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Review paper

Patient-specific tumor and respiratory monitoring phantom design for quality controls of stereotactic ablative body radiotherapy in lung cancer cases

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ABSTRACT

The design, production and adaptability to clinical routine of a patient-specific tumor and respiratory monitoring phantom (TRMP) was investigated using 3D printer technology. TRMP and GTV modelling were done using 4D-CT images of the inhalation phase. The model was converted to STL (Stereolithography) format and printed with STH (Strong Herbal) biopolymer with HU (Hounsfield Unit) suitable for imaging purposes. The assembly of TRMP motorized parts and mechanical equipment has been completed and made suitable for clinical use. In the first part of the study, the deviations of radio-opaque markers attached to the TRMP sternum to perform mechanical quality control tests and T1-7 costal vertebrae in CC, AP, and LAT directions were evaluated. In the second part of the study, in order to evaluate the usability of the TRMP in quality assurance (QA), point dose measurements with BeO OSL dosimetry and EBT3 gafchromic film measurements were taken in Trilogy® radiotherapy accelerator and CyberKnife® robotic radiosurgery accelerator. In this study, we present a highly flexible TMRP capable of performing independent internal and external motions. TRMP was successfully tested in different treatment accelerators, both mechanically and dosimetrically.

Introduction

Stereotactic ablative body radiation therapy (SABR) is an alternative treatment for groups of patients with stage I non-small cell lung cancer (NSCLC). Prospective studies evaluating the use of SABR have shown that local tumor control rates are 78% −97% [1]. However, treatment success depends on an accurate target volume definition [2]. Target definition in the lung is particularly difficult due to tumor movement induced by respiration. The degree of motion depends on the tumor location and the patient's respiratory pattern. For tumors located close to the diaphragm, amplitudes above 2.5 cm were measured [3,4]. The use of four-dimensional computed tomography (4D-CT) is a reliable tool to accurately detect tumor motion [5,6]. The contouring of the tumor is usually performed at each respiratory phase by defining an internal target volume (ITV) which then takes into account the entire cycle of motion. The ITV concept is widely used for motion management. It ensures a great tumor coverage but exposes a larger portion of healthy lung tissue to radiation. Therefore, it requires more sensitive, and professional treatment methods. Active motion management, respiratory-gated and respiratory synchronized tumor tracking methods are the treatment modalities developed for this purpose. But these techniques require real-time information about the tumor position, and therefore a need arose to use different treatment strategies. The complexity of these strategies brings the necessity for accurate and appropriate quality assurance (QA) tests.

While phantoms are used as an important quality control material in the quality assurance tests of CT and radiotherapy systems, they are also used in the development and testing of new imaging and treatment methods. For a phantom to be tissue equivalent, the materials creating the phantom ideally should interact with radiation in the same way as human tissue. Many materials have been used to mimic human tissue considering its interaction with radiation, but current manufacturing techniques make elaborate phantoms expensive and not useful for specific needs. To increase the level of detail and enable the production of

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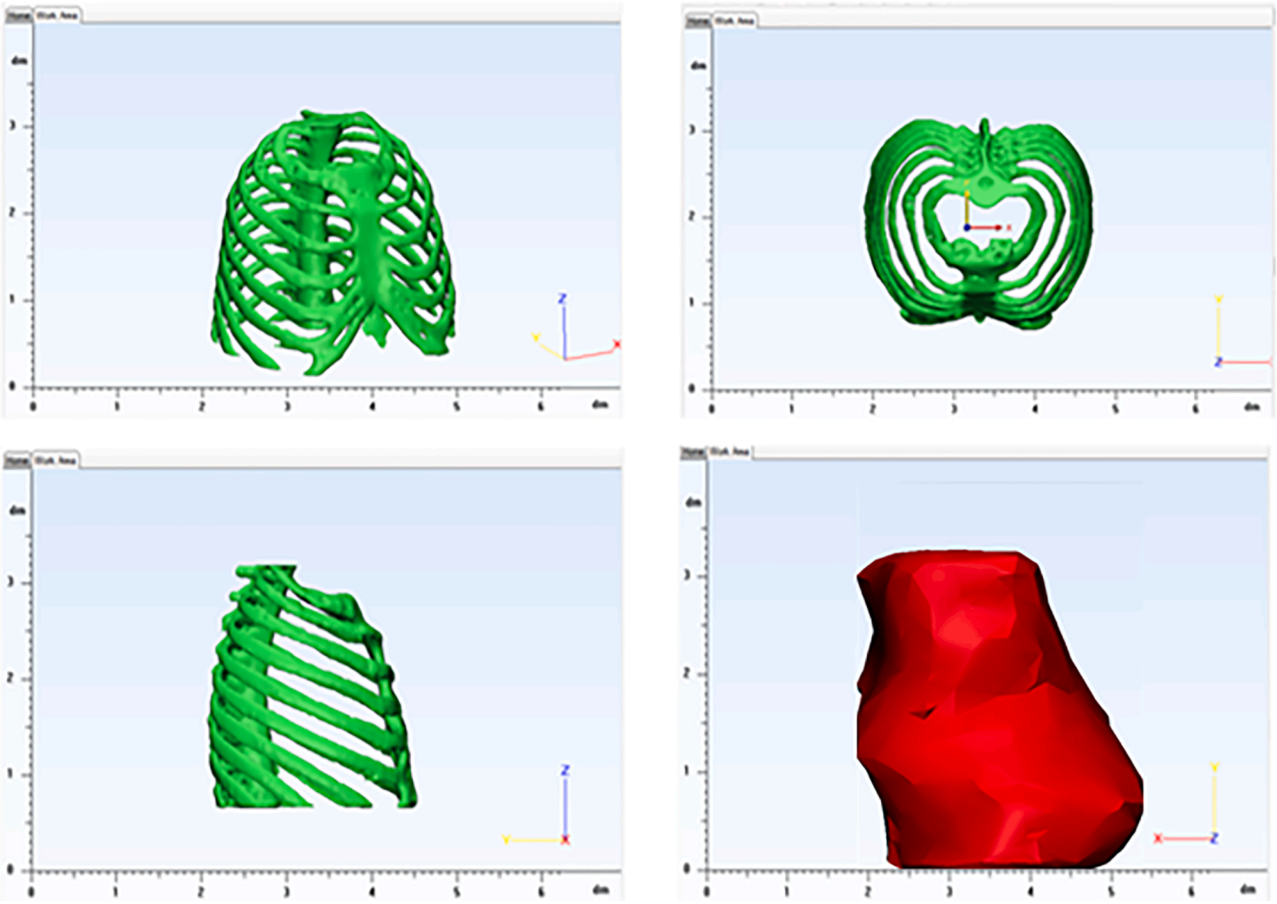

Fig. 1. Anatomical Modeling of TRMP and GTV.

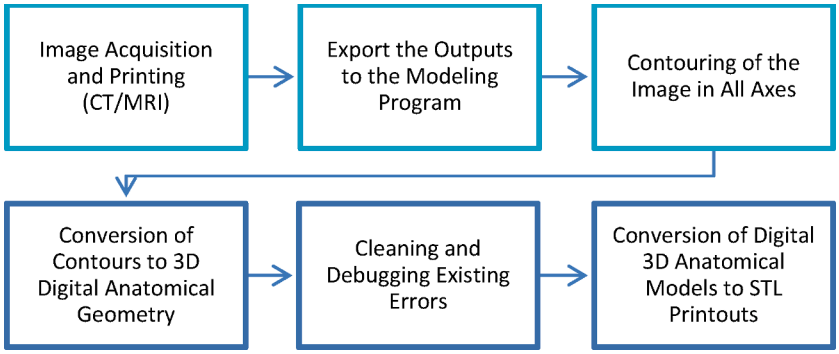

Fig. 2. The workflow chart of the digital 3D anatomical modeling process.

patient-specific phantoms, 3D printing techniques can be used. In external radiotheraphy (ERT) applications, Park et al. [7] revealed that a patient-specific bolus can be produced using 3D printing technology in patients with irregular body contours. Moreover, in their study, Ehler et al. [8] stated that patient-specific quality control phantoms can also be produced in addition to bolus production.

In contrast to the homogeneous phantoms in the literature, it is important to produce non-homogeneous phantoms by taking bone anatomy into account. Kashani et al. [9] combined realistic bone structure and internal composition in their study; however, the developed thorax was unable to perform the respiratory movement. There is a commercial phantom that can deform the thorax according to breathing. Dynamic Breathing Phantom of RSD (Radiological Support Devices Inc., Long Beach, CA, USA) uses compressed air for tumor and breathing motion, however, it can only perform the 1D motion. Most phantoms in the literature can only perform 1D or 2D target motion. Serban et al. [10] and Nioutsikou et al. [11] brought a 3D motion to the tumor by pushing an artificial diaphragm. This motion is reproducible, but not predictable/adjustable. Nioutsikou et al. [11] have constructed a phantom capable of performing 3D motion following regular or even irregular trajectories, but rotations of tumor motion did not include thorax motion. There are also two commercially available systems that provide external motion: the Qasar Respiratory Motion Phantom (Modus Medical Devices Inc., London, CA) and the Dynamic Thorax Phantom (CIRS Inc., Norfolk, VA, USA). However, both systems are produced with standard casting techniques and do not include thorax motion.

This study was conducted with a focus on the development of

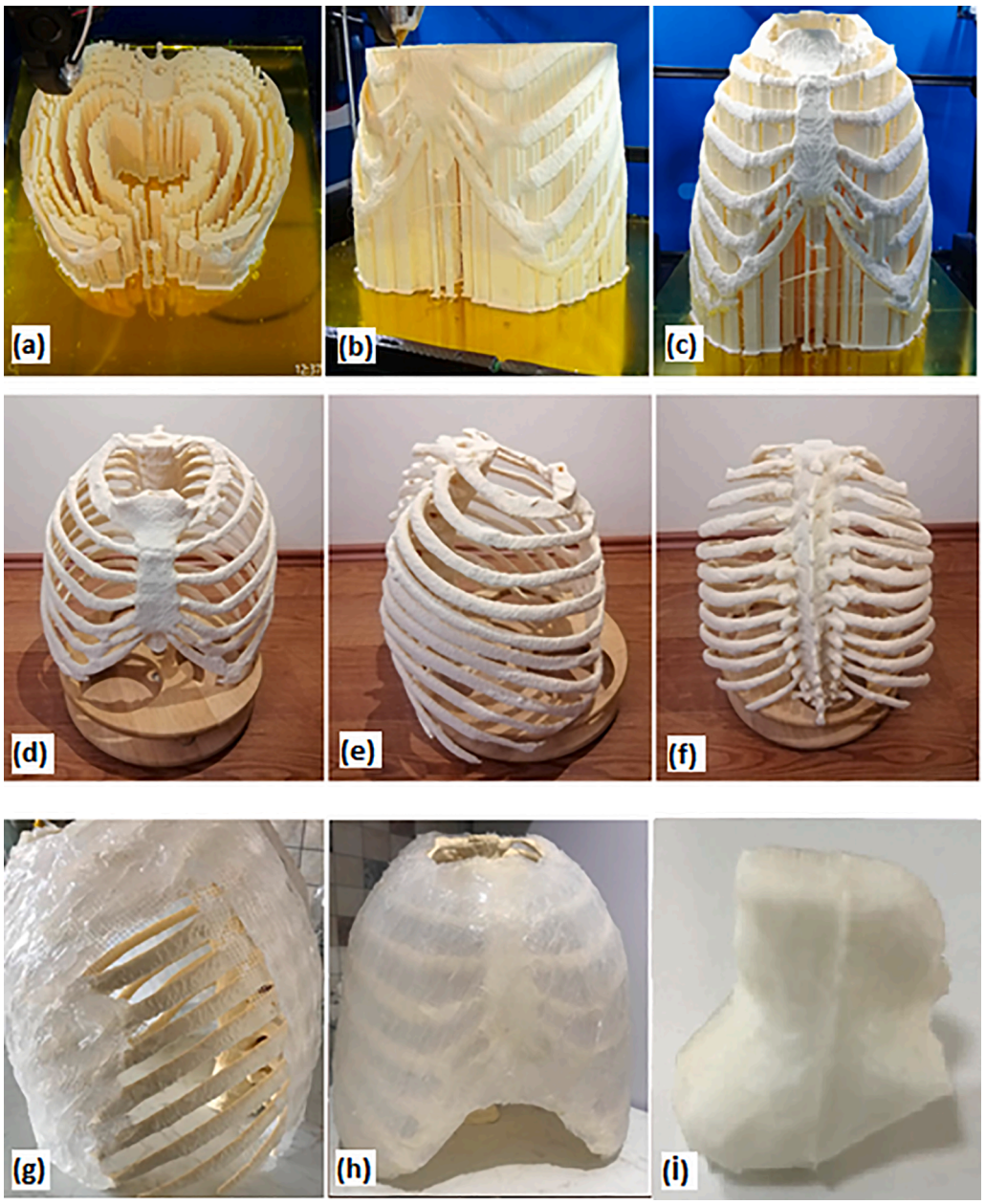

Fig. 3. The anatomical model containing TRMP thorax (costal vertebrae and coated polysiloxane silicone) and GTV, (a,b,c,i) TRMP thorax, costal vertebrae and GTV was printed using the BYM technique on Diamond DT3X branded 3D printer. (d,e,f) TRMP output was 350 × 330 × 330 mm^3 and printing time was completed in 400 h. (h,g) The costal vertebrae was coated with 1 cm thickness using polysiloxane cartridge silicone. (i) GTV output.

standard QA methods for estimating and verifying the dose given to time-dependent geometries. In contrast to QA phantoms produced with standard casting techniques, it was aimed to investigate the patient-specific TRMP design, production, and adaptability to clinical routine in QA tests using 3D printer technology.

Materials and Methods:

Anatomical modeling of TRMP

For the study, the DICOM data of patients with indications of peripherally located NSCLC whose treatment was completed in 2018 were used. The patient-specific phantom design was created by using 4D-CT simulation data previously taken at 1 mm slice thickness for the treatment plan. DICOM images obtained using 4D-CT of the patient with lung SABR indication selected for TRMP anatomical printing were analyzed. DICOM data were imported into the MIMICS v.19 program and the bone tissues of the patient were used to form the basis of anatomical modeling. The aim was to create a completely patient-specific model by not making any manipulation on the original bone tissues of the patient (Fig. 1.). In order to determine the GTV, all of the DICOM data of the 4D-CT phase imaging were imported into the MIMICS v.19 program. GTVs for all phase imagings were drawn one by one by the same radiation oncologist. The maximum volume of GTVs created was chosen to be used in the study. It was made ready for 3D printing by converting it to STL format. The workflow chart of the digital 3D anatomical modeling process is presented in Fig. 2.

TRMP material Selection, 3D Printing, and installation of mechanical equipment

The HU value of bone tissue varies according to location and age.

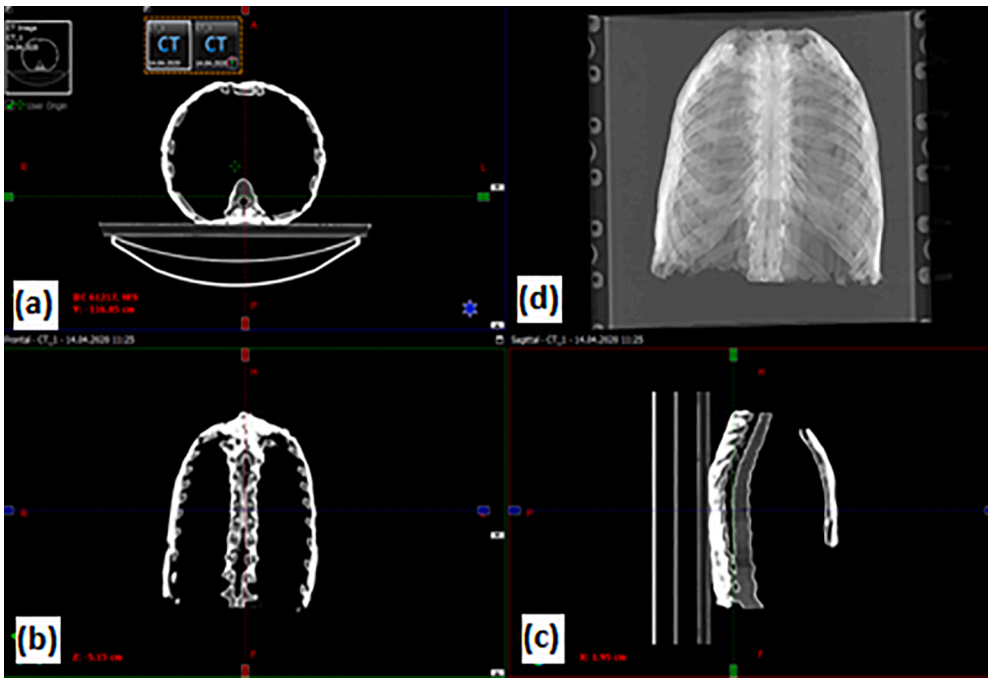

Fig. 4. CT scan of the thorax, (a,b,c) Respectively axial, coronal and sagittal slice, (d) Topogram.

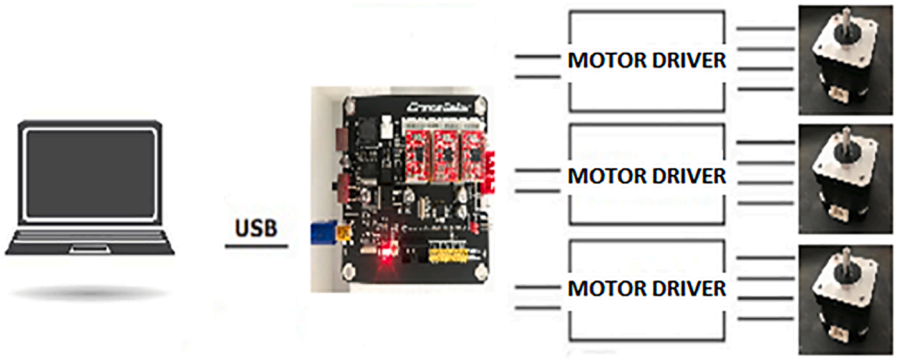

Fig. 5. The Stepper Motors connection on the driver is as shown schematically.

Since our patient selected for TRMP was 75 years old, a plant-based biopolymer STH filament with a 74.4 HU value, 1.22 gr / cm^3 specific weight in bone tissue and GTV production, 50% tensile elongation, 41.0 kg / cm^2 tensile coefficient, 770.0 kg / cm^2 flexural strength, of 35. 0 kg / cm^2 bending coefficient, was used. The anatomical model containing TRMP costal vertebrae and GTV was printed using the Combined Stacking Modelling (CSM) technique on Diamond DT3X branded 3D printer (Fig. 3.(a,b,c,i)). Nozzle diameter 400-μm printing resolution was used. The printing temperature was 218 °C and the tray temperature was 80 °C. Our TRMP output was 350 × 330 × 330 mm^3 (Fig. 3.(d,e,f)) and our printing time was completed in 400 h, with an average print head speed selected at 40 mm / s. The perimeter (shell) thickness was filled in 4 layers in the form of a 300-μm thick grid at a 100% compactness ratio on the outside and with a 30% compactness ratio inside. The pectoralis major muscle tissue of the patient in the study was 50.00 ± 9.85 HU. The costal vertebrae outputs was coated with 1 cm thickness using polysiloxane cartridge silicone, as the equivalent of pectoralis major muscle tissue (Fig. 3.(g)). After the polysiloxane cartridge silicone drying was completed, thorax 4D-CT imaging was performed to evaluate HU value and thickness (Fig. 4). Polysiloxane silicone had a value of 51.85 ± 12.83 HU and a thickness of 1.00 ± 00.7 cm.

The GTV movement was carried out using a linear slide system operating in Cartesian coordinates. A corresponding axis name was defined on the motor driver card for each axis of the linear slide. Z-axis connection for up and down (vertical) was carried out, while x-axis connection for right-left direction (lateral) and y-axis connection for back-forth direction (longitudinal) were carried out. Then the NEMA 17 stepper motors belonging to each axis were mounted. The stepper motor connection on the driver is as shown schematically in Fig. 5.

In thorax motion, a nylon thread attached to the sternum is pulled and released periodically through a NEMA 23 stepper motor. This pull causes contraction and deformation of the thorax, and this cycle provides the motion of the thorax. Thorax motion is monitored by the Synchrony® Respiratory Tracking System or distance sensors of the Real-Time Position Management (RPM) system, depending on the treatment accelerator used. The 3D GTV motion should be as rapid as possible to simulate complex tumor motion. Therefore, the GTV was mounted on a robotic arm belonging to the linear slide system, which was produced and programmed to synchronize with the movement of the thorax. In this way, the target was ensured to be able to perform arbitrary motion patterns regardless of the motion of the thorax.

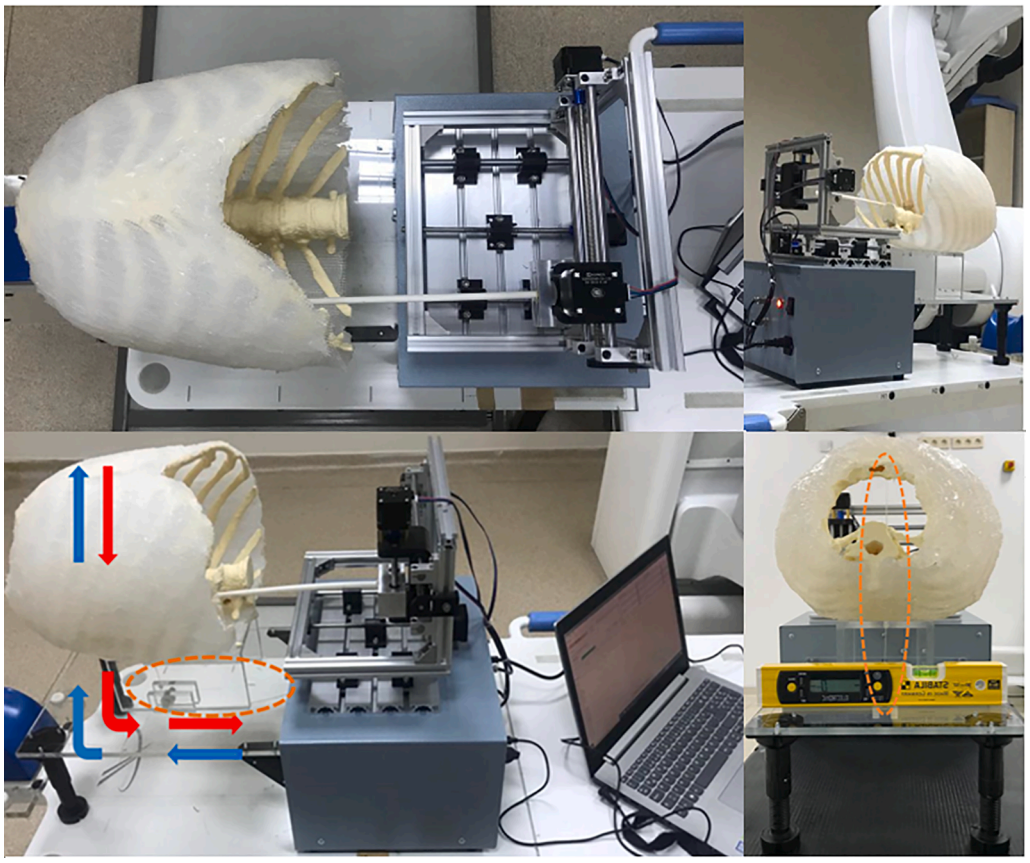

Fig. 6. Patient- Specific Tumor and Respiratory Monitoring Phantom. The sternum moves in the AP direction. The direction of inhalation is indicated by red arrows and exhalation is indicated by blue arrows. The orange circles shows the nylon thread and pulley system that moves the sternum. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

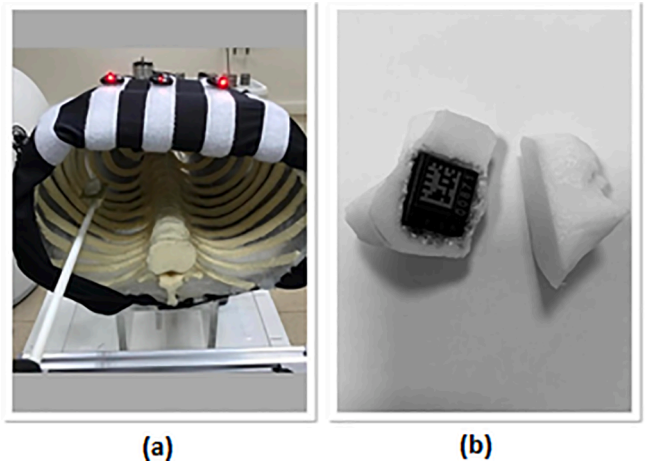

Fig. 7. The EBT3 film (a) and BEO dosimetry (b) were sandwiched between GTVs parts.

TRMP mechanical accuracy and feasibility tests

The TRMP represents a patient-specific thorax that simulates tumor motion inside expanding and contracting lungs within the chest wall, which can move independently or synchronously, covered by the thorax (Fig. 6). The total thorax weight was 6.2 kg and the dimensions of width, height, and length were 32x22x33 cm^3, respectively. The GTV, located peripherally in the right lung of the patient in the study, was also positioned in the same location in the phantom and performs the 3D motion in the specified trajectory.

The thorax was operated continuously for 50 min in quality control for the repeatability and accuracy of the motion. Repeated CT scans with 10-minute intervals to check the positions of markers placed on the costae and sternum. Their measured positions are compared with an initial reference position by using DIR (Deformable Image Registration) software. Repeatability was tested by changing the behavior between different motion detection sequences. In the study of Steidl et al. analyzed one hundred and forty-six log files to determine the sensitivity of target and robotic motion. In all these cases, they concluded that the target motion happens in the trajectory defined by the following time-dependent equations [12]:

$$x(t) = \frac{1}{2}A_P \sin\frac{2\pi t}{T}$$

$$y(t) = \frac{1}{4}A_P \sin\frac{2\pi t}{T} + \frac{\pi}{2}$$

$$z(t) = \frac{1}{4}A_P \sin\frac{2\pi t}{T} + \frac{\pi}{2}$$

They concluded that the peak-to-peak amplitude (AP) varied between 2 and 20 mm and the period T was up to 3 s (12). In our study, a 3D trajectory was plotted with AP = 10 mm and T = 3 s using MATLAB software. By examining the 4D-CT images of our study patient, the maximum motion limits of GTV belonging to the patient were determined as x = 6 mm and y = z = 10 mm and T = 3 s.

Evaluation of TRMP dosimetric quality assurance (QA)

Four different irradiations were made in order to evaluate TRMP for

Table 1
The deviations of radio-opaque markers attached to the TRMP sternum and T1-7 costal vertebrae in CC, AP, and LAT directions.

Region of Interest	T (s)	CC (mm)	AP (mm)	LAT (mm)
T1	10	1	0	0
	20	0	1	1
	30	0	1	2
	40	1	0	1
	50	1	1	2
	AVG	0,6	0,6	1,2
	STD	0,5477	0,5477	0,8367
	P	0,070	0,070	0,033
T2	10	1	0	1
	20	1	1	1
	30	0	1	1
	40	0	1	0
	50	1	1	1
	AVG	0,6	0,8	0,8
	STD	0,5477	0,4472	0,4472
	P	0,070	0,016	0,016
T3	10	1	2	0
	20	1	1	1
	30	1	2	1
	40	2	2	1
	50	1	1	1
	AVG	1,2	1,6	0,8
	STD	0,4472	0,5477	0,4472
	P	0,004	0,003	0,016
T4	10	1	1	1
	20	2	2	1
	30	2	2	0
	40	2	1	1
	50	1	1	1
	AVG	1,8	1,6	0,8
	STD	0,4472	0,5477	0,4472
	P	0,001	0,003	0,016
T5	10	2	3	1
	20	1	2	1
	30	1	3	1
	40	2	3	1
	50	2	2	0
	AVG	1,6	2,6	0,8
	STD	0,5477	0,5477	0,4472
	P	0,003	0,000	0,016
T6	10	2	3	0
	20	1	2	1
	30	2	3	1
	40	2	2	1
	50	1	2	1
	AVG	1,6	2,4	0,8
	STD	0,5477	0,5477	0,4472
	P	0,003	0,001	0,016
T7	10	1	1	0
	20	1	1	0
	30	0	0	1
	40	1	0	0
	50	0	1	0
	AVG	0,6	0,6	0,2
	STD	0,5477	0,5477	0,4472
	P	0,070	0,070	0,374
Sternum	10	1	2	1
	20	1	0	1
	30	2	2	0
	40	1	2	1
	50	2	1	2
	AVG	1,4	1,4	1
	STD	0,5477	0,8944	0,7071
	P	0,005	0,005	0,034

use in treatment QA control tests and to create a real patient scenarios:

a. static thorax and static tumor
b. moving thorax and moving tumor
c. moving thorax and static tumor
d. static thorax and moving tumor

Table 2
Details for the 4D treatment plan created in the Eclipse® planning system.

TPS				
Region of Interest	**Point Dose 1 (cGy)**	**Point Dose 2 (cGy)**	**Point Dose 3 (cGy)**	**Point Dose Average ± SD (cGy)**
GTV	1148,34	1151,72	1157,50	1152,52 ± 4,63
Sternum	15,52	15,80	16,22	15,85 ± 0,35
T6	383,34	376,54	366,18	375,35 ± 8,64
T7	6,27	6,48	5,76	6,17 ± 0,37
L1	154,31	152,01	148,97	151,76 ± 2,68

Table 3
The results of BeO dosimeters irradiated in the Trilogy® radiotherapy accelerators and analyzed using pDose software.

Measurement Scenarios 1: The Static Thorax and The Static Tumor				
Region of Interest	**BeO 1 (cGy)**	**BeO 2 (cGy)**	**BeO 3 (cGy)**	**BeO Average ± SD (cGy)**
GTV	1016,70	1058,32	1033,57	1036,20 ± 20,93
Sternum	14,85	13,60	14,11	14,19 ± 0,63
T6	347,18	338,75	326,61	337,51 ± 10,34
T7	5,33	5,18	5,24	5,25 ± 0,08
L1	154,30	150,88	149,65	151,61 ± 2,41
Measurement Scenarios 2: The Static Thorax and The Moving Tumor				
Region of Interest	**BeO 1 (cGy)**	**BeO 2 (cGy)**	**BeO 3 (cGy)**	**BeO Average ± SD (cGy)**
GTV	1196,71	1207,37	1186,44	1196,84 ± 10,47
Sternum	15,50	16,10	16,71	16,10 ± 0,61
T6	351,70	356,41	347,63	351,91 ± 4,39
T7	5,90	5,32	6,62	5,95 ± 0,65
L1	155,48	156,42	152,30	154,73 ± 2,16
Measurement Scenarios 3: The Moving Thorax and The Static Tumor				
Region of Interest	**BeO 1 (cGy)**	**BeO 2 (cGy)**	**BeO 3 (cGy)**	**BeO Average ± SD (cGy)**
GTV	1028,90	1018,72	1032,10	1026,57 ± 6,99
Sternum	16,32	16,18	16,57	16,36 ± 0,20
T6	343,60	352,40	350,11	348,70 ± 4,57
T7	5,82	6,05	5,88	5,92 ± 0,12
L1	150,13	152,48	154,16	152,26 ± 2,02
Measurement Scenarios 4: The Static Thorax and The Moving Tumor				
Region of Interest	**BeO 1 (cGy)**	**BeO 2 (cGy)**	**BeO 3 (cGy)**	**BeO Average ± SD (cGy)**
GTV	948,30	921,18	930,50	933,30 ± 13,78
Sternum	14,08	13,87	14,27	14,07 ± 0,20
T6	338,30	321,12	331,18	330,20 ± 8,63
T7	5,68	5,21	5,33	5,41 ± 0,24
L1	151,60	154,85	153,10	153,18 ± 1,63

In these four different scenarios, firstly, TRMP phase-binned planning tomography was obtained with 4D-CT. By completing the necessary contouring of the ITV on Average-IP projection, a 4D SABR first treatment plan was prepared with the Eclipse® planning system. PTV was created by giving 3 mm margin to ITV in all axes. In the SABR treatment plan prepared using a 6MV FF photon beam, 2 half arcs were used and the prescribed dose for 2.7x3.33x2.7 cm^3 PTV volume was 10 Gy. It was ensured in all of the plans where the normalization of the plan was created that 95% of PTV received 100% of the defined dose. Optimization has been made in accordance with that the minimum dose received by PTV was not<95% of the prescribed dose and the maximum dose received by PTV was not more than 125% of the prescribed dose. GTV was published in two parts. The BEO dosimetry and EBT3 films were sandwiched between GTVs parts (Fig. 7). In another step of the study, dosimetric measurements were repeated using the Cyberknife® Robotic Radiosurgery accelerator. In the Multiplan® planning system, the 4D SABR second treatment plan prepared using 6 MV FFF photon energy and a maximum dose rate of 800 MU/min was created by using non-coplanar beams and the "sequential multi-objective" optimization of the planning system. In the SABR treatment plan prepared, the prescribed dose for 2.7x3.33x2.7 cm^3 PTV volume was 10 Gy. Three

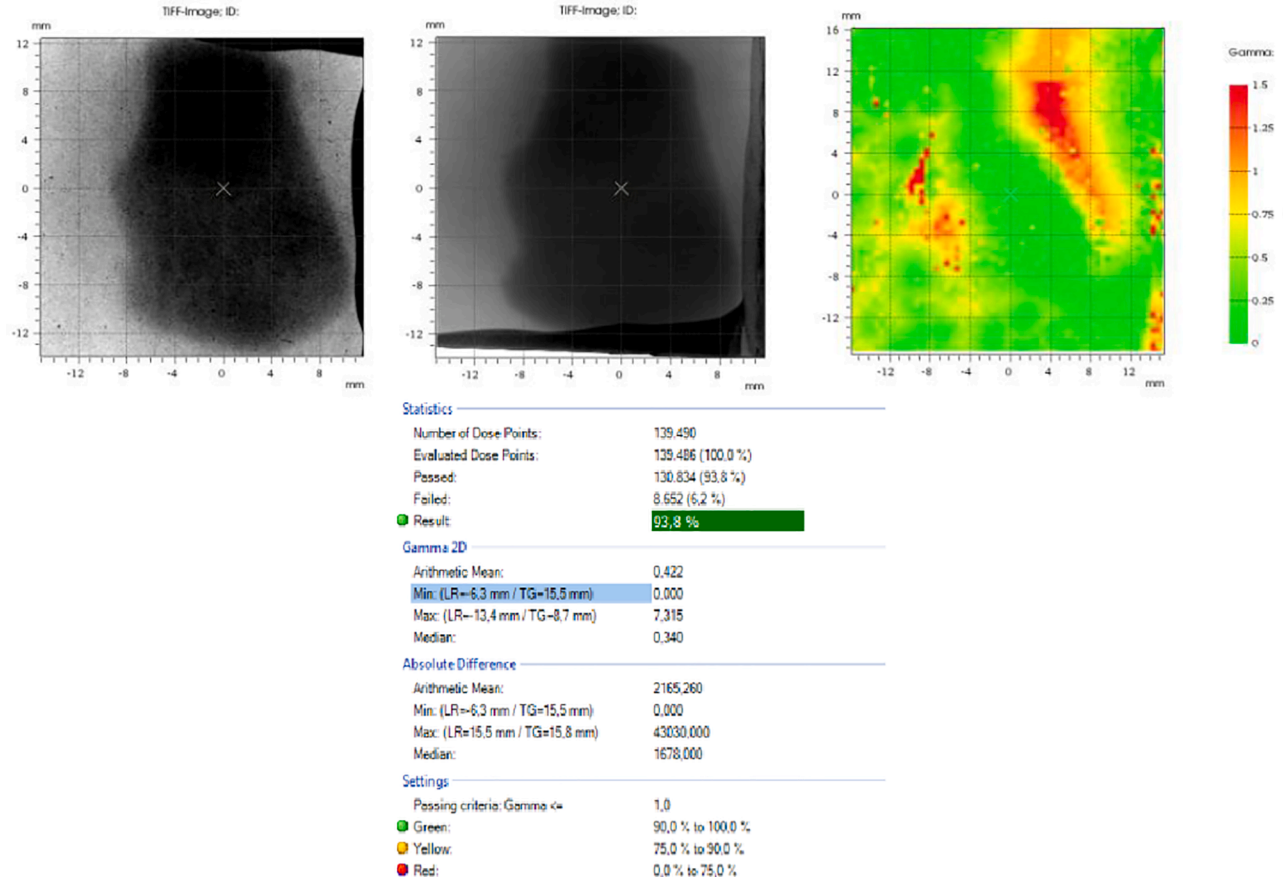

Fig. 8. Gamma index analysis film results for 3 mm DMU and 3% DF criteria of static thorax and static tumor with moving thorax and moving tumor in Trilogy radiotheraphy accelerator were found to be 93.8%.

Table 4
Results obtained from different measurement scenarios in the Trilogy® radiotheraphy accelerator.

Gamma Index Criteria	Moving Thorax and Moving Tumor	Moving Thorax and Static Tumor	Static Thorax and Moving Tumor
3 mm DMU and 3% DF	93,8	97,8	100
3 mm DMU and 5% DF	94,2	99,4	100
5 mm DMU and 3% DF	97,6	99,4	100
5 mm DMU and 5% DF	99,3	99,6	100

Table 5
Details for the 4D treatment plan created in the Multiplan® planning system.

TPS Region of Interest	Point Dose 1 (cGy)	Point Dose 2 (cGy)	Point Dose 3 (cGy)	Point Dose Average ± SD (cGy)
GTV	1047,06	1067,86	1039,25	1051,39 ± 14,79
Sternum	1,60	1,67	1,73	1,67 ± 0,07
T6	25,65	21,94	23,72	23,77 ± 1,76
T7	114,75	111,14	113,82	113,24 ± 1,87
L1	6,44	6,54	6,15	6,38 ± 0,20

separate fiducials positioned in the PTV volume at least 2 cm and 15° angles between them were defined to the treatment planning systems. Optimization has been done in such a way that 100% of the PTV volume would take at least 95% of the defined dose. Optimization has been made in accordance with that the minimum dose received by PTV was not<95% of the prescribed dose and the maximum dose received by PTV was not more than 125% of the prescribed dose. Then, QA measurements performed using the Synchrony ® respiratory tracking system. In the last step, the specific dose values obtained at the end of the measurements were evaluated both in terms of TPS used in different accelerators and in terms of QA suitability for treatment in different accelerators. Evaluation of BeO dosimetry readings is the comparison of it with point dose values calculated by TPS at dosimetry locations. EBT3 film dosimetry evaluation is the comparison of moving tumor and moving thorax, considering them as the base plan, with each other using gamma analysis in other measurement scenarios.

Results

Examination of Time-Dependent thorax motion using 4D-CT of the TRMP

The deviations of radio-opaque markers attached to the TRMP sternum and T1-7 costal vertebrae in CC, AP, and LAT directions were evaluated for each relevant region by applying the Single Sample t-Test. Besides, deviations of the total motion in CC, AP, and LAT directions were evaluated using the Kruskal-Wallis Test (Table 1). When the deviations of T1-7 costal vertebrae in the CC, AP and LAT directions were evaluated statistically, T3 ($p < 0.04$), T4 ($p < 0.001$), T5 ($p < 0.003$) and T6 ($p < 0.003$) costal vertebrae and sternum ($p < 0.003$) < 0.005) deviations in CC direction and T3 ($p < 0.03$), T4 ($p < 0.003$), T5 ($p <$

Table 6
The results of BeO dosimeters irradiated in the Trilogy® radiotherapy accelerator and analyzed using pDose software.

Measurement Scenarios 1: The Static Thorax and The Static Tumor				
Region of Interest	**BeO 1 (cGy)**	**BeO 2 (cGy)**	**BeO 3 (cGy)**	**BeO Average ± SD (cGy)**
GTV	983,12	995,02	953,78	977,30 ± 21,22
Sternum	1,94	2,12	1,83	1,96 ± 0,15
T6	38,17	44,2	37,1	39,82 ± 3,83
T7	122,2	119,8	115,03	119,01 ± 3,65
L1	11,07	10,51	10,88	10,82 ± 0,28
Measurement Scenarios 2: The Static Thorax and The Moving Tumor				
Region of Interest	**BeO 1 (cGy)**	**BeO 2 (cGy)**	**BeO 3 (cGy)**	**BeO Average ± SD (cGy)**
GTV	1040,13	1172,18	1108,95	1107,09 ± 66,04
Sternum	2,52	1,92	1,73	2,06 ± 0,41
T6	27,36	27,13	29,78	28,09 ± 1,47
T7	119,98	121,15	123,48	121,54 ± 1,78
L1	9,25	10,12	10,85	10,07 ± 0,80
Measurement Scenarios 3: The Moving Thorax and The Static Tumor				
Region of Interest	**BeO 1 (cGy)**	**BeO 2 (cGy)**	**BeO 3 (cGy)**	**BeO Average ± SD (cGy)**
GTV	1027,80	1112,47	1090,33	1076,87 ± 43,91
Sternum	2,57	2,85	2,07	2,05 ± 0,40
T6	30,26	35,18	29,72	31,72 ± 3,01
T7	110,25	123,23	118,66	117,38 ± 6,58
L1	10,23	11,86	10,48	10,86 ± 0,88
Measurement Scenarios 4: The Static Thorax and The Moving Tumor				
Region of Interest	**BeO 1 (cGy)**	**BeO 2 (cGy)**	**BeO 3 (cGy)**	**BeO Average ± SD (cGy)**
GTV	1010,26	946,97	1030,11	996,78 ± 41,74
Sternum	1,98	1,61	2,10	1,90 ± 0,26
T6	42,18	36,80	44,03	41,00 ± 3,76
T7	120,50	116,31	118,57	118,46 ± 2,10
L1	9,76	10,22	9,98	9,99 ± 0,23

0.000), T6 ($p < 0.001$) and sternum ($p < 0.005$) deviations in the AP direction were found to be statistically significant, while the deviations in the LAT direction were found to be statistically insignificant. T1 ($p < 0.070$), T2 ($p < 0.070$) and T7 ($p < 0.070$) costal vertebrae deviations in the CC direction, T1 ($p < 0.070$), T2 ($p < 0.016$) and T7 ($p < 0.070$) deviations in the AP direction, and all the deviations in the LAT direction were found to be statistically insignificant. Significant deviations in the CC and AP direction of T5-6 costal vertebrae, motion region of the GTV, indicating that the motion in the relevant region was regular.

Dosimetry findings for TRMP different measurement scenarios

In the first part of the study, point dose measurements with BeO OSL dosimetry were taken in the Trilogy® radiotherapy accelerator in order to evaluate the usability of the TMRP in treatment quality control either using RPM respiratory tracking system or not using it. When Table 2. was examined in detail for the 4D treatment plan created in the Eclipse® planning system, the minimum dose was 97.1% of the prescribed dose, the maximum dose was 123%, and the average dose was 111%. Before each measurement, BeO dosimeters were placed on the reference point, sternum, and T6-7 and L1 vertebra located in the tumor section, and irradiation was performed three times in the phantom for four different scenarios. Table 3. shows the results of BeO dosimeters irradiated in the Trilogy® radiotherapy accelerator and analyzed using pDose software. To determine the statistical significance of dosimetric data, variance analysis was applied in two-factor experimental layouts on the measurement results imported to SPSS v20.0 software. When the BeO measurement results and TPS data were compared, GTV ($p < 0.000$) and T6 ($p < 0.002$), which are the high dose region, measurements and the sternum ($p < 0.001$), which is the low dose region, measurement were significant. The measurements of T7 ($p < 0.244$) and L1 ($p < 0.701$), located in the low dose region, were insignificant.

In order to evaluate different measurement scenarios of measurements made using EBT3 gafchromic film, the gafchromic film of the immobile thorax and immobile tumor irradiation was accepted as the reference measurement and compared with the gamma analysis method. Gamma analysis was performed using 4 different DMU and DF values (3 mm DMU / 3% DF, 3 mm DMU / 5% DF, 5 mm DMU / 3% DF and 5 mm DMU / 5% DF) as criteria. Gamma index analysis results for 5 mm DMU and 5% DF criteria of static thorax and static tumor with moving thorax and moving tumor in Trilogy® radiotherapy accelerator are presented in detail in Fig. 8. Results obtained from different measurement scenarios are shown in detail in Table 4. When the measurement results were analyzed, the result of the gamma analysis was found to be over 99% in 8 of the 12 comparisons made. While the result was 93.8% in the comparison criteria of 3 mm DMU and 3% DF gamma analysis for the mobile thorax and mobile tumor measurement scenario, it was 94.2% in the 3 mm DMU and 5% DF gamma analysis comparison criteria.

In the second part of the study, point dose measurements with BeO OSL dosimetry were taken in the CyberKnife® robotic radiosurgery accelerator in order to evaluate the usability of the tumor and respiratory monitoring phantom in treatment quality control by using the fiducial tracking algorithm and/or Synchrony® respiratory tracking system. Two cones of 12.5 mm and 20.0 mm were used in the treatment plan. When Table 5. was examined in detail for the 4D treatment plan created in the Multiplan® planning system, the minimum dose was 93.9% of the prescribed dose, the maximum dose was 125%, and the average dose was 111%. Before each measurement, BeO dosimeters were placed on the reference point, sternum, and T6-7 and L1 vertebra located in the tumor section, and irradiation was performed three times in the phantom for four different scenarios. The kV imaging frequency was selected as 20 s in treatment irradiations. All irradiations were performed by using 3 fiducial trackings. Also, the Synchrony® tracking algorithm was used in moving thorax irradiations. Table 6. shows the results of BeO dosimeters irradiated in the CyberKnife® robotic radiosurgery accelerator and analyzed using pDose software. To determine the statistical significance of dosimetric data, variance analysis was applied in two-factor experimental layouts on the measurement results imported to SPSS v20.0 software. When the BeO measurement results and TPS data were compared, GTV ($p < 0.013$) and T6 ($p < 0,001$), which are the high dose region, measurements were significant. Sternum ($p < 0.149$), T7 ($p < 0.704$) and L1 ($p < 0.243$), which are the low dose region, measurements were statistically insignificant.

In order to evaluate different measurement scenarios of measurements made using EBT3 gafchromic film, the gafchromic film of the static thorax and static tumor irradiation was accepted as the reference measurement and compared with the gamma analysis method. Gamma index analysis results of different measurement scenarios in CyberKnife ® robotic radiosurgery accelerator are presented in detail in Fig. 9. Results obtained from different measurement scenarios are shown in detail in Table 7. All of the measurement results were found above 95%, which is the tolerance value.

Discussion

Tumor and respiratory monitoring phantom (TRMP), containing anthropomorphic components representing the patient-specific human thorax, was designed and produced by evaluating the deficiencies of many studies such as having a thoracic structure in terms of bone anatomy, lung tissue or anatomical geometry used by some groups in the literature. And its use in SABR quality controls was evaluated both mechanically and dosimetrically.

While the lungs were filled with room air in TRMP, Nioutsikou et al. [11] and Vinogradskiy et al. [13] used sponges to represent the lung tissue equivalent material. Besides, in the study of Serban et al. [10], bronchial tree-like bifurcations were modeled on the sponge tissue. Biederer et al. [14] used real animal lung in their studies. However, the use of real organs is not beneficial in terms of application to the clinical routine, as organs that are separated from their real environment over time lose their properties due to contact with air and their endurance is

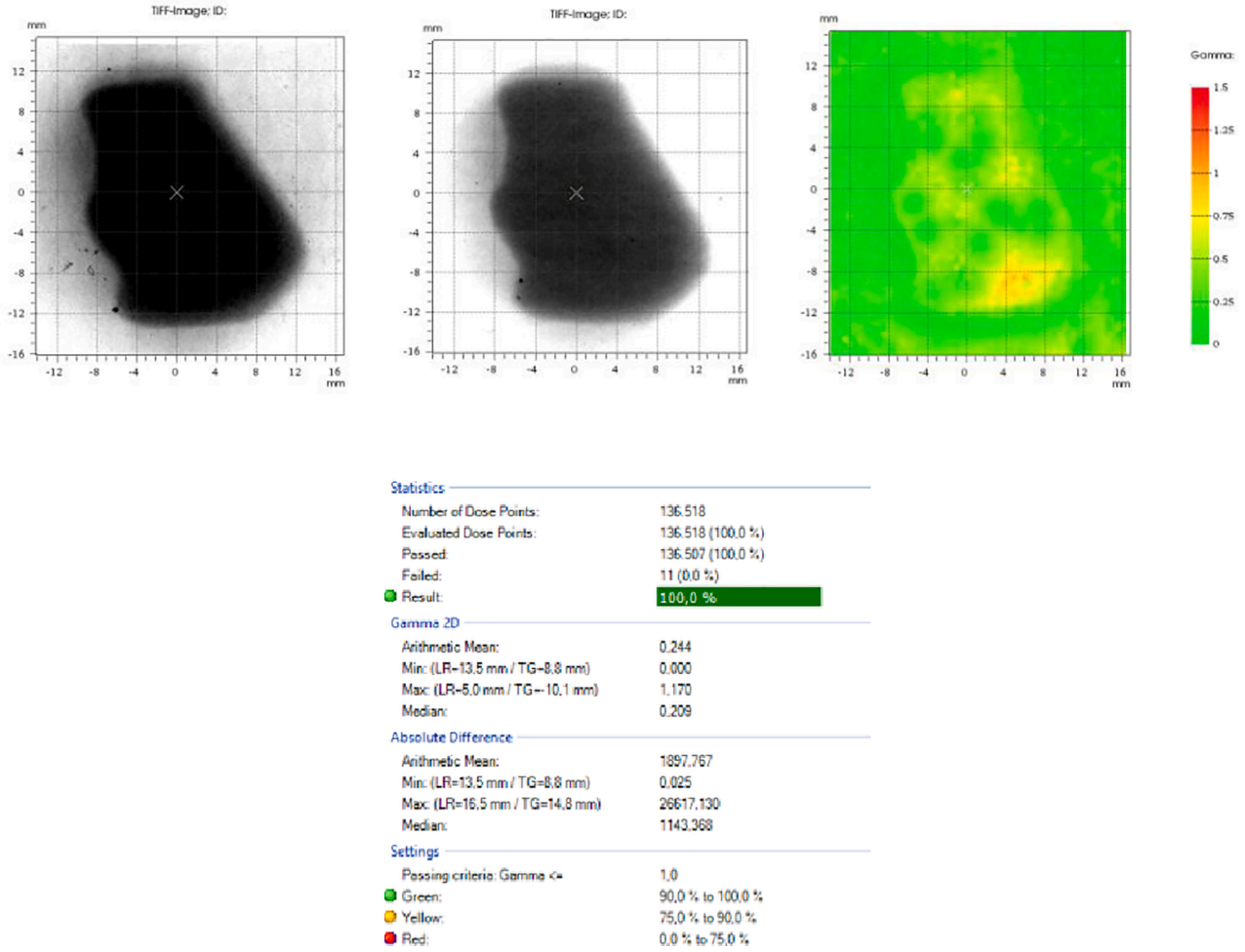

Fig. 9. Gamma index analysis film results for 5 mm DMU and 5% DF criteria of static thorax and static tumor with moving thorax and moving tumor in CyberKnife® radiotheraphy accelerator were found to be 100 %.

Table 7
Results obtained from different measurement scenarios in the Cyberknife® radiotheraphy accelerator.

Gamma Index Criteria	Moving Thorax and Moving Tumor	Moving Thorax and Static Tumor	Static Thorax and Moving Tumor
3 mm DMU and 3% DF	99,1	99,6	100
3 mm DMU and 5% DF	99,3	96,5	100
5 mm DMU and 3% DF	99,9	99,8	100
5 mm DMU and 5% DF	100	100	100

limited. In the tumor and respiratory monitoring phantom, a simple design was modeled without the presence of neighboring organs in order to eliminate the complexity of the motion of respiratory and tumor as well as making the use of the phantom more ergonomic.

The correlation between the tumor and the thorax motion signal needs to be well defined. Beddar et al [15], Gierga et al [16], Hoisak et al. [17], Lonascu et al. [18], Kanoulas et al. [19], Liu et al. [20], Otani et al. [21], Tsunashima et al. [22] compared the external motion signals with the actual tumor motion based on patient data. While some studies detected a good correlation, it was reported, in some of the studies, to be dependent on selected reference points or marker positions. Von Siebenthal et al. [23] and Sonke et al. [24] observed phase shifts (time shifts) and muscle relaxation-induced organ shifts. Examination of patient data is required to assess the clinical significance of the correlation, but systematically appropriate phantoms are needed to estimate the dosimetric effects of spurious correlation. In future studies, the correlation between the marker block and the movement of the tumor mass center can be examined in Deep Breath Hold and Respiratory Gated treatments. TMRP will add a new dimension to the development of patient-specific methods for treatment quality control, as it includes both patient-specific thoracic, GTV volüme and motion is used. Patient-specific TMRP has been very useful in the technical development of treatment plan quality control and correlation models.

Mechanical quality control checks were carried out to have longer treatment times in SABR applications and to evaluate the repeatability of the motion. The means and standard deviations in the position differences between the initial reference images of the radio-opaque markers are shown in Table 1. Time-dependent deformation can lead to dosimetric effects in quality assurance tests. Significant deviations in the CC and AP direction of T5-6 costal vertebrae, motion region of the tumor, indicating that the motion in the relevant region is regular. The thorax motion was found to be very sensitive in both timing and positioning.

Dosimetric quality assurance tests were performed in the second part of the quality control tests of the study. In order to investigate the dosimetric effect of tumor and respiratory motions, the motion equations and measurement scenarios created by Steidl P. et al. [12] were used. The adaptability of TRMP to the clinical routine was evaluated using BeO OSL dosimetry and EBT3 gafchromic film dosimetry in all

measurement scenarios. No respiratory tracking method was used in the study in measurement scenarios involving the static thorax. In measurement scenarios where the thorax was moving, measurements were completed using the RPM method and Synchrony® tracking algorithm. There were interruptions experienced in the measurements taken using the Synchrony ® tracking algorithm during treatment. The connection with the Synchrony ® tracking algorithm has been cut as a result of the LEDs entering between the positions of the camera in a certain node area of the head of the CyberKnife® robotic radiosurgery accelerator. In these specific node areas, the Synchrony ® tracking algorithm was turned off and tracking was provided with fiducial tracking algorithm. Since the thorax was irradiated in the RPM method in an isocentric way, such connection problems were not experienced. In the measurement results, this interruption has been seen not to have a great dosimetric effect. Also, CyberKnife® robotic radiosurgery has been taken by providing a minimum of three fiducial tracking algorithms in all measurement scenarios. In their study, Krona et al. [25] showed that the gafchromic film dosimeter was an appropriate dose control tool for lung SABR. In their study, Thiyagarajan et al. [26] aimed to develop a new method to verify dynamic dosing applications using a 4D phantom. EBT3 film measurement results were evaluated according to gamma analysis results and deemed acceptable for treatment with a pass rate of 92.4–99% (96.6 ± 3.8%) [26]. When the gamma index analysis results of different measurement scenarios in Trilogy® radiotherapy accelerator were analyzed, the results of the gamma analysis were found to be over 99% in 8 of the 12 comparisons made (Table 4.). When the gamma index analysis results of different measurement scenarios in CyberKnife® robotic radiosurgery accelerator were analyzed, the results of the gamma analysis were found to be 100% in 6 of the 12 comparisons and 96.5% in 1 of them (Table 7.). As a result, EBT3 film emerges as a highly efficient tool for small areas when the required sensitivity is shown in dosimetry measurement and reading protocols.

Conclusion and recommendations

In this study, we presented a highly flexible tumor and respiratory monitoring phantom (TRMP) capable of performing independent internal and external motions. TRMP consists of real tissue-equivalent materials for imaging of anthropomorphic components and dosimetric evaluations and is therefore fully compatible with x-rays. The tumor and respiratory monitoring were successfully tested in different treatment accelerators, both mechanically and dosimetrically. The fact that its entire design, including GTV, is unique to the real patient, acting by taking the breathing patterns of the patient into account and being created with a 3D printer using a plant-based STH polymer filament as raw material is a unique study in the literature.

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