Physica Medica (2012) xx, 1–10

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: http://intl.elsevierhealth.com/journals/ejmp

ORIGINAL PAPER

Evaluation of Gafchromic® EBT3 films characteristics in therapy photon, electron and proton beams

J. Sorriaux [a,b,*], A. Kacperek [c], S. Rossomme [a], J.A. Lee [a,b], D. Bertrand [d], S. Vynckier [a,e], E. Sterpin [a]

[a] Center of Molecular Imaging, Radiotherapy and Oncology, Institut de recherche expérimentale et clinique, Université catholique de Louvain, Avenue Hippocrate 54, 1200 Brussels, Belgium
[b] ICTEAM Institute, Université catholique de Louvain, Louvain-la-Neuve, Belgium
[c] Douglas Cyclotron, Clatterbridge Center for Oncology, Wirral, UK
[d] Ion Beam Applications S.A, Louvain-la-Neuve, Belgium
[e] Département de radiothérapie, Cliniques Universitaires Saint-Luc, Avenue Hippocrate 54, 1200 Brussels, Belgium

Received 8 July 2012; received in revised form 7 September 2012; accepted 4 October 2012

KEYWORDS
EBT3;
Dosimetry;
Proton therapy

Abstract *Purpose:* To evaluate the uncertainties and characteristics of radiochromic film-based dosimetry system using the EBT3 model Gafchromic® film in therapy photon, electron and proton beams.
Material and methods: EBT3 films were read using an EPSON Expression 10000XL/PRO scanner. They were irradiated in five beams, an Elekta SL25 6 MV and 18 MV photon beam, an IBA 100 MeV 5×5 cm^2 proton beam delivered by pencil-beam scanning, a 60 MeV fixed proton beam and an Elekta SL25 6 MeV electron beam. Reference dosimetry was performed using a FC65-G chamber (Elekta beam), a PPC05 (IBA beam) and both Markus 1916 and PPC40 Roos ion-chambers (60 MeV proton beam). Calibration curves of the radiochromic film dosimetry system were acquired and compared within a dose range of 0.4–10 Gy. An uncertainty budget was estimated on films irradiated by Elekta SL25 by measuring intra-film and inter-film reproducibility and uniformity; scanner uniformity and reproducibility; room light and film reading delay influences.
Results: The global uncertainty on acquired optical densities was within 0.55% and could be reduced to 0.1% by placing films consistently at the center of the scanner. For all beam types, the calibration curves are within uncertainties of measured dose and optical densities. The total uncertainties on calibration curve due to film reading and fitting were within 1.5% for

* Corresponding author. Center of Molecular Imaging, Radiotherapy and Oncology, Institut de recherche expérimentale et clinique, Université catholique de Louvain, Avenue Hippocrate 54, 1200 Brussels, Belgium. Tel.: +32 27649526.
E-mail address: jefferson.sorriaux@gmail.com (J. Sorriaux).

1120-1797/$ - see front matter
http://dx.doi.org/10.1016/j.ejmp.2012.10.001

photon and proton beams. For electrons, the uncertainty was within 2% for dose superior to 0.8 Gy.
Conclusions: The low combined uncertainty observed and low beam and energy-dependence make EBT3 suitable for dosimetry in various applications.

Introduction

Film dosimeters are often used in various radiotherapy treatment modalities because of their superior resolution and as a natural 2D dosimeter compared to detectors used for point measurements (e.g. ion chambers, silicon diodes...) [1–3]. Radiographic films like EDR2 are often used as standard dosimeters for quality assurance of intensity-modulated radiotherapy treatments (IMRT) [4]. However radiographic films have undesirable drawbacks like energy-dependence and the need of chemical development [5]. Gafchromic films like EBT do not require post-irradiation processing, display advantages concerning energy-dependence compared to radiographic films and sensitivity adapted to common radiotherapy dose per fraction (around 2 Gy). Performances of the EBT1 and EBT2 film models were already studied for a wide range of applications [6–9]. This includes, but is not limited to, quality assurance for IMRT [10–12], measurements of correction factors for reference dosimetry [13], depth-dose measurements for various beam types [14].

The latest EBT3 model Gafchromic® film has been released recently. As claimed by the manufacturer, EBT3 films are constructed similarly to EBT2 films, with similar expected performances, with the added features of a symmetric construction (the effective point of measurement is now at center) and anti-Newton ring artifacts coating. The symmetry of the film should allow a safer procedure for scanning films in clinical routine. The aim of this study was to compare work performed by other authors on earlier versions of EBT films to evaluate the performance of EBT3 in terms of measurement uncertainty in various clinical radiation types (photons, electrons and protons).

Film scanning provides optical density (OD) values, with several sources of uncertainties. These need to be quantified individually to properly assess the global uncertainty, that is the first main objective of this work. Moreover, to be clinically useful, OD need to be converted to dose. Therefore, uncertainty of the reference doses used for calibration of the films need also to be included.

The EBT3 film dosimetry chain was implemented in our research center for clinical radiotherapy with photons and electrons but, as a primary purpose, for future studies in proton-therapy. The behavior of EBT3 dose-calibration curves in photon, electron and proton beams at several energies was therefore investigated, the main question being the sensitivity of relative dosimetry accuracy to the calibration curve used. Arjomandy et al. [14] already showed a weak energy dependence of the response of EBT2 films for different types of beams employed.

Material and methods

Detectors

Film pieces from the same lot (#A07251101) were used for all measurements. The nominal size of the sheets was 20.32 cm by 25.4 cm. According to manufacturer claims, the active layer construction is similar to EBT2 one. The active layer of $\sim$0.028 mm is positioned with a new (slightly denser) matte polyester substrate layer of 0.12 mm on each side. An EPSON Expression 10000XL/PRO scanner was used to read the transmission of the film pieces as recommended by the manufacturer. The scanner was used in 48-bit RGB (Red Green Blue) mode. The transmitted raw intensity values were obtained using the EPSON Scan software delivered with the scanner without any color correction. Each film was read at a resolution of 150 dpi, 48 h after irradiation and saved in uncompressed tagged image file format (TIFF). For each scanning, the films were preferably placed in the center of the bed scanned, in landscape orientation, that is, with the short edge of film parallel to the scanning direction. The orientation was marked for all film pieces. Also, 50 warm-up scans were performed for allowing the scanner to stabilize. One preview scan was also performed before each saved scan.

Net optical densities (of a color channel) were determined through the following formula, according to the definition of Devic et al. [15]:

$$\mathrm{netOD} = \log_{10}\left(\frac{I_{\mathrm{unexp}} - I_{\mathrm{bckg}}}{I_{\mathrm{exp}} - I_{\mathrm{bckg}}}\right) \quad (1)$$

where I_{unexp}, I_{exp} and I_{bckg} are intensities measured for unexposed films, exposed films and zero-light transmitted intensities, respectively.

For the reference dosimetry of the beam qualities used and depending on the beam type, several ion chambers were used: 1) a Farmer IBA FC65-G (Janus electrometer, Precitron AB); 2) a PPC05 IBA (Dose1 electrometer, Wellhoffer); 3) a Markus 1916 (Keithley 6517A electrometer); 4) a Roos PPC40 (Keithley 6517A electrometer). Except the Roos PPC40, the different detectors were chosen because they were used locally for routine dosimetry with dedicated solid phantoms (i.e. with layers specially engineered to be compatible with detector geometry). Since chambers calibrated for different reference proton dosimetry protocols were used in different centers, additional measurements with the PPC40 chamber (TRS-398 [16]) were performed against Markus 1916 measurements at Clatterbridge (ECHED [17,18]) for consistency.

Description of beam types and setups

Measurements were performed for 5 irradiation beams and 5 energies: 1) an Elekta SL25 at 6 MV and 18 MV nominal energy (Cliniques Universitaires Saint-Luc, Radiotherapy department, Brussels, Belgium); 2) a 6 MeV electron beam (same unit as 1)); 3) an IBA proton-therapy gantry with dedicated pencil-beam scanning (PBS) with 100 MeV nominal energy (C230 cyclotron, gantry 2 in Essen, Germany); 4) a fixed 60 MeV proton beam-line used for eye therapy (Douglas Cyclotron, Clatterbridge Cancer Centre, UK). The setups and chambers employed for absolute dose measurements are detailed in Table 1. All phantom dimensions were large enough to ensure full equilibrium conditions. Reference dosimetry protocols are also listed. The protocols listed here are the ones used for calibrating directly or cross-calibrating, the chambers, and to determine quality correction factors, when available, in the reference conditions defined by the protocols. Those are not the measurement conditions used actually for calibration of EBT3 films.

For every setup listed in Table 1, films were placed at the measurement point of the chambers. For each setup, 3 pieces of films were irradiated at every dose step except for electrons where only 2 repetitions were done. For the Elekta SL25 unit, the chosen depths correspond to the position of the chamber in daily monitor check measurements performed at the Saint-Luc hospital. For proton beams, the depth was chosen in order to avoid any build-up effect due to the production of secondaries by nuclear interactions. On the other hand, the chosen depth was far enough from the Bragg peak position to avoid dose gradients within the chambers. The LET (linear energy transfer) being relatively constant up to a few cm before the Bragg peak [19], the chosen depth is expected to have negligible impact around the positions considered in this study. Under dose—response drawback of the film in the Bragg peak region due to known quenching effect was avoided [19].

Uncertainty budget

Uncertainties on dose measured by films have two main origins: uncertainty on the measured dose for calibration of the films and overall uncertainty on the measured netOD.

In TRS-398 document and cited references therein, the uncertainty on measured dose is evaluated to be within 2% when the protocol is properly implemented. In NCS 18, and under the applied clinical conditions, the evaluation of uncertainty on measured dose is within 1% for high-energy photon beams and 1.5% for high-energy electron beams. In ECHED protocol, the overall uncertainty estimation is 4.3% (1σ). The Clatterbrige fixed beam line was also used for calorimetry development [21]. The results of the calorimetry study were used as a benchmark of the dosimetry in reference conditions. Polarity and recombination correction factors (two voltage method, using the formula for continuous beams, as recommended by Palmans et al. [22] and Lorin et al. [23]) were applied when appropriate (i.e. polarity correction not included in the dose-to-water conversion coefficient ($N_{D,w}$)). The continuous beam condition was assumed because frequencies of the cyclotron (of order of 25 and 100 MHz for Clatterbridge and IBA, respectively) made the time between two pulses negligible compared to ion collection time in the chambers [23]. Quality correction factors were applied when available (for Elekta SL25 and Clatterbridge beam for PPC40 chamber). However, those factors are taken directly from protocols and are approximations since the conditions of measurement listed in Table 1 differ from reference conditions listed in TRS-398. Moreover, the TRS-398 correction factor used for the IBA scanned beam may be inappropriate, since it was intended for use with a double-scattering system, increasing the uncertainty on the measured dose for films calibrated on the IBA system. There is however no available code of practice for such beam delivery method and previous work using active scanning proton modality demonstrated that TRS-398 offers suitable reference dosimetry protocol for active scanning proton modality [24]. Those additional uncertainties, which are mainly linked to the quality correction factor, are expected to be significantly less than the total uncertainty on measured dose in TRS-398 protocol (2%). Therefore, the value provided by TRS-398 was kept unchanged.

The overall uncertainty on netOD computed using formula (1) was obtained with the formula [15]:

$$\sigma_{\mathrm{netOD}} = \frac{1}{\ln_{10}} \sqrt{\frac{\sigma^2_{I_{\mathrm{unexp}}} - \sigma^2_{I_{\mathrm{bckg}}}}{I_{\mathrm{unexp}} - I_{\mathrm{bckg}}} + \frac{\sigma^2_{I_{\mathrm{exp}}} - \sigma^2_{I_{\mathrm{bckg}}}}{I_{\mathrm{exp}} - I_{\mathrm{bckg}}}} \quad (2)$$

where$\sigma^2_{I_{\mathrm{unexp}}}$, $\sigma^2_{I_{\mathrm{exp}}}$ and $\sigma^2_{I_{\mathrm{bckg}}}$ are the uncertainties of the measured I_{unexp}, I_{exp} and I_{bckg}.

Uncertainty on background was computed from 10 measurements of I_{bckg} (zero transmitted light, averaged over the whole scanner surface). I_{bckg} was then kept the same for all following computations of netOD. Similarly, I_{unexp} and $\sigma^2_{I_{\mathrm{unexp}}}$ were obtained by computing mean and standard deviation over a set of averaged measured intensities over the entire surface of 10 unexposed films pieces of 5×5 cm^2 (in portrait and landscape orientations)

Table 1 Summary of experimental conditions.

Beam type and nominal incident energy	Nominal field (cm^2)	Phantom material	Measurement depth (cm)	Detectors	Protocol
Elekta SL25 6 MV photon	10×10	Polystyrene	1.5	FC65-G	NCS18 [20]
Elekta SL25 18 MV photon	10×10	Polystyrene	3.0	FC65-G	NCS18
Elekta SL25 6 MeV electron	10×10	Polystyrene	1.4	FC65-G	NCS18
IBA PBS 230 MeV proton	5×5	IBA SP34	5.0	PPC05	TRS-398
Clatterbridge fixed beam line 60 MeV	1.5625π	Perspex	2.0	Markus 1916, PPC40	ECHED

read 10 times each. Again, the same values I_{unexp} (one for portrait and one for landscape) were kept for all determinations of netOD and σ_{netOD}

Uncertainties on measured intensities of exposed films were obtained by quadrature sum of all identified individual sources of uncertainties (assumed as independent). Those were listed in previous publications [8,25] for EBT and EBT2 films: local film uniformity; intra-film and inter-film reproducibility; intra-scanner and whole-film uniformities; film reading delay; film orientation; effect of room light exposition. Depending on the conditions of film conservation and film post-processing, some of those sources of uncertainties may be canceled or reduced.

For quantifying part of the uncertainties, a spatially uniform dose delivery is needed. The 10 × 10 cm^2 Elekta SL25 6 MV beam has very good uniformity properties (within 0.3% in a 5 × 5 cm^2 squared centered on-beam axis) and was therefore used for determining the uncertainty budget, assuming it would remain essentially the same for other beam types.

The following tests were performed to quantify uncertainty components on I_{exp}:

- Single film scanner reading reproducibility was quantified by reading 10 times the same 2 × 2 cm^2 film at the center of the scanner and computing standard deviation over I_{exp} readings.
- Inter-film reproducibility was quantified by measuring the I_{exp} on three different sheets each cut into four equal pieces and a 2 × 2 cm^2 region for 3 pieces of films cut at the center of 3 other sheets, irradiated with the same dose. Each piece was read 10 times to exclude single film reproducibility.
- Intra-scanner uniformity was evaluated by quantifying I_{exp} at the same position within a 5 × 5 cm^2 film scanned over several spots covering the full scanner screen.
- For whole-film uniformity, a single EBT3 sheet was cut into 9 pieces. Each one of them was irradiated with the same beam and the same number of monitor units and read 10 times by the scanner. The intra-film uniformity was obtained by quantifying I_{exp} fluctuation for each film piece placed at the center of the scanner over a 5 × 5 cm^2 irradiated region, where intra-scanner uniformity was ensured in the previous step. To exclude reproducibility uncertainty, each film piece was read 10 times and standard deviation of the 9 average I_{exp} was computed.
- Effect of film reading delay was evaluated by reading 3 sets of films of 2 × 2 cm^2 irradiated with the same dose 48 h after irradiation and during a period of 8 h after.
- The effect of film orientation was quantified by computing the average I_{exp} over a 2 × 2 cm^2 region of 3 films irradiated with the same dose and scanned in both portrait and landscape orientations.
- The effect of room light on measured intensities was investigated every 2 h over a period of 8 h started as well 48 h after irradiation by placing the 2 × 2 cm^2 film pieces on a desk exposed to room light.
- To evaluate dose response (local film uniformity), film pieces of 2.5 × 2.5 cm^2 were prepared and orientation marked. The size of the analysis region dose levels was approximately 2 × 2 cm^2 for each film pieces. Each film irradiated was stored in a black envelope in a closed cupboard until darkening stabilization.

Dose response analysis

Experimental dose response calibration curves are expected to be used in other applications where the dose is an unknown parameter. In this section, functional dose response is introduced and the associated uncertainty is described. To retrieve a dose from the net optical density values, Devic et al. [26] proposed the following analytical function:

$$D = a \times \mathrm{netOD} + b \times \mathrm{netOD}^n \quad (3)$$

where a and b are the fitting parameters. The non-linear n-term is introduced to account for the non-linear saturation process of the film at high doses. Following the same argument of Devic et al. [26], the parameter n was fixed at 3.1 to give the best fitting results for all radiation modalities. This value is slightly higher than the $n = 2.5$ from Devic [26]. This difference is explained by the use of a different film model (EBT3 instead of EBT) and a slightly different protocol (including a different scanner). The Levenberg–Marquardt algorithm was used to optimize the dose response curve fits. The Levenberg–Marquardt, mix of Gauss–Newton and gradient minimization algorithm, is adapted for fitting multiple parameters and non-linear functions. The estimated overall uncertainty is the quadratic sum of the fitting estimated uncertainty and the relative experimental uncertainty. The relative experimental uncertainty is

$$\sigma_{D_{exp}}(\%) = \frac{\sqrt{\left(a + b \times n \times \mathrm{netOD}^{n-1}\right)^2 \times \sigma^2_{\mathrm{netOD}}}}{D_{fit}} \times 100 \quad (4)$$

where σ_{netOD} is the overall uncertainty on optical densities defined in (2). The estimated uncertainty due to fitting parameters, D_{fit}, is expressed as

$$\sigma_{D_{fit}}(\%) = \frac{\sqrt{\mathrm{netOD}^2 \times \sigma_a^2 + \mathrm{netOD}^{2n} \times \sigma_b^2}}{D_{fit}} \times 100 \quad (5)$$

Table 2 Uncertainty budget determination for RBG channels.

	Relative uncertainty (%)		
	R	G	B
Single film reproducibility	<0.01	<0.01	<0.01
Inter-film uniformity	0.04	0.02	0.05
Scanner uniformity	0.31	0.2	0.59
Whole film uniformity	0.07	0.06	0.1
After 48 h irradiation variation	<0.01	<0.01	<0.01
Film orientation	0.45	0.79	1.1
Room light influence	<0.01	<0.01	<0.01
Total uncertainty excluding local film uniformity	0.55	0.67	1.57
Total uncertainty excluding local film uniformity, scanner uniformity and film orientation	0.1	0.08	0.06

where σ_a and σ_b are the uncertainties on the respecting fitting parameters.

Results

Uncertainty budget

Although the determination of the overall uncertainty was described in the last section of the material and methods, it was decided to show this result first. All error bars on optical density readings were computed using the values shown in Table 2. The total uncertainties are 0.55%, 0.67% and 1.57% for the RGB color channels and could be reduced to 0.1%, 0.08% and 0.06%, respectively, if film orientation and film position with respect to scanner flat-bed were kept consistently. The determination of the uncertainties was performed with film pieces irradiated by a 2 Gy uniform dose from the 6 MV photon beam. It is noteworthy to mention that "Single film reproducibility" was tested with film pieces

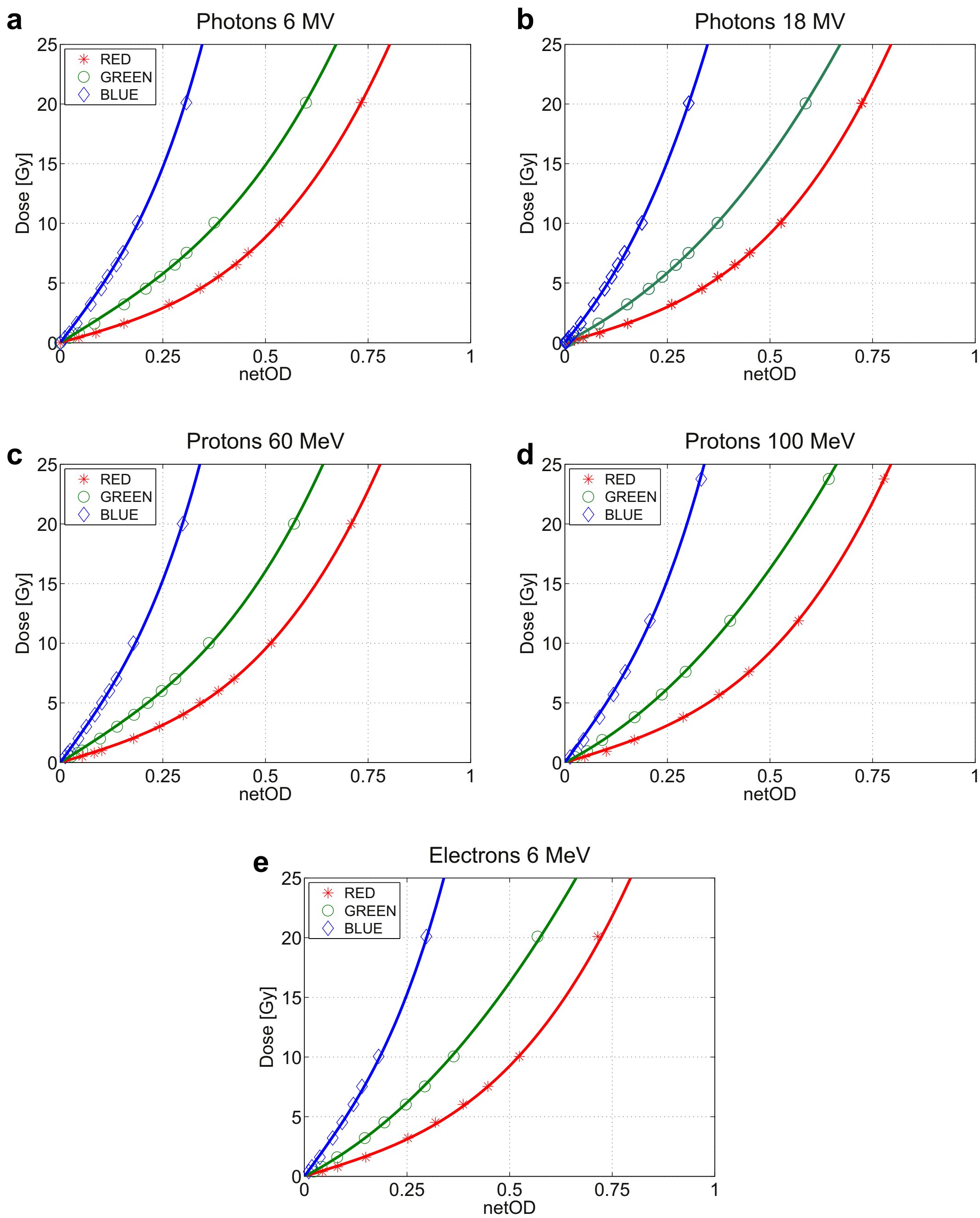

Figure 1 EBT3 Gafchromic dose—response curves for a 6 MV photon beam (a), a 18 MV photon beam (b), a 60 MeV proton beam (c), a 100 MeV proton beam (d) and a 6 MeV electron beam (e). Experimental points are shown for the red (stars), green (circles) and blue (diamonds) channels. Fitting dose—response curves are represented by solid line for each color response of the scanned films in each beam modality. Error bars have a similar size than data-points and are not displayed for readability. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Please cite this article in press as: Sorriaux J, et al., Evaluation of Gafchromic® EBT3 films characteristics in therapy photon, electron and proton beams, Physica Medica (2012), http://dx.doi.org/10.1016/j.ejmp.2012.10.001

irradiated with a low dose (0.4 Gy), an intermediate dose (2 Gy) and a high dose (6.5 Gy) in the same beam. Reproducibility was in each case lower than 0.01%. Whole-film uniformity determined here only quantifies the standard deviation of the mean response over several film pieces of a single film sheet. The local film uniformity response within one film piece was quantified on an individual basis for every piece irradiated by a uniform dose. The standard deviation corresponding to local film uniformity was implicitly included for further estimation of σ_{netOD}. The local film uniformity increased with respect to the dose and was on average 0.79% and 0.94% for the 6 MV and 18 MV photon beam, 1.38% and 0.74% for the 60 MeV and 100 MeV proton beams and 0.89% for the 6 MeV electron beam. Also, the local unirradiated-film uniformity is on average within 0.52%.

Individual color response

Dose response curves for the different beam qualities are presented in Fig. 1 for the three color channels of the scanned images. Uncertainties on measured intensities are part of the previous uncertainty budget results. One should note that uncertainties listed in Uncertainty budget Section on the measured dose with the different ionization chambers have to be added. As explained in Uncertainty budget Section, the measured points were fitted using equation (3) and the results of the fitting procedures are presented by solid lines in Fig. 1. The three color channels represent different dose responses to irradiation. Error bars at the one-sigma level uncertainties are of similar sizes than the data points and were not shown for the readability of the figures.

In order to choose the most sensitive color channel to the dose the first derivative of the fitted netOD with respect to the dose was computed [27]. Figure 2 represents one of these sensitivity derivations for the 18 MV photon beam. For dose below 12.15 Gy, the red channel is the most sensitive. Similar observations can be performed for other beam qualities.

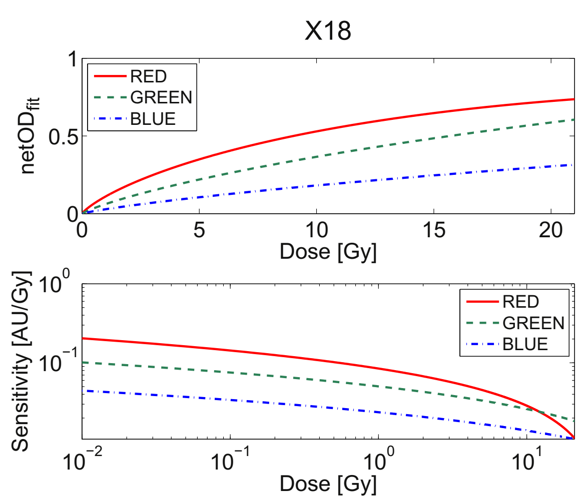

Figure 2 Inverse dose—response curve for the color channels (top) and their respective sensitivity (bottom) to the dose in a dose range of 0.4—20 Gy for the 18 MV photon beam. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Uncertainties on the fitting process

Uncertainties on expected dose related to the fitting process and the reading experimental errors are shown in Fig. 3 for all modalities. For all modalities, the experimental standard deviation is about 1% at low doses (~0.5 Gy) and decreases with dose. For photon beams (Fig. 3 (a) and (b)), total errors amount to 1.5% for low dose values and decrease below 1% at higher doses. Proton calibration curves (Fig. 3 (c) and (d)) required a two-steps fitting with: a 'low dose' fit for doses between 0 and 2 Gy and a second fit for higher doses. This was performed to keep the fitting standard deviation component below one percent. In the typical radiotherapy dose range 1.5 Gy—2.5 Gy the difference between the two fitting curves is constant and less than 0.01% leading to a dose error of 0.015 Gy. Therefore the total standard deviations are at most 1.15% and 1.09% respectively for the 60 MeV and 100 MeV protons low dose fit. In this dose range for the 100 MeV proton beam, the total standard deviation is lower than 1% because of parameters determination. For electrons (Fig. 3 (e)), the total standard deviation is at most 2.2% and decreases below 2% for doses above 1 Gy. Despite a fit per dose-range, the error due to fitting has not been able to be reduced to 1% for electrons unlike photon and protons beams.

Figure 4 shows fitting uncertainty as a function of dose and number of regions of interest (ROI) for film pieces irradiated by the electron beam. The 2 × 2 cm^2 film pieces irradiated by the electron beam were divided equally in four ROI's. The fitting error decreases as more ROIs are taken into account inside a same film piece. For one film piece, the standard deviation is at most 1.83% for 1 ROI, 1.74% for 2 ROIs, 1.51% for 3 ROIs and 1.41% for 4 ROIs (whole surface of the scanned film). For the second irradiated film piece, the same behavior is observed and the optimal fitting error is at most 3.31%. By taking into account the two film pieces, the fitting uncertainty is in agreement with Fig. 3 (e).

Calibration curves for various beam types

Figure 5 shows a superposition of red channel calibration curve of EBT3 films calculated above in a dose range of 0—10 Gy for the 6 MV and 18 MV photon beams, 60 MeV and 100 MeV proton beams and 6 MeV electron beam. For the readability of the figure, error bars are not shown, but standard deviations displayed in Fig. 3 should be taken into account for each beam modality. In a dose range from 0 to 10 Gy, we observed an average difference of 4.2% between the calibration curve of the 6 MV and 18 MV photon beams and an average difference of 2% between the two proton calibration curves. However, over the netOD range 0—10 Gy, the maximum spread based on the two extreme calibration curves is 11.5% at low dose value to 7.1% at 10 Gy. This maximum spread corresponds to the difference between the 6 MV photon curve and the 100 MeV proton curve. The global spread of the dose calibration curves for

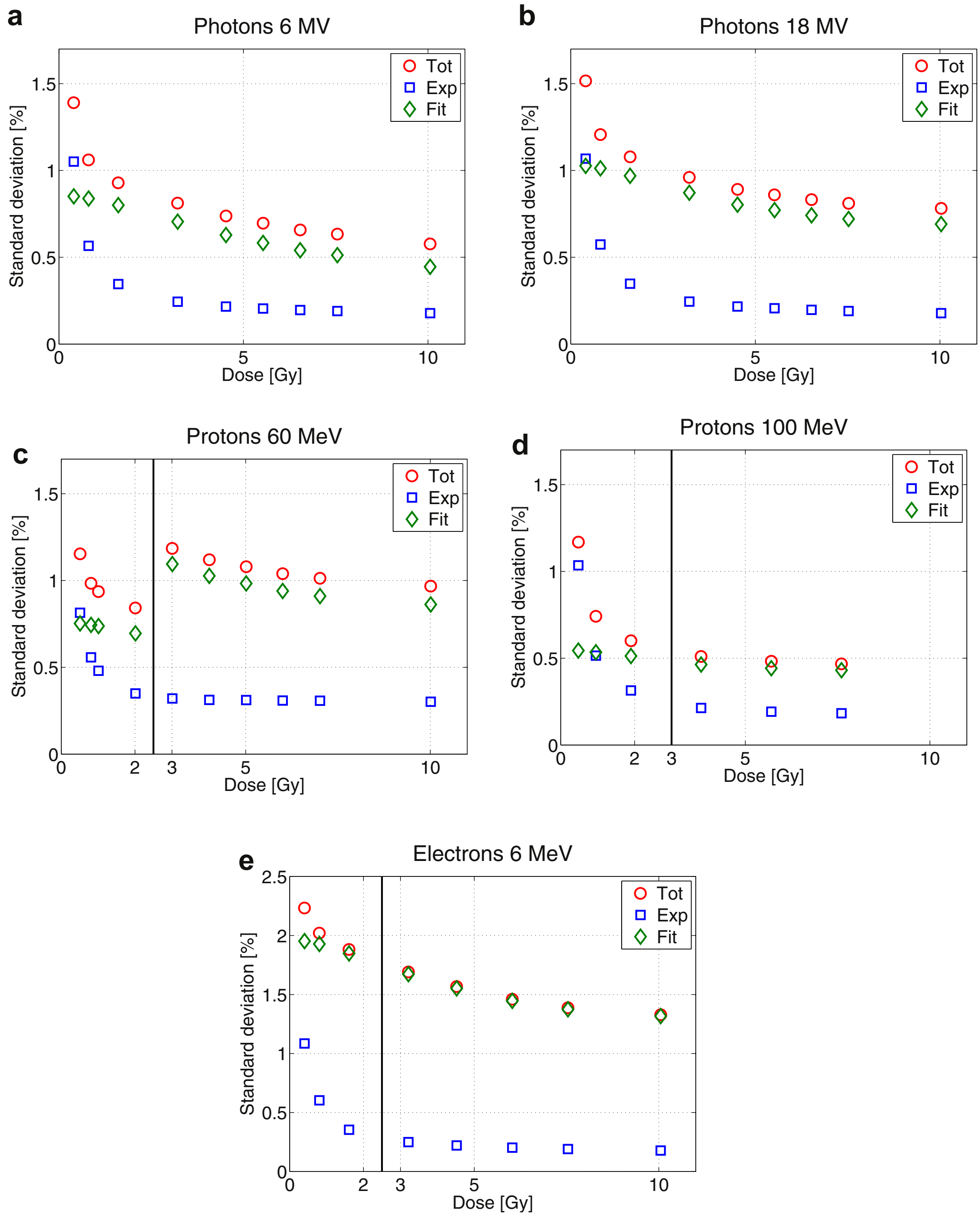

Figure 3 Standard deviation as a function of delivered dose to EBT3 films between 0 and 10 Gy for each modality. Experimental uncertainties (squares) are low compared to fit propagated errors (diamonds). Total uncertainties (circles) remain below 1.5% for photon and proton beam and are of the order of 2% for the 6 MeV electron beam. In the case of proton and electron beams, fits are performed at two different dose ranges (vertical line) to keep the fitting error as low as possible.

all energies and modalities around average equals 2.9% (one standard deviation).

Discussion

A complete uncertainty budget on EBT3 Gafchromic film was performed; including reading reproducibility, inter- and intra-film uniformity, reading delay after irradiation, orientation and room light effect. Previous work [8] showed that the single film reproducibility is part dose-dependent. This effect was tested for 0.4 Gy, 2 Gy and 6.5 Gy. In each case, the reading reproducibility is ensured with less than 0.01% of standard deviation. The film uniformity was also tested for each unexposed and exposed piece of film. The local film uniformity increases with respect to the dose as for EBT2 [8]. As observed by Reinhard et al. [28] the local film uniformity was found to be smaller than 1.5% on

Please cite this article in press as: Sorriaux J, et al., Evaluation of Gafchromic® EBT3 films characteristics in therapy photon, electron and proton beams, Physica Medica (2012), http://dx.doi.org/10.1016/j.ejmp.2012.10.001

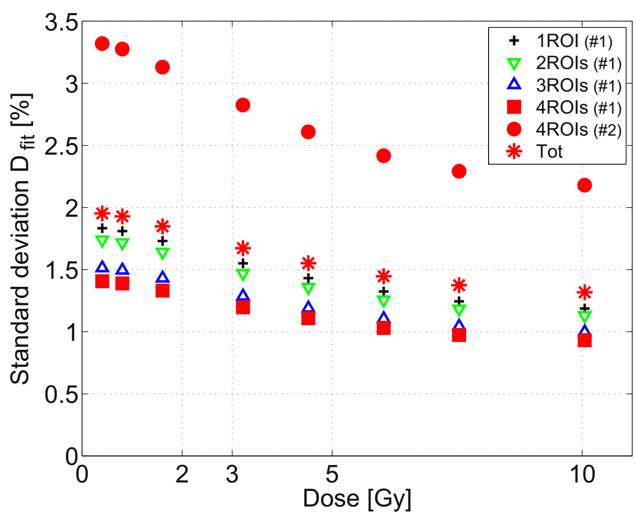

Figure 4 Standard deviation of the fitting uncertainty as a function of dose and the number of ROI for a same film piece irradiated by the electron beam. The fitting errors for 1 ROI (crosses), 2 ROIs (down triangles), 3 ROIs (up triangles), 4 ROIs (squares) decrease as the number of ROI increases. The optimal fitting error for film piece #2 (circles) is at most 3.31% for low dose. The total fitting uncertainty is reduced to 2% (stars) by taking into account the 4 ROIs of each film piece.

average for unexposed as well as exposed films. From our test, films are darkening until 46 h after irradiation and are stabilized with less than 0.01% of variation (1σ) after 48 h. Room light influence is minimal. The higher uncertainties are those related to the scanner uniformity (0.55%, 0.67% and 1.57% for the RGB color channels) and those due to film orientation. Film symmetry is ensured by an error inferior

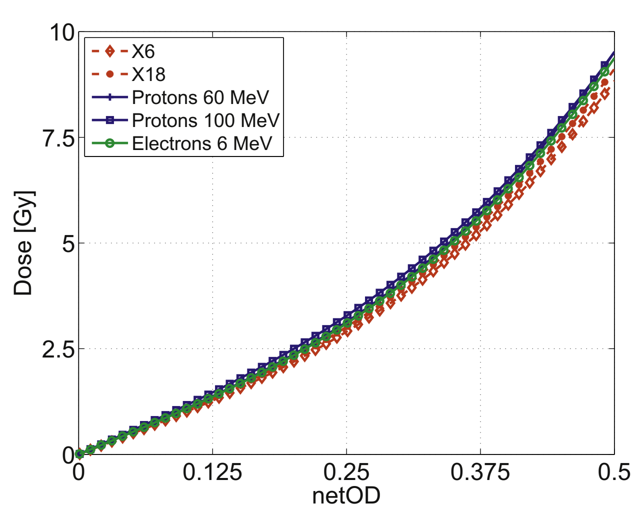

Figure 5 Superposition of red channel calibration curves for each modalities: 6 MV (diamonds, dotted line), 18 MV (stars, dotted line), 60 MeV protons (plus signs, solid line), 100 MeV (squares, solid line) and 6 MeV electrons (circles, solid line). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

to 0.01% and is included in the film orientation error. Film pieces are small enough (at most 5 $\times$ 5 cm^2) to ensure independence of film uniformity and scanner uniformity errors. The total uncertainties excluding local film non-uniform response can be reduced to 0.1% or less by reading the film always at the center of the scanner and by keeping the same orientation of the film on the flat bed. Average local uniformity was within 1.38% and even below 1% excluding results from the 60 MeV proton beam in agreement with previous findings for EBT2 films [14,28]. According to the manufacturer, EBT3 films have surrounding matte polyester components, which are different than those of the EBT and EBT2 [29]. This increases homogeneity and therefore decreases Newton's artifact halos (likely due to the surface treatment). The uncertainties are significantly lower due to a better homogeneity and symmetry of EBT3 compared to the EBT and EBT2 [8,25,30,31]. The uncertainty budget is well controlled and quite promising for future dosimetric applications of films EBT3. However, compared to an ionization chamber measurement, the disadvantage of the films remains the time necessary for post-irradiation processing and stabilization.

EBT and EBT2 Gafchromic films seem to be more sensitive to radiation exposure in the red color of the RGB analysis mode [32]. From the first derivative of the fitted calibration curves shown in Fig. 2, the red channel was shown the most sensitive for EBT3 to the dose for the low dose up to 12 Gy for photon beams and 14 Gy for protons and electrons. These values can be taken as an average for the different beam qualities with a standard deviation of 0.2%. In a dose range of 12 (or 14) Gy to 20 Gy the green channel has the highest sensitivity to the dose and should be preferred. The dose fractionation in radiotherapy applications is usually about 2 Gy and the red channel is therefore more appropriate for optical density conversion.

As shown in Fig. 3 fitting procedure is a particularly important step as long as the experimental standard deviation on the estimated dose is relatively low. The total uncertainty on expected dose determination due to the fitting is in general at most 1.5% for photons and protons. Electrons present poorer results as the fitting errors dominate. We suspect that our repetition statistics was not sufficient enough compared to the 3 repetitions made for all other modalities. We evaluate this hypothesis in Fig. 4. The standard deviation due to fitting process decreases as we take into account more ROI from a same film piece. The same behavior is observed for the second irradiated film piece but with a higher optimal fitting error than for the first film piece. On one hand, the optimal surface to get the minimal fitting error is, in this case, limited by the surface of the film piece but is close to "saturation". On the second hand, the variability between the two irradiated films is higher than the variability inside a film piece so that the fitting uncertainty cannot be lower with 2 repetitions.

The calibration curves (Fig. 5) show overall a weak energy and particle type dependencies. Arjomandy et al. [14] observed a maximum difference between proton and photon calibration curves for EBT2 films of 18% and a global spread of 4.5% (1σ) over the dose range 0–10 Gy. Those values are comparable with the maximum difference of 11.5% and the global spread of 2.9% observed in Fig. 5. In recent research on EBT3 films published by Reinhardt et al. [28], maximum differences of 6% were observed between EBT3 photon and proton calibration curves. Considering the uncertainties in netOD and dose determination, our results are compatible with aforementioned studies. As mentioned by Arjomandy et al. [14], the user is expected to have a curve calibration for the used beam, in clinical applications. The energy and LET spread with depth or field size is expected to be significantly smaller than the ranges of energy and LET studied here. Also the LET-dependence appearing at low residual proton energy [28] was not investigated in this study.

Conclusion

This work provides guidelines for optical density determination of EBT3 Gafchromic films for a wide variety of beam qualities and energies. The methodology leads to small uncertainty on reading processes dealing with the intrinsic characteristic of the films and reducing total uncertainty for a dose determination. The red channel is more appropriate at the therapeutic dose range. The low combined uncertainty observed and low beam-type and energy dependence make EBT3 a promising candidate for dosimetry in various applications.

Acknowledgments

The authors would like to thank the radiotherapy department of Cliniques Universitaires Saint-Luc, Clatterbridge Cancer Center and Ion Beam Application s.a for making available the material and structure needed to carry out this study. E. Sterpin is a research fellow of the Belgian 'Fonds National pour la Recherche Scientifique' (Charge de recherches du F.R.S – FNRS FC 73512). J. A. Lee is a Research Associate of the Belgian 'Fonds National pour la Recherche Scientifique' (Research Associate-FC 63880).

This work is supported by the Walloon Region under the project name InVivoIGT, convention number 1017266.

References

[1] Zhu XR, Jursinic PA, Grimm DF, Lopez F, Rownd JJ, Gillin MT. Evaluation of Kodak EDR2 film for dose verification of intensity modulated radiation therapy delivered by a static multileaf collimator. Med Phys 2002;29(8):1687–92.
[2] Tsai J-S, Wazer DE, Ling MN, Wu JK, Fagundes M, DiPetrillo T, et al. Dosimetric verification of the dynamic intensity-modulated radiation therapy of 92 patients. Int J Radiat Oncol Biol Phys 1998;40:1213–30.
[3] Xing L, Curran B, Hill R, Holmes T, Ma L, Forster KM, et al. Dosimetric verification of a commercial inverse treatment planning system. Phys Med Biol 1999;44:463–78.
[4] Childress NL, Salehpour M, Dong L, Bloch C, White RA, Rosen II. Dosimetric accuracy of Kodak EDR2 film for IMRT verifications. Med Phys 2005;32(2):539–48.
[5] Pai S, Das IJ, Dempsey JF, Lam KL, LoSasso TJ, Olch AJ, et al. TG-69: radiographic film for megavoltage beam dosimetry. Med Phys 2007;34(6):2228–58.
[6] Fiandra C, Ricardi U, Ragona R, Anglesio S, Giglioli FR, Calamia E, et al. Clinical use of EBT model Gafchromic film in radiotherapy. Med Phys 2006;33:4314–9.
[7] Fiandra C, Ragona R, Ricardi U, Anglesio S, Giglioli FR. Absolute and relative dose measurements with Gafchromic™ EBT film for high energy electron beams with different doses per pulse. Med Phys 2008;35:5463–70.
[8] Martišíková M, Ackermann B, Jäkel O. Analysis of uncertainties in Gafchromic® EBT film dosimetry of photon beams. Phys Med Biol 2008a;53:7013–27.
[9] Butson MJ, Cheung T, Yu PK. Weak energy dependence of EBT Gafchromic film dose response in the 50 kVp–10 MVp x-ray range. Appl Radiat Isot 2006;64:60–2.
[10] Low DA, Moran JM, Dempsey JF, Dong L, Oldham M. Dosimetry tools and techniques for IMRT. Med Phys 2011;38(3):1313–38.
[11] Sohn JW, Dempsey JF, Suh TS, Low DA. Analysis of various beamlet sizes for IMRT with 6 MV Photons. Med Phys 2003; 30(9):2432–9.
[12] Niroomand-Rad A, Blackwell CR, Coursey BM, Gall KP, Galvin JM, McLaughlin WL, et al. Radiochromic film dosimetry: recommendations of AAPM radiation therapy committee task group 55. American association of physicists in medicine. Med Phys 1998;25:2093–115.
[13] Zeverino M, Agostinelli S, Pupillo F, Taccini G. Determination of the correction factors for different ionization chambers used for the calibration of the helical tomotherapy static beam. Radiother Oncol 2011;100:424–8.
[14] Arjomandy B, Tailor R, Anand A, Sahoo N, Gillin M, Prado K, et al. Energy dependence and dose response of Gafchromic EBT2 film over a wide range of photon, electron, and proton beam energies. Med Phys 2010;37(5):1942–7.
[15] Devic S, Seuntjens J, Hegyi G, Podgorsak EB, Soares CG, Kirov AS, et al. Dosimetric properties of improved GafChromic films for seven different digitizers. Med Phys 2004;31: 2392–401.
[16] IAEA Technical Reports Series No. 398. Absorbed dose determination in external beam radiotherapy. Vienna: International Atomic Energy Agency; 2004.
[17] Vynckier S, Bonnett DE, Jones DTL. Code of practice for clinical proton dosimetry. Radiother Oncol 1991;20:53–63.
[18] Vynckier S, Bonnett DE, Jones DTL. Supplement to the code of practice for clinical proton dosimetry. Radiother Oncol 1994; 32:174–9.
[19] Kirby D, Green S, Palmans H, Hugtenburg R, Wojnecki C, Parker D. LET dependence of GafChromic films and an ion chamber in low-energy proton dosimetry. Phys Med Biol 2010; 55:3741–51.
[20] NCS (Nederlandse Commissie voor Stralingsdosimetrie). Code of practice for the dosimetry of high-energy photon beams. NCS; 2008. Report NCS-18.
[21] Palmans H, Thomas R, Simon M, Duane S, Kacperek A, DuSautoy A, et al. A small-body portable graphite calorimeter for dosimetry in low-energy clinical proton beams. Phys Med Biol 2004;49:3737–49.
[22] Palmans H, Thomas R, Kacperek A. Ion recombination correction in the Clatterbridge Centre of Oncology clinical proton beam. Phys Med Biol 2006;51:903–17.
[23] Lorin S, Grusell E, Tilly N, Medin J, Kimstrand P, Glimelius B. Reference dosimetry in a scanned pulsed proton beam using ionisation chambers and a Faraday cup. Phys Med Biol 2008; 53:3519–29.
[24] Medin J. Implementation of water calorimetry in a 180 MeV scanned pulsed proton beam including an experimental determination of kQ for a Farmer chamber. Phys Med Biol 2010;55:3287–98.
[25] Hartmann B, Martisıkova M, Jäkel O. Homogeneity of Gafchromic® EBT2 film. Med Phys 2010;37:1753–6.
[26] Devic S, Seuntjens J, Sham E, Podgorsak EB, Ross Schmidtlein C, Kirov AS, et al. Precise radiochromic film dosimetry using a flat-bed document scanner. Med Phys 2005; 32:2245–53.

Please cite this article in press as: Sorriaux J, et al., Evaluation of Gafchromic® EBT3 films characteristics in therapy photon, electron and proton beams, Physica Medica (2012), http://dx.doi.org/10.1016/j.ejmp.2012.10.001

[27] Devic S, Tomic N, Soares CG, Podgorsak EB. Optimizing the dynamic range extension of a radiochromic film dosimetry system. Med Phys 2009;36:429—37.
[28] Reinhardt S, Hillbrand M, Wilkens JJ, Assmann W. Comparison of Gafchromic EBT2 and EBT3 films for clinical photon and proton beams. Med Phys 2012;39(8):5227—62.
[29] International Specialty Products. Gafchromic® EBT2 self-developing film for radiotherapy dosimetry. Wayne, NJ: ISP; 2009.
[30] Fuss M, Sturtewagen E, De Wagter C, Georg D. Dosimetric characterization of GafChromic EBT film and its implication on film dosimetry quality assurance. Phys Med Biol 2007;52:4211—25.
[31] Zeidan OA, Stephenson SAL, Meeks SL, Wagner TH, Willoughby TR, Kupelian PA, et al. EBT radiochromic film for IMRT dose verification. Med Phys 2006;33(11):4064—72.
[32] Butson MJ, Cheung T, Yu PKN. Absorption spectra variations of EBT radiochromic film from radiation exposure. Phys Med Biol 2005;50:135—40.