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Original research article

Radiation dose verification of an X-ray based blood irradiator using EBT3 radiochromic films calibrated using Gamma Knife machine

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ABSTRACT

Aim: Blood irradiators (BI) initial acceptance testing and routine annual dosimetry checks require radiation dose measurements in order to comply with regulatory requirements.
Background: Traditionally thermo-luminescence dosimeters (TLD) have been used to measure the dose. The EBT3 film is reported to be a better dosimeter for low energy X-rays than its predecessors EBT2 and EBT. To the best of our knowledge, the use of EBT3 films to perform dosimetry on X-ray based BI has not been reported yet.
Materials and methods: We performed routine radiation dosimetry checks using EBT3 films on a new X-ray based BI and compared the results with TLD dosimetry. Calibration films were irradiated with radiation beam from a Co-60 Gamma Knife (GK) radiosurgery machine and, alternatively, using an Ir-192 high dose rate (HDR) brachytherapy device. The films were calibrated to cover a wide dose range from 1 to 40 Gy. Such a wide dose range has not been reported yet in BI film dosimetry.
Results: We obtained a relative difference of about 6.6% between doses measured using TLD and those measured using EBT3 films. Both irradiation methods using GK or HDR were found to be adequate for the calibration of the EBT3 Gafchromic films.
Conclusions: We recommend the use of EBT3 films in routine X-ray based BI dosimetry checks. The presented method takes advantage of available radiotherapy equipment that can be efficiently used for EBT3 films calibration. The method is fast, reproducible and saves valuable medical physicist's time.

1. Background

Irradiation of whole blood components before transfusion is currently the only accepted method to prevent transfusion-associated graft-host-disease (TA-GVHD).[1] An absorbed dose of 25 Gy is necessary to prevent TA-GVHD.[2]

The American Food and Drug Administration (FDA) recommend the use of 25 Gy delivered to the center of the canister with maximum and minimum doses of 50 and 15 Gy, respectively, anywhere in the irradiated blood bags.[3]

It is necessary to have a procedure that enables the blood bank staff to verify the accuracy of the radiation dose delivered to the blood bags during irradiation using blood irradiators.

The use of thermoluminescence dosimeters (TLD) is the most prevalent method in dosimetry of blood irradiators.[4] Lately, Films have been used as dosimeters for blood

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irradiation[5]; most of the reported studies are for Cs-137 and Co-60 irradiators and none for X-ray based ones.

EBT and EBT2 Gafchromic films have displayed significant energy dependence in kilovoltage energy range.[6] The EBT3 Gafchromic films exhibit low energy dependence for energies in the order of 1.25 MeV, the same energy of the cobalt 60 was used for film calibration in this study; eliminating energy correction to the measured doses.

Another study suggested EBT3 as a more suitable dosimeter for kilo-voltage X-rays beams since it has a weaker energy dependence than EBT2 and EBT in that range.[7] Furthermore, EBT3 was found to be useful dosimetric tool for absolute Quality assurance and depth dose measurements of kV contact radiotherapy[8]; and as a dosimeter for kV X-ray applications, such as a small animal irradiator.[9]

To the best of our knowledge the use of EBT3 films to perform dosimetry on X-ray based BI has not been reported yet in the literature.

2. Aim

We are proposing to compare the doses measured using EBT3 films to those measured using the standard TLD. The objective of the present work is to evaluate EBT3 radiochromic films as practical dosimeters that can be used for radiation dose verifications and routine annual quality assurance of blood irradiators. The ^{60}Co radiation of a gamma knife radiotherapy machine will be used to calibrate the films against specific dose levels in the range of 1–40 Gy.

We are claiming a practical and efficient method for blood irradiators' radiation dose verification using Gafchromic EBT3 film calibrated using Leksell Perfexion Gamma Knife (GK) radiosurgery machine (Elekta, Stockholm, Sweden) available at the radiation oncology department in our tertiary care medical center.

3. Materials and methods

A quality assurance method consisting of measuring the dose distribution inside the irradiator canisters was established in our medical institution. The method uses EBT3 radiochromic films as radiation dosimeters. The film net optical density (NOD) is linked to the radiation dose in (Gy) using a lookup table generated by the PTW FilmCal software version 2.3.

Dosimetry phantoms provided by the vendor of the BI equipment RS 3400 X-ray Blood Irradiator (Rad Source, Suwanee, Georgia, USA) was used to irradiate the EBT3 dosimetry films. Fixing the films strips at the same location as the TLD allowing direct comparison of the measured doses using the 2 methods.

The irradiator is self-contained with 4 Pi emitter X-ray technology, the photons energy is 140 kV, and it produces 25 Gy at the center of a one liter canister housing the blood bags in 4.67 min, the approximate dose rate of 5 Gy/min. The irradiator has 6 canisters that circulate around the X-ray Source providing acceptable dose distribution uniformity.

Fig. 1(a) shows the blood irradiator, (b) the dosimetry phantom simulating a blood irradiator canister and (c) the EBT3 films strips.

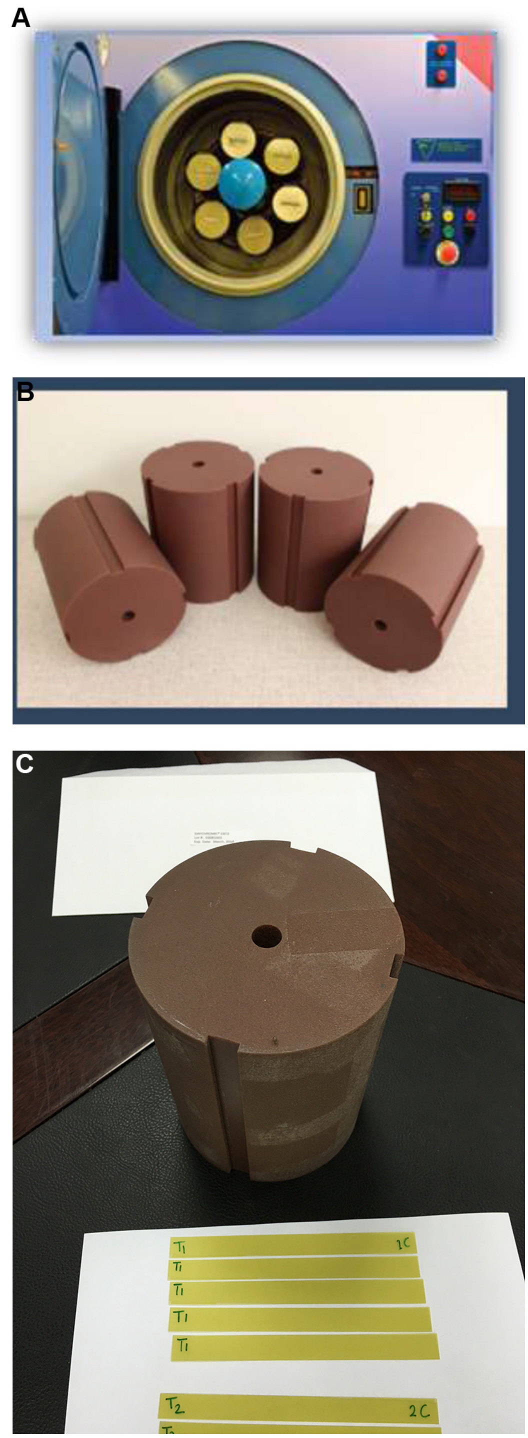

Fig. 1 – Blood irradiator (a) view and the dosimetry phantom (b) simulating blood irradiator canister and EBT3 films strips (c).

3.1. *Film calibration using GK*

9 film pieces of 4 cm × 4 cm of Gafchromic EBT3 films (Lot Number: 03081601), were used to create the film calibration curve. The films were irradiated using Perfexion Gamma Knife machine (^{60}Co, dose rate = 2.474 Gy/min) using 16 mm collimator. The films were placed separately in the GK brown phantom

at the isocenter level, keeping the same orientation for all films. Irradiation time was calculated to deliver 5, 10, 15, 20, 25, 30, 35 and 40 Gy. Another piece of film was irradiated with 28 Gy to check the accuracy of the procedure.[10]

The radiation doses delivered by the Perfexion machine are calibrated using the PTW Semiflex 31010 chamber, which has been calibrated at PTW facility with calibration traceable to the national standard of the German National Laboratory with uncertainty of 1.1%. 1 cm × 12 cm strips of film were cut from the same film sheet as used earlier and irradiated using the blood irradiator. All films were left for 24 h before reading. PTW (PTW, Freiburg, Germany) FilmCal version 2.3 software was used to read the dose values on both the calibration films irradiated using the GK machine and the actual film strips irradiated by the blood irradiator.

The films were scanned using Epson Expression 10000 XL flatbed scanner. Fig. 2 shows a screenshot of the PTW FilmCal software showing the film OD versus the true dose in (Gy).

3.2. *EBT3 film scanning procedure*

In order to improve the accuracy of the dose measurement method, both calibration and measurement films were irradiated at the same time.[11]

To eliminate film non-uniformity due to post-exposure darkening evolution of EBT3 films, both calibration and measurement films were scanned and analyzed at the same time 24 h post-exposure to radiation to ensure film darkening stabilization.[12]

To eliminate other non-uniformities during scanning, all used films were taken from the film sheet of the same batch; they were placed in the landscape orientation and positioned at the center of the flatbed scanner surface. Both calibration and measurement films were scanned in the same orientation as recommended.[13]

Three pre-scans were performed prior to scanning for the scanner lamb to warm-up. We marked the films to ensure positioning regularity, and with dose information for identification purposes.

The films were scanned in the red-blue-green (RGB) image format using Epson Expression 10000 XL flatbed color scanner (Epson, Long Beach, CA, USA). Positive film mode was selected with 72 dpi for resolution, 48-bits color depth and without image correction.

A non-irradiated reference film piece was scanned and used to correct for the background reading of the EBT3 films; all calibration films were digitized in a single scan to eliminate scan-to-scan variability.[14]

3.3. *Film calibration using ^{192}Ir from HDR afterloader*

We also used another commonly available radiotherapy source of radiation to calibrate the EBT3 films for medical centers that do not have a GK machine. The source is a ^{192}Ir HDR machine. For the purpose of using ^{192}Ir with averaged energy of 380 keV to calibrate films, small strips of 1 cm × 4 cm were used. The film strips were taped at the surface of a 3.0 cm diameter vaginal vault applicator and warped with a 0.5 cm bolus, taking into account the orientation of the films.

The position of the source was calculated and marked on each film. The dose delivered was 10, 20, 25, 30, 35, 40 Gy. Another film strip was irradiated with 23 Gy to check the accuracy of the procedure. The dose rate of the ^{192}Ir source at the time of irradiation was 13,451 cGy/min cm^2, the ^{192}Ir on

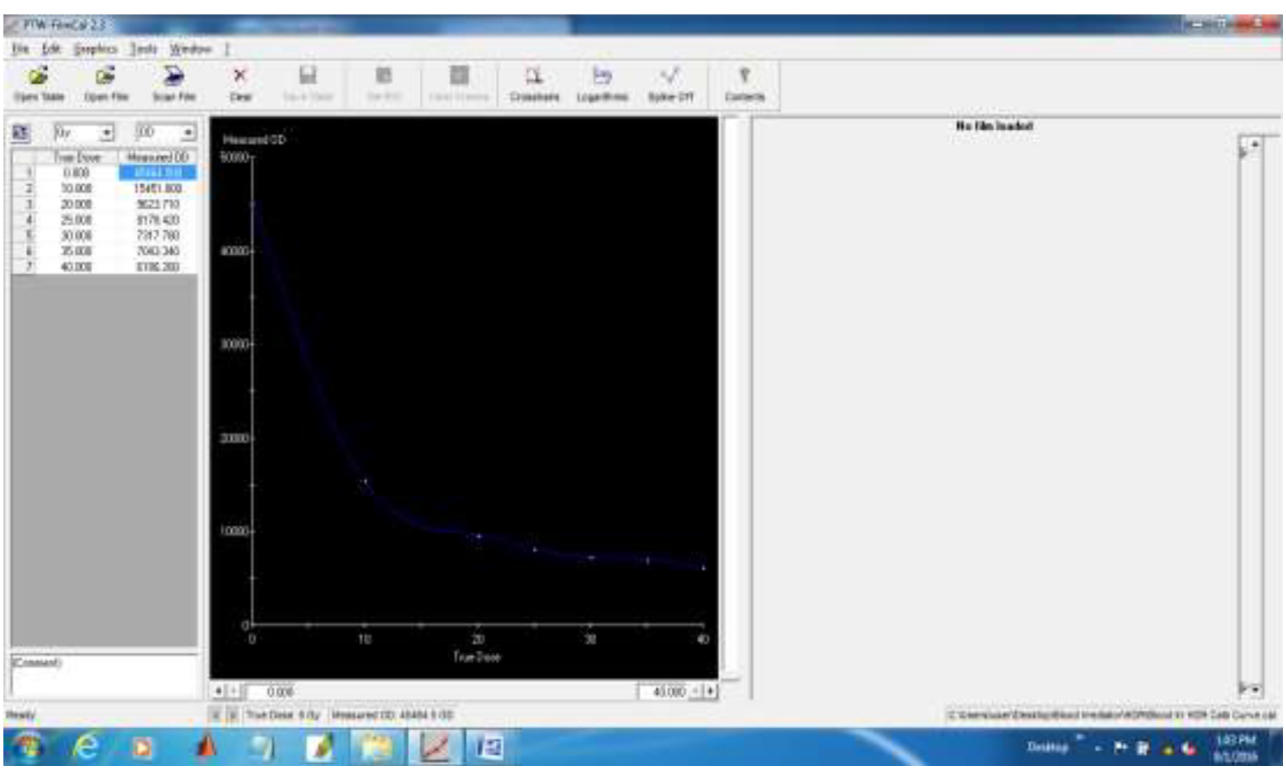

Fig. 2 – Screen shot of the PTW FilmCal 2.3 software.

Varisource machine (Varian Palo Alto, CA. USA) is calibrated using Standard Imaging well type HDR 1000 plus an ionizing chamber. The agreement between the measured source activity and the one provided by the manufacturer is less than 1%.

3.4. *Calculation of the film net optical density (NOD) and fitted film calibration curve*

The PTW FilmCal Ver 2.3 software displays the film optical density along with the corresponding radiation dose in (Gy). In order to be consistent with the way radiochromic films calibration is presented in the literature, we calculated the NOD and plotted the radiation dose as a function of the NOD. Matlab curve fitting toolbox was used to drive a fit function that best describes the film radiation dose and the NOD relationship.

The film optical density is given by (Eq. (1)):

$$OD(x, y) = \log\left[\frac{I_0(x, y)}{I(x, y)}\right] \tag{1}$$

where $I(x,y)$ is the intensity of the pixel value located at line (x) and colom (y) of the film image matrix. I_0 is the background intensity.

And the film net optical density (NOD) is defined in Eq. (2):

$$\text{NOD} = -\log(\text{signal exposed film} - \text{signal control film}) \tag{2}$$

3.5. *Advantages of EBT3 film dosimetry*

The EBT3 films were recently shown to be dose rate independent in the range of 2–40 Gy/min.[15] Low uncertainty and energy-dependence make EBT3 films suitable for dosimetry in various applications, with the red channel being the most sensitive to the measured dose.[16]

Furthermore, EBT3 films response was not dependent on photons energy levels or on the dose rates used during film irradiation.[17]

There are a number of advantages of using film dosimetry to check the delivered radiation dose to the blood components being irradiated for clinical utilization in hematology departments. The first one is the two-dimensional dose distribution information available on the irradiated films; the distribution reflects the expected dose distribution inside the sample compartment of the blood irradiator[18]; Secondly, the visual observation of the irradiated film could be used as an indication of irradiated blood and serve to ensure the distinction between blood bags being irradiated from those that have not been irradiated. A small piece of un-irradiated film can be fixed at the surface of the blood bag being irradiated.

3.6. *Differences between EBT3 and EBT-XD films for blood irradiator dosimetry*

We used Gafchromic EBT3 films since they had been recommended for measurements involving low energy X-rays as in X-ray based blood irradiators.[19]

It is important to mention that this work was performed in early 2016. At that time the EBT-XD model was just newly introduced with no reference studies in the literature that validated EBT-XD films to measure kilo-voltage X-rays. Only recently, in March 2018, did a study conclude that EBT-XD films showed the same characteristics on film darkening as EBT3. And EBT-XD films showed a similar dosimetric response for photon and proton irradiation with low energy and beam quality dependency as EBT3 films.[20]

EBT3 has been tested for radiation dose dynamic range including calibration curves for doses of up to 40 Gy in numerous publications,[21–23] and up to 30 Gy in Refs. 15,24 and has been used to measure radiation doses upwards of 35 Gy from 75 kVp, 200 kVp, 6 MV and (28 keV) I-125 photon sources in Ref. 25. It has been evaluated for dose uncertainties for doses of up to 120 Gy in Ref. 26. We can conclude from this that EBT3 films can be used to measure radiation doses of up to 40 Gy. Lewis and Chen[27] mentioned: EBT-XD is less sensitive than EBT3, a greater exposure dose is required to reach the same net response. On this basis, the lower sensitivity of EBT-XD relative to EBT3 results in less net response change for equal exposure and a reduction in the impact of the lateral response artifact. For doses $\geq$10 Gy, the slopes of the EBT-XD red and green channel dose response curves are greater than the corresponding ones for EBT3. For these two reasons, the authors prefer EBT-XD for doses exceeding approx. 10 Gy.[27] We conclude from this that the advantage of EBT-XD film over EBT3 for doses above 10 Gy is useful for applications requiring a great deal of precision such as stereotactic radiosurgery (SRS) dosimetry but not required for blood irradiator dosimetry verifications.

3.7. *Advantages of using GK or HDR to calibrate EBT3 films*

The main advantage of using GK or HDR radiotherapy machines in EBT3 film calibration is being able to deliver a large radiation dose of up to 40 Gy in short time, taking advantage of the inherent high dose rates delivered by these machines. Most of published work regarding dosimetry of blood irradiators do not cover the radiation dose range covered in this work (1–40) Gy, which proves the originality of this work. We should remember that according to the clinical requirement for blood irradiation, dose levels of 30 Gy are often measured.

4. Results

Using EBT3 films and for 14 dose positions over the irradiation volume throughout the simulated blood bags the minimum and maximum doses were 24.8 and 37.4 Gy, respectively.

The mean dose was (30.3) Gy with a standard deviation of 4.4 Gy and the coefficient of variability was 14%. Table 1 shows the results of 14 points of dose measurements using both methods: EBT3 and TLD.

TLD dosimetry was performed by the Radiation Dosimetry Services at the MD Anderson Cancer Center (Houston, Texas, USA). The measured doses in the TLD dosimetry report are accurate to ±10% and traceable to the national institute of standards and technology (NIST).

Table 1 – The radiation doses measured at 14 different locations on the blood irradiator sample irradiation canisters.

TblColHeadDose measured using (D_{EBT3}) in (Gy)	Dose measured using (D_{TLD}) in (Gy)	Dose difference abs($D_{TLD} - D_{EBT3}$) in (Gy)	% Dose difference [abs($D_{TLD} - D_{EBT3}$)/D_{TLD}]*100%
25.5	27.9	2.4	8.6%
27.9	29.7	1.8	6.1%
24.8	23.7	1.1	4.6%
31.0	32.7	1.7	5.2%
37.2	34.9	2.3	6.6%
28.6	28.7	0.1	0.3%
34.6	31.0	3.6	11.6%
26.0	26.2	0.2	0.8%
28.2	28.5	0.3	1.1%
26.6	21.8	4.8	22.0%
31.8	31.3	0.5	1.6%
37.4	33.5	3.9	11.6%
29.4	26.9	2.5	9.3%
35.6	34.4	1.2	3.5%
Average = 30.3 Gy	Average = 29.4 Gy	Average = 1.9 Gy	Average = 6.6%

The relative average difference in percentage between the measured doses using the EBT3 films calibrated using GK and the reported TLD measurements was 6.6%; calculated as:

$$\%\ \text{difference} = \left[\frac{D_{TDL} - D_{EBT3}}{D_{TLD}}\right] \times 100 \quad (3)$$

We also measured a 7% difference between the dose measured by EBT3 films and calibrated using the HDR machine and the TLD method.

We fitted the film dose response for both the GK and the HDR methods. We noticed that there was a small but significant difference in the film response, especially at dose levels above 25 Gy. The observed difference indicates that EBT3 film responds differently to the two methods of calibration, namely GK and HDR, probably due to the energy difference between Co-60 and Ir-192.

The observed difference does not affect the accuracy of the measured doses using EBT3 films in comparison with the TLD. The overall uncertainty of the measured dose using EBT3 film is in the order of 7% based on the method described in Ref. 26.

We found that an exponential function given in Eq. (4) below produces the best fit for our data using Matlab curve fit tool.

$$\text{Dose (Gy)} = a * \text{Exp}(b * \text{NOD}) \quad (4)$$

In Eq. (4), parameters a and b for the GK fit were 1.245 and 3.859, respectively, and for the HDR fit they were equal to 1.615 and 3.723, respectively. Fig. 3 shows the exponential fit function for both calibration sources.

With this observation made, we can recommend that both sources can be used depending on their availability in medical centers offering radiation therapy services to oncology patients.

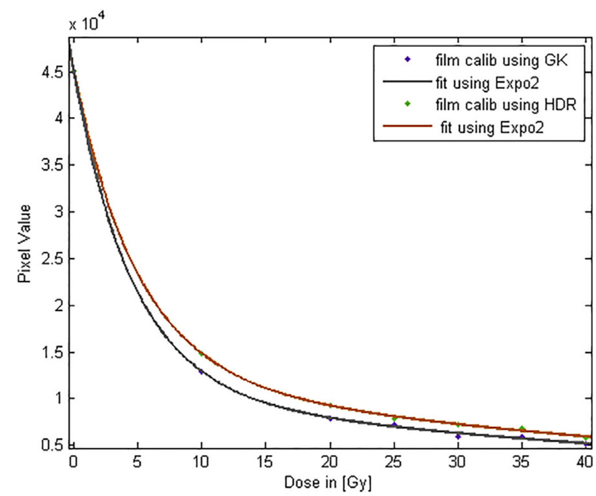

Fig. 3 – Film response in terms of radiation dose in (Gy) as a function of the net optical density (NOD) for two calibration methods using ^{60}Co gamma rays from GK machine and ^{192}Ir gamma rays from HDR machine.

5. Discussion

The dose delivered by the GK system is accurate and traceable to international primary standard laboratory according to the available system calibration certificate.

The proposed dosimetry method was compared to the gold standard dosimetry system in the field of blood irradiation which is the thermoluminescence dosimetry (TLD) system and found to be in good agreement.

The method is simple, reproducible and less time consuming than the TLD system; it also has better spatial resolution characteristics allowing the possibility of obtaining radiation dose profiles along different axes in the canister cylindrical geometry. The films calibration can be done using either a GK or HDR radiotherapy machines available in radiation therapy departments. The entire dosimetry and calibration procedures can be done on the same day and take about few hours only saving valuable medical physicist's time.

We encourage medical institutions to use the proposed method in acceptance testing and in the routine annual quality assurance testing of blood irradiators.

6. Conclusions

EBT3 radiochromic films are useful and accurate dosimeters with 6.6% mean error compared to TLD, they can be used for the verification and measurement of absorbed dose delivered to cellular blood products as a result of routine blood irradiation procedure in hematology departments.

Conflict of interest

None declared.

Financial disclosure

None declared.

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