

APPENDIX 7: RANDOMIZED CONTROLLED TRIALS OF LOW LEVEL LIGHT THERAPY FOR THE PREVENTION OF ORAL MUCOSITIS IN ADULT AND PEDIATRIC PATIENTS RECEIVING TREATMENT FOR CANCER OR UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION - STUDY CHARACTERISTICS

First Author (reference)	Year Pub	Age	Underlying Condition	Setting	N Randomized	Type of Laser	Wavelength (nm)	Energy (J/m ²)	Laser Schedule
Antunes[1 2]	2013	Adults	Head and neck cancer	Chemo-radio	94	InGaAIP	660	4	5 sessions/week during radiation
Arbabi-Kalati[3]	2013	Adults	Oncologic disorders	Chemo	48	Mustang	630	5	Prior to chemotherapy
Gautam (a)[4 5]	2012	Adults	Head and neck cancer	Chemo-radio	239	He-Ne	632.8	3	5 sessions/week x 45 days
Gautam (b)[6]	2012	Adults	Oral carcinoma	Chemo-radio	121	He-Ne	632.8	3.5	5 sessions/week during radiation
Gouvea de Lima[7]	2012	Adults	Head and neck cancer	Chemo-radio	75	GaAIAs	660	2.5	5 sessions/week during radiation
Hodgson (a)[8]	2012	Both	Hematologic, oncologic disorders	HSCT (allo, auto)	40	Infrared LED	670 ± 10	4	Daily from day 0 to day +14
Hodgson (b)[8]	2012	Adults	Multiple myeloma	HSCT (auto)	40	Infrared LED	670 ± 10	4	Daily from day 0 to day +14
Oton-Leite[9 10]	2012	Adults	Head and neck cancer	Radio or Chemo-radio	60	InGaAIP	685	2	5 sessions/week during radiation
Pires-Santos[11]	2012	Adults	Breast cancer	Chemo	12	NA	NA	NA	Day 0 to day +7 q 48 hours
Silva[12]	2011	Both	Hematologic, oncologic disorders	HSCT (allo, auto)	42	InGaAIP	660	4	Daily from day -4 to day +4
Chor[13]	2010	Adults	NA	HSCT (auto)	34	AsGaAl	660	NA	Daily from day -7 to day 0
Khouri[14]	2009	Both	Hematologic disorders	HSCT (allo)	22	InGaAIP and GaAIAs laser	660 and 780	6.3	Daily until day +15 or day of engraftment
Antunes[15]	2007	Adults	Hematologic Disorders	HSCT (allo, auto)	38	InGaAIP	660	4	Daily from day -7 until neutrophil recovery
Cruz[16]	2007	Children	Hematologic and solid malignancies	Chemo or HSCT (auto)	62	NA	780	4	Daily from start of chemo x 5 days
Schubert[17]	2007	Both	Hematologic, oncologic disorders	HSCT (allo, auto)	47	GaAIAs	650	2	Daily from day -1 of conditioning to day +2
Arun Maiya[18]	2006	Adults	Oral carcinoma	Radio	50	He-Ne	632.8	1.8	5 sessions/week during radiation
Lopes[19]	2006	Adults	Head and neck cancer	Chemo-radio	60	InGaAIP	685	2	NA
Bensadoun[20 21]	1999	Adults	Head and neck cancer	Radio	30	He-Ne	632.8	2	5 sessions/week during radiation
Cowen[22]	1997	Adults	Hematologic malignancies	HSCT (auto)	30	He-Ne	632.8	1.5	Daily from day -5 to day -1

Adapted from Oberoi et al. For more detailed information and outcomes, see [23]

Abbreviations: N – number; allo - allogeneic; auto-autologous; chemo – chemotherapy; GaAIAs/AsGaAl – gallium-aluminium-arsenide/arsenate; He-Ne- helium-neon; HSCT – hematopoietic stem cell transplantation; InGaAIP – indium-gallium-aluminium phosphide; LED – light emitting diode; NA – not available; pub – published; radio- radiotherapy

REFERENCES

1. Antunes HS, Herchenhorn D, Small IA, et al. Phase III trial of low-level laser therapy to prevent oral mucositis in head and neck cancer patients treated with concurrent chemoradiation. *Radiother Oncol* 2013;**109**(2):297-302
doi: <http://dx.doi.org/10.1016/j.radonc.2013.08.010published> Online First: Epub Date]].
2. Antunes HS, Herchenhorn D, Small I, et al. Cost-effectiveness of low-level laser therapy (LLLT) in head and neck cancer patients submitted to concurrent chemoradiation. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer* 2013;**21**:S199 doi: <http://dx.doi.org/10.1007/s00520-013-1798-3published> Online First: Epub Date]].
3. Arbabi-Kalati F, Arbabi-Kalati F, Moridi T. Evaluation of the effect of low level laser on prevention of chemotherapy-induced mucositis. *Acta Medica Iranica* 2013;**51**(3):157-62
4. Gautam AP, Fernandes DJ, Vidyasagar MS, Maiya AG, Vadhiraja BM. Low level laser therapy for concurrent chemoradiotherapy induced oral mucositis in head and neck cancer patients - a triple blinded randomized controlled trial. *Radiother Oncol* 2012;**104**(3):349-54
doi: <http://dx.doi.org/10.1016/j.radonc.2012.06.011published> Online First: Epub Date]].
5. Gautam AP, Fernandes DJ, Vidyasagar MS, Maiya AG, Nigudgi S. Effect of low-level laser therapy on patient reported measures of oral mucositis and quality of life in head and neck cancer patients receiving chemoradiotherapy--a randomized controlled trial. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer* 2013;**21**(5):1421-8 doi: <http://dx.doi.org/10.1007/s00520-012-1684-4published> Online First: Epub Date]].
6. Gautam AP, Fernandes DJ, Vidyasagar MS, Maiya GA. Low level helium neon laser therapy for chemoradiotherapy induced oral mucositis in oral cancer patients - a randomized controlled

trial. *Oral Oncol* 2012;**48**(9):893-7

doi: <http://dx.doi.org/10.1016/j.oraloncology.2012.03.008published> Online First: Epub Date]].

7. Gouvea de Lima A, Villar RC, de Castro G, Jr., et al. Oral mucositis prevention by low-level laser therapy in head-and-neck cancer patients undergoing concurrent chemoradiotherapy: a phase III randomized study. *Int J Radiat Oncol Biol Phys* 2012;**82**(1):270-5

doi: <http://dx.doi.org/10.1016/j.ijrobp.2010.10.012published> Online First: Epub Date]].

8. Hodgson BD, Margolis DM, Salzman DE, et al. Amelioration of oral mucositis pain by NASA near-infrared light-emitting diodes in bone marrow transplant patients. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer* 2012;**20**(7):1405-

15 doi: <http://dx.doi.org/10.1007/s00520-011-1223-8published> Online First: Epub Date]].

9. Oton-Leite AF, Correa de Castro AC, Morais MO, Pinezi JCD, Leles CR, Mendonca EF.

Effect of intraoral low-level laser therapy on quality of life of patients with head and neck cancer undergoing radiotherapy. *Head Neck* 2012;**34**(3):398-404

doi: <http://dx.doi.org/10.1002/hed.21737published> Online First: Epub Date]].

10. Oton-Leite AF, Elias LS, Morais MO, et al. Effect of low level laser therapy in the reduction of oral complications in patients with cancer of the head and neck submitted to radiotherapy.

Spec Care Dentist 2013;**33**(6):294-300 doi: 10.1111/j.1754-4505.2012.00303.xpublished Online First: Epub Date]].

11. Pires-Santos GM, Ferreira MFL, Oliveira SCPS, Monteiro JSC, Brugnera A, Pinheiro ALB.

Use of Laser photobiomodulation in the evolution of oral mucositis associated with CMF chemotherapy protocol in patients with breast cancer-Case Report. *Med Oral Patol Oral Cir*

Bucal 2012;**17**:S252 doi: <http://dx.doi.org/10.4317/medoral.17643752published> Online First: Epub Date]].

12. Silva GBL, Mendonca EF, Bariani C, Antunes HS, Silva MAG. The prevention of induced oral mucositis with low-level laser therapy in bone marrow transplantation patients: a

randomized clinical trial. *Photomed Laser Surg* 2011;**29**(1):27-31

doi: <http://dx.doi.org/10.1089/pho.2009.2699published> Online First: Epub Date]].

13. Chor A, Torres SR, Maiolino A, Nucci M. Low-power laser to prevent oral mucositis in autologous hematopoietic stem cell transplantation. *Eur J Haematol* 2010;**84**(2):178-9

doi: <http://dx.doi.org/10.1111/j.1600-0609.2009.01336.xpublished> Online First: Epub Date]].

14. Khouri VY, Stracieri ABPL, Rodrigues MC, et al. Use of therapeutic laser for prevention and treatment of oral mucositis. *Braz Dent J* 2009;**20**(3):215-20

15. Antunes HS, de Azevedo AM, da Silva Bouzas LF, et al. Low-power laser in the prevention of induced oral mucositis in bone marrow transplantation patients: a randomized trial. *Blood* 2007;**109**(5):2250-5

16. Cruz LB, Ribeiro AS, Rech A, Rosa LGN, Castro CG, Jr., Brunetto AL. Influence of low-energy laser in the prevention of oral mucositis in children with cancer receiving chemotherapy. *Pediatr Blood Cancer* 2007;**48**(4):435-40

17. Schubert MM, Eduardo FP, Guthrie KA, et al. A phase III randomized double-blind placebo-controlled clinical trial to determine the efficacy of low level laser therapy for the prevention of oral mucositis in patients undergoing hematopoietic cell transplantation. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer* 2007;**15**(10):1145-54

18. Arun Maiya G, Sagar MS, Fernandes D. Effect of low level helium-neon (He-Ne) laser therapy in the prevention & treatment of radiation induced mucositis in head & neck cancer patients. *Indian J Med Res* 2006;**124**(4):399-402

19. Lopes CdO, Mas JRI, Zângaro RA. Prevenção da xerostomia e da mucosite oral induzidas por radioterapia com uso do laser de baixa potência. *Radiol. bras* 2006;**39**(2):131-36

20. Bensadoun RJ, Franquin JC, Ciais G, et al. Low-energy He/Ne laser in the prevention of radiation-induced mucositis. A multicenter phase III randomized study in patients with head and

neck cancer. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer* 1999;**7**(4):244-52

21. Bensadoun RJ, Ciais G. Radiation-and chemotherapy-induced mucositis in oncology: results of multicenter phase III studies. *J Oral Laser App* 2002(2):115-20

22. Cowen D, Tardieu C, Schubert M, et al. Low energy Helium-Neon laser in the prevention of oral mucositis in patients undergoing bone marrow transplant: results of a double blind randomized trial. *Int J Radiat Oncol Biol Phys* 1997;**38**(4):697-703

23. Oberoi S, Zamperlini-Netto G, Beyene J, Treister N, Sung L. Effect of prophylactic low level laser therapy on oral mucositis: a systematic review and meta-analysis *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2014;**PlosOne (in press)**