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Authors: Agnieszka Walewska, Paweł Kukołowicz

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In-vivo dosimetry with Gafchromic films for patients with sarcoma

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Agnieszka Walewska, Paweł Kukołowicz

Medical Physics Department, Maria Skłodowska Curie Memorial Cancer Centre and Institute of Oncology in Warsaw, Warszawa, Poland

Corresponding Author: Paweł Kukołowicz, Maria Sklodowska-Curie National Research Institute of Oncology in Warsaw, Medical Physics Department, Warsaw, Roentgena 5, 02–781 Warszawa, Poland; e-mail: pawel.kukolowicz@pib-nio.pl

Abstract

Background: The aim of the study was to evaluate Gafchromic films as in-vivo detectors for intensity modulated radiation therapy for patients with sarcomas and to assess the quality of irradiation in these patients.

Material and methods: Phantom measurements were used to validate the measurements performed with the Gafchromic. The uncertainty of the measurement method and that in determining the reference dose value obtained from the treatment planning system (TPS) were independently estimated. In-vivo measurements were performed in 21 patients with sarcomas who were irradiated with dynamic techniques using a 5 × 5 Gy. For each patient, measurements were taken at four points using films placed on the skin under a 1 cm bolus. The results of the measurements obtained in the 96 treatment sessions were analysed. The treatment quality was assessed based on the differences between the doses calculated using the TPS and those measured.

Results: The uncertainty of measurements was less than 0.8% (one standard deviation). Owing to differences in the dose gradient, the uncertainty of the reference dose reading from the TPS had an individual value at each measurement point. The uncertainties were less than 3% for more than 95% of the points; 93% of the in vivo measurements showed a difference of less than 7% between the measurements and calculations.

Conclusions: Gafchromic films can be used for in vivo dosimetry using dynamic techniques. This method made it possible to detect errors of 7% with a probability of approximately 95%.

The results obtained for 21 patients with sarcoma demonstrated high-quality preparation and delivery of irradiation.
Keywords: in vivo dosimetry; Gafchromic EBT3 film; soft tissue sarcoma

Introduction

In the 1990s, *in vivo* dosimetry was often used for detecting major errors between planned and delivered doses, and evaluating the quality of irradiation [1]. Most often, semiconductor detectors were used for in-vivo dosimetry. One of the most significant limitations of semiconductor detectors for in-vivo measurements in dynamic techniques is their angular dependence and, to some extent, also their energy dependence (scattered radiation). Radiochromic EBT films have many attractive properties that make them good candidates for *in vivo* dosimetry, such as high spatial resolution, near-tissue equivalence, absence of angular dependence, and weak energy response. The only real disadvantage of using Gafchromic films as *in vivo* dosimeters is that the measurement results are not obtained immediately after irradiation. Gafchromic films have been used for dose control in total body irradiation and intraoperative therapy [2–4]. Several studies demonstrated the suitability of Gafchromic film for surface dose measurements in external radiotherapy with megavoltage photon beams [5–10] or external electron beams [11]. With the development of dynamic irradiation techniques, *in vivo* dosimetry has been replaced by other verification methods [12–17]. These methods are based on a comparison of the calculated dose distribution with the dose distribution measured in the phantom, the fluence of photons emitted by the therapeutic device, and the planned fluence. Solutions also exist where the fluence transmitted throughout the patient's body is measured during irradiation to calculate a “reconstructed” dose distribution in patient’s body. The essence of each of these methods is to compare the quantity calculated using the treatment planning system (TPS) or other software with the measured quantity. All of these methods provide indirect evidence that the treatment instituted is appropriate. Thus, old methods of verification with *in vivo* measurements are more reliable. However, in vivo dosimetry is no longer used in intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) for several reasons.

In this study, we present a method for film detector measurements of the dose received by patients with sarcomas treated with IMRT/VMAT techniques.

Materials and methods

Patients

Twenty-one consecutive patients with sarcoma were preoperatively treated with IMRT/VMAT. The planning target volume (PTV) ranged from 1210 cm^3 to 10817 cm^3. Truebeam or Clinac 2300 CD (Varian) 6 MV X-ray accelerators were used. The VMAT plan consisted of 2–6 arcs, while the IMRT plans consisted of 7–9 fields. Treatment plans were prepared using the Eclipse Treatment Planning System (Varian, Analytical Anisotropic Algorithm, version 13.6.23). For each patient, a 1 cm bolus was used to deliver the complete dose to the skin. Each patient received 5 daily fractions at a total dose of 25 Gy. The prescribed dose was calculated as the mean PTV dose. An example of the dose distribution is shown in Figure 1.

Detectors

The EBT3 and EBT-XD Gafchromic films were used in this study. A description of the detector can be found in previous studies [18, 19]. The measurements were performed using small square pieces ($2 \times 2cm^2$) of Gafchromic films.

Reference calibration curve

Separate reference calibration curves were constructed for each film type. Seven rectangular pieces of film placed at a depth of 10 cm and a distance of 100 cm were irradiated in a solid water phantom with a 6 MV photon beam. A TrueBeam accelerator (Varian) was used for irradiation of Gafchromic films. Each calibration strip was exposed to different doses in the range of 2–10 Gy (EBT3) or 4–20 Gy (EBT-XD). One strip of each type of film was left unexposed. The films were analysed after 48 h. The film samples were scanned in the transmission mode using a Perfection V750 flatbed scanner in the 48-bit RGB colour mode at a resolution of 72 dpi. The scanner was warmed prior to scanning. Five consecutive preview scans were performed to stabilise the state of the scanner lamp [20]. The strips were always placed at the centre of the scanning area along the direction of the lamp movement. The Gafchromic films were maintained in the same orientation during scanning and were covered with thin glass to avoid curling of the film. The average pixel values were read from a 1 cm × 1 cm square region of interest (ROI) located at the centre of each strip [21, 22]. A three-channel method was used [23]. Reference calibration curves were obtained by fitting the curves (Equation 1) to the data. The least-squares method was used.

$$PV_{x,cal}(D) = \frac{(\alpha_x + \beta_x D)}{(\gamma_x + D)} \quad (1)$$

where α_x, β_x , γ_x – parameters, D – dose, $PV_{x,cal}$ – mean of the pixels' value in ROI.

One reference calibration curve was used for the films with the same LOT number.

Actual calibration curve

Calibration curves were rescaled according to the Lewis procedure [24] and obtained for each therapeutic session. To determine the scaling coefficients, two 2 cm × 4 cm film-scaling strips were prepared for each film type. Immediately after each therapy session, one strip was irradiated at a dose of 5 Gy. The second group was not irradiated.

In vivo measurements

For each patient, the doses were measured at four points. At each measurement point two films (2 x 2 cm^2) located on the skin, one on top of the other, were used. Figure 2 (left) shows the locations of these points. Figure 2 (right) shows the computed tomography (CT) cross-section of a random patient. The positions of the two sets of films labelled B and D under bolus are marked. Before planning CT, three set-up tattoos were administered, the anterior tattoo and two lateral tattoos. During treatment setup, patients were aligned to room lasers using these three tattoos. Next, the appropriate shifts were made to find the position of isocentre. The first (central) *in-vivo* detector was placed on the body surface above the isocentre. The rest of the detectors were placed at a distance of 5 cm towards the head, legs and outwards on the irradiated side of the body. The detectors were always placed between two very thin foils. The foils were sterilized just before placing. The film-scaling strips were exposed immediately following the exposure. They were scanned together so that the actual calibration curve could be used for each *in vivo* measurement. The dose measured with a single piece of Gafchromic film was represented by the mean value of the pixels in the 1 × 1 cm^2 ROI located at the centre of the detector. The measured dose was the mean dose obtained from the readings from the two detectors. The ImageJ plugin, GAFchromic software (GAFchromic is a program written in our department), and triple channel method were used.

For each patient, the reproducibility of irradiation was evaluated in terms of the standard deviation of the mean differences between the measured and calculated doses normalised to the reference dose calculated in the TPS for each measurement point.

Reference value of the dose obtained with the TPS

The centre of the detector, i.e. the point Q, was defined in the TPS on the CT scans. In a square of 1 cm × 1 cm around Q the doses were read every 0.1 cm using Eclipse software. Next, the mean dose to all 1 cm x 1 cm squares which centres were displaced of the vector (n,k), where n x 0.1 cm, n = –5,–4, …, 5 and k x 0.1 cm, k = –5,–4, …, 5, was calculated. The

reference dose at point Q was represented by the mean of 121 mean values obtained for each square (equation 2).

$$D_Q = \frac{\sum D_{nk}}{121} \qquad (2)$$

So, as a reference dose value from the treatment planning system (TPS) at a given measurement point, the average dose value from 121 regions of interest (ROIs) measuring 1 x 1 cm² around the given measurement point was adopted. The uncertainty in determining the dose in the 1 x 1 cm² ROI was taken as the standard deviation SD_{ROI}. This is individualized for each measurement point, for each patient, and primarily depends on the dose gradient in the vicinity of the measurement point.

To estimate the uncertainty of dose readings from profiles calculated in the treatment planning system, for a randomly selected patient, the reading from profiles at each measurement point (A, B, C, D) was repeated ten times according to the rule described above. The relative uncertainty of dose readings from the profiles of the treatment planning system was assumed to be the highest standard deviation SD_{TPS} from all measurement points.

For the uncertainty of calculations of the treatment planning system SD_{TPScal}, the standard deviation for a rectangular distribution with a width of (–3%, 3%) was adopted. Before the clinical use of the TPS, a wide range of tests was performed according to Polish recommendations [25]. A comparison of dose distribution calculations and measurements of depth dose curves (DDC) and profiles showed very good agreement, except for the first few millimetres DDC below the surface, where differences of 1% were observed. At larger depths, the differences in the DDC were less than 0.1%.

In this study, the total uncertainty in determining the dose from the treatment planning system at each measurement point was determined according to the equation 3.

$$\Delta D^{I,J}_{TPStotal} = ¿ \quad \sqrt{\left(SD^{I,J}_{ROI}\right)^2 + \left(SD_{TPS}\right)^2 + \left(SD_{TPScal}\right)^2} \qquad (3)$$

$\Delta D^{I,J}_{TPStotal}$ – the total uncertainty in determining the dose calculated in the treatment planning system for the I-th patient at the J-th measurement point;

$SD^{I,J}_{ROI}$ — uncertainty of dose determination in 1 x 1 cm² ROI calculated in a treatment planning system for the I-th patient, at the J-th measurement point;

SD_{TPS} — uncertainty of reading the doses calculated in the treatment planning system from the profiles for the I-th patient, at the J-th measurement point;

SD_{TPScal} — uncertainty of the dose calculation in the treatment planning system for the I-th patient, at the J-th measurement point (uniform distribution).

The relative uncertainty of the dose calculation in the treatment planning system and the relative uncertainty of the readout of the dose calculated in the treatment planning system assumed in this study have a constant percentage value for the methodology used. In contrast, the uncertainty of the dose determination in the ROI is an individual value for each point, depending on the homogeneity of the dose in its surroundings.

Measurement uncertainty

To evaluate the uncertainty of the measurement method, measurements were performed in a solid water phantom at a depth of 1 cm (under a 1 cm bolus) with a 6 MV X-ray beam. The experiment was repeated ten times. The source-skin distance was 90 cm. Measurements were performed separately for the EBT3 and EBT-XD films. For each film type, a set of two additional 2 × 4 cm film fragments (scaling strips), necessary for rescaling the calibration curve, was prepared. In each set, one of the scaling strips remained unirradiated and the other was irradiated with a 5 Gy dose. The reference dose was measured using an ion chamber according to the *International Atomic Energy Agency* (IAEA) 398 protocol. The difference between the chamber and film measurements was calculated for each piece of film. The mean difference over 10 measurements and standard deviation of these values were calculated.

Additional dose delivered by setup imaging

The positioning of patients with sarcoma is challenging. Therefore, the position of each patient in each fraction is usually checked several times using kV and/or MV planar images or cone-beam CT (CBCT). The film detectors were placed before the setup control, resulting in an additional dose. The doses registered by single CBCT, kV, and MV were estimated to be 2, 1, and 3 cGy, respectively [26–28]. The total additional dose for each patient was estimated by considering all the setup images.

Results

Uncertainty of reference dose estimation from the TPS

The standard deviation of a uniform distribution with limits of ± 3% was adopted as the relative uncertainty of the dose calculation in the Eclipse, which is 1.73%.

As we highlighted previously, the uncertainty of the reference dose determination was dependent on the dose gradient around the measurement point. The relative uncertainties of doses from TPS for individual measurement points ranged from 0.1% to 15.4%. However, for 88.5% and 94% of measurement points the uncertainty was smaller than 1% and 2.6% of dose calculated in the treatment planning system, respectively.

Film measurement uncertainty

Considering that the measurement result was determined as the average of the readings from two pieces of Gafchromic films, the uncertainty of the dose reading from two film pieces for EBT3/EBT-XD and EBT3/EBT3 were 0.64% and 0.73%, respectively, which were 0.03 Gy and 0.04 Gy for the 5 Gy dose, respectively.

Action level

Uncertainties in the differences between the reference doses estimated by the TPS and the measured doses were less than 3% for more than 95% of the points. Based on this result, we assumed that the measurement results did not indicate a treatment error if the deviation between the measured and calculated doses was less than 7%.

Results of the in vivo measurements

For 21 patients in 7 of the 105 treatment sessions, the measurements were not performed owing to varying technical challenges. A total of 760 film readings were analysed.

The difference between the measured and reference doses did not exceed 7% at 95.5% of the points where the dose gradient was small (i.e. the uncertainty in the determination of the reference dose was< 2.6%). The results for all the patients and their points are shown in Figure 3. Patients 7 and 16 exhibited the greatest variations between the measured and reference doses. In these cases, the dose gradient near Point C is very large. In 85% of the cases, the differences between the measured and reference doses were positive, indicating that the measured dose was higher than the calculated dose. This systematic difference may be due to two reasons. It is likely that the extra dose obtained from the setup control was underestimated. Positioning the patients with sarcomas was challenging and several controls were required. A second source of this difference may simply be the treatment planning

system and the inaccuracy of the calculations in the build-up region. The repeatability of the irradiation, in terms of the standard deviation of the differences between the delivered and calculated doses for each patient at each measurement point normalised to the calculated doses, is shown in Figure 4. The mean values calculated for all patients of the standard deviations at points A, B, C, and D were 1.6%, 1.1%, 2.2%, and 1.3%, respectively. The results demonstrated good reproducibility, except in patients #16 and #17.

Discussion

A key issue for in-vivo dosimetry is the determination of a reference dose. In our case, the reference dose is determined in the treatment planning system which is not easy. Numerous studies, including ours, have reported that surface doses are calculated in TPS with large uncertainties [29–32]. The uncertainty decreases with an increase in the calculation depth. Therefore, *in vivo* measurements are usually performed using a bolus or build-up cap. In our case, the doses were measured using a 10 mm bolus. The uncertainty in the dose calculation was very small and did not exceed 0.1%. However, the dose gradient near the measurement point significantly affected the accuracy of determining the reference dose for dynamic plans. This was caused by the rather low precision of detector positioning. The greater the gradient, the greater is the error in determining the reference dose. We estimated that this uncertainty was less than 2.6% of the prescribed dose at 94% of the measurement points. However, at some points, this uncertainty was much higher. Therefore, the precise selection of measurement points plays an important role. Considering the other factors influencing the uncertainty in determining the difference between the calculated reference dose and the measured dose, we estimated that it was possible to detect a difference of 7% with 95% probability. These results indicate that Gafchromic detectors can be used for *in vivo* dosimetry using dynamic techniques. However, it should be emphasised that this type of dosimetry requires a great deal of care and skill on the part of the person performing the measurement. Precise positioning of the detector on the patient's body is important. Incorrect positioning can significantly increase measurement uncertainty. To make the method more accurate and to reduce the uncertainty of the detector position, a better method for defining the position of the detector should be established. CBCT could be used for this task. A limitation of the method is that the result is obtained a few hours after the measurement is taken. The method is quite time-consuming.

In this study, *in vivo* dosimetry was performed on patients with sarcomas. Irradiation of patients is challenging and requires high-quality preparation and delivery. Our results show

that the entire procedure was performed very well. The standard deviation between the measured and calculated doses, normalised to the calculated reference doses, was less than 2% for 87% of the measurements. The measured dose was higher than the calculated dose in 85% of the measurements. This result can be explained by the underestimation of additional doses registered by the Gafchromic films during setup control. One of the most challenging tasks for patients with sarcoma is to obtain the planning position of the patient. To achieve this goal, position control was repeated several times for most patients, that is, planar portal control or CBCT was performed. Although the doses were estimated for each patient, this dose was underestimated. The uncertainty of the dose measurement method using the Gafchromic film estimated in our study (SD < 0.8%) was similar to that reported in previous studies [33–35].

Conclusion

With the dynamic irradiation technique, performing *in vivo* dosimetry is possible using small pieces of Gafchromic film. The uncertainty of this method is not greater than that of other *in vivo* dosimetry methods. For almost all patients and all fractions the difference between expected and measured dose was small and the reproducibility of measured doses was very good, which indicates high quality of preparation of treatment and irradiation.

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Conflict of interests

Authors declare no conflict of interests

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Figure 1. Example of dose distribution in radiotherapy of sarcoma localized in the extremities and trunk; 95% isodose is presented

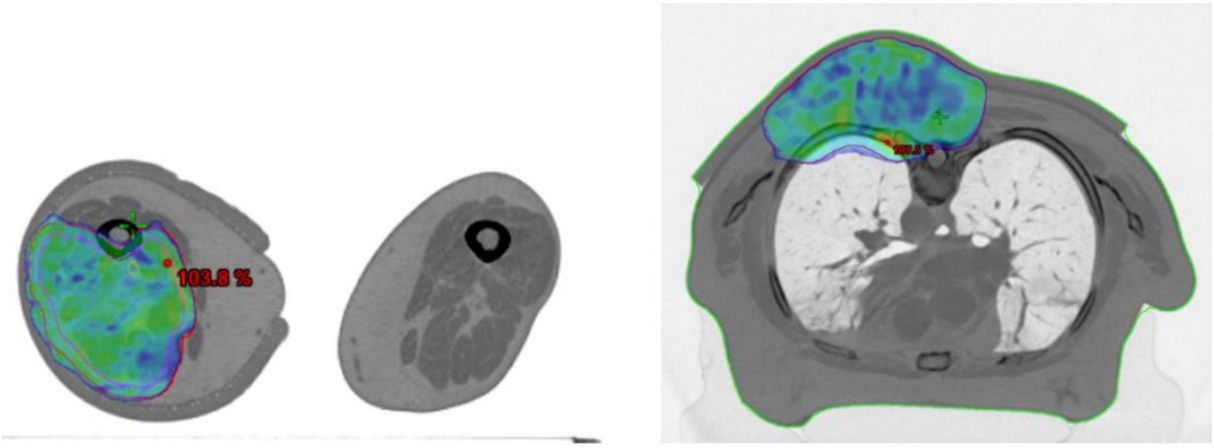

Figure 2. Locations of the measurement points

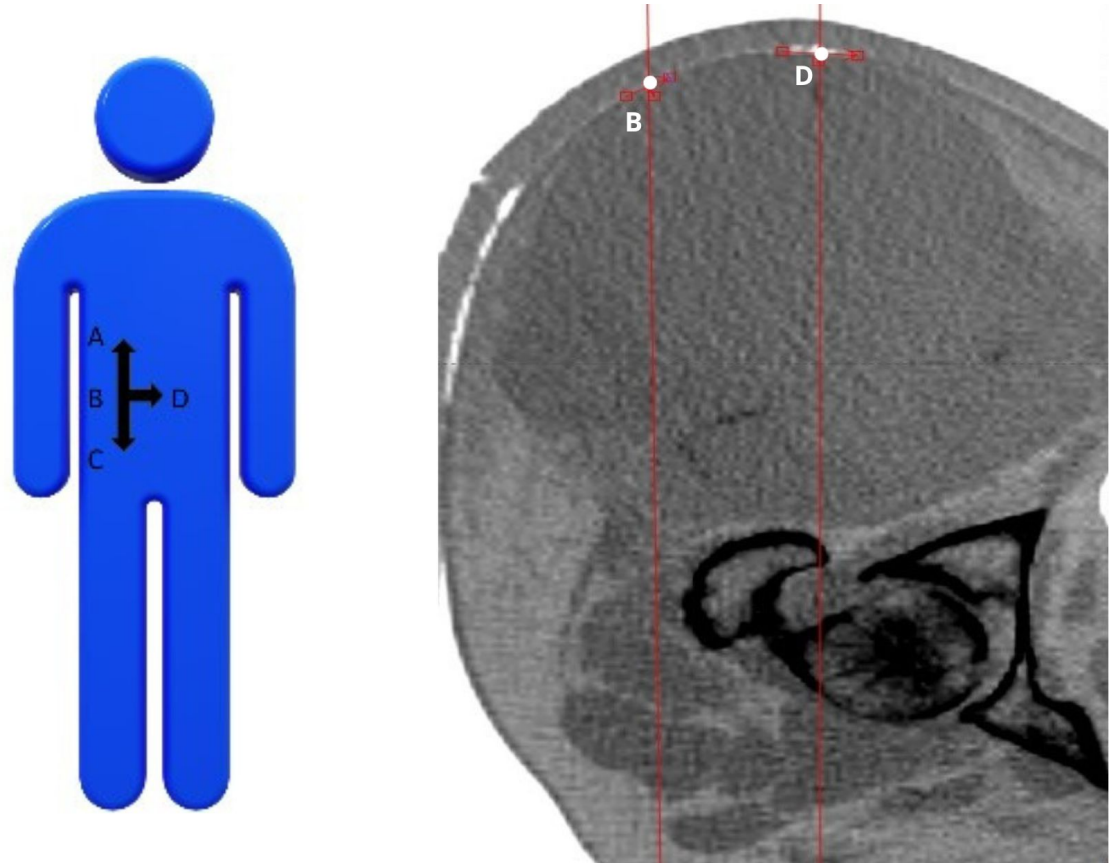

Figure 3. Difference between measured and reference doses for all patients and points, expressed as a percentage of the reference dose

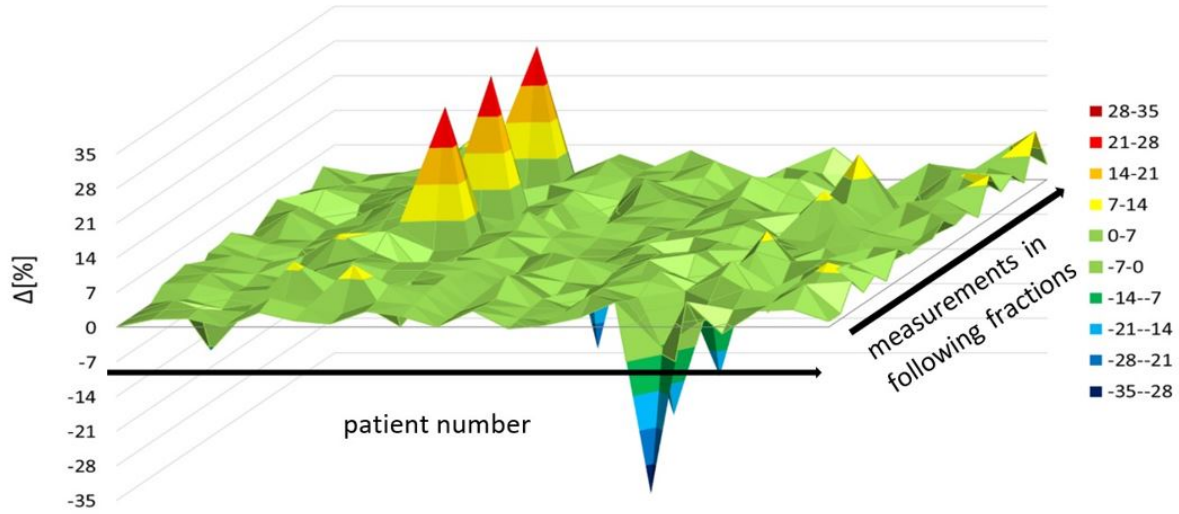

Figure 4. The normalized standard deviation of the measured doses in all the fractions at each of the measurement points A, B, C and D