

INVESTIGATION OF DOSIMETRIC IMPACT OF ORGAN MOTION IN STATIC AND DYNAMIC CONDITIONS FOR THREE STEREOTACTIC ABLATIVE BODY RADIOTHERAPY TECHNIQUES: 3D CONFORMAL RADIOTHERAPY, INTENSITY MODULATED RADIATION THERAPY, AND VOLUMETRIC MODULATED ARC THERAPY BY USING PRESAGE 3D DOSIMETERS

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Aim: To investigate the use of PRESAGE 3D dosimeters to quantify the dosimetric variation between the static and dynamic conditions of three stereotactic ablative body radiotherapy techniques. **Materials and Methods:** An in-house custom-designed thorax dynamic phantom was designed to simulate the tumor motion in two directions (i.e., superior/inferior (Z-axis) and anterior/posterior (Y-axis)). The PRESAGE dosimeter was attached to the moving arm of the phantom and irradiated in two scenarios (static and dynamic) using three stereotactic ablative body radiotherapy (SABR) techniques: 3D conformal radiotherapy (3D CRT), intensity-modulated radiation therapy (IMRT), and volumetric modulated arc therapy (VMAT). **Results:** The highest differences in the mean volume measurements between the two conditions were noticed in IMRT (0.14 cm³) and 3D CRT (0.13 cm³). The mean volume measurements of the VMAT showed the lowest difference between the static and dynamic conditions of 0.10 cm³. The gamma analysis for 3%, 3-mm criterion showed passing rates of < 1 for 3D CRT, IMRT, and VMAT. **Conclusion:** This study quantify the dosimetric variations which are caused by the tumor motion in lung cases. In the SABR of the lung for QA purposes, this could help in identifying the prescription dose coverage due to tumor movement and correlate with the planned dose using 3D dosimeters like PRESAGE.

Key Words: 3D conformal radiotherapy (3D CRT), stereotactic ablative body radiotherapy (SABR), PRESAGE 3D dosimeter, intensity-modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT).

Stereotactic ablative body radiotherapy (SABR) for lung cancer has shown promising results compared to the conventional radiotherapy treatment, with tumor control rates of up to 90% over 3 years [1–3]. The SABR technique is characterised by the precise delivery of a few high dose fractions (typically 3–5) and up to 60 Gy to a small target volume [4]. SABR for lung cancer can be compromised by tumor motion, resulting in irradiation to normal tissue and decrease in the local control to/of the targeted tumor [5]. To quantify the dosimetric variation due to tumor motion, several dynamic, high-resolution devices have been proposed [4, 6, 7]. However, these devices offer two-dimensional analysis of the three-dimensional dose distribution [8]. Three-dimensional analysis of the dose distribution is preferable because the two-dimensional plane is not representative of the entire dose distribution [8].

PRESAGE 3D dosimeters have shown promising results for analysing and visualising the dose in three dimensional planes. The application of PRESAGE

as a 3D dosimeter has several advantages: 1) it exhibits “robustness to laboratory environment, i.e., no O₂ sensitivity” [8]; 2) it has very low scatter due to the absorption medium [8]; 3) it can be prepared in any external container allowing better dosimeter edge resolution through improved refractive index (RI) matching [9]. Dynamic thorax phantoms that can be integrated with the PRESAGE 3D dosimeters are limited to specific small PRESAGE sizes, thus allowing for dosimetric studies in a small field size, e.g., 2 × 2 cm² [8]. For example, a commercial CIRS dynamic thorax phantom accommodates PRESAGE with a length less than 5 cm and diameter of 5 cm [8, 10]. Large PRESAGE sizes are preferable to visualise the dose distribution of the planned dose or the static condition to compare it with the dynamic condition [10]. To date, no commercial phantom is available to measure the dose in a large PRESAGE dosimeter.

The aim of this study was 1) to design an in-house custom-designed thorax dynamic phantom to accommodate a large PRESAGE 3D dosimeter and also 2) to propose a method to quantify the dosimetric impact of organ motion (such as tumors in the lung) using the above phantom and PRESAGE 3D dosimeters. The investigation of the dosimetric variation includes a retrospective clinical case of patients that underwent SABR of the lung using a 3D CRT technique, and it was replanned for

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Abbreviations used: 3D CRT – 3D conformal radiotherapy; GTV – gross tumor volume; IMRT – intensity-modulated radiation therapy; MLC – multileaf collimator; PTV – planning target volume; SABR – stereotactic ablative body radiotherapy; VMAT – volumetric modulated arc therapy.

intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT). Before the static and dynamic studies were conducted, the designed phantom and PRESAGE dosimeters were tested.

MATERIALS AND METHODS

The custom-designed thorax dynamic phantom and the PRESAGE 3D dosimeters. An in-house custom-designed thorax dynamic phantom was designed to simulate the motion of lung tumors in two directions: superior/inferior motion and anterior/posterior motion. The development of the custom-designed thorax dynamic phantom was achieved by 1) designing and integrating the mechanical parts, 2) developing source codes using Keil C [11] and C++ programs [12] to control the mechanical parts and provide the required motions.

The PRESAGE 3D dosimeters were prepared and the fabrication process utilised four different compounds: 1) polyurethane resin precursors, Crystal Clear® 204 part A and part B (Smooth-On, Inc., Easton, PA, USA); 2) leucomalachite green (LMG) (Sigma-Aldrich®), which “acts as a dye when oxidised by free radicals created by the irradiation of the radical initiator chloroform” [13]; 3) chloroform (Chem-Supply); 4) the catalyst dibutyltin dilaurate (DBTDL) (Merck KGaA, Darmstadt, Germany) [14]. The catalyst increases the post response stability and sensitivity. It also changes the effective atomic number (Z_{eff}) to be radiological equivalent to that of water [15, 16].

Two sizes of PRESAGE 3D dosimeters were used in this study, a small size with 4 cm length $\times$ 4 cm diameter and a larger size with 8 cm length $\times$ 8 cm diameter (Fig. 1). The small PRESAGE was used to generate the calibration curve for the PRESAGE dosimeters. The larger PRESAGE was utilised to demonstrate the dose distribution and the penumbra of the retrospective lung SABR for static and dynamic conditions. Both PRESAGE sizes were prepared from the same batch. The PRESAGE dosimeters were kept at a temperature of 4 °C before and after the irradiation. Furthermore, before the irradiation and optical computed tomography (CT) readout, the PRESAGE dosimeters were allowed to reacclimatise to room temperature (22 °C). After irradiation, the PRESAGE was given 12 h for the post-irradiation polymerisation reaction to stabilise before the optical CT readout.

To create the calibration curve, 10 small-sized PRESAGE dosimeters were irradiated with various doses. The irradiation of the 10 PRESAGE dosimeters ranged from 5 Gy to 50 Gy. When the PRESAGE is irradiated, free radicals are produced due to radiolysis of the radical initiator, i.e., chloroform. Then free radicals oxidise the leuco dye causing an alteration in the optical density or the absorbance, i.e., colour. Thus, the change in the optical density (ΔOD) can be measured at a particular wavelength when dealing with such dosimeters [17]. To ensure that the ΔOD of the PRESAGE dosimeters are obtained owing to the absorbance of the radiation dose only, the ΔOD values

are measured by subtracting the ΔOD value of the irradiated dosimeters from the reference or blank (radiation dose = 0) by using an optical CT scanner [15, 18]. The pixel values and the doses were recorded and plotted for 10 PRESAGE dosimeters using image J software (Fig. 2).

CT scan for the in-house phantom and PRESAGE dosimeter.

The in-house custom-designed thorax dynamic phantom, including the PRESAGE 3D dosimeter, was CT scanned in the static condition using a Philips BrillianceTM CT scanner (Koninklijke Philips Electronics, Amsterdam, The Netherlands). The CT scan protocol for the static condition was as follows: helical mode, 140 KV and 300 mAs, slice thickness and increment = 3 mm, field of view (FOV) = 600, pitch (table feed per rotation) = 0.68, rotation time = 0.5 s, and matrix size = 512 with standard resolution. The image reconstruction was performed with a slice thickness and increment of 5 mm. The CT DICOM datasets were transferred to the treatment planning system for contouring.

Static and motion conditions for three techniques of lung SABR: 3D CRT, IMRT, and VMAT.

The ethics approval was approved for all patients who participated in this study. To study the dosimetric impact of organ motion, the treatment plan of a previously treated patient who underwent SABR for the lung, i.e., Patient 1 who was treated by 3D CRT with a prescription dose of 28 Gy (gross tumor volume (GTV) = 3.4 cm³, planning target volume (PTV) = 14 cm³), was used for

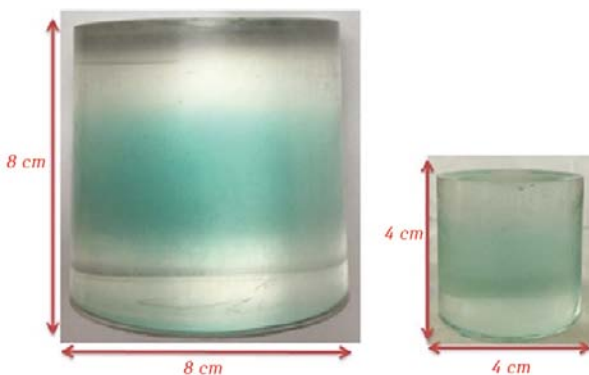


Fig. 1. Two sizes of PRESAGE dosimeters. A large PRESAGE dosimeter irradiated by 28 Gy with dimension of 8 cm length $\times$ 8 cm diameter (left image). A PRESAGE dosimeter irradiated by 10 Gy with dimension of 4 cm length $\times$ 4 cm diameter (right image)

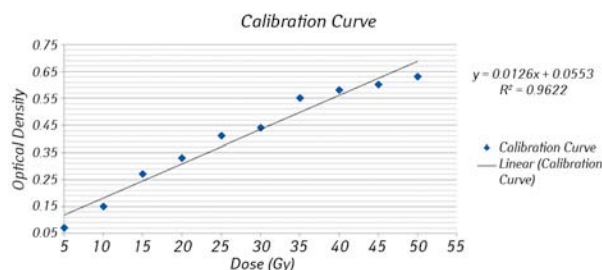


Fig. 2. Relationship between optical attenuation per pixel and dose. The correlation coefficient parameters of fitted line are shown in the inset of the graph

Table 1. Beam configurations and monitor units in the original treatment plan of *Patient 1* treated by SABR with 3D CRT technique

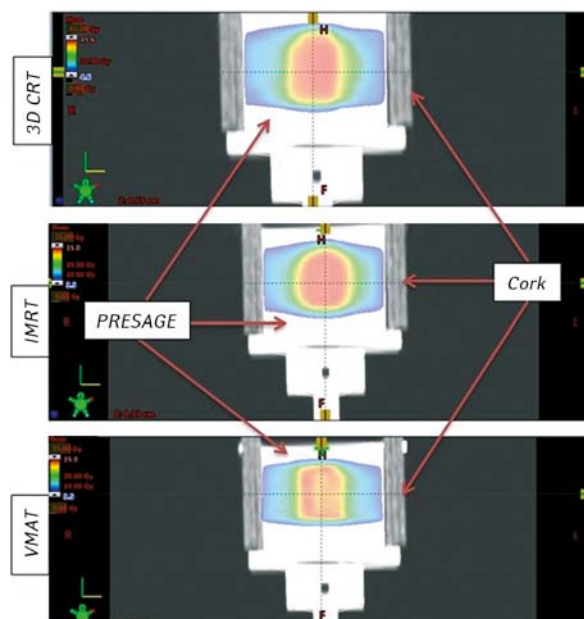
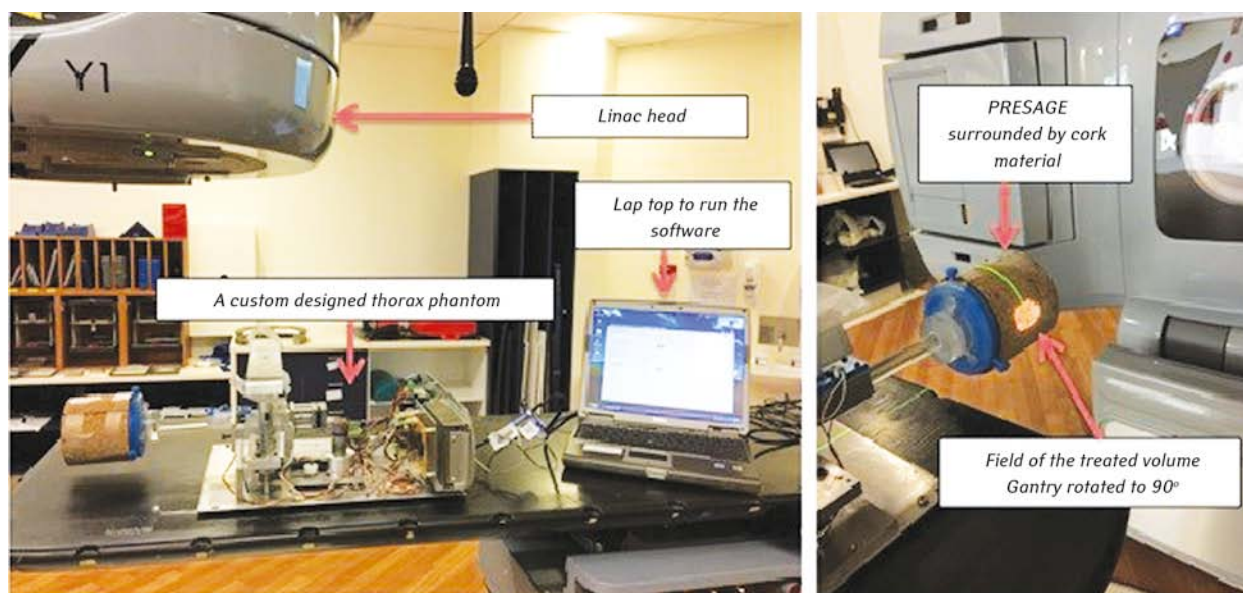
Beams number	Patient 1 (tumor is located in the left lung) PTV = 14 cm ³	
	Beam configurations	Monitor unit (MU)
1	Anterior Gantry rotation 0° Couch rotation 0° Collimation rotation 90°	456
2	Oblique Gantry rotation 30° Couch rotation 0° Collimation rotation 90°	408
3	Oblique Gantry rotation 60° Couch rotation 0° Collimation rotation 90°	791
4	Lateral Gantry rotation 90° Couch rotation 0° Collimation rotation 90°	759
5	Oblique Gantry rotation 120° Couch rotation 0° Collimation rotation 90°	764
6	Oblique Gantry rotation 150° Couch rotation 0° Collimation rotation 90°	382
7	Oblique Gantry rotation 210° Couch rotation 0° Collimation rotation 90°	432
8	Oblique Gantry rotation 195° Couch rotation 90° Collimation rotation 0°	403
9	Oblique Gantry rotation 155° Couch rotation 90° Collimation rotation 0°	354

the static and dynamic conditions. Table 1 presents the beam configurations for Patient 1.

Six identical large PRESAGE dosimeters (8 cm length × 8 cm diameter) were used to investigate three treatment plans that include 3D CRT, IMRT,

and VMAT under the static and dynamic conditions. The PRESAGE dosimeters were fit into the PRESAGE holder attached to the in-house custom-designed thorax dynamic phantom.

The phantom is capable of simulating the tumor motion in two directions: A/P (Y axis) and S/I (Z axis). The tumor motion or the movement distance in Patient 1 was recorded to be 2 mm in the A/P direction, 13 mm in the S/I direction, and 0 mm in the R/L (X-axis) direction. The 4D CT monitored the trace of the tumor motion for Patient 1. Fig. 3 shows the position of the phantom, including the PRESAGE dosimeter on the couch, for the static condition. In the dynamic condition, the phantom simulated the motion in both

**Fig. 4.** CT images of three SABR techniques in TPS: 3D CRT, IMRT, and VMAT. The planning process was applied to large PRESAGE dosimeters to study the static and dynamic conditions**Fig. 3.** Process of irradiating large PRESAGE dosimeters for the static and dynamic conditions using in-house custom-designed thorax dynamic phantom: *left*) setup position of the in-house custom designed thorax dynamic phantom on Linac treatment table; the phantom motion was controlled by the designed software using a laptop; *right*) irradiated large PRESAGE dosimeter surrounded by cork material (equivalent to lung density) showing the tumor field in the 90° gantry angle

directions with the same movement distance of the tumor motion, as described above.

Treatment plan and delivery. Three SABR techniques were used in this study for the static and dynamic conditions. The treatment plan of Patient 1 using 3D CRT was replanned using IMRT and VMAT. The three plans were then copied onto the CT PRESAGE images using Eclipse-TPS (Fig. 4). The beam orientations were optimized according to the location of the PTV in all three plans. The beam configurations with the MU for 3D CRT and IMRT plans are summarised in Table 1.

The IMRT and VMAT plans were generated according to the departmental protocols. As a starting point, the multileaf collimator (MLC) was conformed with zero margins to the PTV using the outbound method of leaf positioning, and the MLC leaf positions were individually adjusted to provide adequate target coverage. The VMAT plans were composed of two arcs. The first arc was defined with the gantry start angle at 181° and stop angle at 0° clockwise for right-sided lesions. For left-sided lesions, the start angle was 0°, and the stop angle was 179°. The second arc was defined with the gantry start angle at 0° and stop angle at 181° counter clockwise for right-sided lesions. For left-sided lesions, the start angle was 179°, and the stop angle was 0°. The collimator angles were 30° and 330° for arc 1 and arc 2, respectively. The MUs for arc 1 and arc 2 were 4279. The maximum gantry speed was 4.8°/s, and the maximum dose rate was 600 MU/min. All the plans were planned using 6 MV X-rays.

Data analysis. The dosimetric variation between the static and dynamic conditions for the three SABR plans 3D CRT, IMRT, and VMAT was calculated by the PolyGeVero® software [19]. The calibration curve information was imported to the PolyGeVero® to calculate the dose distribution for the PRESAGE dosimeters. The data analysis for this study includes gamma index and dosimetric volumes of the three plans in two conditions.

PolyGeVero® software is able to calculate the dose in PRESAGE and gel dosimeters. It consists of four workspaces: 1) calibration workspace; 2) calibration curve with summary table workspace (named CCTW); 3) gel dosimetry dose distribution workspace; and 4) gel dosimetry versus treatment planning system workspace (gel dosimetry vs TPS) [19, 20]. The software was designed to allow the user to calculate data acquired by scanning the 3D dosimeters with CT, magnetic resonance imaging and optical CT. The calculation includes two file formats: 1) VFF files of a VISTA cone beam optical CT (modus medical device, Canada) and 2) the DICOM files from a CT scanner. The calculations can be exported to the BMP and TXT file format, for example, 1D and 2D graphs, in the form of reports and signal and dose maps [19, 20].

Statistical analyses. The statistical analyses were performed by Graph Pad PRISM 6 software, v. 6.03. A paired *t*-test was used to investigate the statistical significances ($p < 0.05$) and mean differences between the two conditions (static and dynamic).

RESULTS

Fig. 5 and 6 show the dose distribution of the static and dynamic conditions for the three SABR techniques: 3D CRT, IMRT, and VMAT in the ZX and YZ planes. The images in dynamic mode exhibited broadening of the penumbra compared with the images acquired in static mode, especially in the (Y and Z directions) for all three SABR techniques. The dose

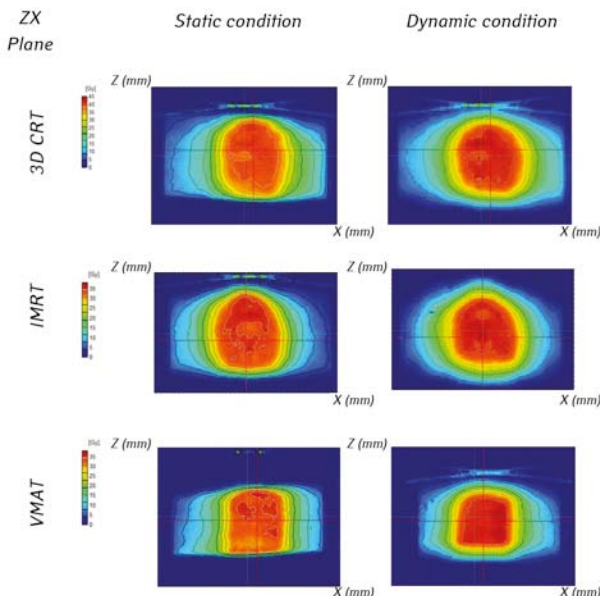


Fig. 5. Coloured wash dose distribution of six large PRESAGE dosimeters irradiated in two conditions (static and dynamic) for three SABR techniques: 3D CRT, IMRT and VMAT in the ZX plane

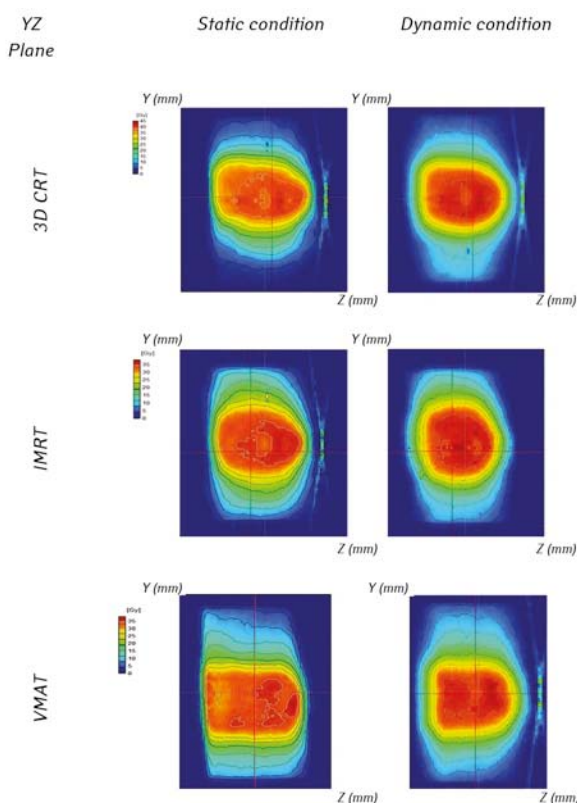


Fig. 6. Coloured wash dose distribution of six large PRESAGE dosimeters irradiated in two conditions (static and dynamic) for three SABR techniques: 3D CRT, IMRT, and VMAT in the YZ plane

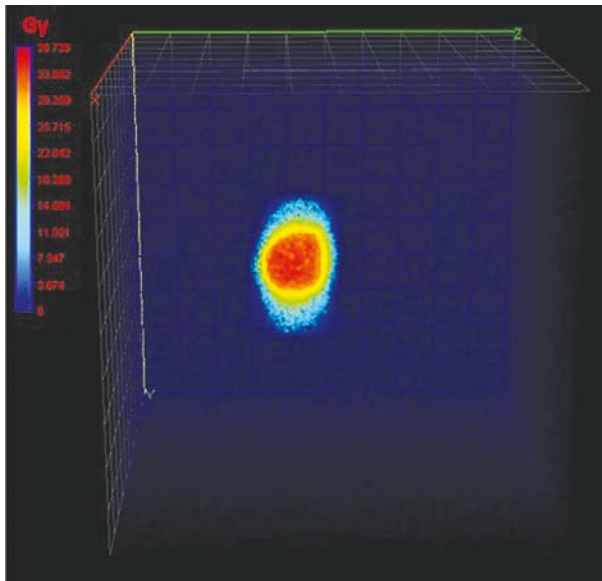


Fig. 7. Three-dimensional image of the irradiated PRESAGE dosimeters in dynamic condition using IMRT technique for Patient 1. The three axes were assigned as follows: X (red colour), Y (yellow colour), and Z (green colour)

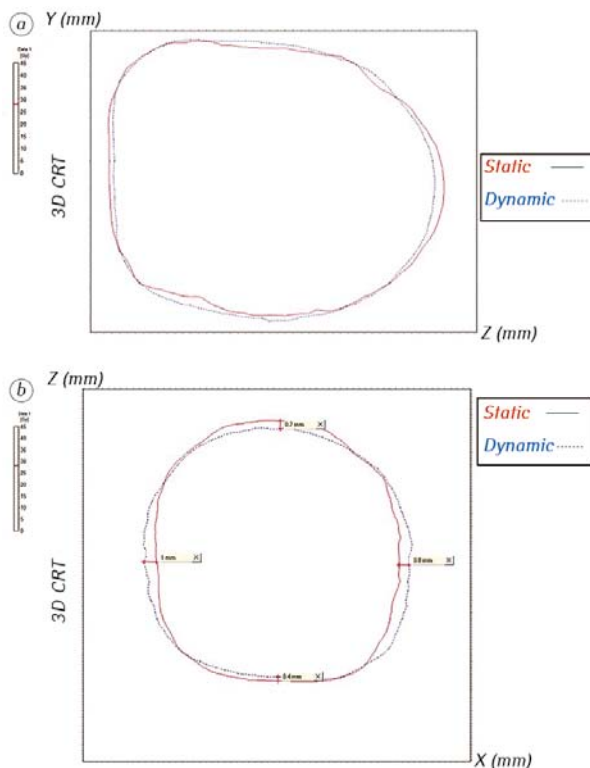


Fig. 8. Dosimetric variation between the static and dynamic conditions for individual plane/layer of SABR technique using 3D CRT for the 28 Gy isodose line in: a) YZ axes and b) ZX axes. The displacement measurements (in millimetres) between the static and dynamic conditions are displayed in (b) for ZX axes

Table 2. Mean volume measurements of the static and dynamic conditions for the three SABR techniques: 3D CRT, IMRT, and VMAT. The data presented in this Table was the result of three independent measurements ($n = 3$)

SABR techniques	Volume of 28 Gy isodose line (cm^3) using TPS	Mean volume of 28 Gy isodose line (cm^3) Static condition using PRESAGE, Mean $\pm$ SD	Mean volume of 28 Gy isodose line (cm^3) Dynamic condition using PRESAGE, Mean $\pm$ SD	Differences (Dynamic – Static volume), cm^3
3D CRT	32.7	31.56 $\pm$ 0.83	31.69 $\pm$ 0.81	0.13
IMRT	26	25.61 $\pm$ 0.38	25.75 $\pm$ 0.35	0.14
VMAT	21	20.43 $\pm$ 0.42	20.53 $\pm$ 0.46	0.10

distributions in the three-dimensions (X, Y, and Z) are illustrated in Fig. 7. Owing to the movement, the dose distributions were/are varied between the static and dynamic conditions. For the known movement distance of the phantom in the Y- and Z-axes, the dose distribution showed an elongation and shortening in the former and later axes for the 3D CRT technique (Fig. 8, a). This elongation was also visualised in the X-axis (Fig. 8, b). This trend was consistent for the three SABR techniques with the prescription dose of 28 Gy. Table 2 summarised the isodose line volumes for the static and dynamic conditions using the three SABR techniques with 28 Gy isodose line. The highest differences in the mean volume measurements between the two conditions were noticed in IMRT (0.14 cm^3) and 3D CRT (0.13 cm^3). The mean volume measurements of the VMAT showed the lowest difference between the static and dynamic conditions of 0.10 cm^3 (Table 2). The gamma analysis for 3%, 3-mm criterion showed passing rates of < 1 for 3D CRT, IMRT, and VMAT (Fig. 9). This suggested a good agreement between the two sets of data (static and dynamic) for the three SABR techniques. Also, the statistical analysis showed no significant difference between the static and dynamic conditions.

DISCUSSION

This study investigated the impact of tumor motion using PRESAGE 3D dosimeters and in-house custom-designed thorax dynamic phantom in three SABR techniques: 3D CRT, IMRT, and VMAT. Studies related to the investigation of the motion using PRESAGE 3D dosimeter are very limited [8, 10]. Brady *et al.* [8], irradiated the PRESAGE (< 5 cm length $\times$ 5 cm diameter) with small field sizes (~ 2 cm) in three scenarios: static, motion, and gated, by using the commercial CIRS dynamic thorax phantom [8]. They recorded an elongation in the axis directions that were parallel and perpendicular to the edge of the MLC leaf [8]. The gamma analysis results showed that the passing rates were 84.7%, 84.5%, and 100% for the static, motion, and gated treatment scenarios, respectively [8]. Another study by Thomas *et al.* [10], used the same commercial CIRS dynamic thorax phantom to assess the differences in the PTV and CTV for the IMRT and rapid arc plans using PRESAGE in the static and dynamic states. They found that the isodose distributions were varied between the static and dynamic on the order of millimetres, and the dynamic isodoses provided significant deviations in the form of shifting and stretching in the motion directions [10]. Our results agreed with those of Brady *et al.* [8]. The observed elongations in the three SABR techniques were consistent in the X- and Y-axes. Moreover, the gamma analysis showed good agreement between the

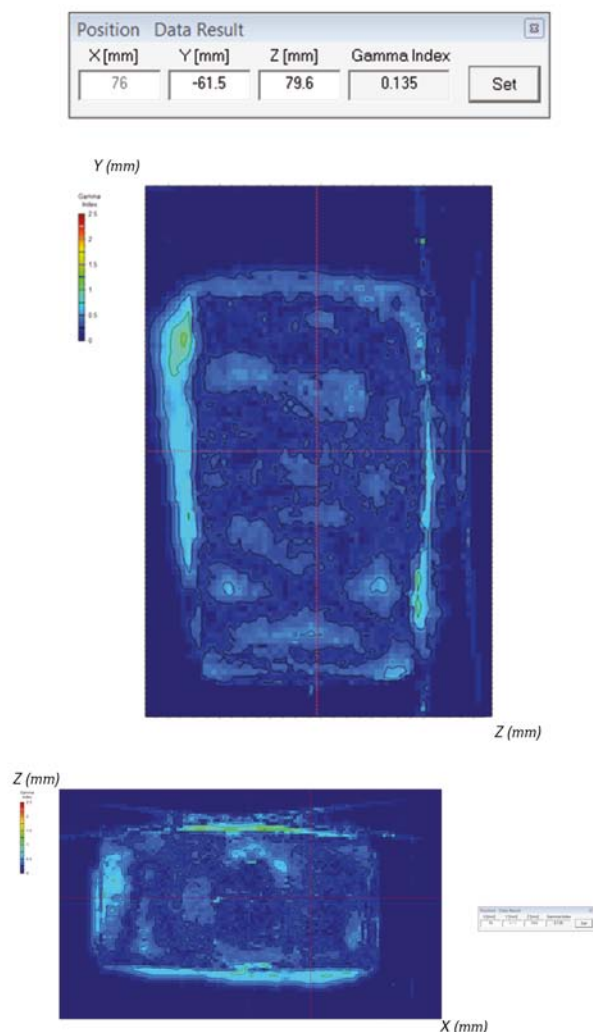


Fig. 9. Gamma index analysis using 3%, 3 mm criterion for 3D CRT technique demonstrating that most of the PRESAGE dosimeter was < 1 in the YZ plane (top image) and ZX plane in the (bottom image). The red cursor in the box tool shows the gamma index value of 0.135

static and dynamic condition for the 3D CRT, IMRT, and VMAT, i.e., (< 1). The differences between the static and dynamic conditions were quantified in this study, and the recoded variations were small ($< 0.5\%$) among the three plans (Table 2).

From the two previous studies [8, 10], it was clear that the isodose distributions during the motion were exhibited by elongation or stretching and shifting compared to the static plans [8, 10], leading to the under-dosing of the PTV [10]. The elongation of the dose distribution can be attributed to the X-ray beams passing through the rounded end of the Varian MLC leaf, which has been exhibited to increase penumbral blurring by approximately 2 mm [8, 21]. Apart from the elongation of the isodose distribution, the results in this study monitored shortening isodose distribution on the Z-axis. The shortening phenomenon by the motion was proposed by Clements *et al.* [22]. They compared the ITV between the 4D CT and CBCT images obtained during the phantom motions using QUASAR phantom for small, medium, and large lesions moved by 0 cm, 1 cm, 2 cm, and 4 cm. They found that when the mo-

tion was present, the ITV in 4D CT and CBCT were shortened by 7 mm to 11 mm [22].

The main aspects of this study are summarised as follows: 1) the use of larger size PRESAGE samples allows for better demonstration of the dose distribution, especially for the penumbra area (Fig. 5 and 6) of a retrospective clinical case of lung SABR; 2) analysis of the PRESAGE data by the PolyGeVero® software [19] to quantify the dosimetric variation between the two conditions; 3) simulation of the target motion by designing an in-house custom-designed thorax dynamic phantom that featured larger PRESAGE sizes, unlike the commercial CIRS dynamic thorax phantom that is limited to a specific PRESAGE size (< 5 cm in diameter). The limitation of this work was the lack of motion in the X-direction (R/L) for the designed phantom, which may occur in some lung cases during the tumor motion [23]. Therefore, the current phantom design was suitable for evaluating the tumor motion in two directions, and as an example, patient 1 was considered in this study. Also, this study was specified for patients with regular breathing with a small tumor displacement of < 2 cm.

CONCLUSION

The trend of the dose distribution results during the tumor motion cannot be predicted to cause over- or under-dosing to the targeted volume. This study proposed a method to quantify the dosimetric impact of organ motion by using an in-house custom-designed thorax dynamic phantom and PRESAGE 3D dosimeters in the static and dynamic conditions for a known distance motion in two directions. In the SABR of the lung for QA purposes, this could help in identifying the prescription dose coverage due to tumor movement and correlate with the planned dose.

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