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THE ROLE OF BRACHYTHERAPY IN THE TREATMENT OF NON-MELANOMA SKIN CANCERS: A NARRATIVE REVIEW

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ABSTRACT

Background. Basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (SCC) are the two most frequent malignancies worldwide, and their incidence continues to rise with the ageing of the population. Although surgical excision remains the gold standard, radiotherapy — including brachytherapy — constitutes a valuable alternative in selected clinical situations, particularly in elderly patients and in tumours located in cosmetically or functionally sensitive areas.
Aim. This narrative review aims to define the role of brachytherapy in the treatment of non-melanoma skin cancers, with emphasis on currently used techniques (surface, contact, mould-based, and interstitial methods, including Leipzig- and Valencia-type applicators and electronic brachytherapy), as well as on indications, patient selection, efficacy, and safety profile.
Methods. The PubMed/MEDLINE and Google Scholar databases were searched for English-language publications, and 44 articles published between 2011 and 2025 were included and analysed descriptively.
Conclusions. The available literature indicates that brachytherapy is an effective treatment strategy for selected non-melanoma skin cancers, providing high local control rates (reported between 71% and 99%), good cosmetic outcomes, and low toxicity. High dose conformity and effective sparing of healthy tissue make brachytherapy a valuable component of multidisciplinary skin cancer care.

KEYWORDS

Brachytherapy, Skin Cancer, Basal Cell Carcinoma, Squamous Cell Carcinoma, Radiotherapy, Skin Cancer Treatment

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1. Introduction

1.1 Epidemiology and Clinical Presentation of Skin Cancers

Skin cancers are primarily divided into melanoma and non-melanoma skin cancers (NMSCs) (Zhang et al., 2021). NMSCs comprise tumors that develop from keratinocytes, namely basal cell carcinomas (BCCs) and cutaneous squamous cell carcinomas (SCCs) (Perry et al., 2017). In 2017, NMSCs accounted for the highest rates of cancer incidence worldwide. An observational study conducted in Japan found that the percentage of skin cancer patients aged 70 and over has increased from 44% in 1989 to 74% in 2021 (R. Wang et al., 2025). Epidemiologically, the burden of NMSCs has been driven by population growth and marked by disparities in sex and sociodemographic index, cumulative ultraviolet radiation, and an increase in the number of screenings and biopsies (M. Wang et al., 2025; R. Wang et al., 2025; Zhou et al., 2025); diagnostic accuracy varies with lesion type and examination method (Chen et al., 2025).

As indicated by epidemiological data, the risk of skin cancer rises with advancing age, reaching its peak around 80 years of age (M. Wang et al., 2025; R. Wang et al., 2025; Zhou et al., 2025). In addition, skin cancers exhibit the highest incidence and prevalence levels in North America, followed by Europe and Asia (M. Wang et al., 2025). Consequently, there is a demand for effective skin cancer treatment methods suitable for use in elderly individuals with comorbid conditions and in hard-to-access anatomical sites (M. Wang et al., 2025; R. Wang et al., 2025).

1.2 Conventional Treatment Methods and Their Limitations

Treatment of NMSCs depends on tumor size, histopathologic type, depth of invasion, location, and the medical condition of the patient (J. Y. S. Kim et al., 2018a; Marzuka & Book, 2015; Waldman & Schmults, 2019). Presently, the main treatment approach for these cancers involves surgery, which includes electrodesiccation and curettage, surgical excision, and Mohs micrographic surgery (J. Y. S. Kim et al., 2018a). Radiotherapy serves as an alternative to surgery in cases of inoperability in elderly patients, in patients with

serious medical problems where general anesthesia cannot be performed, or in anatomical sites that are difficult to operate on and where surgery may impair organ functionality and aesthetics, particularly within the facial "H-zone," which includes the nose, eyelids, lips, and ears. Although surgical excision and Mohs micrographic surgery provide excellent oncologic control, obtaining adequate margins in these areas may require extensive tissue removal and complex reconstruction procedures (Chicheł et al., 2023; J. Y. S. Kim et al., 2018a; Marzuka & Book, 2015).

1.3 Rationale for the Use of Brachytherapy

Brachytherapy, also referred to as interventional radiotherapy permits the delivery of a concentrated radiation dose to the target lesion while minimizing the irradiation of normal surrounding tissues due to a steep dose gradient (Chicheł et al., 2023; Fionda et al., 2023; Monge-Cadet et al., 2024; Shah et al., 2020).

Data from clinical series published in the literature indicate that brachytherapy offers considerable local control together with tolerable toxicity and good cosmetic outcomes in properly selected patients (Doggett et al., 2023; Esmati et al., 2024; Laliscia et al., 2021a; Monge-Cadet et al., 2024; Tagliaferri et al., 2021). Moreover, brachytherapy proves particularly useful in elderly individuals who cannot be operated upon, as well as in tumors situated in irregular facial areas, where custom moulds or contact applicators may ensure conformity of the radiation dose distribution (Chicheł et al., 2023; Esmati et al., 2024; Laliscia et al., 2021a; Shah et al., 2020). Another benefit of brachytherapy is the possibility of using hypofractionated treatment plans, thereby reducing the number of clinic visits — an issue of major importance in elderly and multi-morbid patients (Chicheł et al., 2023; Fionda et al., 2023; Krzysztofiak et al., 2022; Shah et al., 2020).

1.4 Purpose of the Study

The purpose of this study is to establish the current role of brachytherapy in skin cancer management by discussing its indications, technique, oncological results, and toxicity. Specific emphasis is placed on its application in anatomical sites where surgical or external radiation therapy may be challenging due to either practical or cosmetic considerations.

2. Materials and Methods

This study is a narrative review of the literature on the use of brachytherapy in the treatment of skin cancers, with particular emphasis on basal cell carcinoma (BCC) and squamous cell carcinoma (SCC).

Search strategy. The PubMed/MEDLINE database and Google Scholar were searched for studies published in English. The search was conducted from February to May 2026. The following keywords and their combinations with logical operators (AND/OR) were used: brachytherapy, skin cancer, basal cell carcinoma, squamous cell carcinoma, radiotherapy, skin cancer treatment. In addition, the reference lists of selected articles were analyzed to identify further relevant studies (snowballing).

Inclusion criteria. The following were eligible for analysis: original studies (prospective and retrospective clinical series), systematic reviews and meta-analyses, consensus statements and guidelines from scientific societies, as well as review articles and epidemiological studies concerning the epidemiology, techniques, efficacy, toxicity profile, and cosmetic outcomes of brachytherapy in skin cancers. Full-text articles available in English were included.

Exclusion criteria. Studies not directly related to the topic and publications concerning melanoma exclusively were excluded.

Selection and data analysis. Titles and abstracts were subjected to an initial assessment for relevance to the topic, followed by an analysis of the full texts of publications meeting the criteria. For some studies where full-text access was not available, the analysis was based on data contained in their abstracts. Data on tumor type, the brachytherapy technique used, fractionation schedule, local control rate, cosmetic outcomes, and complications were extracted from the selected studies, and the collected information was presented descriptively.

Characteristics of the included literature. The review included 44 publications from 2011 to 2025. Original clinical studies predominated (18 studies; 40.9%) and review articles (14; 31.8%); the remainder consisted of systematic reviews and meta-analyses (4; 9.1%), epidemiological studies (4; 9.1%), consensus statements and guidelines (3; 6.8%), and a case report (1; 2.3%). Half of the studies (22; 50.0%) were published between 2021 and 2025, which demonstrates the up-to-date nature of the analyzed literature.

3. Epidemiology of Skin Cancers

The main skin cancers include keratinocyte carcinomas, which encompass two major subtypes based on their histology, namely BCC and SCC (J. Y. S. Kim et al., 2018a; Perry et al., 2017; R. Wang et al., 2025).

BCC is the most frequent type of skin cancer (Marzuka & Book, 2015; Zhang et al., 2021). According to a population-based study conducted in Rochester, Minnesota, BCC incidence was estimated at 146 per 100,000 Caucasians annually (Marzuka & Book, 2015). BCC has slow-growing features and rarely metastasizes; however, a delay in diagnosis and/or treatment may lead to the progressive destruction of tissues, including subcutaneous tissue, cartilage, muscle, and bone (D. P. Kim et al., 2019; J. Y. S. Kim et al., 2018a; Marzuka & Book, 2015). The dysregulation of the Hedgehog signaling pathway underlies the mechanism of BCC development. Most often, it involves PTCH1 inactivating mutations or SMO activating mutations, causing abnormal cellular proliferation (J. Y. S. Kim et al., 2018a; Marzuka & Book, 2015). BCC develops primarily due to ultraviolet (UV) radiation, the main environmental etiological factor (J. Y. S. Kim et al., 2018a; Marzuka & Book, 2015; Perry et al., 2017).

The clinical presentation of BCC is highly variable. This type of skin cancer typically affects chronically sun-exposed areas of skin such as the face, earlobes, scalp, and neck. Nodular BCC has a typical appearance as a pearly papule or nodule characterized by a raised, pearly border, telangiectasias, and usually central ulceration. In addition to the nodular form, other types include superficial, pigmented, and scleroderma-like lesions (D. P. Kim et al., 2019).

The second most common form of keratinocyte cancer is SCC. This type of cancer develops in epidermal keratinocytes and is caused by chronic cumulative damage from UV radiation, which results in DNA damage and mutations, especially in tumor suppressor genes such as TP53. Additional risk factors include immunosuppression, recurrent skin injury, the presence of precancerous lesions, and exposure to carcinogens (Que et al., 2018; Waldman & Schmults, 2019).

Even though both diseases occur due to exposure to UV rays and share the same background, their biological behavior, growth characteristics, risk of metastasis, and treatment approach are different. BCC is more common than SCC, and its growth rate is slower and involves mostly local invasion, while SCC grows faster and has a much higher risk of metastasis (J. Y. S. Kim et al., 2018b; Leiter et al., 2020). As far as the biology of sunlight exposure is concerned, BCC is more typical for intensive UV exposure, which occurs usually in younger age groups, while SCC is related more often to long-term cumulative exposure to radiation (Leiter et al., 2020).

In contrast to BCC, SCC more often develops secondary to precancerous lesions, such as actinic keratosis and Bowen's disease (J. Y. S. Kim et al., 2018b; Que et al., 2018). Clinically, SCC appears as an infiltrative nodule, ulcer, or hyperkeratotic lesion with irregular borders (Waldman & Schmults, 2019). In general, this malignancy has a higher proliferation rate and deeper penetration into the skin and underlying tissues compared with BCC (Leiter et al., 2020; Waldman & Schmults, 2019). Histologically, tumor differentiation, depth of infiltration, and perineural involvement are of considerable prognostic value (J. Y. S. Kim et al., 2018b; Que et al., 2018). The risk of metastases increases in the presence of larger lesion size, deep infiltration, poor differentiation, recurrence, perineural involvement, lesions on the ears or lips, and immunosuppression (J. Y. S. Kim et al., 2018b; Que et al., 2018).

4. Radiotherapy in the Management of Cutaneous Malignancies

Although surgery remains the standard primary treatment for NMSC, radiation therapy has gained an increasingly important role, particularly in patients of advanced age, with significant comorbidities, or with contraindications to surgery (Chicheł et al., 2023; Goyal et al., 2021; Laliscia et al., 2021a). BCC and SCC often respond well to radiation-based treatment modalities, especially in anatomically sensitive regions such as the nose, eyelids, and ears, where surgical excision may compromise cosmetic or functional outcomes (Doggett et al., 2023; Monge-Cadet et al., 2024; Yadavalli et al., 2024). Mohs micrographic surgery continues to achieve excellent local control rates approaching 95% (J. Y. S. Kim et al., 2018a); however, radiotherapy represents an effective non-invasive alternative in selected clinical settings.

4.1 External Beam Radiotherapy (EBRT)

Principles of Action and Technical Context

External beam radiotherapy (EBRT) uses externally generated photon or electron beams to deliver ionizing radiation to the target tissue. (Goyal et al., 2021) In cutaneous malignancies, the transition from orthovoltage X-rays to megavoltage beams introduced several dosimetric challenges. Megavoltage electron beams exhibit a build-up effect, in which the maximum radiation dose is deposited beneath the skin surface rather than directly at it. To ensure adequate superficial dose delivery, a bolus material is applied to shift the dose distribution toward the skin surface and achieve the prescribed therapeutic dose (Goyal et al., 2021; Tagliaferri et al., 2021).

Indications

EBRT serves as a definitive treatment option for large lesions and as adjuvant therapy following surgery in the presence of high-risk pathological features (Goyal et al., 2021; Tagliaferri et al., 2021). These include positive or close surgical margins, perineural invasion, infiltration of bone or cartilage, and lymph node involvement (Goyal et al., 2021; Rodríguez Villalba et al., 2021). Although EBRT remains highly effective, recent comparative studies increasingly evaluate its outcomes against brachytherapy, which has demonstrated superior cosmetic results in several meta-analyses (Chicheł et al., 2023; Doggett et al., 2023; Monge-Cadet et al., 2024).

Limitations

One important limitation of EBRT is the difficulty in achieving optimal dose conformality on highly irregular anatomical surfaces, such as the auricle or nasolabial fold (Esmati et al., 2024; Goyal et al., 2021). Short source-to-skin distances in these regions may result in dose inhomogeneities and localized “hot spots” (Goyal et al., 2021). In addition, megavoltage photon beams penetrate deeply, potentially exposing adjacent healthy tissues to unnecessary irradiation (Goyal et al., 2021). From a logistical perspective, EBRT typically requires multiple treatment fractions delivered over several weeks and depends on dedicated shielded facilities, which may present challenges for elderly or frail patients (Goyal et al., 2021; Monge-Cadet et al., 2024).

4.2 Brachytherapy — Definition and Advanced Principles

Definition and Classification

Brachytherapy (BT), also referred to as interventional radiotherapy, involves the placement of radioactive sources directly within or adjacent to the target volume, allowing the delivery of high localized radiation doses while sparing surrounding healthy tissues (Monge-Cadet et al., 2024). The technique is broadly divided into surface brachytherapy (plesiotherapy), in which sources are positioned on the skin using customized moulds or dedicated applicators such as Leipzig or Valencia systems, and interstitial brachytherapy, where catheters or needles are implanted directly into the tumor tissue (Esmati et al., 2024; Monge-Cadet et al., 2024; Yadavalli et al., 2024).

Radiation Sources and Dosimetric Methods

Modern brachytherapy predominantly employs high-dose-rate (HDR) remote afterloading systems. Iridium-192 is the most commonly used isotope because of its high activity and rapid dose fall-off outside the target region. However, its relatively short half-life of approximately 74 days necessitates regular source replacement (Esmati et al., 2024). Cobalt-60 provides a substantially longer half-life of approximately 5.27 years, offering logistical advantages for treatment centers; nevertheless, its higher average photon energy of 1.25 MeV requires more extensive radiation shielding (Esmati et al., 2024).

Local Irradiation and Intensity Modulation

The effectiveness of brachytherapy depends heavily on accurate clinical target volume (CTV) delineation. For BCC, treatment margins of 5–10 mm are typically added to the gross tumor volume (GTV), whereas SCC generally requires wider margins of 10–20 mm because of its greater infiltrative potential (Tagliaferri et al., 2021). Lesions exceeding 5 mm in thickness, historically considered less suitable for surface brachytherapy, can now be treated using multilayer catheter configurations (Esmati et al., 2024; Fionda et al., 2023). This approach enables dynamic intensity modulation by varying the distance between the radiation sources and the skin surface (Fionda et al., 2023). Additional catheter layers expand the therapeutic window between the prescribed treatment isodose and toxicity-limiting dose levels, thereby improving deep tumor coverage while reducing the risk of excessive surface toxicity (Esmati et al., 2024; Fionda et al., 2023).

Protection of Healthy Tissues and Quality of Life

Protection of organs at risk (OARs) relies on both physical shielding and advanced imaging guidance. During periocular irradiation, internal lead ocular shields protect the lens and retina, while customized lead

splints may be used during lip irradiation to shield the mandibular region (Monge-Cadet et al., 2024; Tagliaferri et al., 2021). High-frequency ultrasound and CT-based three-dimensional planning provide accurate evaluation of tumor depth and lead to a significant decrease in major toxicities such as tissue necrosis and non-healing ulceration (Fionda et al., 2023; Goyal et al., 2021). Long-term local control rates remain excellent, up to 98.9% in some studies, and patient-reported quality of life measures including DLQI and UW-QOL scores report high satisfaction levels (Doggett et al., 2023; Monge-Cadet et al., 2024; Yadavalli et al., 2024). Chronic adverse effects such as telangiectasia or hypopigmentation are generally limited to low-grade toxicities and are acceptable given preserved anatomy and function (Doggett et al., 2023; Monge-Cadet et al., 2024).

Electronic brachytherapy represents a newer technological approach that uses miniature X-ray sources generating low-energy photons of approximately 50 keV (Doggett et al., 2023; Goyal et al., 2021). Because it does not require radioactive isotopes or extensive shielding infrastructure, electronic brachytherapy enables treatment in outpatient and ambulatory settings with greater logistical flexibility (Doggett et al., 2023; Goyal et al., 2021). Dosimetric calculations are commonly based on the TG-43 formalism, which assumes full-scatter conditions; studies suggest that this model may overestimate skin surface dose by approximately 5% because of reduced backscatter at the skin-air interface.

5. Brachytherapy in Non-melanoma Skin Cancer

5.1 Types of Brachytherapy

The selection of a brachytherapy technique in skin cancer should be based on tumor thickness, surface extent, anatomical location, and the geometry of the treated area (Likhacheva et al., 2017; Shah et al., 2020). In clinical practice, several main delivery methods are distinguished: standardized surface applicators, custom moulds, multicatheter flap systems, electronic brachytherapy, and, less commonly, interstitial techniques (Likhacheva et al., 2017; Shah et al., 2020).

Surface applicators, including the Leipzig and Valencia systems, provide a reproducible, factory-defined dose distribution and are intended mainly for small, regular, and superficial lesions. Custom moulds, fitted to the individual patient, allow coverage of larger surfaces and irregularly shaped areas such as the nose or the auricle. Interstitial techniques, which involve implanting catheters or needles directly within the tumor, are used for thicker and more deeply infiltrating lesions, whereas electronic brachytherapy, which employs miniature X-ray sources, represents an emerging alternative to conventional radioactive sources (Shah et al., 2020).

The extent of variation in clinical practice is illustrated by the survey by Likhacheva et al., in which the most frequently used methods were Leipzig applicators and custom moulds (each in 75% of centers), followed by multicatheter flap systems (69%), Valencia applicators (50%), electronic brachytherapy (31%), and interstitial techniques (6%) (Likhacheva et al., 2017). The same study revealed considerable variation in treatment planning: lesion depth was routinely assessed by ultrasound in 60% of centers, margins around the gross tumor ranged from 3 to 15 mm (median 5 mm), and the prescribed fractionation schedules ranged from 30 Gy in 5 fractions to 64 Gy in 32 fractions (Likhacheva et al., 2017). These data indicate that skin brachytherapy requires individualized planning rather than a uniform treatment scheme (Likhacheva et al., 2017).

Among the dose-rate modalities, high-dose-rate (HDR) brachytherapy remains the best-documented technique in non-melanoma skin cancer. Its efficacy is supported by the systematic review by Krzysztofiak et al., which included 14 studies and 2,403 patients (Krzysztofiak et al., 2022). A summary of the principles guiding technique selection in clinical practice is provided in Table 1.

Table 1. Brachytherapy technique selection in non-melanoma skin cancer based on tumor characteristics.

Tumor characteristic	Best-fit brachytherapy technique	Notes and references
Superficial, regular lesion (<3 cm²)	Surface applicator (Leipzig or Valencia)	Reproducible, factory-defined dose distribution (Likhacheva et al., 2017; Shah et al., 2020)
Large or irregularly shaped surface	Custom mould	Conforms to complex curved surfaces (Laliscia et al., 2021a; Likhacheva et al., 2017)
Lesion depth ≤5 mm	Surface applicator or custom mould	Standard surface brachytherapy (Likhacheva et al., 2017; Shah et al., 2020)
Lesion depth >5 mm	Interstitial implant or multilayer mould	Intensity modulation extends the therapeutic depth window (Esmati et al., 2024; Fionda et al., 2023)
Curved anatomy (nose, auricle, eyelid)	Custom mould or multicatheter flap	Conformity to anatomy (Laliscia et al., 2021a; Likhacheva et al., 2017)
Outpatient setting with minimal shielding	Electronic brachytherapy	No radioactive sources; low-energy photons (Doggett et al., 2023; Goyal et al., 2021; Kuo et al., 2023)
Deeply infiltrative tumor	Interstitial implant (LDR or HDR)	Allows full coverage of deep target volumes (Ducassou et al., 2011)
Nasal vestibule SCC (Wang T1–T2)	Interstitial implant with image guidance	5-yr local control up to 100% in modern image-guided series (Czerwinski et al., 2019)

5.2 Indications and Patient Selection

The selection of patients for brachytherapy in non-melanoma skin cancer requires a multidisciplinary assessment, taking into account tumor characteristics (size, depth, histology, location), patient factors (age, general condition, comorbidities, life expectancy, anticipated cosmetic and functional outcomes), and the technical feasibility of the planned treatment (Shah et al., 2020; Veness et al., 2019).

Definitive treatment. Brachytherapy is most commonly used as a definitive, radical treatment in patients in whom surgery is contraindicated, technically difficult, or likely to compromise cosmetic and functional outcomes (Chicheł et al., 2023; Shah et al., 2020; Veness et al., 2019). Particularly favorable indications include small and superficial BCC and SCC lesions located in the so-called facial H-zone (nose, eyelids, lips, ears, and adjacent regions), where wide excision and reconstruction may be challenging (Goyal et al., 2021; J. Y. S. Kim et al., 2018a; Shah et al., 2020). The American Brachytherapy Society identifies tumors smaller than 5 cm with limited depth of infiltration as particularly suitable for surface brachytherapy, while deeper or more complex lesions may require interstitial techniques or custom moulds (Shah et al., 2020). Brachytherapy is also a valuable option in elderly patients and those with significant comorbidities, who often poorly tolerate extensive surgery or prolonged courses of external beam radiotherapy; in such cases, the limited treatment volume and the possibility of using hypofractionated schedules reduce the overall treatment burden (Albert et al., 2019; Chicheł et al., 2023; Shah et al., 2020).

Adjuvant treatment. In selected cases, brachytherapy may also serve as an adjuvant modality after surgery, particularly in high-risk cutaneous SCC with positive or close surgical margins, perineural invasion, or other adverse pathological features (Muto & Pastore, 2021; Stevenson et al., 2020). However, the role of adjuvant radiotherapy in cSCC with clear surgical margins remains debated; a recent systematic review and meta-analysis by Kim et al. did not demonstrate a significant impact of adjuvant radiotherapy on outcomes in patients with clear margins (Y. Kim et al., 2022). Decisions regarding adjuvant brachytherapy should therefore be individualized within a multidisciplinary team.

Contraindications. Brachytherapy is generally not recommended for tumors with deep invasion of bone or cartilage, lesions that exceed the technical coverage of available applicators, or patients with active connective tissue disease that may exacerbate radiation toxicity. Previous irradiation of the same field is a relative contraindication that requires careful re-evaluation of the cumulative dose to organs at risk. Pre-treatment assessment of lesion depth — most commonly using high-frequency ultrasound or CT-based three-dimensional planning — is essential to confirm that the prescribed dose adequately covers the tumor volume while sparing critical structures (Likhacheva et al., 2017). The principal patient- and tumor-related factors guiding the choice between brachytherapy, surgery, and external beam radiotherapy are summarized in Table 2.

Table 2. Patient and lesion factors favoring brachytherapy, surgery, or external beam radiotherapy in non-melanoma skin cancer.

Patient / lesion factor	Favors brachytherapy	Favors surgery	Favors EBRT
Small, superficial lesion (<2 cm, <5 mm depth)	Strong indication	Strong indication	Acceptable alternative
Lesion in facial H-zone (nose, eyelids, lips, ears)	Strong indication (preserves anatomy)	Often requires complex reconstruction	Limited dose conformality on curved surfaces
Deep infiltration (>5 mm)	Interstitial BT only	Strong indication	Strong indication
Bone or cartilage invasion	Generally contraindicated	Preferred	Considered if surgery declined
Elderly or multiple comorbidities	Strong (hypofractionated, short course)	Anesthesia and recovery risk	Feasible but logistically demanding
Need for histological margin control	Not applicable	Preferred (especially Mohs)	Not applicable
Recurrent tumor in a previously irradiated field	Relative contraindication	Preferred	Usually contraindicated
Cosmetic preservation as priority	Strong (cosmetic superiority in SCRiBE meta-analysis (Zaorsky et al., 2018))	Depends on reconstruction quality	Inferior cosmesis vs BT (Zaorsky et al., 2018)
Adjuvant treatment after positive surgical margins	Feasible for small volumes (Tagliaferri et al., 2021)	Re-excision first if feasible	Standard for high-risk SCC (Muto & Pastore, 2021; Stevenson et al., 2020)

5.3 Dose and Fractionation

A wide variety of dose–fractionation schedules has been employed in skin brachytherapy, reflecting differences in tumor characteristics, applicator type, and institutional preferences. The survey by Likhacheva et al. reported prescribed regimens ranging from 30 Gy in 5 fractions to 64 Gy in 32 fractions, illustrating the lack of a single universally adopted standard (Likhacheva et al., 2017). The American Brachytherapy Society consensus statement provides recommended dose–fractionation schemes for both definitive and post-operative settings, with multiple acceptable regimens depending on tumor depth and applicator type (Shah et al., 2020).

Frequently used schedules in the included literature include 36 Gy delivered in 12 fractions of 3 Gy with Leipzig applicators (Gauden et al., 2013), 40 Gy delivered in 8 fractions of 5 Gy with custom moulds (Laliscia et al., 2021a), and similar regimens with Valencia applicators (Delishaj et al., 2015; Laliscia et al., 2021b). For electronic brachytherapy, a commonly applied regimen is 40 Gy in 8 fractions delivered twice weekly (Kuo et al., 2023). The optimal dose–fractionation regimen for non-melanoma skin cancer remains a subject of debate, and direct comparisons across studies are limited by the heterogeneity of prescribed doses, applicator types, and reporting criteria (Krzysztofiak et al., 2022; Likhacheva et al., 2017).

5.4 Treatment Efficacy

Available evidence indicates that brachytherapy is a highly effective treatment modality for non-melanoma skin cancer, providing high local control and favorable cosmetic outcomes. In the systematic review by Krzysztofiak et al., comprising 14 studies and 2,403 patients treated with HDR brachytherapy, local control rates ranged from 71% to 99%, cosmetic results were most commonly described as good or very good, and radiodermatitis was the most frequently reported adverse effect (Krzysztofiak et al., 2022).

In a prospective study by Gauden et al., involving 200 patients and 236 lesions treated with HDR brachytherapy using Leipzig applicators (36 Gy in 12 fractions of 3 Gy), a local control rate of 98% was achieved after a median follow-up of 66 months (range, 25–121 months). Treatment was well tolerated, with predominantly mild skin reactions and excellent or good cosmetic results in 88% of cases; only four patients required further surgical treatment due to recurrence (Gauden et al., 2013). In a mono-institutional series by Tagliaferri et al., including 51 patients with 67 lesions treated with contact HDR brachytherapy using ^{192}Ir flap applicators, the 2-year local control rate was 94.0% (93.5% in the definitive setting and 100% in the adjuvant setting after positive surgical margins), with disease-specific survival of 100% and cosmetic outcomes rated as excellent or good in 73.7%, fair in 19.3%, and poor in 7.0% of cases; acute toxicity remained limited (grade 1 in 24.6%, grade 2 in 3.5%, and grade 3 in 3.5% of lesions, with no grade 4 events) (Tagliaferri et al., 2021).

Favorable outcomes have also been reported in elderly patients treated with the Valencia applicator. In the study by Delishaj et al., including 57 lesions in 39 patients, complete response was achieved in 96.25% of lesions after a median follow-up of 12 months, with no recurrences and no grade 3 or higher acute or late toxicity (Delishaj et al., 2015). Similar results were reported by Laliscia et al., who, in 95 patients (182 lesions; median age 83 years) treated with HDR brachytherapy using Valencia applicators, achieved a complete response in 97.3% of lesions and a 2-year local control rate of 96%, with excellent or good cosmetic results in 77.5% and 18.7% of cases, respectively (Laliscia et al., 2021b).

Good outcomes have also been observed for lesions located in anatomically challenging facial regions. In an analysis of 147 periorificial facial carcinomas treated with low-dose-rate interstitial brachytherapy, the 5-year locoregional recurrence-free survival rate was 87.3% (90.4% for BCC and 70.8% for SCC), with no grade 3 complications (Ducassou et al., 2011). In SCC of the nasal vestibule, the 3-year local, regional, and locoregional control rates were 91%, 93%, and 84%, respectively (Lipman et al., 2015), while in a more recent image-guided brachytherapy series by Czerwinski et al., the corresponding 5-year rates were 95%, 91%, and 83% (Czerwinski et al., 2019). In the subgroup treated after April 2010 with three-dimensional image guidance and a standardized regimen of 49 Gy in 14 fractions of 3.5 Gy (EQD2 67.8 Gy), 5-year local control reached 100% (n = 42), supporting the role of image-guided brachytherapy and contemporary fractionation in the management of nasal vestibule carcinoma (Czerwinski et al., 2019). Of note, the series by Lipman et al. (Lipman et al., 2015) represents an earlier subset of the institutional cohort subsequently expanded and analyzed with image guidance by Czerwinski et al. (Czerwinski et al., 2019).

Table 3. Summary of clinical studies included in the review on brachytherapy in non-melanoma skin cancer.

Study	n (pts / lesions)	Technique	Dose / fractionation	Local control	Follow-up	Cosmetic outcome	Toxicity / notes
Krzysztofiak et al. (2022)	14 studies / 2,403 pts	HDR (various)	Various	71–99%	Various	Good / very good (most studies)	Radiodermatitis most frequent
Gauden et al. (2013)	200 / 236	HDR, Leipzig	36 Gy in 12 × 3 Gy	98% (232/236)	Median 66 mo (25–121)	Excellent or good 88%	Acute G1 71% / G2 34%; no >G2; late hypopigmentation 5.5%; no telangiectasia; 74 lesions adjuvant after surgery
Tagliaferri et al. (2021)	51 / 67	Contact HDR, ^{192}Ir flap applicators	40 Gy/8 fx BID or 54 Gy/18 fx	2-yr LC 94.0%	Median 10 mo (6–27)	Excellent/good 73.7%; fair 19.3%; poor 7.0%	Acute G1 24.6%; G2 3.5%; G3 3.5%; no G4; DSS 100%
Delishaj et al. (2015)	39 / 57	HDR, Valencia (^{192}Ir)	40 Gy/8 fx or 50 Gy/10 fx (BED 60–75 Gy)	CR 96.25%	12 mo (3–29)	Excellent 86%; good 12.3%; fair 1.7%	Acute G1–G2 63.2%; late G1–G2 19.3%; no grade ≥3; cohort 77.2% BCC / 21.1% SCC / 1 Kaposi
Laliscia et al. (2021b)	95 / 182	HDR, Valencia (^{192}Ir)	NR*	CR 97.3%; 2-yr LC 96%	Median 14 mo (3–59)	Excellent 77.5%; good 18.7%	Dermatitis G1 16.0% / G2 6.0%; hypopigmentation 27.5%; no grade ≥3
Ducassou et al. (2011)	132 / 147	LDR interstitial, ^{192}Ir wire (Paris System)	Median 60 Gy (60–70 Gy)	5-yr LRRFS 87.3% (BCC 90.4%; SCC 70.8%)	Median 72 mo	Hypopigmentation, atrophy, telangiectasia (each 12.9%)†	G1 28.6%; G2 7.5%; no grade ≥3 (CTCAE v3.0); BCC 82% / SCC 18%; primary BT > salvage
Lipman et al. (2015)	60 (T1:50, T2:10)	HDR; interstitial (38) + mould (22), ^{192}Ir	42–54 Gy	3-yr: local 91%; regional 93%; locoregional 84%	NR*	NR*	Moist desquamation 64%; confluent mucositis 82%; chondritis/chondronecrosis 19% (actuarial); nasal vestibule SCC
Czerwinski et al. (2019)	102	HDR ^{192}Ir; interstitial (77) or mould (25)	49 Gy in 14 fx of 3.5 Gy (EQD2 67.8 Gy)	5-yr: local 95%; regional 91%; locoregional 83%	Median 42 mo (3–210)	High satisfaction (NAFEQ; n = 42)	Nasal crusts most prevalent mild complication; Wang T1–T2 SCC nasal vestibule; image-guided since 2010

HDR — high-dose-rate; LDR — low-dose-rate; BT — brachytherapy; LC — local control; CR — complete response; LRRFS — locoregional recurrence-free survival; BID — bis in die (twice daily); NR — not reported in the original publication / not available. † Ducassou et al. assessed side effects using CTCAE v3.0 rather than the RTOG–EORTC cosmetic scale (excellent / good / fair / poor) used by Delishaj, Laliscia, Tagliaferri, and others; cosmetic outcomes between these studies are therefore not directly comparable.*

5.5 Complications

Most adverse effects associated with brachytherapy for non-melanoma skin cancers are confined to the irradiated area, and the overall toxicity profile remains acceptable. The most common reactions include erythema, dry or moist desquamation, and post-irradiation skin changes, with post-irradiation dermatitis (radiodermatitis) being the main problem during HDR treatment (Krzysztofiak et al., 2022).

The toxicity observed in clinical trials was predominantly mild in nature. In the series by Delishaj et al., the most severe acute skin reaction reached only grade 1 severity and occurred in 58% of patients, while late changes of the same grade were reported less frequently — in less than one-fifth of cases; no severe early or late complications were observed (Delishaj et al., 2015). In the study by Laliscia et al., covering 182 lesions treated with Valencia applicators, the most common acute reaction was radiation dermatitis (grade 1 in 16.0%, grade 2 in 6.0%), while pain (8.2%) and dry skin (2.8%) were less common. Among late complications, hypopigmentation predominated (27.5%), while fibrosis (8.2%), skin atrophy (1.0%), and ulceration (0.5%) were observed sporadically; no grade 3 or higher toxicity was reported (Laliscia et al., 2021b).

Complications were more pronounced in tumors located in anatomically challenging areas. In SCC of the nasal vestibule, Lipman et al. reported moist desquamation in 64% of patients, confluent mucositis in 82%, and an actuarial incidence of chondritis or chondronecrosis of 19% (Lipman et al., 2015). In contrast, in an analysis by Ducassou et al. of low-dose-rate interstitial implants in the periorificial regions of the face, no grade 3 or higher adverse events were observed; the most frequent late effects were hypopigmentation, skin atrophy, and telangiectasia, each in 12.9% of treated lesions (Ducassou et al., 2011). Despite the variability of results between individual reports, serious complications were rare; however, tissues in areas with complex anatomical structures may be at greater risk of permanent sequelae (Ducassou et al., 2011; Krzysztofiak et al., 2022; Laliscia et al., 2021b; Lipman et al., 2015).

6. Discussion

Brachytherapy, once reserved for inoperable or recurrent tumors, is now a recognized treatment option for selected keratinocyte tumors (Krzysztofiak et al., 2022; Ota et al., 2018; Shah et al., 2020; Veness et al., 2019). Its use is most strongly justified in BCC and in some cases of squamous cell carcinoma located on the face and neck, where preservation of function and aesthetic outcome is of key importance (Monge-Cadet et al., 2024; Shah et al., 2020; Tagliaferri et al., 2021; Veness et al., 2019). With appropriate patient selection, the method ensures high local control — in the systematic review by Krzysztofiak et al., covering 14 studies and 2,403 patients treated with HDR brachytherapy, local control rates ranged from 71% to 99% (Krzysztofiak et al., 2022).

The particular clinical value of brachytherapy is evident in the therapeutic space between surgical treatment and external beam radiotherapy (EBRT) (Shah et al., 2020; Veness et al., 2019). Surgery remains the standard of care for many primary tumors; however, brachytherapy proves useful where resection would require extensive reconstruction or carry a risk of deformity of the nose, eyelids, lips, or auricle (J. Y. S. Kim et al., 2018a; Shah et al., 2020; Veness et al., 2019). It also offers an alternative to EBRT in situations where teleradiotherapy is less conformal on curved surfaces or more logistically burdensome due to the long duration of treatment (Shah et al., 2020; Veness et al., 2019). Available comparative analyses indicate that brachytherapy may provide a more favorable cosmetic outcome than EBRT with comparable local efficacy, although the data do not confirm its universal superiority (Haseltine et al., 2016; Zaorsky et al., 2018). The SCRiBE meta-analysis demonstrated the superiority of brachytherapy over EBRT in terms of cosmetic outcome (Zaorsky et al., 2018), while the analysis by Haseltine et al. found no statistically significant differences in local efficacy, toxicity, or cosmetic outcome between the compared techniques (Haseltine et al., 2016).

A key determinant of the efficacy of brachytherapy remains appropriate patient selection (Albert et al., 2019; Chicheł et al., 2023; Shah et al., 2020). The greatest benefit is derived by elderly patients, those in poor general condition, or those with multiple comorbidities, in whom the method allows surgery to be avoided while maintaining high efficacy (Albert et al., 2019; Chicheł et al., 2023; Shah et al., 2020). The possibility of applying hypofractionated schedules further reduces the treatment burden and the number of visits. Albert et al. indicated that elderly patients with skin cancers may achieve good outcomes with hypofractionated radiotherapy combined with HDR brachytherapy instead of surgical treatment (Albert et al., 2019), while Chicheł et al. emphasized the flexibility of the method, particularly in locally advanced cases in which surgery is not feasible (Chicheł et al., 2023). This is confirmed by the data of Delishaj et al., who, in 39 elderly patients (57 lesions) treated with the Valencia applicator, achieved a complete response in 96.25% of lesions after a

median follow-up of 12 months, with no recurrences and no grade ≥3 toxicity (Delishaj et al., 2015). In the study by Monge-Cadet et al., the median age of patients treated for facial cancers was 81 years, and more than three-quarters of those surveyed would recommend the method (Monge-Cadet et al., 2024). Treatment decisions in older adults should therefore take into account not only tumor eradication but also treatment tolerability, the impact on daily functioning, and quality of life (Albert et al., 2019; Chicheł et al., 2023; Monge-Cadet et al., 2024).

Beyond patient-related factors, tumor characteristics also influence outcomes after brachytherapy. In their image-guided series of 102 patients with squamous cell carcinoma of the nasal vestibule, Czerwinski et al. identified tumor volume as a significant prognostic factor for regional recurrence, proposing a threshold of 2.3 cm^3 above which the risk of regional failure increased substantially (Czerwinski et al., 2019). However, because the ultimate 5-year regional control rate after salvage treatment in their cohort reached 96%, the authors did not recommend elective neck treatment on the basis of tumor volume alone, underscoring the role of close follow-up and individualized risk assessment in anatomically challenging sites (Czerwinski et al., 2019).

The variety of skin brachytherapy techniques is both an advantage and a source of heterogeneity in the available data (Likhacheva et al., 2017; Ota et al., 2018; Pashazadeh et al., 2019; Shah et al., 2020). On the one hand, surface applicators, Leipzig and Valencia-type applicators, custom moulds, interstitial implants, and electronic brachytherapy allow treatment to be tailored to the depth, shape, and location of the lesion (Ota et al., 2018; Pashazadeh et al., 2019; Shah et al., 2020). According to the American Brachytherapy Society, standardized surface applicators are best suited to small, regular, and superficial lesions, while custom moulds and interstitial techniques are used for tumors with complex geometry, located on curved surfaces, or with deeper infiltration (Ota et al., 2018; Pashazadeh et al., 2019; Shah et al., 2020). In the survey by Likhacheva et al., surface applicators were most commonly used, while customized forms were selected mainly to cover a larger area or lesions with irregular shapes (Likhacheva et al., 2017). A practical example of such customization is the work by Laliscia et al., in which 40 lesions with a depth of ≤5 mm — including those on the scalp, nose, and auricle — were treated using custom-made moulds (median of 5 catheters per applicator) (Laliscia et al., 2021a), while Fionda et al. described multilayer contact brachytherapy with intensity modulation as a solution for lesions thicker than the traditional 5 mm threshold (Fionda et al., 2023). However, this technical flexibility comes at the cost of difficulty in comparing results between centers and partly explains the variability in reported cosmetic outcomes and toxicity (Fionda et al., 2023; Likhacheva et al., 2017; Pashazadeh et al., 2019).

Electronic brachytherapy deserves a separate discussion (Doggett et al., 2023; Goyal et al., 2021; Kuo et al., 2023; Ota et al., 2018). Its advantages include the absence of the need for radioactive sources, reduced requirements for radiation shielding, and easier integration into outpatient settings (Goyal et al., 2021; Ota et al., 2018). Long-term observations indicate high local efficacy — in the study by Doggett et al., local control was achieved in 98.9% of patients (Doggett et al., 2023) — and in the multicenter study by Kuo et al., an improvement in quality of life and resolution of early symptoms were noted between 6 and 12 weeks after treatment (Kuo et al., 2023). However, the available data are mainly derived from non-randomized studies involving selected low-risk lesions (Doggett et al., 2023; Goyal et al., 2021; Kuo et al., 2023; Ota et al., 2018). For this reason, electronic brachytherapy should currently be regarded as a promising but still evolving option, rather than a proven alternative to HDR isotope brachytherapy, surgical treatment, or teleradiotherapy (Doggett et al., 2023; Goyal et al., 2021; Ota et al., 2018).

The interpretation of the available data is limited by the predominance of retrospective, single-center clinical series and the lack of randomized controlled trials directly comparing brachytherapy with other treatment methods (Haseltine et al., 2016; Krzysztofiak et al., 2022; Zaorsky et al., 2018). Variations in techniques, fractionation schedules, and evaluation criteria further complicate direct comparisons and the synthesis of results (Krzysztofiak et al., 2022; Likhacheva et al., 2017; Pashazadeh et al., 2019). Nevertheless, the consistency of results regarding high local control and acceptable toxicity observed in independent clinical series supports the reliability of the described benefits (Delishaj et al., 2015; Ducassou et al., 2011; Krzysztofiak et al., 2022).

Future directions

Several questions remain unresolved and warrant prospective investigation. First, the optimal dose–fractionation schedule for brachytherapy in non-melanoma skin cancer has not been defined; randomized comparisons between commonly used regimens (e.g., 36 Gy in 12 fractions, 40 Gy in 8 fractions, 49 Gy in 14 fractions of 3.5 Gy) are needed to clarify which schedules best balance local control with long-term cosmesis

(Czerwinski et al., 2019; Krzysztofiak et al., 2022; Likhacheva et al., 2017). Second, the role of advanced imaging guidance — including high-frequency ultrasound and three-dimensional CT-based planning — should be examined prospectively, as preliminary data suggest improved local control and reduced toxicity with image-guided approaches (Czerwinski et al., 2019). Third, the position of electronic brachytherapy in routine practice will depend on long-term, comparative data; ongoing multicenter studies should clarify whether its logistic advantages translate into outcomes equivalent to those of isotope-based HDR brachytherapy (Doggett et al., 2023; Goyal et al., 2021; Kuo et al., 2023; Ota et al., 2018). Finally, structured patient-reported outcome measures (such as DLQI, UW-QOL, or NAFEQ for nasal lesions) should be applied systematically across studies to enable meaningful comparison of cosmetic and functional results between brachytherapy, surgery, and EBRT (Czerwinski et al., 2019; Kuo et al., 2023; Monge-Cadet et al., 2024).

7. Conclusions

Brachytherapy is a well-established, tissue-sparing method for treating selected non-melanoma skin cancers. It is particularly valuable for small, superficial lesions located in areas of anatomical and aesthetic importance, and for elderly patients who are not suitable candidates for surgical treatment. Available data indicate high local control, good cosmetic results, and an acceptable toxicity profile, although the strength of the evidence remains limited by the predominance of retrospective studies and the lack of randomized trials. Brachytherapy should therefore be regarded as an important component of multidisciplinary treatment for skin cancers, rather than a universal substitute for surgery or teleradiotherapy — its greatest advantage lies in its precision and selectivity, not its universality.

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REFERENCES

1. Albert, A., Knoll, M. A., Conti, J. A., & Zbar, R. I. S. (2019). Non-melanoma skin cancers in the older patient. *Current Oncology Reports, 21*(9), 79.
2. Chen, J. Y., Fernandez, K., Fadadu, R. P., Reddy, R., Kim, M. O., Tan, J., et al. (2025). Skin cancer diagnosis by lesion, physician, and examination type: A systematic review and meta-analysis. *JAMA Dermatology, 161*(2), 135–146.
3. Chicheł, A., Chyrek, A. J., Kluska, A., & Burchardt, W. M. (2023). Advanced non-melanoma skin cancer in elderly patients: When surgery says no, interventional radiotherapy (brachytherapy) says yes. *Journal of Contemporary Brachytherapy, 15*(4), 235–244.
4. Chlebicka, I., Stefaniak, A., Matusiak, Ł., & Szepietowski, J. C. (2021). Basal cell carcinoma: What new can be learned about the most common human cancer? A cross-sectional prospective study of 180 cases in a single centre. *Advances in Dermatology and Allergology, 38*(6), 1086–1091.
5. Czerwinski, M. D., van Leeuwen, R. G. H., Kaanders, J. H. A. M., Zwijnenburg, E. M., Lipman, D., Takes, R. P., et al. (2019). Image guided brachytherapy for cancer of the nasal vestibule: Local control and cosmesis. *International Journal of Radiation Oncology, Biology, Physics, 103*(4), 913–921.
6. Delishaj, D., Laliscia, C., Manfredi, B., et al. (2015). Non-melanoma skin cancer treated with high-dose-rate brachytherapy and Valencia applicator in elderly patients: A retrospective case series. *Journal of Contemporary Brachytherapy, 7*(6), 437–444.
7. Doggett, S. W., Willoughby, M., Miller, K. A., et al. (2023). Long-term clinical outcomes of non-melanoma skin cancer patients treated with electronic brachytherapy. *Journal of Contemporary Brachytherapy, 15*(1), 9–14.
8. Dreyfuss, I., Kamath, P., Frech, F., et al. (2022). Squamous cell carcinoma: 2021 updated review of treatment. *Dermatologic Therapy, 35*(4), e15308.

9. Ducassou, A., David, I., Filleron, T., Rives, M., Bonnet, J., & Delannes, M. (2011). Retrospective analysis of local control and cosmetic outcome of 147 periorificial carcinomas of the face treated with low-dose-rate interstitial brachytherapy. *International Journal of Radiation Oncology, Biology, Physics, 81*(3), 726–731.
10. Esmati, E., Abyaneh, R., Jaberi, R., Naderinasab, S., Gholami, S., Payandeh, M., et al. (2024). Surface mold brachytherapy for head and neck non-melanoma skin cancer—Local control rates and survival: A retrospective analysis. *Journal of Contemporary Brachytherapy, 16*(5), 323–334.
11. Fionda, B., Placidi, E., Rosa, E., et al. (2023). Multilayer intensity modulated contact interventional radiotherapy (brachytherapy): Stretching the therapeutic window in skin cancer. *Journal of Contemporary Brachytherapy, 15*(3), 220–223.
12. Gauden, R., Pracy, M., Avery, A., & Hodgson, D. (2013). HDR brachytherapy for superficial non-melanoma skin cancers. *Journal of Medical Imaging and Radiation Oncology, 57*(2), 212–217.
13. Goyal, U., Cheung, M. K., Suszko, J., Laughlin, B., Kim, Y., Askam, J., et al. (2021). Electronic brachytherapy for treatment of non-melanoma skin cancers: Clinical results and toxicities. *Journal of Contemporary Brachytherapy, 13*(5), 497–503.
14. Haseltine, J. M., Parker, M., Wernicke, A. G., Nori, D., Wu, X., & Parashar, B. (2016). Clinical comparison of brachytherapy versus hypofractionated external beam radiation versus standard fractionation external beam radiation for non-melanomatous skin cancers. *Journal of Contemporary Brachytherapy, 8*(3), 189–194.
15. Kim, D. P., Kus, K. J. B., & Ruiz, E. (2019). Basal cell carcinoma review. *Hematology/Oncology Clinics of North America, 33*(1), 13–24.
16. Kim, J. Y. S., Kozlow, J. H., Mittal, B., Moyer, J., Olencki, T., & Rodgers, P. (2018a). Guidelines of care for the management of basal cell carcinoma. *Journal of the American Academy of Dermatology, 78*(3), 540–559.
17. Kim, J. Y. S., Kozlow, J. H., Mittal, B., Moyer, J., Olencki, T., & Rodgers, P. (2018b). Guidelines of care for the management of cutaneous squamous cell carcinoma. *Journal of the American Academy of Dermatology, 78*(3), 560–578.
18. Kim, Y., Lehrer, E. J., Wirth, P. J., Khesroh, E. A., Brewer, J. D., Billingsley, E. M., et al. (2022). Adjuvant radiotherapy may not significantly change outcomes in high-risk cutaneous squamous cell carcinomas with clear surgical margins: A systematic review and meta-analysis. *Journal of the American Academy of Dermatology, 86*(6), 1246–1257.
19. Krzysztofiak, T., Kamińska-Winciorek, G., Pilśniak, A., & Wojcieszek, P. (2022). High dose rate brachytherapy in non-melanoma skin cancer—Systematic review. *Dermatologic Therapy, 35*(9), e15675.
20. Kuo, A. M., Lee, E. H., Rossi, A. M., Nehal, K. S., Cordova, M. A., Steckler, A. M., et al. (2023). A multicenter prospective trial of electronic skin surface brachytherapy for keratinocyte carcinoma: Early cosmesis, quality of life, and adverse events. *International Journal of Radiation Oncology, Biology, Physics, 116*(3), 544–550.
21. Laliscia, C., Coccia, N., Fuentes, T., Perrone, F., & Paiar, F. (2021b). Two different sizes of Valencia applicators in non-melanoma skin cancer treatment with iridium-192 high-dose-rate brachytherapy. *Journal of Contemporary Brachytherapy, 13*(6), 650–656.
22. Laliscia, C., Fuentes, T., Coccia, N., Mattioni, R., Perrone, F., & Paiar, F. (2021a). High-dose-rate brachytherapy for non-melanoma skin cancer using tailored custom moulds—A single-centre experience. *Contemporary Oncology, 25*(1), 12–16.
23. Leiter, U., Keim, U., & Garbe, C. (2020). Epidemiology of skin cancer: Update 2019. *Advances in Experimental Medicine and Biology, 1268*, 123–139.
24. Likhacheva, A. O., Devlin, P. M., Shirvani, S. M., et al. (2017). Skin surface brachytherapy: A survey of contemporary practice patterns. *Brachytherapy, 16*(1), 223–229.
25. Lipman, D., Verhoef, L. C., Takes, R. P., Kaanders, J. H., & Janssens, G. O. (2015). Outcome and toxicity profile after brachytherapy for squamous cell carcinoma of the nasal vestibule. *Head & Neck, 37*(9), 1297–1303. https://doi.org/10.1002/hed.23758
26. Marzuka, A. G., & Book, S. E. (2015). Basal cell carcinoma: Pathogenesis, epidemiology, clinical features, diagnosis, histopathology, and management. *The Yale Journal of Biology and Medicine, 88*(2), 167–179.
27. Monge-Cadet, J., Vairel, B., Meresse, M., et al. (2024). High-dose-rate brachytherapy for treatment of facial skin cancers: Local control, toxicity, and quality of life in 67 patients. *Cancers, 16*(15), 2742.
28. Muto, P., & Pastore, F. (2021). Radiotherapy in the adjuvant and advanced setting of cSCC. *Dermatology Practical & Conceptual, 11*(Suppl. 2), e2021168S.
29. Ota, K., Adar, T., Dover, L., & Khachemoune, A. (2018). The re-emergence of brachytherapy as treatment for non-melanoma skin cancer. *Journal of Dermatological Treatment, 29*(2), 170–175.
30. Pashazadeh, A., Boese, A., & Friebe, M. (2019). Radiation therapy techniques in the treatment of skin cancer: An overview of the current status and outlook. *Journal of Dermatological Treatment, 30*(8), 831–839.
31. Perry, D. M., Barton, V., & Alberg, A. J. (2017). Epidemiology of keratinocyte carcinoma. *Current Dermatology Reports, 6*(3), 161–168.
32. Que, S. K. T., Zwald, F. O., & Schmults, C. D. (2018). Cutaneous squamous cell carcinoma: Incidence, risk factors, diagnosis, and staging. *Journal of the American Academy of Dermatology, 78*(2), 237–247.

33. Rodríguez Villalba, S., Pérez-Calatayud, M. J., Pérez-Calatayud, J., Richart Sancho, J., & Ortega, M. (2021). Acute parotitis in high-dose-rate brachytherapy treatment for skin cancer: A case report. *Journal of Contemporary Brachytherapy, 13*(5), 493–496.
34. Shah, C., Ouhib, Z., Kamrava, M., et al. (2020). The American Brachytherapy Society consensus statement for skin brachytherapy. *Brachytherapy, 19*(4), 415–426.
35. Stevenson, M. L., Criscito, M. C., Wilken, R., Doudican, N. A., Bain, E. E., III, Parashar, B., & Carucci, J. A. (2020). Use of adjuvant radiotherapy in the treatment of high-risk cutaneous squamous cell carcinoma with perineural invasion. *JAMA Dermatology, 156*(8), 918–921.
36. Tagliaferri, L., Ciardo, F. G., Fionda, B., Casà, C., Di Stefani, A., Lancellotta, V., et al. (2021). Non-melanoma skin cancer treated by contact high-dose-rate radiotherapy (brachytherapy): A mono-institutional series and literature review. *In Vivo, 35*(4), 2313–2319.
37. Veness, M. J., Delishaj, D., Barnes, E. A., Bezugly, A., & Rembielak, A. (2019). Current role of radiotherapy in non-melanoma skin cancer. *Clinical Oncology, 31*(11), 749–758.
38. Waldman, A., & Schmults, C. (2019). Cutaneous squamous cell carcinoma. *Hematology/Oncology Clinics of North America, 33*(1), 1–12.
39. Wang, M., Gao, X., & Zhang, L. (2025). Recent global patterns in skin cancer incidence, mortality, and prevalence. *Chinese Medical Journal, 138*(2), 185–192.
40. Wang, R., Chen, Y., Shao, X., et al. (2025). Burden of skin cancer in older adults from 1990 to 2021 and modelled projection to 2050. *JAMA Dermatology, 161*(7), 715–722.
41. Yadavalli, P., Pareek, V., Barthwal, M., Bharat, R., Mullassery, S., Aashita, et al. (2024). Clinical and toxicity outcomes with 3D-based HDR surface mold brachytherapy in skin cancer. *Journal of Cancer Research and Therapeutics, 20*(3), 930–934.
42. Zaorsky, N. G., Lee, C. T., Zhang, E., & Galloway, T. J. (2018). Skin CanceR Brachytherapy vs External beam radiation therapy (SCRiBE) meta-analysis. *Radiotherapy and Oncology, 126*(3), 386–393.
43. Zhang, W., Zeng, W., Jiang, A., He, Z., Shen, X., Dong, X., et al. (2021). Global, regional and national incidence, mortality and disability-adjusted life-years of skin cancers and trend analysis from 1990 to 2019: An analysis of the Global Burden of Disease Study 2019. *Cancer Medicine, 10*(14), 4905–4922.
44. Zhou, L., Zhong, Y., Han, L., Xie, Y., & Wan, M. (2025). Global, regional, and national trends in the burden of melanoma and non-melanoma skin cancer: Insights from the Global Burden of Disease Study 1990–2021. *Scientific Reports, 15*(1), 5996.