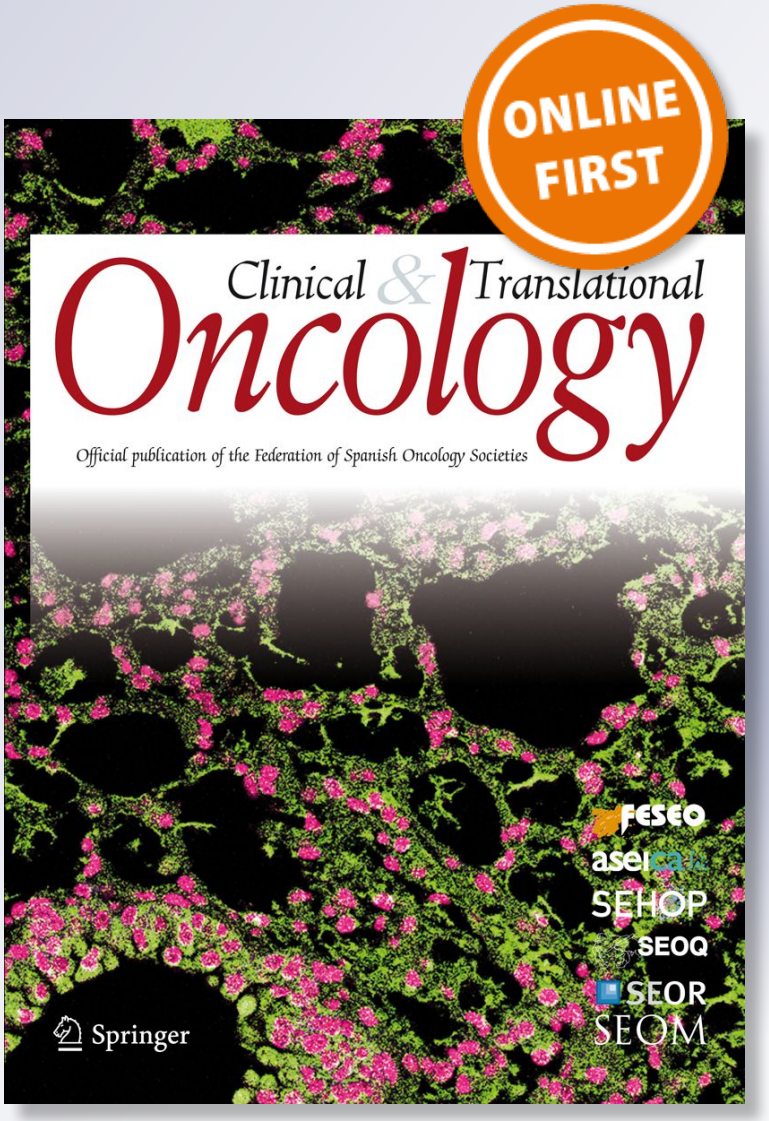
Recommendations of the Spanish brachytherapy group (GEB) of Spanish Society of Radiation Oncology (SEOR) and the Spanish Society of Medical Physics (SEFM) for high-dose rate (HDR) non melanoma skin cancer brachytherapy

S. Rodríguez, M. Arenas, C. Gutierrez, J. Richart, J. Perez-Calatayud, F. Celada, et al.

Clinical and Translational Oncology

ISSN 1699-048X

Clin Transl Oncol
DOI 10.1007/s12094-017-1733-z



Springer

Clin Transl Oncol
DOI 10.1007/s12094-017-1733-z

CLINICAL GUIDES IN ONCOLOGY

Recommendations of the Spanish brachytherapy group (GEB) of Spanish Society of Radiation Oncology (SEOR) and the Spanish Society of Medical Physics (SEFM) for high-dose rate (HDR) non melanoma skin cancer brachytherapy

S. Rodríguez[1] · M. Arenas[2] · C. Gutierrez[3] · J. Richart[1] · J. Perez-Calatayud[4] · F. Celada[4] · M. Santos[1] · A. Rovirosa[5]

Received: 22 July 2017 / Accepted: 28 July 2017

Abstract Clinical indications of brachytherapy in non-melanoma skin cancers, description of applicators and dosimetry recommendations are described based on the literature review, clinical practice and experience of Spanish Group of Brachytherapy and Spanish Society of Medical Physics reported in the XIV Annual Consensus Meeting on Non Melanoma Skin Cancer Brachytherapy held in Benidorm, Alicante (Spain) on October 21st, 2016. All the recommendations for which consensus was achieved are highlighted in blue. Regular and small surfaces may be treated with Leipzig, Valencia, flap applicators or electronic brachytherapy (EBT). For irregular surfaces, customized molds or interstitial implants should be employed. The dose is prescribed at a maximum depth of 3–4 mm of the clinical target volume/planning target volume (CTV/PTV) in all cases except in flaps or molds in which 5 mm is appropriate. Interstitial brachytherapy should be used for CTV/PTV >5 mm. Different total doses and fraction sizes are used with very similar clinical and toxicity results. Hypofractionation is very useful twice or 3 times a week, being comfortable for patients and practical for Radiotherapy Departments. In interstitial brachytherapy 2 fractions twice a day are applied.

Keywords Skin brachytherapy · Technical · Dosimetric aspects · Consensus

Introduction

Brachytherapy (BT) is being increasingly used for the treatment of Non melanoma skin cancer (NMSC) with evident good results, especially in patients in whom surgery may produce esthetic defects or in those with comorbidities who are unable to undergo an invasive intervention.

We describe the clinical indications, applicators, and aspects related to physics (dosimetry, reconstruction, prescription, and reporting) defined by a group of expert Radiotherapy Oncologists and Medical Physicists of the Spanish Brachytherapy Group (GEB) and the Spanish Society of Medical Physics (SEFM) based on personal experience and literature after the XIV Annual Consensus meeting of the two societies held on the 21st of October, 2016 in Benidorm, Alicante (Spain). The results of this consensus are presented here as recommendations for medical practice.

Prior to the meeting, an electronic survey was sent to 25 out of 69 Radiotherapy Departments with Brachytherapy Units in which skin BT is routinely performed. Twenty-four surveys (96%) were returned completed (Addendum 1 is a list of these 24 hospitals).

✉ S. Rodríguez
atosrodriguez@gmail.com

[1] Radiation Oncology Department, Hospital Clínica Benidorm, Av. Alfonso Puchades 8, 30501 Benidorm, Alicante, Spain

[2] Radiation Oncology Department, Hospital Universitari Sant Joan de Reus, Tarragona, Spain

[3] Radiation Oncology Department, Institut Català d'Oncologia, Hospitalet de Llobregat, Catalonia, Spain

[4] Radiation Oncology Department, Hospital La Fe-IRIMED, Valencia, Spain

[5] Radiation Oncology Department, ICMHO, Hospital Clínic I Universitari, Barcelona, Spain

Published online: 14 August 2017

- ***Skin BT has demonstrated to be a safe reliable technique for the treatment of NMSC.***

Indications/patient selection/contraindications

The advantage of BT over external beam radiation in NMSC is that the dose remains on the surface and the dose gradient is smaller. BT provides both, very good local control and excellent cosmetic results [1–4]. BT treatment can be performed using plesiotherapy or interstitial techniques. In plesiotherapy, the radiation source is placed directly over the target skin and in the second modality the radioactive sources are implanted directly "in contact" with the target tissue. BT can be delivered by both, low-dose-rate (LDR) or high-dose-rate (HDR) radiation sources which allow fractionation of the total dose in an outpatient setting. Superficial BT or plesiotherapy can be delivered by radionuclide-based applicators for treating small tumors in flat areas [5, 6] or by customized molds that adapt radiation doses to very uneven surfaces without the need to shield surrounding areas [4, 7].

Radionuclide-based applicators may include Leipzig applicators of 10, 20, or 30 mm in diameter, Valencia applicators of 20 or 30 mm in diameter and flaps (HAM applicator, Freiburg flap or Catheter flap). Molds can be handmade or customized and more recently are made by automated 3D printing [8]. Both types of BT treatment (applicators or customized molds) are used depending on the lesion size and skin surface shape. Another technique developed in the last years is HDR electronic BT with surface applicators [9, 10]. When the area to be treated is more than 5 mm in depth or it has very irregular surfaces or special anatomic areas (i.e., lower eyelid) interstitial BT is indicated Fig. 1.

The availability of a complete pathologic report (biopsy/surgery) is essential in the treatment of NMSC. Clark invasion should be reported. Patients with special clinical histopathologies including primary cutaneous lymphoma, metastasis, Merkel carcinoma, Kaposi, or dermatofibrosarcoma protuberans have also been treated with BT, and treatment should be individualized.

The prognostic factors of skin cancer are: histological type (morpheaform, basosquamous (metatypical), sclerosing, mixed infiltrative or micronodular features for basal cell carcinoma (BCC) and adenoid (acantholytic), adenosquamous, desmoplastic or metaplastic (carcinomatous subtypes) for squamous cell carcinoma (SCC), lesion size (>20 mm in area L, >10 mm in area M or area H independently of the size. See Addendum 2 for a description of the areas), depth (>2 mm or Clark level >IV), invasion of bone or cartilage structures, deep soft tissue, margins, recurrent or prior radiotherapy, poor differentiation, perineural invasion, vascular invasion, and lymph node involvement. These prognostic factors help in the decision making related to the indications for radiotherapy [11, 12].

The indications of BT are: radical or definitive treatment, adjuvant or postoperative treatment (after local excision due to positive or close margins or other bad prognostic factors. The definition of margins is described by each Institutional Tumor Board), and for a boost after external beam radiotherapy.

With regard to radical treatments, radiotherapy may be indicated in T1–T2 lesions [13] in non-surgical candidates due to the physical inability of the patient undergo invasive tumor removal or surgical reconstruction (comorbidities), or because of tumor size and anatomic location, such as in facial localizations (internal eye corner, nasogenian fold, nasal wing, auricular pavilion, lips, among others). BT may also be an alternative therapy in elderly patients or those with limited functional status as well as in patients with multiple tumors in whom surgery is ruled out.

Contraindications include malignant melanoma of the skin which is not radiosensitive and requires broader therapeutic strategies, skin cancers invading bony structures, upper eyelid localization, pinna tumor involving both the helix and the external auditory canal, ear conduct or any other site in which the anatomical situation makes the source positioning needed to provide adequate covering of the target volume impossible, as well as genetic or connective tissue diseases. Perineural invasion or repair DNA diseases are a relative contraindication. Age is NOT a contraindication for the use of BT [11, 12].

An imaging technique must be used to define CTV/PTV, with ultrasound being a simple, easy to use, and affordable tool. High frequency ultrasound with specific skin probes has been shown to be very useful for this purpose. However, several studies have questioned [14] the use of frequency values of 18 MHz since more accurate determinations and image quality are obtained with 35 MHz (Allen 2016 Personal communication). The depth of the macroscopic lesion or surgical bed helps to define the prescription point and the most adequate applicator to be chosen.

The recommended CTV is the macroscopic gross tumor volume (GTV) with a safety margin of 3–5 mm for BCC and 7–10 mm for SCC [15]. In adjuvant/postoperative cases the radial safety margin recommended is 10 mm around the scar.

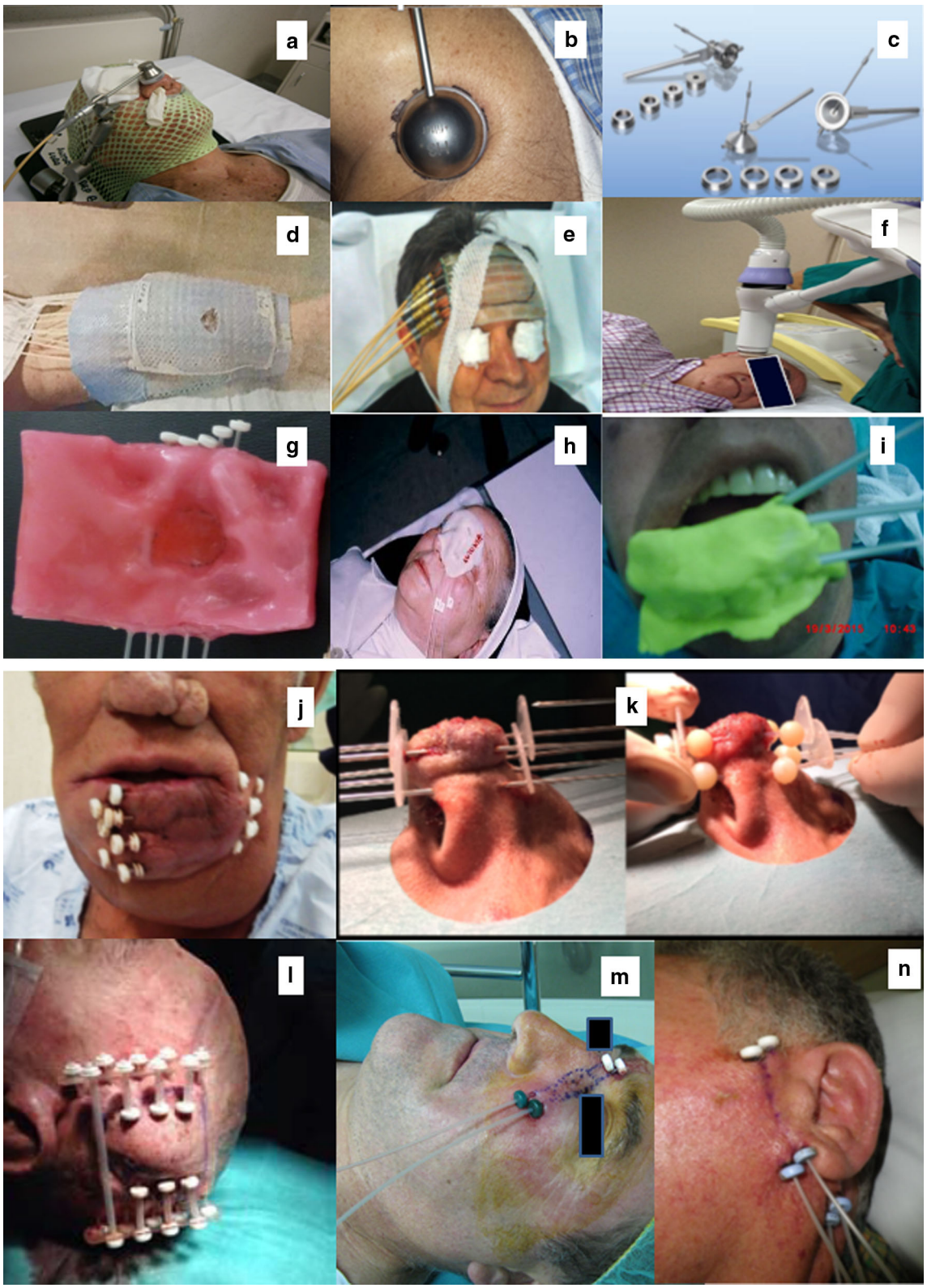


Fig. 1 Skin BT techniques. **a**, **b** Valencia applicator. **c** Leipzig applicator. **d**, **e** Flaps. **f** Electronic BT Esteya®. **g**, **h**, **i** Molds. **j**, **k**, **l**, **m**, **n** Interstitial BT. Courtesy of attendees to the XIV Annual Consensus Meeting on non melanoma skin cancer

- ***BT plays an important role in the treatment of skin tumors located on the face, irregular surfaces or areas in which an important surgical defect does not achieve the esthetical objective and/or functionality.***
- ***Age is NOT a CONTRAINDICATION of BT treatment.***
- ***Relative contraindications: Perineural invasion or repair DNA diseases.***
- ***PATHOLOGY:***
  - ***Depth must be correctly defined (Clark invasion).***
  - ***Histologies other than NMSC (cutaneous lymphoma, metastasis, Merkel carcinoma, Kaposi or dermatofibrosarcoma protuberans) can be treated with BT. Individual clinical situations must be considered.***
- ***MARGINS (always with considerations in specific areas) :***
  - ***Macroscopic GTV:***
    - ***3-5 mm for BCC***
    - ***7-10 mm for SCC.***
  - ***Adyuvant/postoperative: 10 mm radially around the scar.***
  - ***The definition of margin values is made by each individual Institutional Tumor Board.***
  - ***Ultrasound is useful for depth evaluation although an adequate frequency is required, ideally being higher than 30 MHz.***

Applicators/clinical implementation/dosimetric aspects

Radionuclide-based applicators

The PTV may be relatively small in some cases of superficial skin BT (i.e., less than 30 mm in maximum diameters and up 3–5 mm in depth). In this scenario, the use of molds or flaps is difficult in clinical practice, mainly due to the poor conformation and the significant peripheral dose. These difficulties led to the development of small shielded applicators, as accessories of HDR, acting as mini-beams with one single dwell position, allowing good collimation together with excellent preservation of normal tissue, and integral dose to the patient. At the same time, these applicators allow for very simple treatment setup and planning procedures.

The first applicator developed was the Leipzig (manufactured by Varian Medical System Palo Alto, California, USA and Elekta Brachytherapy, Veenendaal, The Netherlands). Applicators consist in a cup of high-density tungsten, with the dwell position at the vertex. There are two configurations based on whether the HDR source runs parallel or perpendicular to the treatment surface. The most extended in clinical practice are the horizontal configurations because of the higher robustness in source positioning and easier setup. This shielded applicator allows great protection to the surrounding healthy tissue. It is essential to consider the dose gradient, full contact between the applicator and surface, avoiding gaps, thereby limiting the use of this type of applicator to flat areas.

The dosimetry of the Varian Leipzig applicators was evaluated by Fulkerson et al. [16, 17] whiles the Leipzig Elekta applicators were assessed by Perez-Calatayud et al. [18]. The Leipzig applicators present significant penumbra and non-flattened fields that should be taken into account because of their implication in PTV coverage. The Valencia applicators were developed in 2008 [19] with the aim of improving the flatness and penumbra (1.9 mm). This was achieved using a flattening filter to homogenize the dose distribution. The treatment time with the Valencia applicators is significantly longer than that of the Leipzig applicators due to filter attenuation. The Valencia applicator was modified in 2012 [20] providing an extra shield at the dome to minimize leakage in this direction.

Both Leipzig and Valencia applicators are typically used to treat lesions of up to 3–4 mm as recommended by the American Brachytherapy Society (ABS) report [15]. The dose gradient is 12%/mm. Prescription at 3 mm involves a maximum dose at the surface of 136%.

The Elekta Leipzig and Valencia applicators are provided with plastic cup of 1 mm in thickness to avoid electronic contamination. The applicators must always be used with the cap on since the absence of the cap produces a very large overdose in the first mm of the skin of 2.8 and 15-fold with the Valencia and Leipzig applicators, respectively [21].

The development of electronic brachytherapy (eBT) has gained importance in the last decade, including specific applicators for skin treatment. The aim of this technique is to reproduce the radionuclide-based applicators while improving the treatment time, leakage, radiation-protection constraints, shielding, HDR Ir-192 dependence, and regulatory agency requisites.

These devices use miniature X-ray sources producing low energy radiation at a HDR. With the use of specific applicators that collimate the beam and that are placed in contact with the skin surface, these devices allow the treatment of skin lesions combining the benefits of the classical approaches with essential advantages. Due to the low energy used, shielding requirements are minimal [22] and radiobiological effectiveness (RBE) is potentially increased [23]. Since a radioactive source of activity is not necessary, treatment times are shorter and more stable [24]. Moreover, these devices are portable, allowing treatments according to patient and/or department needs. There are currently three eBT systems for the treatment of skin lesions: the 50 kVp Xoft Axxent (iCad, San Jose, CA, USA) with applicators of 10, 20, 35, and 50 mm in diameter [16, 17, 25], the 50 kVp Zeiss INTRABEAM (Carl Zeiss Surgical Gmbh, Oberkochen, Germany) with 10–60 mm diameter applicators [26, 27], and the most recent is the 69.5 kVp Esteya (Elekta) which has applicators of 10–30 mm in diameter [14]. Esteya is the only device specifically developed for HDR-BT treatment of skin lesions, and taking into account the experience of the Valencia applicator, it was designed to provide a similar dose profile but with smaller percentage of dose depth (PDD) [24].

One of the main improvements of the Esteya vs. Valencia applicators is the treatment time. For example, a typical treatment with a 30 mm applicator at a depth of 3 mm with 7 Gy takes 153 s with the Esteya while the Valencia applicator takes 373–898 s based on the air kerma strength of the source.

Another potential benefit of the Esteya is a lower skin overdose thanks to a lower dose compared to standardized applicators or Xoft Axxent. Clinical uses of eBT devices are analogous to standardized BT applicators. Treatment of NMSC lesions is the main target of eBT. These lesions usually fulfill the criteria for treatment with eBT devices according to their specific dosimetry. These lesions must be located on a flap surface, their depth should not exceed 4 mm in order to avoid overdose to the skin due to the high gradient, and their size must be adequate for the different sizes of the applicators. All these benefits need to be further correlated with clinical outcomes. Initial reports show excellent control rates and cosmetic results [9, 10, 28–30], but literature on eBT is still very limited. High-level evidence in the form of large-scale randomized clinical trials and longer follow-up are need to define the role of eBT in the treatment of NMSC.

With the Leipzig, Valencia and Xoft applicators the PDD is 12%/mm in contrast with Esteya, which is 8%/mm. Thus, on prescribing at 3 mm, the overdose at the skin is 136 and 124%, respectively, with the dose to underlying tissues (i.e., 5 mm in depth) of 76 and 84%, respectively.

In the ABS skin report, [15] the maximum recommended prescription depth in the case of molds and flaps is 5 mm in contrast with the shielded applicator for which the recommended value is 3–4 mm. This recommendation is based on clinical experience. In a Monte Carlo study comparing these modalities, Granero et al. [31] concluded that the average PDD for the shielded applicators at 3 mm is approximately the same as for 5 mm in the case of flaps, Fig. 2.

- ***Flatness, penumbra and useful field must be considered in the selection of an applicator for a specific PTV.***
- ***The recommended maximum prescription depth with surface applicators (Leipzig, Valencia or eBT) is 3-4 mm.***
- ***Special quality measurements must be included to assure the use of the plastic cap.***

Clinical implementation

Different aspects must be considered in the implementation of surface applicators in clinical practice. A joint AAPM-ESTRO report (TG-253) is currently ongoing to develop recommendations to be published in 2018. This report will include detailed recommendations on commissioning and quality assurance that should be followed by medical

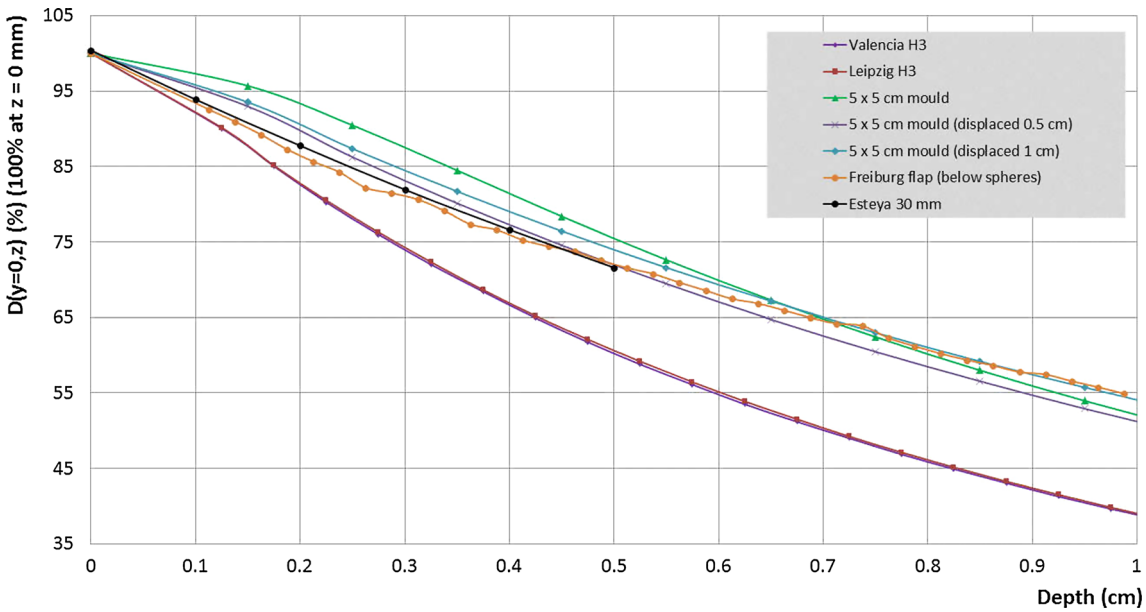


Fig. 2 Comparison of the percentage of dose depth (PDD) curves for all the configurations (100% at the surface)

physicists. In this section, we are going to briefly discuss the publications available on two specific applicators, the Valencia and Esteya.

Applicators must be commissioned and a quality assurance program must also be established. In a recent study of Granero et al., [32] detailed procedures are described for the use of the Valencia applicator. These include general considerations, verification of the manufacturer documentation and physical integrity, evaluation of the source-to-indexer distance and reproducibility, setting the library plan in the treatment planning system (TPS), evaluation of flatness and symmetry, absolute output and percentage depth dose verification, independent calculation of the treatment time, and visual inspection of the applicator before each treatment. The proposed methodology, equipment, frequency, expected results, and tolerance levels (when applicable) are provided for each test.

Candela-Juan et al. [33] described the complete commissioning and periodic testing of the Esteya device according to the AAPM, GEC-ESTRO guidelines for linear particle accelerators (LINACs), and brachytherapy units as well as their personal experience. In addition to the methodology, recommendations on the equipment required for each test are provided, taking into consideration their availability and the traceability of detectors. Finally, tolerance levels for all the tests are given, and a specific frequency for each test is suggested.

The treatment conditions of this therapy are well-defined (only one dwell position, fixed field size and flap surface), therefore the dose distribution is based on atlas for which the PDD, flatness (especially with the Leipzig) penumbra, and output are well established. For the Valencia applicator, the option proposed by Granero et al. [21] is very efficient and practical, consisting in a library plan built in the TPS with which the HDR source decay is automatically considered.

Depth determination is a critical point in this modality due to the high dose used. The CTV is an expansion of the GTV to account for possible microscopic tumor extension. The PTV is an expansion of the CTV due to setup variation. As discussed in the ABS Report, [15] PTV derivation from CTV is controversial in BT. It seems logical that in an interstitial implant, the PTV equals the CTV. Expansion from CTV to PTV is required in cases of superficial lesions using radionuclide-based BT or eBT, custom molds, or flap applicators. For radionuclide-based BT and eBT applicators, a realistic margin of approximately 2 mm should be added to the CTV to build the PTV to account for any misalignment.

The applicator setup is a critical point because of the high gradient and then full contact with patient skin must be guaranteed and monitored (the use of a zoomed TV image is very useful). First, the applicator selected for the treatment should provide an adequate margin for the target, and second, the applicator should be precisely positioned before each treatment fraction. In a recent study by Rodriguez Villalba et al., [34] some simple acrylic templates called Template La Fe-ITIC were developed. These templates were specifically designed to help clinical users to select the most adequate size applicator, and to assist medical staff in reproducing the positioning of the applicator. For each Valencia and Esteya applicator, a crosshair and two different circles are drawn on these templates: the

inner circle corresponds to the useful beam, while the outer circle represents the external perimeter of the applicator. The outer circle contains slits that facilitate the drawing of a circle on the skin of the patient for exact positioning of the applicator. In addition, there are two perpendicular rulers to define the most adequate margin.

In some special cases such as eyelid treatment, internal shielding is needed, requiring special caution due the backscatter that must be neutralized with bolus [35]. For example, in case of an eyelid a lead thickness of 2 mm is typically used (dose reduction of 60%), then 0.5 and 1 mm of bolus must be used in front of and behind the lead, respectively.

- ***In case of Valencia and Esteya, commissioning and quality assurance should be done according to the studies of* Granero et al *[32] and Candela-Juan* et al *[33] respectively.***
- ***Surface applicator planning can be done with just atlas.***
- ***For Leipzig and Valencia applicators it is convenient to use TPS library plans as described by* Granero et al *[34].***
- ***Evaluation of set-up constancy with adequate applicator position must be performed, for example with zoomed TV.***
- ***Plastic templates such as the La Fe-ITIC should be used for PTV definition and marking, helping in the inter-fraction applicator set-up.***
- ***Moderate pressure is required to guarantee full contact between the applicator surface and the skin, avoiding any gaps.***
- ***To preserve from patient to patient different plastic caps are used.***
- ***When internal shielding is required, bolus must be used to avoid backscatter. For example, in the case of an eyelid a lead thickness of 2 mm is typically used (dose reduction of 60%), then 0.5 mm and 1 mm of bolus must be used in front of and behind the lead, respectively.***
- ***Use of the AAPM-ESTRO TG-253 guidelines is recommended on their publication in 2018.***
- *In surface applicators CTV≠PTV*
- ***In case of use of templates, a typical margin from CTV to PTV is 2 mm.***

Flap applicators, custom molds applicators, and interstitial BT

Flaps

Superficial applicators include the Freiburg flap by Elekta, HAM by Mick Radio-nuclear instruments (Eckert and Ziegler BEBIG Company) or the Catheter flap by Varian. They are used on regular surfaces and are manufactured with a fixed geometry. For example, the Freiburg flap (Elekta) consists of 10 mm silicon spheres with catheters 10 mm apart embedded in the spheres at 5 mm from the surface.

Molds

Molds are customized to the patient skin surface. They allow housing the catheters with a, appropriate geometry (parallelism, specified distance, etc.). Like flaps, the separation between catheters should be less than 10 mm, and they should allow dwell positions of the source at a distance of 5 mm from the skin surface [15].

Molds can be constructed of different materials such as thermoplastic, silicone, high viscosity silicone (polyvinyl siloxane), wax, or rubber. 3D printed molds are also being introduced. The catheter pathway must be carefully designed in order to minimize transit dose from the after loader, and to avoid the source passing through organs at risk or the irradiation of non-interest areas.

- ***The recommended distance between catheters is 10 mm with a distance to skin of at least 5 mm.***
- ***The maximum prescription depth with flaps or customized molds is 5 mm.***
- ***Automated 3D individual printer molds are under development.***
- ***In molds and flaps CTV ≠PTV.***

Interstitial brachytherapy

Lesions with a depth greater than 5 mm require an interstitial approach. Implants are generally performed under local or regional anesthesia and sedation if necessary. The number of catheters (usually plastic tubes) and length of the implant are selected based on the clinical findings. Lines representing the location of the catheters can be drawn on the skin for guidance. Most skin cancers suitable for interstitial implants can be treated with a single plane. Implants too superficial (less than 5 mm in depth) may result in late visible telangiectasia, skin necrosis, or delayed healing along the source positions. Possible changes in the target volume due to local anesthesia injected into the dermis and epidermis should be evaluated. To avoid the effect of the temporary swelling on the resulting dosimetry, it is recommended to wait before the acquisition of the treatment planning CT images. Removal of the implants is usually done without anesthesia.

For lesions up to 10 mm in depth, only one plane of inserted catheters may be necessary. Catheters should be spaced less than 10 mm apart and located at half distance within the target. For lesions deeper than 10 mm, two of more planes of inserted catheters may be necessary. The recommended separation between planes is 5–7 mm. Catheter location will follow the SSDS system as far as possible. Special care is needed to avoid hot spot areas (>200%), and consider to add extra catheters if necessary. Ideally, the shallowest plane will be at least at 5 mm beneath the skin surface to avoid overdoses to the skin. In this type of implants, the CTV equals the PTV.

The design of the PTV should be GTV or CTV if irradiating the surgical bed, plus a margin of 10 mm in all directions. The margin can be greater in the direction of the tubes. The depth of the implant should be about 5 mm to cover the deep margin. The entrance and exit points must be at least 10 mm outside the CTV in order not to irradiate.

Treatment planning

Prescription

A written treatment prescription should be made, including:

- Treatment site, total target dose, dose per fraction, and the fractionation plan (twice a day, daily, twice a week, three times week…).
- Treatment depth
- Modality used (radionuclide, eBT, etc.)
- Applicator type and size
- Critical organs and dose constraints
- Previous treatment (if any)

Image acquisition and contouring

Both the reconstruction process and the target delineation are mainly CT image based. Other imaging modalities (US, MRI) may be used with CT to help in the reconstruction process or for target evaluation.

CT acquisition should be contiguous; with a slice thickness of no more than 2 mm. CT should be extended 10–20 mm beyond the PTV.

In some special situations with flap applicators and very simple geometry and with flap surfaces, the acquisition of a CT study set is discarded and library plans may be used.

Caution should be exercised in relation to the presence of air gaps between the applicator and patient's skin when setting up the applicators or molds on the patient, especially on non-uniform surfaces. Careful placement of the applicator is also mandatory because the PTV ≠ CTV in these situations.

To help in the contouring process, a thin wire may be located on the skin surface prior to the study set acquisition. Since this wire is visible on CT images, it may be used to outline the target in each slice.

- ***Interstitial BT is recommended in PTVs deeper than 5 mm.***
- ***Catheter location should follow the SSDS system. It is important to avoid hot spot areas (> 200%) to cover the CTV.***
- ***In interstitial implants the CTV = PTV***

- ***CT acquisition should be with a maximum slice size of 2 mm.***
- ***A thin wire delimiting the lesion can help in the image acquisition process of the delimitation of the GTV or scar.***

Catheter reconstruction

Dummies may be employed for better visualization of catheter pathways. The relative position between the tip of the catheter tunnel or the tip end of dummies and the distal dwell position must be determined during the commissioning process.

In the case of interstitial procedures, basal points are used, based on the SSDS system as the starting point. Graphic optimization may be used afterward for slight corrections, paying attention to hot spot regions.

The dose should be limited to 125% on the skin surface for flaps and to 140% for custom molds [15].

- ***Optimization/prescription points in flaps or molds must be the depth surface of the CTV.***
- ***Optimization/prescription points in interstitial implants must be the basal point (SSDS system). Graphic optimization should be done (with particular attention to hot spots).***

Source dwell activation should guarantee adequate coverage of CTV. Catheters in the proximity of the borders of the CTV should be available and source dwell positions outside the CTV may be required to cover the extension of the CTV. The absence of catheters may lead to unacceptable hot spot areas.

The source step should be the minimum compatible with the extent of the target. A default value of 2.5 mm is desirable.

Reporting

The following parameters are recommended for data reporting:

- Modality used.
- Applicator type and size.
- Lesion type, size, location, and imaging used for evaluation.
- GTV, CTV, and PTV.

- ***A library plan may be used with flap applicators with a very simple geometry and flap surfaces.***
- ***Source dwell positions outside the CTV may be required to cover the complete CTV.***

Optimization

Several target point- and catheter point-based and hand-made defined point optimization methods, among others, are currently available in the TPS. In the case of flaps or molds, special caution must be considered with automatically generated points around the target, since only deeper points at prescription depth should be considered.

- Prescription dose, prescription depth, dose per fraction, treatment schedule.
- Air Kerma strength used for daily fractions and kV and dose rate for eBT.
- Output factor of the applicator.
- Skin surface dose and skin Dmax.
- Dose to critical structures.

- ***Always report the Dmax on the skin.***

Practical dosimetric considerations

Most TPS are based on TG-43 U1. Calculations are made assuming the source in full scatter conditions into a medium of water density. However, real situations in the case of flaps or a source 5 mm below the patient skin are different from full scatter conditions. Some authors have studied the use of bolus to compensate the lack of scatter near the surface. The study by Granero et al. [36] concluded than no bolus is required if the source is located on the surface of the patient, since the impact on the dose gradient is minimal. If the source is located 5 mm under the skin, a 1–2 mm bolus may be required if Co-60 is employed.

Another study regarding lead shielding [37], indicated that the placement of lead shielding directly over the surface of the patient may lead to overdoses of up to 300% to the skin. This may be avoided by administering a 1 mm bolus for I^{192} sources or 2–3 mm in the case of Co-60 sources between the patient's skin and the lead shielding.

In lesions in close proximity to the underlying bone, such as the shin or scalp, the dose might be lower than expected because of a reduction in bone backscatters. In these situations, the recommendations of the TG-253 report may be followed.

Caution should be exercised in eBT applied to lesions in close proximity to the underlying bone. Recent studies [38] have shown that eBT gives an excessive bone dose compared with HDR I^{192} or electrons at 4–6 MeV.

To minimize errors, adequate identification of catheters should be made, with numbering, labeling, and color code etc. Correspondence between catheter numbering and both, transfer tubes and after loader channels is advisable.

Table 1 Resume of different schedules (number of fractions, size of fraction, and total dose)

Type of skin BT	# Fractions	Size of fraction	Frequency
Leipizg/Valencia applicators	6 Fx	7 Gy	Twice a week
	7 Fx	6 Gy	Twice a week
Interstitial BT			
Radical (exclusive)	9–10 Fx	3.6–5.5 Gy	Twice a day
Adjuvant	9–10 Fx	3–5 Gy	Twice a day
Molds/flaps			
Radical (exclusive)	33–40 Fx	2 Gy	Daily
	15–20 Fx	2.5 Gy	Daily
	12 Fx	3.5 Gy	Daily
	10 Fx	4 Gy	Daily
	10–12 Fx	4 Gy	3 Times a week
	6–7 Fx	6–7 Gy	Twice a week
	8–10 Fx	5 Gy	Twice a week
Adjuvant	10 Fx	3 Gy	Twice a day
	30 Fx	2 Gy	Daily
	17 Fx	2.5 Gy	Daily
	10 Fx	3.5–4 Gy	Twice a week
	8–9 Fx	5 Gy	Twice a week
	6 Fx	6.5 Gy	Twice a week
Electronic BT	8 Fx	5 Gy	Twice a week
	7 Fx	6 Gy	Twice a week
Special clinical situations			
Anatomical areas with risk of necrosis	18 Fx	3 Gy	3 Times a week
75 years/low Karnofsky index	5 Fx	7 Gy	Twice a week
	2 Fx	8 Gy	Once a week
	2 Fx	10 Gy	Once a week

- ***A bolus is no necessary with flaps and molds.***
- ***In interstitial BT with catheters at 5 mm from the skin a bolus is only necessary when Co-60 (2-3 mm) is employed.***
- ***If lead is indicated a bolus or gauze should be placed under it.***
- ***If the CTV is close to subjacent bone, TG-253 recommendations may be followed.***
- ***The position of the catheters must be made taking in account the dose in transit of the isotope.***

Adequate catheter placement pre-planning is useful in order to reduce the transit dose to normal tissues or organ at risk structures.

Dose (fraction/total dose/frequency)

Different fractionated BT regimens are currently used, achieving excellent local control and cosmetic results. The literature available is based on individual experience and the different BT regimens have been widely analyzed and described [3, 15, 39]. Daily standard fractionations (Monday–Friday) similar to those used in standard external radiotherapy must be applied and too different fraction sizes (hypofractionation regimens) twice or 3 times a week in radical treatments, reducing the fraction size in clinical situations adjuvant to surgery. In interstitial BT, 2 daily fractions separated by 6 h in 9–10 fractions are usually employed. The size of the CTV and anatomical areas should be taken into account to choose the most adequate fraction size and total dose.

Different schedules based on the clinical experience of the members of SEOR and SEFM are summarized in the Table 1 according to the responses to the survey sent prior to the annual meeting.

Conclusions

- Skin BT is a safe reliable technique for the treatment of NMSC and is an alternative to surgery or other topical techniques as a first indication.
- BT is mandatory if surgery is contraindicated.
- Technique selection depends on individual clinical experience and the availability of a brachytherapy unit.
- Volume definition must be objective (based on imaging techniques).
- The dosimetry report must be uniform.
- Physicians have based their practice on their own individual experience and training and limited retrospective literature. A wide variability in fraction sizes and total doses and a lack of literature require prospective studies to unify criteria.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Appendix

Addendum 1

- Hospital Universitario Quirónsalud Madrid
- Fundación Instituto Valenciano de Oncología (FIVO). Valencia
- Hospital Universitario Ramón y Cajal. Madrid
- Complejo Hospitalario de Navarra. Pamplona
- Hospital Universitario Marqués de Valdecilla. Santander
- Hospital Universitario Infanta Cristina. Badajoz
- Fundación Rioja Salud. Logroño
- Hospital Universitario Sant Joan de Reus. Tarragona.
- Institut Català d'Oncologia (ICO). Barcelona
- Hospital Universitario HM San Chinarro. Madrid
- Hospital Universitario La Paz. Madrid
- Hospital de Cruces. Vizcaya
- Hospital Universitario La Fe. Valencia
- Hospital Clínico Universitario de Valladolid. Valladolid
- Hospital Regional de Málaga (Carlos Haya). Málaga
- Hospital Clínica Benidorm. Benidorm. Alicante
- Hospital Universitario Virgen de la Victoria. Málaga
- Hospital la Ribera. Alzira. Valencia
- Hospital Universitario de Gran Canaria Dr. Negrín. Las Palmas de Gran Canaria
- Centro Oncológico de Galicia. La Coruña
- Hospital de la Esperanza. Barcelona
- Hospital do Mixoeiro. Vigo
- Hospital 12 de octubre. Madrid
- Instituto IMOR. Barcelona

Addendum 2

AREA H: "Mask areas" of face (central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermillion], chin, mandibule, preauricular and postauricular skin/sulci, temple, ear), genitalia, hands, and feet.

AREA M: cheeks, forehead, scalp, neck, and pretibial.

AREA L: trunk and extremities (excluding pretibial, hands, feet, nail units, and ankles).

References

1. Alam M, Nanda S, Mittal BB, Kim NA, Yoo S. The use of brachytherapy in the treatment of nonmelanoma skin cancer: a review. J Am Acad Dermatol. 2011;65:377–88.
2. Kowalik L, Lyczek J, Sawicki M, Kazalsky D. Individual applicator for brachytherapy for various sites of superficial malignant lesions. J Contemp Brachytherapy. 2013;5:45–9.
3. Skowronek J. Brachytherapy in the treatment of skin cancer: an overview. Postepy Dermatol Alergol. 2015;5:362–7.
4. Arenas M, Arguis M, Diez-Presa L, Henriquez I, Murcia-Mejía M, Gascón M, et al. Hypofractionated high-dose-rate plesiotherapy in nonmelanoma skin cancer treatment. Brachytherapy. 2015;14:859–65.
5. Kwan W, Wilson D, Moravan V. Radiotherapy for locally advanced basal cell and squamous cell carcinomas of the skin. Int J Radiat Oncol Biol Phys. 2004;60:406–11.
6. Köhler-Brock A, Prager W, Pohlmann S, Kunzw S. The indications for and results of HDR after loading therapy in diseases of the skin and mucosa with standardized surface applicators (the Leipzig applicator). Strahlenther Onkol. 1999;175(4):170–4.
7. Rose JN, McLaughlin PY, Hanna TP, D'Souza D, Sur R, Falkson CB. Surface mold brachytherapy for nonmelanoma skin cancer: Canadian patterns of practice. Pract Radiat Oncol. 2014;4:398–403.
8. Arenas M, Sabater S, Sintas A, Arguis M, Hernandez V, Arquez M, et al. Individualised 3D scanning and printing for non-melanoma skin cancer brachytherapy: a financial study for its integration into clinical workflow. J Contemp Brachytherapy. 2017;9(3):270–6.
9. Bhatnagar A, Loper A. The initial experience of electronic brachytherapy for the treatment of non-melanoma skin cancer. Radiat Oncol. 2010;5:87.
10. Ballester-Sánchez R, Pons-Llanas O, Candela-Juan C, Celada-Alvárez FJ, de Unamuno-Bustos B, LLavador-Ros M, et al. Efficacy and safety of electronic brachytherapy for superficial and nodular basal cell carcinoma. J Contemp Brachytherapy. 2015;7(3):331–8.
11. NCCN Clinical Practice Guidelines in Oncology. Squamous Cell Skin Cancer Version 1.2017 NCCN.org.
12. NCCN Clinical Practice Guidelines in Oncology. Basal Cell Skin Cancer Version 1.2017 NCCN.org.
13. TNM staging American Joint Committee on Cancer. 7th ed. In: Sobin LH, Gospodarowicz MK, Wittekind Ch, editors. TNM Classification of Malignant Tumors, 7th ed. Oxford: Wiley-Blackwell, 2009. 310 p. ISBN 978-1-4443-3241-4.
14. Pons-Llanas O, Ballester-Sánchez R, Celada-Álvarez FJ, Candela Juan C, García-Martinez T, Llavador-Ros M, et al. Clinical implementation of a new electronic brachytherapy system for skin brachytherapy. J Contemp Brachytherapy. 2014;6:417–23.
15. Ouhib Z, Kasper M, Calatayud JP, Rodríguez S, et al. Aspects of dosimetry and clinical practice of skin brachytherapy: the American Brachytherapy Society working group report. Brachytherapy. 2015;14(6):840–58.
16. Fulkerson RK, Micka JA, DeWerd LA. Dosimetric characterization and output verification for conical brachytherapy surface applicators. Part I. Electronic brachytherapy source. Med Phys. 2014;41(2):022103.
17. Fulkerson RK, Micka JA, DeWerd LA. Dosimetric characterization and output verification for conical brachytherapy surface applicators. Part II. High dose rate 192Ir sources. Dosimetric characterization and output verification for conical brachytherapy surface applicators. Part II. Med Phys. 2014;41(2):022104.
18. Perez-Calatayud J, Granero D, Ballester F, Puchades V, et al. A dosimetric study of Leipzig applicators. Int J Radiat Oncol Biol Phys. 2005;62(2):579–84.
19. Granero D, Pérez-Calatayud J, Gimeno J, Ballester F, et al. Design and evaluation of a HDR skin applicator with flattening filter. Med Phys. 2008;35(2):495–503.
20. Granero D, Pérez-Calatayud J, Ballester F, Ouib Z. Radiation leakage study for the Valencia applicators. Med Phys. 2013;29:60–4.
21. Granero D, Candela-Juan C, Ballester F, Ouib Z, et al. Commissioning and quality assurance procedures for the HDR Valencia skin applicators. J Contemp Brachytherapy. 2016;8(5):441–7.
22. Ibañez-Rosello B, Bautista-Ballesteros JA, Candela-Juan C, Villaescusa JI, et al. Evaluation of the shielding in a treatment room with an electronic brachytherapy unit. J Radiol Prot. 2017;37(2):N5–12 **(epub ahead of print)**.
23. Brenner DJ, Leu CS, Beatty JF, Shefer RE. Clinical relative biological effectiveness of low-energy X-rays emitted by miniature X-ray devices. Phys Med Biol. 1999;44(2):323–33.
24. García-Martinez T, Chan J-P, Perez-Calatayud J, Ballester F. Dosimetric characteristics of a new unit for electronic skin brachytherapy. J Contemp Brachytherapy. 2014;6:45–53.
25. Rivard MJ, Davis SD, De Werd LA, Rusch TW, Axelrod S. Calculated and measured brachytherapy dosimetry parameters in water for the Xoft Axxent X-ray source: an electronic brachytherapy source. Med Phys. 2006;33:4020–32.
26. Lam SCP, Xu Y, Ingram G, et al. Dosimetric characteristics of INTRABEAM® flat and surface applicators. Transl Cancer Res. 2014;3:106–11.
27. Schneider F, Clausen S, Thölking T, Wenz F, Abo-Madyan Y. A novel approach for superficial intraoperative radiotherapy (IORT) using a 50 kV X-ray source: a technical and case report. J Appl Clin Med Phys. 2014;5:4502.
28. Bhatnagar A. Nonmelanoma skin cancer treated with electronic brachytherapy: results at 1 year. Brachytherapy. 2013;12:134–40.
29. Bhatnagar A, Patel R, Werschler WP, Ceilley RI, Strimling R. High-dose rate electronic brachytherapy: a nonsurgical treatment alternative for nonmelanoma skin cancer. J Clin Aesthet Dermatol. 2016;9(11):16–2.
30. Jankarashvili N, Topeshashvili M. Treatment of skin cancer with intrabeam. 9th ZEISS INTRABEAM User Meeting. 2015.
31. Granero D, Vijande J, Ballester F, Rodríguez S, et al. Prescription depth in surface skin brachytherapy. Brachytherapy. 2017;16(3):S1.
32. Granero D, Candela-Juan C, Vijande J, Ballester F, et al. Technical note: dosimetry of Leipzig and Valencia applicators without the plastic cap. Med Phys. 2016;43(5):2087.
33. Candela-Juan C, Niatsetski Y, Ouhib Z, Ballester F, et al. Commissioning and periodic tests of the Esteya® electronic brachytherapy system. J Contemp Brachytherapy. 2015;7(2):189–95.
34. Rodriguez-Villalba S, Perez-calatayud MJ, Bautista JA, Carmona V, et al. Novel simple templates for reproducible positioning of skin applicators in brachytherapy. J Contemp Brachytherapy. 2016;8(4):1–5.
35. Lliso F, Granero D, Perez-Calatayud J, Carmona V, Pujades MC, Ballester F. Dosimetric evaluation of internal shielding in a high dose rate skin applicator. J Contemp Brachytherapy. 2011;3(1):32–5.
36. Granero D, Pérez-Calatayud J, Vijande J, Ballester F, Rivard MJ. Limitations of the TG-43 formalism for skin high-dose-rate brachytherapy dose calculations. Med Phys. 2014;41(2):021703.
37. Candela-Juan C, Granero D, Vijande J, Ballester F, Rivard MJ, et al. Dosimetric perturbations of a lead shield for surface and interstitial high-dose-rate brachytherapy. J Radiol Prot. 2014;34(2):297–311.
38. Safigholi H, Song WY, Meigooni AS. Optimum radiation source for radiation therapy of skin cancer. J Appl Clin Med Phys. 2015;16(5):5407.
39. Delishaj D, Rembielak A, Manfredi B, Ursino S, Pasqualetti F, Laliscia C, et al. Non-melanoma skin cancer treated with high-dose-rate brachytherapy: a review of literature. J Contemp Brachytherapy. 2016;8(6):533–40.