Photodermatol Photoimmunol Photomed 2000; **16**: 34–37
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Munksgaard · Copenhagen

Photodermatology
Photoimmunology
& Photomedicine
ISSN 0905-4383

Communication

Low intensity laser irradiation in the treatment of recalcitrant radiation ulcers in patients with breast cancer – long-term results of 3 cases

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Radiotherapy can be followed by recalcitrant skin ulcers. As low intensity laser irradiation has been demonstrated to have a beneficial effect on impaired wound healing, we investigated its efficacy and safety in three patients with chronic radiation ulcers. The three patients, previously mastectomized due to breast cancer, with recalcitrant radiation ulcers of the skin were treated with a 30 mW helium-neon laser (wavelength: 632.8 nm, intensity: 3 mW/cm^2, dose: 30 J/cm^2) three times weekly. In all patients, complete wound closure was achieved within a period of 7, 5, and 8 weeks. One patient died 6 weeks after laser treatment due to tumor cachexia. Neither of the other patients showed recurrence of radiation ulcers or neoplasm during a follow-up of 36 months. Low intensity helium-neon laser irradiation has been shown to be effective in the induction of wound healing in radiotherapy-induced ulcers in three patients with breast cancer.

Key words: **biostimulation; neoplasma; wound healing.**

Although the risk of local recurrence of breast cancer can be significantly reduced by adjuvant radiation therapy there is a relatively high risk for some degree of radiation damage within the first 10 years after radiation therapy (1). These late complications may be represented by distinct skin reactions, ranging from subcutaneous induration to dermal necrosis with subsequent ulceration developing several months and even years after exposure. Both ulcerating breast tumors and radiation ulcers can be treated by surgical intervention, using a great variety of different flaps and grafting methods. Due to the reduced microcirculation in the fibrotic skin, however, surgical treatment often fails. In these cases, the only alternative is a non-invasive treatment approach aiming at inducing epithelialization (2). Among such conservative treatment modalities, low intensity laser irradiation is of growing interest for the induction of wound healing. Therefore, we investigated the efficacy of laser therapy in recalcitrant radiation ulcers in patients with breast cancer.

Patients and methods

Patients

Between March 1993 and April 1994, three consecutive female patients with metastatic breast cancer and histology-proven radiation ulcers persisting for at least 9 weeks consented to participate in our study. The age of the patients was: 42, 69, and 42 years. All patients had previously undergone mastectomy, two of them received anti-estrogen medication and in one patient eight cycles of polychemotherapy had been administered until 4 weeks before the first laser irradiation. After the radiotherapy-induced occurrence of ulcerous lesions several attempts to close these ulcers by both surgical and conservative means had failed in all three patients. The duration of radiation ulcers was: 9, 10, and 19 weeks. Further patient characteristics can be seen in Table 1. The clinical status at the initial examination is shown in Fig. 1 a–c.

Irradiation procedure and follow-up

For the laser irradiations a continuous wave 30 mW helium-neon laser (wavelength: 632.8 nm) was used. The beam (original spot-diameter: 5 mm) was diverged by the instrument's scanner to cover the edges of the ulcers. The intensity used was 3 mW/cm^2 and the irradiation time was set, dependent on the wound area, to achieve a dose of 30 J/cm^2 at skin level. Laser therapy was carried out in an outpatient setting three times weekly and was continued until the closure of the radiation ulcers. The only con-

Table 1. Patients characteristics, irradiation protocols, and treatment outcome

Patient	Age	Staging at first visit Receptors Localisation (quadrant)	Total dose of radiotherapy	Time between radiation and development of ulcers	Medication	Previous treatments for wound closure/ complications	Duration of ulcer and size at first visit	Time of irradiation until wound closure	# of laser sessions	Follow-up period	Staging at follow-up	Clinical situation at radiation site at follow-up
# 1	42	T1mult N1 M0 ER-, PR- upper/medial	5100 cGy	24 months	–	Necrosectomy Thiersch plastic Lung infarction	9 weeks 40×35 mm	7 weeks	24	36 months	T1mult N1 M0	scar
# 2	69	T4 N1a M2, ER+ PR+ Upper/medial	5500 cGy	3 months	Tamoxifen 30 mg/d	Necrosectomy Tanin lotion	10 weeks 25×32 mm	5 weeks	15	36 months	T4 N1a M2	scar (histology-proven)
# 3	42	T4c N2 M1 ER+ PR− Upper/medial	5129 cGy (focal dose) plus 960 cGy (tumor bed)	13 months	Tamoxifen 30 mg/d	Necrosectomy Split skin from thigh	19 weeks 65×35 mm plus exulcerating skin metastases	8 weeks	10	1.5 months (Pat. died)	T4c N2 M1	scar

ER = estrogen receptor, PR = progesterone receptor.

comitant topical therapy consisted of rinsing with saline and dry sterile cotton dressings. During a 36-month follow-up the patients were regularly monitored by clinical and radiographic means for recurrence of both the radiation ulcers and the tumor. At the final control, a tumor restaging was performed and the local status at the radiation site was evaluated clinically.

Results

The short-term and long-term results for each individual are summarized in Table 1. In all three patients a complete closure of the radiation ulcers could be achieved by low dose laser irradiations within a period of 7, 5, and 8 weeks (Fig. 1 d–f). One patient (patient #3) died 6 weeks after finishing laser treatment due to tumor cachexia; the two remaining patients were regularly controlled clinically and by radiographic means for recurrence of the radiation ulcers and recurrence or progression of the breast tumor. After the follow-up period of 36 months, neither of the remaining two patients showed recurrence of radiation ulcers or neoplasm. In patient #2 a control biopsy was taken from a suspicious nodule at the radiation site, revealing only scar tissue and a pseudocyst.

Discussion

Low intensity laser irradiation was introduced as a non-invasive, athermic therapeutic modality for acceleration of wound healing by Mester and co-workers (3) and has since been used successfully for the treatment of chronic ulcers, particularly due to poor microcirculation (4). During the last decade it has been demonstrated that low intensity laser radiation is able to enhance metabolic pathways by different mechanisms. These include activation of previously partially inactivated enzymes, mainly ATPases (5), induction of reactive oxygen species (6), stimulation of Ca^{2+}-influx and mitosis rate (7), augmented formation of mRNA and protein secretion (8, 9). At the cellular level, enhancement of cell proliferation and motility of fibroblasts and keratinocytes were frequently noted after laser irradiation (7, 10–12), which are of significant importance for wound healing procedures. Moreover, there is evidence for the possible improvement of skin circulation (13) and induction of neoangiogenesis due to low dose laser exposure under both *in vitro* and *in vivo* conditions (14–16).

The beneficial use of low intensity light irradiation for the reduction of dermal necrosis after X irradiation in animals has been reported by Rezvani and co-workers (17). Our group recently demonstrated complete wound healing in recalcitrant ulcers resulting from radiotherapy used to treat benign lesions (18, 19). The duration of laser-induced wound healing was found to depend on the wound size and cause with radiotherapy-triggered ulcerations

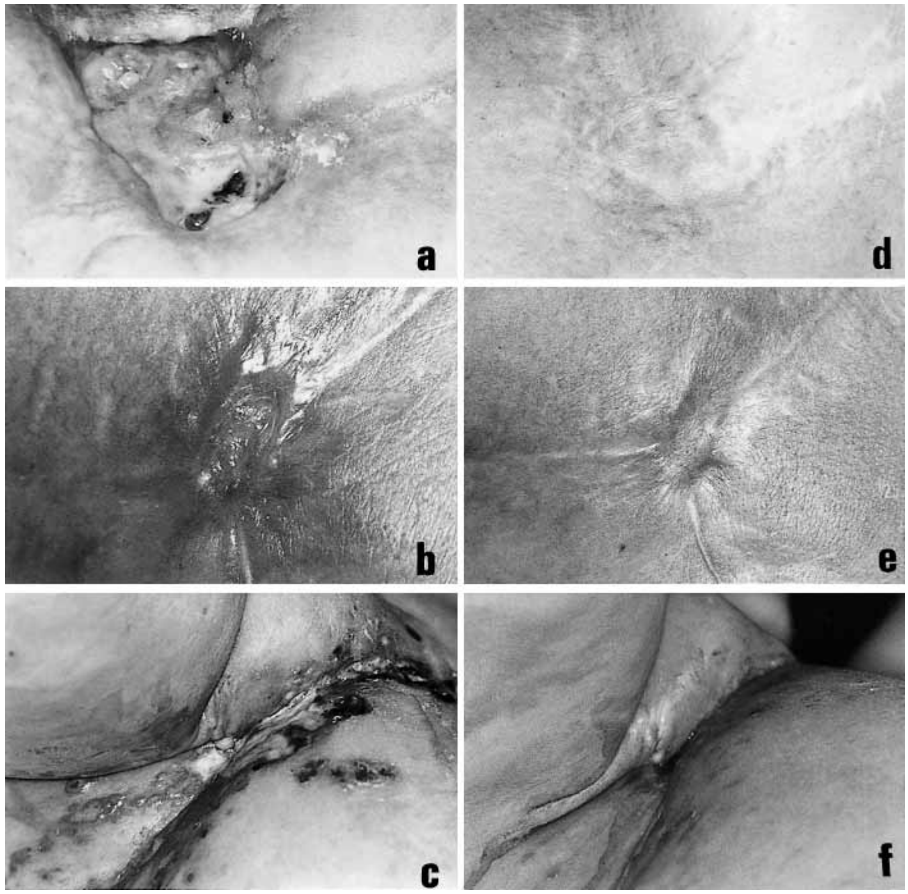

Fig. 1. a–c. Clinical status at time of first visit; d–f: Clinical status at the end of laser therapy.

showing the fastest response (20). A study by Barasch and colleagues (21) describes a protective effect of prophylactically applied helium-neon laser irradiations against the occurrence of conditioning-induced oral ulcerous mucositis in bone marrow transplantation patients. As in the only comparable report (22) on effects of low intensity light irradiation on malignant ulcers, this phototherapy was applied as an adjuvant therapy and no substantial period of follow-up was included. The present study is thus unique because we used laser therapy as monotherapy for the induction of wound healing and have a 36-month period of follow-up, demonstrating the long-term efficacy and safety of this type of phototherapy.

Due to the fact that these observations represent uncontrolled cases, we are well aware that properly controlled studies have to be performed and we hope to encourage further research in that direction.

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Accepted for publication August 10, 1999

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