Title

Characterization of Stochastic Noise and Post-irradiation Density Growth for Reflective-type Radiochromic Film in Therapeutic Photon Beam Dosimetry

Authors and Affiliations

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Abstract

The aim of this study is to investigate the dosimetric uncertainty of stochastic noise and the post-irradiation density growth for reflective-type radiochromic film to obtain the appropriate dose from the exactly controlled film density. Film pieces were irradiated with 6-MV photon beams ranging from 0 to 400 cGy. The pixel values (PVs) of these films were obtained using a flatbed scanner at elapsed times of 1 min to 120 h between the end of irradiation and the film scan. The means and standard deviations (SDs) of the PVs were calculated. The SDs of the converted dose scale, u_{sd}, and the dose increases resulting from the PV increases per ±29 min at each elapsed time, u_{time}, were computed. The combined dose uncertainties from these two factors, u_c, were then calculated. A sharp increase in the PV occurred within the first 3 h after irradiation, and a slight increase continued from 3 h to 120 h. u_{sd} was independent of post-irradiation elapsed time. Sharp decreases in u_{time} were obtained within 1 h after irradiation, and slight decreases in u_{time} were observed from 1 to 24 h after irradiation. u_c first decreased 1 h after irradiation and remained constant afterward. Assuming that the post-irradiation elapsed times of all of the related measurements are synchronized within ±29 min, the elapsed time should be at least 1 h in our system. It is important to optimize the scanning protocol for each institution with consideration of the required measurement uncertainty and acceptable latency time.

Key words: radiochromic film, stochastic noise, post-irradiation density growth, dosimetric uncertainty

Introduction

In recent years, highly precise and accurate radiotherapy techniques such as stereotactic irradiation, intensity-modulated radiotherapy, and volumetric-modulated arc therapy combined with image guidance functions have rapidly evolved [1-3]. These treatment technologies can realize spatially suitable irradiation that leads to improvements in the survival outcomes and fewer treatment-related side effects [4-6]. However, the quality assurance (QA) of these new treatment techniques has become more important for the exact and safe delivery of radiotherapy [7].

A radiochromic film (RCF) is one of the most useful devices for the QA of radiotherapy equipment. The advantages of RCFs are their high spatial resolution, small energy dependence, tissue equivalence, and self-development without processing in a darkroom [8]. For quantitative dosimetry using an RCF, the film densities are quantitatively measured after irradiation. Formerly, the optical density obtained using a densitometer was used as the film density, but currently, a pixel value (PV) obtained using the film scanner is generally used. Subsequently, the dose distribution on the film is calculated using a dose calibration curve (film PVs versus dose values) that is prepared in advance or simultaneously.

Several studies have discussed the characteristics of RCF dosimetry [8, 9]. In the same absorbed dose range, it is well known that the radiation sensitivity of an RCF is relatively lower than that of a radiographic film, which is a traditional silver-halide-based film [10]. We have previously investigated the radiation sensitivity of an RCF and proposed a new technique for optimizing the sensitivity by using optical band-pass filters [11]. The important point is that the

low radiation sensitivity directly degrades the signal-to-noise ratio (SNR) that represents the image quality [8, 12]. In addition, the stochastic noise present within the digitized image becomes an important factor for controlling the quality of RCF dosimetry [13].

An RCF possesses certain characteristics called the post-irradiation density growth [14, 15]. The RCF density continuously increases after irradiation owing to a radiation-induced polymerization reaction within the sensitive layer. Therefore, when performing quantitative dosimetry with an RCF, the elapsed time between the end of irradiation and the film scan needs to be maintained at a constant value in all related measurements including the preparation of the dose calibration curve. An inconsistency in the post-irradiation elapsed time causes a systematic and/or random measurement error.

RCFs may be roughly classified as transmission-type and reflective-type. A reflective-type RCF, e.g., GAFCHROMIC® RTQA2, has been developed for qualitative dosimetry such as radiation-field and light-field alignment [16]. However, it is necessary to convert the film density to the dose scale to provide an accurate radiation field size because the dose calibration curves of the RCF are nonlinear [11]. Moreover, several studies employed this reflective-type RCF for quantitative dosimetry [17, 18]. Although a reflective-type RCF is not designed to be used for quantitative dosimetry, it is still useful to know its characteristic in dosimetry to obtain the appropriate dose from the exactly controlled film density.

To the best of the authors' knowledge, the dosimetric characteristic of stochastic noise and the post-irradiation density growth for reflective-type RCF has not been evaluated. Therefore,

the aim of this study is to quantitatively investigate the uncertainty of stochastic noise and post-irradiation density growth for reflective-type RCF.

Materials and Methods

Film irradiation

A reflective-type RCF, GAFCHROMIC® RTQA2 (Lot No. A11171101; Ashland corporation, NJ, USA), was evaluated in this study. The films were handled in accordance with the recommendations outlined in the American Association of Physicists in Medicine Task Group No. 55 report [8]. For irradiation, 6.0 × 6.0 cm^2 pieces of film were placed in a water equivalent phantom (TM phantom, Taisei Medical Inc., Osaka, Japan) at a 10-cm depth. The field size was set to 10 × 10 cm^2, and the source-axis distance was 100 cm. The film pieces were irradiated to the following doses: 0, 25, 50, 75, 100, 125, 150, 175, 200, 225, 250, 275, 300, 325, 350, 375, and 400 cGy with a 6-MV photon beam supplied by a Vero 4DRT accelerator (Mitsubishi Heavy Industries Inc., Tokyo, Japan).

Quantification of the film density

The effects of temperature on the film density growth and scanner response have been previously reported [19, 20]. In this experiment, film storage and analysis were performed at a temperature of 22 ± 2°C. Additionally, all films were kept in a light-tight envelope to reduce the effect of ambient light [20, 21].

An ES-10000G flatbed scanner (Epson Seiko Corporation, Nagano, Japan) was used for quantification of the film density. The films were scanned in the reflection mode with the software package EPSON Scan (Epson Seiko Corporation, Nagano, Japan; Ver. 3.685). All filters and image enhancement options were turned off, and images were obtained at 150 dpi in the 48-bit RGB mode (16 bits per channel). Before film scanning, the scanner was prepared with five empty scans. The scanned data were saved in an uncompressed tagged image file format. The films were scanned before irradiation and as soon as possible after irradiation (i.e., 1 min); then, the films were repeatedly scanned at 0.5, 1, 2, 3, 4, 5, 6, 12, 18, 24, 36, 48, 60, 72, 96, 108, and 120 h after irradiation. To eliminate the effects of the film orientation and the lateral density variation of the scanner bed [9], the films were placed at the same position with the same film orientation for every scan.

The region of interest for the measurement of the PV was set at 2.0×2.0 cm^2, and the means and standard deviations (SDs) of the PVs from the separated RGB color images were obtained by using Image J software (Wayne Rasband, National Institutes of Health, USA, Ver.1.46). Prior to a detailed analysis, the PVs were preprocessed as follows. In order to confirm the increasing/decreasing direction of the film density with the PV, the PV scale was transformed using the following formula: $65535 - PV$. Then, the amount of change in the PV caused by irradiation was set as the net pixel value (*netPV*), which was calculated as the difference between the PVs of the irradiated and nonirradiated films.

Analysis of the stochastic noise

For each of the elapsed times, dose calibration curves relating the PV to the dose were generated. We then derived the differential coefficients, *F′*, of all data points of the dose calibration curves. By using linear functions with the slope *F′* at each data point, the SDs of the converted dose scale from the SDs of the PVs were calculated and defined as the uncertainty of the stochastic noise u_{sd}. A schematic of this process is shown in Fig. 1. u_{sd} was analyzed according to the post-irradiation elapsed time.

Figure 1. Schematic of the conversion of the PV to the dose scale. The conversion of the PV to the dose scale was performed by using linear functions (red line) with slope *F′*, which is the differential coefficient of the dose calibration curve at each data point. The blue arrows indicate the calculation processes.

Analysis of the post-irradiation density growth

The variations in *netPV* with the post-irradiation elapsed time *t* are defined as follows:

$$\Delta PV_t = netPV_t - netPV_{1st}, \quad (1)$$

where $netPV_{1st}$ is the initial value of *netPV* obtained 1 min after irradiation. For a detailed analysis of the post-irradiation density growth, we derived the time constants of the elapsed time until ΔPV reached 63.2%, 86.5%, or 95.0% of the reference time. In this study, we defined the latest datum 120 h after irradiation as the reference time.

It is difficult to achieve completely coincident post-irradiation elapsed times for all of the related measurements in complex and busy clinical situations. Because the film density grows with the elapsed time, the inconsistency in the scan timing between the dose calibration curve and the target films will cause a dosimetric error. Therefore, the uncertainty of the post-irradiation density growth, u_{time}, was defined as the dose variation induced by the inconsistency in the post-irradiation elapsed time. First, the fluctuation in the post-irradiation elapsed time was assumed to be ±29 min, and the variations in the PV per ±29 min at each elapsed time were calculated. Subsequently, the dose variations per ±29 min, $u_{time\ (\pm 29\ min)}$, were computed from the variations in the PV by using the linear functions with the slope *F'*, which were estimated in the above section. In addition, the dose variations per ±15 min, $u_{time\ (\pm 15\ min)}$, and the dose variations per ±59 min, $u_{time\ (\pm 59\ min)}$, were estimated for comparison.

Integrated evaluation

The combined dose uncertainty was calculated on the basis of an uncertainty budget [22] as follows:

$$u_c = \sqrt{{u_{sd}}^2 + \left(\frac{u_{time\ (\pm 29\ min)}}{\sqrt{3}}\right)^2}. \quad (2)$$

Assuming $u_{time\ (\pm 29\ min)}$ has a rectangular distribution, a type-B evaluation (divided factor: $\sqrt{3}$) was selected for the uncertainty budget.

Results

The values of *netPV* for all color channels are shown in Fig. 2, and Fig. 3 shows a detailed plot of *netPV* versus the post-irradiation elapsed time (red color channel data for a radiation dose of 225 cGy). A sharp increase in *netPV* occurred within 3 h after irradiation. Then, a slight increase in *netPV* was observed from 3 h to 120 h after irradiation.

Figure 2. Transition of the net pixel value (*netPV*) with the post-irradiation elapsed time. The values of *netPV* were calculated as the differences between the pixel values of the irradiated and nonirradiated films at post-irradiation elapsed times of 1 min to 120 h between the end of irradiation and the film scan. The (a) upper, (b) middle, and (c) lower charts correspond to the red, green, and blue color channel values, respectively.

Figure 3. A detailed plot of the net pixel value (*netPV*) versus the post-irradiation elapsed time. Data are plotted for the red color channel for a radiation dose of 225 cGy. A sharp increase in *netPV* occurred within 3 h after irradiation. Then, slight increase was observed afterward.

The values of u_{sd} were independent of the post-irradiation elapsed time for all color channels, as shown in Fig. 4. The magnitude of u_{sd} depended on the absorbed dose and scanned color channel. Increases in u_{sd} were observed depending on the absorbed dose. The values of u_{sd} were the lowest for the red color channel, followed by those for the green color channel, and then

those for the blue color channel. In particular, u_{sd} for the blue color channel had a value that was approximately 10 times higher than those of the red and green color channels.

Figure 4. Standard deviations of the converted dose scale u_{sd} versus the post-irradiation elapsed time.

The results for the time constant of the PV increase are listed in Table 1. The time constants were not influenced by the color channel. The mean time constants for the three color channels when ΔPV = 63.2%, 86.5%, and 95.0% of the reference time at 120 h were 3.4 h, 32.5 h, and 73.9 h, respectively.

Table 1

Mean values and standard deviations of the time constant, *T*, when the variations in the increase in the pixel value reached 63.2%, 86.5%, and 95.0% of the reference value at 120 h post-irradiation.

Color channel	$T_{63.2\%}$ (h)	$T_{86.5\%}$ (h)	$T_{95.0\%}$ (h)
Red	3.5 ± 0.3	33.1 ± 1.1	74.4 ± 0.9
Green	3.6 ± 0.3	33.2 ± 2.2	74.5 ± 1.9
Blue	3.2 ± 1.2	31.3 ± 4.6	72.8 ± 4.1

The results of u_{time} are shown in Fig. 5. u_{time} depended on the absorbed dose, the post-irradiation elapsed time, and the fluctuation in the post-irradiation elapsed time. For $u_{time\ (\pm 29\ min)}$, a sharp decrease occurred within 24 h after irradiation, and a slight decrease was observed 24 to 120 h after irradiation. However, the sharp decrease in $u_{time\ (\pm 15\ min)}$ occurred more immediately than that in $u_{time\ (\pm 29\ min)}$; on the other hand, the decrease in $u_{time\ (\pm 59\ min)}$ occurred more slowly than that in $u_{time\ (\pm 29\ min)}$. The values of $u_{time\ (\pm 15\ min)}$ are approximately two times smaller than $u_{time\ (\pm 29\ min)}$, and the values of $u_{time\ (\pm 59\ min)}$ are approximately two times larger than $u_{time\ (\pm 29\ min)}$. The results for u_{time} for the red, green, and blue channels exhibited approximately the same tendency.

Figure 5. The dose variations per ±15 min, $u_{time\ (\pm 15\ min)}$; per ±29 min, $u_{time\ (\pm 29\ min)}$; and per ±59 min, $u_{time\ (\pm 59\ min)}$. The (a, d, g) upper, (b, e, h) middle, and (c, f, i) lower charts correspond to the red, green, and blue color channel values, respectively.

The increase in the combined dose uncertainty u_c depends on the absorbed doses for all color channels (Figs. 6a–c). A decrease in u_c occurred within 1 h after irradiation for the red and green color channels; then, u_c remained constant afterwards. For the blue color channel, a clear change in u_c with the post-irradiation elapsed time was not observed. The results for u_c per absorbed dose are shown in Figs. 6d–f. u_c per absorbed dose in the low-dose regime (< 50 cGy) was higher than that in the middle- and high-dose regimes. A decrease in u_c per absorbed dose also occurred within 1 h after irradiation for the red and green color channels.

Figure 6. (a, b, c) Combined dose uncertainty, u_{time}, calculated from equation (2) and (d, e, f) u_{time} per absorbed dose.

Discussion

In the reflective-type RCF, a sharp increase in the PV occurred within the first 3 h, followed by a slight increase from 3 to 120 h after irradiation. These results represented the same tendency as the results for the transmission-type RCF. Fuss *et al*. demonstrated rapid post-irradiation density growth for a GAFCHROMIC® EBT film within 2–4 h after irradiation [23]. Cheung *et al*. reported that the post-irradiation density growth mostly occurs within 6 h after irradiation and recommended leaving the film undisturbed for a period of 6 h after irradiation to improve the stability of the measurements [14]. Moreover, Martisikova *et al*. investigated the changes in the PV within ±3 h at 24 h after irradiation for an EBT film and found that they were ±0.1% for 0.3 Gy and ±0.2% for 1 Gy [24]. In comparison, the results in the present study were ±0.1% for 0.25 Gy and ±0.2% for 1 Gy. Hence, we conclude that there was no discrepancy between the transmission-type RCF and the reflective-type RCF with regard to the properties of the post-irradiation density growth. For the blue color channel, discontinuous changes in *netPV* occurred in the films irradiated at 170 cGy (see Fig. 2c). We assume that this discontinuous change is caused by both the extremely low-dose response in the blue color channel and the intrasheet uniformity [25].

Rink *et al.* evaluated the intra-irradiation changes in the optical density for a GAFCHROMIC® MD-55 film and EBT film using an in-house measurement device [26, 27]. The precipitous change in the optical density observed with irradiation and the pre-, intra-, and after-irradiation changes in the optical density were represented by three regression lines. These inter-irradiation data were not obtained in this study. However, we accurately executed film scanning as quickly as possible after irradiation (i.e., 1 min). Within the results of this experiment, we infer that the same precipitous inter-irradiation change and a consecutive post-irradiation change occur.

In this study, the film storage and analysis were performed at an ambient temperature of 22 ± 2°C that has been adopted by previous studies related to RCF dosimetry [28-30]. However, Mclaughlin *et al*. and Ali *et al*. demonstrated the dependence of the film response on the temperature during film readout [19, 28]. Moreover, Reinstein *et al*. proposed a rapid color stabilization procedure by utilizing the fact that the post-irradiation optical density depends on the temperature [30]. Furthermore, some authors have discussed the batch-to-batch variation in the sensitivity of the RCF. A slight change in the dose calibration curves dependent on the batch number was reported by Mizuno *et al.* [25]. The ambient temperature could potentially affect the systematic and/or random dosimetric error; thus, the variation in the ambient temperature should be considered during film storage and analysis. Although we have not evaluated the batch-to-batch variation in this study; this is a potential limitation of our study, and it might be particularly important to prepare dose calibration curves for each batch number to avoid an undesirable dosimetric error in a clinical situation.

On the assumption that the reference time was 120 h after irradiation, the time constants when ΔPV reached 63.2%, 86.5%, and 95.0% were approximately 3.5 h, 33 h, and 74 h after irradiation, respectively. According to the results of the time-constant measurement, it is clear that precipitous changes in the PV increase occurred within the first 3.5 h after irradiation. On the other hand, Fuss *et al*. reported that the optical development of a transmission-type RCF during 4 months consisted of a slow but steady increase and suggested that the increase in the optical density measured for very long post-irradiation times (~months) could be due to natural film aging [23]. Therefore, we did not execute a very long post-irradiation evaluation and defined the latest datum 120 h after irradiation as the reference time.

The uncertainties of the stochastic noise u_{sd} were independent of the post-irradiation elapsed time, and they were absolutely large compared to the uncertainty of the post-irradiation density growth effect u_{time} (e.g., $u_{sd} \approx 10$ cGy; $u_{time} < 0.5$ cGy at an absorbed dose of 200 cGy*)*. Stochastic noise is caused by the stochastic nature of optical photon detection in a charge-coupled device embedded in the flatbed scanner. The main stochastic noise sources are shot noise, dark noise, readout noise, and photoresponse nonuniformity noise [13]. Moreover, in this study, u_{sd} includes the film and irradiation variations. Hupe *et al*. stated that the noise is independent of the color channel [31]. However, u_{sd} depended on the color channel. This phenomenon is the cause of the difference in the evaluation scale. In this study, we employed the SDs of the converted dose scale instead of the SDs of the PV scale. Therefore, for the clinical evaluation, it will be important to ensure that the scales (unit) between the real clinical use and the evaluation of the uncertainty

are coincident. As for the uncertainty of the post-irradiation density growth effect, the values of $u_{time\ (\pm 15\ min)}$ are approximately two times smaller than $u_{time\ (\pm 29\ min)}$, and the values of $u_{time\ (\pm 59\ min)}$ are approximately two times larger than $u_{time\ (\pm 29\ min)}$. As might be expected, the scan timing of all related measurements should be synchronized as much as possible because the inconsistency in the scan timing clearly affects the dosimetric uncertainty.

For the red and green color channels, a decrease in u_c is observed within the first 1 h after irradiation. Because u_{sd} for each absorbed dose was constant throughout the post-irradiation elapsed time, the major factor in the characteristics of u_c was u_{time} until 1 h after irradiation. On the other hand, the predominant influence on u_c changed from u_{time} to u_{sd} after the first hour. From these results, the elapsed time should be at least 1 h in our system, assuming that the post-irradiation elapsed times of all the related measurements are synchronized within ±29 min. However, the impact of stochastic noise will depend on the scanner type and scanning parameters. Therefore, the scanning protocol should be optimized for each institution with consideration of the required measurement uncertainty and acceptable latency time. In our institution, we developed two scanning protocols. In the case where a prompt result is required, a film analysis is performed 1 h after irradiation according to these results. For other cases, the film analysis is performed 24 h after irradiation according to the recommendation of radiochromic film dosimetry [8]. For both protocols, the inconsistency in the scan timing between the calibration curve and the target films is synchronized within ±30 min.

Lewis *et al.* established an efficient protocol that combines calibration and measurement

in a single scan and enables measurement results to be obtained less than 30 min after irradiation [32]. This method is a highly useful tool in clinical situations. However, this method has several disadvantages: dedicated software is required, it is necessary to verify the uncertainty in this method, and it is difficult to estimate the source of error resulting from the special calibration. Therefore, we strongly believe that the simple and economical method described in this study is the fundamental technique for radiochromic film dosimetry, and we need to know and understand the uncertainty of this basic technique.

Conclusion

The uncertainties of stochastic noise and post-irradiation density growth for reflective-type RCF were investigated quantitatively. u_{sd} was independent of the post-irradiation elapsed time, and the inconsistency in the scan timing resulted in an increase in u_{time}. u_c decreased in the first 1 h after irradiation and remained constant afterwards at all dose ranges. Assuming that the post-irradiation elapsed times of all of the related measurements are synchronized within ±29 min, the elapsed time should be at least 1 h in our system. It is important to optimize the scanning protocol for each institution with consideration of the required measurement uncertainty and acceptable latency time.

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