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Dose Distribution Evaluation and Independent Quality Check of Spherical INTRABEAM™ Applicators via Radiochromic EBT2 Film Measurement

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ABSTRACT

Introduction: The present study was conducted to implement a simple practical independent quality check of depth dose and isotropy of the Intrabeam™ therapeutic X-ray machine using radiochromic EBT2 film.

Material and Methods: The independent quality check of 1.5, 3.5, and 5-cm spherical Intrabeam™ applicators was accomplished using particular EBT2 film cutting pieces with internal rounded edges in a water phantom. Prior to this measure, the film was calibrated at three distances from the 5-cm applicator in water to clarify the effects of beam spectrum and dose rate alteration on film response. To this end, three calibration curves were plotted.

Results: The results of the one-way analysis of variance showed a critical difference between film pieces receiving equal doses at various distances ($P<0.05$). Therefore, depth dose curves were designed using all three calibration curves. Smaller applicators represented steeper dose fall-off, compared to the larger sizes. In this regard, 14.97%, 17.59%, and 30.92% of the relative mean doses were measured at 1 cm depth of 1.5-cm, 3.5-cm, and 5-cm applicators, respectively. A 10%/1mm gamma index was satisfied for the lateral dose evaluation of corresponding depth relative to Z-direction.

Conclusion: The approach implemented in this study could be carried out as a rapid monthly quality check method for the dose distribution evaluation of the Intrabeam device.

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Introduction

Cancer treatment via various electronic brachytherapy systems has attracted attentions in recent years, mostly, due to the possibility of localized irradiation, which is considered as a desirable characteristic in all radiotherapy modalities [1, 2]. Electronic brachytherapy machines are divided into two main categories, including electron and low-energy X-ray beam generators, each of which has its own specialties and characteristics. The differences are mostly about the penetration depth and treatment duration. In this regard, electron beams have a higher penetration, compared to low-energy X-rays, and the treatment duration of electron radiator systems is much lower.

Zeiss Intrabeam™ (Carl Zeiss Surgical, Oberkochen, Germany) is one of the well-known intra-operative radiation therapy machines, used partially for irradiation purposes, mostly after breast conservative surgery among early-stage breast cancer patients [3]. The unit produces an approximate isotropic dose distribution at the end of a 10-cm evacuation probe tip by striking 50 keV electrons irradiated from an electron gun [4].

Prior to each treatment, the isotropy and output of the X-ray Source (XRS) are checked via quality assurance and accessories, including a Photodiode array (PDA) and a Probe adjuster ionization chamber holder (PAICH) respectively. These pretreatment procedures are considered as internal quality assurance (QA) that must be verified by various independent QA approaches [5]. This study aimed to apply a simple, practical, independent quality check technique for evaluating the dose distribution of the Intrabeam therapeutic X-ray machine using radiochromic EBT2 film. Some aspects of film dosimetry via radiochromic films are discussed in the following paragraphs.

Film dosimetry is considered as a suitable approach, providing high spatial resolution for the dosimetry of complex radiation fields and facilitating the achievement of two-dimensional dose distribution maps [6]. Gafchromic™ EBT2 as a self-developing film is used to access such purposes [7]. External beam

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therapy (EBT) film generation was initially designed for dosimetry purposes of high-energy complex radiation fields, including intensity-modulated radiation therapy (IMRT), which needs high spatial resolution to be assessed [8, 9].

Some investigations show energy dependence in EBT film response. In a study, about 7.7% difference was observed in EBT film dose responses varying from 50 kV to 10 MV at energy ranges lower than 100 keV [10], which seems to be significant for implementing an accurate dosimetry procedure. The second generation , EBT2 film, contains some additional components in its active layer, including sulfur, sodium, and bromine derivatives, leading to an increase in photoelectric coincidence that is desirable for kV dosimetry range [6].

Butson et al. (2010) represented 6.5% energy dependence in EBT2 film, compared to the energy dependence of 7.7% reported in the aforementioned study [10]. The EBT2 film is actually composed of three main layers, including a 30-µm thickness active layer and two polyester layers above and under the active layer with the thicknesses of 50 and 175 µm, respectively. In addition, a 5-µm top coat with a 25-µm adhesive layer above is placed between the active layer and the superior polyester layer (adopted from GAFCHROMIC® EBT2 Self-Developing Film for Radiotherapy Dosimetry, February 19, 2009. Rev1).

In 2012, the ISP® company presented EBT3 film. The main difference between EBT2 and EBT3 film is the symmetrical configuration of EBT3 composed of three layers, including an approximate 28-µm active layer between two 100-µm polyester layers [11]. The symmetric configuration of the EBT3 film resolves the concern about the side orientation placement of the film on the scanner bed [12]. This issue is reported to be a potential source of deviation in optical density measurements with the EBT2 film. However, it could be prevented by placing the reference side of the film on the scanner bed in all scan procedures as suggested by the manufacturer [13].

Materials and Methods

In this study, particular EBT2 film cutting pieces were used for dose distribution assessment around 1.5, 3.5, and 5-cm spherical applicator sizes of the low-energy therapeutic X-ray Intrabeam™ device as an in-house independent quality check manner. For this purpose, three continuous “8×10“Gafchromic® EBT2 lots with a batch number of #06241302 were prepared. An industrial CO_2 laser with 10,600 nm wavelength [14] was used for cutting the film pieces safely since the EBT2 film has a maximum absorption at 420 nm due to the presence of a yellow marker dye in the active layer and a milder absorption at 636 nm according to the manufacturer declaration.

Film Calibration

Prior to initiating the dose distribution assessment procedure, a calibration stage was performed to obtain the film response in terms of net optical density (net OD) against the reference doses delivered to film pieces at various distances according to the Intrabeam™ treatment planning system (TPS). The calibration stage seemed to be necessary due to the noticeable energy dependence and other factors affecting the EBT2 film response mentioned in previous studies [10, 13, 15], which may influence the dose distribution assessment.

The response of the film depends on radiation type [7, 16], beam energy, and dose rate [10, 17]. The two latter factors could be assessed by changing the distance between the source and detector in water. The dose rate and beam spectrum do not vary independently by changing the source and detector distance in water. In this regard, the beam hardens and dose rate decreases with increasing the distance between source and detector in water [17, 18].

Therefore, calibration was performed using 20 EBT2 film pieces with an approximate dimension of 2×2 cm^2 using 5-cm applicator attached to the probe in the Zeiss water phantom along the probe axis. In a way that 10 pieces out of the calibration films received 1-10 Gy doses at the applicator surface (zero depth) with 1 Gy increment intervals, six of which received 1-6 Gy at 5 mm from the applicator surface, and the four remaining calibration film pieces received 1-4 Gy doses at 10 mm from the applicator surface.

One other film piece with the same dimensions was used to assess the background response of the film and measure the net OD. Following the irradiation of the calibration film pieces, three calibration curves were plotted in terms of net OD and dose for each distance. According to the calibration setup, there were three corresponding film pieces that received equal doses between 1 and 4 Gy, each of which was irradiated at 0, 5 and 10 mm depths in water. The responses of corresponding film pieces at each distance were compared to evaluate the energy and dose rate affecting them.

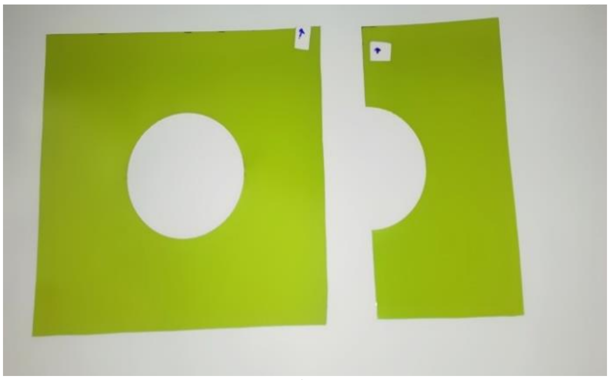


Figure 1. Particular EBT2 film cutting pieces prior to being perpendicularly attached to 5-cm Intrabeam™ spherical applicator. The left-sided piece used for lateral dose assessment and the right one for dose assessment along probe axis (Z-direction). Similar film pieces were prepared for 3.5-cm and 1.5-cm applicators using industrial CO2 laser as well.

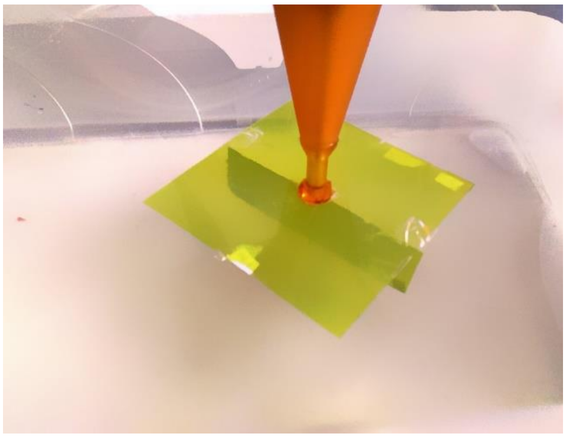


Figure 2. Perpendicularly attached EBT2 film pieces to 1.5-cm applicator submerged in water for being irradiated. The special Zeiss water phantom was not used because of large film piece dimensions. The same set up was implemented for 3.5 and 5-cm applicators as well.

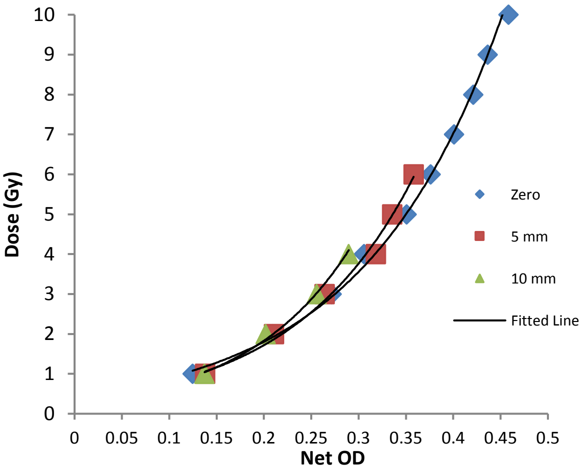


Figure 3. Calibration curve of EBT2 film at three depths in water. As shown in the plot, doses between 1 and 4 Gy (according to Intrabeam™ TPS) represent a bit different net ODs at the mentioned distances. Each point represents the mean pixel value of 5 × 5 cm2 pixels of a region of interest defined at each calibration film piece.

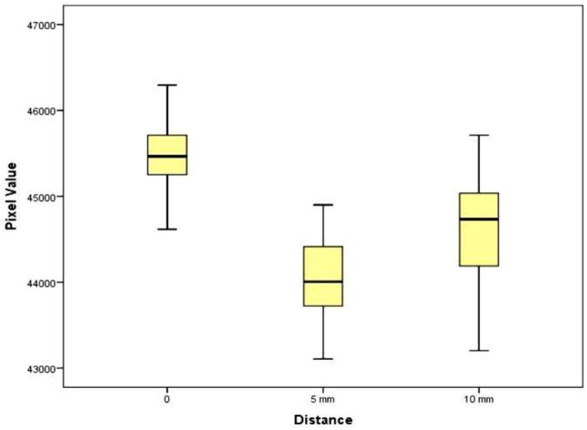


Figure 4. Comparing mean pixel values of 5 × 5 pixel regions of interest of EBT2 calibration films receiving 1-Gy dose at three distances.

Dose distribution assessment

Dose distribution parameters, including depth dose, and isotropy of the applicators were evaluated. To do so, as shown in Figure 1, a circular and semicircular cut with diameters corresponding to each applicator were excised from some film pieces by an industrial CO_2 laser to be accurately matched with each applicator. Therefore, the two particular cutting film pieces were perpendicularly attached to the corresponding applicator size to assess three-dimension dose distribution. Then, the whole setup was submerged in a water phantom for irradiation as shown in Figure 2. The special shielded Zeiss water phantom could not be utilized due to the large dimensions of film pieces.

Subsequently, the Intrabeam™ control console was placed at the entrance of the L-shaped examination room to keep the examiners protected. After preparing the setup, a 10-Gy dose was prescribed at the surface of each applicator with radiation times equal to 3:31, 9:51, and 25:31 (mm:ss) for 1.5, 3.5, and 5-cm applicators respectively. Finally, depth dose curves, isodose curves, and dose fluctuation curves were plotted for each applicator size.

Film scanning and analysis

All the calibration and rounded film pieces were marked to eliminate potential scanning faults including the film side orientation and the film direction orientation relative to the scanner bed. All the films are scanned in portrait while they are placed from the same side on the scanner bed for all scanning procedures in order to receive the best possible response [11, 16, 17]. This procedure was carried out 24 hours post irradiation with a Microtek flatbed 1000 XL document scanner (ScanMaker 1000XL Pro: Microtek International Inc., Hsinchu, Taiwan) in transmission mode. Prior to each scan procedure, five scan processes with no film on the scanner bed was performed to warm up and stabilize the temperature. Both calibration and main film pieces were placed on a similar region located at the scanner flatbed center. Film pieces were scanned in 48-bit RGB mode (16-bit per color channel) with full dynamic range, positive film mode, spatial resolution of 72 dpi and all the image correction modes on the scanner software were turned off.

All images were saved as Tagged Image File Format (TIFF) for being analyzed using MATLAB software (version R2015a) in red color channel according to the implemented dose level [6]. Afterwards, a 5 × 5 pixel region of interest (ROI) was defined at the center of each calibration film piece for measuring mean pixel values. Then, the mean of three groups of 25 pixel values corresponding to three distances for each dose from 1-4 Gy were compared using one-way analysis of variance (ANOVA) at a significance level of 0.05 using SPSS, version 20.0. Our purpose was to determine whether the responses of film pieces receiving equal doses, according to the Intrabeam™ TPS, at 0, 5 and 10 mm distances were significantly different.

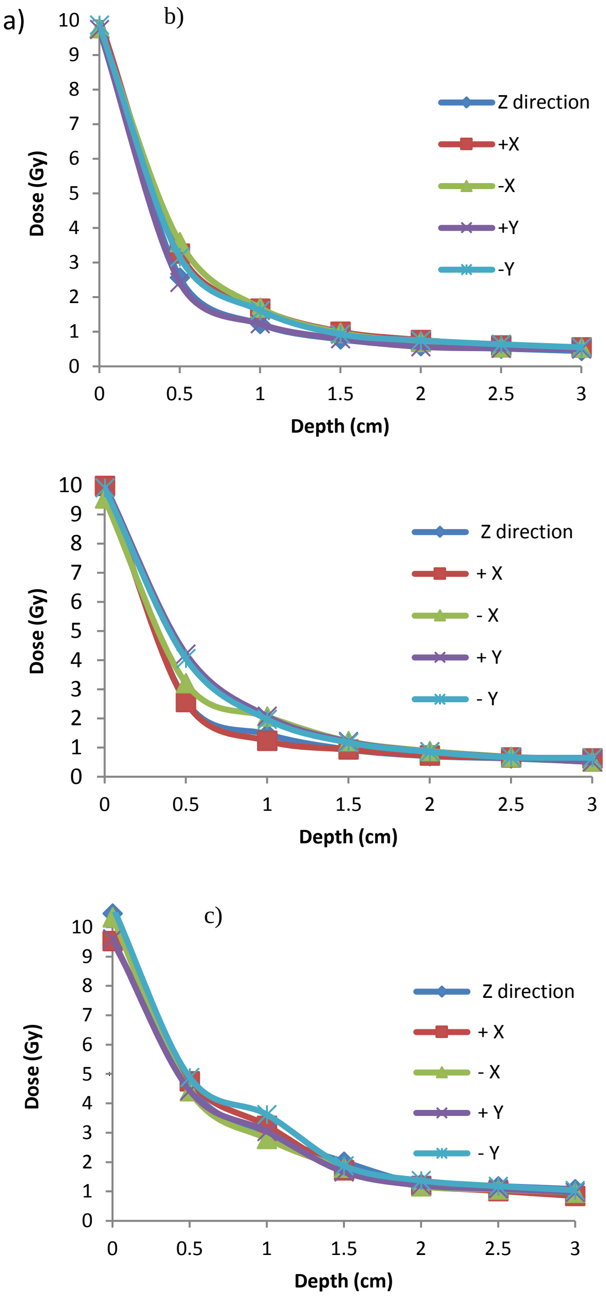
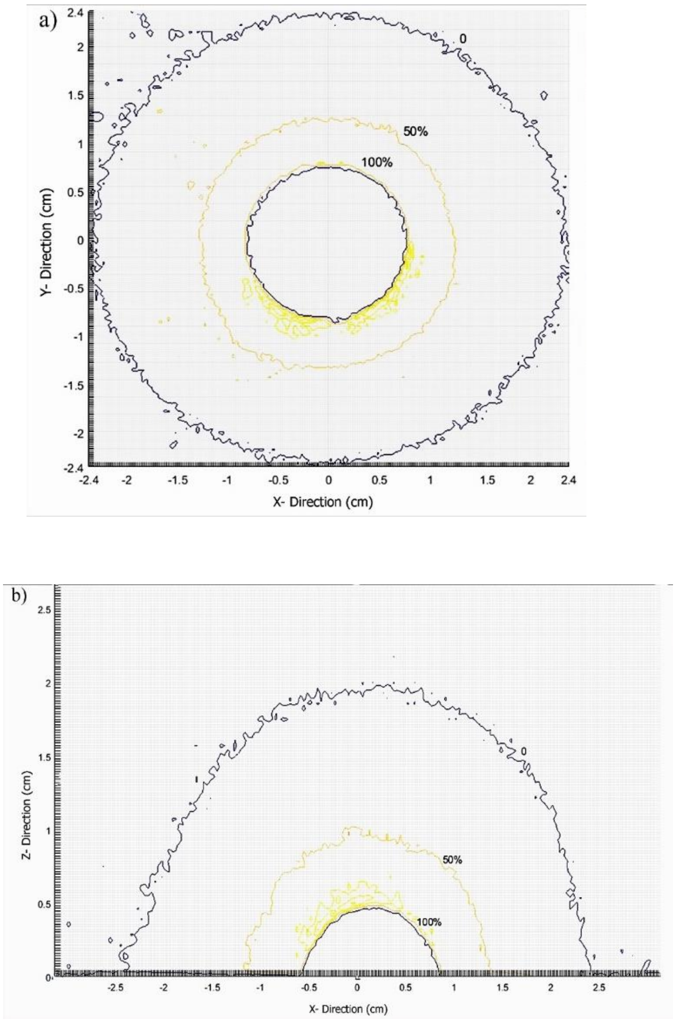


Figure 5. Depth dose curve of a) 1.5 cm, b) 3.5 cm, and c) 5 cm spherical Intrabeam™ applicators from each applicator surface to the depth of 3 cm in the lateral (±X, ±Y) and longitudinal planes (Z)

Results

Figure 3 shows the calibration curve of the EBT2 film in terms of dose (Gy) and net OD at zero depth and 5 mm and 10 mm from the 5-cm applicator surface. Mean differences between net OD of film pieces receiving same dose at three distances were calculated as 9.9%, 4.32%, 5.97% and 9.41% for 1-4 Gy doses, respectively. Furthermore, a one-way ANOVA test, at significance level of 0.05, was implemented to determine possible dose response dependency of the film to distance. The results of the test showed that the Sig was equal to 0.000 for all doses from 1-4 Gy.

Figure 4 represents the plot of the mean pixel values against three distances for 1-Gy dose as a sample. Similar plots were provided for 2-4 Gy doses, which are not shown. Subsequently, the EBT2 film response dependence to beam energy and dose rate was proved. According to the significant statistical differences between mean pixel values of calibration films receiving equal doses at three distances, the three calibration plots were used for measuring depth doses of 1.5, 3.5, and 5-cm applicators from each applicator surface to the depth of 3 cm in water. The calibration curve of the zero depth was used for dose measurements from each applicator surface to a depth of 0.5 cm. Further, the 5 mm calibration curve was utilized for 0.5-1 cm depth dose measurements, and the 10-mm calibration curve was applied for 1-3 cm dose measurements. Figure 5 displays the depth dose curve for each applicator.



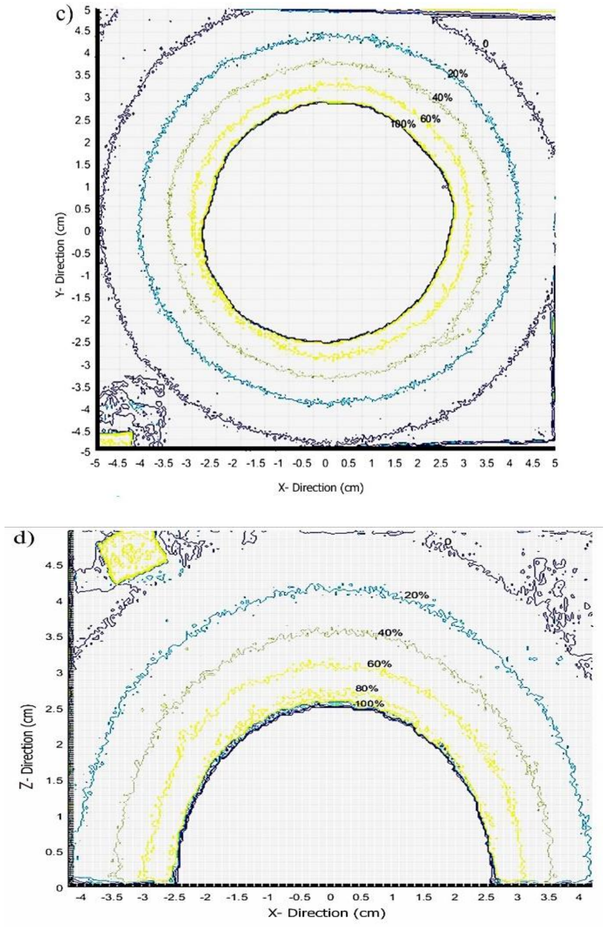


Figure 6. Isodose curves of 1.5 cm (a, b) and 5 cm (c, d) spherical Intrabeam™ applicators provided using EBT2 film. a, c curves represent dose distribution on the lateral plane (±X, ±Y) and b, d curves represent it on the longitudinal plane of applicators. The percent depth doses are shown on each distinct curve as well.

The steep dose fall-off of the applicators is recognizable on each plot. According to relative dose fluctuation curves (not shown) of each applicator, different relative mean doses were observed at corresponding distances from each applicator surface. Somehow that 14.97%, 6.8% and 5.19% relative doses at 1, 2, and 3 cm depths were observed for the 1.5-cm applicator, respectively. A corresponding measurement was performed for 3.5-cm and 5-cm applicators, which showed 17.59%, 9.7%, and 7.4% relative mean doses at the depths of 1, 2, and 3 cm, respectively, for the 3.5-cm applicator, and finally, 30.92%, 12.26%, and 9.68% relative mean doses were measured at the depths of 1, 2, and 3 cm from the 5-cm applicator, respectively. A 10%/1mm gamma analysis was also used to compare the measured doses at corresponding distances (with 0.5 cm increment intervals) on various directions of lateral plane (±X, ±Y) relative to Z-direction for isotropy evaluation of the applicators. The results were satisfied completely for all applicators. Moreover, the dose distribution evaluation was carried out by drawing isodose curves based on processing performed on EBT2 films in MATLAB, which recognized steep dose fall-offs and dose distribution differences between applicators. Figure 6 depicts the isodose curves of 1.5 and 5-cm (without 3.5 cm) applicators on the lateral plane and along longitudinal direction for each one.

Discussion

Film response evaluation

In this study, EBT2 film response dependence to beam energy and dose rate were assessed prior to initiating the main evaluation procedure in order to eliminate potential deviations in dose measurements in an incremental depth range. The importance of implementing such assessment became more obvious after proving the film response dependence to its distance from the source. Energy dependence of radiochromic films is one of the most important parameters for dose measurement, which is studied separately or along with some other measurement factors such as direction, side orientation, and light sensitivity for EBT2 films [7, 10, 13, 15, 16]. Ebert et al. 2008 evaluated the response of three radiochromic film types including XR-QA, XR-RV2, and EBT by drawing dose response curves of the films in terms of net OD and reference doses at 5 mm, 15 mm, and 30 mm from the tip of an Intrabeam™ bare probe. None of the film types represented linear response and all of them showed a considerable difference in response (net OD) against equal doses delivered from three distances by the XRS [17].

No applicator usage and considerable distance (30 mm) from the probe tip led to such significant discrepancy due to the remarkable X-ray spectrum changes following the penetration in water. Such evaluation on EBT2 film in the present study showed lower discrepancies relative to the EBT film compared to the previous study. That's probably due to the different active layer components, shorter distance between source and film (10 mm in the present study against 30 mm in Ebert's study), and attachment of a 5-cm applicator to the probe tip, which changes the beam spectrum considerably. Somehow that the beam needs to pass longer depth in the water to represent the same spectral changes occurring in first few millimeters. However, the lower response dependence of EBT2 film to distance from the source remained statistically significant.

In another study, Guerda et al. 2012 studied energy dependence of EBT3 film at 6 MV, 15 MV, and 50 kV as a low energy beam between 0.5-32 Gy dose ranges. According to the results, energy dependence of EBT3 film response at high energies was negligible, but about 11% variation was observed particularly at higher doses in response to the low energy (50 kV) photon beam [11]. Reinhardt et al. 2012 compared EBT2 and EBT3 film responses to clinical proton and photon beams. Comparable results were observed between these two consecutive film generations almost in all aspects of dose measurement including response to proton and photon beams, batch-to-batch uniformity, and response dependence to scanner direction. The result of the last parameter could be due to needle-shaped structures in the active layer, which scatters light in an anisotropic manner. However, side orientation dependence of EBT3 film response was acceptably eliminated due to the symmetric structure of EBT3 film relative to asymmetric ones of the EBT2 film [16]. Similar active layer components in EBT2 and EBT3 films (based on manufacturer declaration) result in comparable responses in similar circumstances. Therefore, considering the lack of energy independency progression and dose rate independency of such films claimed by the manufacturer, measurements must be taken cautiously, particularly in low energy ranges, through a well suited calibration stage based on the device used and the examination condition.

Dose distribution evaluation

Independent quality check measurements performed in the present study indicated a dramatically steep dose fall-off for spherical Intrabeam™ applicators, which was already proved for low-energy therapeutic X-ray devices in some previously published studies [2, 19, 20]. This characteristic is always considered to provide two potential benefits such as applying low doses to healthy adjacent tissues and meeting the needs of implementing structural shielding for the operating room, which enabled it to accomplish low kV intraoperative radiation therapy (IORT) treatments in normal operating theatres. Herein, a different dose fall-off among three investigated applicator sizes was observed as mentioned in the results. The main dose drop occurred at the first 1 cm depth in water as shown in depth dose curves of the three applicators. However, smaller applicators showed a steeper dose fall-off relative to the larger diameter applicators. That is to say, 1.5, 3.5, and 5-cm applicators represented 14.97%, 17.59%, and 30.92% relative mean doses of all directions at the depth of 1 cm, respectively, which indicates about 15% slower dose fall-off in the 5-cm applicator relative to the 1.5 cm diameter. This leads to a higher dose level to normal adjacent tissues being treated using larger diameter applicators.

Since a single high fraction of dose, usually 20-Gy, is delivered to breast tumor bed via Intrabeam™, approximately 3 Gy higher dose will be deposited in tissues at the depth of 1 cm of 5 cm applicator compared to the corresponding depth of 1.5 cm applicator. Therefore, treatments using larger applicator sizes must be carried out cautiously to prevent high dose absorption of surrounding healthy tissues. At least 1-cm interval between applicator surface to the breast skin is recommended by some authors [21]. Such distance from 5-cm applicator surface leads to an approximate 6-Gy dose in water, which corresponds to 5 Gy in breast skin due to steeper dose fall-off in breast tissue relative to water [2] that is tolerable by the skin [22].

Some deviations are observed on depth dose curves particularly at the first centimeter depth. This issue could be raised from the steep dose drop and probable measurement errors like film deviation from the correct alignment. Isotropy evaluation of the applicators with gamma analysis met the 10%/1mm criterion. Using such index raised from the extremely high dose gradient of the device makes accurate dose measurement around the applicator challenging. In fact, this index is used based on the assumption of 10% dose reduction for each millimeter depth in water [5, 23].

However, a more accurate investigation on isotropy, particularly in longitudinal isodose curves (along Z-direction), does not indicate an absolute isotropic dose distribution around the spherical applicators. This is simply recognized by considering whether each isodose curve on the Z-direction, passing from equal distances in the lateral plane, proceeds through similar depth on the Z-direction. Such investigation shows that the isodose curve, passing from ±2.5 cm depth on lateral plane of the 1.5-cm applicator, penetrates through a depth of 2 cm on the longitudinal direction, which indicates a lower beam penetration along the Z-direction relative to the lateral plane. The corresponding consideration on the 5-cm applicator showed the isodose curve, passing from ±3 cm on the lateral plane, penetrates about 3.2 cm on the Z-direction. This observation indicates an increase in beam penetration along the Z-direction compared to the lateral plane by increasing the applicator diameter.

Eaton et al. 2013 measured an isotropy range of 3.4% to 16% on the Z-direction compared to the lateral plane for 4.5-cm applicators among seven therapeutic centers with a 5-cm applicator exceptionally in one center. They used thermoluminescence dosimeters during an audit [23]. A similar higher dose on the Z-direction relative to the lateral plane of 5-cm applicator was observed in some other studies [5, 24]. This characteristic is sometimes considered clinically insignificant [23]. However, having a deeper understanding of dose distribution characteristics of therapeutic system and using an accurate and reliable treatment planning system are of great value.

Conclusion

An independent quality check of the Intrabeam™ therapeutic machine implemented in this study, using EBT2 film, resulted in a proper understanding of dose distribution properties of various spherical applicator sizes of the system. The novelty of this study is mainly about different dose distribution of the spherical Intrabeam™ applicators. We assessed EBT2 film and tried to eliminate the film response deviations as much as possible. Regarding the results of the present study and importance of independent check of radiation therapy systems, that is strongly recommended on resources, the implemented manner could be used as a quick quality check approach at least for one applicator monthly. In addition, lack of a reliable TPS of the device makes the importance of acquiring such accurate knowledge of radiational properties of various applicator sizes more clear. Such investigation is of significance for other Intrabeam™ applicator types such as flat and surface ones.

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