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9.1 Introduction

Epithelial skin cancers are very common neoplasms. The majority of them are basal cell carcinoma followed by squamous cell carcinoma [1, 2]. Among the different treatment options (surgery, Mohs' surgery, radiotherapy, cryotherapy, curettage, electro-desiccation, photodynamic therapy, topical treatment, etc.), surgical excision and radiation therapy are the most effective modalities to achieve local control [3].

Indeed, radiation therapy is one of the best treatment modalities available to treat skin carcinomas and represents a particularly important option when the preservation of normal tissue and the cosmetic result are essential. It allows treating the tumor and the area of subclinical spread with a margin without significant damage to normal tissues [4, 5]. Radiation therapy can be administered by superficial X-rays, brachytherapy, megavoltage photons, or electron beams.

Since 1949, electron beam therapy has been used for cutaneous malignancies [6]. Its applications in the treatment of mycosis fungoides are well known and described in the literature, but only few articles are available on their use for skin carcinomas. The main advantage of electron beam therapy is to make the treatment of epithelial skin cancers easier when their size and/or localization presents difficulties in their management, as described by Friedman and Pearce and by Braun-Falco et al. [7, 8]. Generally speaking, the electron beam therapy is preferred for large

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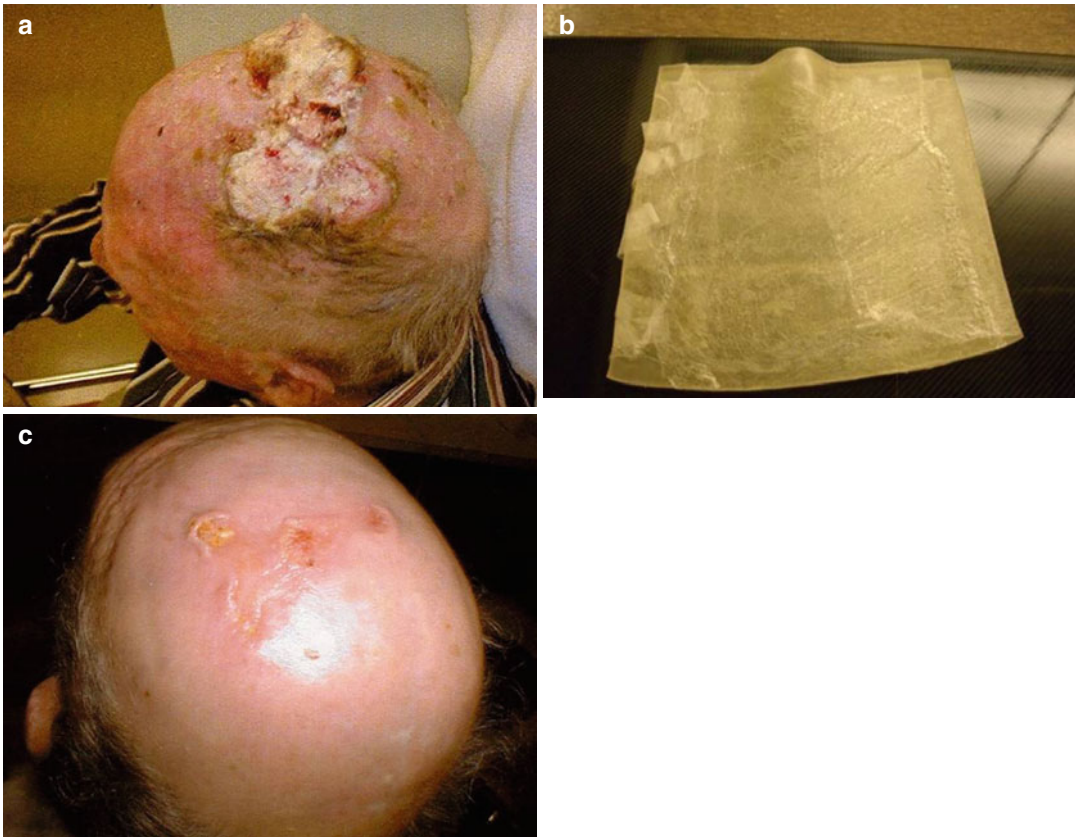


Fig. 9.1 (a–c) Large squamous cell carcinoma on the scalp treated with electrons and bolus. Result 6 weeks after the end of the treatment

lesions to decrease the radiation exposure to subcutaneous tissues compared with X-rays treatments [9] (Fig. 9.1) or when their thickness is too important to allow a treatment with X-rays. To avoid large dose inhomogeneities observed with superficial X-ray treatments on irregular surface (i.e., the pinna or the nasolabial fold), electron beams are also preferable [10] (Fig. 9.2).

9.2 Electron Beam Characteristics

Some characteristics of the electron beams make them interesting for the treatment of certain skin carcinomas, especially when their localization makes the surgery or the treatment by X-rays less relevant. Electron beams are characterized by a rapid isodose falloff at depth below the skin

surface, which means that there is little or no radiation exposure beyond a defined depth. The range of the depth to be irradiated is controlled by the selection of the appropriate energy. Although differences in body densities represent important inhomogeneities for electrons, the additional problem of strong atomic number dependence is not an issue here. So a high dose of radiation can be delivered to superficial skin lesions with limited damage to underlying and adjacent normal tissues. This can be particularly advantageous when the skin cancer to be treated is located over bone or cartilage. In contrast, the high density of bone and cartilage is responsible for a high relative absorption of radiation when X-rays are used, and these tissues are therefore more at risk to develop radionecrosis. For low energy electron beams (2–10 MeV), the dose distribution to the level of 80 % isodose is uniform.

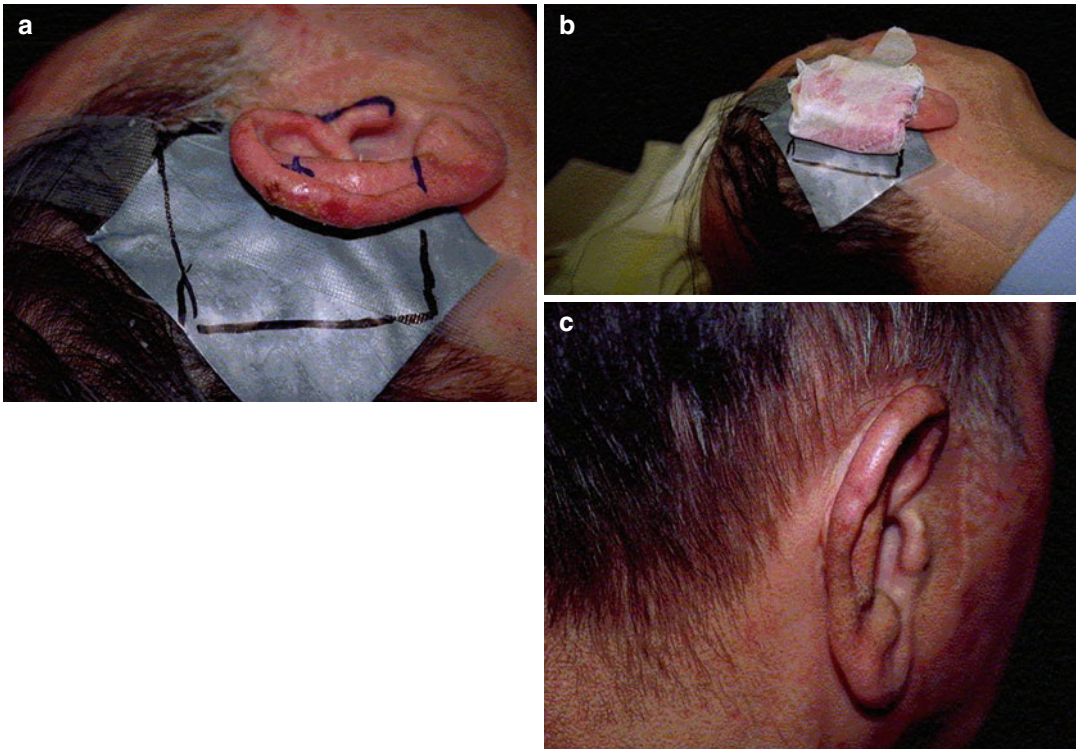


Fig. 9.2 (a–c) Basal cell carcinoma treated with electron beam. A wax mold is placed to diminish the dose inhomogeneity. Result 6 months later

As their energies are higher than those of X-rays, electrons can treat thicker lesions much more efficiently [4, 11].

this case, superficial X-rays are preferable for a better eye protection.

9.3 The Margins

The determination of the margins for lesions treated with electron beams must absolutely take into account the fact that the area of high dose intensity is constricted inside the borders of the radiation fields by as much as 1 cm (blurred field edge). A larger field size than the one used with superficial X-rays may be necessary to cover the target area adequately to counterbalance the penumbra region of the electron beams [4]. To underestimate this physical fact can be responsible for a higher recurrence rate after treatment with electron beams. Tumor localization near the eye is a relative contraindication to perform an electron beam treatment because of the lack of sharpness at the edge of the electron fields. In

9.4 The Buildup

Because of the electrons' buildup, the maximum dose is localized under the surface of the skin, and its depth depends on the electron energy. As the target for epithelial carcinomas is the skin, it is essential to use a bolus (tissue-equivalent material) to be placed on the skin. The thickness of the bolus depends on the depth of the buildup [4].

9.5 Local Control and Treatment Modality

Griep et al. have presented a retrospective analysis of 389 basal or squamous cell carcinomas treated either with superficial X-ray (99) or

electrons (290). Local or loco-regional recurrence was 4.9 %. The local control of the 99 lesions treated with superficial X-rays was 97 %, whereas it was 94.5 % for the 290 lesions treated with electrons ($p=0.30$). Similar rates of local control are reported in the literature [12]. The overall local tumor control rate in the study reported by Locke et al. in 531 patients was 89 % with a median follow-up of 5.8 years [2]. Tapley and Fletcher [2] have reported a local control of 86 % in 156 patients treated for epithelial skin carcinomas with electron beam therapy, with follow-up between 2 and 8.5 years [13]. In Zablow et al.'s analysis, the local control of 115 skin cancers (99 patients) was 88 % with a follow-up between 24 and 47 months [14]. In Miller and Spittle's study, a primary control of 82 % in 29 patients was found with a follow-up between 2 and 6 years [11].

The results reported above on the local control with electron beam therapy contradict the initial data reported by Lovett et al. in their retrospective analysis on 339 basal (242) and squamous cell (97) carcinomas treated with either superficial X-rays (187), electrons (57), megavoltage photons (15), or combined treatment (80). Overall, local control was achieved in 86 % of the patients: 91 % for basal cell carcinoma and 75 % for squamous cell carcinoma. They found that local control was dependant both on the tumor size and on the modality of treatment. Regarding superficial X-rays, the local control was 98 % for lesions less than 1 cm, 93 % for lesions 1–5 cm, and 100 % for lesions more than 5 cm. Regarding electrons, the tumor control was 88, 72, and 78 %, respectively, whereas for megavoltage photons (60Co, 4 MV photons) tumor control was 100, 67, and 33 % respectively. Finally with mixed treatments, local control was 90, 76, and 64 %, respectively [5]. In an updated analysis after more than 10 additional years, Locke et al. have reported an overall local tumor control rate of 94 % for superficial X-rays modality, of 82 % for electron beam, of 82 % for mixed treatment, and of 50 % for megavoltage photons. Nevertheless, in multivariate analysis, the treatment modality was not significant (electron versus other treatment modalities, $p=0.345$). On one hand, these results may reflect

an improvement over the years in the use of electrons as a modality of treatment for epithelial skin cancer. On the other hand, electrons were generally used for more advanced tumors than those treated with superficial X-rays, and this can explain the poorer local control in that group [2].

Silva et al. from the Princess Margaret Hospital have reported their experience in the treatment of carcinoma of the pinna. Among the 334 lesions treated, 278 (83 %) were treated with orthovoltage radiotherapy and 39 (12 %) with electron beams. The local control was worse in the group treated with electrons. However, after the correction of the RBE (relative biological effectiveness), there were no more statistically significant increased local failure rates with electrons [15]. The different results reported in the literature for treatment with electron beam therapy are summarized in Table 9.1.

9.6 Prognostic Factors

9.6.1 Tumor Size

One of the main prognostic factors for local control is the tumor size: the larger the tumor, the higher the recurrence rate. Irradiated region of less than 10 cm² had a local recurrence rate of 2.2 %, versus 13.8 % for irradiated areas of more than 50 cm² [12]. Lovett et al. found also a relationship between the tumor size and local control. Tumor control was 97, 87, and 87 % for basal cell less than 1 cm, 1–5 cm, and greater than 5 cm, respectively, versus 91, 76, and 56 %, respectively, for squamous cell carcinoma [5]. In Silva's study, a tumor size of more than 2 cm had a statistically significant worse local control ($p=0.02$) [15].

9.6.2 Previously Treated Skin Cancer

Other factors are also important regarding local control, such as previous treatments and histology. Patients treated with radiation therapy for relapse showed a recurrence rate of 9.9 %, while

Table 9.1 Studies on skin carcinomas including electron beam therapy

Literature	Number of patients	Follow-up	Local control	Local control in basal cell carcinoma	Local control in squamous cell carcinoma
<i>Locke J 2001</i> ^{ab}	531	5.8 years	89 %	92 %	80 %
Superficial X-rays	317		94 %		
Electron beam	100		82 %		
Combination of treatment	108		82 %		
Megavoltage photon	6		50 %		
<i>van Hezewijk M 2010</i>	434	3.6 years (median)	96.5 %		
54 Gy (18 fractions) electron beam	159	5.4 years	97.5 % (actuarial at 3 years)	97.6 % (actuarial at 3 years)	97 % (actuarial at 3 years)
44 Gy (10 fractions) electron beam	275	2.6 years	96.1 % (actuarial at 3 years)	96.9 % (actuarial at 3 years)	93.6 % (actuarial at 3 years)
<i>Griep C 1995</i>	389	1.98 years (average)	95.1 %	95.9 %	92.5 %
Electron beam	290		Actuarial 93 % at 2 years		
Superficial X-rays	99		Actuarial 90 % at 2 years		
<i>Lovett RD 1990</i> ^a	339	min 2 years	86 %	91 %	75 %
Superficial X-rays	187		95 %		
Electron beam	57		77 %		
Combination of treatment	80		76 %		
Megavoltage photon	15		67 %		
<i>Silva JJ 2000</i> , carcinoma of the pinna	334	3.3 years (median)	86.6 % (actuarial at 2 years)	93 % (actuarial at 2 years)	82 % (actuarial at 2 years)
Orthovoltage X-rays	278		79.2 % (actuarial at 5 years)	83 % (actuarial at 5 years)	79 % (actuarial at 5 years)
Electron beam	39				
Other	17				
<i>Zablow AI 1992</i>	115	3.9 years (mean)	88 %		
Electron beam					
<i>Tapley Ndu V 1975</i>	111/156	2-8.5 years	86 %		
<i>Miller RA 1982</i>	29	2-6 years	82 %		
Electron beam					

^aStudies from the same institution (Mallinckrodt Institute of Radiology, Washington University Medical Center, St. Louis, MO)

^bIn multivariate analysis, the treatment modality was not significant (electrons versus other types, $p=0.345$)

patients primarily treated with radiation therapy had a recurrence rate of only 3.1 % [12]. Lovett et al. have reported a local control rate for untreated lesions of 93 %, versus 75 % for previously treated lesion. The recurrence rate for basal cell carcinoma previously treated was 18 % versus 5 % for untreated basal cell carcinoma and 35 % versus 13 %, respectively, for squamous cell carcinoma [5]. In their 10-year updated analysis, Locke et al. found a local control rate of 93 % for previously untreated cancer and 80 % for recurrent lesions. Previously treated basal cell cancer had a local control rate of 86 % compared to 94 % for untreated lesions and 68 % for previously treated squamous cell carcinoma compared to 89 % for untreated lesions [2].

9.6.3 Histology

In Griep's study, the local control rate was 95.9 % for basal cell carcinoma versus 92.5 % for squamous cell carcinoma [12]. Locke et al. reported a local control of 92 % with basal cell carcinoma versus 80 % with squamous cell carcinoma [2]. In contrast, van Hezewijk et al. found no difference in local control between basal and squamous cell carcinoma [16].

In morpheaform basal cell carcinoma, the limits of the lesion are difficult to assess as they are mostly poorly defined. Surgery allows having a better assessment of the margin since the pathologist will analyze the entire lesion. However, if the radiation therapy indication is confirmed, an appropriate margin (at least 1.5 cm) should be given [17].

9.7 Dose and Fractionation

The same total dose and fractionation should be used with electron beam and superficial X-ray therapy. In the literature, different schedules are found such as 6–10-times 6–10 Gy, 33–35 Gy in five fractions, 42.5–45 Gy in 10 fractions, 50–60 Gy in 20–30 fractions, or the more standard 60–66 Gy in 2 Gy per fractions. Usually the same treatment schedule is prescribed both in basal cell carcinoma and in squamous cell carcinoma [2, 11, 12, 15, 16].

These different schedules found in the literature make a comparison between these treatment modalities difficult. Usually small lesions are treated with lower total dose and higher fractionation, whereas larger tumors are irradiated with higher total dose and lower fractionation [2, 5].

van Hezewijk et al. have compared two different electron beam fractionations for epithelial skin carcinoma. Their standard treatment was 54 Gy in 18 fractions of 3 Gy (159 lesions) and their hypofractionated schedule was 44 Gy in 10 fractions (275 lesions). The actuarial 3-year local recurrence-free rate was 97.5 % in the group treated with 54 Gy versus 96.1 % in the group treated with 44 Gy ($p=0.22$). They neither found any differences between the two schedules in the basal cell carcinoma (97.6 % vs. 96.9 %, respectively) nor in the squamous cell carcinoma subgroups (97 % vs. 93.6 %, respectively) [16]. Locke et al. found a better local control with higher total dose and with a higher fraction size (≤ 2 Gy vs. 2.01–3, 3.01–4, >4 $p=0.01$) [2].

9.8 Tissue Reaction

The same tissue reactions are observed after electron beam or X-ray therapy. The importance of the reaction depends on the total dose, the fractionation (dose/fraction), and the field size. Most common acute reactions are erythema, dry desquamation, and moist desquamation. With a treatment on the nose, one can observe a vestibular irritation, sometimes with minor nosebleeds. The late reactions comprise hypopigmentation, subcutaneous fibrosis, skin atrophy, teleangiectasia, and epilation [18]. Residual scarring depends on the initial lesion. Complications can affect soft tissues, they can also include cartilaginous and bone necrosis, but they are altogether very rare (0–6 %), as are the radiation-induced malignancies (1/1,000). For young patients, surgery is a better choice than radiation therapy, particularly for lesions developed on burn scars. Radiation oncologists are concerned with the risk of radiation-induced malignancies even if the probability is very small, but it is an important issue in younger patient treated for skin cancers which have a very good prognostic [18].

9.9 Cosmetic

Good to fair cosmetic and functional result are observed in the majority of patients, namely, between 75 and 97 % [12, 14, 16, 19]. Locke et al. have reported excellent to good cosmetic results in 92 % of their patients. They found worse cosmetic results in patients treated with high total dose, in lesions previously treated, and lesions treated with electrons [2]. Griep et al. have reported a better cosmetic result with electrons, probably due to the fact that in their institution, lesions were treated with small dose per fraction because of their large size [12]. van Hezewijk et al. found no significant difference in terms of cosmetic result between the various dose and fractionation schedules [16].

Conclusion

Radiotherapy is an excellent treatment modality for skin cancer. Electron beam therapy proves to be a good option in skin carcinoma when there is a large and/or thick lesion or because its localization makes surgery more difficult.

As the tumor's local control depends on the tumor size, an early diagnostic is an important issue. Patients with recurrent skin cancers experience a poorer local control. So, early detection and treatment intervention improve the local control and the final cosmetic result.

With electron beam treatment, special knowledge in treatment techniques is mandatory in order to provide the best tumor control, with special attention to the margins, the bolus, the energy's choice, and the total dose and fractionation.

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