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# Non Melanoma Skin Cancer of the Scalp

## *On the Etiology*

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In order to evaluate the relative significance of previous grenz-ray treatment for human non melanoma skin carcinogenesis, the files were studied of all patients treated for non melanoma skin cancer of the scalp ($n$ = 82, male/female ratio 1.1) at the Department of Dermatology, the Finsen Institute, from 1976 to 1985. Fourteen patients, with a male/female ratio of 3.7, were treated for squamous cell cancer (SCC). Sixty-five patients, with a male/female ratio of 0.9, were treated for basal cell cancer (BCC). Twelve patients (15%, 11 with BCCs, 1 SCC), of which eight with psoriasis, were previously treated with grenz rays on the scalp, and two of them had not been exposed to additional skin carcinogens. Comparably, malignant conversion in sebaceous and verrucous nevi accounted for 9 cases or 11%. Characteristically, scalp cancers associated with previous grenz-ray treatment were BCCs, the male/female ratio were <0.1 and two-thirds occurred in patients with multiple skin cancer. That grenz-ray related scalp cancers more often develop in females than in males was further confirmed by comparison to the sex distribution among patients treated on the scalp with grenz rays in the years 1950, 1960 and 1970 ($p<0.01$). (Accepted August 10, 1988.)

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Ultraviolet light and conventional X-rays are established etiological factors associated with the development of human skin cancer (1). Grenz rays have photon energies between these sources of radiation and are able to give rise to skin cancers in experimental animals when given in large doses (for review see Lindelöf & Eklund (2)). The role of grenz rays in human skin carcinogenesis has been difficult to assess statistically, the number of cases published until now being less than twenty (2). Among the public, grenz-ray therapy in these years is considered hazardous (3).

In order to assess the relative significance of previous exposure to grenz rays in human skin carcinogenesis we have evaluated possible etiologic factors in non melanoma skin cancer (NMSC) of the scalp in a ten-year material from the Department of Dermatology at the Finsen Institute.

## MATERIAL

The records of all patients registered as having non NMSC of the scalp and neck (diagnosis code common) in the years 1976–1985 were studied. The records of patients whose cancers were located on the scalp were evaluated for these parameters: sex, age at debut of the lesion, histological diagnosis (basal or squamous cell cancer or other types), whether the patient had multiple skin cancer ($n\geq2$) or not, and any information which might have etiological implications. For this purpose we registered previous skin diseases and the treatment of them (X-rays, grenz rays, artificial ultraviolet light, radium, thorium, coal tar products applicated to the scalp, and oral arsenic; exposure to more than one of these was designated "combined exposure"), scarring, exposure to unusual amounts of sunlight, defined as >5 years with out-door work or prolonged stay in sunny climates. Furthermore, information on sensitivity to sunlight (skin types I and II) was registered and, according to the clinical description and/or photographic registration, whether the cancer arose from an actinic keratosis. Skin

cancers arising in sun-sensitive individuals, in actinic keratoses and in previously strongly sun-exposed individuals were considered related to sunlight.

Whenever possible, patients who previously had been subjected to grenz-ray therapy on the scalp were examined and questioned further. The exact dose given to the scalp could not always be established, because many of the patients had been treated many years previously in other—generally private—clinics which are not by law obliged to keep patient records that long. In these cases an approximated dose was calculated based on the patients' estimate of the number of treatments given. For the time period in question the usual scalp treatment schedule was 200–300 r (2–3 gy) 10–15 KV three times at 1–2 week intervals, if necessary given repeatedly at 1–2 month intervals. In most clinics the radiation source was of the type Siemens/Dermopan. In some cases, no information on dose and latency time could be obtained.

## RESULTS

Eighty-two patients were treated for non melanoma skin cancer of the scalp at the Department of Dermatology at the Finsen Institute in the 10-year period from 1976–85. The overall male/female ratio amounted to 1.1. Sixty-five tumors were BCCs histologically, 14 (17%) were SCCs, while 2 were described as metatypical skin cancers. These metatypical cancers arose in actinic keratoses in elderly males. For one tumor, arising in a 45-year-old scar second to scalding, the diagnosis was changed from basal to squamous cell cancer from the first to the final histological examination. Thirty patients (37%) had multiple skin cancer, i.e. two or more malignant tumors. In six of them the cancers were restricted to the scalp area.

The distribution among patients with BCC and SCC respectively, to sex, age at debut of symptoms, multiplicity of tumor lesions, carcinogenic exposures, and preexisting nevi is seen in Tables I (BCC) and II (SCC). The distribution of the carcinogenic factors incriminated is graphically shown in Fig. 1.

Table I. *Predisposing conditions and carcinogenic exposure in 65 patients with BCC on the scalp according to sex, multiplicity of tumors and age at tumor debut*

| | Sun-related | Nevi | Grenz rays only | Combined exposure | Unknown | Total/ Median |
|---|---|---|---|---|---|---|
| *Females* | | | | | | |
| Number | 5 | 5 | 1 | 9 | 15 | 35 |
| Multiple tumors, % | 80 | 0 | 100 | 67 | 40 | 49 |
| Median age at debut | 70 | 57 | 69 | 61 | 72 | 65 |
| *Males* | | | | | | |
| Number | 4 | 4 | 1 | | 19 | 30 |
| Multiple tumors, % | 50 | 0 | 100 | | 42 | 37 |
| Median age at debut | 74 | 44.5 | 76 | | 69 | 68 |
| Number | 9 | 9 | 2 | 9 | 34 | 63[a] |

[a] Two males with personal histories of exposure to tar and X-radiation, respectively, are omitted in the Table.

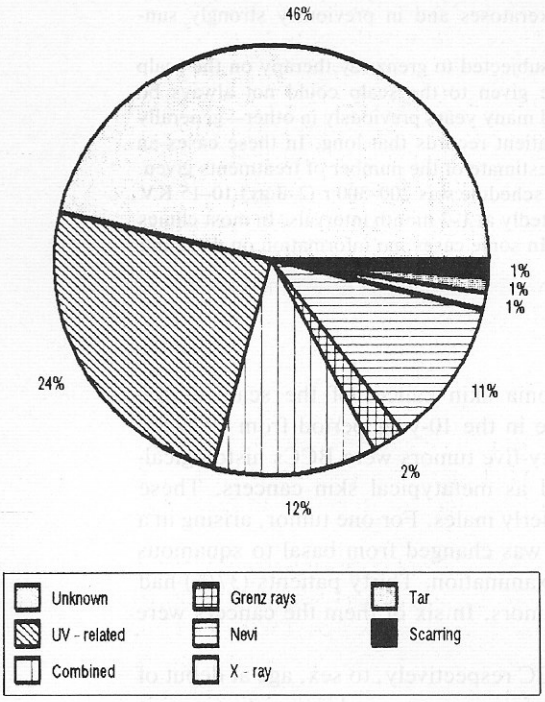


*Fig. 1.* The distribution of predisposing/carcinogenic parameters in 82 patients with non melanoma skin cancer of the scalp.

Table III concerns the clinical data of 12 patients, 11 with BCC and 1 with SCC, 8 with multiple skin cancer, who in the past had been subjected to grenz-ray treatment of the scalp. Two-thirds had been treated for psoriasis, and 10 patients were in the past exposed to at least one additional skin carcinogen, i.e. radium, thorium, artificial UV light, topical tar preparations applicated to the scalp, or oral arsenic. The female sex was significantly overrepresented in these cases of grenz-ray related scalp cancers, when comparison was made to the sex distribution among patients subjected to grenz-ray treatment on the scalp (194 males and 222 females) in the years 1950, 1960 and 1970 at the University Clinic for Dermatology in Copenhagen ($p<0.01$ by normal approximation).

Eight patients out of 82 with NMSC of the scalp were psoriatics against 1–2% in the general Danish population. Out of 14 SCCs, 11 occurred in males, predominantly elderly, seven of these arose in actinic keratoses, as a rule on the bald fronto-parietal area.

## DISCUSSION

In about half of the cases of non melanoma skin cancer of the scalp no specific carcinogenic exposure could be traced. In 24% exposure to sun appeared to be important, character-

Table II. *Carcinogenic exposures in 14 patients with SCC on the scalp*

| | Sun-related | Thorium + grenz rays | Unknown |
|---|---|---|---|
| Number | 9 | 1 | 4 |
| Multiple tumors, % | 11 | 0 | 25 |
| Median age at debut | 78 | 71 | 69–80 |

istically in elderly males with solitary SCCs. A second, characteristic group consisted of younger persons (sex ratio equal) with solitary BCCs arising in sebaceous or verrucous nevi (11%).

Fifteen percent of the patients had previously been treated with grenz rays on the site of their tumour(s). All but one were BCCs, and all but one occurred in a female. Comparably, the overall male/female ratio for NMSC in Denmark is 1.4 (1.3 for BCC and 2.8 for SCC) and the overall BCC/SCC ratio 5.7 (4.0 for males and 8.5 for females) as calculated from figures from the Danish Cancer Registry (4). Ten out of these 12 individuals who previously were treated with grenz rays had been exposed to at least one additional relevant skin carcinogen. In these 10 cases grenz-ray treatment in itself cannot be proclaimed the agent responsible for the malignant conversion. Experiments on mice have shown that additional chemical carcinogenic stimuli significantly accelerate tumor growth in animals irradiated with grenz rays (5). In two patients with multiple BCCs on the previously irradiated scalp, no skin carcinogen other than exposure to grenz rays could be incriminated. However, it cannot be excluded that the hyperproliferative skin disorders for which the treatment was given may predispose to skin cancer (1, 6). Furthermore, in considering these figures, it should be mentioned that psoriatics in Denmark rather often are subjected to grenz-ray therapy (7).

Recently, we have evaluated human non melanoma skin cancer occurring on previously grenz-ray exposed areas over the total integument (8). When patients with and without additional carcinogenic exposures were compared, the latency times from the first exposure to grenz rays to tumor appearance were significantly different, the group exposed to grenz rays alone having the shortest. Also in this group of monofactorially grenz-ray exposed skin tumor patients the female sex and multiple BBCs predominated. From these studies we hypothesized that a—presumably very small—subgroup of the human popula-

Table III. *Clinical data of 12 patients with non melanoma skin cancer arising on scalp skin previously exposed to grenz radiation*

| Pt. | Sex | Age at debut | Tumor type | Multiple, type | Grenz ray dose (gy) | Latency (years) | Additional therapy | Skin disease |
|---|---|---|---|---|---|---|---|---|
| 1[a] | F | 60 | BCC | BCCs | >18 | 27 | Thorium tar, arsenic | Psor. |
| 2[a] | F | 60 | BCC | BCCs | >124 | 21 | Tar, UV arsenic | Psor. |
| 3[a] | F | 40 | BCC | BCC+ SCC | >28 | 20 | Thorium, UV arsenic, tar | Psor. |
| 4 | F | 63 | BCC | BCCs | High | Unknown | Tar | Psor. |
| 5 | F | 62 | BCC | O | High | 30 | UV | Pity. |
| 6 | F | 67 | BCC | BCCs | High | Unknown | Thorium, UV radium, tar | Psor. |
| 7[a] | F | 61 | BCC | BCCs | >14 | 33 | Thorium, UV | Psor. |
| 8 | F | 71 | SCC | O | High | 40? | Thorium, UV arsenic | Psor. |
| 9 | F | 64 | BCC | O | ? | 36 | Tar | Pity. |
| 10 | F | 45 | BCC | O | 84 | 20 | Tar, UV | Pity. |
| 11 | M | 76 | BCC | BCCs | ? | Unknown | O | Psor. |
| 12[a] | F | 69 | BCC | BCCs | 103 | 22 | O | Pity/ neurod. |

[a] These patients are previously incorporated in the material in ref. (8). High dose: exact dose uncertain, by estimate >100 gy (8).

tion might be abnormally sensitive to the carcinogenic effect of grenz rays (8). Further support for this point of view is gained from in vitro studies on the cellular sensitivity to X-rays in patients with multiple non melanoma skin cancer showing an increased sensitivity in white blood cells from patients with grenz-ray related cancers (9).

The predominance of BCC over SCC in previously grenz-ray treated areas contrasts the general literature review made by Lindelöf & Eklund (2). However, the cases in the present study are systematically sampled, while the literature review is based on case reports and one systematical study not taking BCCs in account at all (2). Also in studies on NMSC related to conventional X-rays the BCC/SCC ratio has changed against a predominance of BCC in the course of time (10).

The findings in the present study suggest that exposure to radium, thorium, tar, large amounts of ultraviolet light and/or oral arsenic should call for caution on additional grenz-ray therapy, and that skin cancer screening should be performed in previously multifactorially exposed dermatological patients, e.g. with severe psoriasis, as also proposed by Stern and coworkers (6). The underlying biochemical mechanism and the role of the dose of grenz radiation still remain to be understood (1, 2, 8).

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