

Improvement in quality of life of an oncological patient by laser phototherapy

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Improvement in quality of life of an oncological patient by laser phototherapy.

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OBJECTIVE AND BACKGROUND DATA: Common side effects of radiotherapy (RT) to the head and neck include oral mucositis, xerostomia, and severe pain. The aim of this study is to report improvement in the quality of life of an oncological patient by laser phototherapy (LPT). **CLINICAL CASE AND LASER PHOTOTHERAPY PROTOCOL:** The patient, a 15-year-old girl diagnosed with mucoepidermoid carcinoma, underwent surgical excision of a tumor of the left palatomaxilla. After that, she was subjected to 35 sessions of RT (2 Gy/d). Clinical examination revealed the spread of severe ulcerations to the jugal mucosa, gums, lips, hard palate, and tongue (WHO mucositis score 3). She had difficulty in moving her tongue and she was unable to eat any solid food. Oral hygiene orientation and LPT were performed throughout all RT sessions. A continuous diode laser, 660 nm, 40 mW, 6 J/cm², 0.24 J per point in contact mode, with spot size of 0.04 cm² was used in the entire oral cavity. A high-power diode laser at 1 W, 10 sec per cm of mucositis, approximately 10 J/cm², was used in defocused mode only on ulcerative lesions. After the first laser irradiation session, decreases in pain and xerostomia were reported; however, a more significant improvement was seen after five sessions. At that point although the mucositis score was still 2, the patient reported that she was free of pain, and consequently a palatine plate could be made to rehabilitate the entire surgical area. Seventeen laser irradiation sessions were necessary to eliminate all oral mucositis lesions. **CONCLUSION:** Normal oral function and consequent improvements in the quality of life of this oncologic patient were observed with LPT.

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Effects of diode 808 nm GaAlAs low-power laser irradiation on inhibition of the proliferation of human hepatoma cells in vitro and their possible mechanism.

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Low-power laser irradiation (LPLI) has come into a wide range of use in medical field. Considering basic research, LPLI can enhance DNA synthesis and increases proliferation rate of human cells. But only a few data about the effects of LPLI on human liver or hepatoma cells are available. The cytoskeleton plays important roles in cell function and therefore is implicated in the pathogenesis of many human liver diseases, including malignant tumors. In our previous study, we found the stability of cytokeratin molecules in human hepatocytes was related to the intact microtubule network that was influenced by colchicine. In this study, we are going to search the effect of LPLI on proliferation of human hepatoma cell line HepG2 and J-5 cells. In addition, the stability of cytokeratin and synemin (one of the intermediate filament-associated proteins) were analyzed under the action of LPLI to evaluate the possible mechanism of LPLI effects on proliferation of human hepatoma cells. In experiment, HepG2 and J-5 cells were cultured in 24-well plate for 24 hours. After irradiation by 130 mW diode 808 nm GaAlAs continue wave laser in different time intervals, the cell numbers were counted. Western blot and immunofluorescent staining examined the expression and distribution of PCNA, cytokeratin and synemin. The cell number counting and PCNA expression were evaluated to determine the proliferation. The organization and expression of cytokeratin and synemin were studied to identify the stability of cytoskeleton affected by LPLI. The results revealed that proliferation of HepG2 and J-5 cells was inhibited by LPLI since the cell number and PCNA expression was reduced. Maximal effect was achieved with 90 and 120 seconds of exposure time (of energy density 5.85 J/cm² and 7.8 J/cm², respectively) for HepG2 and J-5, respectively. The decreased ratio of cell number by this dose of irradiation was 72% and 66% in HepG2 and J-5 cells, respectively. Besides that, the architecture of intermediate filaments in these cells was disorganized by laser irradiation. The expression of intermediate filament-associated protein, synemin, was also reduced. Two significant findings are raised in this study: (1) Diode 808 nm GaAlAs continuous wave laser has an inhibitory effect on the proliferation of human hepatoma cells line HepG2 and J-5. (2) The mechanism of inhibition might be due to down-regulation of synemin expression and alteration of cytokeratin organization that was caused by laser irradiation.

Med Surg. 2002; 20 (1): 23-26.

Effects of low-level laser therapy on malignant cells: In vitro study. J Clin

Pinheiro A L, Carneiro Nascimento S, De Barros Vieira A L et al.

The aim of a study by Pinheiro was to assess the effect of 635- and 670-nm laser irradiation on H.Ep.2 cells in vitro using MTT. It was decided to evaluate the effect of increased doses of laser light on these cells. The cells, obtained from SCC of the larynx. The cultures were kept either at 5% or 10% of FBS. Twenty-four hours after transplantation, the cells were irradiated with laser light (5 mW diode lasers; 635 and 670 nm; beam cross section 1 mm at local light doses between 0.04 and 4.8.10(4) J cm². For 670 nm, significant differences in the proliferation were observed between the two concentrations of FBS and between

irradiated cultures and controls. Although the results were not significant, 635-nm irradiated cells also proliferated more than non-irradiated ones. This occurred under both conditions of nutrition. It was concluded, that irradiation with 670 nm laser light applied at doses between 0.04 and 4.8104 J/cm² could significantly increase proliferation of laryngeal cancer cells.

Anesteziol Reanimatol. 2001 Sep-Oct;(5):47-50.

[Validation and approaches to correction of hemorheologic disorders in patients with gastrointestinal cancer]

[Article in Russian]

Karabanov GN, Karimov AI, Ogi II, Gantsev KSh, Khalikov RA, Ishmuratova RSh.

A total of 237 patients were examined: 127 with gastric cancer and 110 with colonic cancer, 99 women and 138 men, mean age 57.5 years. Erythrocyte deformability and aggregation were studied by original methods. Red blood, protein metabolism, and endogenous intoxication parameters were evaluated by routine laboratory tests. Increased aggregation and volume of erythrocytes and decrease of their deformability and hemoglobin content in parallel with hypo- and dysproteinemia and increased level of endogenous intoxication were observed in all patients with gastrointestinal cancer. Correction of these disorders by intravenous laser exposure of the blood essentially improved the erythron status and protein metabolism and decreased endotoxiosis. Infusion/transfusion therapy also notably improved the erythron function and decreased endogenous intoxication. Analysis of the results of surgery showed decreased incidence of complications and lethal outcomes, which was due to methods of corrective therapy.

Klin Khir. 1999;(5):27-9.

[Intravascular laser irradiation of the blood in complex treatment of the patient with esophageal cancer]

[Article in Ukrainian]

Hanul VL, Zaitsev SL, Kirkilevs'kyi SI, Fil'chakov FV.

Complex treatment of 41 patients with intrathoracic esophageal cancer using intravascular laser irradiation of the blood was done. The immunorehabilitating method application had promoted the postoperative complications rate lowering, the mortality reduction, the three-year survival rate indexes improvement.

Vopr Onkol. 1998;44(6):672-5.

[Microcirculation in gastrointestinal cancer and some possibilities of its correction]

[Article in Russian]

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Microcirculation and blood rheology were studied in 348 patients with tumors of the gastrointestinal tract. Such disorders as increased blood and plasma viscosity, aggregates of erythrocytes and their increased stability of shape were recorded in conjunction with hypo- and dysproteinemia, endogenous intoxication syndrome and microvascular disturbances. Microcirculation significantly improved and endoxemia was alleviated following photomodification of the blood by use of helium-neon laser radiation and application of an original procedure of infusion.

Klin Khir. 1998;(3):40-1.

[Results of the clinical use of laser therapy in malignant tumors]

[Article in Ukrainian]

Dryzhak VI, Halaichuk II, Dombrovich MI, Oleksii OP, Zahurs'ka NO.

The raise of natural antitumoral resistance level, the reduction of intoxication severity, the raise of an organism tolerance to irradiation and polychemotherapy were permitted by adjuvant low-energy laser therapy absorption in the complex of treatment of 27 patients with colonic cancer in early postoperative period, 16--cervix uteri cancer while irradiation therapy conduction, and 14--with cutaneous melanoma during polychemotherapy.

Biomodulation of normal and tumor cells

J Photochem Photobiol B: Biology. 1997; (40): 253-257

In a study by Schaffer et al. various cells were irradiated by 805 nm laser light. The cells were (1) murine skeletal myotubes, (2) normal urothelial cells, (3) human squamous carcinoma cells of the gingival mucosa and (4) urothelial carcinoma cells. Mitotic index for 1, 2 and 4 increased at fluences of 4 J/cm² while irradiation at 20 J/cm² resulted in a slight decrease. The no 3 cells showed a decrease of the mitotic index with both fluences. The most interesting observation is the different reaction of the two carcinoma cells.

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Biological Effect of Helium-Neon (He-Ne) Laser Irradiation on Mouse Myeloma (Sp2-Ag14) Cell Line In Vitro

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Received for publication 22 July 1997; accepted following revision 6 February 1998.

We examined the effect of helium-neon (He-Ne) laser irradiation with a wavelength of 632.8 nm on cell cycle synchronisation of monolayer growing mouse myeloma (Sp2-Ag14) cell line. The monolayer cultures were exposed to repeated doses of different energy densities (4-64 J/cm²). The nuclear DNA content has been studied by flow cytometry to obtain the cell percentage in each cell cycle phase. Results showed that the He-Ne laser irradiation at energy densities of 8-64 J/cm² produced a significant and different effect on the G0-G1 and S phases of cell cycle over control. In contrast, no significant effect in G2-M phase was produced by He-Ne laser irradiation at any energy density compared with non-treated control. These results support previous observations suggesting that He-Ne laser irradiation of low energy density interferes with cell cycling and may inhibit cell proliferation when irradiation is performed at doses of 8 J/cm² or more.

[Nizkointensivnaia lazernaia terapiia v detskoj onkologii] Voprosy onkologii. 2000; 46 (4): 459-461.

Balakirev S A, Gusev L I, Kazanova M B et al.

The study by Balakirev suggests that the application of laser therapy makes it possible to reduce the time needed for the management of radiation injury and chemotherapy complications in pediatric patients 1.5-2-fold. It was shown that exposure to laser caused mononuclear levels of donors' blood to rise, which in turn led to release, in higher concentrations, of IL-1 and FNO cytokins, major factors of immune response development.

[Low-intensity lasers in pediatric oncology]. Vestn Ross Akad Med Nauk. 2000; (6): 24-27.

Durnov L A, Gusev L I, Balakirev S A et al

The study by Durnov outlines the outcomes of treatment for complications associated with chemo- and radiation therapy in children with malignant neoplasms by using low-intensity laser radiation. The use of this therapy may reduce the duration of treatment of these complications by 1.5-2 times. The use of low-intensity laser radiation in the treatment of other complications that are common in pediatric oncological care is briefly described..

[The correction of the subcellular postradiation changes in the hypothalamus and parathyroid gland by using low-intensity laser radiation. An experimental study]. Vopr Kurortol Fizioter Lech Fiz Kult. 2000; (3): 3-4.

Korolev Iu N, Panova L N, Geniatulina M S

The study by Korolev showed that exposure of the rat adrenals 30 days after radiation (1 Gy) to infrared laser radiation arrested the development of ultrastructural disorders in the cells of the hypothalamus and the parathyroid gland and enhanced subcellular manifestations of adaptation and rehabilitation processes.

USE OF LOW-LEVEL LASER THERAPY (LLLT) FOR TREATMENT OF THE PATIENTS WITH A CANCER OF A ESOPHAGUS T3N0MX

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In this part of work at 20 patients received the laser therapy (LLLT) in a combination with external radial therapy under the radical program (1 group), 15 patients (2 groups) received only one laser therapy, the control group consist of 18 men receiving only external radial therapy on the radical program (3 groups), 10 patients received only symptomatic therapy (4 groups). The stage of disease T3N0MX and spent treatment in skilled and control groups was identical. Radial therapy carried out on kettles "Lutch-1" and "Agat-?" on a procedure from three fields (1 parasternal, 2 and 3 - juxtaspinal under an angle of 40 degrees to a backbone) with a single dose till 90 % on doses by a curve 1,8 Gr and cooperative dose 64-66 Gr. The irradiation was carried out 5 days per one week with a break 2 days. A GaAs semiconductor laser (wavelength 890 nm., pulsed mode, pulse power 5-10 W.) was used for laser therapy. Laser therapy carried out after leading to a tumor of a dose 15-20 Gr. The sessions LLLT carried out 3 times per one week in day. A cooperative dose - 5,8 J/cm² The analysis of lifespan of the patients in group receiving LLLT with radial therapy and in control group has shown, that use of laser therapy increases lifespan of the patients: 1 group - up to 10,28 ±2,03 months, in 2 groups up to 11,4 ±3,02 months, in 3 groups it makes 7,35 ±2,4 months, in 4 groups - 6,3 ± 1,94 months. Use LLLT allows to reduce quantity of occurrence of complications after radiation therapy in 2,9 times.

HeNe laser reduces mucositis

a) Barasch B et al. Helium-neon laser effects on conditioning-induced mucositis in bone marrow transplantation patients. *Cancer*. 1995; 76 (12): 2550-2556.

Oral mucositis is a common complication of bone marrow transplantation conditioning therapy. Different drugs are given in order to reduce rejection of the implant. These drugs induce an oral mucositis. The mucositis is painful and complicates nutrition. Sometimes the intake of the drug has to be stopped due to complications. In the study above 20 patients received HeNe to their oral mucosa, either right or left of midline. One side was sham irradiated. Laser treatment was well-tolerated and reduced the severity of oral mucositis.

b) Cowen D 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): 697-707. Significant reduction of oral mucositis using a 60 mW HeNe laser

CHEMO-AND RADIATION-INDUCED MUCOSITIS : RESULTS OF MULTICENTER PHASE III STUDIES.

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Considerable buccal toxicity of radiotherapy and/or chemotherapy in patients with cancer can cause patients to become discouraged and can alter their quality of life. In addition, such toxicity often necessitates alterations of treatment planning, with grave consequences in term of tumor response and even survival (concept of dose-intensity). With 5-fluorouracil and head and neck radiotherapy for example, acute mucosal toxic effect is the main limiting factor for which no clinically appropriate prophylaxis or efficacious antidote has been found to date. Management of oral mucositis is currently primarily directed at palliation of the symptoms, and prevention of infections. Low Level Laser Therapy (LLLT) has been reported effective in reducing the severity of oral mucositis lesions in a non-randomized trial, initiated in Nice (France) by Ciais et al. (1). The efficacy of this method in the prevention of chemotherapy induced oral mucositis has been subsequently confirmed in two prospective, double-blind randomized trials, in

patients undergoing bone marrow transplant (2 ; 3). These initial findings and the high incidence of radiation-induced mucositis prompted a randomized multicenter trial to evaluate LLLT for the prevention of acute radiation-induced oropharyngeal mucosal lesions. The trial was open to patients with carcinoma of the oropharynx, hypopharynx and oral cavity being treated by external radiotherapy, with a total dose of 65 Gy at a rate of 1 fraction of 2 Gy/day, 5 days a week, from cobalt-60 or linear accelerator photons, without prior surgery or concomitant chemotherapy. Between September 1994 and March 1998, thirty patients entered this double-blind randomized study conforming to the Huriet law. The goal was to determine whether preventive HeNe laser beam applications could reduce or prevent oropharyngeal mucositis caused by radiotherapy.

Patients characteristics: There were 26 men and 4 women. Mean age was 60.4 years (range 36 - 78). Oral examination and preventive dental management were performed prior to radiotherapy. Daily oral hygiene (cleaning of the teeth and dental prosthesis) during treatment was recommended. Patients were assigned to either laser treatment (L+) or sham-treatment (L-) by computer blocked randomization. The protocol called for the inclusion of 30 patients, 15 in each arm. No associated anti-inflammatory or other treatment was authorized. Analgesics could be prescribed, but not during the 2 days preceding each week evaluation. Patients received HeNe laser applications daily for five consecutive days (Monday to Friday) each week, during the seven weeks of radiotherapy. The malignant tumor had to be located outside the areas selected for randomized preventive LLL application. Laser was delivered to the tissues by a straight optical fiber with a 1.2 mm spot size. The 9 treatment areas included : posterior third of buccal mucosa, soft palate and anterior tonsillar pillars. Laser illumination consisted of a continuous beam (wavelength: 632.8 nm; power: 60 mW), calibrated at the end of the optical fiber every day. The treatment time (t) for each application point was given by the equation : $t \text{ (sec)} = \text{energy (J/cm}^2) \times \text{surface (cm}^2) / \text{Power (W)}$. The average energy density delivered to the treatment areas was 2 J/cm², and was applied on these nine points, equally distributed on the treated surfaces, for 33 s per point (each specific LLL session lasted approximately 5 minutes). The 60 mW lasers were designed and produced by Fradama S.A. (Geneva, Switzerland). All laser illuminations were performed by the same individual in each center. This operator was the only person to know whether or not the patient was sham-treated, and did not participate in the evaluation and scoring mucositis. During the sessions, patients wore wavelength-specific dark glasses and were instructed to keep their eyes closed, to assure that they did not know whether they were sham-treated or whether they received laser applications. The laser made the same noises, and the probe was held in the mouth exactly the same way, when treating control subjects and when treating laser patients. The whole irradiation field, the oral cavity and the visible oropharynx were inspected weekly during seven weeks by the same physician (head and neck surgeon, or radiation oncologist), blinded to the result of randomization. The evaluation of mucositis and pain was performed on the oropharyngeal areas (9 points). Criteria for evaluation were the standard WHO scale for mucositis in the oropharynx; and a segmented visual analogic scale for pain (patient self evaluation). In this phase III study, no adverse effect was noted with the use of a 60-mW HeNe laser, though it is important to emphasize the importance of preventing retinal damage by the use of wavelength-specific goggles. This is consistent with previous reports. Laser applications delayed time of onset, attenuated the peak severity and shortened the duration of oral mucositis. The difference between L+ and L- patients was statistically significant from week 4 to week 7. With the total delivered dose of 65Gy, conventionally fractionated, all L- patients developed mucositis at week 2, with a peak at week 5 (13 with grade 3 mucositis, and 2 with grade 2 mucositis). All L+ patients also had mucositis at week 2, with a peak at week 5 (5 with grade 3 mucositis, 9 with grade 2, 1 with grade 1). During the 7 weeks of treatment, the mean grade of mucositis in L+ patients was significantly lower (p=0.01) than the mean grade in L- patients. Results on decrease in pain intensity were also quite convincing. Laser applications reduced the incidence and duration of morphine administration. Ability to swallow was also improved. These results confirm previous data collected with this method, especially for patients undergoing bone marrow transplant (BMT). In a prospective study, Barasch et al. (2) used a 25- mW laser on one side of the mouth only and reported a statistically significant reduction in oral mucositis on that side, according to the scoring system they used. In the Barasch study, each patient was his or her own control, which could be of importance, since mucosal damage on the sham-treated side could have benefited also from a distant systemic laser effect. Cowen et al. (3), using a 60 mW HeNe laser, performed a double-blind randomized phase III trial, in which laser was administered to the treatment group during conditioning, prior to the day of transplant. This study showed a 33% reduction of grades 3 and 4 mucositis in L+ patients. In this trial, mucositis was scored according to an oral examination guide, with a 16 items scale, of which 4 were assessed by the

patients themselves. Daily mucositis index was significantly lower in L+ patients ($p < 0.05$) from d+2 to d+7 after BMT. The duration of grade 3 stomatitis was also reduced in L+ patients ($p = 0.01$). Oral pain was lower ($p = 0.05$), and L+ patients required less morphinomimetics ($p = 0.05$). Finally, xerostomia and ability to swallow were improved among L+ patients ($p = 0.05$, and $p = 0.01$, respectively). All these results were in keeping with previous observations, suggesting the efficacy of the method (1, 4). Schubert et al. for example (4), identified a trend towards lower oral mucositis scores, on all examination days, in an interim results report of a phase I/II study, in which laser application was performed prophylactically during conditioning before BMT.

In conclusion, LLLT seems to be a safe and efficient method for the prevention of chemo- and radiation-induced mucositis, with a tremendous potential interest for combined modality treatment. The concomitant use of chemo- and radiotherapy is becoming the new standard of care in advanced head and neck cancer, with very encouraging results, even in nonresectable cases. Since the main limiting factor of these combined protocols is the acute mucositis, this complementary treatment option with low level HeNe laser could be important in enhancing the feasibility of such regimens, and especially in the conservation of dose-intensity effect. At Nice, where the method is now used routinely during head and neck radiation, we project a new study testing LLL in patients being treated with concomitant chemo- and radiotherapy for advanced head and neck cancer. Even more than the improvement of patient comfort, the therapeutic index of combined specific treatment should be increased by the use of LLLT, besides standard supportive care, oral care and enteral nutrition (5). During this study, other laser wavelengths and powers could be tested, and compared to 60-mW HeNe laser.

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5. R. J. BENSADOUN, J. C. FRANQUIN, G. CIAIS, V. DARICOURT, M. M. SCHUBERT, M. VIOT, J. DEJOU, C. TARDIEU, K. BENEZERY, T. D. NGUYEN, Y. LAUDOYER, O. DASSONVILLE, G. POISSONNET, J. VALLICIONI, A. THYSS, M. HAMDI, P. CHAUVEL, F. DEMARD. 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. *Support Care Cancer* 7(4):244-252, 1999.

J Clin Laser Med Surg. 2002 Feb;20(1):23-6

Effects of low-level laser therapy on malignant cells: in vitro study.

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The aim of this study was to assess the effect of 635- and 670-nm laser irradiation on H.Ep.2 cells in vitro using MTT. In addition to our previous report on the effects of LLLT on the proliferation of laryngeal carcinoma cells in which it was found that

irradiation H.Ep.2 cells with 670-nm laser results in increased cell proliferation, it was decided to evaluate the effect of increased doses of laser light on these cells. The cells, obtained from SCC of the larynx, were routinely processed from defrost to the experimental condition. The cultures were kept either at 5% or 10% of FBS. Twenty-four hours after transplantation, the cells were irradiated with laser light (5-mW diode lasers; 635 and 670-nm; beam cross section approximately 1 mm) at local light doses between 0.04 and 4.810(4) Jm(-2). For 670 nm, significant differences in the proliferation were observed between the two concentrations of FBS ($p = 0.002$) and between irradiated cultures and controls ($p = 0.000$). Although the results were not significant, 635-nm irradiated cells also proliferated more than nonirradiated ones. This occurred under both conditions of nutrition. It is concluded, that irradiation with 670-nm laser light applied at doses between 0.04 and 4.810(4) Jm(-2) could significantly increase proliferation of laryngeal cancer cells.

J Photochem Photobiol B. 2000 Dec;59(1-3):1-8.

Magnetic resonance imaging (MRI) controlled outcome of side effects caused by ionizing radiation, treated with 780 nm-diode laser -- preliminary results.

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BACKGROUND and OBJECTIVE: Ionizing radiation therapy by way of various beams such as electron, photon and neutron is an established method in tumor treatment. The side effects caused by this treatment such as ulcer, painful mastitis and delay of wound healing are well known, too. Biomodulation by low level laser therapy (LLLT) has become popular as a therapeutic modality for the acceleration of wound healing and the treatment of inflammation. Evidence for this kind of application, however, is not fully understood yet. This study intends to demonstrate the response of biomodulative laser treatment on the side effects caused by ionizing radiation by means of magnetic resonance imaging (MRI). **STUDY DESIGN/PATIENTS and METHODS:** Six female patients suffering from painful mastitis after breast ionizing irradiation and one man suffering from radiogenic ulcer were treated with $\lambda=780$ nm diode laser irradiation at a fluence rate of 5 J/cm². LLLT was performed for a period of 4-6 weeks (mean sessions: 25 per patient, range 19-35). The tissue response was determined by means of MRI after laser treatment in comparison to MRI prior to the beginning of the LLLT. **RESULTS:** All patients showed complete clinical remission. The time-dependent contrast enhancement curve obtained by the evaluation of MR images demonstrated a significant decrease of enhancement features typical for inflammation in the affected area. **CONCLUSION:** Biomodulation by LLLT seems to be a promising treatment modality for side effects induced by ionizing radiation.

Lasers Med Sci. 2003;18(2):100-3.

Low-level 809 nm GaAlAs laser irradiation increases the proliferation rate of human laryngeal carcinoma cells in vitro.

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The aim of the study was to investigate the effect of low-level 809 nm laser irradiation on the proliferation rate of human larynx carcinoma cells in vitro. Epithelial tumor cells were obtained from a laryngeal carcinoma and cultured under standard conditions. For laser treatment the cells were spread on 96-well tissue culture plates. Sixty-six cell cultures were irradiated with an 809 nm GaAlAs laser. Another 66 served as controls. Power output was 10 mW(cw) and the time of exposure 75-300 s per well, corresponding to an energy fluence of 1.96-7.84 J/cm². Subsequent to laser treatment, the cultures were incubated for 72 h. The proliferation rate was determined by means of fluorescence activity of a redox indicator (Alamar Blue Assay) added to the cultures immediately after the respective treatment. The indicator is reduced by metabolic activity related to cellular growth. Proliferation was determined up to 72 h after laser application. The irradiated cells revealed a considerably higher proliferation activity. The differences were highly significant up to 72 h after irradiation (Mann-Whitney U test, $p < 0.001$). A cellular responsiveness of human laryngeal carcinoma cells to low-level laser irradiation is obvious. The cell line is therefore suitable for basic research investigations concerning the biological mechanisms of LLLT on cells.

Braz Dent J. 2002;13(2):109-12.

Does LLLT stimulate laryngeal carcinoma cells? An in vitro study.

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Low level laser therapy (LLL) has been used successfully in biomedicine and some of the results are thought to be related to cell proliferation. The effects of LLLT on cell proliferation is debatable because studies have found both an increase and a decrease in proliferation of cell cultures. Cell culture is an excellent method to assess both effects and dose of treatment. The aim of this study was to assess the effect of 635nm and 670 nm laser irradiation of H.Ep.2 cells in vitro using MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide). The cells were obtained from squamous cell carcinoma (SCC) of the larynx and were routinely processed from defrost to the experimental

condition. Twenty-four hours after transplantation the cells were irradiated with doses ranging from 0.04 to 0.48 J/cm² for seven consecutive days (5 mW diode lasers: 635 nm or 670 nm, beam cross-section approximately 1 mm) at local light doses between 0.04 and 0.48 J/cm². The results showed that 635 nm laser light did not significantly stimulate the proliferation of H.Ep.2 cells at doses of 0.04 J/cm² to 0.48 J/cm². However, 670 nm laser irradiation led to an increased cell proliferation when compared to both control and 635 nm irradiated cells. The best cell proliferation was found with 670 nm laser irradiated cultures exposed to doses of 0.04 to 0.48 J/cm². We conclude that both dose and wavelength are factors that may affect cell proliferation of H.Ep.2 cells.

ANZ J Surg. 2002 Feb;72(2):95-9.

Combined endoscopic laser and radiotherapy palliation of advanced rectal cancer.

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BACKGROUND: In the palliative treatment of patients with advanced, inoperable rectal cancer, combined endoscopic laser and radiotherapy have been claimed to be more effective than laser therapy alone. The number of laser treatments, laser energy used, relapse rate, treatment of relapse, morbidity and survival in consecutive patients who were treated either by laser therapy alone or laser plus radiotherapy was compared.

METHODS: Prospective data were analysed with regard to number of treatments, laser energy used, relapse rate, morbidity and survival for 56 consecutive patients. **RESULTS:** The crude relapse rate was significantly higher in the laser only group than in the laser plus radiotherapy group (58 and 15%, respectively; $P = 0.002$). There was no difference between the groups in the median total number of laser treatments or the mean total laser energy used. In patients experiencing a relapse, there was no difference in the median number of relapses, the number of laser treatments post-relapse or the total energy used post-relapse. Survival did not differ between the groups and there were no treatment-related deaths. **CONCLUSIONS:** These findings demonstrate a clear reduction in relapse after using combined laser and radiotherapy to palliate patients with advanced rectal cancer with no appreciable additional morbidity and have encouraged continuing use of this treatment.

LASER THERAPY IN CLINICAL ONCOLOGY

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The methodological basis for the treatment of malignant tumors will remain multivariant combinations of surgical, radiation and medicinal methods in the next century just like in this century. Such approach undoubtedly provides some results although the effectiveness

of the treatment, rehabilitation indices and the existing standards of oncological patients do not meet requirements of society, physicians and patients. It is for the first time that system of Low Intensity Laser Therapy (LILT) has been used. From the position of the system approach LILT technologies with oncological patients represent complicated biotechnical processes and at its application specific features of the system, i.e. "tumor-organism", technology of the irradiation as well as professional experience of the operator (i.e. physician) play a very important role and should be taken into account. LILT has been applied for 1000 patients with oncologic pathology of major localizations, different clinical states and morphological forms, independent of sex, age, psychosomatic features and other standard factors. The main trends of LILT in the treatment of oncological patient were: protective action during the antitumorogenic and radiation therapy (hemo-clinical correction); stimulation of growth-inhibiting factors and increase of the tumor sensivity to special and other additional means of treatment; preventive measures and treatment of complications after surgical operations; improvement of the results and quality of rehabilitation therapy and palliative treatment; treatment of opportunist pathologies with oncological patients; provides elimination of reaction for radiation therapy in 93,6% of cases; elimination of surgical complications in 89,4%. Effectiveness of the palliative LILT is 68,4%. Absolute contraindications of LILT have not been revealed. The analysis of immediate and long- term results reveals a complete absence of oncostimulating influence of LILT. Thus, it is possible to say that LILT is a new mean, improving the quality and results of a combined treatment of patients with malignant tumors.