

Healthcare Professional Guide

Brachytherapy:

The precise answer for tackling skin cancer



Because life is for living

Skin cancer

Worldwide, the incidence of skin cancer is higher than all other cancers combined.¹ Skin cancers include:

Basal cell carcinoma (BCC):²⁻⁶

- Most common form
- Growth patterns include nodular (nBCC), superficial (sBCC) and morpheaform
- Approximately 1–2 million newly diagnosed cases in United States every year
- Most often seen in 50–80 year-olds, but increasing incidence in under 50's

Squamous cell carcinoma (SCC):^{2,3}

- Includes Bowen's disease (SCC *in-situ*)
- May arise out of solar keratosis (actinic keratosis)
- Lower incidence than BCC (1:4 ratio)

Malignant melanoma:⁷

- Arises from melanocytes
- More aggressive but less common than BCC and SCC
- Varying sensitivity to radiation

Non-melanoma skin cancer (NMSC)

BCC and SCC are classified as NMSCs.² Although the incidence is rising, **the mortality rate for NMSC is very low**, due in part to the ease of detection, the low metastatic rate of the more common BCC and the high success rates of therapy.³

Staging of NMSC

Staging of NMSC is determined by the clinical extent of the disease and the appearance of high risk features which can help guide treatment decisions and prognosis.³ This brochure primarily discusses treatment for early stage (T1–T2) NMSC.

In the United States over 2.1 million people are treated for NMSC annually⁸

Treating early NMSC

There are a variety of treatments, most often used as monotherapy in early stage cancers (T1–T2). Historically, treatment of early stages has been with simple excision or cryotherapy. However, as NMSC most commonly occurs on sun-exposed skin areas and patients' rate cosmetic outcome as an important factor when choosing a treatment,⁹ there is a greater demand for more patient-friendly options.

NMSC treatment choices

Radiotherapy:^{2,3}

- Brachytherapy
- External beam radiotherapy (EBRT)

Surgery:^{2,3}

- Simple excision
- Mohs' micrographic surgery: excised tissue assessed microscopically to ensure entire tumor removed

Destructive therapies:^{2,3}

- Cryotherapy: tumor destroyed with, most often, liquid nitrogen
- Electrodessication and curettage (ED&C): exposed cell layers in turn necrotized then scraped free until all tumor tissue removed

Photodynamic Therapy: (PDT)²

- Photosensitizing cream (methyl aminolevulinate or 5-aminolevulinic acid) activated with light to produce free radicals that destroy tumor tissue
- Mainly for sBCC and Bowen's disease

Topical therapies:²

- Imiquimod 5% cream: stimulates immune cells and cytokines to destroy tumor tissue
- 5% 5-fluorouracil cream: interferes with tumor cell growth
- Mainly for sBCC and Bowen's disease

Brachytherapy: targeted treatment for early NMSC

Radiotherapy can be divided into **external beam radiotherapy** (EBRT) and **brachytherapy**. In EBRT, the radiation source is placed at a measured distance from the skin. In brachytherapy, the source is placed in, on, or directly next to the tumor.^{10,11}

The precise approach of brachytherapy allows direct delivery of radiation to the target tissue, while sparing surrounding, healthy tissues.^{10,11}

Role of brachytherapy in early NMSC

While surgery can provide excellent cure rates, cosmetic results are often less acceptable due to scarring and deformity.^{2,3} **Brachytherapy is an outstanding alternative or complement to surgery**, offering considerable patient benefits, including excellent cosmetic outcomes.

Brachytherapy could be considered treatment of choice:¹²⁻¹⁴

- When surgery is contraindicated e.g. for elderly or diabetic patients, or those taking blood thinners.
- When scarring needs to be minimal as the tumor is in a visible or uncomfortable position, e.g. nose or shin.
- In areas with poor wound-healing capacity, e.g. scalp or shin.
- When it is vital to preserve structure and function of the area being treated, e.g. hand or lip.
- Where surgery may lead to nerve damage and permanent numbness or paralysis.
- If surgical excision could leave a wound that requires complicated reconstruction.
- For lesions too hard to reach or too anatomically awkward for EBRT, e.g. ear pinna.

Benefits of brachytherapy in early NMSC

With excellent functional and cosmetic results and a more comfortable and convenient procedure compared to both surgery and EBRT, **brachytherapy is a patient-centered treatment choice**.

Brachytherapy can be used in all lesion types, including Bowen's disease and recurring lesions. Additionally, brachytherapy can be used for other skin disorders including keloids¹⁵ and Kaposi's sarcoma.¹⁶

Benefits of brachytherapy in early NMSC:

- **Demonstrated efficacy:** Excellent local control rates of up to 100% in early stage disease; comparable to surgery and EBRT and more favorable than PDT and topical treatments.¹²
- **Excellent cosmesis:** Little or no tissue destruction, so minimal or no scarring and excellent cosmetic results compared to surgery and EBRT.^{12,17-20}
- **Precision:** A tailored radiation dose delivered precisely to target tissue, unlike surgery where surrounding tissue is destroyed.^{10,11}
- **Minimized side effects:** Unlike EBRT, nearby healthy tissue is spared from unnecessary radiation, minimizing short- and long-term side effects and treatment discomfort, resulting in favorable functional outcomes.¹²
- **Pain free:** Surface brachytherapy is non-invasive and painless and is both anesthesia and needle free; ideal for locations where surgery and/or scarring will be painful.¹²
- **Convenience:** Short treatment time of days, compared to weeks with EBRT; shorter recovery time compared to surgery.¹⁹



Brachytherapy delivery

An advantage of brachytherapy over EBRT is that it delivers a tailored radiation dose directly to the target area. The intensity of radiation decreases rapidly the further it is from the source. As a result, higher doses of radiation can be delivered to small volumes of target tissue with brachytherapy. **Surrounding healthy tissues therefore receive as minimal a dose as possible, limiting toxicity.**¹⁰

Treatment schedule

Delivery of brachytherapy may be carried out at different dose rates: a high dose rate (HDR) over a short time (> 12Gy/Hr), or low dose rate (LDR) over a longer period (0.4–2Gy/Hr). **HDR brachytherapy is most widely used for NMSC treatment** and may be delivered in as little as 1–3 treatment sessions.

HDR brachytherapy is delivered via a computer-controlled 'afterloader' (Figure 1), which delivers radiation via specialized applicators. Applicators deliver radiation at the tumor surface (Figure 2; surface brachytherapy) or interstitially via catheters.



Figure 1. A fully-automated afterloader controls delivery of radiotherapy according to a pre-devised plan



Figure 2. Delivery of brachytherapy using a flat, fixed-diameter applicator

Leading innovation in radiotherapy

Scientific and technical advances in imaging, computerized treatment planning, customizable applicators and dose delivery have resulted in considerable improvements in patient outcomes and provide additional options in the treatment of difficult-to-reach lesions.

These advances build on the established principles of brachytherapy to facilitate **even greater levels of precision**, thereby delivering highly individualized patient care.²¹

Other treatment advances include electronic brachytherapy – where treatment is delivered via small X-ray sources positioned close to, or directly on to, the skin. Current preliminary data for this therapy shows promising control rates in NMSC.²²

Specialized applicators

Surface applicators range from flat, fixed diameter applicators (Figure 3A–C) to cuttable mats (Figure 3D). The choice is partly dependent on the size and location of the tumor.

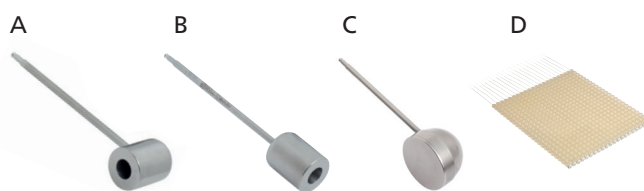


Figure 3. Brachytherapy applicators. A) horizontal Leipzig applicator; B) vertical Leipzig applicator; C) Valencia applicator; D) Freiburg flap

Use of specialized applicators extends the range and complexity of tumors that can be treated, meaning HDR brachytherapy is a treatment choice available to most people with early NMSC.^{12,23,24}

HDR surface brachytherapy in early NMSC

High efficacy

HDR surface brachytherapy in early stage NMSC provides **a highly effective option with excellent cancer control rates**. Many studies report complete control in all patients, maintained at 5 years follow-up (Table 1).

Location	N	Type	Control rate (%)	Minimum follow-up (months)
Ear	13	M	100	18
Face	136	M	98	12
Various	53	M	100	20
Various	106	M	96	5
Various	11	M	100	3
Various	67	FD	96	18*
Various	92	FD	97	10
Hand (SCC)	25	M	100	1.5

Table 1. Control rates for primary NMSCs following HDR surface brachytherapy (both BCC and SCC unless indicated otherwise)^{14,17,19,25-29}
Type of applicator: M: Mold; FD: Fixed diameter; *median follow-up recorded

Favorable efficacy compared to other treatments

Five-year control rates for HDR brachytherapy are comparable to EBRT and surgery (Table 2), demonstrating that **HDR brachytherapy is as efficacious as these treatments in early stage NMSC**.

Location	N	Control rate (%)	Minimum follow-up (months)
EBRT			
Various	339	86	NS
Various	531	89	24
Ear	334	87	1.4
Surgery			
Various (BCC)	1516	99	60
Head & neck (BCC)	3370*	97.4	60
Head & neck (SCC)	381*	96	60

Table 2. Control rates for primary NMSCs following EBRT or surgery (all BCC and SCC unless indicated)³⁰⁻³⁵
NS: Not Stated; *Mohs' micrographic surgery

Furthermore, **HDR brachytherapy is often more efficacious than other NMSC treatments**, including ED&C, imiquimod cream and PDT (Table 3).

Treatment	Control rate (%)	Lesion type	Follow-up (months)
ED&C	94	SCC	50*
Cryotherapy	80	BCC	60**
Imiquimod	89	sBCC	60*
PDT	78 86	sBCC nBCC	24

Table 3. Control rates for primary NMSCs following ED&C, imiquimod cream and PDT³⁶⁻³⁹
*Average follow-up; **estimate of overall treatment success at end of follow-up period

This proven efficacy profile establishes brachytherapy as a viable treatment option for early NMSC and a feasible alternative to EBRT and surgery. As such, brachytherapy can be considered part of the standard of care for early NMSC.



Side effects and quality of life

Excellent cosmetic outcomes

With comparable efficacy between treatments, other factors such as cosmesis and impact on patients' quality of life become important considerations.

As brachytherapy minimizes radiation to surrounding healthy tissues, patients experience reduced side effects, improved cosmetic outcomes and better quality of life compared to surgery and EBRT.

Studies show that excellent cosmetic results with minimal scarring can be achieved with surface HDR brachytherapy.

In one investigation, at 6 months post-brachytherapy to the face, appearance at the treatment site was rated by physicians as 'good to excellent' in the vast majority of cases (Figure 4).¹⁷

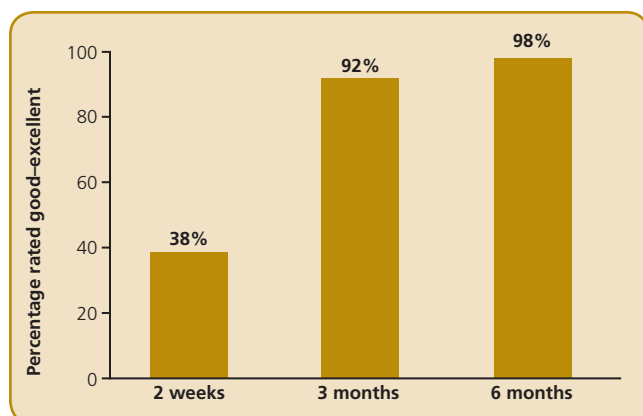


Figure 4. Physician-rated cosmetic outcome following HDR brachytherapy (Adapted from Guix *et al*, 2000)¹⁷

Similar studies of cryotherapy, surgery, EBRT and PDT have produced investigator-rated cosmetic 'excellent or good' scores of only 61%, 38%, 74% and 79% respectively.^{18,20,37}

Maximized functional outcomes

Limited damage to surrounding tissue with brachytherapy means that **functional outcomes can also be maximized**. For instance, an investigation of brachytherapy on the hand showed no significant differences between treated and opposite hands with regard to range of motion, grip strength, fine touch sensitivity, deformity and overall disability at 5-years follow-up.²⁹

Reduced side effects and optimal quality of life

Side effects

Short-term side effects in the first few days following treatment are most often of Grades 1–2. When a Grade 4 side effect does occur it normally resolves within 3 weeks.⁴⁰

Brachytherapy offers reduced potential for post-treatment side effects such as scarring, necrosis, rash, depigmentation and skin ulceration. This limits the need for post-treatment corrective procedures (Figure 5).^{17,40}



Figure 5. Results before (left) and 5 years after (right) treatment with HDR surface brachytherapy for SCC^{17†}

Short treatment and recovery time

In many cases, brachytherapy treatment is only a limited number of sessions compared to the numerous daily sessions over a number of weeks required for EBRT. Moreover, brachytherapy is nearly always carried out on an outpatient basis, with no recovery time needed.^{14,19,41}

Minimized pain

Surface HDR brachytherapy is a painless treatment that preserves tissue functionality. Therefore, it is particularly suitable for areas where surgery could be painful, result in functional defects, or have problematic wound healing such as the shin, palm of hand, fingers, lips, eyelids, scalp, nose or ear.^{17,19,25,42}

Brachytherapy is a painless and effective therapy option that requires few treatment sessions. It often results in better cosmetic and functional outcomes than surgery or EBRT, making it a **more comfortable and convenient option** for many patients.

Summary

Using techniques established and refined over several decades, brachytherapy has proven to be an effective treatment for early stage NMSC.

Advances in imaging, treatment planning and applicator design facilitate even **greater precision** in dose delivery and minimizes harmful radiation to surrounding healthy tissues. **These advances are enabling brachytherapy to be utilized in a wide range of NMSC treatments.**

Excellent efficacy, cosmetic and functional outcomes, combined with reduced risk of side effects, short outpatient treatment times and improved quality of life indicate that **brachytherapy is a patient-centered treatment choice.**

The shorter treatment duration of HDR surface brachytherapy also lowers the total treatment costs.

Brachytherapy should be considered as a part of the standard of care for NMSC.

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For further information on brachytherapy for skin cancer, consult the following resources:

Speak to colleagues who have successfully integrated brachytherapy into their practice

ESTRO (European Society for Therapeutic Radiology and Oncology)
www.estro.org

ASTRO (American Society for Therapeutic Radiology and Oncology)
www.astro.org

GEC-ESTRO (Groupe Européen de Curiethérapie and the European Society for Therapeutic Radiology and Oncology)
www.estro.org/about/Pages/GEC-ESTRO.aspx

ABS (American Brachytherapy Society)
www.americanbrachytherapy.org

NCCN (National Comprehensive Cancer Network)
www.nccn.org



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Brachytherapy:

The precise answer for tackling skin cancer

Reasons to consider brachytherapy in skin cancer management

- Demonstrated efficacy
- Precision radiotherapy
- Minimized toxicity
- Patient-centered
- Cost-effective
- State-of-the-art

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