JOURNAL OF BIOMEDICAL OPTICS 1(4), 448–454 (OCTOBER 1996)

TREATMENT OF SKIN MELANOMA WITH PULSED RADIATION FROM A NEODYMIUM LASER

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(Paper JBO-081 received Feb. 26, 1996; revised manuscript received June 25, 1996; accepted for publication June 28, 1996)

ABSTRACT

Pulsed radiation generated by powerful neodymium glass lasers was used to treat 272 cases of stage I skin melanomas; 250 patients (91.9%) patients were treated 5 years ago or earlier. Local recurrences of melanoma were detected in 2 (0.7%) cases within 1 to 8 years of followup. Regional metastases developed in 45 (16.5 ±3.3%) cases and distant ones in 12 (4.4±1.6%); 1 (0.4%) female patient presented with a transport metastasis. In patients treated 5 years ago or earlier, regional metastases occurred in 16.2±3.8% cases, distant ones in 4.4±1.6%, and transport ones in 0.4%. Five-year survival was registered in 84.5±2.8% of patients. Powerful pulsed laser radiation is effective in treating flat and slightly elevated skin melanomas that are up to 4.5 cm thick and that are characterized by levels I to IV of invasion. © *1996 Society of Photo-Optical Instrumentation Engineers.*

Keywords skin melanoma; pulsed laser therapy.

1 INTRODUCTION

A beam of pulsed radiation generated by a powerful laser has found effective application in treating various benign tumors of the skin as well as cutaneous cancers (stages I to II).[1,2] Attempts have been made to use laser radiation for treating skin melanomas. Our earlier work using pulsed laser radiation to treat skin melanomas has been reported.[3,4] This present paper discusses the results of neodymium laser therapy of stage I skin melanomas.

2 MATERIALS AND METHODS

The studied group included 272 cases of stage I cutaneous melanomas without clinically detectable regional or distant metastases. The age of the 51 males and 221 females varied from 17 to 83 years. The face was the most frequent site (34.3%) (Table 1). Seventy-one (26.1%) tumors were less than 1.0 cm in diameter, while 57 tumor species (21.0%) were more than 2.0 cm in breadth (Table 2). The diameter of the largest tumor was 4.5 cm. Out of 272 skin melanomas, 119 (43.7%) were flat ones; 153 of the tumors (56.3%) rose over the skin surface by 2 to 4 mm. The data presented in Table 3 show that the most frequent lesion was presented by epithelial cell melanomas. The histological pattern was not identified in 20 (7.4%) patients.

The source of radiation was the powerful neodymium plus laser installation Pulsar-1000 and its modification Pulsar-1000 M (wavelength, 1060 nm; pulse energy densities, 700 and 1000 J; impulse time, 1 and 4 to 5 msec, respectively).[5]

A total of 177 patients received standard treatment: a ring of normal skin chosen at a distance of 1 to 1.5 cm from the visible rim of the tumor was exposed to a series of successive and partially overlapping impulses of 300 to 400 J/cm^2. Irradiation was started on a site close to the nearest regional lymph collector. This resulted in the formation of a raised 1 to 1.5-cm-wide circular coagulative scar that protected the adjacent normal tissue from tumor cell infiltration. It was also supposed to prevent dissemination of tumor cells via blood and lymph vessels during subsequent irradiation of tumors. The area of suspected subclinical dissemination of tumor cells was also exposed to radiation. Once the tumor was blocked, samples were taken from it for cytological examination. Subsequently the tumor was exposed to 300 to 400 J/cm^2 of laser radiation. No general or local anesthesia was used.[1]

As one can see, the procedure used cannot provide any information on the extent of tumor invasion into the skin (Clark[6]) or its thickness (Breslow[7]), which can be of clinical importance for prognosis. Therefore, energy densities to induce coagulation of tumor tissue were selected empirically. Sometimes they were not sufficient to affect the entire mass of the tumor and as a result a repeated exposure was required. In addition, the area of coagulated tissue was relatively large and it took a long time for the wound to heal. Therefore, not

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Table 1 Localization of skin melanomas treated with laser therapy.

Site	No. of patients	%
Face	93	34.3
Hairy part of head and neck	12	4.4
Trunk	57	20.9
Arms and hands	52	19.1
Legs and feet	58	21.3
Total	272	100

many advantages may be gained in treating melanomas of the nose near natural orifices, or on the fingers and toes, which are not fleshy.

To solve the problem, we developed another procedure of pulsed laser therapy for skin melanomas and tested it in 95 patients. In this procedure, a 1.0 to 1.5-cm-wide blocking scar was formed at a distance of 0.5 to 0.8 cm from the visible rim of the tumor [Figure 1(a)]. The width of the ring of normal skin exposed to radiation was selected according to the type of tumor growth and site. It was narrower in flat tumors and those located on the face, and relatively wider in the cases of elevated tumors and those located on the trunk and extremities. Two to 3 ml of 0.5 to 1.0% solution of Novocain were injected into the submelanoma fat tissues from the outer rim of the blocking scar ring to achieve local anesthesia. An 8 to 9-mm long and a 4 to 5-mm wide skin-thick cone of the melanoma and of normal tissue between the tumor and the inner rim of the block was dissected using a scalpel [Figure 1(b)] for biopsy. The thickness of the melanomas was measured on the basis of the sample. Subsequently the latter were used to determine the extent of tumor invasion after Clark[6] and thickness after Breslow[7] in the course of histological examination. After biopsy the whole area within the blocking ring (both normal skin and tumor) was subjected to laser-induced coagulation from the periphery to the center according to the method used originally to form the circular blocking scar.

Table 2 Size of skin melanomas treated with laser therapy.

Tumor diameter (cm)	No. of patients	%
Under 1.0	71	26.1
1.1–2.0	144	52.9
Over 2.0	57	21.0
Total	272	100

Table 3 Morphological pattern of skin melanomas treated with laser radiation.

Morphological pattern	No. of patients	%
Epitheloid-cell	109	40.0
Spindle-cell	49	18.0
Mixed-cell	84	30.9
Nevocellular	10	3.7
Melanoma (Histological Pattern Not Identified)	20	7.4
Total	272	100

An energy density ranging from 200 to 400 J/cm^2 for the creation of the block was selected in each case individually, depending on the skin thickness at the tumor site and on the basis of the energy density (penetration ratio of 100 J/cm^2) at 1 mm.[8] The densities of the pulsed energy were selected using the sample material to carry out coagulation and were 200 to 300 J/cm^2 for thick tumors.[9]

Laser radiation destroyed the melanomas and adjacent normal tissues, causing necrosis. The scabs formed on the necrotic tissue would pull off 3 to 4 weeks later, revealing the granulated wound surface, and samples for cytological examination were removed. Laser therapy was repeated when viable

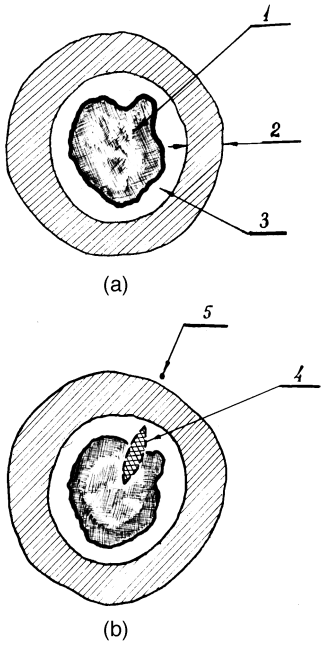


Fig. 1 (a) Melanoma after laser formation of a circular block: 1: melanoma; 2: 1 to 1.5 cm-wide blocking ring; 3: 0.5 to 0.8 cm-wide normal tissue area between melanoma rim and inner rim of circular block. (b) Melanoma after biopsy: 4: melanoma segment with adjacent normal tissue after biopsy; 5: puncture point for Novocain to be injected underneath the melanoma.

tumor cells were detected. The wound on the tumor site would heal, leaving a smooth scar (Figures 2 to 4).

Out of 95 patients, the invasion level (Clark[6]) and melanoma thickness (Breslow[7]) were identified in 93 cases. Table 4 shows the distribution of skin melanoma patients treated with laser radiation versus invasion level and tumor thickness: levels I and II, 33.4% and levels III and IV, 66.6% (Clark[6]). Level V was not detected. The thickness of the melanomas was no more than 1.5 mm in 33 (35.4%) patients and more than 1.51 mm in 60 (64.6%) patients. The maximum thickness recorded in the studied group was 4.5 mm.

The skin melanoma treatment was carried out under outpatient conditions. The data were evaluated using Student t test and χ^2 criteria.

3 RESULTS AND DISCUSSION

The followup lasted 1 to 8 years. In 250 (91.9%) cases, laser treatment was given 5 years ago or earlier. Local recurrences of melanomas were detected in 2 (0.7%) female patients on the basis of cytological examination. A node (0.4 cm) was detected in the skin at the edge of the scar in one of those patients 20 months after therapy and it was removed surgically. In the other case, recurrence involved a large skin melanoma on the right cheek which was thereafter treated by laser radiation in two steps. Since the patient refused to undergo surgery, the relapse was repeatedly exposed to laser radiation. The patient has survived for 3 years without any signs of tumor recurrence or regional or distant metastases. While recurrence in the former case might have been due to incomplete exposure of the entire area of subclinical extension of the melanoma, in the latter case it may be accounted for by incomplete exposure of the entire mass of the tumor.

During the 1 to 8 years of followup, regional and distant metastases were detected in 58 (21.3±2.7%) patients; lesions was detected in regional lymph nodes in 45 (16.5±3.3%); distant metastases were found in 12 (4.4±1.6%) patients, and transport metastasis was detected in 1 (0.4%) patient. Among patients treated 5 years ago or earlier, metastases were detected in 57 (22.8±3.0%): they were regional in 44 (16.2±3.8%), distant in 12 (4.4±1.6%), and transport in 1 (0.4%) case.

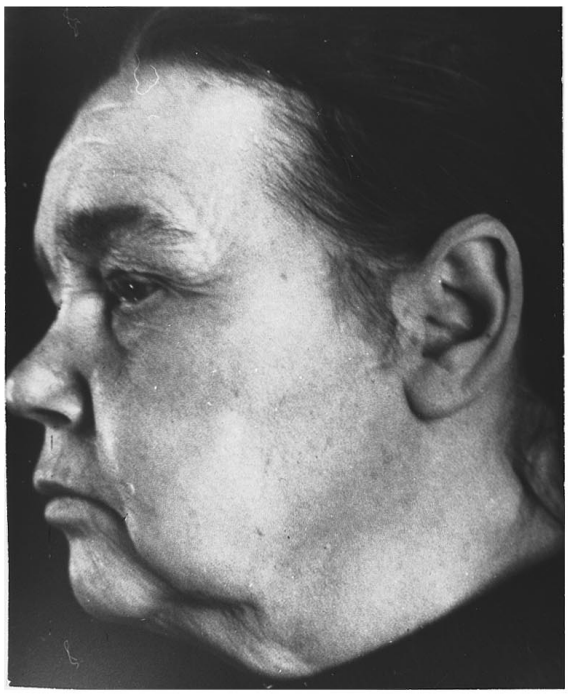
In the 1 to 8 years in the followup group, regional and distant metastases were confirmed histologically in 34 (19.2±3.6%) cases and in 24 (25.2±4.3%) patients examined by incision biopsy. In patients treated 5 years ago or earlier, regional and distant metastases were detected in 33 (21.3±3.9) and 24 (25.2±4.3%) cases, respectively. Metastases were more frequent, with melanomas localized on the skin of the hirsute part of the head, neck, and trunk, and in the cases of epithelioid cell melanomas. The results indicate a correlation between the spreading frequency of metastases and tumor size and the

(a)

(b)

Fig. 2 Female patient P., aged 47. Mixed-cell melanoma on the skin of the right side temporal region. One exposure to 21 impulses with energy density of 350 to 400 J/cm^2 each. (a) Before treatment and (b) 9 years after treatment.

(a)



(b)

Fig. 3 Female patient K., aged 63. Epithelioid cell melanoma of the skin, level IV of invasion, on the left side of preauricular region. One exposure to 30 impulses with energy density of 350 to 400 J/cm^2 each. (a) Before treatment and (b) 5.5 years after treatment.

type of growth: there is a direct connection between tumor size and incidence of metastases. Similarly, elevated melanomas involved the spread of metastases more frequently than flat ones. Metastases were more frequent in males than in females. The formation of metastases also appeared to be in direct correlation to the invasion level (Clark[6]) and melanoma thickness (Breslow[7]) (Tables 5 and 6).

Out of 58 patients with regional and distant metastases detected after laser therapy, these lesions were identified in 26 (44.8±3%) cases within 12 months of followup either by cytological examination (45±6.2%) or by melanoma tissue biopsy

(a)

(b)

Fig. 4 Male patient G., aged 73. Mixed-cell melanoma of the skin in the second interdigital space of the left hand. Two exposures: 20 impulses of 300 to 350 J/cm^2 each. (a) Before treatment and (b) 4 years after treatment.

Table 4 Distribution of skin melanoma patients treated with laser radiation versus invasion level (Clark[6]) and tumor thickness (Breslow[7]).

Level of invasion	Thickness (mm)					Patients	
	<0.75	0.75–1.50	1.51–3.0	3.1–4.0	>4.0	No.	%
I	2					2	2.2
II	8	11	9	1		29	31.2
III	4	3	11	4	1	23	24.7
IV		5	24	8	2	39	41.9
Total	14	19	44	13	3	93	100
	(15.0%)	(20.4%)	(47.3%)	(14.0%)	(3.3%)	(100%)	

(44.1±5.9%). Total 5-year survival was registered in 84.5±2.8% of all melanoma patients treated with pulsed radiation, cytological confirmation of the diagnosis accounting for 83.4±3.5% and incision biopsy for 86.4±4.6% (Table 7).

All patients with a level I invasion (Clark[6]) have survived 5 and more years. For invasion levels II, III, and IV, the survival rates during 5 and more years were 92.3±5.4, 85.7±6.0, and 81.1±5.1%, respectively. For melanomas that were less than 1.5 mm or 1.51 to 4.5 mm thick, the 5-year survival rates were 96.7±6.5% and 80.9±4.9%, respectively.

The 5-year survival of skin melanoma patients receiving laser therapy was assessed according to tumor localization, its histological pattern and size, and the type of growth, as well as the patients' sex and age. For melanomas on the face; hairy parts of the head, neck, and trunk; and arms and legs, the survival rates were 84.6±4.2, 83.3±9.9, 75.5±7.1, 83.3±5.8, and 94.2±2.9%, respectively. A survival of more than 5 years was recorded in 79.2±5.1% of patients with epithelioid cell melanomas, 95.2±3.9% ($p<0.05$) with spindle cell melanomas, 85.5±5.9% with mixed cell melanomas, 77.7±8.4% with histologically unidentified melanomas, and 100% with nevocellular melanomas. For melanomas under 1.0 cm, 1.1 to 2.0 and more than 2.1 cm in breadth, the 5-year survival rates were 96.5±3.6, 85.6±3.6 ($p<0.01$), and 68.6±7.7% ($p<0.05$), respectively. These rates for elevated and flat melanomas were 77.8±4.0 and 93.8±3.3%, respectively. Among patients with stage I skin melanomas, 68.0±7.7% of males and 88.3±2.8% of females ($p<0.01$) survived 5 years. A particularly distinct relationship between sex and 5-year survival was observed in the group under 39 years of age, with 42.8±10.2% of males and 90.9±4.3% of females among the survivors ($p<0.01$). In contrast, 73.1±8.3% of males and 84.5 ±3.7% of females aged more than 39 years survived 5 years. No age-related differences in this parameter were found in males and females in the same age groups: 84.3±5.1% in patients under 39 and 81.8±3.7% in those aged more than 39.

Regional metastases were detected in 17 to 31% of patients following surgery for stage I skin melanoma, while in distant ones it was 2.8 to 24.2%,[10–12] their frequency ranging from zero for level I of the invasion (Clark[6]) to 48.9 to 56.9% for level IV. The incidence of metastases within the first 12 months after operation was 50.0 to 87.5%.[10–12] There were

Table 5 Relationship between the frequency of regional and distant metastases in melanoma patients after laser therapy depending on invasion (Clark[6]).

Level of invasion[a]	No. of patients	No. of metastases	$M \pm m$ (%)
I	2	0	—
II	29	3	10.3±5.7
III	23	8	34.7±6.7
IV	39	13	33.3±7.5
Total	93	24	—

[a] The difference between levels I+II and III+IV is statistically significant: $\chi^2=3.99$, $p<0.05$.

Table 6 Frequency of regional and distant metastases in melanoma patients after laser therapy depending on tumor thickness (Breslow[7]).

Thickness of tumor (mm)[a]	No. of patients	No. of metastases	$M \pm m$ (%)
Under 1.50	33	3	9.1± 4.9
1.51–3.0	44	13	29.5± 6.9
3.1–4.5	16	8	50.0±12.9
Total	93	24	

[a] The difference between the groups is statistically significant: $\chi^2=10.84$, $p<0.05$.

Table 7 Total 5-year survival in skin melanoma patients after laser therapy.

No. of patients treated 5 years ago or earlier	Victims of skin melanoma	Victims of other cases	No. of patients less victims of other cases	Survivors for 5 years and longer	% of patients less victims of other causes
I. With and without biopsy					
250	36	17	233	197	84.5±2.8
II. Without biopsy					
155	24	10	145	121	83.4±3.5
III. With biopsy					
95	12	7	88	76	86.4±4.6

virtually no fatalities among cases of skin melanomas with level I invasion after surgery. However, the 5-year survival for invasion levels II, III, and IV was 62 to 100, 46 to 95, and 30 to 72%, respectively.[13–16]

Our results demonstrate that radiation from a powerful pulse laser is effective in treating both flat and slightly elevated skin melanomas with invasion levels I to IV (Clark[6]) and with a thickness up to 4.5 mm (Breslow[7]). Laser radiation can find applications for treating skin melanomas in different locations. It is particularly useful for skin melanomas of the face, hands, and feet when sufficiently extensive excision of tumor tissue is impossible. Anatomical and functional losses can be avoided if laser radiation therapy is used on such sites. The use of the laser also has a beneficial psychological effect because this kind of treatment can be conducted in outpatient clinics, allowing rapid social and occupational rehabilitation.

Similar to surgical excision of stage I skin melanomas,[12–17] the prognosis when pulsed radiation therapy is used is determined by several clinico-morphological parameters, including the extent of invasion (Clark[6]); the thickness of the tumor (Breslow[7]); tumor localization; its histological pattern, size, and type of growth; and the age and sex of patients. There is an inverse correlation between the survival rates for 5-year patients on the one hand, and invasion level and tumor thickness, on the other. The prognosis is worse for skin melanomas localized in the hirsute part of the head and neck and on the trunk, for epithelial cell melanomas, tumors more than 1.0 cm in diameter, and elevated melanomas, especially for males of young ages. It is noteworthy that the frequency of local recurrence following laser treatment is lower than after surgery (3 to 8%).[18,19] This may be because pulsed radiation treatment, unlike surgery, involves profuse lymphoid histocytic infiltration[20] which, in turn, is capable of preventing local recurrence by destroying tumor cells. It was also established that tumor dissemination is curbed by incision biopsy of skin melanomas conducted after the formation of a circular blocking scar around the tumor with the aid of a laser beam. This finding is corroborated by the data on the low incidence of metastases and the high rates of 5-year survival in skin melanoma patients treated this way.

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