Original

Extraction of Respiratory Signal Based on Image Clustering and Intensity Parameters at Radiotherapy with External Beam: A Comparative Study

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ABSTRACT

Background: Since tumors located in thorax region of body mainly move due to respiration, in the modern radiotherapy, there have been many attempts such as; external markers, strain gage and spirometer represent for monitoring patients' breathing signal. With the advent of fluoroscopy technique, indirect methods were proposed as an alternative approach to extract patients' breathing signals.

Materials and Methods: The purpose of this study is to extract respiratory signals using two available methods based on clustering and intensity strategies on medical image dataset of XCAT phantom.

Results: For testing and evaluation methods, correlation coefficient, standard division, amplitude ratio and different phases are utilized. Phantom study showed excellent match between correlation coefficient, standard division, amplitude ratio and different phase. Both techniques segmenting medical images are robust due to their inherent mathematical properties. Using clustering strategy, lung region borders are remarkably extracted regarding intensity-based method. This may also affect the amount of amplitude signal.

Conclusion: To evaluate the performance of these methods, results are compared with slice body volume (SBV) method. Moreover, all methods have shown the same correlation coefficient of 99%, but at different amplitude ratio and different phase. In SBV method, standard division and different phase are better than clustering and intensity methods with SDR=4.71 mm, and SDL=4.12 mm and average different phase 1.47 %, but amplitude ration of clustering method is significantly more remarkable than SBV and intensity methods.

Keywords
Surrogate Breathing Signal, Motion Management, Clustering Method, Intensity Method, Slice Body Volume, External Beam Radiotherapy

Introduction

In external beam radiotherapy, the tumor motion is a crucial and challenging issue that is increasingly becoming important at the image-guided radiotherapy area. The uncertainty motion errors lead to undesired planned dose distribution on tumor and the surrounding tissues while some over- and under- dosage will happen. Several motion management strategies have been proposed to compensate for the effect of tumor motion errors in external beam radiotherapy [1-3]. Since tumors located in thorax region of patients' body mainly move due to

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respiration, in modern radiotherapy, there have been many attempts to represent methods for monitoring patients' breathing signal. Patients' breathing signal as main part of total motion management is highly applicable at 1) real-time tumor tracking and 2) motion-gated radiotherapy [4-6].

As a surrogate method, several efforts have been proposed to extract respiratory signals ranging from continuous x-ray imaging in the chest or abdomen region of patients [7, 8], but there is still great endeavor in modern radiotherapy which represents a novel method or methods to extract patients' breathing signal with low cost of treatment taking into account that the patients' safety is kept as a crucial issue. Although in conventional surrogate methods, to extract breathing signal, some additional hardware instruments such as strain gage, spirometer and external markers are utilized [6, 9, 10], physical instruments are invasive and may cause medical risk increasing the cost of treatment. Moreover, in latter case, finding a proper correlation model between external surrogate markers and internal tumor motion within less uncertainty errors is complicated which may reduce the accuracy of performance model. For tumor motion estimation, this issue highly depends on variabile respiratory motion database [11, 12].

With the advent of continuous x-ray imaging strategy to extract breathing signals as a part of the conventional surrogate methods, the surrogate methods, as a respiratory signal were represented. In clinical application, surrogate methods are utilized by means of fluoroscopy system or 4D CBCT technique. In this method, the patient's breathing signal is exactly and directly extracted from the process of fluoroscopy or 4D CBCT images as real time. Moreover, by implementing surrogate methods, physical instruments are required as conventional surrogate method is omitted, the cost of the treatment is saved and the patient feels more comfortable. As a drawback, using continuous x-ray imaging may increase additional dose received by patient. This issue must be addressed according to ALARA principle [1, 13-16]. In previous methods, in order to extract respiratory signal, fluoroscopy images captured by imaging systems have been processed based on image features such as: lung air volume, lung air density, deformable image registration (DIR) [17-19] and sliced body volume (SBV) based on image registration method [1]. Some of these proposed methods have been clinically available to extract patients' breathing signals [1, 13-16].

In this study, we utilized the information of 4DCT images of the XCAT phantom to extract breathing signals. While, during respiration the human body is expanded, the displacement of lungs margin is identified as a robust potential respiration surrogate. Two available methods, based on the clustering and intensity, were proposed as a respiration surrogate. 4DCT images taken from 4D XCAT anthropomorphic phantom and developed by Dr. WP Segars [20-22] were utilized to extract breathing signals. Moreover, final results were compared with real phantom breathing signal as benchmark. The major advantage of using clustering and intensity methods is that both phase and magnitude information are available for extracting respiratory signals from CT images.

The clustering method was based on k-means algorithms for segmentation of 4DCT images. Although the margin of lung is extracted from each slice of 4DCT segmentation data, the total numbers of pixels in the margin of lungs were calculated. Moreover, an individual number of pixels as a result of the breathing signals were plotted. In addition, the mean values of clustering method were set to zero. Transfer axis to zero was used to compare extracted breathing signal with the benchmark. The proposed intensity-based method was based on two predefined thresholds. The first threshold was used to extract slice body volume and the second threshold was used to extract margin of lungs from each slice of 4DCT images. After extracting the margin of lungs, the process is used in the same way as the clustering method for plotting breathing signals.

To test and evaluate the performance of these methods, the results of two models are expressed by computing the correlation coefficient (R), standard division (SD), amplitude ratio and different phases between surrogates breathing signals given through two proposed models and real respiration signal extracted from phantom as a benchmark were compared. Although the results of two available methods based on the testing and evaluation models were compared, the performance of two available methods were compared with sliced body volume (SBV) method [1] using XCAT phantom data

Material and Methods

Properties of Data and Software

In this study, a simulation study was performed on 4D XCAT anthropomorphic phantom using NURBS base which is commercially available to simulate motions of dynamic organs caused mainly by breathing phenomena. This phantom was chosen due to combined advantages of pixel-based and geometry-based phantoms which were quite robust to simulate human body with multiple resolutions and various anatomies. XCAT phantom enables user to change functional variables that control respiration, in order to generate deformable 4DCT models, simulating condition must be simulated. The main controllable parameters are: 1) motions of beating heart only, respiration only or combined mode, 2) Maximum diaphragm motion and 3) Maximum anterior-posterior expansion of chest wall [21-23]. Moreover, using this phantom, tumors with Spherical shape can be added at each arbitrary organ with various sizes. Organs margin and deformable registration map can also be extracted from the spline-based representation approach [24].

In this study, five different respiratory cycles were generated with reasonable breathing amplitudes and frequency to mimic real respiratory (Table 1). To do this, required parameters such as maximum anterior-posterior expansion of chest wall and time of respiratory period were determined using amplitude and frequency of respiratory motion signals of real patients treated with Cyberknife Synchrony System (Georgetown University Medical Center, Washington DC). Also, the 4DCT image size used in this study is 512*512*381 with 0.5*0.5*0.5 mm3 voxel size.

Clustering Methodology at Image Segmentation

The assessment of clustering method to extract breathing signals was executed using unsorted 4DCT images of the phantom. Since unsorted 4DCT images represent slice by slice including human anatomy during res-

Table 1: Characteristics of five different respiratory cycles created by XCAT Phantom.

breathing cycle number	Time of respiratory period(sec.)	Maximum diaphragm motion(cm)	Maximum Anterior-Posterior expansion of chest wall (cm)
1	5	2	1.2
2	5	1.7	0.7
3	4	1.2	0.5
4	6	2.2	1.3
5	5.5	1.8	1

piration, tracking the contour of lung (inside and encompassed) provides a continuous trace of respiration status of the phantom. In this study, the clustering was done using k-means strategy on 4DCT image data. K-means clustering or Hard C-means clustering is an algorithm based on defining clusters in a dataset such that the cost function of dissimilarity criterion is minimized. The Euclidean distance is mostly used as the dissimilarity measure [20-21]. A set of N vectors X_k and k =1, … , N, are to be divided into C groups G_i , i =1, … , C. The cost function based on the Euclidean distance between vectors X_k in group i and the corresponding cluster center V_i, can be defined by the following equation. Although, based on the trial and error method, the number of clusters used in this study was set to be three clusters. Clustering method is an automatic way to segment 4DCT images based on the number of definite clusters. The main advantage of clustering method is efficient computing capability and robustness property that prove our model can correct lung boundary reliably and reproducibly.

$$j = \sum_{i=1}^{c} j_i = \sum_{i=1}^{c} \left(\sum_{k, Xk \in G_i} \left\| x_k - v_i \right\|^2 \right)$$

Figure 1 shows the workflow of the implemented method. As seen, in the first step, the total number of pixels in the contour of the lung (inside and encompassed) was calculated to represent the amplitude of breathing signal. In the next step, individual amplitude of the breathing signal was generated for slice of 4DCT image plotted in the breathing curve. Finally, the mean value of clustering method was set to zero. In this study, transfer axis to zero was used to compare extracted breathing signal with the benchmark breathing signal.

Intensity-Based Method in Image Segmentation

In computer vision, image registration based on intensity method is the process of partitioning a digital image into multiple segments (sets

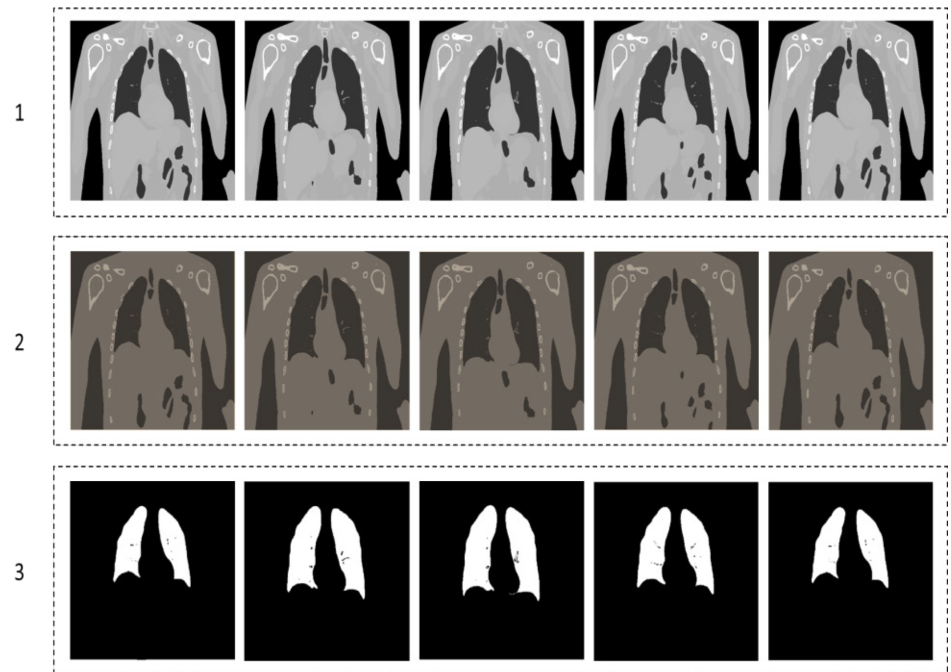


Figure 1: Workflow of breathing signal extraction from 4DCT image with clustering method based on k-means strategy. In the first step, the 4DCT images of the phantom are imported in the clustering method and in the second step the images of the phantom are clustered based on tree cluster and finally the margin of lung were extracted.

of pixels also known as super pixels). The goal of segmentation is to simplify and/or change the representation of an image into something that is more meaningful and easier to analyze [25]. Intensity method based on the threshold was typically used to locate objects and boundaries in images. More precisely, image segmentation is the process of assigning a label to every pixel in an image such that pixels with the same label share certain characteristics. The result of intensity- based method is a set of segments that collectively cover the entire image, or a set of contours extracted from the image. Each pixel in a region is similar to some characteristics or computed properties such as color, intensity or texture. Adjacent regions are significantly different with respect to the same characteristic. Workflow of intensity method is shown in Figure 2. As seen in this figure, for segmentation of 4DCT images, the two thresholds are defined and then patient body (inside and encompassed) and right/left lung (inside and encompassed) are reconstructed on the basis of pre-defined thresholds. As next step, total numbers of pixels in the margin of lungs (inside and encompassed) were calculated. Then, an individual breathing curve was generated for each slice by plotting the intensity means value as a function of image acquisition time. Also, for comparing the extracted breathing signals with the benchmark breathing signal, the means of intensity means values were set to zero. Moreover, the minimum values of red, green and blue (RGB) light were definite to segmentation images that made a poor boundary edge detection. These is as a drawback for intensity method.

Sliced-Body-Volume (SBV) Method

Since during patient respiration, human body is expanded, body volume (BV) method can be used to extract patients' breathing signals. In SBV method, a threshold was defined to reconstruct contour of the patient body from

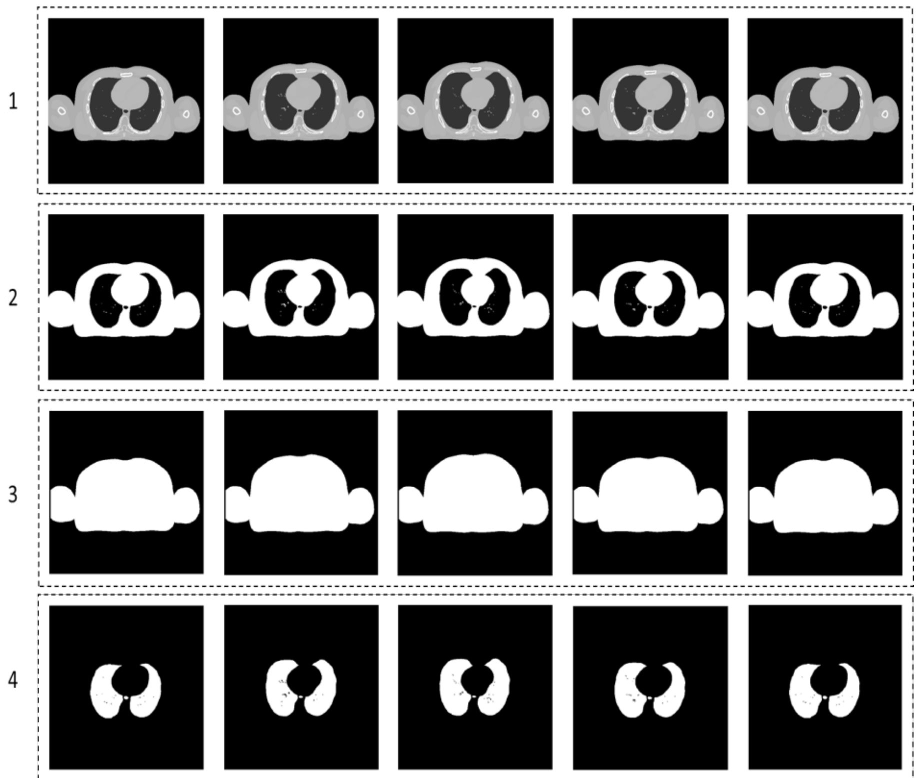


Figure 2: Workflow of breathing signal extraction from 4DCT image using intensity based method. Based on two thresholds, the first contour of body was extracted and then the margin the second threshold was used to extract margin of the each lungs in the 4DCT images.

4DCT images. This way, the desired signal is achieved by calculating the number of pixels in contour of the patient body, and plotting SBV value as the breathing curve generated from slice of 4DCT image as a respiration function of time. After plotting SBV value as respiration curve, the means of SBV value were set to zero [1].

The process of extraction surrogate breathing signal was shown in Figure 3. Firstly, the body contour was determined for each 4DCT image by applying a threshold and then performing morphological operations to exclude extraneous pixels due to noise. SBV is the total area (or simply the total number of pixels) encompassed by the body contour. Secondly, an individual breathing curve was generated for each slice by plotting SBV value as a function of image acquisition time. The means of SBV values were set to zero. Thirdly, the complete breathing signal was generated by sequentially appending all individual breathing curves.

Results

In this study, two available methods, based on clustering and intensity, were presented to extract patients' breathing signal from 4D XCAT anthropomorphic phantom. For testing and evaluation the performance of the proposed methods, correlation coefficient (R), standard division (SD), amplitude ratio (amplitude ratio of method divided to amplitude ration of benchmark) and different phase were utilized. Although in first part, the results of breathing signals reconstructed from two available methods (clustering and intensity) were compared with real breathing signal of the phantom, in the second part, all results obtained by three proposed methods (clustering, intensity and SBV) were compared with benchmark respiration signals. In Table 2, the accuracy of correlation coefficient, different phase and amplitude ratio determined by using a 4DCT dataset of XCAT phantom are shown.

Moreover, the results of segmentation region of lung and body by three methods were shown in figure 4. In figure 4, the results of

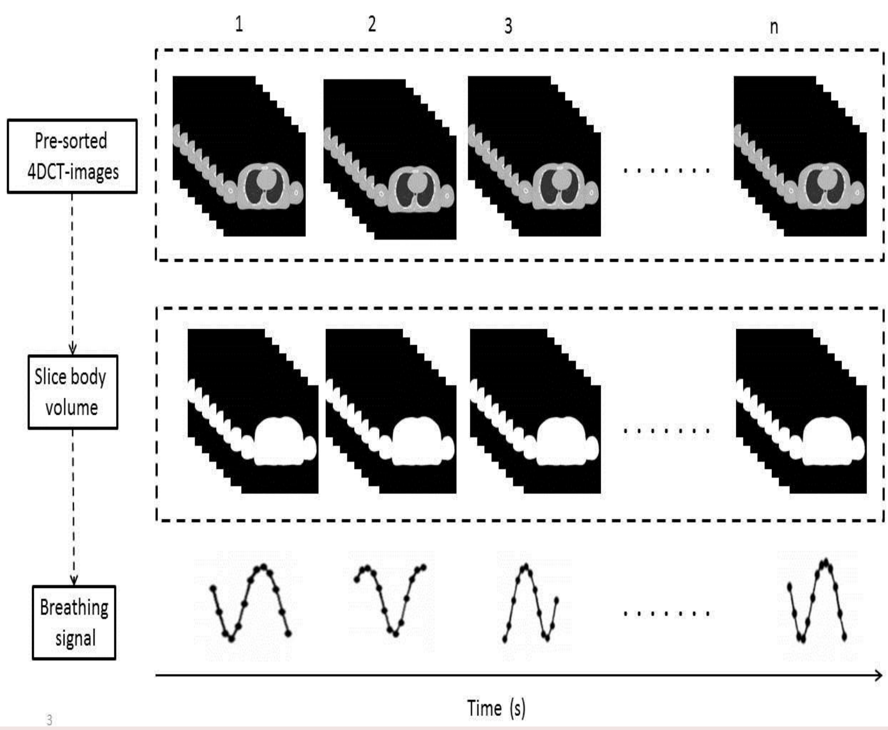


Figure 3: Workflow of sliced body volume for extract surrogate patient breathing signal. For illustration purpose, only one slice is shown per couch position.

Table 2: Accuracy of correlation coefficient, different phase and amplitude ration, determination by using a 4DCT dataset of the XCAT phantom

Time		Intensity method	Clustering method	SBV method
1	Correlation Coefficient	99 %	99 %	99 %
	Different Phase (%)	1.71 %	1.68 %	1.65 %
	Amplitude Ratio	1	1	1
2	Correlation Coefficient	99 %	99 %	99 %
	Different Phase (%)	1.63 %	1.61 %	1.58 %
	Amplitude Ratio	0.68	0.73	0.65
3	Correlation Coefficient	99 %	99 %	99 %
	Different Phase (%)	1.77 %	1.74 %	1.7 %
	Amplitude Ratio	0.69	0.72	0.63
4	Correlation Coefficient	99 %	99 %	99 %
	Different Phase (%)	0.86 %	0.84 %	0.84 %
	Amplitude Ratio	0.66	0.73	0.69
5	Correlation Coefficient	99 %	99 %	99 %
	Different Phase (%)	1.67 %	1.65 %	1.61 %
	Amplitude Ratio	1	1	1

4DCT SBV, 4DCT clustering, 4DCT intensity, and 4DCT phantom (RPM) are shown, respectively. As shown in Figure 4, all of the methods are able to segment and extract body and lung boundaries well.

The average correlation coefficient and average standard division for the right and left lung calculated for clustering based are R=99%, with SDR=4.8 and SDL=4.22 mm, while this parameter is R=99%, with SDR=4.9 and SDL=4.22 mm for intensity-based method against real breathing signal as benchmark. Using SBV method, the correlation coefficient and standard division for the right and left lung are R=99%, with SDR=4.71 and SDL=4.12 mm. Figure 5 represents breathing

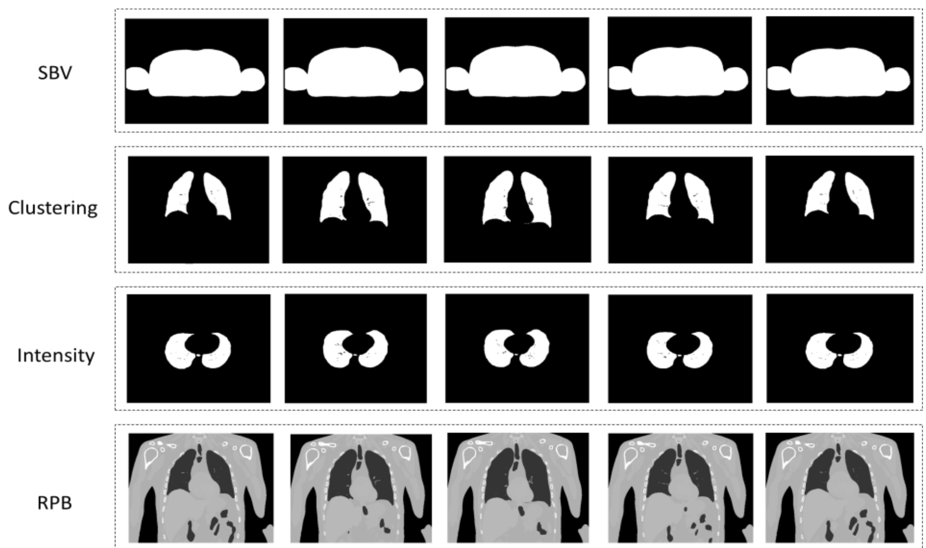
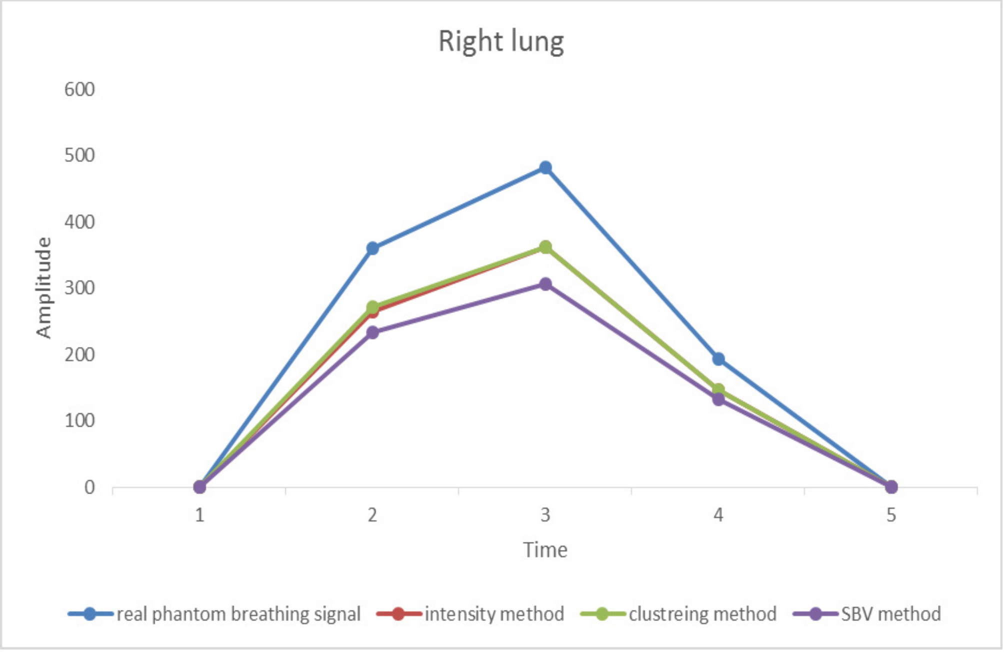
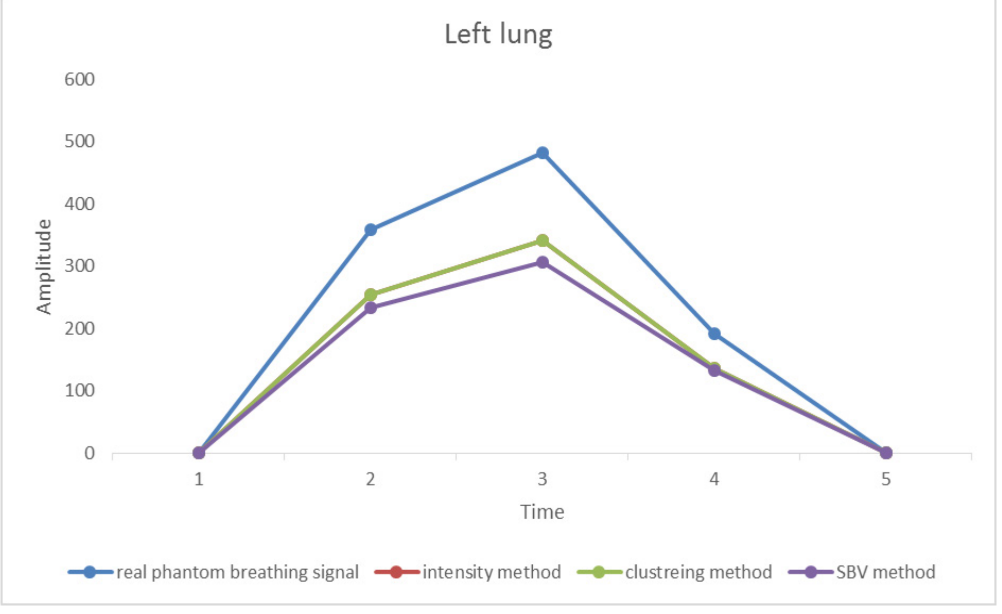


Figure 4: Boundary organ and body delineation using 4DCT image by three proposed methods

signals extracted from three proposed methods as motion amplitude vs. time for right (5-a), left (5-b) and total lung organ (5-c). Also, the different phase of three methods (clustering, intensity and SBV) is shown in figure 6.



(5-a)



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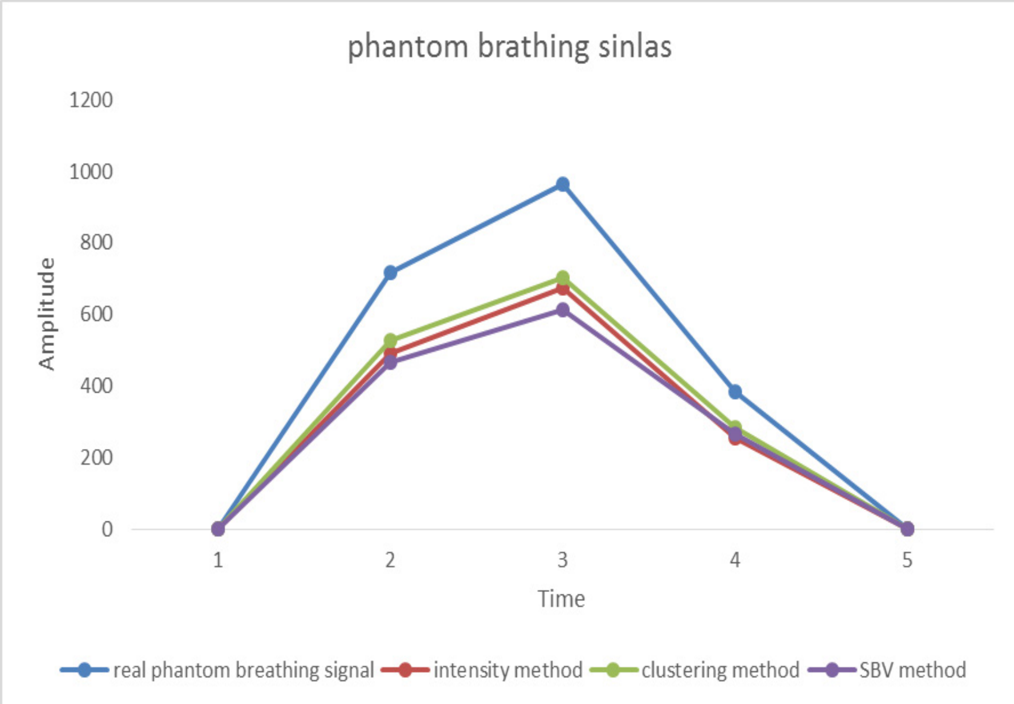

(5-c)

Figure 5: Breathing signals extracted from three proposed methods compared with the real breathing signals on right lung (5-a), left lung (5-b) and total lung organ (5-c).

Discussion

In modern radiotherapy, many tumors located in thorax and abdomen regions move semi-regularly mainly due to respiration. To compensate this inter- and intra- fractional motion errors, several strategies were proposed to compensate for this effect onto prescribed dose distribution. In different treatment modalities, accuracy of each treatment dependents highly on patients' breathing signal obtained from physical instruments such as: external markers, strain gage and spirometer. In recent strategies, there is a great seeking to extract patients' breathing signal with low cost of treatment and patient safety avoiding implementation of additional devices for gathering breathing motion database. With the advent of fluoroscopy and 4D CBCT technique, indirect methods were proposed as alternative approaches to extract patients' breathing signals. In these methods, the patients' breathing signals are exactly extracted from fluoroscopy image or 4D CBCT image as real time.

In this approach, two available methods based on clustering and intensity were proposed to extract patients' breathing signal from 4DCT images including respiratory motion data. To do this, a validated computational 4D XCAT phantom was used to produce 4DCT images. Using this phantom, one of the difficulties to study on patient's body that is lack of real motion information is addressed precisely. Our proposed method is applicable on 4DCT and 4D CBCT data of real patients. In this study, we comprehensively evaluated the clustering and intensity surrogate methods for signal extraction in comparison with real breathing signal extracted by phantom.

As mentioned before, although in image segmentation by clustering method, three clusters are used, at intensity-based method, two predefined threshold values are utilized for image segmentation. Both techniques that segment medical images have robust and weakness

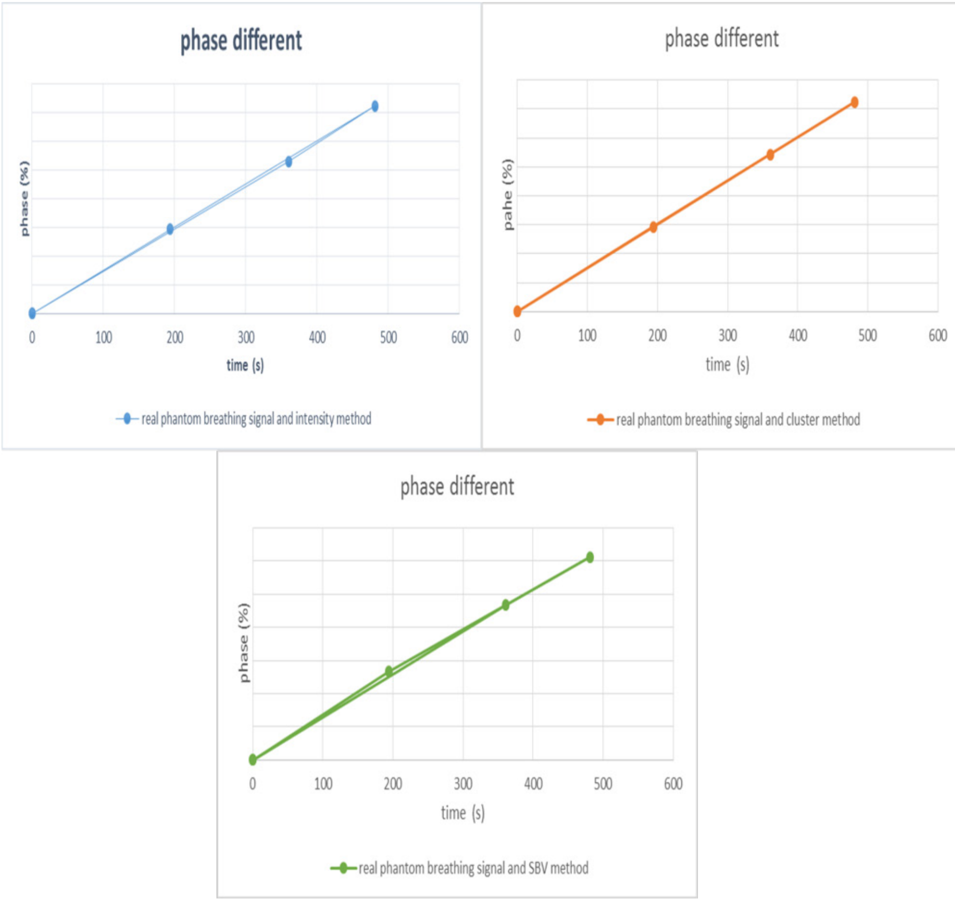

Figure 6: Different phases of the three methods (clustering, intensity, and SBV) are shown.

points due to their inherent mathematical properties. Using clustering strategy, lung region borders were remarkably extracted regarding intensity-based method since the latter case uses minimum image intensity value. This may affect the amount of amplitude signal.

According to final analyzed results using correlation coefficient, different phase parameters and amplitude ration based on table 1, two proposed methods are robust to extract breathing signal. While the correlation coefficient is more that 99%, different phases are assorted for each method. Moreover, the performance of clustering and intensity-based methods was compared with SBV method as an alternative method. As results from all figures (5-a, b, c) and figure 6, three of the methods (clustering, intensity and SBV) show the same correlation coefficient 99%, but different in amplitude ratio and different phase. In SBV method, standard division and different phase are better than clustering and intensity methods with SDR=4.71 mm and SDL=4.12 mm and average different phase 1.47 %, but the amplitude ration of clustering method is significantly more remarkable than SBV and intensity methods. In addition, the clustering method with the same average different phase 1.48 % shows more remarkable amplitude ration than other methods. Moreover, this different significantly remarked in the time 2 (s) figure (5-a) and in the time 3 (s) figure (5-c). Maximum displacement in the abdomen region occurred in the time 2-4 (s). Especially, the best correlation and maximum amplitude occurred in the time 3 as in figure (5-c), while the inhale and exhale in time 1 and time 5 were set up to zero for adjustment and comparison of the breathing signals with the benchmark breathing signals.

Conclusion

In this study, we used a 4D XCAT phantom to extract phantom breathing signal to find and present alternative respiration methods which have the best correlation coefficient, high amplitude and low standard division. We found that the best alternative methods to extract patients' breathing signal are clustering method and SBV methods. Clustering and SBV methods both represented the best performance. Also, using alternative methods to extract respiration caused to eliminate requirement devices and reduced cost of treatment. Although the method used to extract surrogate respiration was not without any limitation. The limitation of this method is if these methods cannot be used as a real-time monitoring system or if we want to use as real time method, continuous x-ray imaging, fluoroscopy technique or 4DCBCT images may increase additional dose received by patient; this issue must be addressed according to ALARA principle. Finally, although the study here focuses on extracting surrogate respiration using XCAT phantom, the proposed idea can be implemented on real patient data.

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Conflict of Interest

None

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