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Comparison of two different respiratory monitoring systems with 4D-CT images for target volume definition in patients undergoing para-aortic nodal irradiation

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ABSTRACT

OBJECTIVE: Today, respiratory movement can be monitored and recorded with different methods during a simulation on a four-dimensional (4D) computed tomography (CT) device to be used in radiotherapy planning. A synchronized respiratory monitoring system (RPM) with an externally equipped device is one of these methods. Another method is to create 4D images of the patient's breathing phases without the need for extra equipment, with an anatomy-based software program integrated into the CT device. Our aim is to compare the RPM system and the software system (Deviceless) which are two different respiratory monitoring methods used in tracking moving targets during 4D-CT imaging and to assess their clinical usability.

METHODS: Ten patients who underwent paraaortic nodal irradiation were enrolled. The simulation was performed using intravenous contrast material on a 4D-CT device with both respiratory monitoring methods. The right/left kidneys and renal arteries were chosen as references to evaluate abdominal organ movement. It was then manually contoured one by one on both sets of images. The images were compared volumetrically and geometrically after rigid reconstruction. The similarity between the contours was determined by the Dice index. Wilcoxon test was used for statistical comparisons.

RESULTS: The motion of the kidneys in all three directions was found to be 0.0 cm in both methods. The shifts in the right/left renal arteries were submillimetric. The Dice index showed a high similarity in both kidney and renal artery contours.

CONCLUSION: In our study, no difference was found between RPM and Deviceless systems used for tracking and detection of moving targets during simulation in 4D-CT. Both methods can be used safely for radiotherapy planning according to the available possibilities in the clinic.

Keywords: Four-dimensional computed tomography; respiratory monitoring system; RPM; smart deviceless 4D.

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External beam radiotherapy (RT) is a commonly used treatment modality in cancer treatment. Nowadays, modern radiotherapy applications such as 3-dimensional conformal radiotherapy (3-DCRT), intensity-modulated radiotherapy (IMRT) and stereotactic body radiotherapy (SBRT) deliver the prescribed dose accurately to the target while reducing toxicities by maximizing the protection of organs at risk. Since these techniques deliver a high-precision dose delivery to irregularly shaped volumes, accurately defining the target volume is most important before treatment. However, planning images obtained by conventional tomography may cause difficulties in determining the exact location of the target due to respiratory movement, especially in tumors located in the chest and abdomen [1, 2].

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In recent years, four-dimensional computed tomography (4D-CT) devices have been developed that monitor respiratory movements to overcome this problem [3–7]. 4D-CT images are performed showing volumetric changes at different stages of the respiratory cycle over time. Then, all acquired images are divided into 10 phases between 0% and 90% of the breathing cycle and reconstructed. In addition, by merging several CT series at different breathing phases, maximum intensity projections (MIP), average intensity projection (Ave-IP), and minimum intensity projection (Min-IP) are generated. The MIP displays the highest intensity value for each voxel over a full respiratory cycle, thus allowing the most accurate visualization and identification of tumors. In general, MIP image sets are preferred by physicians for contouring the target volume as they show the maximum extent of the tumor [8–11].

In 4D CT, respiratory tracking and the method of generating respiratory signals can be done in two different ways. One of them performs external motion tracking by recording respiratory signals with an external instrument as well as CT images [12–15]. The other method generates respiratory signals directly from axial CT images and sorting based on the patient's internal anatomy which is called deviceless respiratory tracking [10, 16].

External respiratory signals can be generated with different techniques in clinical practice [12–15]. One of them is Varian's Real-Time Position Management (4D-RPM) (Varian Medical Systems, Inc., Palo Alto, CA, USA) system. The 4D-RPM system consists of a marker block and an infrared camera that can track motion. The infrared camera emits infrared light toward the markings on the block. The external surface of the RPM block has two or six dots, and these dots reflect the infrared light back to the camera. The block is placed on the surface of the upper abdomen of the patient close to xyphoid notch and moves synchronized with the patient's breathing. The infrared camera captures its motions, and the respiratory movement is monitored [10, 17].

The Deviceless 4D (4D-DL) respiratory monitoring concept is a new software system implemented by GE Medical Systems, Chicago, USA as Smart Deviceless 4D. In this system, unlike the RPM system, there is no external instrument to monitor and record the respiratory signal. The patient's internal anatomical features are used as a surrogate to track the movement of the target [16]. There are several studies in the literature comparing different respiratory monitoring systems [10, 13, 15, 17–19]. In most of them, tumor movement in the thoracic region has been evaluated. There are very few studies comparing external surrogates with deviceless systems and investigating the motion of abdominal organs [10, 17].

Highlight key points

- The basic principle in radiotherapy applications is to protect the normal tissues at the maximum level while delivering the treatment dose to the target accurately and precisely.
- In modern radiotherapy techniques such as 3-dimensional conformal radiotherapy (3-DCRT), intensity-modulated radiotherapy (IMRT), and stereotactic body radiotherapy (SBRT), it is necessary to accurately determine the target volume and consider respiratory-related internal organ motions due to the sharp dose gradient.
- Currently, moving organs can be followed with different methods during imaging in 4-dimensional computed tomography devices, and obtained images are used in radiotherapy planning.
- Real-Time Position Management (RPM) and 4D-Deviceless techniques are the most commonly used respiratory monitoring systems and there is no difference between them in terms of respiratory monitoring.

In the present study, two different respiratory monitoring systems (RPM vs. 4D-DL) were compared to determine intra-abdominal organ motion in patients who underwent paraaortic nodal irradiation and the differences between them were evaluated.

MATERIALS AND METHODS

Patients' Data

Ten consecutive patients who received radiotherapy to abdominal regions at our clinic between 2020 and 2021 were enrolled in our study. Six of them were diagnosed with upper gastrointestinal system cancer and four with gynecological cancer. Six of the patients were women. The inclusion criteria for the study were to be 18 years of age and older, to receive radiotherapy to the abdominal region, to have a planning tomography scan taken with 4D-CT and to have a regular respiratory cycle. Patients with superficial respiration or patients who received treatment other than the abdominal region were not included in the study.

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Table 1. Volumetric comparison results of renal contours

	RPM		4D-DL		Volume difference (4D-RPM vs.4D-DL)		p
	Mean (cc)	SD	Mean (cc)	SD	Mean (cc)	Mean (%)	
Right kidney	249.42	206.21	249.76	206.48	-0.34	0.13	0.257
Left kidney	255.59	257.91	255.74	257.35	-0.15	0.05	0.646
Right renal artery	3.76	1.24	3.92	1.30	-0.16	4.25	0.083
Left renal artery	3.17	1.06	3.18	1.16	-0.01	0.31	0.811

RPM: Real-time position management; 4D-DL: Four dimension-deviceless; SD: Standard deviation.

4D-CT Simulation

In this present study, two different methods of tracking respiratory motion, RPM (Varian Medical Systems, Inc., Palo Alto, CA, USA) and Deviceless 4D system were used from the 4D-CT Discovery RT model (GE Medical Systems, Chicago, USA). At first, the infrared camera was mounted on the end of the CT couch and calibrated. The patient was laid in the supine position on the CT table. The RPM marker box was placed on the xiphoid process of each patient for respiratory movement monitoring and respiratory signals were recorded during CT scanning. The respiratory signal obtained from the device was transferred to the RPM software. Then the RPM box was removed, and a second CT scan was performed using the deviceless method by placing a short metallic wire marker in the same location. The 4D-CT scan was performed in axial cine mode with a slice thickness of 2.5 mm. The images obtained were then reconstructed and binned into respiratory phases. The 4D-CT images were sorted into 10 phases according to the respiratory cycle. The MIP, Ave-IP and Min-IP image sets were generated and all images were transmitted to the Varian Velocity software v4.0 (Varian Medical Systems, Palo Alto, CA).

Study Design

Since paraaortic lymph node involvement is usually at the infrarenal level in gynecological cancer patients, the right and left kidneys and renal arteries were taken as a reference to evaluate respiration-induced organ motions in our study [20]. CT scans were performed in the arterial phase (30–35 seconds) using 1 g/kg IV contrast material to visualize the renal arteries.

Right (R), left (L) kidney and renal artery contouring were performed manually by an experienced radiation oncologist on the ten breathing phases image sets that were taken in both protocols and then the contoured volumes were transferred to the Ave-IP image set.

Statistical Analysis

The contoured CT images were transferred from Velocity software V4.0 to Eclipse 15.6 treatment planning system for rigid image registration and statistical evaluation. The motion of the kidneys and renal arteries were compared geometrically. The geometric comparison was used by measuring the volume change in cc, using the DICE similarity coefficient, and calculating the center of mass displacement in the Eclipse statistics tool.

The DICE similarity coefficient was used as a statistical validation metric to evaluate the spatial overlap accuracy of the R/L kidneys and renal artery contours. DICE value is a scalar coefficient and ranges from 0 (no overlap) to 1 (complete overlap).

To assess the geometrical displacement of R/L kidneys and renal arteries between 4D-RPM CT and 4D-DL CT, shifting in the left-right (LR), superior-inferior (SI) and anterior-posterior (AP), directions were identified and the X, Y, Z coordinates were recorded with the DICOM system. Wilcoxon test was used to compare volumes. All statistical analyses were done using the SPSS software program version 20 (IBM SPSS, Chicago, IL, USA). The significance level was accepted as $p<0.05$.

RESULTS

For this study, the abdominal region images obtained from 4D-CT using RPM and 4D-DL system of a total of ten patients were evaluated.

TABLE 2. Displacement values of both kidneys in LR, SI and AP directions

Number of patients	Right kidney			Left kidney		
	X-axes (L-R) shifting (cm)	Y-axes (S-I) shifting (cm)	Z-axes (A-P) shifting (cm)	X-axes (L-R) shifting (cm)	Y-axes (S-I) shifting (cm)	Z-axes (A-P) shifting (cm)
1	0.00	0.00	0.01	0.00	0.00	-0.01
2	0.00	0.00	0.01	0.00	0.01	0.01
3	0.00	0.00	0.02	-0.01	-0.02	-0.07
4	0.00	0.00	0.00	0.00	0.01	0.01
5	0.00	0.00	0.00	0.00	0.01	0.01
6	0,00	0.00	-0.01	0.00	0.00	-0.01
7	0.00	-0.01	-0.02	-0.01	0.00	0.02
8	0.00	0.00	0.00	0.00	-0.01	0.01
9	0.00	0.00	0.01	0.01	0.00	0.01
10	0.03	0.04	0.02	0.01	0.05	0.06
Median	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.01**

L-R: Left-right; S-I: Superior-inferior; A-P: Anterior-posterior.

TABLE 3. Displacement values of both renal arteries in LR, SI and AP directions

Number of patients	Right renal artery			Left renal artery		
	X-axes (L-R) shifting (cm)	Y-axes (S-I) shifting (cm)	Z-axes (A-P) shifting (cm)	X-axes (L-R) shifting (cm)	Y-axes (S-I) shifting (cm)	Z-axes (A-P) shifting (cm)
1	-0.08	0.05	0.02	-0.03	0.01	0.12
2	0.02	-0.02	0.00	0.12	0.03	-0.07
3	0.01	-0.02	-0.01	-0.01	-0.02	-0.07
4	0.02	-0.02	0.01	0.00	0.01	0.00
5	-0.03	0.01	-0.02	-0.12	-0.03	0.00
6	0.00	0.00	0.01	0.00	0.01	0.01
7	0.00	-0.01	-0.02	-0.05	-0.02	-0.01
8	-0.02	0.01	-0.08	-0.02	-0.01	-0.01
9	-0.01	0.01	-0.01	-0.01	-0.01	-0.01
10	-0.02	0.00	-0.05	-0.02	-0.07	-0.38
Median	**0.00**	**0.00**	**-0.01**	**0.015**	**-0.01**	**-0.01**

L-R: Left-right; S-I: Superior-inferior; A-P: Anterior-posterior.

The volumetric comparison results of renal contours are shown in Table 1. The mean percentage of volume difference between RPM and 4D-DL renal contours ranged from 0.05% to 4.25%. The maximum percentage of volume difference was observed in right renal artery contour. All 4D DL volumes were larger than RPM volumes, but no significant difference was found between them.

The AP, SI and LR displacement values of the R/L kidneys and renal arteries are reported in detail in Table 2–3. The median shifts of both kidneys in the AP, SI and LR directions were found to be 0.0 cm. The median shift of the right renal artery in the LR and SI directions was 0.0, and the median shift in the AP direction was -0.01 cm. The median shifts of the

Table 4. Dice similarity coefficient values of both kidneys and renal arteries

Number of patients	Dice index			
	R kidney	L kidney	R renal artery	L renal artery
1	0.98	0.99	0.69	0.81
2	0.99	0.99	0.80	0.74
3	0.99	0.84	0.79	0.84
4	0.99	0.99	0.83	0.84
5	0.99	0.99	0.87	0.81
6	0.99	0.98	0.94	0.94
7	0.99	0.99	0.99	0.81
8	0.98	0.98	0.81	0.84
9	0.99	0.98	0.87	0.84
10	0.98	0.97	0.89	0.83
Mean	**0.98**	**0.97**	**0.84**	**0.83**

SD: Standard deviation

left renal artery in the AP, SI and LR directions were -0.01 cm.

The mean DICE similarity coefficient of R kidney, L kidney, R renal artery and L renal artery were 0.98, 0.97, 0.84, 0.83, respectively. The DICE index values found for each patient are presented in Table 4.

DISCUSSION

Today, the effect of respiration-related internal organ motion on the dose distribution is very well known, especially during radiotherapy is applied to the thoracic and abdominal regions. The breast, lungs, esophagus, pancreas, liver, and kidneys are the most displaced organs during breathing. Abdominal organ motion is reported generally in the superior-inferior direction, while the movement in the anterior-posterior and lateral directions is minimal. In lung tumors, the amount of movement is highly variable and greater in all three directions. Currently, to reduce the respiratory-related motion effects on dose distribution, some strategies are used such as forced shallow breathing with abdominal compression, breath-holding on deep inspiration, respiratory-gating and tracking techniques integrated into the treatment planning system [19–21].

The above-mentioned techniques are applied with the help of images obtained from the 4D-CT device that shows time-dependent volumetric changes in the respiratory cycle. The respiratory monitoring method in 4D-CT scans is usually performed on an external device-based system. Several studies have reported that external surrogate-based 4D-CT images are superior to conventional 3D-CT in terms of accuracy and functionality [17, 22–24]. The most important issue to be considered while using these systems is the breathing pattern of the patient. If the patient has irregular or superficial breathing, respiratory signals recorded by external surrogates may not always accurately represent internal target motions [12, 25, 26]. The location of the external marker on the patient and the tumor localization also affect the results [17]. In addition, it has been reported that the use of the six-dot marker box has advantages over the two-dot box in terms of showing real-time patient position [10].

The 4D-DL, a new system which monitors respiration according to the anatomical features of the internal organs, does not require any extra respiratory monitoring equipment and does not have the disadvantages mentioned above [10, 17].

There are several studies showing good agreement between external surrogate systems and internal organ motion in respiratory gating treatment [10, 16, 17, 19]. In most of these studies, the Varian RPM system and the 4D-DL system were compared. However, these studies have mostly been done on phantoms, and the number of clinical studies with patients is much less [15, 18, 19]. In the study of Yip et al. [17] external device-based 4D-CT and anatomy-based device-free 4D-CT were compared geometrically and dosimetrically in lung tumor patients who underwent SBRT, and it was reported that there was no significant difference between them. Furthermore, Li et al. [16] compared external and internal surrogate systems in ten cancer patients and reported that the deviceless 4D system can be used more easily in clinical settings. In Sprouts' study [10], there were 35 cases, 20 were diagnosed with lung cancer, 8 pancreatic cancer, and 7 liver cancer. The evaluation was made for both the thoracic and abdominal regions. The comparisons were made quantitatively and qualitatively for two reconstruction methods. As a result, both methods were found to be similar. Unlike our study, they used diaphragm and body region as comparing metrics for liver and pancreatic cancers. However, the diaphragm movement due to respiration affects the displacement of tumors in the lung more than the abdominal tumors. Since some people do abdominal breathing, the diaphragm movement is not sufficient to predict the motion of organs located in the abdomen (such as the kidneys). Similarly, in the study of Panandiker et al. [27] the physiological renal motions were evaluated with 4D-CT in pediatric patients; however, no significant correlation could be shown between the diaphragm and renal motion.

On the other hand, Holla et al. [19] have compared another monitoring system the Anzai belt and the 4D-DL system on the phantom and showed that the 4D-DL system is more useful if the target movement is small. However, Liu et al. [13] investigated the combined use of two different respiratory monitoring systems (RPM and Anzai belt) for 4D-CT simulation in 15 patients with lung cancer and reported that they should not be used together because there is no correlation between them.

In the current study, the motion of the abdominal organs was compared in 4D-CT images obtained using the 4D-RPM and 4D-DL systems in patients. There was no difference between the external and internal organ motion monitoring systems in terms of geometric and volumetric variations. Especially mean difference between the right-left, superior-inferior, and anterior-posterior displacement of the kidneys in both respiratory monitoring systems was determined as 0.0 cm. Also, there was a high similarity between the delineated right and left kidney volumes in both respiratory monitoring systems (0.98 and 0.97, respectively).

The 4D-Deviceless respiratory monitoring system is generally developed for lung tumors. However, both in this study and in Sprouts' study [10], it was observed that the 4D-DL system was not different from the Varian RPM system for abdominal region radiotherapy.

Although it seems like a limitation that our study is retrospective and has a small number of patients, it was planned as a prospective study but analysed retrospectively. Also, since the number of patients varies between 10–15 in most of the studies on this subject in the literature and it is a technical study comparing two respiratory monitoring systems, the number of our patients is relatively low. In addition, unlike other studies, we did not prefer gross tumor volume to determine organ motion, but rather the kidneys and renal arteries. The reason for this is that the paraaortic lymph nodes are mostly located around the vessels and at the infrarenal level.

Despite these, the most important feature is that our study is the only study in the literature comparing device-based (RPM) and 4D deviceless respiratory monitoring systems when evaluating abdominal organ motion in patients.

Conclusion

For 4D-CT, external device-based and deviceless respiratory monitoring systems were not different from each other in tracking and detecting moving targets. The 4D-Deviceless system can be preferred in routine practice as an alternative, as it eliminates the need for an external monitoring instrument and provides ease in workflow and greater patient comfort. Either one of them can be used safely for abdominal region radiotherapy planning according to the available possibilities in the clinic.

Ethics Committee Approval: The Istanbul University-Cerrahpasa Clinical Research Ethics Committee granted approval for this study (date: 08.01.2019, number: A-44).

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