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New Technology in High-Dose-Rate Brachytherapy with Surface Applicators for Non-Melanoma Skin Cancer Treatment: Electronic Miniature X-Ray Brachytherapy

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1. Introduction

The number of skin cancers diagnosed in the United States is higher than all other cancers combined, and approximately one in five Americans will develop skin cancer in their life [1]. Non-melanoma skin cancer (NMSC) is estimated to affect more than 1 million persons in the United States annually[2]. Of these, the majority (75-80%) of them are basal cell carcinoma (BCC) [3]. Non-melanoma skin cancers very rarely metastasize, with a few rare exceptions such as Merkel cell carcinomas. The remainder of non-melanoma skin cancers are squamous cell carcinomas (SCC). Squamous cell skin cancers are more aggressive than BCC and have a tendency to spread into fatty tissues beneath the skin and in contrast to BCC, SCC has a small but definite risk of metastasizing to distant organs. When this happens, SCC can become a life-threatening disease, similar to metastatic squamous cell cancer from any other organ. Most NMSCs are curable with less than 1000 deaths reported annually [2]. If identified at an early stage and given appropriate treatment, excellent local control and cosmesis can be achieved for many patients. Treatment options include, but are not limited to, simple surgical excision [4], Moh's micrographic surgery [5], radiation therapy (RT) [6,7,8,9], laser surgery [10,11], topical chemotherapy [12] and cryosurgery [13]. Flexibility in the application of these modalities is important for offering patients the best method for the skin cancer treatment. Selection of the appropriate modality requires professional considerations of effective tumor control, cosmetic outcome, possible toxicities, and patient's preference. Many factors, including the cancer type, size, specific location of the cancer, primary or recurrent disease, and the extent of the invasion affect treatment options. The National Comprehensive Cancer Network (NCCN) has established guidelines and treatment algorithms for the evaluation and management of BCC and SCC [14].

NMSC is generally treated with surgical excision or Moh's micrographic surgery. Standard surgical excision is simple and effective, providing complete clearance with an appropriate margin assessment [15,16]. Moh's micrographic surgery has been shown to have superior cure rates for primary and recurrent BCCs (1% and 5.6%, respectively) and for primary and

recurrent SCCs (3% and 10%, respectively) [17,18]. Treatment with RT provides a viable alternative for those patients who refuse or are medically unsuitable for surgery or when surgery might lead to unacceptable cosmesis. It is generally reserved for patients at the age of 60 years or older, given concerns of potential long-term sequelae. Clinical considerations are required from the radiation oncologist when RT is selected, such as the appropriate dose-fractionation regimen, patient setup, bolus use, field size, and the specific RT treatment modality. Several groups have reported results for NMSC treatment using different RT modalities. Treatments with superficial x-rays presented a 93-100% tumor control in one group [6] but 78% tumor control in another group [19]. Differences are mainly attributed to tumor size, dose fractionation scheme, and the total dose. Excellent tumor control was observed in treatments with fraction size between 3Gy and 5Gy, and total dose <60Gy [6]. RT treatment with orthovoltage x-rays or megavoltage electrons achieved 72-88% 5-year overall tumor control [6,7,9,20]. Sykes et al reported 100% local control with a median follow-up of 31months for T1/2 SCC on the lip using electron beams. Lesion size may explain some of the discrepancies in reported results. The continuous technology advances in the field of brachytherapy have made possible the use of precise after-loader equipment for high-dose-rate (HDR) irradiation using radioactive sources, i.e. ^{192}Ir. Isotope-based HDR brachytherapy, in conjunction with the standard surface applicators or custom-made molds, has become a highly effective treatment method of skin carcinomas in recent years. Favorable cosmetic outcomes and excellent local control with minimal complications have been reported with this method [8, 21, 22]. Post-operative RT is also considered an adjuvant therapy to surgery for multimodality treatment of NMSCs with favorable outcomes [23].

The increased demand for RT of small superficial lesions has revived the interest in HDR brachytherapy techniques using skin surface applicators or surface molds [8, 22, 23]. The available HDR afterloaders and applicators on the market include Varian GammaMedPlus™ afterloader unit with Varian surface applicators (Varian Brachytherapy, Charlottesville, VA) and Nucletron microSelectronHDR system with Leipzig and Valencia surface applicators (Nucletron, Veenendaal, The Netherlands). Both of these units utilize an HDR ^{192}Ir source, which requires experienced personnel with NRC Authorized User and Authorized Medical Physicist status, a shielded radiation treatment room, special handling of the isotopes, etc. A recently available alternative is the electronic brachytherapy (EBT) miniature tube, such as the model S700 Axxent® X-ray source (Xoft Inc., Fremont, CA), which generates an x-ray beam in the low kilovoltage (kV) energy range and provides dose-rates comparable to 7-Ci ^{192}Ir sources, with similar dose distributions [24, 25]. In contrast to a conventional radioisotope-based HDR unit, the radiation from the EBT system can be switched on and off through this water-cooled miniature x-ray tube. It has been used for accelerated partial breast irradiation (APBI) treatments [26, 27] with breast balloon applicators and endometrial treatments [28] with dedicated endometrial applicators. Dosimetric advantages have been demonstrated for normal lung and heart tissues in APBI treatment and rectum in endometrial treatments [25-29]. The advantages of the EBT device include less shielding requirements for the 50kVp x-ray source and lower exposure rate to personnel that allows staff to remain in the treatment room in close proximity to the patient [29, 30], compared to isotope based brachytherapy (HDR ^{192}Ir source has a mean energy 380keV). The dosimetric properties and energy spectrum of the 50kVp miniature x-ray source have been well studied [25, 26, 31]. System commissioning procedures have been well described in several publications [30, 31] for breast intracavitary treatment using breast applicators. The new surface applicators for skin cancer treatments were approved by the FDA in March 2009 and

first used for patient treatments at our facility (University of Wisconsin Riverview Cancer Center, Wisconsin Rapids, WI) in July 2009. In contrast to prior applications of the EBT device for APBI and endometrial treatments, the soft x-rays are delivered through surface applicators externally to the patient's skin for skin treatments. Thus, this delivery setup is quite different from most brachytherapy delivery. The output calibration and treatment planning procedures for such applications have recently been reported [30].

2. Novel technology on isotope-free brachytherapy using miniature x-ray tube

2.1 System description

2.1.1 Axxent Xoft EBT controller and miniature x-ray source

The EBT system consists of the Xoft controller, miniature x-ray source, and the treatment applicators. The Xoft controller, as shown in Figure 1, includes a touch-screen monitor, USB port, barcode reader, pullback arm, x-ray source cooling system, Standard Imaging Well Chamber, and a Standard Imaging Max-4000 Electrometer. The pullback arm, as indicated in Figure 1(a) and 1(b), has three adjustable joints and they are all adjustable for better positioning the source. There is a high voltage port on the arm for the source connection (not shown on the figure). The on-board well chamber (Figure 2a) and electrometer (Figure 2b) make the source pre-treatment calibration possible. The most essential part of this novel system is the design of the miniature x-ray source, as shown in Figure 3.

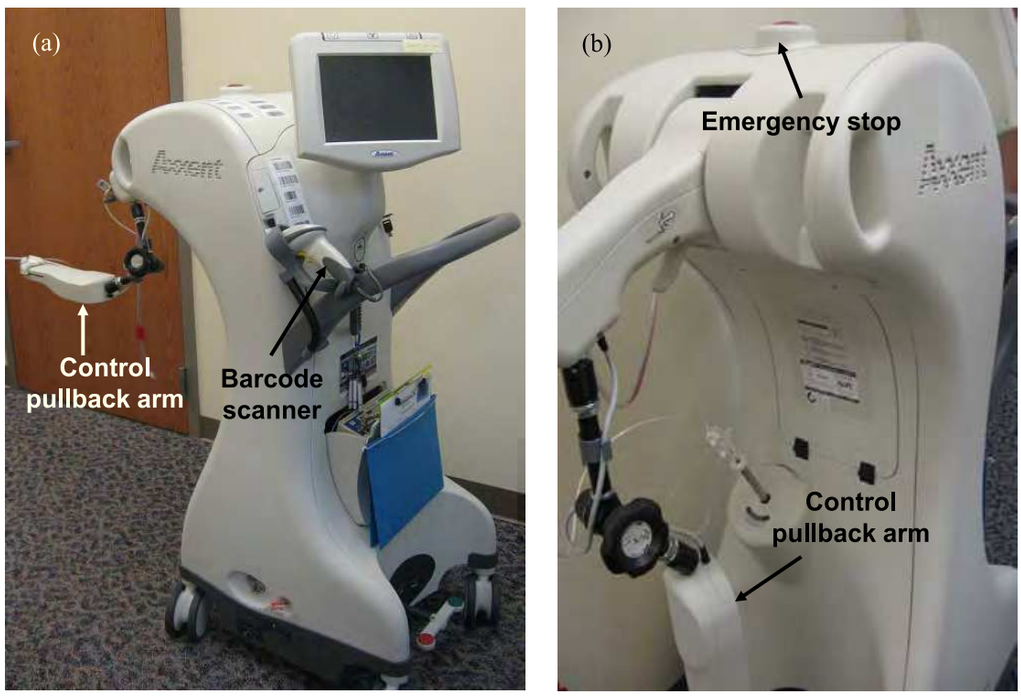


Fig. 1. Axxent Xoft electronic brachytherapy controller with (a) adjustable control pullback arm and barcode scanner; and (b) emergency stop and pullback arm pointing down

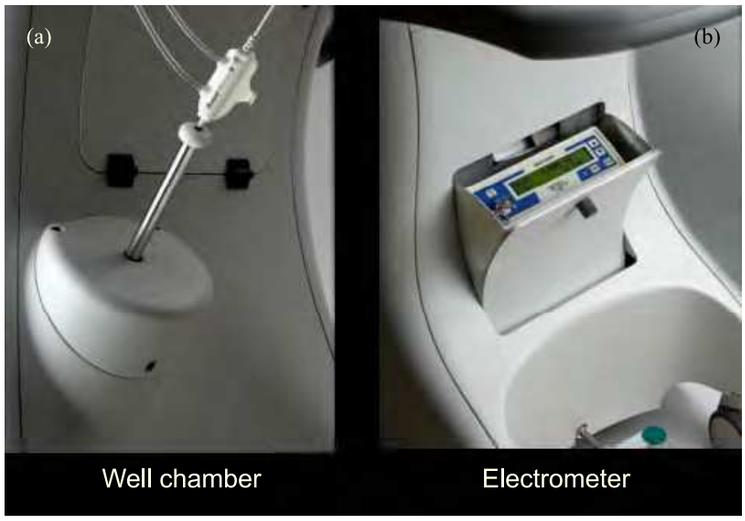


Fig. 2. (a) The well chamber and (b) electrometer are monted on the controller

Figure 3a shows the overview of the x-ray source, which consists of an x-ray tube as small as a finger tip (Figure 3b) located at the tip of a flexible cooling catheter (25 cm in length and 5.4 mm in diameter, as shown in Figure 3c), a white mounting clip with a pair of cooling connection tubes (which need to be connected with the cooling system on the Xoft controller during the treatment), and a high voltage connector. Water circulating inside the catheter cools the surface of the source, this allows maximum air kerma strength of 1400 Gy/hr at 1cm for 50kV and 300 μA beam current [25]. The miniature x-ray tube is only 2.3 mm in diameter and 1.5 cm in length and generates 50kVp bremsstrahlung x-rays with a mean energy of 26.7 kV photons.

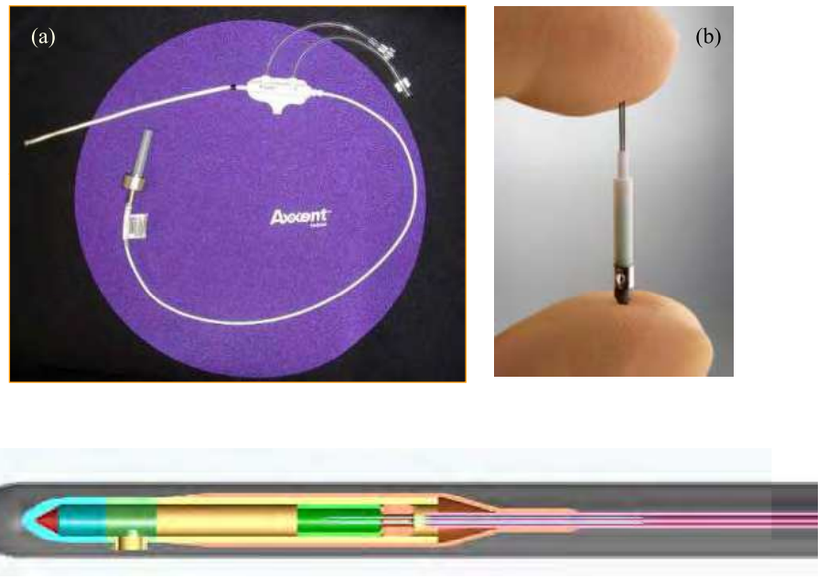


Fig. 3. (a) Axxent Xoft miniature x-ray source inserted into to a flexible cooling catheter; (b) The actual size of the miniature x-ray source; (c) The x-ray source tip detail including miniature x-ray tube and HV cable.

2.1.2 Xoft surface applicators and target collimator

For treating superficial lesions on skin, Xoft surface applicators are used, as shown in Figure 4. The cone connects to one end of the applicator source channel, whose other end connects to an adapter that is designed to lock the source in place for treatment (Figure 4a). Four applicator cone sizes are available including 10 mm, 20 mm, 35 mm, and 50 mm. A disposable end cap that is made of 0.5mm plexiglas is used to cover the cone in order to protect it from the direct contact with patient and to ensure a flat treatment area. X-ray beams are further shaped for the clinical target with the custom-made lead shields (Axxent® FlexiShield Mini) (Figure 4b), which are disposable, non-sterile, flexible devices with a circular shape (12.7 cm in diameter and 1mm in thickness). It has a lead equivalency of 0.45mm at 50kVp, which provides about a 30-fold reduction in radiation.

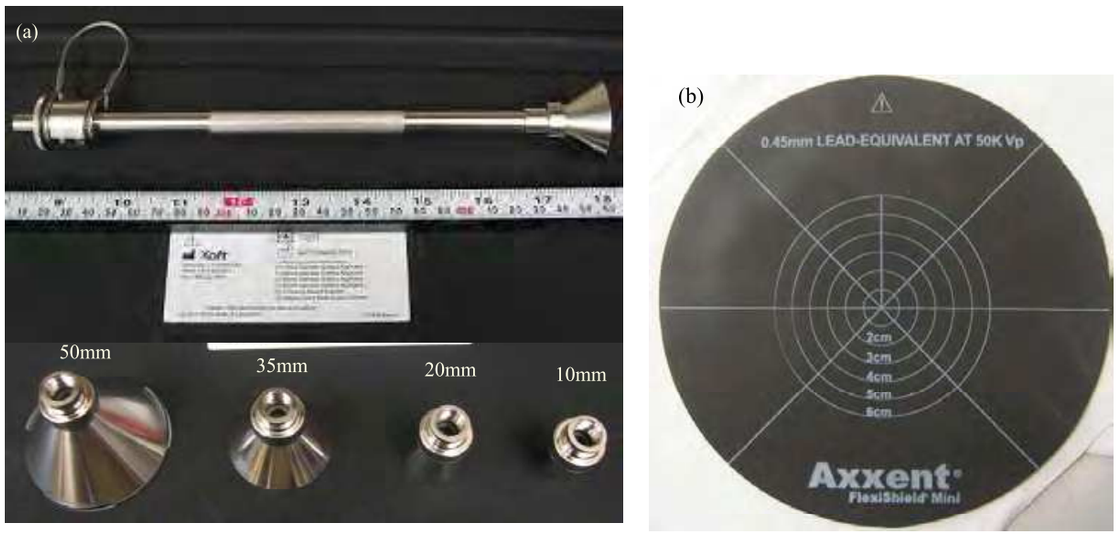


Fig. 4. (a) Applicator source channel connecting to the 35mm cone on the right end and the Touhy Burst adaptor on the left. Below are four skin applicator cones with different sizes; (b) The Axxent® FlexiShield Mini with drawn circles representing different field sizes

2.2 Physics aspects

2.2.1 Dose rate output calibration and stability

The source nominal dose rate at the skin surface with the applicator needs to be calibrated prior to treatment. It is recommended to use the protocol AAPM TG-61 in-air method[32] for the soft x-ray dose calibration, using a soft x-ray parallel plate chamber (PTW T34013) mounted to a L-shaped in-air calibration fixture (Figure 5), which is commercially available through Xoft, Inc.

Dose to water at surface can be determined by:

$$D_w = MN_k B_w P_{stem,air} [(\frac{\overline{\mu}_{en}}{\rho})^w_{air}]_{air} \quad (1)$$

Where M is the corrected ion chamber reading, $M = M_{raw} P_{TP} P_{pol} P_{ion} P_{elec}$

N_k is the air-kerma calibration factor for the given beam's quality. B_w is the backscatter factor which accounts for the effect of the phantom scatter and $P_{stem,air}$ is the stem correction factor

which accounts for the change in photon scatter from the chamber stem between the calibration and measurement (mainly due to the change in field size). The mass energy-absorption coefficient ratio of water-to-air $[(\frac{\overline{\mu}_{en}}{\rho})^{w}_{air}]_{air}$ can be determined by the look-up table given in TG-61 Table IV. The dose rate to water at surface can be calculated by

$$\dot{D}_w = \frac{D_w}{t} \ (\mathrm{Gy/min}) \tag{2}$$

Finally, the nominal dose rate to skin at surface can be calculated by

$$\dot{D}_{skin,n} = C_w^{med} \dot{D}_w \frac{\mathrm{No\,min\,al} S_k}{\mathrm{Actual} S_k} \tag{3}$$

Where C_w^{med} is the conversion factor from dose-to-water to dose-to-medium, which can be looked-up from the table provided in TG-61 Table X. For skin treatment, C_w^{skin} has a value of 0.91. S_k is the air-kerma strength. The nominal S_k is set to be 110000U in the EBT system and the actual S_k is obtained from the well chamber measurement.

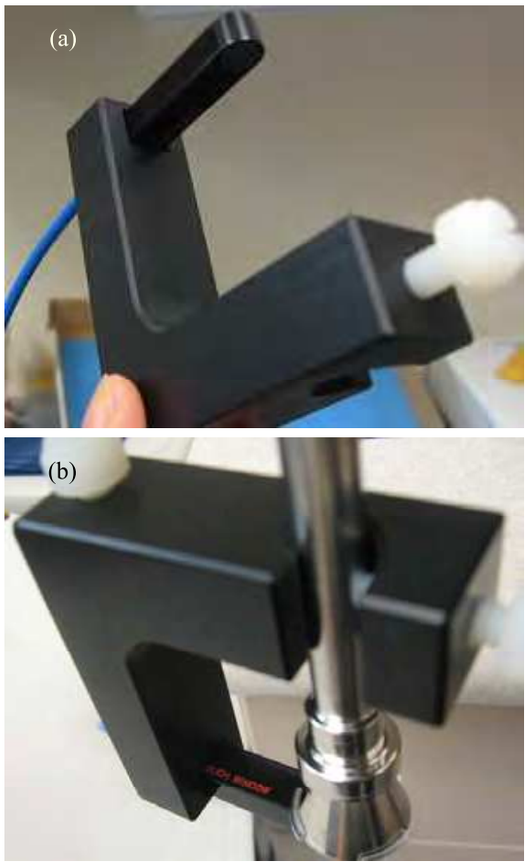


Fig. 5. L-shaped in-air calibration fixture with the PTW T34013 parallel plate chamber centrally placed under the 10mm applicator for the in-air measurement.

The nominal skin surface dose-rate of 35mm applicator cone is reported to be 1.35 Gy/min averaged over sixteen sources, with a ±5% variation [31]. For the same source, the output variation is within 2%. Due to the differences in the design of the flattening filters and cone sizes, the dose rate output varies. The average dose-rates are 1.52, 1.39, 1.35, and 0.67 Gy/min for 10, 20, 35, and 50mm applicators. Smaller cone sizes produce higher dose rates, due to the design of the flattening filter and the in-field scattering from the applicator.

2.2.2 Field flatness and symmetry

The reported beam flatness and symmetry (mean and standard deviation) for ten sources over the central 80% of the field width are well within 5% from all four sizes of the applicator cones. With a flattening filter built in the applicator cone, it is possible to obtain a uniform dose distribution on the surface of the applicator as well as at a depth beneath the skin. As shown in Figure 6(a), the radiation field was tightly conformed by the applicator cone. Film profiles (background subtracted) for five sources all normalized to the profile center at 100% are shown in Figure 6b and 6c. The dose penumbra region is smaller than 2.0 mm at surface, sharp enough to spare surrounding normal tissues.

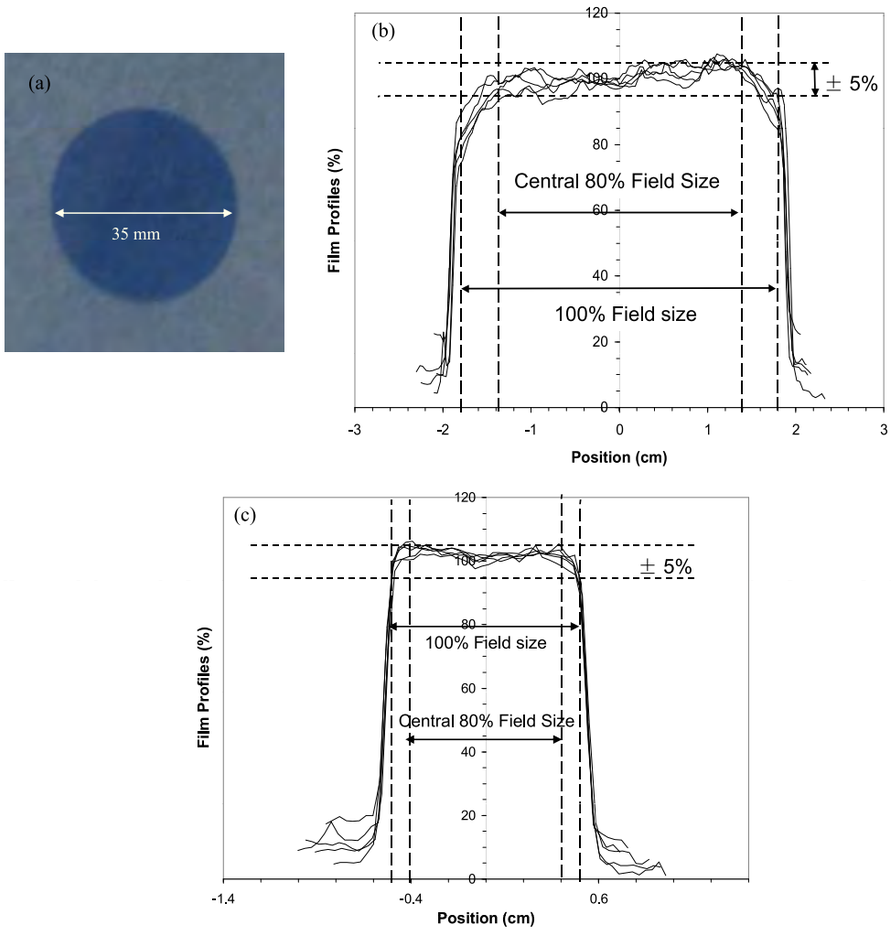


Fig. 6. (a) EBT Gafchromic film exposure at surface for a 35 mm cone. (b) Relative dose profiles for the 35mm cone from the EBT Gafchromic films exposed to five sources. (c) Relative dose profiles for the 10mm cone from the EBT Gafchromic films exposed to five sources.

2.2.3 Percentage depth dose (PDD)

The factory data is provided for clinical use based on the measurements averaging over ten sources for all four applicators. Factory PDD data was obtained using a water tank with sealed ion-chamber and applicators (Figure 7). Surface dose was obtained by extrapolation. Skin dose is about 126%-174% for a standard prescription depth of 2-5 mm. For the treatment range up to 6 mm, the dose fall-off is more rapid for smaller cone size, except for 10mm size, which resides between 20 mm and 35 mm probably due to the scattered electron contamination, which is more significant with such a small size.

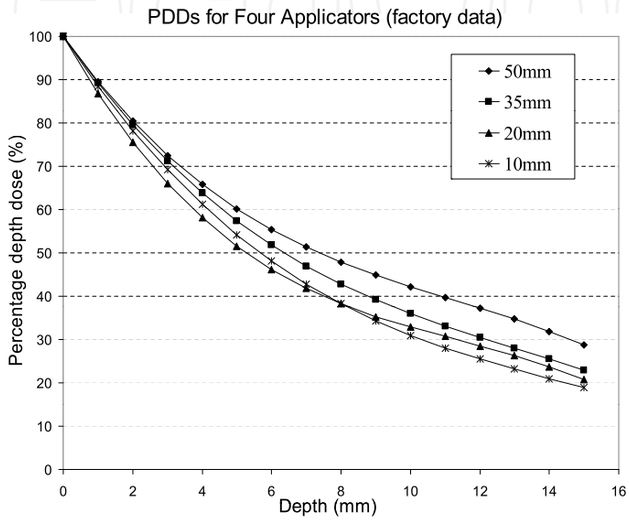


Fig. 7. Factory data of PDDs for four applicator cones: diamonds, squares, rectangles and stars represent the PDD curves for 50, 35, 20 and 10 mm cones.

2.2.4 Nominal SSD and correction factors

Low energy x-ray beam should also obey the inverse square law, $\frac{I_o}{I_g} = \left(\frac{f + d_m + g}{f + d_m} \right)^2$ where d_m is the measurement depth, g is the air gap, and f is the nominal SSD. By plotting $\sqrt{\frac{I_o}{I_g}}$ as a function of gap g, a straight line is obtained, the slope of which is $\frac{1}{f + d_m}$. Thus $f = \frac{1}{slope} - d_m$. Therefore, the nominal SSD can be verified clinically by measuring the correction factors with different air-gaps. The nominal SSD were calculated for all four applicators.

Moreover, if an air gap is inevitable in a treatment setup, the correction factor for the dose output (CF_{air}) can be calculated using the nominal SSD:

$$CF_{air} = \left(\frac{f + d}{f + g + d} \right)^2 \tag{4}$$

where d is the calculating depth.

The presence of an air-gap greatly affects the output at the skin surface. The dose fall off can be higher than 10% when there is more than 1mm air gap. The nominal SSDs are determined to be 20 mm for the 10 mm cone, 20 mm cone and 35 mm cone; and the nominal SSD is 30 mm for the 50 mm cone. Note that the nominal SSD varies with different cones due to the different filter manufacturing.

The cutouts made by the Xoft Axxent® Mini lead shield can be used to collimate the beam to accommodate the treatment area. Cutout correction factors (CF_{cone}) need to be measured prior to the treatment by qualified personnel to correct for the output change due to the use of the lead collimation. It can be calculated by:

$$CF_{\text{cone}} = M_{\text{cone}}\ (\text{uncollimated}) / M_{\text{cone}}(\text{collimated}) \tag{5}$$

Measurements of the specific cutout factors were performed using the surface applicator QA test fixture (Figure 8). The applicator QA text fixture consists of inserts for the ion chamber (left figure) and the applicator (right figure). A custom-made plastic slab with a groove can be used to accommodate the parallel-plate chamber, so that the chamber surface is flush to the phantom surface. This fixture allows measurements with additional solid water slabs placed on top of the chamber and centrally fixed applicator.

Fig. 8. Surface applicator QA test fixture with the PTW T34013 parallel plate chamber centrally inserted under the applicator for shielded measurements.

2.3 Clinical management

2.3.1 Prescription and treatment time calculation

The treatment area was determined by physician as the visible tumor (i.e. gross tumor volume or GTV) plus estimated microscopic extension (i.e. clinical target volume or CTV), with an additional margin depending on tumor size (planning target volume or PTV). A smaller margin (typical 5 mm) than typically used with electron beam or ^{192}Ir HDR brachytherapy is recommended, given the beam flatness of the Xoft 35 mm surface applicator (with a mean and SD of 3.2%±1.2% as stated in the Xoft Axxent® system manual). Physicians make the selection of applicator cone size depending on the treatment area. Common prescription doses are 3 Gy per fraction to 45~48 Gy total for larger lesions or 5 Gy per fraction to 40 Gy total for smaller lesions. The prescription depth varies from 2 to 6 mm,

depending on the characteristics of the tumor. Patient with lesion thicknesses larger than 6 mm generally should not be treated with EBT treatment, due to the rapid dose fall-off with depth. Very close contact should be maintained between the applicator end-cap and skin so that the air gaps can be eliminated.

Treatment duration (in seconds) can be calculated based on the prescribed fractionated dose D_p, the nominal dose-rate $\dot{D}_{skin,n}$ (Gy/min), the percentage depth dose at depth $PDD(d)$, and the cutout factor CF_{cone} using the equation:

$$T(s) = \frac{D_p}{\dot{D}_{skin,n} \times PDD(d) \times CF_{cone}} \times 60$$

Cutout factors need to be pre-measured for each patient case since patients have very different target areas, as shown in Figure 9, using the method mentioned in section B.4. Bolus materials have multiple purposes for skin cancer treatment including immobilizing the collimation material and attenuating radiation outside the treatment field. For cases shown in Figure 9a and 9b, bolus materials are used for filling the gap between the collimator cutouts and the mask in order to ensure minimum air gap and for protecting the scalp area behind the ear.

Treatment time usually takes 4 to 6 minutes for each session. The source stays in one position inside the applicator throughout the entire session. In the early clinical application of this new technology there were no cases of interruption of treatment resulting from malfunction of the applicator or patient movements. Source arcing did occur a few times during a few treatments, leading to an interruption of the treatment and recalculation for the remaining dose. The air-kerma strength was re-measured prior to the continuation of the treatment using the on-board well chamber and electrometer. In all cases, the treatment was successfully continued and finished after replacing the source.

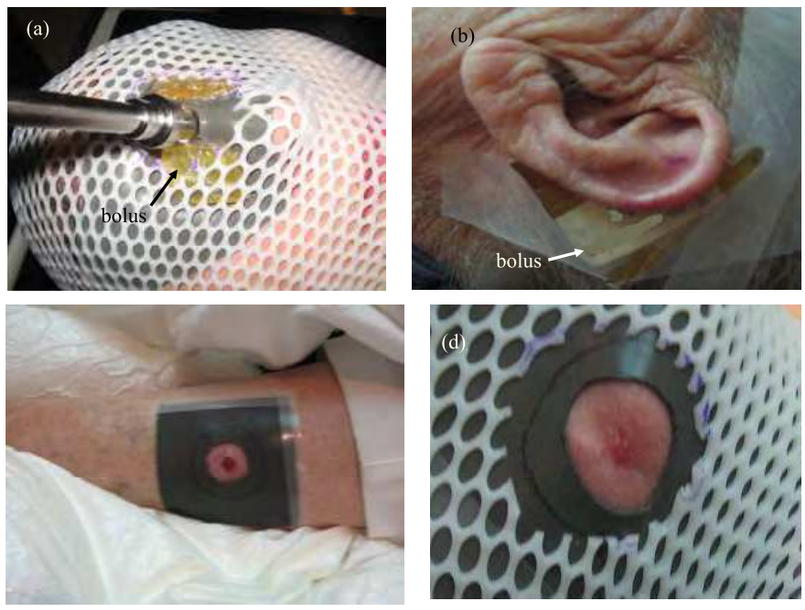


Fig. 9. Different collimations using the Flexishield lead material for targets located at (a) the bridge of the nose, (b) the left ear, (c) the left leg, and (d) the left temple.

2.3.2 Room setup and exposure to the personnel

In our clinic, patients lie on a flat "couch" (a linac table is what we use in our clinic) with clinically appropriate immobilization systems devised by the radiation therapists and physician to ensure minimal patient motion at applicator placement and during the treatment. For example, a thermoplastic facemask (WFR-Aquaplast, Avondale, PA) is normally used for lesions located on the face and other areas in the head and neck (Figure 10a). Patient positioning is not essential in this type of treatment since physicians can visually locate the treatment area and accurately place the applicator (although it is preferable to have the applicator oriented downwards rather than upwards or horizontally when possible for ease of set-up and reproducibility). A 0.5 cm lead equivalent rolling shield (2 meter tall and 1 meter wide) is used to reduce radiation exposure to the therapy personnel (Figure 10b). The therapy team can stay in the room and monitor the treatment through a small viewing window on the rolling shield. The room exposure measured with a survey meter was reported for three patients with the skin lesions located at their scalp, left ear, and left leg [31]. These three patients were scheduled on the same day for treatment using the same x-ray source. Seven positions in the treatment room were surveyed during the treatment session (Figure 11). As shown in Table 1, the highest room exposures were 70 mR/hr, 43 mR/hr, and 6.7 mR/hr at 1 m superior to the lesion for the scalp, left ear, and left leg. As expected, the further away from the source, the lower the exposure. The exposure rate was consistently at background reading (<1 mR/hr) behind the rolling shield. Therefore, the clinical personnel are safe and receive essentially no radiation behind the rolling shield.

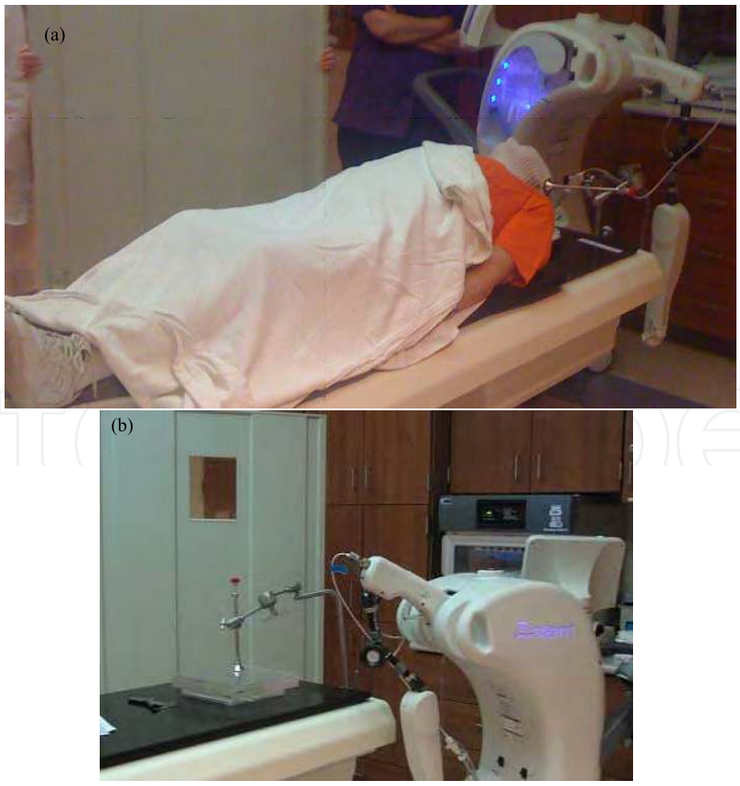


Fig. 10. (a) Patient setup with a thermoplastic facemask for skin treatment on the ear; (b) Radiation protection with the rolling shield in place.

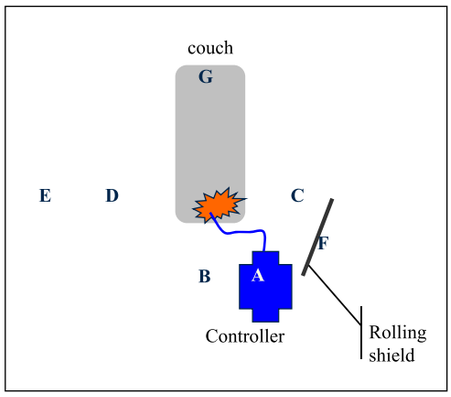


Fig. 11. Diagram of measurement points with clinical setup for ear, scalp and leg cases. Point A is right behind the controller. Point B, G, C, and D are 1 meter from the source superior, inferior, right and left. Point E is 1 meter from the source to the left. Point F is behind the rolling shield.

Table 1: Room Exposure (mR/hr)			
Measured points	Scalp	Left Ear	Left Leg
A (controller)	1.2	1.8	0.5
B (1meter Sup)	70	43	6.7
C (1meter right)	24	18	7.2
D (1meter left)	50	37	26
E (2meter left)	18	9.3	4.1
F (lead shield)	0.8	0.1	0.2
G (1meter Inf)	0.7	0.3	0.9

Table 1. Room exposure at different locations during the treatment of several patient setups

2.3.3 Initial clinical experience and patient follow-up

Similar to isotope-based HDR brachytherapy, the primary radiation oncologist and a medical physicist are currently required to be present for each treatment. After patient is comfortably lying down on the table, the radiation oncologist directly visualizes the target location and places the applicator with minimal air gap and at an appropriate angle. The physicist and therapists help the physician to secure the applicator using a clamp system. As shown in Figure 12, the surface applicator needs to be placed close to the target or pressing the collimator for various lesion locations, such as on the left ear, the left leg, and the scalp.

As in Figures 13, 14, and 15, most non-melanoma skin cancers responded fully to the treatment. During the course of treatment, most lesions demonstrated increased erythema. Many lesions became slightly ulcerated or turned into eschars in the first one to four weeks following the completion of treatment. However, by three to six months of follow up most cases showed resolution of acute radiodermatitis and no evidence of remaining malignancy. Due to the early stage of clinical practice using the surface applicators and EBT system, there is only one publication so far to provide the initial experience for treatment of 37 patients

with 44 cutaneous malignancies in terms of tumor control, acute toxicity, and cosmesis [33]. No recurrences had been seen for a median of 4.1 months (range 1-9 months) follow-up, with acceptable acute toxicity and good to excellent early cosmesis.

Early clinical experience of EBT shows favorable tumor control as well as cosmetic outcomes. Using the hypofractionated approach, the treatment duration is short and convenient for patients. Direct visualization of the target location helps radiation oncologist to accurately place the applicator, thus accurately direct the radiation.

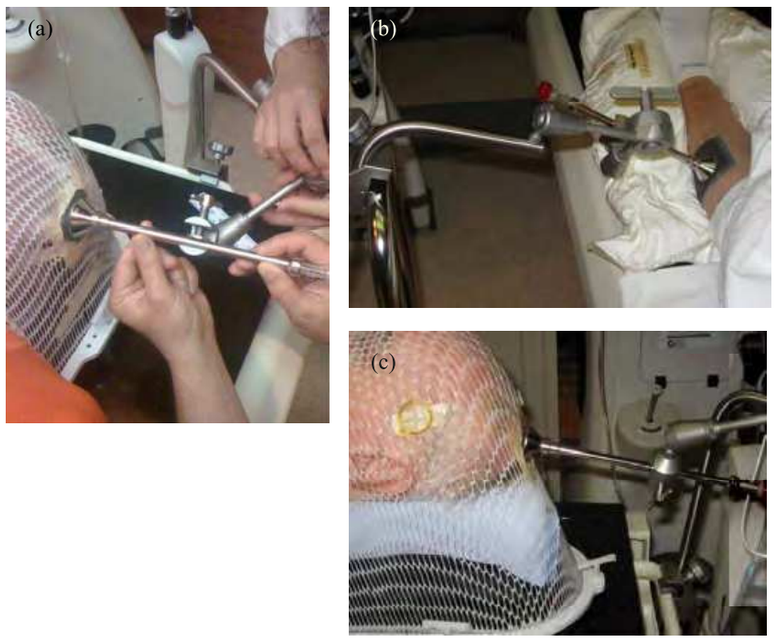


Fig. 12. The surface applicator setup immobilized with an Elmed Retract-Robot clamp system for different lesion locations, including (a) the left ear, (b) the left leg, and (c) the scalp.

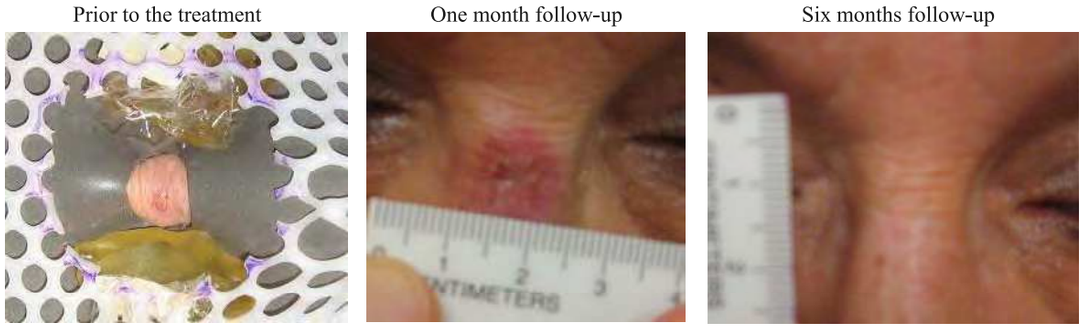


Fig. 13. Patient follow-ups for basal cell carcinoma on the nose, with pictures showing (a) prior to the treatment, (b) one month after the treatment, and (c) six months after the treatment.

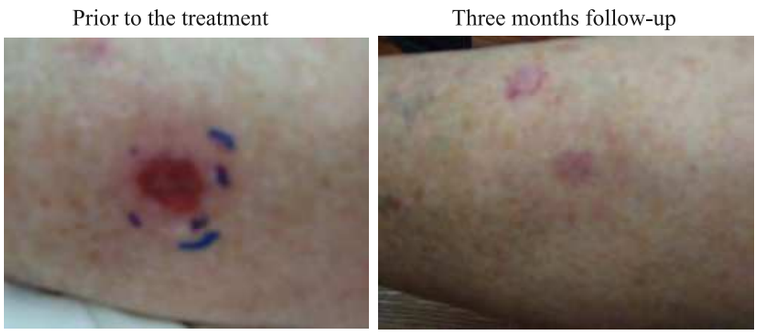


Fig. 14. Patient follow-ups for basal cell carcinoma on the left leg, with pictures showing (a) prior to the treatment and (b) three month after the treatment.

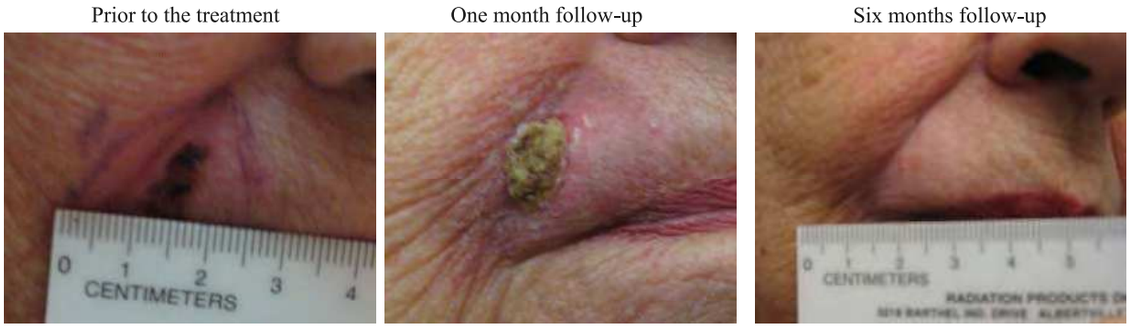


Fig. 15. Patient follow-ups for basal cell carcinoma on the face, with pictures showing (a) prior to the treatment, (b) one month after the treatment, and (c) six months after the treatment.

2.4 Technical and clinical considerations

2.4.1 Dose output uncertainty

As suggested in TG-61, the in-air method is recommended for measuring the absorbed dose to water at surface for low energy x-rays with tube potential between 40 kV and 300 kV. The Xoft source has an operating voltage of 50 kV, which falls within this region. Based on equation (1), several factors need to be pre-determined for the surface dose measurements. Similar to TG-51 for high-energy external beam, the calibration factor N_k and the electrometer correction (P_{elec}) are provided by the Accredited Dosimetry Calibration Laboratory (ADCL) or **National Institute of Standards and Technology (**NIST). The mass energy-absorption coefficient ratio $[(\overline{\frac{\mu_{en}}{\rho}})^{w}_{air}]_{air}$ is a function of half value layer (HVL) in Al of the beam. The nominal beam quality (1st HVL in mm Al) is provided by factory measurements to be 1.39, 1.53, 1.57 and 1.56 mm Al for 10, 20, 35, and 50mm cones for the Xoft 50kVp x-ray beam. Thus, based on AAPM TG-61 Table IV, $[(\overline{\frac{\mu_{en}}{\rho}})^{w}_{air}]_{air}$ is 1.017. The backscatter factor B_w is a function of nominal SSD, field size, and HVL. Interpolated from

Table V in TG-61, the backscatters used in the calculation are 1.049, 1.081, 1.102, and 1.130 for 10, 20, 35, and 50 mm cone sizes, respectively. The stem correction factor $P_{stem,air}$ is set to 1 if the change of field size and beam quality between the calibration and actual measurements is minimal. Including all calibration parameters, the combined uncertainty at the surface in low energy x-ray beams using the in-air calibration method is 5%. Since the other part of uncertainty associated with the clinical setup and immobilization during treatment can be considered negligible due to the ease and stability of the setup using this skin applicator system, the final uncertainty in the absorbed dose should satisfy a tolerance of ±5% [34].

2.4.2 Treatment consideration

The presence and specific magnitude of electron contamination generated in air and on the inside surface of the treatment cone might contribute to an enhanced surface dose, which largely depends on the material from which the treatment cone is fabricated. A five-fold increase was reported in relative surface dose with lead lined treatment cones[35, 36]. The selection of an ionization chamber for a proper window thickness used in surface dose determination is crucial to the x-ray source calibration. The entrance window thickness should not be so thick that it absorbs low-energy photons nor so thin that it can be contaminated by photoelectrons. The surface points on the PDD curves provided by the company were determined by extrapolation. Its accuracy is questionable due to the possible effect of enhanced surface dose with the applicator cone. Further studies with Monte Carlo simulation are needed for accurately modeling the PDD in tissue with the surface applicators. It also implies that correction factors, i.e. cutout factors or air gap factors are more accurate if measured at depth.

It is recommended that close contact between skin surface and applicator end-cap be maintained to avoid underdosing due to the presence of an air-gap. The effective SSD is different for different applicators, but it can be determined for all applicators by measuring the air-gap correction factors as we described above. For treatment areas where a flat surface is hard to achieve, thin bolus material can be use to facilitate the treatment.

As to date, the largest available cone size is 50 mm in diameter for the Xoft surface applicators. This limits the application of EBT for lesions with a diameter larger than 40 mm. One possible solution is to combine multiple fields to cover the target. However, with the round shape of the field and manual positioning of the applicator, this technique might requires more practice and better design, to avoid overdosing or underdosing at the junction of two fields.

2.4.3 Room exposure to personnel

Room exposure varies with patient setups. As shown in Table 1, the scalp case represents an extreme scenario where no lead collimation was used due to a large treatment area and a very loose contact with the skin (due to patient discomfort when the applicator was pressed onto the lesion). The left ear case has an oblique skin surface but the use of bolus and lead collimation helped to reduce radiation exposure to staff. The left leg case was a small lesion and had very flat skin surface and thus close contact was achieved. This case represents the other extreme. Even for the scalp case, where the room exposure was maximal, the survey meter reading was below 1 mR/hr behind the rolling shield. The rolling shield does effectively minimize radiation exposure to personnel when properly used. Moreover, the

use of Flexi-shield or bolus significantly reduces the room exposure, thus is recommended when possible.

2.4.4 Comparison with isotope-based HDR brachytherapy

Overall, it has been shown that Xoft miniature x-ray source can produce comparable dose distribution for intracavitory brachytherapy treatment compared to ^{192}Ir source [26-28]. One major concern is the relatively more rapid dose fall off with distance in tissue compared to ^{192}Ir source, which results in a higher surface dose near the MammoSite balloon applicator for APBI treatment or the Vaginal cylinder applicator for endometrial treatment. This is due to the lower energy (50keV) emitted from the miniature x-ray tube, compared to the effective energy of about 380keV for ^{192}Ir [37]. The size of the source is also a limitation. The miniature x-ray source is 2.3 mm in diameter, and it has to be housed in a cooling catheter in order to maintain a long time function. The apparent size of the source is 5.4 mm in diameter, which is too large for interstitial brachytherapy treatments. However the economics and safety favor the use of EBT over ^{192}Ir, in terms of minimal shielding required, less regulations over radioactive materials, initial cost of the unit, etc.

Favorable cosmetic outcomes and excellent local control (97~98% for primary tumors and 87% for recurrence) with minimal complications have been reported with isotope-based brachytherapy method for a follow-up study of 117 patients[8]. Clinical follow-up of a total of 85 patients have shown that the local control for the skin cancer using the isotope-based brachytherapy is 97%, with good cosmetic results (grade 1 (58%) and grade 2 (24%) acute skin toxicity)[22]. Since the electronic brachytherapy for skin cancer is still at its early stage for clinical management, patient follow-up reports are limited. Initial experience at University of Pittsburgh was published for treatment of 37 patients with 44 cutaneous malignancies using the electronic brachytherapy in terms of tumor control, acute toxicity, and cosmesis. No recurrences had been seen for a median of 4.1 months (range 1-9 months) follow-up, with acceptable acute toxicity and good to excellent early cosmesis [33]. We anticipate increased clinical applications of this technology in the near future.

3. Summary

The application of EBT for skin treatment is still relatively new and consequently is unfamiliar to many medical physicists and physicians. It is relatively simple to implement technically. With limited clinical experience and short follow-up it appears to be safe and effective for small non-melanoma skin cancers. Each source needs to be carefully calibrated with the surface applicator prior to treatment. The electronic brachytherapy is a feasible approach for treatment of non-melanoma skin cancer.

4. References

[1] Christenson LJ, Borrowman TA, Vachon CM, et al. Incidence of basal cell and squamous cell carcinomas in a population younger than 40 years. JAMA 294, 681-690 (2005)

[2] http://www.cancer.gov/cancertopics/types/skinCancer, National Cancer Institute 2009, Website last accessed January 11, 2010.

[3] http://www.cancer.org/downloads/STT/2008CAFFfinalsecured.pdf, American Cancer Society. Cancer Facts and Figures 2008.

[4] Freeman RG, Knox JM, Heaton CL. The treatment of skin cancer: A statistical study of 1341 skin tumors comparing results obtained with irradiation, surgery and curettage followed by electrodesiccation. Cancer 17, 535–538 (1964)
[5] Mohs FE. The chemosurgical method for microscopical controlled excision of cancer of the skin. NY State J. Med. 56, 3486 –3492 (1956)
[6] Lovett RD, Perez CA, Shapiro SJ, et al. External irradiation of epithelial skin cancer. Int. J. Radiat. Oncol. Biol. Phys. 19, 235–242 (1990)
[7] Silva JJ, Tsang RW, Panzarella P, et al. Results of radiotherapy for epithelial skin cancer of the pinna: the Princess Margaret Hospital experience, 1982-1993. Int. J. Radiat. Oncol. Biol. Phys. 47, 451-459 (2000)
[8] Guix B, Finestres F, Tello J, et al. Treatment of skin carcinomas of the face by high dose rate Brachytherapy and custom made surface molds. Int. J. Radiat. Oncol. Biol. Phys. 47, 95-102 (2000)
[9] Kwan W, Wilson D, Moranvan V. Radiotherapy for locally advanced basal cell and squamous cell carcinomas of the skin. Int. J. Radiat. Oncol. Biol. Phys. 60, 406-411 (2004)
[10] Klein E, Fine S, Laor Y et al., Laser irradiation of the skin. J. Invest. Dermatol. 43, 565–570 (1964)
[11] Spicer MS, Goldberg DJ, Lasers in dermatology. J. Am. Acad. Dermatol. 34, 1-25 (1996)
[12] Heidary N, Naik H, Burgin S, Chemotherapeutic agents and the skin: an update. J Am Acad Dermatol. 58, 545-570 (2008)
[13] Kuflik EG, Gage AA, The five-year cure rate achieved by cryosurgery for skin cancer. J. Am. Acad. Dermatol. 24, 1002-1004 (1991)
[14] Lee DA, Miller SJ, Nonmelanoma Skin Cancer. Facial Plast Surg Clin N Am 17, 309-324 (2009)
[15] Wolf DJ, Zitelli JA. Surgical margins for basal cell carcinoma. Arch Dermatol. 123, 340-344 (1987)
[16] Brodland DG, Zitelli JA. Surgical margins for excision of primary cutaneous squamous cell carcinoma. J Am Acad Dermatol. 27, 241-248 (1992)
[17] Greene F, Page DL, Fleming ID. AJCC cancer staging manual. 6th edition. New York: AJCC Springer-Verlag; 2001. Berlin, Heidelberg.
[18] Rowe D, Caroll RJ, Day CL Jr. Mohs Surgery is the treatment of choice for recurrent (previously treated) basal cell carcinoma. J Dermatol Surg Oncol 15:424-432 (1989)
[19] Caccialanza M, Piccinno R, Kolesnikova L, Gnecchi L. Radiotherapy of skin carcinomas of the pinna: a study of 115 lesions in 108 patients. Int J Dermatol. 44, 513-7 (2005)
[20] Barnes EA, Breen D, Culleton S, et al. Palliative radiotherapy for non-melanoma skin cancer. Clin Oncol. 22, 844-849 (2010)
[21] Kohler-Brock A, Prager W, Pohlmann S, Kunze S. The indications for and results of HDR afterloading therapy in diseases of the skin and mucosa with standardized surface applicators (the Leipzig applicator). Strahlenther. Onkol. 175, 170-174 (1999)
[22] Gauden S, Egan C, Pracy M, HDR brachytherapy for the treatment of skin cancers using standard surface applicators. Brachytherapy 7, 159 (2008)
[23] Mebed AH, Soliman HO, Gad ZS, et al. Multimodality treatment for non melanoma skin cancer: a prospective study done on 120 Egyptian patients. J Egyp Nat Cancer Inst. 22, 49-55 (2010)

[24] Rivard MJ, Davis SD, DeWerd LA, Rusch TW, and Axelrod S, Calculated and measured brachytherapy dosimetry parameters in water for the Xoft Axxent X-Ray Source: An electronic brachytherapy source. Med. Phys. 33, 4020–4032 (2006)

[25] Mille MM, Xu XG, Rivard MJ. Comparison of organ doses for patients undergoing balloon brachytherapy of the breast with HDR 192Ir or electronic sources using monte carlo simulations in a heterogeneous human phantom. Med Phys. 37, 662-71 (2010)

[26] Dickler A, Kirk MC, Seif N, et al, A dosimetric comparison of MammoSite high dose-rate brachytherapy and Xoft Axxent electronic brachytherapy. Brachytherapy. 6, 164–168 (2007)

[27] Dickler A, Dowlatshahi K. Xoft Axxent electronic brachytherapy. Expert Rev Med Devices. 6, 27-31 (2009)

[28] Dickler A, Kirk MC, Coon A, et al, A dosimetric comparison of Xoft Axxent electronic brachytherapy and iridium-192 high-dose-rate brachytherapy in the treatment of endometrial cancer. Brachytherapy. 7, 351-354 (2008)

[29] Hiatt J, Cardarelli G, Hepel J, et al, A commissioning procedure for breast intracavitary electronic brachytherapy systems. J. App. Clin. Med. Phys. 9, 58-68 (2008)

[30] Rong Y, Welsh JS. Surface applicator calibration and commissioning of an electronic brachytherapy system for nonmelanoma skin cancer treatment. Med Phys. 37, 5509-5517 (2010)

[31] Liu D, Poon E, Bazalova M, Reniers B, Evans M, Rusch T, Verhaegen F. Spectroscopic characterization of a novel electronic brachytherapy system. Phys Med Biol. 53, 61-75 (2008)

[32] Ma CM, Coffey CW, DeWerd LA, et al. AAPM protocol for 40-300kV x-ray beam dosimetry in radiotherapy and radiobiology. Med. Phys. 28, 868-893 (2001)

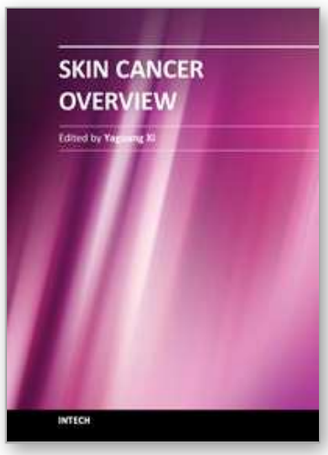
[33] Bhatnagar A, Loper A, The initial experience of electronic brachytherapy for the treatment of non-melanoma skin cancer. Radiat Oncol. 28, 87 (2010)

[34] Brahme A, Dosimetric precision requirements in radiation therapy, Acta. Radiol. Oncol. 23, 379-391 (1984)

[35] Aldrich JE, Meng JS, and Andrew JW, The surface doses from orthovoltage x-ray treatment, Med. Dosim. 17, 69-72 (1992)

[36] Podgorsak MB, Schreiner LJ and Podgorsak EB, Surface dose in intracavitary orthovoltage radiotherapy, Med. Phys. 17, 635-640 (1990)

[37] Holt RW, Thomadsen BR, Orton CG. Miniature x-ray tubes will ultimately displace Ir-192 as the radiation sources of choice for high dose rate brachytherapy. Med Phys. 35, 815-817 (2008)



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The book Skin Cancer Overview is divided into three sections to cover the most essential topics in skin cancer research: Etiology, Diagnosis and Treatment, and Prevention. Due to the complexity of skin cancer, this book attempts to not only provide the basic knowledge, but also present the novel trends of skin cancer research. All chapters were written by experts from around the world. It will be a good handbook for researchers with interests in skin cancer.

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