

Probability Distribution of Pixel Intensities of EBT3 Films and its Application in the Correction of Uncertainty Budget

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Abstract

Background and Aim: Modern radiotherapy modalities, such as Intensity-Modulated Radiotherapy and Volumetric Modulated Arc Therapy involve complex dose delivery. The dose delivery is complex as it involves beam modulation, hence, manual dose calculations for these techniques are not possible. Film dosimetry is commonly used method of dose verification for these modalities because of the advantages associated with it. The quantification of uncertainty associated with a film dosimetry system under clinical use becomes important for accurate dosimetry. The spread in the distribution of the pixel values (PV) of the irradiated film contributes to the uncertainty. The probability distribution (PD) of the PV was studied for the clinical photon beam energies of 6, 10, and 15 MV. **Methods and Materials:** Gafchromic EBT3 film and EPSON 10000XL flatbed scanner were used for this purpose and using the resulting PD, the uncertainty budgets for these energies in the red, green and blue color channels were estimated. **Results:** The PV of exposed films for the energies studied follows t-distribution, the sum of the squares of the deviation of the measured data from the fitted value was of the order of 10^{-7} , this indicates the goodness of fit. The “t” value corrected combined standard uncertainty (CSU) at 1σ confidence level for exposed film and dose measurement at 200 cGy were 1.42%, 1.48%, and 1.63% and 1.99%, 3.23%, and 5.08% for 6, 10, and 15 MV energies, respectively, in the red colour channel. **Conclusion:** In the case of the limited number of measurements of a quantity, the SU values must be corrected using the “t” value to get the correct CSU.

Keywords: EBT3 films, film dosimetry, flatbed scanners, uncertainty budget

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INTRODUCTION

Modern radiotherapy techniques, such as intensity-modulated radiotherapy and volumetric modulated arc therapy involve complex dose delivery. Manual calculations of the dose are not possible for these modalities. Hence, the pre-treatment dose verification of these techniques is often done by comparing the planned dose distribution, calculated by the treatment planning system with the measured dose distributions and performing the gamma analysis. The measurement of the dose distribution is done by two-dimensional arrays or radiochromic films.

Radiochromic films such as Gafchromic EBT3 (Ashland International Speciality Products Advanced Materials, Wayne, NJ, USA) are frequently used in radiotherapy dosimetry because of the known advantages associated with it, such as, nearly tissue equivalent composition,^[1] weak energy dependence,^[1-4] dose rate independence of response^[5] and high spatial resolution.^[6] The radiochromic films undergo polymerization and develop self-darkening when irradiated by

the ionizing radiations. The darkening developed in the film as a result of the irradiation is quantified in the terms of net optical density (NOD) which is the measure of absorbed dose.

In order to digitize the films, film scanners are used. Film scanner consists of the light source and a charge-coupled device to receive the light transmitted through the irradiated film. The radiochromic film along with the scanner constitutes the film dosimetry system (FDS).

Over the years, different models and types of film scanners have been used for film dosimetry, for example, roller-based (VIDAR VXR Dosimetry Pro Advantage, VIDAR Systems

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Corporation, VA, USA) and commercially available flatbed scanners (FBS) such as EPSON 10000XL (Seiko Epson Corporation, Nagano, Japan), etc. These scanners have been studied in detail by various groups,^[7-9] FBS are widely used with Gafchromic EBT film types because of the better results shown, as compared to the roller-based scanners.^[10]

Film dosimetry requires precautions during the handling, irradiation and scanning to minimize the sources of uncertainty and to improve the accuracy. Therefore, uncertainty quantification of the FDS for clinical energies becomes necessary for the success of treatment.

It has been observed that, during the analysis of scanned film image, there is a spread in the pixel values (PV) of the irradiated film, this introduces uncertainty in the measurement of the absorbed dose. The spread of the PV is described by the probability distribution (PD) curve and its nature is important in the determination of uncertainty. In the present study, the nature of PD of the PV has been studied for the dose of 200 cGy, delivered by 6, 10, and 15 MV photon beams.

The resulting PD (t-distribution [TD]) was applied to estimate the uncertainty budgets of 6, 10, and 15 MV photon beams, which were otherwise, estimated assuming the Gaussian distribution of measurement (or sample) data.^[6-8] In the absence of sufficient data, this assumption may decrease the confidence in the value of reported combined standard uncertainty (CSU). TD has been used to correct the SU values, associated with individual components of radiochromic film dosimetry in the cases, involving the limited number of measurements of a quantity.

MATERIALS AND METHODS

Film handling and sample preparation

EBT3 films have an expiry period of about 30 months from the date of manufacturing. EBT3 films within the expiry date were used for dosimetry purposes. The films were handled either using gloves or vacuum tweezers, films were kept in the dark when not in use and were handled in the interior room light as per the recommendations of the EBT3 film specifications manual.^[11]

Square film pieces of 5 cm × 5 cm were used for the study, film samples were numbered at the top right corners to maintain the identity of orientation at the time of placing the film samples on the glass plate of FBS.

Flatbed scanner settings and film scan

Flatbed scanner settings

The EPSON scan software (version 3.49 A) was used for the scan of the film on the FBS. The films were scanned in 48 bit red, green and blue (RGB) colour mode at 72 dots per inch resolution.^[12] The image enhancement features were turned off and scanned images were saved in Tiff format.

Film scan

The EPSON 10000XL scanner's lamp turns on at the time of preview or scan. In order to stabilize the response of scanner,

the practice of ignoring first seven scans was followed before starting the actual measurements.^[8] Since portrait orientation of the film has higher dose-response and lesser uncertainty in determining the dose than landscape orientation,^[13] the films were scanned in the portrait orientation at the center of glass plate of FBS to minimize the effect of non-uniformity of response of the scanner.^[14] This also ensures the reproducibility of film positioning.

The compression glass plate is recommended above the film to ensure flat-film scanning.^[15] This removes the uncertainty arising due to the non-contact of the film with the glass plate of the scanner. Figure 1 shows an example of the placement of the glass plate to make the film in perfect contact with the scanner's glass plate. The films were read after the waiting period of 48 h post irradiation.^[16]

Film irradiation and image analysis

Irradiation geometry and uncertainty in the dose delivery

The irradiations were carried out on the True Beam® linear accelerator (Varian Medical Systems, Palo Alto, USA). Prior to the irradiation of the films on the linear accelerator, the uncertainties in the outputs of 6, 10 and 15 MV beams were estimated following the procedure mentioned in IAEA-TECDOC-1585.^[17] The film irradiation and ionization chamber measurements were done using the slab phantom in the isocentric geometry at 10 cm depth by 10 cm × 10 cm field size. Twelve calibration doses extending through the optimum range of EBT3 films, i.e., 0.2–10 Gy were delivered for the calibration of EBT3 films.^[18]

Image analysis

Image J software (Version 1.51a, National Institute of Health, Bethesda, Maryland, USA) was used for the image analysis. The region of interest (ROI) of 4 cm × 4 cm was chosen for reading the PV in the RGB colour channels.^[18]

Probability distribution of the pixel values

The nature of spread in the PV of films, irradiated by 6, 10 and 15 MV beams to the dose of 200 cGy was determined by

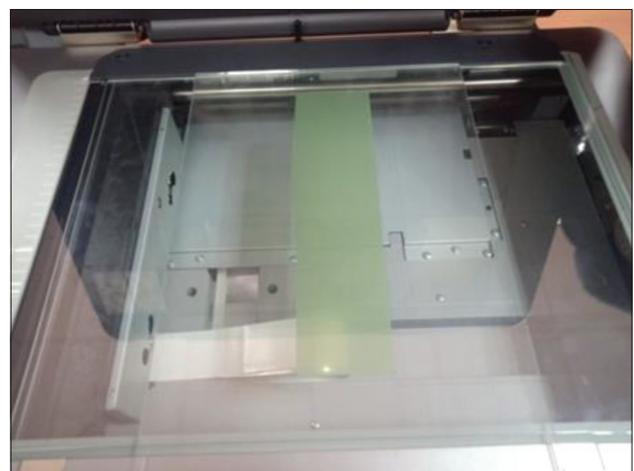


Figure 1: Photograph of the placement of glass sheet over the film to make it in perfect contact with the glass plate

plotting the PD function of PV in the RGB channels for above-mentioned energies. The probabilities of PV were obtained by taking the ratio of the counts of particular PV to the total pixels counts in the ROI. For better readability of the data, corresponding normalized histograms and 1σ confidence levels have also been plotted. The data was fitted with TD and the goodness of fit was estimated by the sum of squares of the deviation of measured data from the fitted value.

The “*t*” value of TD was used for determining confidence intervals (CI) and hence, SU of the components of the exposed films, this was used further in determining the CSU (total uncertainty) of the exposed films and the experiment.

The CI of the mean PV of the data following TD is given by

$$\left[\mu - t \times \frac{\sigma}{\sqrt{n}}, \mu + t \times \frac{\sigma}{\sqrt{n}} \right] \quad (1)$$

here, μ = Mean of the samples

σ (Sigma) = Standard deviation of the mean of samples

t = TD critical value for the given degrees of freedom (DF) and probability, available from standard tables

n = sample size

In this study, the SU of the components of the exposed film has been obtained from error (\pm) term of eq. (1), expressed as the percentage of the mean PV.

Film calibration and curve fitting

Calibration curves were plotted between the NOD and delivered doses for the three colour channels. The expression used for the calculation of NOD^[19] is as follows:

$$\text{NOD} = \log_{10} \frac{I_{\text{unexp}} - I_{\text{bckg}}}{I_{\text{exp}} - I_{\text{bckg}}} \quad (2)$$

here, I_{exp} , I_{unexp} and I_{bckg} are the PV for exposed, unexposed films and dark sheet, respectively.

Non-linear relationship was used to obtain dose from the measured NOD,^[20]

$$D = a \cdot \text{NOD} + b \cdot \text{NOD}^c \quad (3)$$

Here, *a* and *b* are fitting parameters and *D* is the delivered dose. Parameter *c* has the value that gives the best fitting results and generally lies between 2 and 3. For our experimental data, the value of 2.5 gave the best fitting results. Levenberg-Marquardt optimization algorithm was used for the fitting of experimental data, this is because this algorithm is adapted for the fitting of multiple parameters and non-linear functions.^[21]

Uncertainty estimation

The uncertainty in the film dosimetry is divided into two parts (1) experimental uncertainty and (2) uncertainty due to curve fitting. The overall uncertainty is the sum in quadrature of relative experimental uncertainty and relative fitting uncertainty.^[21]

Relative experimental uncertainty

The relative experimental uncertainty is given by the expression^[19]

$$\sigma_{D_{\text{exp}}} (\%) = \frac{\sqrt{(a + b \times c \times \text{NOD}^{c-1})^2 \times \sigma_{\text{NOD}}^2}}{D_{\text{fit}}} \times 100 \quad (4)$$

Here, σ_{NOD} is the SU in the NOD value which is calculated by using the error propagation expression,^[22]

$$\sigma_{\text{NOD}} = \frac{1}{\ln 10} \sqrt{\frac{\sigma_{I_{\text{unexp}}}^2 + \sigma_{I_{\text{bckg}}}^2}{(I_{\text{unexp}} - I_{\text{bckg}})^2} + \frac{\sigma_{I_{\text{exp}}}^2 + \sigma_{I_{\text{bckg}}}^2}{(I_{\text{exp}} - I_{\text{bckg}})^2}} \quad (5)$$

here, $\sigma_{I_{\text{unexp}}}$, $\sigma_{I_{\text{exp}}}$ and $\sigma_{I_{\text{bckg}}}$ are the SU of measured I_{unexp} , I_{exp} and I_{bckg} respectively, estimated using eq. (1). D_{fit} is the dose estimated as the result of fitting of the calibration data. The I_{bckg} was measured by placing a completely dark sheet over the scanner’s glass plate and taking the average of the scan values over the whole glass surface. These values remained constant throughout the experiment. Figure 2 shows the arrangement to scan the black sheet for the measurement of I_{bckg} . Similarly, I_{unexp} was obtained by computing the mean of the response of unexposed film samples of size 5 cm × 5 cm. These values also remained constant throughout the experiment.^[21]

To find the CSU of the exposed films, the SU due to the individual components (intra sheet, inter sheet, intra scanner uniformity, scanner reproducibility, scanner warm up effect, output of linac, film orientation, effect of reading delay, film positioning reproducibility, gap between film and glass plate of the scanner) were assumed independent of each other and the CSU of the exposed film was obtained by adding the SU of components in the quadrature. Table 1 describes the method to estimate the uncertainty due to the individual components (except, the output of linac) as mentioned above.^[21]

Fitting uncertainty

The relative fitting uncertainty is given by,



Figure 2: Arrangement to scan the black sheet to measure the I_{bckg}

$$\sigma_{D_{fit}} (\%) = \frac{\sqrt{NOD^2 \times \sigma_a^2 + NOD^{2c} \times \sigma_b^2}}{D_{fit}} \times 100 \quad (6)$$

Here, σ_a and σ_b are the uncertainties associated with fitting parameters a and b, respectively.^[19]

RESULTS

Film calibration and curve fitting

Figures 3-5 show the calibration curves for 6, 10, and 15 MV energies, respectively in the RGB color channels. Table 2 shows the values and uncertainties of the fitting parameters of the fitted non-linear equations in the RGB channels for the photon energies under the study.

Uncertainty in the output of the linear accelerator

The uncertainty in the output of linear accelerator was quantified by the ionization chamber measurements. The uncertainty in the output was <1% for all the photon beams under the study, which is in agreement with the other studies.^[23] This value was

considered for the uncertainty budget estimation.

Probability distribution of the pixel values

Figures 6-8 show the PD curves of the PV along with the normalized histograms of the films in the RGB colour channels, irradiated to the dose of 200 cGy by 6, 10 and 15 MV energies, respectively. It can be observed that, the PD curves are symmetrical about the mean PV for all the color channels for the studied energies. The sum of squares of the difference between measured and TD fitted data was of the order of 10^{-7} , this shows the goodness of fit of the TD. The 1σ CI of mean is shown by shaded area on the PD curves.

Uncertainty budget

The uncertainty budget of exposed film is shown in Table 3. The relative experimental uncertainty and fitting uncertainties at 1σ confidence level for 6, 10 and 15 MV energies in RGB color channels are shown in Table 4.

Table 3 shows that the CSU of the exposed films are 1.42%, 1.48% and 1.63% for 6, 10 and 15 MV energies, respectively

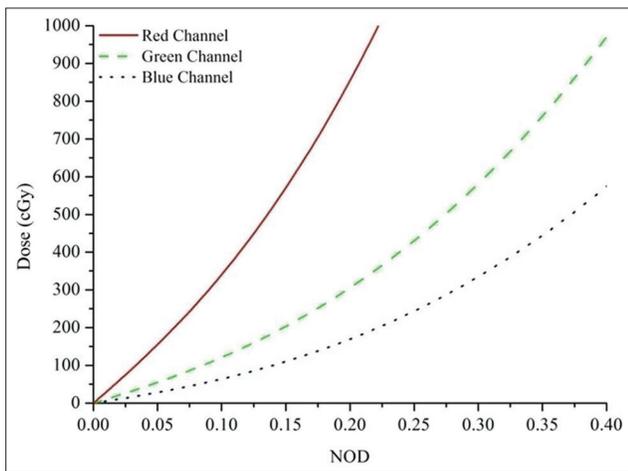


Figure 3: Calibration curves for 6 MV energy in the red, green and blue colour channels

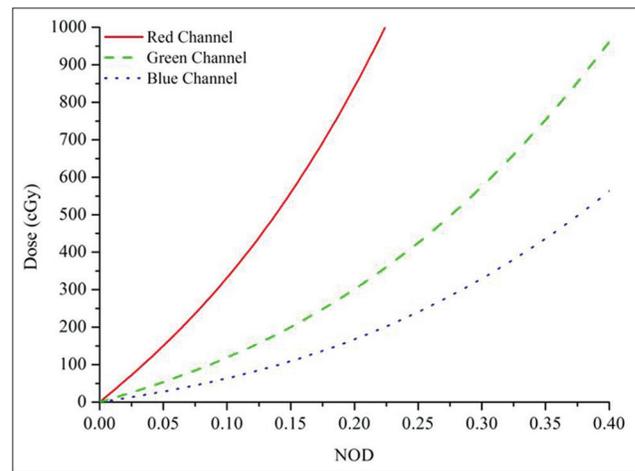


Figure 4: Calibration curves for 10 MV energy in the red, green and blue colour channels

Table 1: Components of the uncertainty of an exposed film and the methods to estimate them

Component of uncertainty	Method of estimation
Intra film uniformity	Sheet of film was cut into multiple pieces and exposed to same dose of 200 cGy, each one was read 3 times and the standard deviation of the average value I_{exp} of 3 readings of film pieces was computed
Inter-film reproducibility	Quantified by measuring the I_{exp} of the film pieces from three different sheets, irradiated with the same dose. Each film piece was read 3 times to exclude single film reproducibility and standard deviation of mean values for three film pieces was computed
Intra-scanner uniformity	Evaluated by quantifying I_{exp} at the same position within $5\text{ cm} \times 5\text{ cm}$ film piece, scanned over several spots covering the full scanner screen and standard deviation of the mean values was computed
Scanner reproducibility	Multiple scans of the same film at the centre of the scanner were read over the same area and standard deviation was computed
Scanner warm up effect	Initial seven scans were ignored, standard deviation of the mean of the later scans was computed
Effect of film orientation	Eliminated by adopting the portrait orientation of film scan throughout the experiment
Effect of reading delay	Eliminated by reading the films 48 h post irradiation
Reproducibility in film positioning	Film pieces were placed at the centre of scanner with the help of in-house made template
Effect of the gap between the film and glass plate of scanner	Eliminated by placing the glass plate over the film at the time of film scan

Table 2: Values of the fitting parameters and associated uncertainties for 6, 10 and 15 MV energies in red, green and blue colour channels

Parameter	Value (cGy)								
	6 MV			10 MV			15 MV		
	Red	Green	Blue	Red	Green	Blue	Red	Green	Blue
a	524.9	1035	2930	526.1	1016	2831	490.56	1064	2712
b	3598	5492	1.50E+04	3483	5486	1.54E+04	3592.91	5082	1.59E+04
σ_a	15.38	25.63	55.51	24.56	36.59	42.75	37.98	15.91	73.06
σ_b	48.72	118.2	627.2	76.45	167.7	477.2	118.68	71.44	804.9

Table 3: Uncertainty budget of the exposed film for 6, 10 and 15 MV energies in red, green and blue colour channels at 1 σ confidence level

Components of uncertainty	Uncertainty (%)								
	6 MV			10 MV			15 MV		
	Red	Green	Blue	Red	Green	Blue	Red	Green	Blue
Intra sheet uniformity	0.21	0.25	0.08	0.38	0.28	0.22	0.59	0.11	0.02
Inter sheet uniformity	0.51	0.31	0.32	0.70	0.63	0.52	0.66	0.70	0.48
Intra scanner uniformity	0.82	0.70	0.82	0.73	0.57	0.65	0.87	0.84	0.95
Scanner reproducibility	0.13	0.12	0.03	0.07	0.03	0.11	0.33	0.26	0.29
Scanner warm up effect	0.14	0.08	0.04	0.07	0.05	0.05	0.02	0.02	0.03
Linac output uncertainty	1	1	1	1	1	1	1	1	1
Film orientation	Eliminated (≤ 0.01)								
Effect of reading delay									
Reproducibility in film positioning									
Effect of the gap between the film and glass plate of scanner									
Film handling and sample preparation									
Combined standard uncertainty	1.42	1.29	1.34	1.48	1.34	1.33	1.63	1.51	1.49

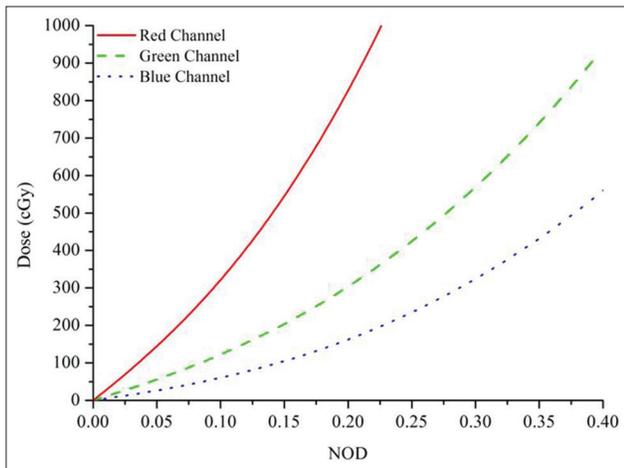


Figure 5: Calibration curves for 15 MV energy in the red, green and blue colour channels

in the red color channel. Red color channel has the highest CSU for the exposed film, whereas, rest of the color channels have almost similar uncertainties for all the energies studied.

It can be observed from Table 4 that, total uncertainty in the dose determination is 1.99%, 3.23% and 5.08% for 6, 10 and 15 MV energies respectively, in the red color channel.

DISCUSSIONS

The PD of the PV in the EBT3 film dosimetry was studied, and it was found that the PV PD fits well TD. The TD approaches the Gaussian behavior for large sample size or degrees of freedom.

Earlier studies have estimated the uncertainty budget associated with radiochromic film dosimetry assuming the Gaussian distribution. This assumption may underestimate the confidence level for the limited number of measurement data. Application of the TD in the estimation of the SU corrects the uncertainty budget.

TD has been applied here because, the data of any film dosimetry experiment is assumed to be the sample from Gaussian distribution, whereas the sample size (generally 3 or 5 readings) itself is too small to be normally distributed, in these situations TD corrects for this assumption, this is achieved by including the “*t*” value in the expression for CI (eq. [1]).

The uncertainty budget for EBT3 film and EPSON 10000XL FBS FDS has been estimated on the basis of TD. Wherever possible, the sources of the uncertainty were reduced to $\leq 0.01\%$ and were therefore excluded in the estimation of uncertainty budget. The remaining sources of the uncertainty were kept as minimum as possible following the procedures mentioned in

Table 4: Relative experimental and fitting uncertainties for 6, 10 and 15 MV energies in red, green and blue colour channels at 1σ confidence level

Uncertainty type	Relative uncertainty (%)								
	6 MV			10 MV			15 MV		
	Red	Green	Blue	Red	Green	Blue	Red	Green	Blue
Experimental	0.90	1.20	1.51	1.34	1.23	2.04	2.03	0.54	0.76
Fitting	1.77	1.94	1.75	2.94	2.83	1.41	4.66	1.21	2.43
Total	1.99	2.28	2.31	3.23	3.09	2.48	5.08	1.33	2.54

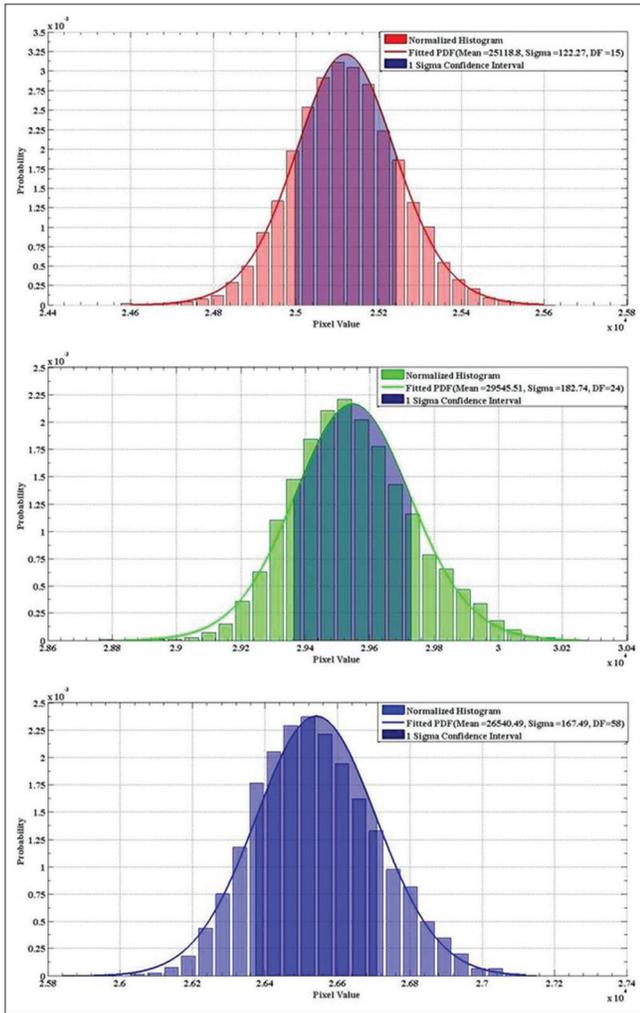


Figure 6: Probability distribution curves, normalized histograms and 1σ CI of red (top), green (middle) and blue (bottom) colour channels for EBT3 films irradiated by 6 MV energy

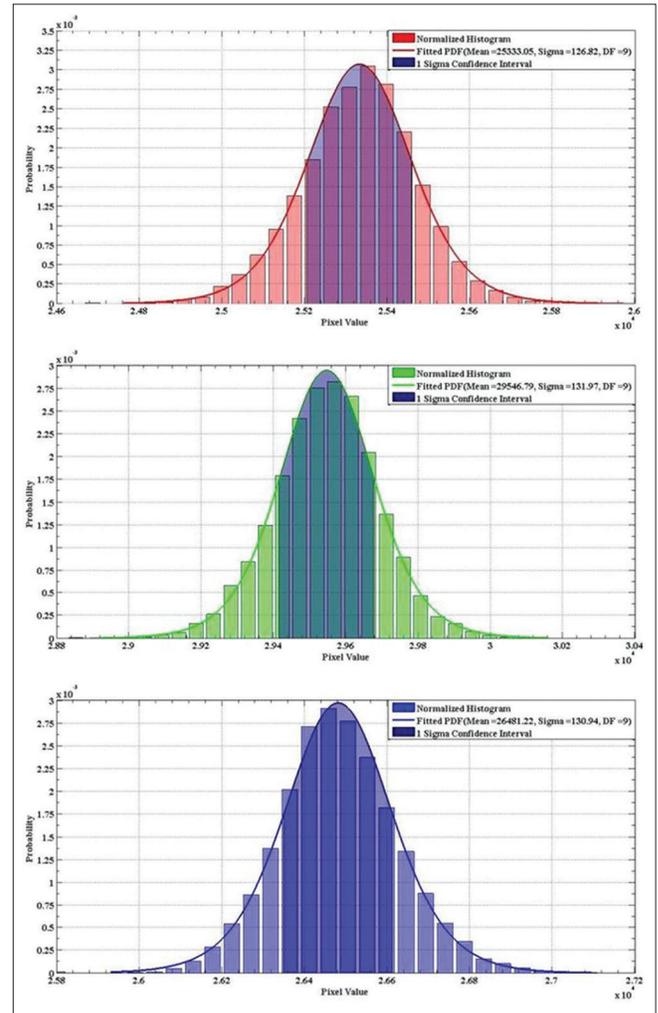


Figure 7: Probability distribution curves, normalized histograms and 1σ CI of red (top), green (middle) and blue (bottom) colour channels for EBT3 films irradiated by 10 MV energy

this study. The uncertainty budget presented here is usable and is valid for the FDS of the current study. The method described here for correcting the uncertainty budget in the absence of the sufficient data is independent of the FDS.

The red color channel has the highest uncertainty for all the energies and color channels studied, this is because of the highest sensitivity of response with delivered dose for the red color channel. As a result of this, any error impacts the

uncertainty in this channel the most. The increase in total uncertainty in dose determination with the energy of the beam is consistent with the findings of the past study.^[21]

For the completeness of the study, the most commonly used 9 MeV electron energy was also studied (not described here) and it was found that the total uncertainty behavior was similar to 6 MV energy for the RGB color channels studied.

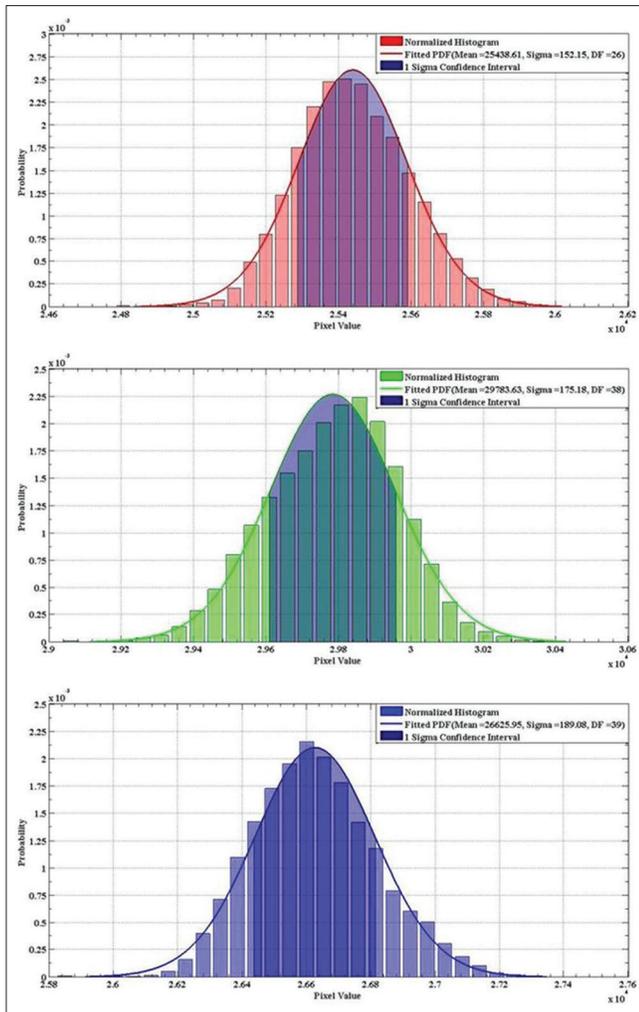


Figure 8: Probability distribution curves, normalized histograms and 1σ CI of red (top), green (middle) and blue (bottom) colour channels for EBT3 films irradiated by 15 MV energy

CONCLUSIONS

The PD of the PV of the irradiated film fits TD well, this distribution approaches to normal behavior for large sample sizes. CI must be corrected by “ t ” value in the case of radiotherapy dosimetry, where, limited measurements of the quantity of interest are made and distribution of the measured values is assumed to be Gaussian.

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