HDR BRACHYTHERAPY FOR NON-MELANOMATOUS SKIN CANCER
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The scope of the problem
Cancer of the skin (including melanoma, basal cell, and squamous cell skin cancer) is by far the most common of all types of cancer worldwide. In fact, there are more cases of skin cancer diagnosed in the United States each year than all other cancer types combined with an estimated 3.5 million non-melanomatous skin cancers (NMSC) occurring in about 2.2 million Americans primarily in sun-exposed areas of the body. Remarkably, one in five individuals will develop skin cancer in their lifetime. The skin cancer incidence increases in older patients (over age 60 years) with a 4.2 percent increase every year from 1992 to 2006. In similar fashion, the number of new skin cancer procedures being performed has increased 4-6% per year. NMSC is highly curable due to most lesions being detected in early stage (T1 and T2) with low risk of metastases and the broad availability of effective therapy.

Common treatment options
The vast majority of early skin lesions are diagnosed and treated by primary care physicians or general dermatologists. There are several commonly used treatment options that are available with varying degrees of effectiveness. The optimal choice of therapy is based on lesion extent, body site location, histopathology, grade, access to specialized procedures and patient preference. The standard of care for early stage skin cancers has traditionally been surgical excision. While simple excision is limited by requisite removal of larger tissue volume, the advent of Mohs micrographic surgery has allowed for precise and systematic removal of thin sections until negative margins are achieved. This allows maximal tissue preservation and has demonstrated very high local control rates (>97%). Although the cosmetic outcome is usually quite favorable, Mohs surgery requires subspecialty training/expertise and can be a long, invasive procedure requiring local anesthesia and possible skin grafts for adequate reconstruction. It is also relatively contraindicated in patients on blood thinners or with healing issues.

Other alternatives include cryotherapy in which the tumor is typically destroyed with liquid nitrogen or electrodesiccation and curettage (ED&C) where exposed cell layers are necrotized then scraped free until all tumor tissue is removed. Photodynamic therapy involves applying sensitizing cream to the surface lesion (methyl-aminolevulinate or 5-aminolevulinic acid), which is then activated with light to produce free radicals that locally destroy tumor tissue. Although relatively simple to deliver in the office, patients do report some discomfort, scarring, and skin sensitivity especially to light and sun exposure. The recurrence risk is higher than surgery at 20-30%.

Topical ointments have been used for decades including the chemotherapeutic agent, Fluorouracil (Efudex) and the immune modulator, Imiquimod (Aldara) that is typically applied multiple times per week for several weeks. These treatments therefore require significant patient compliance and proper application techniques to assure adequate lesion coverage. They are also limited to superficial penetration and thus also have higher local recurrence rates than other methods.
The role of radiation therapy

The National Comprehensive Cancer Network (NCCN) guidelines suggest that in a review of literature, the best results for NMSC were obtained with surgery. However, consideration of function, cosmetic outcome, less scarring and patient preference may lead to the choice of radiation therapy as primary treatment in order to achieve optimal overall results. Radiation therapy has demonstrated excellent local control rates and may indeed be preferable in elderly patients with health issues such as peripheral vascular disease, diabetes mellitus or on blood thinners in which case anesthesia and surgery may be contraindicated. This includes complex lesion locations such as those in cosmetically sensitive areas of the face including the nose, eyelids, lips, ears, or in parts of the body with thin, delicate tissue such as the preauricular area of the leg or the dorsum of the hand. Radiation therapy can be used as an adjunct to surgery for higher risk lesions with positive margins, perineural invasion or high grade as well as recurrent tumors.

Therapeutic x-rays have been used for the definitive treatment for skin cancer for nearly a century. In fact, superficial radiation therapy (kilovoltage X-ray machines) was commonly used for skin treatments by dermatologists in their office in the 1970s and 1980s. These dedicated machines were costly to maintain, and offered much less conformity. newer superficial radiation therapy machines have been developed; however, this technique still delivers a low dose rate with greater doses to tissues at depth thereby requiring a protracted 20-25 daily treatment course.

Modern electron beam radiation therapy is more readily available and allows three-dimensional treatment planning. However, small skin lesions such as those on the face can offer challenges with dosage of irregular or curved surfaces and with reliability of calibration of small fields or cutouts. The relatively large penumbra requires a broader surface area to be irradiated than with more targeted techniques.

HDR brachytherapy

High-dose rate (HDR) surface brachytherapy places an Iridium-192 source in close proximity to the target lesion to deliver the treatment using a remote afterloader. The afterloader houses a radioactive source and delivers it precisely within specialized catheters or applicators that are applied to the target tissue. There are a variety of applicators available which can be tailored to the complexity and extent of skin lesions, which are outlined below. This technique can be used for all NMSC subtypes as well as keloids.

Advantages of HDR brachytherapy

HDR brachytherapy allows a more custom, direct radiation dose delivery to the surface with rapid falloff thereby aiming to maximally spare adjacent, deeper healthy tissues. During the treatment course, patients may develop mild skin rash, itching and dryness limited to the lesion area. This resolves within a couple weeks of completing therapy. Several studies have reported excellent local control rates (>90%), and favorable cosmetic outcomes with minimal long-term side effects.10, 11, 12

The treatment is pain-free and noninvasive and therefore does not require needles, cutting, or sutures. This is a distinct advantage especially for elderly patients with comorbidities such as diabetes, peripheral vascular disease or if they are on blood-thinners, where surgery is relatively contraindicated due to challenges in wound healing. The treatment may also result in less tissue destruction and scarring in sensitive facial areas such as the nose, ear, lip, or eyelid which may help bypass the need for reconstructive procedures.

Due to its localized nature, the treatment time is significantly less than external beam radiotherapy, with faster recovery times than invasive techniques. A course of therapy is accelerated and hypofractionated; it is typically delivered over a few minutes, twice weekly, for less than eight treatments compared to a four- to six-week daily fractionated course of external beam radiotherapy.

HDR solutions

Surface applicators

These simple applicators are ideally suited for flat, well-circumscribed lesions. The optimal scattering of the tungsten alloy shielding creates a homogenous dose pattern in the treatment area to a specified depth, typically 3 mm. Once commissioned, surface applicators are simple to use. The treatment planning process can be simplified to a nomogram to determine the specific dwell time based on the prescription depth. Alternatively, for a more complete approach Acuros® BV advanced dose calculation can be utilized in conjunction with BrachyVision. Acuros BV allows the user to calculate with Monte-Carlo like accuracy the complete dose distribution based on specific patient anatomy.

HDR workflow

1. Consultation (Pathology review & patient selection)
2. Simulation (Target delineation, including surface area and depth)
3. Treatment planning (With 3D catheter reconstruction if required)
4. Quality assurance (Physics)
5. Treatment delivery (Outpatient, twice weekly)
6. Follow-up (Routine)

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Common HDR dose/fractionation schemes shown above. (Typical external beam radiotherapy schedules are 20-30 fractions to 50-60 Gy.)

Catheter flaps

For more irregular surfaces or areas too large to treat with a surface applicator, multi-lumen catheter flaps can be utilized. The Catheter Flap Set, GM1004370 (available for GammaMedplus only), is a 200 x 290 x 10 mm flap of medical-grade silicone with a treatment channel possible every 0.5 cm. The catheter flap can be customized to the size and shape of the target lesion. Mould probes or treatment catheters are then inserted within the flap. For the Varisource, a Harrison-Anderson-Mick (H.A.M.) applicator (available from Mick-Radio Nuclear Instruments, Inc.) can be used. 3D treatment planning with advanced imaging (X-ray, CT, or MRI) can be utilized to assure optimal conformity.

Custom moulds

Conformable custom moulds are often utilized for complex shapes and irregular surfaces like the ear or nose. A custom mould can be constructed from specialized polymers (such as those used in dentistry) or a thermoplastic sheet. Treatment catheters can be embedded or affixed to the material, providing a custom fit to the treatment site. Care must be taken to ensure that the catheters meet the afterloader’s minimum turn radius so that the source wire can negotiate the catheter.

Varian offers two types of surface applicators: one with the source axis parallel to the skin (available only for GammaMedplus20), and one with the source axis parallel to the skin (available for Varisource® and GammaMedplus). Both are offered with an assortment of insert sizes to accommodate different lesion shapes. A thermoplastic sheet or the Universal Clamping Device, GM1008700, can be used to hold the surface applicator next to the skin.

To aid in the commissioning of the surface applicators, Standard Imaging, Inc. manufactures a fixture (Surface Applicator In-Air Calibration Fixture that works with Varian applicators, p/n 71737) which holds a small ion chamber (Exradin A20, 0.074 cc, p/n 92736) at a fixed distance to the surface applicator in air. With this setup, output measurements are easy to obtain and can be used to verify the output data supplied with the surface applicator sets.

Clinical perspectives | HDR brachytherapy for skin cancer

This figure illustrates the differences in dose distribution between an Acuros BV calculation (left) and a TG-43 calculation.
Summary

Brachytherapy is a viable treatment modality for early stage NMSC patients. The advent of sophisticated planning software, integration of imaging, and introduction of novel applicators has expanded the number of early stage patients that are potentially eligible for this non-invasive and painless procedure. With excellent local control rates, cosmetic outcomes, and minimal long-term toxicities, HDR brachytherapy with surface applicators should be considered in the frontline of primary treatment for NMSC patients.

References


Intended Use Summary

Varian Medical Systems’ software, afterloaders, and applicators are intended to provide radiotherapy for lesions, tumors, and conditions anywhere in the body where radiation treatment is indicated.

Safety

Radiation treatments may cause side effects varying with the part of the body being treated. This may include, but not be limited to irritation to the mouth, respiratory system, digestive system, genitourinary system, fatigue, nausea, skin irritation, and hair loss. In a minority of patients, side effects can be severe. Typically, the side effects are temporary. Radiation treatment is not appropriate for all cancers. Treatment sessions may vary in complexity and time. Patients should discuss the treatment and side effects with their physicians before starting. Side effects of applicator placement and/or implantation may occur. These side effects may include, but are not be limited to, localized discomfort, bleeding, and infection or other localized side effects based on the location the applicator is placed. Patients should discuss the treatment and side effects with their physicians before starting.

Medical Advice Disclaimer

Varian as a medical device manufacturer cannot and does not recommend specific treatment approaches. Individual treatment results may vary.