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Characterization of small PRESAGE® samples for measurements near the dosimeter edges

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Abstract. Measurements near the edges of PRESAGE® 3D dosimeters will be important for validating the electron return effect (ERE) that can occur at tissue-air interfaces during radiotherapy treatment delivered with the Elekta MR-linac. We investigate and characterize the spatially non-uniform response of small samples of PRESAGE® to radiation in a conventional linac. We develop a correction to compensate for these non-uniformities and obtain dose values near the dosimeter edges. Five samples from the same batch were uniformly irradiated in a water tank with a broad beam. The non-uniform response of the samples to radiation was investigated and a radial dose-correction function was generated from each sample to obtain a correction image. We then applied these correction images to another sample from the same batch, irradiated with four beams in an inhomogeneous medium, and compared this with the relevant simulated data. Additionally, we irradiated samples after physically removed their edges (axially and top and bottom edges). Higher sensitivity to radiation was observed at the edges (~6mm) of the samples in comparison with the central region. Applying the dose correction function improved agreement between simulations and measurements, but only partial correction was possible. A uniform response was observed on the samples with the edges removed, which we propose as the best option to measure dose at the edges of PRESAGE® samples.

1. Introduction

Radiotherapy for lung cancer can benefit greatly from real-time plan adaptation as motion is always present and high doses of radiation are given [1]. In the MR-linac the constant B0 magnetic field can create a strong dose increase at the proximal side of air cavities and a decrease at the distal side. This is known as electron return effect (ERE) and is a consequence of the Lorentz force acting perpendicularly to the motion of the electrons [2]. In previous work [3] we have shown that small diameter PRESAGE® 3D dosimeters [4] can be used to measure dose at dosimeter-air interfaces and to detect accurately the ERE using the flat end of a cylindrical dosimeter. Non-uniform radiation sensitivities within the samples were observed in that work. Different radiation sensitivities at the center and the edges have also previously been reported for large PRESAGE® samples [5, 6] by other groups, and are thought to arise as a result of the manufacturing process. In addition, measurements near the interfaces between the dosimeter and surrounding optical matching liquid have historically been regarded as problematic

because of the potential for refractive index mismatches. Thus, the outermost 5mm of data are often disregarded in studies using PRESAGE®. This is normally of little consequence either because the samples used are large and so the discarded fraction of data is insignificant, or because these outer shells of data contain only very low doses (dose penumbra region).

In this work we investigate and characterize the non-uniform response of small samples of PRESAGE® to radiation in a conventional linac, using samples from the same batch in order to develop a correction image to compensate for those non-uniformities. We tested the correction on a dosimeter which was irradiated with a simple dose distribution, but in a clinical relevant scenario, inside a lung phantom and mimicking a tumour. Alternative ways to measure doses near the PRESAGE® samples edges were also investigated.

2. Material and Methods

2.1. Presage® 3D dosimeters
A PRESAGE® (Heuris Pharma, Skillman, NJ) 3D dosimeter consists of a solid-state polyurethane matrix with a free radical initiator and a leuco-dye. When irradiated, the leuco-dye oxidises from leuco malachite green to malachite green showing an optical density (OD) change whose peak absorption maximum is at around 633 nm. A batch of cylindrical PRESAGE® samples was manufactured using silicone moulds developed in house, in order to obtain samples with a smooth finish and consistent diameter throughout the length of the sample. Each sample was 3.5 cm in diameter and 5.5 cm ($\pm$0.2 cm) long, had a flat side (region corresponding to the bottom of the mould) and a curved side (meniscus region corresponding to the top of the mould). Five samples were randomly selected from the batch and their flat side glued to a 3D printed cap. The cap shape was created so each sample could be positioned in a reproducible way when being scanned and irradiated.

2.2. Optical-CT scan
To measure changes in optical-CT pixel value, PRESAGE® samples were always scanned before and after being irradiated (within the same day). The scanner used in this work was a modified version of the one described by McErlean et al 2016 [7], which includes a new telecentric lens (TC2MHR096-C, Opto-Engineering, Italy) to allow to image samples up to 10 cm diameter and a new rotation stage (CR1/M-Z7K, Thorlabs Ltd., Ely, UK). Each sample is placed inside a tank with a matching liquid, which was carefully adjusted to the same refractive index as PRESAGE® in order to minimize edge artefacts originating from index mismatch. Raw data consisting of 1000 projections each of matrix 320 × 320 pixels were obtained over 180° rotation to create reconstructed images with a voxel size of 0.2mm^3.

2.3. Non-uniform dose response characterization and correction
The existence of a non-uniform dose response of the dosimeter to radiation was initially investigated using only two samples. Irradiations were carried out at our research Elekta Synergy Linac. The sample holder was placed inside a water tank (MP1, PTW, Germany) at 90 cm source-to-surface (SSD) distance and 10 cm depth (Figure 1a). To deliver a uniform dose of 2Gy, the dosimeter was irradiated with a 6 MV beam, a 10 x 10cm^2 field size and gantry at 0° with four equal beams. The sample was rotated by 90° between each beam irradiation. This process was repeated to irradiate uniformly the samples with accumulated doses of 4Gy, 6Gy, 8Gy and 10Gy. An optical-CT scan was performed between irradiations, always 60 minutes after the delivery of the last beam. This experiment was performed for both Sample 1 and 2. Two months later, three further samples (3 to 5) were irradiated under the same experimental conditions but with different doses (2Gy + 4Gy + 4Gy), thus obtaining accumulated doses of 2Gy, 6Gy and 10Gy. A pre-scan was taken for each sample. All samples were kept in a fridge (~8°C) and taken out 90 minutes prior to the pre-scan to allow for equilibration with the ambient temperature.

A possible correction to a dosimeter non-uniform response to dose at the edges was investigated by taking the radial average of each sample (averaged in lengths thought the middle region of the sample

(from slices 100-250 in Figure 1c), for each dose level). The relation (always found to be linear) between dose and optical-CT pixel value was characterised separately for each radial distance, leading to both a gradient m and intercept value c that varied as a function of radial distance from the central axis of the sample. Thus, each of our correction image datasets was reduced to a calibration of form:

$$\Delta I(D,r) = c(r) + m(r)D \qquad (1)$$

where ΔI is the change in optical-CT pixel value between the pre-scan and the post-irradiation scan. D corresponds to the dose and r is the radial distance of each sample which is given by $r^2 = x^2 + y^2$. Since ΔI corresponds to the variation in optical-CT pixel value, $c \approx 0$, and we can ignore it. Note that, although the calibration is obtained via a radial average, the correction is applied on a voxel-by-voxel basis i.e.:

$$D(x,y,z) = [I_{\text{post}}(x,y,z) - [I_{\text{pre}}(x,y,z)]/m(r) \qquad (2)$$

where z corresponds to the direction along the sample length. The calibration from each correction image series was tested on a dose distribution obtained with another sample from the same batch. Note that this only corrects axial edge effect, and not the top and bottom edges. The research version of Monaco (5.19.03, Elekta AB, Stockholm, Sweden) treatment planning system (TPS) was used to simulate a plan consisting of four equidistant 6 MV beams delivered to a sample of PRESAGE® placed within a lung phantom (QUASAR™ MRI4D motion phantom, Modus Medical, London, Ontario) to a maximum 9.7Gy. The sample was cut at both ends to be 5 cm long. For comparison, EBT3 Gafchromic films (ISP Corp, Wayne NJ, USA) were irradiated in the same conditions as the PRESAGE® samples. A pieces of film was placed between two sets of two half Perspex cylinders of 5 cm length and oriented in the sagittal direction, while a second piece of film was oriented in the coronal direction. Films were scanned 24 hours after irradiation and data analysis was performed, in the red and green channels, using Film QA Pro software (Ashland Inc., Wayne, NJ).

2.4. Physical removal of the dosimeters edge

On the assumption that the varying sensitivities to radiation were introduced into the samples during the manufacturing processes the edges of the samples were removed. Sample 1 was reduced in diameter from 3.5 cm to 2.5 cm using a metal lathe, and Sample 2 was reduced in length by removing 6mm from each end. Both samples were scanned after being cut and then uniformity irradiated with additional 6Gy. The samples were then scanned 60 minutes after the irradiation.

3. Results and discussion

3.1. Non-uniform dose response characterization and correction

Results obtained with all five samples showed that the samples responded linearly with dose as expected, but seem to have higher sensitivity to radiation in the edges when compared to the middle. This effect is clearly visible for both axial edges and also top and bottom edges of the samples. This is shown in Figure 1b and c for Sample 1 with accumulated dose of 10Gy. In Figure 1d, the radial average of optical-CT pixel value is shown for each accumulated dose. Here we can see that this effect occurs on the last 25-30 pixels (corresponding to 5 to 6mm), and the remaining dosimeter shows a relatively flat profile (i.e., uniform dose sensitivity). Absolute differences between sample central region and edges can go up to 20%. The magnitude of the edge effect is dependent on the accumulated dose and increases with dose. In Figure 1e the relationship between optical-CT pixel value and dose is shown for Sample 1 for different radial distances. For larger radial distances (near the edges), the gradient of the fitted lines increase, but the linearity between optical-CT pixel value and dose is kept. This happens for all five samples. As the absolute gradient values for each sample were different (data not shown), the gradient values were normalized to the central region of each sample as shown in Figure 2a. Figure 2a shows how the profiles are broadly comparable between samples, but sample 3, 4 and 5 have a longer edge effect, which could be due to their age in relation to Sample 1 and 2. A 2D gradient map correction image was calculated

for each sample based on the normalized gradient for each radial position as shown in Figure 2b for Sample 1.
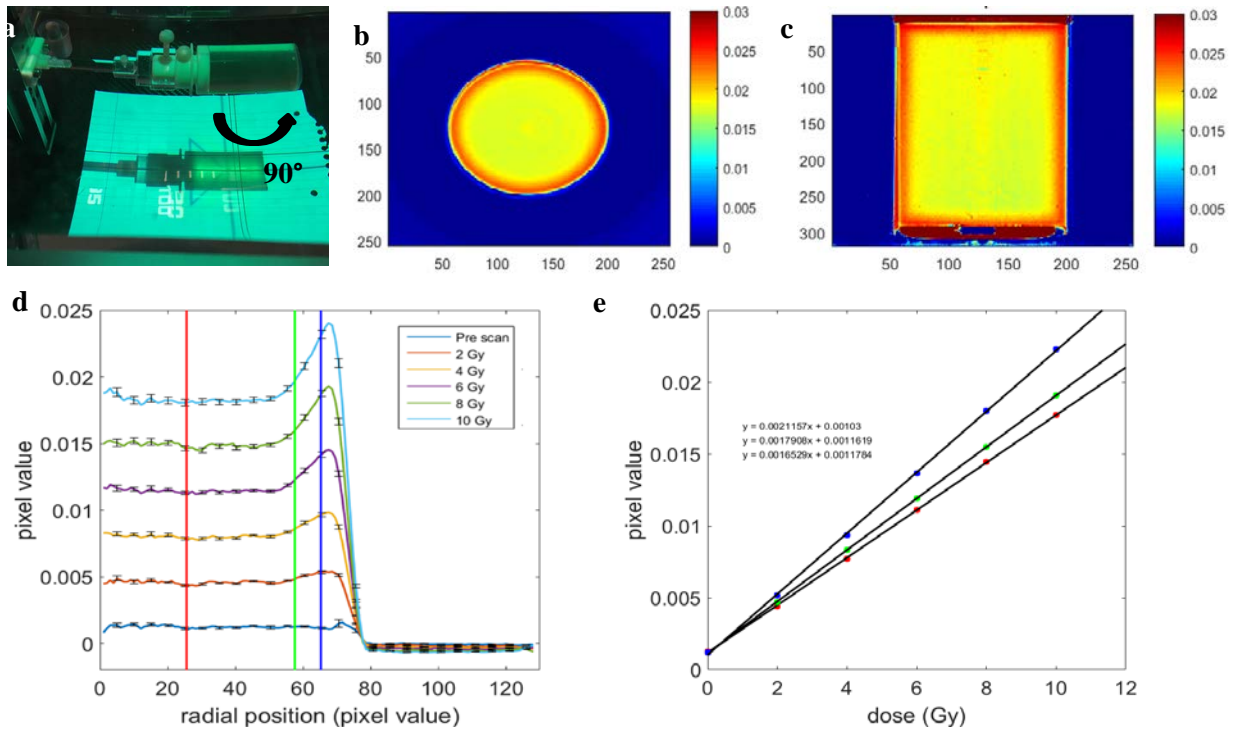

Figure 1. (a) Experimental set-up with a sample positioned in the water tank at 10 cm depth. The holder allows rotating the sample by 90° and locking it in position. 2D reconstructed optical-CT pixel image of a central (b) axial and (c) sagittal slices taken from Sample 1, with 10Gy accumulated dose. (d) Radial average for each accumulated dose obtained by averaging central region (from pixel 100-250) of the sample shown in c. One standard deviation is also shown. (e) Dose versus optical-CT pixel value obtained for three different radial positions taken from Sample 1 and given by the vertical lines in d.
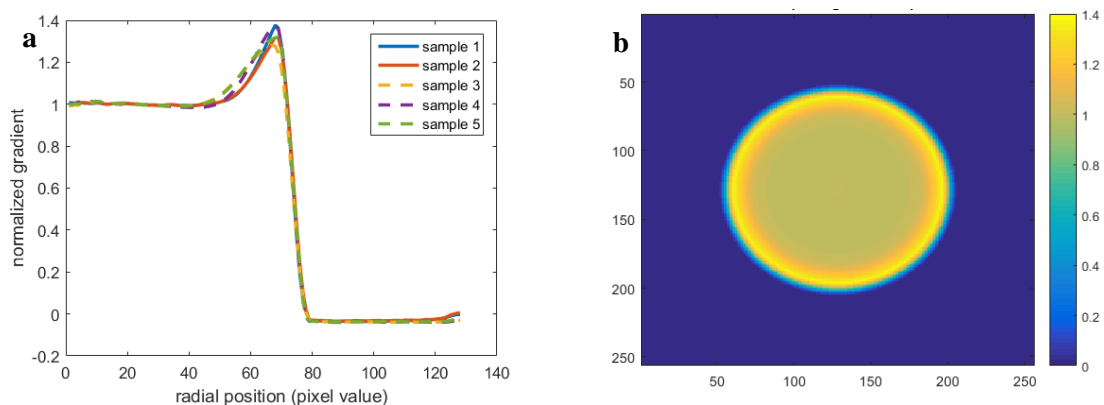

Figure 2. (a) Normalized gradient values versus radial position for all the 5 samples, obtained by plotting dose in relation to optical-CT pixel value, for different radial distances. Radial position > 80 correspond to the background. (b) 2D gradient map correction image obtained from Sample 1, based on the normalized gradient for each radial position.

In Figure 3, 2D reconstructed normalized optical-CT image and profiles obtained with a PRESAGE® sample irradiated with a lung phantom are shown. Measured profiles, taken in the middle of the target in several directions, are compared with the research Monaco simulated data, after normalizing both to the region of maximum dose. Measured profiles are shown with and without applying a 2D normalized gradient correction image (Presage corrected and Presage not corrected respectively). Despite the differences between all five samples, the correction images are comparable. For this reason in Figure 3, we applied a correction image that corresponds to an average of all five corrected images obtained from each sample. When a correction image is applied to the PRESAGE® data, in the regions with worse agreement, the difference between simulated and measured doses can be reduced by 12%. However, by comparison with simulations we can say that only partial correction is observed. A "bump" seems to be visible on two of the sides of the samples (at the left-right (LR) and anterior-posterior (AP) directions) even after correction, which could be a residual optical artefact at the boundary. As expected from the results in Figure 1d, which shows a very small edge effect for lower doses, the edge effect only occurs when the doses are high (here ≥ 30% of the maximum dose used). No effects are visible in the diagonal and sagittal profiles as, at the edges, only very low doses are present.
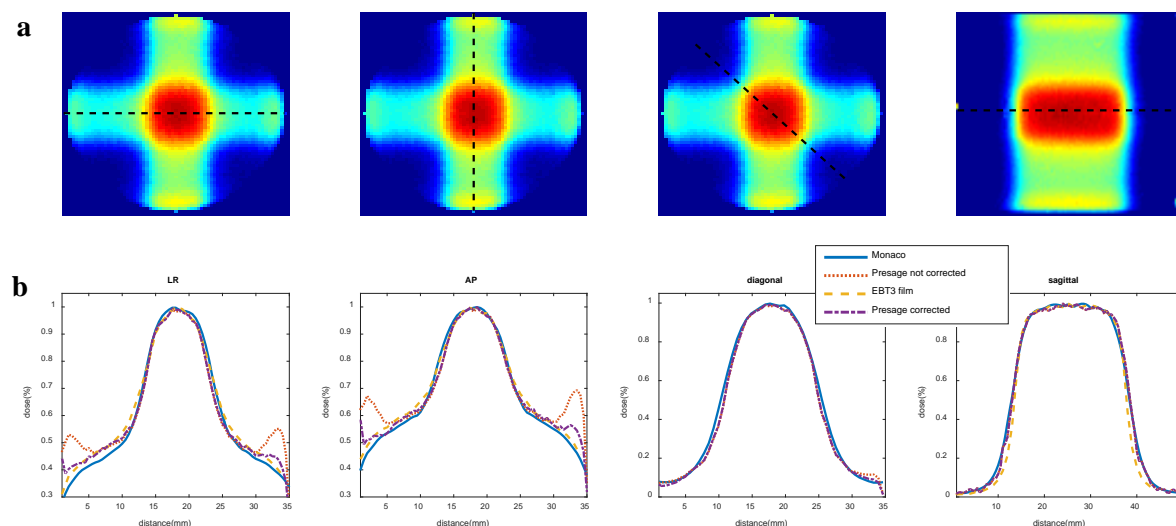

Figure 3. (a) Central axial slice 2D color-coded normalized optical-CT pixel value image showing results from a sample of PRESAGE® irradiated inside a lung phantom with no correction applied. Central sagittal slice is also shown. (b) Normalized simulated profiles taken at the central axial slice at left-right (LR), anterior-posterior (AP), diagonal and sagittal directions are plotted against measured data with and without correction. Green channel EBT3 film results are also shown.

Film results taken from the green channel are also shown in Figure 3 and were normalized to the maximum value of the profile. Higher doses at the edges are visible agreeing well with PRESAGE® when a "bump" is not present. Normalized results on the red channel showed values at the edges higher than the green (up to 3%). Further measurements are needed to obtain a better understanding of these differences.

3.2. Physical removal of the dosimeters edge

In Figure 4, we observe the disappearance of the edge effect in the regions where the sample edges are removed, and the non-reappearance of the edge effect after each sample is irradiated with an additional 6Gy. A long vertical line is visible in the profile (~1mm) which we attribute to an optical-CT edge effect. This could be due to the roughness of the sample surface after being cut and a possible slight mismatch between the samples and matching liquid. The dose increase at the sample edges on the non-cut regions

is still visible. This is clearly visible on the profiles but also looking at the 2D sagittal reconstructed images.
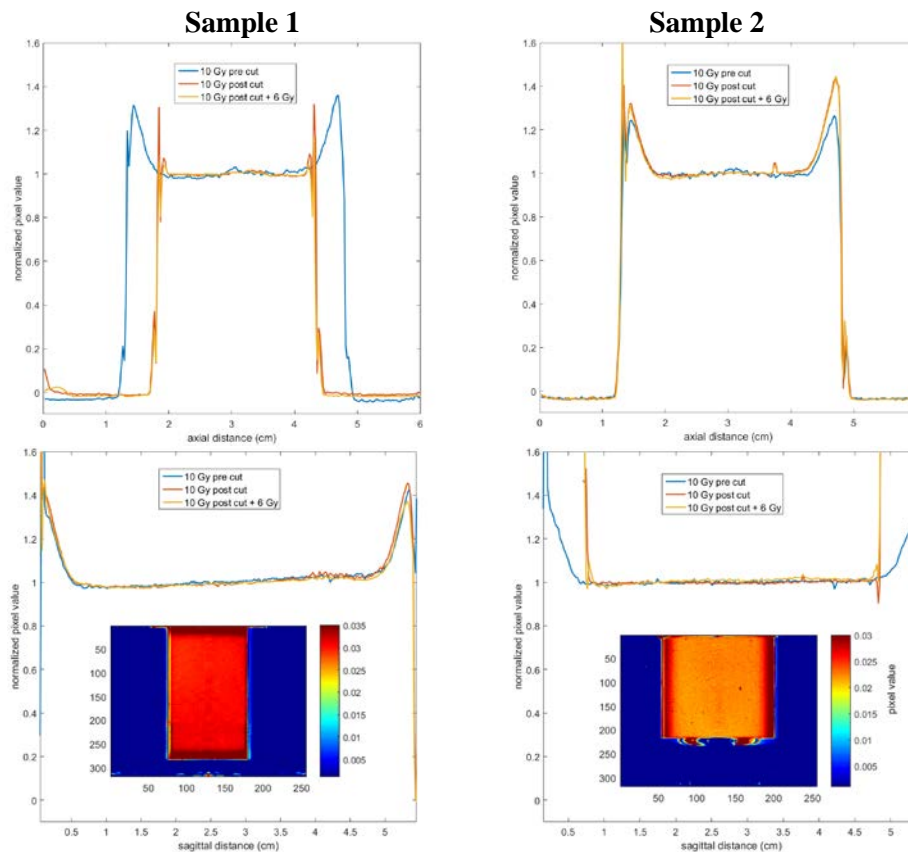

Figure 4. Normalized axial (top) and sagittal (bottom) 1D central optical-CT pixel values taken from Sample 1 (cut in diameter) and Sample 2 (cut in lengths) before being cut (10Gy pre cut), after being cut (10Gy post cut) and after irradiating with 6Gy more (10Gy post cut + 6Gy). A sagittal 2D pixel value image of the samples after being cut and irradiated with 6Gy more (10Gy post cut + 6Gy) are displayed.

4. Conclusion

In this work we show that small cylindrical PRESAGE® samples (3.5 cm diameter) have a different response to radiation in the central region in comparison to the edges. We propose a correction to compensate for this effect and investigate alternatives to obtain a uniform response throughout the samples, so that the dose can be measured right up to the boundary of the sample. Partial correction is possible and was applied here using data from homogeneous irradiated samples, but further work is still needed to develop a robust correction. However, we believe that physically removing the edges of the samples is a good alternative for measurements near dosimeter-air interfaces, provided that bigger samples are obtained. This will be important for studies on the MR-linac to measure accurately the ERE and will be tested in the future.

5. Acknowledgements

6. References

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