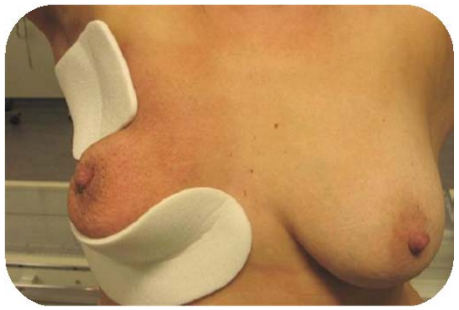
→

- Affects daily activities ➔ Quality of life
- Radiotherapy interruption

Prevention & treatment

- General skin care advice
- Hydrating creams/gels
- Topical steroids
- Wound dressings

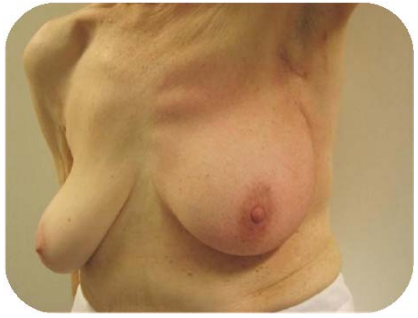
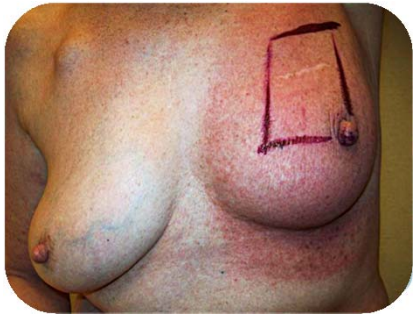
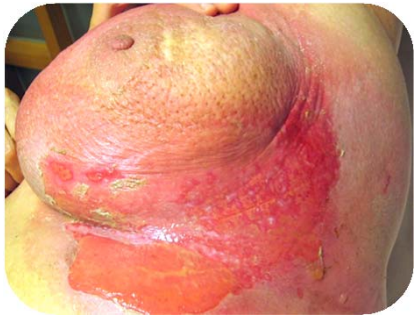
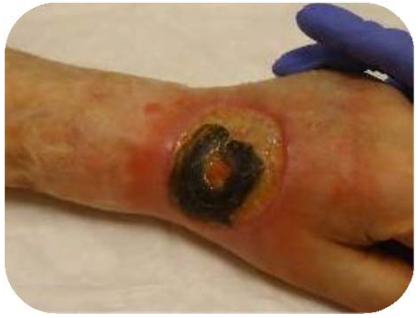
→ **No consensus on standardised guidelines**



Singh, M et al. Am J Clin Dermatol, 2016.

Grading acute RD

Radiotherapy Oncology Group Criteria

RTOG grade 1	RTOG grade 2	RTOG grade 3	RTOG grade 4
Acute follicular erythema / depilation / dry peeling / decreased sweating	Bright erythema / moist desquamation in the skin folds/ moderate oedema	Confluent moist areas of peeling outside the folds / pitting oedema	Ulceration, bleeding, necrosis (rarely seen)
			

Cox et.al. Int J Radiat Oncol Biol Phys, 1995

PBMT and acute RD

	Schindl et al.(1999)	DeLand et al. (2007)	Fife et al. (2010)	Strouthos et al. (2017)
PBMT type **•Wavelength** **•Fluence** **•Irradiance**	Laser diode •632.8 nm •30 J/cm^2 •3 mW/cm^2	LED •590 nm •0.15 J/cm^2 •Not specified	LED •590 nm •0.15 J/cm^2 •Not specified	LED •660 + 850 nm •0.15 J/cm^2 •44.6 mW/cm^2
Patient type				cer
PBMT set up				arting at RT, RT
Control group	/	Retrospective	Placebo	Institutional skin care
Results	Accelerated wound healing	Significantly reduced incidence of RD grade ≥ 2	No significant effects	Significantly reduced incidence of RD grade ≥ 2

Limited scientific evidence

Schindl et. al. Photodermatology, photoimmunology & photomedicine, 1999
DeLand et.al. Lasers in Surgery and Medicine, 2007.
Fife et. al. Dermatol Surg, 2010
Strouthos et. al. Strahlenther Onkol, 2017

Our own experience

01

DERMIS trial

2013-2014

DERMIS trial

Goal

Investigate the efficacy of PBMT in the **treatment** of ARD in **breast cancer patients** undergoing RT

DERMIS trial

Study design

Prospective, quasi-experimental study

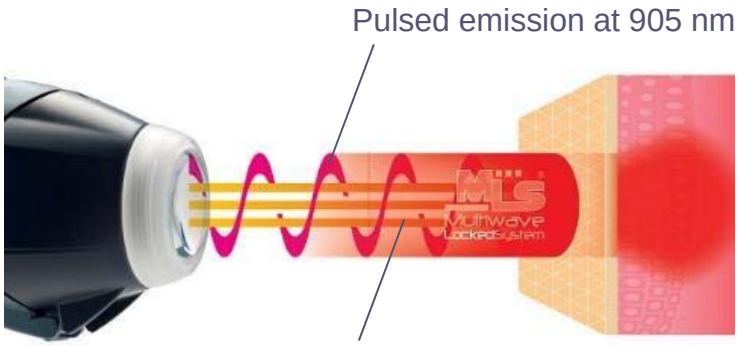
Patients

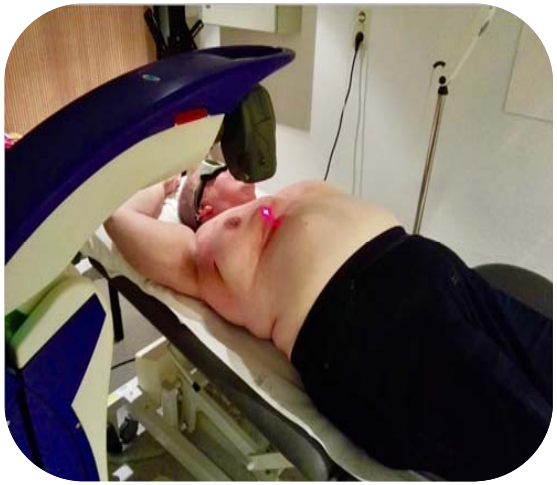
- Breast cancer patients
- Post-lumpectomy
- RT regimen: 25x2Gy (whole breast) + 8x2Gy (boost)
- Jessa Hospital– LOC (Hasselt)

DERMIS trial

PBMT

Parameter	Laser diode 1	Laser diode 2
Emission mode	Pulsed mode	Continuous mode
Wavelength	905 nm	808 nm
Dose	4 J/cm^2	
Treatment area	Whole breast, axilla, inframammary fold	
Treatment time	10-15 min. depending on the size of treated area	





DERMIS trial

Study groups

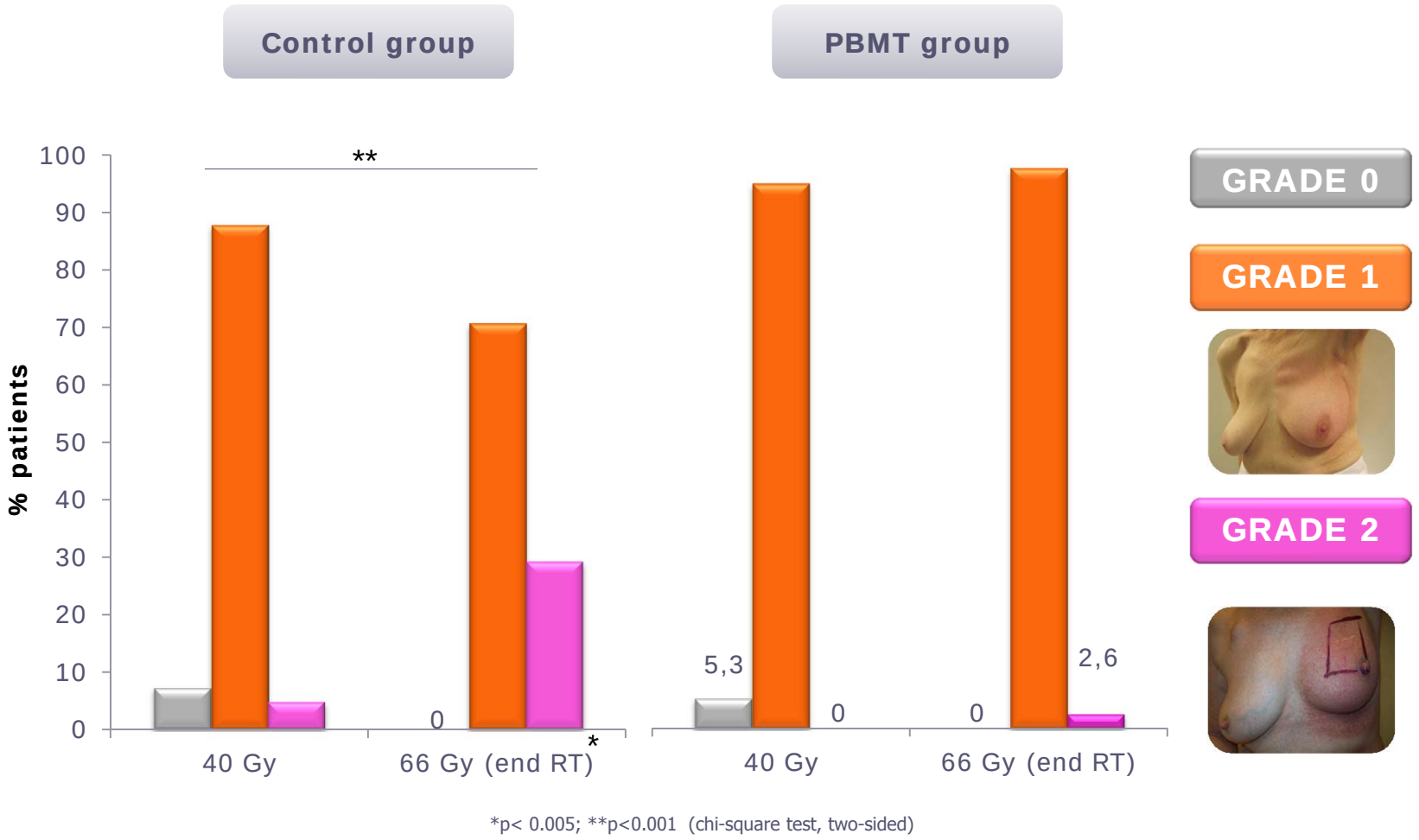
Control group	PBMT group
• 41 patients • Standard skin care	• 38 patients • Standard skin care • **PBMT from RT dose 40 Gy (2x/week, 6 sessions in total)**

Aug 2013 –Nov 2013 → *Nov 2013 –April 2014*

Outcome measures

- RTOG score
- Time points:
  - Fraction 20 RT
  - End RT

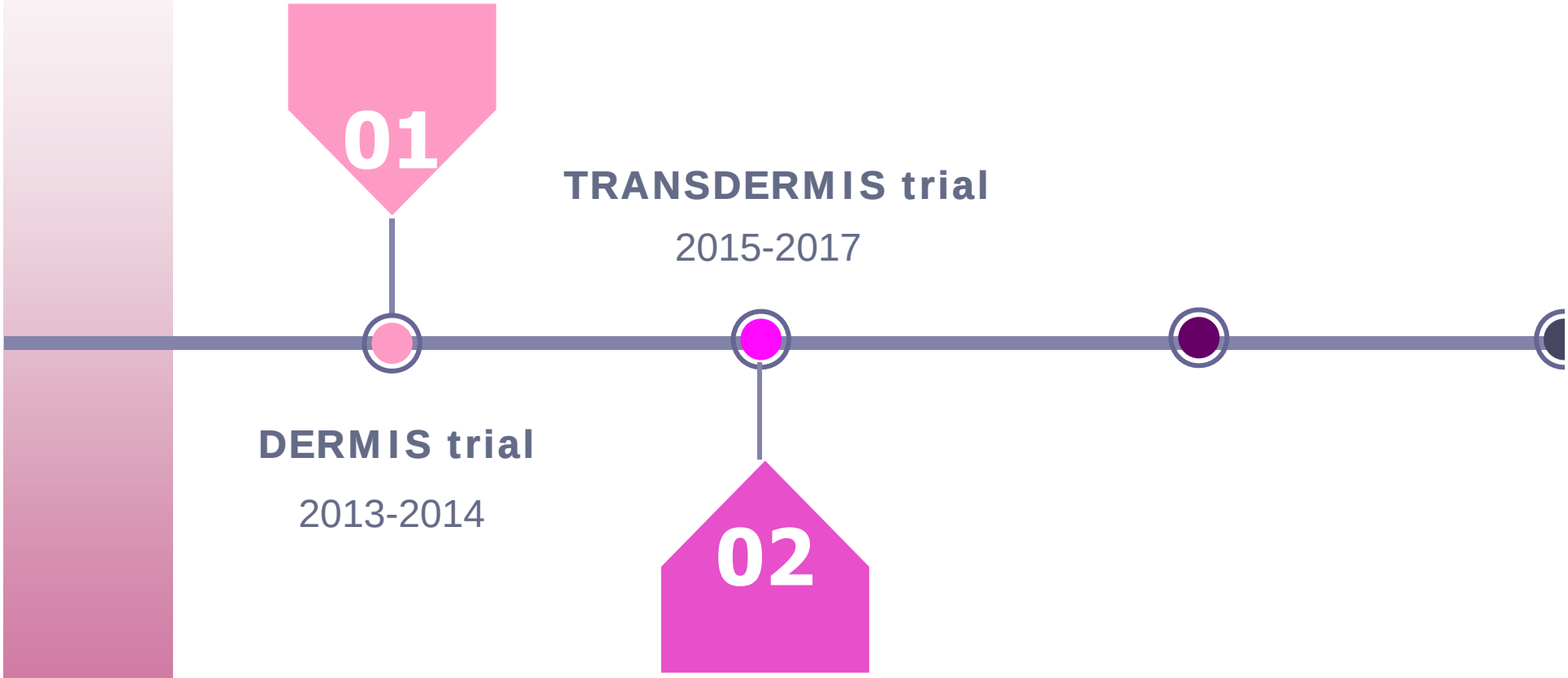
DERMIS trial: skin assessemnt



*p< 0.005; **p<0.001 (chi-square test, two-sided)

Censabella et.al. Support Care Cancer, 2016

Our own experience



TRANSDERMIS trial

Goal

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

TRANSDERMIS trial

Study design

Prospective, randomized placebo-controlled trial

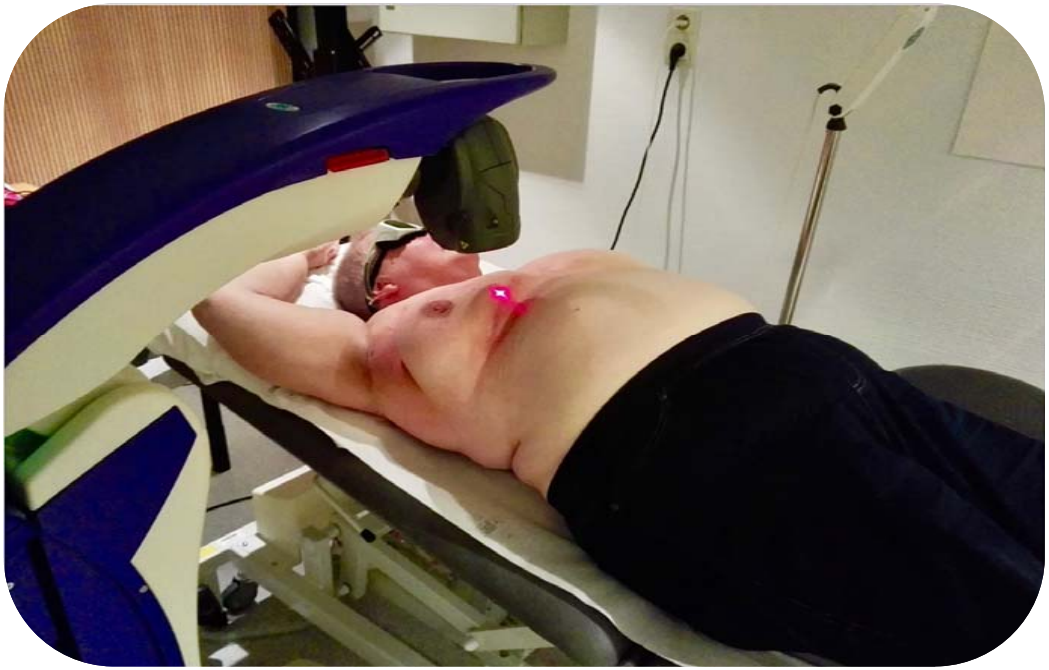
Patients

- Breast cancer patients
- Post-lumpectomy
- RT regimen: 25x2Gy (whole breast) + 8x2Gy (boost)
- Jessa Hospital– LOC (Hasselt)

TRANSDERMIS trial

PBMT

Same parameters as in the DERMIS trial



TRANSDERMIS trial

Study groups

Randomisation based on breast volume (small, medium, large)

Control group	PBMT group
• 60 patients • Standard skin care • Placebo laser from start RT (2x/week, 14 sessions)	• 60 patients • Standard skin care • **PBMT from start RT (2x / week, 14 sessions)**

Patient characteristics	
• **Mean age**	65 y
• **Mean breast volume**	25 cm^3
• **Mean percentage chemotherapy patients**	74%
• **RT energy**	
• 6 MV	77%
• 6 + 15 MV	23%
• **Type boost**	
• Photons	50%
• Electrons	50%

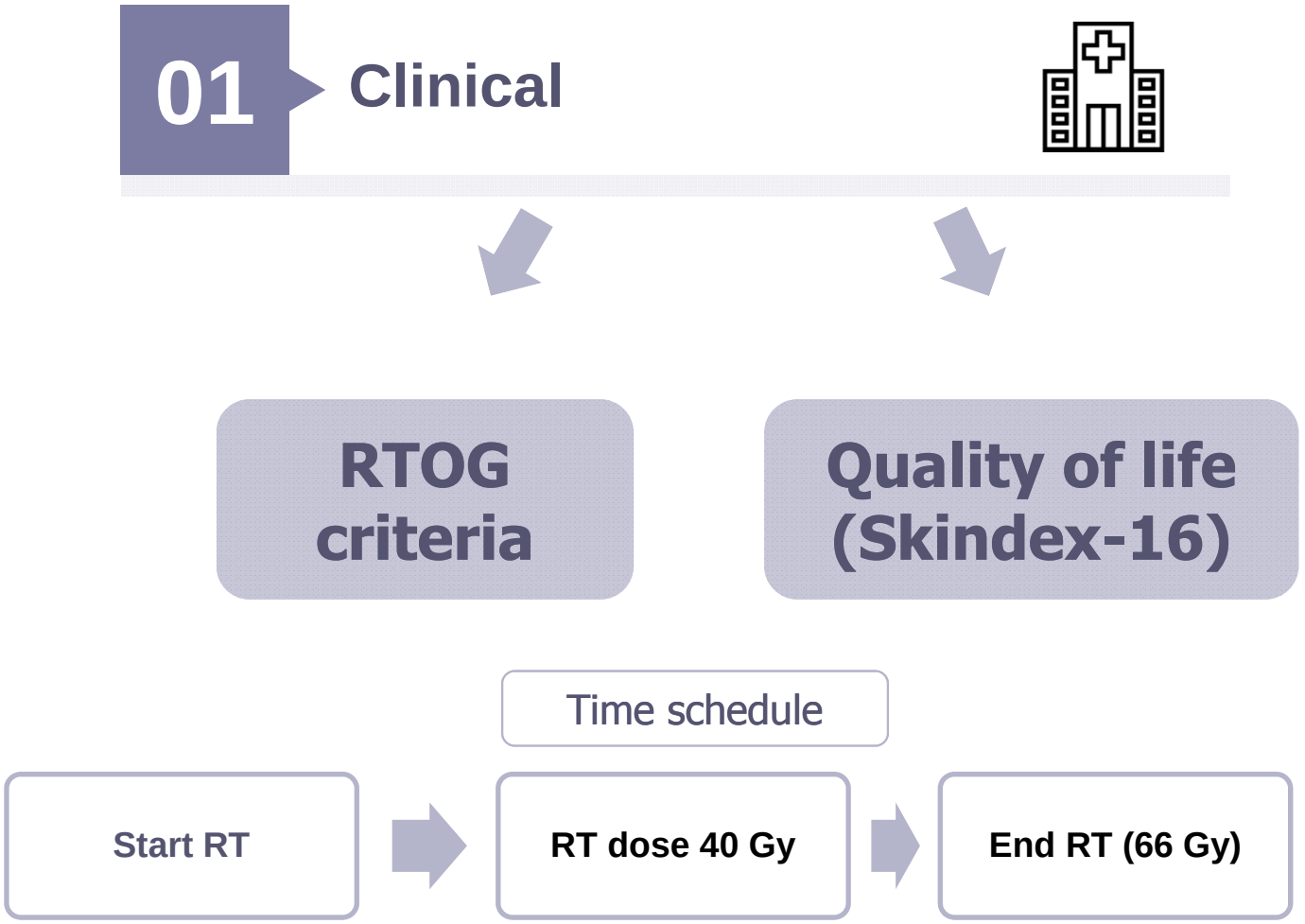
TRANSDERMIS trial

Outcome measures

01 Clinical

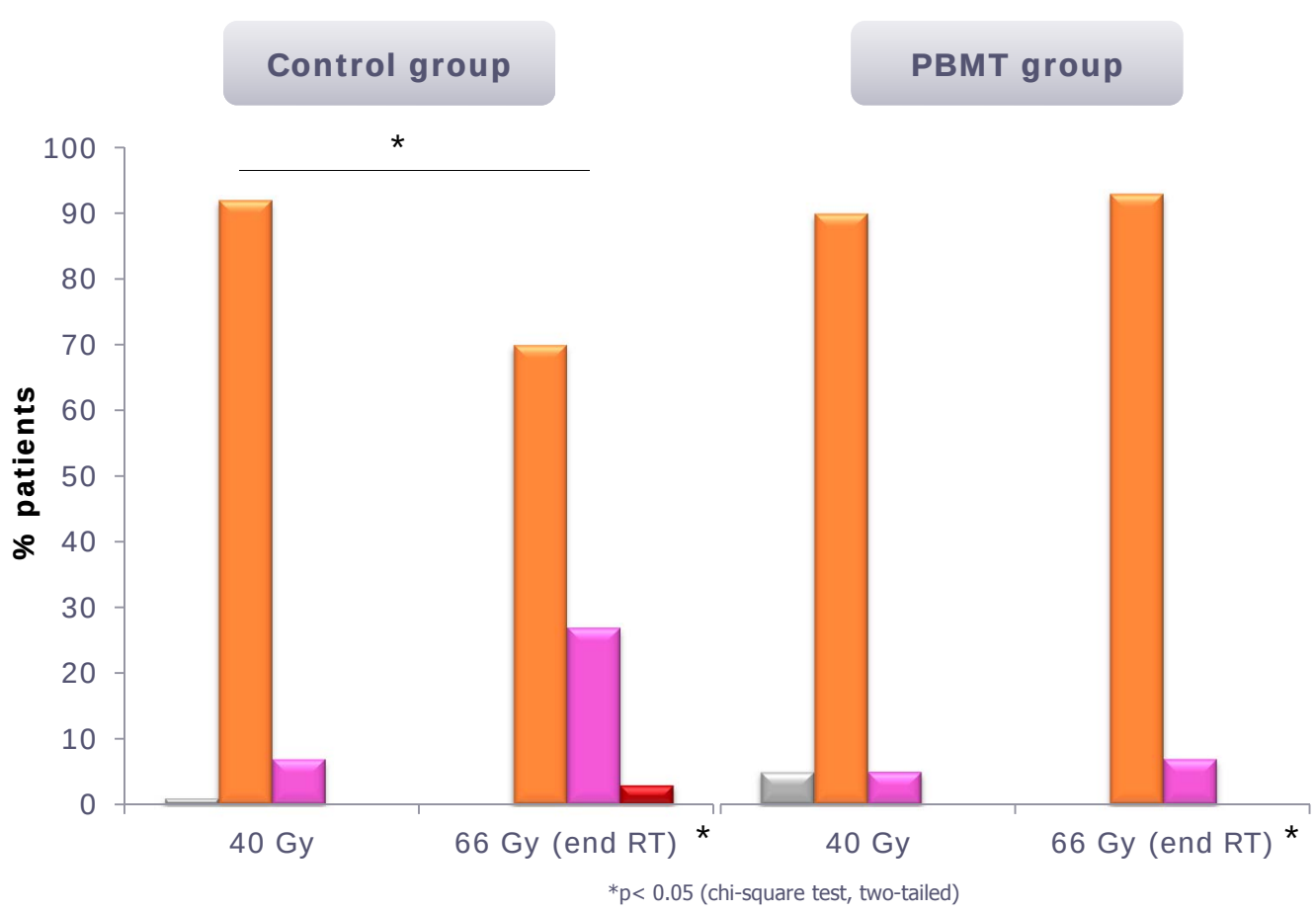
02 Biophysical

TRANSDERMIS trial



Robijns et al. Lasers Surg Med. 2018

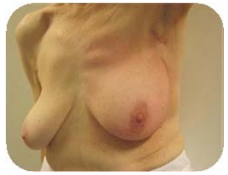
TRANSDERMIS trial: Skin assessment



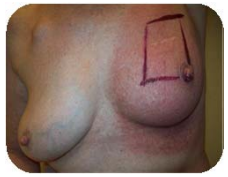
Significant less patients with ≥ grade 2 acute RD in PBMT group

GRADE 0

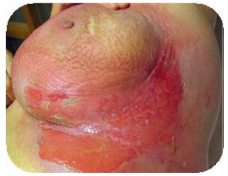
GRADE 1



GRADE 2

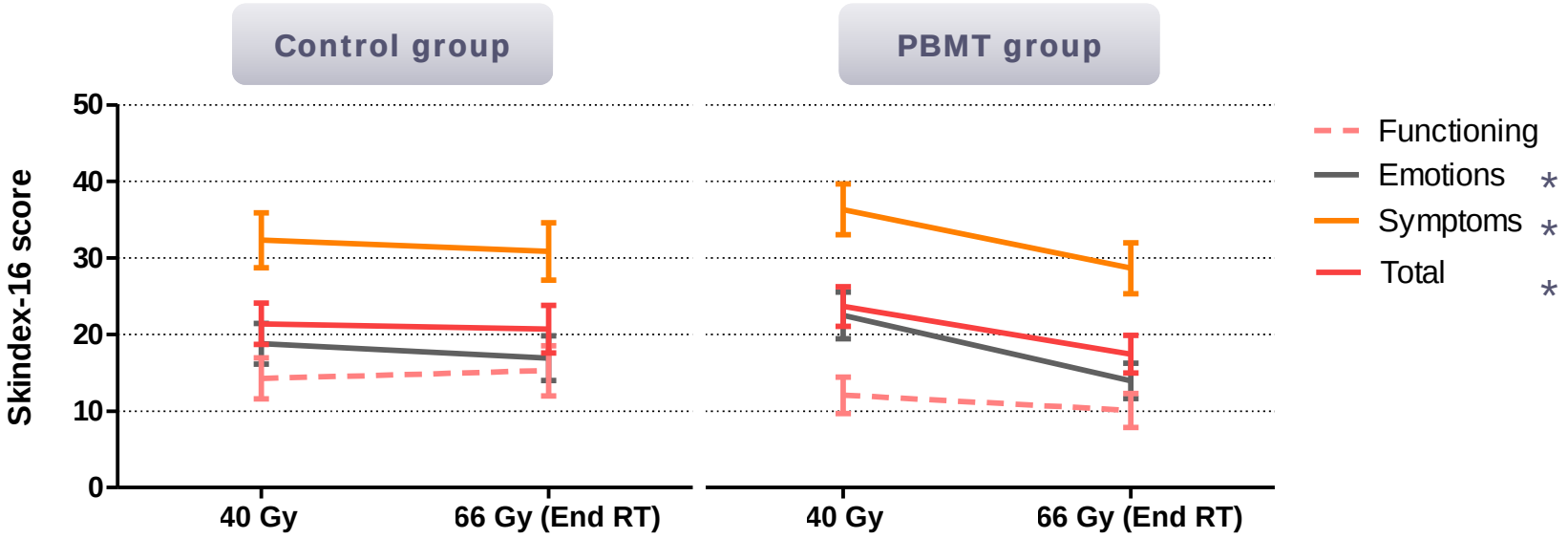


GRADE 3



Robijns et al. Lasers Surg Med. 2018

TRANSDERMIS trial: Quality of life



** Significant main time, group and interaction effect (group x time) p<0.05, 2X2 ANOVA*

Significant increase in quality of life in PBMT group

Robijns et al. Lasers Surg Med. 2018

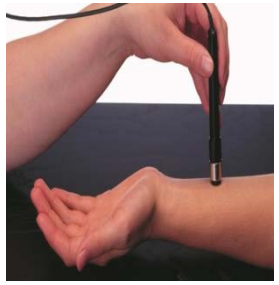
TRANSDERMIS trial

02 **Biophysical**

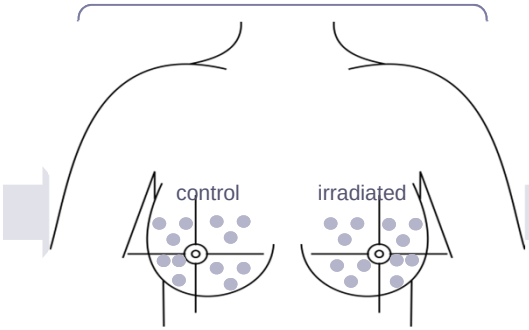
Pigmentation

Trans epidermal water loss (TEWL)

Hydration

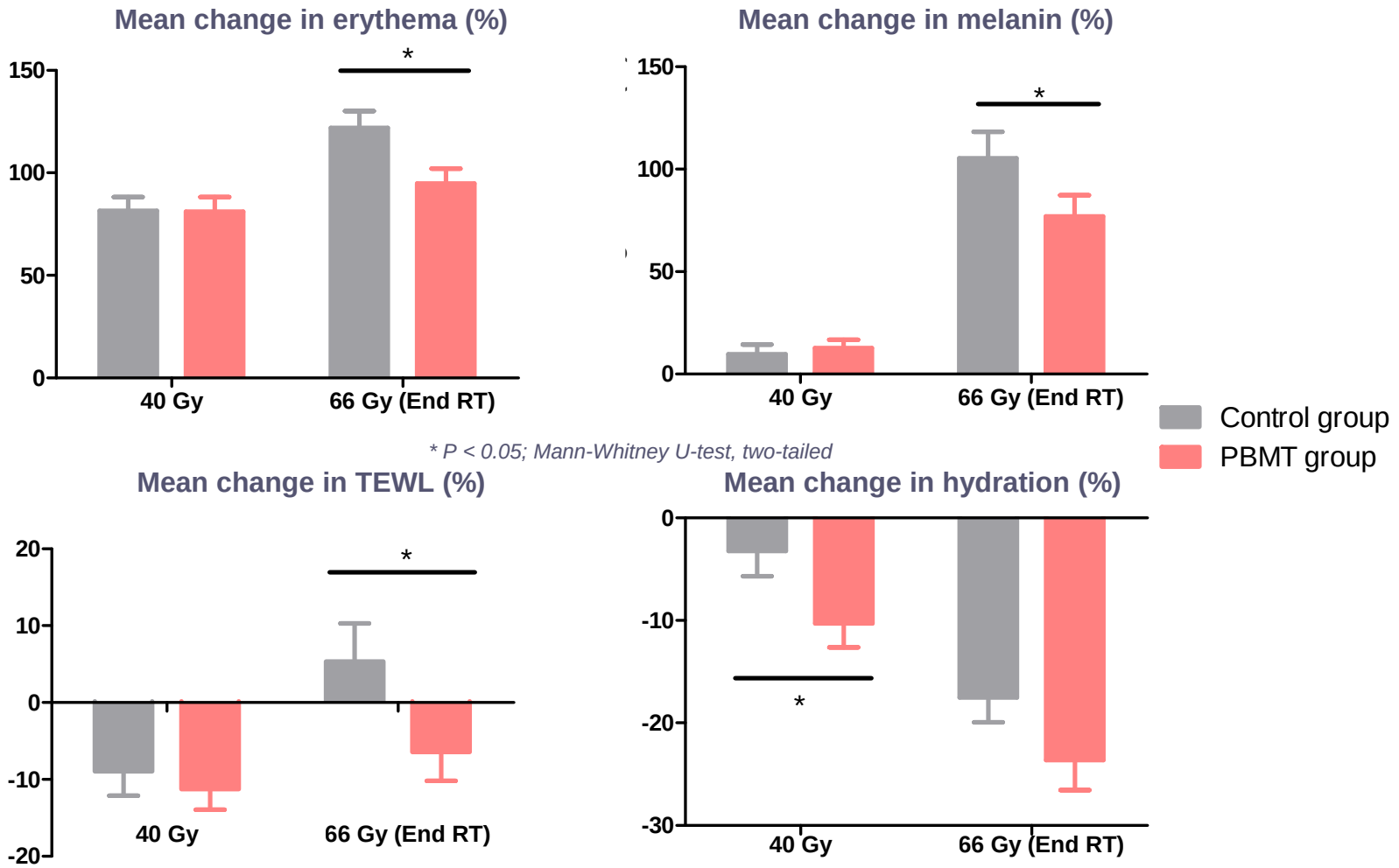


Baseline



End RT (66 Gy)

TRANSDERMIS trial: biophysical measures



PBMT reduces the degree of pigmentation and improves the skin barrier function

Robijns et al. Support Care Cancer. 2018

Our own experience

01

DERMIS trial

2013-2014

TRANSDERMIS trial

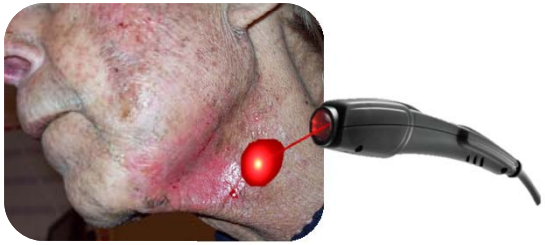
2015-2017

02

03

DERMISHEAD trial

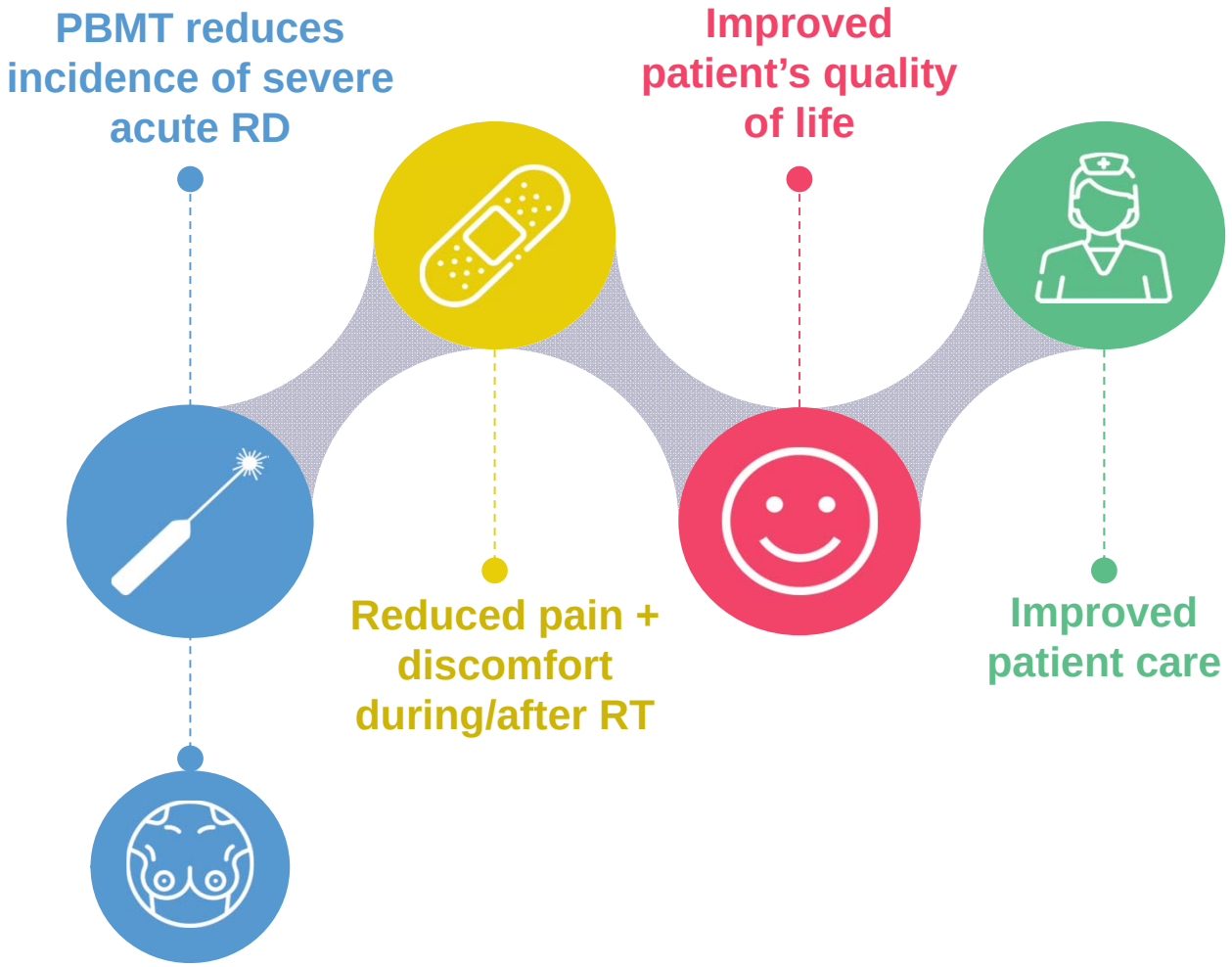
2016-…



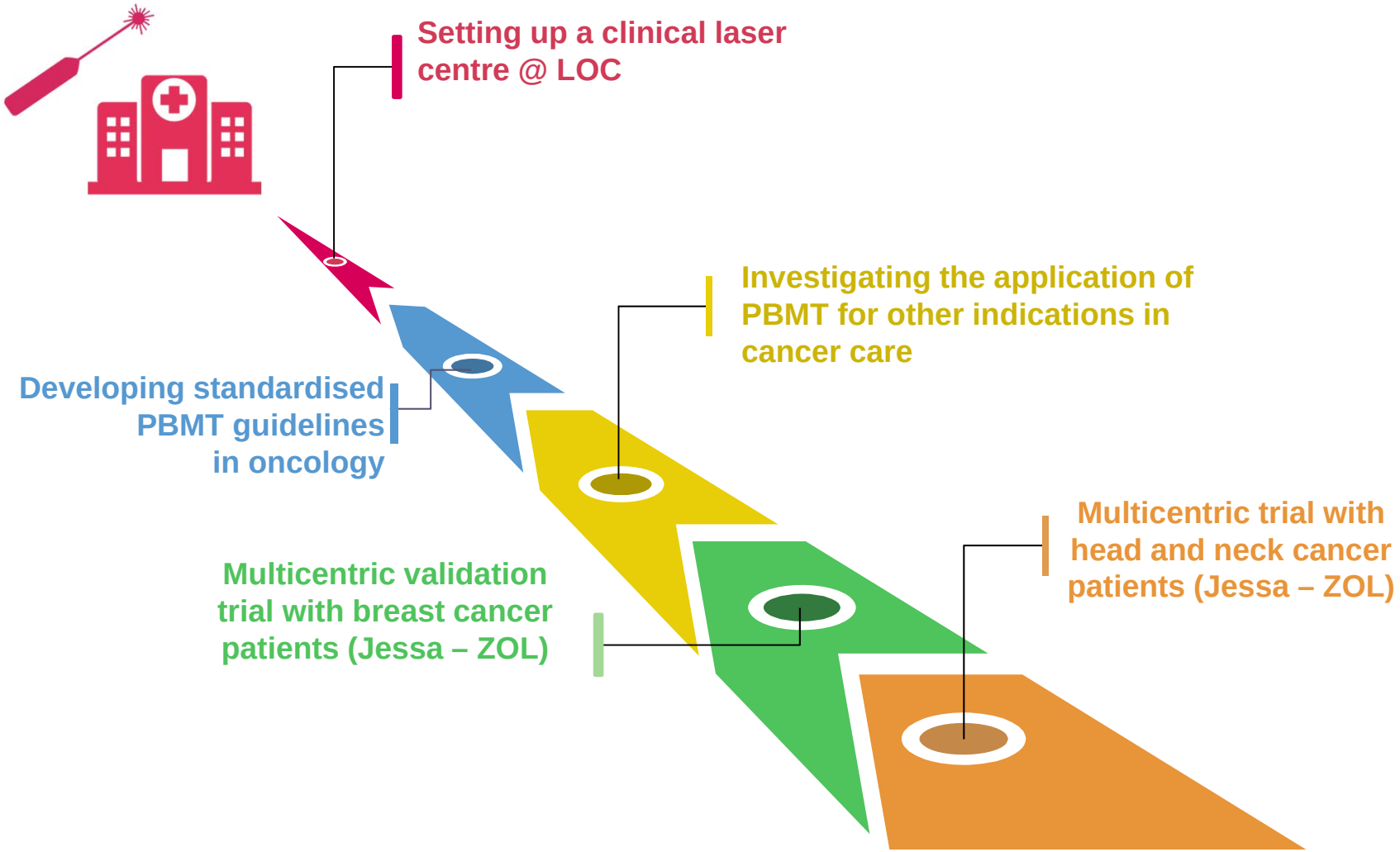
jessa ZIEKENHUIS

Ziekenhuis Oost-Limburg

Conclusion part 2



Future perspective



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