Dynamic MLC Tracking Using 4D Lung Tumor Motion Modelling and EPID Feedback

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ABSTRACT

Background: Respiratory motion causes thoracic movement and reduces targeting accuracy in radiotherapy.

Objective: This study proposes an approach to generate a model to track lung tumor motion by controlling dynamic multi-leaf collimators.

Material and Methods: All slices which contained tumor were contoured in the 4D-CT images for 10 patients. For modelling of respiratory motion, the end-exhale phase of these images has been considered as the reference and they were analyzed using neuro-fuzzy method to predict the magnitude of displacement of the lung tumor. Then, the predicted data were used to determine the leaf motion in MLC. Finally, the trained algorithm was figured out using Shaper software to show how MLCs could track the moving tumor and then imported on the Varian Linac equipped with EPID.

Results: The root mean square error (RMSE) was used as a statistical criterion in order to investigate the accuracy of neuro-fuzzy performance in lung tumor prediction. The results showed that RMSE did not have a considerable variation. Also, there was a good agreement between the images obtained by EPID and Shaper for a respiratory cycle.

Conclusion: The approach used in this study can track the moving tumor with MLC based on the 4D modelling, so it can improve treatment accuracy, dose conformity and sparing of healthy tissues because of low error in margins that can be ignored. Therefore, this method can work more accurately as compared with the gating and invasive approaches using markers.

Citation: Rostampour N, Jabbari K, Nabavi Sh, Mohammadi M, Esmaeili M. Dynamic MLC Tracking Using 4D Lung Tumor Motion Modelling and EPID Feedback. *J Biomed Phys Eng*. 2019;9(4):417-424. https://doi.org/10.31661/jbpe.v0i0.769.

Keywords

Real-time Tracking, Lung Tumor Tracking, Respiratory Motion Prediction, Neuro-fuzzy Model, EPID

Introduction

Giving sufficient dose to target and reducing normal tissue toxicity is the main goal in radiation therapy. Accurate delivery of the beam is one of the main challenges in lung tumor radiation therapy as a result of respiration. Respiration is a source of inaccuracy in radiation therapy because it causes significant motion of thoracical and abdominal organs [1]. Respiration significantly impacts dose distribution, and thereby clinical results in lung cancer radiation therapy.

There are several techniques that have been proposed and evaluated in clinical use to take into account such dynamic nature of the lung

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Received: 30 April 2017
Accepted: 14 October 2017

tumor motion during the course of radiation therapy. These techniques are not desirable for patients [2-7]. Gating and tracking approaches have been developed to adapt a proper beam delivery for breathing or lung tumor motion. The main objective in the gating technique is to synchronize the delivery of beam with the specified condition of respiratory cycle [3, 8-10], but the beam follows the moving tumor in the tracking technique [11-14]. Few tracking approaches with the use of moving radiation source have also been studied such as direct measurement of fiducial marker [15-18], external marker tracking (indirect measurement) [7, 19, 20] and breath monitoring approaches [21]. Respiratory surrogates or implant markers are monitored and used to synchronize the treatment with tumor motion. Treatment of the patient and dose delivery can be interrupted and restarted if target motion differs from the average trajectory.

Previous studies which have been conducted to move the radiation conforming to the lung tumor motion used extra monitoring hardware such as fluoroscopy and optical tracking for real time tumor tracking [22-26]. In this study, lung tumor motion was predicted without any markers by using neuro-fuzzy method to combine the numeric power of neural adaptive network systems with abilities of fuzzy systems. As a simple description about neuro-fuzzy method, assume x and y are input variables, the output variable is determined by applying neuro-fuzzy rules to a fuzzy set of the input variables. According to the following rules, the set of rule includes two fuzzy if-then rules for the first order Sugeno fuzzy model:

If x is A1 and y is B1 then, f1=p1x+q1y+r1 (1)
If x is A2 and y is B2 then, f2=p2x+q2y+r2 (2)

where p_i, q_i, and r_i (i=1 or 2) are linear parameters, and A_i, B_i are linguistic labels. These parameters are characterized by appropriate membership functions (MF) [27].

The principle aim of this work is to provide a markerless method for the prediction of the tumor position based on 4D computed tomography (4DCT) images of the patients.

Material and Methods

At first, 4D-CT images for 10 patients were obtained on a 16-Slice Brilliance CT Big Bore Oncology™ configuration (Philips) placed at the Léon Bérard Cancer Center, Lyon, France [28]. Breathing correlated information was acquired using the associated Pneumo Chest bellows™ (Lafayette Instruments). Each data set including a respiratory cycle consists of ten 3D-CT phases. A radiation oncologist contoured all the slices which contained tumor for 10 patients. The tumor margins were delineated in the selected images. A respiratory cycle for each patient contained 10 phases.

After receiving four-dimensional CT images as an input, the end-exhale phase of these images has been considered as a reference for calculations related to the modelling of respiratory motions. These reference images were analyzed using neuro-fuzzy method for predicting the magnitude of displacement of the tissue in lung.

To train the algorithm, the contoured tumors in each slice of 4D-CT images were considered as an input. The algorithm was used to predict the next phase as the output. The training was performed for the first 6 patients and the left four patients were used to evaluate the algorithm to predict tumor motion. All algorithms in this work were applied on the 4D-CT images using MATLAB software.

The most widely used MF in neuro-fuzzy method is Bell MF which is based on a generalized bell-shaped curve. According to Figure 1, the following formula shows the generalized bell-shaped curve:

$$\text{Bell}\,(x;a,b,c) = \frac{1}{1+\left|\dfrac{x-c}{a}\right|^{2b}} \qquad (3)$$

where parameter a is the width of the curve, b is usually positive and parameter c locates the center of the curve [29, 30].

The hybrid learning algorithm used in neu-

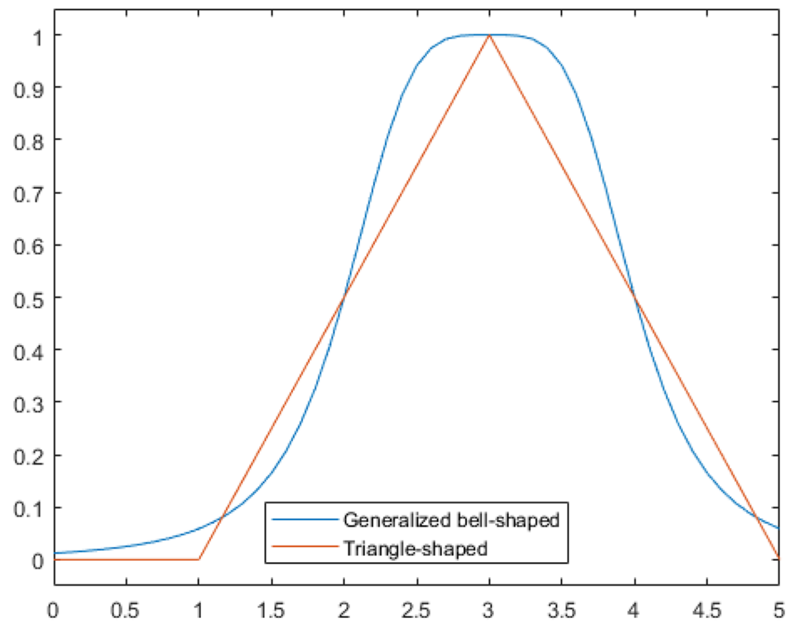

Figure 1: The generalized bell membership function (gbellmf) curve.

ro-fuzzy consists of gradient descent and the least-squares method. The measured error to train is defined as [30]:

$$RMSE = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(A_i - P_i)^2} \quad (4)$$

where N is the number of predicted samples, A_i and P_i are i_{th} desired and predicted outputs, respectively. To predict lung tumor motion, the results from different patients should be combined and RMSE is computed for each patient and then the average RMSE is used.

These reference images and predicted data from respiratory motion were used to determine the leaf motion in MLC. For this purpose, the authors have developed a new software to control each of individual leaves of MLC during tumor motion. This software imports the input from the user as a simple contour which is drawn on the CT images related to the end-exhale phase of respiration and after making other phases of respiration using an artificial neural network method, the amounts of movement of each leaf are determined in different phases of respiration. Finally, the software generates an MLC file which can be delivered as an input to Varian MLC Shaper (Varian Medical System, Palo Alto, CA) to manage MLC movements during radiotherapy of moving tumors.

In this software, with the calculation of dynamic mode, all produced data were validated and the results were entered to Linac for EPID (electronic portal imaging device) imaging. To verify the amount of error in the method, the results of these changes in MLC shape were compared with observed MLC movements resulted from four-dimensional plan using four-dimensional CT images.

The trained algorithm was evaluated by Shaper software to show how MLCs could track the moving tumor. Shaper software loads, opens and displays any plan that MLC physically can achieve. Shaper is a Microsoft Windows-based application that allows you to: a) autofit MLC leaves around a digital shape to create a field, b) edit the leaf positions of a field, c) save Shaper data in a computer file that is readable by the MLC workstation and d) print leaf plan information on any Windows-compatible printer or output device. Shaper creates a file containing the field information. MLC workstation software can read and use the information in the MLC plan files. An MLC plan file can contain one or more fields. Each field represents one field shape. The MLC workstation software can use one filed at a time for a static plan or several fields in succession for a dynamic plan.

Finally, the Shaper-validated MLC plans were tested on a Varian (CLINAC 600 CD) clinical linear accelerator equipped with AS-1000 electronic portal imaging device (EPID). EPID was set up at SID = 140 cm and the images were acquired at a frame rate of 12.86 Hz with a pixel resolution of (0.43 × 0.43) mm in the isocenter plane. The obtained images by EPID were compared with the images acquired by the Shaper software.

The obtained images by EPID and the Shaper software (Figures 2 and 3) were compared in terms of area by ITK-SNAP software [31] and the mean values of them in each phase of one respiratory cycle were calculated. ITK-SNAP is a software application used to segment structures in 3D medical images. It provides semi-automatic segmentation using active contour methods, as well as manual delineation and image navigation.

Results

To investigate the accuracy of neuro-fuzzy performance in order to predict the tumor motion, the root mean square error (RMSE) was used as a statistical criterion. RMSE is a frequently used measure of differences among values predicted by a model and corresponding observed values. In this study, the differences were squared and then averaged over the samples. So, the square roots of the average values were taken for the evaluation of results. In order to predict the positions of contoured tumors, the means of RMSE per patient were calculated for all patients. Tables 1 and 2 show the parameters for training neuro-fuzzy and means calculated from RMSE of patients, respectively.

Figures 2 and 3 illustrate the images obtained by EPID device and Shaper software for one inhalation and exhalation, respectively. A complete inhalation and exhalation contained 10 phases.

Table 3 shows the mean area of the desired

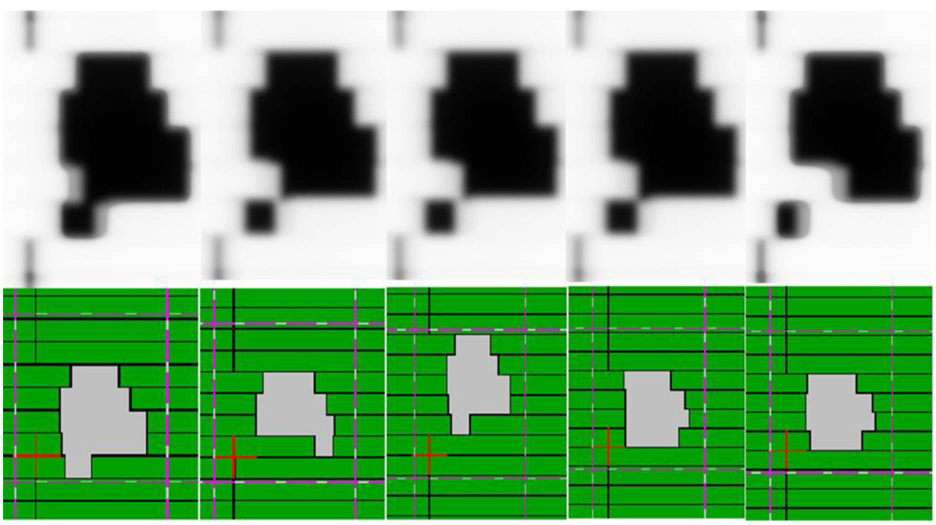

Figure 2: The images of five phases of inhalation from left to right. Top: Images obtained by EPID; Down: Images obtained by the Shaper.

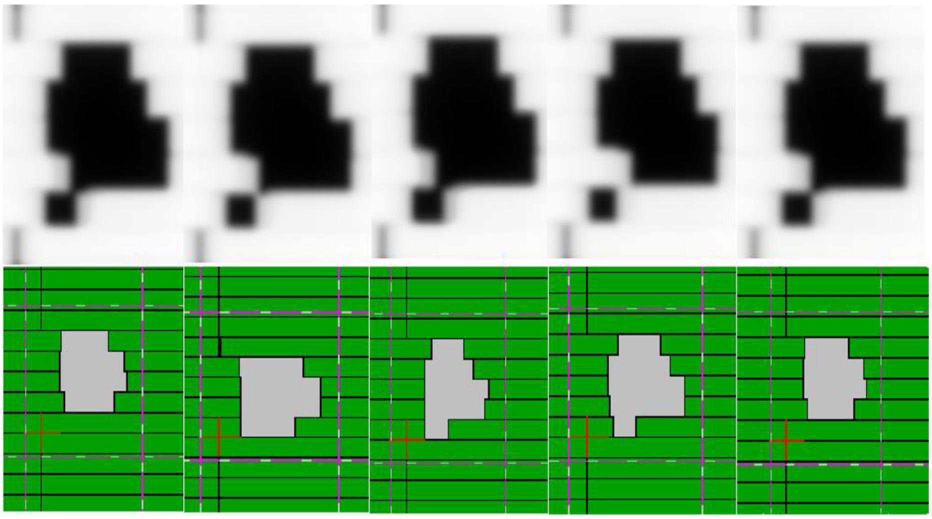

Figure 3: The images of five phases of exhalation from left to right. Top: Images obtained by EPID; Down: Images obtained by the Shaper.

contour images obtained by EPID and the Shaper software illustrated in Figures 2 and 3 for one respiratory cycle containing ten phases.

In order to compare the mean areas of the desired contour obtained by EPID and Shaper software, the independent t-test was performed. Statistical results showed that $P = 0.187$ (P-value > 0.05), so the differences among means are not significant.

Table 1: Various parameters which were used to train the neuro-fuzzy approach.

Neuro-fuzzy parameters	Value
MF type	Bell function
Number of MFs	8
Output MF	Linear
Number of nodes	1451
Number of linear parameters	3783
Number of non-linear parameters	63
Total number of parameters	3846
Number of training data pairs	449
Number of checking data pairs	449
Number of fuzzy rules	707

Discussion

Several methods have been proposed and evaluated to track organ motion in a real time such as respiratory-induced tumor motion [32]. The correlation between respiratory phase and external surrogate marker is generally high; however, the correlation between tumor motion and respiratory phase due to phase shift is less verified. Therefore, tracking is performed using a measured correspondence model between internal tumor motion inside the body and external marker motion placed on the surface.

Internal fiducial marker tracking can be used to accurately indicate tumor motion during breathing; however, the tracking requires invasive marker implantation inside the body. In previous studies, several additional tumor

Table 2: The RMSE results for each patient calculated by the neuro-fuzzy approach.

Statistical parameters	Direction	Average RMSE
Mean ± SD	X	0.1256 ± 0.004
	Y	0.1742 ± 0.003
	Z	0.3980 ± 0.007

Table 3: The mean area of the desired contour images obtained by EPID and the Shaper software for one respiratory cycle.

Respiratory phase		Mean area (mm^2)	
		EPID	Shaper
1	Inhalation	2201±1.49	2175±1.15
2		2087±1.25	2021±0.67
3		2045±1.05	2112±0.94
4		2077±1.25	2008±0.63
5		2055±1.83	1993±1.05
6	Exhalation	2011±1.56	1982±0.82
7		2081±1.63	2033±1.15
8		2124±1.15	2022±0.67
9		2074±1.05	2102±0.82
10		2042±0.94	1990±0.94

tracking approaches have been reported with the use of molecular imaging device such as positron emission tomography (PET). In the near future, novel tumor tracking approaches such as direct fluoroscopic and MRI tracking are expected to be commercially available. The centers which are intended to irradiate moving tumors using a tumor tracking device must provide the user with the characteristics of the device and they should apply an adequate margin for treatment planning.

The neuro-fuzzy approach used in this study showed that RMSE did not have a major variation in results. In this neuro-fuzzy program, the training process was done for the first six patients and the left four patients were used as a test to evaluate lung tumor tracking accuracies.

According to Figures 2 and 3, there is good agreement between EPID and Shaper images related to a cycle of respiration for a desired contour moving on a vertical path based on the used neuro-fuzzy approach. The independent t-test demonstrated that the mean area differences were not significant (P = 0.187).

The selected method in this study can be used to track any tumor with MLC and no access to 4DCT imaging equipment; it can prevent the damage to normal tissue. Moreover, instead of using markers, the data in the images were used to track the tumor motion. Therefore, this approach results in more information of tumor motion compared to the methods based on marker location.

Conclusion

This method has some advantages with respect to methods based on surgical implants, invasive methods and inaccurate methods in respiratory gating. In this method there is no need for an extra hardware that can slow down the treatment process. Because using this extra hardware such as IR system, breathing holder makes the treatment less convenient, more labor work would be needed.

Acknowledgment

Authors are grateful to the Vice Chancellor for Research and Technology, Isfahan University of Medical Sciences grant (2015) for supporting this project (No. 394530).

Conflict of Interest

None

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