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journal homepage: www.elsevier.com/locate/radphyschemQuality assurance of alpha-particle dosimetry using peeled-off Gafchromic EBT3[®] filmC.Y.P. Ng^a, S.L. Chun^a, K.N. Yu^{a,b,*}^a Department of Physics and Materials Science, City University of Hong Kong, Tat Chee Avenue, Kowloon Tong, Hong Kong^b State Key Laboratory in Marine Pollution, City University of Hong Kong, Hong Kong

HIGHLIGHTS

- Proposed method to fabricate peeled-off EBT3 films for alpha dosimetry.
- Proposed integrity check of peeled-off EBT3 films using X-ray irradiation.
- Highlighted importance of scanning directions of EBT3 films.
- Cautioned the need for uniformity check on alpha-particle source.

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ABSTRACT

A novel alpha-particle dosimetry technique using Gafchromic EBT3 film has recently been proposed for calibrating the activity of alpha-emitting radiopharmaceuticals. In the present paper, we outlined four measures which could further help assure the quality of the method. First, we suggested an alternative method in fabricating the peeled-off EBT3 film. Films with a chosen size were cut from the original films and all the edges were sealed with silicone. These were immersed into deionized water for 19 d and the polyester covers of the EBT3 films could then be easily peeled off. The active layers in these peeled-off EBT3 films remained intact, and these films could be prepared reproducibly with ease. Second, we proposed a check on the integrity of the peeled-off film by comparing the responses of the pristine and peeled-off EBT3 films to the same X-ray irradiation. Third, we highlighted the importance of scanning directions of the films. The “landscape” and “portrait” scanning directions were defined as the scanning directions perpendicular and parallel to the long edge of the original EBT3 films, respectively. Our results showed that the responses were different for different scanning directions. As such, the same scanning direction should be used every time. Finally, we cautioned the need to confirm the uniformity of the alpha-particle source used for calibration. Radiochromic films are well known for their capability of providing two-dimensional dosimetric information. As such, EBT3 films could also be conveniently used to check the uniformity of the alpha-particle source.

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1. Introduction

Mukherjee et al. (2015) have recently proposed a novel alpha-particle dosimetry technique using Gafchromic EBT3[®] film and studied its feasibility for calibrating the activity of alpha-emitting radiopharmaceuticals. This pioneering research has provided a valuable method for inexpensive and convenient calibration of these radiopharmaceuticals, which is particularly needed by the community engaging in targeted internal therapy using alpha-particle emitters.

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Radiochromic films were originally designed for industrial applications and for clinical dosimetry applications (e.g., Butson et al., 1998, 2003). The color of the films changes due to polymerization when they are exposed to radiation such as X-ray and protons. According to the manufacturer, the Gafchromic EBT3 film consists of a 30 μm active layer sandwiched between two 125-μm clear polyester covers (see Fig. 1(a)). Since the ranges of alpha particles are much shorter than 125 μm in polyester, they cannot reach the active layer. As such, in developing the alpha-particle dosimetry technique, Mukherjee et al. (2015) proposed to peel off the polyester cover using a surgical scalpel. The authors determined the alpha-particle dose D_a deposited in the active layer as $D_a = AS(\Delta E/\Delta M)$, where ΔE was the alpha-particle energy loss, ΔM was the mass of stopping material within the energy loss volume, A was the time-integrated specific alpha surface activity,

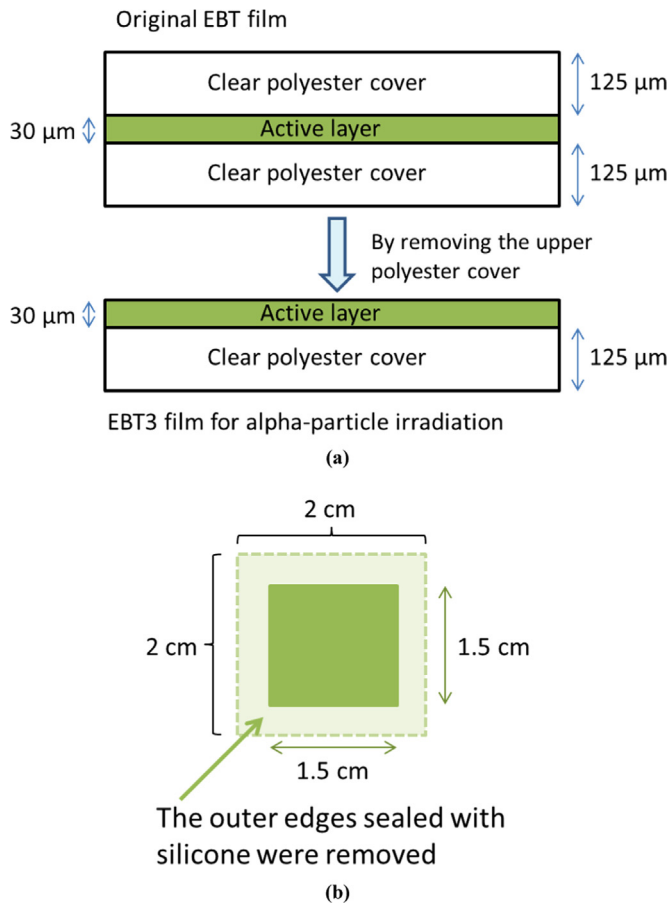


Fig. 1. (a) Physical configuration of the pristine EBT3 film and the peeled-off EBT3 film with the upper clear polyester cover removed. (b) Dimensions of the cut EBT3 film prepared for the peeled-off EBT3 film.

and S was the base area of a right cylinder in the active layer in which the alpha-particle energy was deposited. The diameter of this cylinder was assumed to be 0.7 cm (Mukherjee et al., 2015).

Although in the market there is another Gafchromic HD-V2 film which has an extremely thin layer of protective film so that alpha particles can hit the active layer, this film is designed for high-dose applications with doses between 10 and 1000 Gy. For a comparison, the Gafchromic EBT3[®] film is designed for recording doses between 1 cGy and 40 Gy, so this is more suitable for common applications.

The results obtained by Mukherjee et al. (2015) successfully established the EBT3 film as a calibrator for alpha-particle activity. However, we believe that a few extra measures, and probably an alternative method in fabricating the peeled-off EBT3 film, can further help assure the quality of the method. In the present work, we will first describe a simple method in fabricating the peeled-off EBT3 film and check the integrity of this film. The effects of scanning directions of the peeled-off films will also be described. Finally, a check on the uniformity of the alpha-particle source used for calibration is suggested.

2. Materials and methods

2.1. ISP Gafchromic EBT3 films

In the present work, ISP Gafchromic EBT3 films (Lot no. A03181301) were employed. Subsequent to each (alpha-particle or X-ray) irradiation, the films were kept in light-tight containers and

stored at room temperature. After at least 24 h, a selected part at the center of the irradiated area (with a size of $0.2 \times 0.2 \text{ cm}^2$) of each film was scanned at the same position at the center of an Epson Perfection V700 desktop flatbed scanner. The reflected mode was employed to capture 48 bit RGB color images. Filters and all color correction features were disabled and thus only the raw pixel value results were recorded. The red component of each image was analyzed using the ImageJ software (<http://imagej.nih.gov/ij/>). The color change in the scanned area of the irradiated film was characterized by the average net reflective optical density (ROD) defined as

$$\text{Net ROD} = \log_{10}(P_u/P_t) \quad (1)$$

where P_u and P_t were the average pixel values of the reflected intensity through an unexposed area and an exposed area of the film, respectively. This relation was also previously adopted for determining the ROD for an EBT3 film (Chun and Yu, 2014).

2.2. Peeled-off EBT3 films and integrity check

An alternative method was employed to prepare the peeled-off EBT3 films to ensure that the entire active layer remained intact. The original EBT3 film was cut to a size of $2.0 \times 2.0 \text{ cm}^2$ and all the edges were then sealed with silicone (Solid Firm) (see Fig. 1(b)) to prevent water from interacting with the active layer on the side. The sealed films were immersed into deionized water and placed inside a dark container for 19 d at room temperature. Some small weights (agate marbles) were placed on the films to prevent the films from floating. After 19 d, the films were dried and the outer edges of the films, which were sealed with silicone, were cut away to prepare the peeled-off EBT3 films.

The integrity of a peeled-off film was checked by comparing the responses of the pristine and peeled-off EBT3 films to X-ray irradiation, which was performed using the X-RAD 320 irradiator (Precision X-Ray, Inc., Connecticut) with the voltage and current set at 320 kV and 12.5 mA, respectively, and using a 0.5 mm thick filter which consisted of aluminum, copper and tin. The EBT3 films were irradiated within a uniform irradiation field size of $10 \times 10 \text{ cm}^2$ and at source-to-surface distance of 50 cm, and with an average dose rate of 85.6 cGy/min. The doses and dose rates were measured and monitored using the Universal dosimeter (UNIDOS[®] E Universal Dosimeter, PTW, Freiburg, Germany). A total of 16 and 18 X-ray doses up to $\sim 1500 \text{ cGy}$

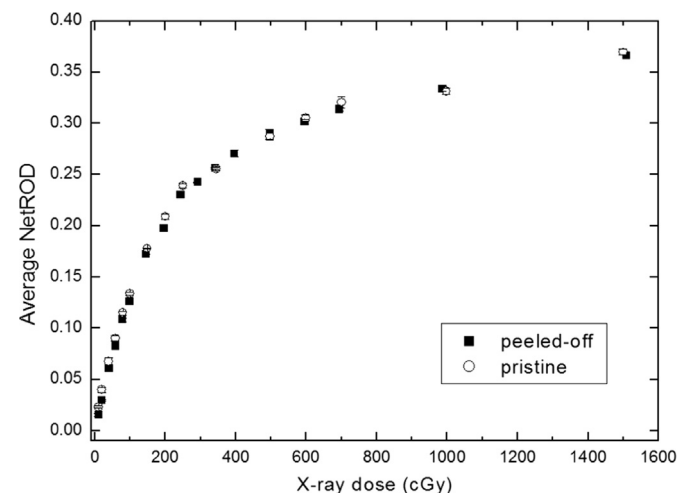


Fig. 2. Comparison between the responses in terms of average Net RODs of the pristine and peeled-off EBT3 films to X-ray doses (320 kV, 12.5 mA, with 0.5 mm thick filter consisting of aluminum and copper, irradiation field size = $10 \times 10 \text{ cm}^2$, source-to-surface SSD = 50 cm). The films were scanned in the landscape scanning direction. Each data point represents the mean value (\pm SEM) from three films.

were adopted to study the responses of the pristine and peeled-off EBT3 films, respectively, and both experiments were repeated with three different films. The films were scanned in the landscape scanning direction (see Section 2.3 below).

2.3. Effects of scanning directions

All EBT3 films came in a rectangular shape with a long edge and a short edge. The “landscape” and “portrait” scanning directions were defined as the scanning directions perpendicular and parallel to the long edge, respectively. The landscape scanning direction was usually adopted. Alpha-particle irradiation was performed using a planar ^{241}Am alpha-particle source (AF 241, Isotope Products Labs, Valencia, CA USA) with an activity of 4.26 kBq and a circular active area with a diameter of 5 mm. The emitted alpha particles have an energy of 5.49 MeV. During irradiation, the active area of the alpha-particle source was placed above and facing the active layer of the peeled-off film. Irradiation was performed in a dark box to avoid light or UV exposures from the surrounding. The films were irradiated for different durations up to 210 min. The films were scanned in both landscape and portrait scanning directions in this part of the experiments.

2.4. Uniformity check of alpha-particle source

As described in the beginning, Mukherjee et al. (2015) determined the alpha-particle dose D_a deposited in the active layer of the EBT3 film as $D_a = AS(\Delta E/\Delta M)$, which had effectively assumed that the Net ROD resulted from the alpha-particle irradiation was uniform. To ensure a correct calibration, however, a check on the uniformity would be required. Radiochromic films are well known for their capability of providing two-dimensional dosimetric information (Butson et al., 2003). As such, EBT3 films could also be conveniently used to check the uniformity of the alpha-particle source. In the present work, we exposed a peeled-off EBT3 film for 5 min to an ^{241}Am alpha-particle source (AF-241-A1, Isotope Products Labs, Valencia, CA USA) with an activity of 186 kBq and a circular active area with a diameter of 12 mm to obtain an image to check for uniformity. The results were confirmed by comparing with the chemically etched pits formed on a polyallyldiglycol carbonate (PADC) film which had also been exposed to the same ^{241}Am source for 5 min and subsequently chemically etched in 6.25 M NaOH solution at 70 °C for 3 h. PADC film was a commonly used solid-state nuclear track detector (see Nikezic and Yu, 2004) and could reveal the positions of alpha-particle traversals in the film through the corresponding developed etched pits.

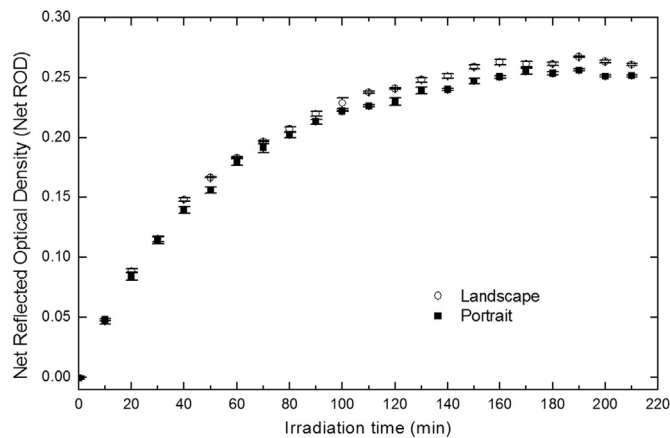
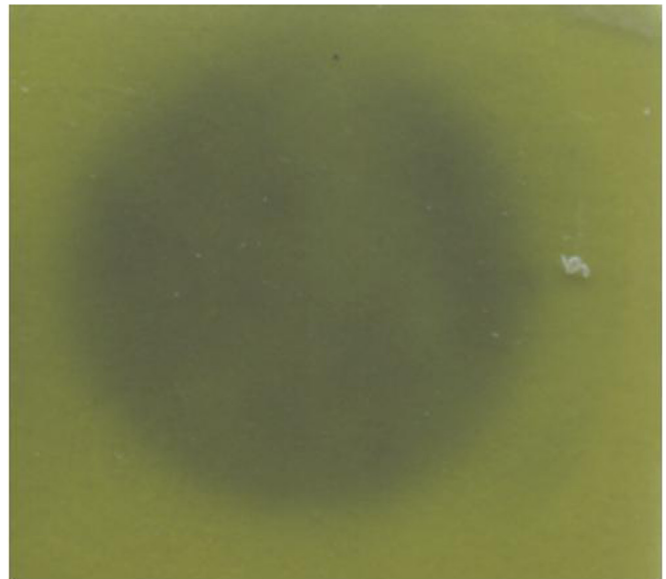


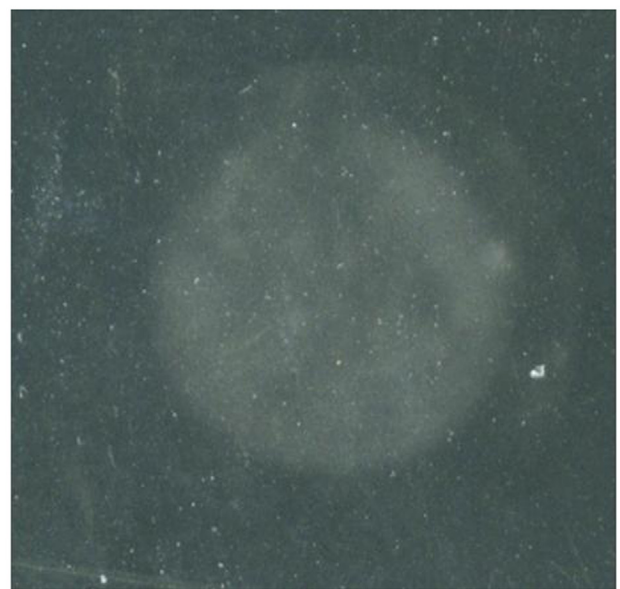
Fig. 3. Comparison between the responses in terms of average Net RODs of EBT3 films to irradiation time to alpha particles from an ^{241}Am alpha source scanned in the landscape and portrait directions. Each data point represents the mean value (\pm SEM) from three films.

3. Results and discussion

After the silicone-sealed EBT3 films were immersed in deionized water for 19 d and then dried, the polyester covers of the EBT3 film could be easily peeled off (see Fig. 1(a)). The EBT3 films with one of the polyester covers removed will be used as the peeled-off films. This “spontaneous” peeled-off method might help reduce the potential risk of breaching the integrity of the films through the “scalpel” peeled-off method. The results on integrity check are shown in Fig. 2, which demonstrate that our procedures to peel off a polyester cover of the EBT3 film has not affected the performance of the film to X-ray irradiation, and as such the integrity of the EBT3 film has been maintained. Although 19 d might appear at first sight to be a long time which can cause inconvenience, it is remarked here that these films are just left alone in



(a)



(b)

Fig. 4. Images of (a) a peeled-off EBT3 film after exposed to an ^{241}Am source for 5 min, and (b) a PADC film exposed to the same ^{241}Am source for 5 min and subsequently chemically etched in 6.25 M NaOH solution at 70 °C for 3 h.

the deionized water and no further actions are needed until they are harvested. As such, these peeled-off films could be prepared reproducibly with ease. The films with a final size of $1.5 \times 1.5 \text{ cm}^2$ (see Fig. 1(b)) were then ready for alpha-particle irradiation.

Fig. 3 shows the comparison between the responses in terms of average Net RODs of EBT3 films (scanned in the landscape and portrait directions) to irradiation time. The results showed that the responses were different for different scanning directions. As such, the scanning direction of the films should be noted carefully and the same scanning direction should be used every time to ensure accurate calibrations of the activities. The active layer in EBT3 films consists of rod-shape polymers which can lead to different scattering effects of light with different rotational reference during scanning. Scanning orientation effects of radiochromic films were better known for X-ray irradiations, which were attributed to the partially polarized light produced by desktop scanners when light was reflected or transmitted through the glass plates (e.g., Zeidan et al., 2006; Butson et al., 2006; Alnawaf et al., 2010). These scanning orientation effects were not previously shown for alpha-particle irradiation (Mukherjee et al., 2015). As the objective of the present work was to outline measures which could help assure the quality of the method, this information is also important.

As regards the uniformity check of alpha-particle source, Fig. 4(a) shows the image of a peeled-off EBT3 film after exposed for 5 min to the ^{241}Am alpha-particle source (AF-241-A1, Isotope Products Labs, Valencia, CA USA) with an activity of 186 kBq. Here, the image was scanned with a higher resolution of 600 dpi. Non-uniformity of the irradiation source was apparent. For confirmation, Fig. 4(b) shows the image of the etched pits captured with 600 dpi on the PADC film which had been exposed to the same ^{241}Am source for 5 min and subsequently chemically etched in 6.25 M NaOH solution at 70 °C for 3 h. The same pattern of non-uniformity was observed. Apparently, the peeled-off EBT3 film provided the information within a much shorter time frame than the PADC film. Now that the EBT3 film could be used as a two-dimensional alpha-particle dosimeter, it might also be considered for α -camera applications in the future, e.g., in ex vivo detection of α -particles in tissues as a tool for assessing the heterogeneous distributions in organs and tumors of α -particle-emitting

bioconjugates designed for α -radioimmunotherapy (Bäck and Jacobsson, 2010).

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