Original Article

The Robustness of Various Intelligent Models in Patient Positioning at External Beam Radiotherapy

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ABSTRACT

Purpose- Patient setup optimization has been required to fill the gap between individual treatment and uncertainty in the external beam radiotherapy at each of the treatment sessions. This uncertainty error consists of patient body misalignments and patient body displacement between different fractions.

Methods- In this study, the patient geometrical set-up has been simulated comprehensively by 4D XCAT anthropomorphic phantom where the XCAT phantom was used to access 4D modeling of dynamic organs motion. All of the possible roto-translation displacement parameters that were effective on instigate patient position before re-alignment were considered. While the data set was assembled from XCAT phantom including 2D translation and 2D rotation, the parallelisms of the dada set between position of the external markers and reference point (patient couch) were considered. Moreover, the experimental validation models for further investigation were considered. For this aim, the captured data from XCAT phantom was extended to four real patients. In some clinically available strategies, the corrective models have been implemented to estimate patient displacement of patient setup. In this study, four intelligent models were proposed for set-up, realignment, and continuous tracking of the patient positioning.

Results- Final results illustrate that Adaptive Neuro Fuzzy Interference System with all markers can estimate the true patient position with less error.

Conclusion- In this study, the four intelligent models were demonstrated to investigate the robustness of various intelligent models in re-alignment and patient set-up at external beam radiotherapy. Finally, our correlation model “ANFIS” can estimate the true patient position with less error.

1. Introduction

In the external radiotherapy, the patient set-up has used to immobilize target (tumor) in front of beam. Since many uncertainty errors during each treatment session of the radiotherapy caused inappropriate 3D prescribed uniform dose that must have been delivered into tumor volume, the result showed some over and/or under dosage in tumor and healthy surrounding organs [1]. In the external radiotherapy, the uncertainty errors are categorized into two group: 1) inter-fraction motion errors and 2) intra-fraction motion errors. Inter-fraction motion errors have been caused by patient body displacement between daily fractions

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of the radiotherapy, intra-fraction motion error results motion deformation organ in daily and/ or even patient set on the treatment coach during radiotherapy. These uncertainties may have been occurred alone or combined together that have caused poor targeting accuracy [2-4]. Therefore, patient positioning set-up was a challenge crucial issue in the quality of the dose delivery at tumor volume in external radiotherapy. For this aim, the patient positioning verification at each irradiation fraction and/or between different fractions may have been significantly important to align 3D tumor volume against the irradiation beam during treatment.

For the verification of the patient position in the external beam radiotherapy, it is necessary to provide a reproducible method with accuracy [2]. Conventional patient positioning set-up have been done by several methods: immobilization system and/or experience of operators to immobilized localization target in front of beam at each treatment session [2], then the patient dose received is not a serious concern according to ALARA principle [25-26], or body detection systems [opto-electronic or laser spot scanning] with combination indication markers were used for calculation misalignment between patient position and reference point [4-7]. So the gap has filled between the un-couched patient position and uncertainty each session treatment. Recently, a method based on Artificial Neural Network and registration was proposed to alignment patient geometrical set-up in breast radiotherapy. In this method, while the treatment parameters were calculated by registration method and then applied to the artificial neural network (ANN) model, the ANN model was used to fill the gap between individual treatment and uncertainty even at the each session treatment [6-9]. Some of these methods have been applied clinically and commercially available [10, 11]. Moreover, in the intelligent models, it is necessary to find the best correlation between external markers and reference points [12, 13]. Previous studies have been examined to used body detection systems [opto-electronic or laser spot scanning] to combination indication markers to re-alignment patient set-up. Also a significant difference exists between body detection systems and external markers or landmark-based image fusion. In our model, laser spot scan was removed and the ANN model and external markers are used to fill the gap between the patient coach position and reference point.

These investigations were simulated with all of the possible position patient coaches with nine external markers that were put on the chest of the XCAT phantom in the text file [21, 22]. Finally, our system can assemble two large dataset 1) symmetric and 2) asymmetric. By training four intelligent models by these data set, configuration of the models were created. After that configuration models, four intelligent models were used to re-alignm un-couched patient position. These models have been studied including: Artificial Neural Network (ANN) [14], Adaptive Neuro Fuzzy Interference System (ANFIS) [15], Adaptive Neuro Fuzzy Interference System with input selection model based on 98% canonical correlation analysis, and Adaptive Neuro Fuzzy Interference System with input selection model based on 70% principle component analysis [16-19]. Also, using the input selection models that lead to decrease the run-time of the training prediction model, and feasibility update predicative model duration treatment. In the previous methods, since the body detection methods such as opto-electronic or laser spot scanning system were used, the system use of processing data was passive, or these systems typically need extra equipment that increase the cost of treatment. In this study, besides using external marker, the body detection system has been used to fill the gap between un-couched patient positions, and the intelligent models with all of the possible roto-translation data set were proposed to set up and re-alignment un-couched patient position. The intelligent models were also used set-up, realignment, and continuous tracking.

Artificial neural network is a computational tool based on the properties of biological neural systems. Neural network as a non-linear method is robust to realize the complex relationships through imperfect, missing information, or where the outputs of conventional mathematical approaches are with large errors [20]. On the other hand, Adaptive Neuro Fuzzy Interference System (ANFIS) is a computational tool, and by enchasing a Fuzzy Inference System (FIS) in the foundation of an adaptive network, ANFIS is obtained. The ANFIS compound learning procedures with the help of inputs/outputs data pairs and fuzzy if-then rules were enabled to create a correlation between inputs data and outputs data [15]. In fact, the reasoning capabilities of fuzzy inference systems and learning skills of neural networks are combined together in a unique system known as ANFIS [27].

Canonical correlation analysis (CCA) is a way of measuring a linear relationship between two multidimensional variables. The CCA is an optimal way to respect correlations and at the same time find a corresponding correlations. In other words, it finds the two bases in which the correlation matrix between the variables is diagonal and the correlations on the diagonal are maximized. The dimensionality of these new bases is equal to or less than the smallest dimensionality of the two variables [28]. Principal component analysis (PCA) involves a mathematical procedure that transforms a number of possibly correlated variables into a smaller number of uncorrelated variables called principal components. The first principal component accounts for as much of the variability in the data as possible, and each succeeding component accounts for as much of the remaining variability as possible [28].

In order to determine models structure parameters, each correlation models should have been initially learnt by means of training dataset. The training dataset assembled from XCAT phantom which included possible patient position and location of the nine external markers in the one cycle of respiration. After registering data set in the text file, for the developing dataset to real patient, two corrective parameters were calculated which include: 1) the distance between external markers were put on the surface of patients and phantom, and 2) the coefficient of the rotation-torsion parameters in the new position of the each markers. While at pre-treatment step, our models were configured using training dataset, un-couched patient position can be estimated by output models and then patient position re-alignment new position according to principle of the ALARA. Moreover, between models were introduced, models were selected which have high accuracy with less error.

Final analyzed results represent that the ANFIS and ANN model respectively can estimate reasonable patient position with less error. Furthermore, the performances of the accuracy models are different for each patient uniquely in a case by case basis.

2. Materials and Methods

In this study, the XCAT phantom and the AMIDE software package have used to assess displacements during patient geometrical set-up. The XCAT phantom, developed by W.P. Segars, is anthropomorphic phantom. This phantom is commercially spline-based anthropomorphic model to create the Visible Human Dataset which includes: a) 3D human anatomy information, b) patient respiration, and c) heartbeat motions versus time as fourth dimension [21, 22]. The AMIDE software is a Medical Image Data Examiner to process and visual 4DCT data [23]. At first, a set of 4DCT data was generated XCAT phantom in a predefined respiratory cycle with a reasonable breathing amplitude and frequency to mimic real respiratory pattern. The 4DCT data has been generated to give the AMIDE (v.1.15) software and then a fiducial marker mode has been used to adding nine external in the nine region surface of the phantom surface body. Figure 1 was shows the location of each external marker on the surface of the phantom. It should be considered that the external markers can be located on every point onto chest and abdomen region of phantom surface body, while the location of the each markers considered based on the previous study about the optimal location of the external markers and clinically. In this work, for defining the motion parameters of XCAT phantom, we utilized motion information (respiration amplitude and frequency) of some real patients treated with Cyberknife synchrony module [29-31].

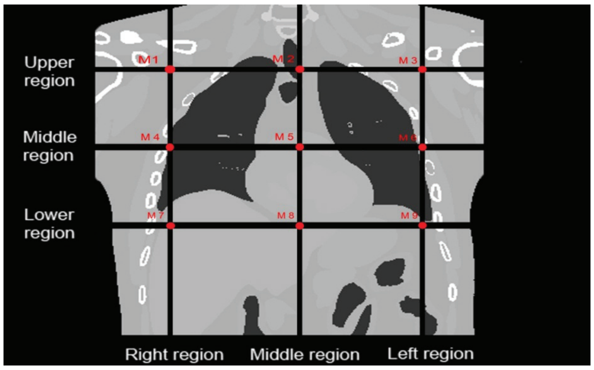

Figure 1. The figure was shown the location of each external marker on the surface of phantom body. (M1) Right upper lobe, (M2) Middle upper lobe, (M3) Left upper lobe, (M4) Right middle lobe, (M5) XIPHOID, (M6) Left middle lobe, (M7) Right down lobe, (M8) Navel upper, (M9) Left down lobe.

In order to investigate patient displacements, all of the possible roto-translation is changed which may have happened during patient setup, by the AMIDE software simulated. Table 1 illustrates a displacement range of patient positioning in both rotation and translation modes. After that simulation, the necessary information about patient geometric set-up was registered in the text file (the 7360 data point was assembled) which includes: a) the location of external markers and b) the patient positioning. Although the dataset have been high quality to model training, the position of coach and external markers were considered in one cycle of respiration (one cycle of respiration was considered five second). Moreover, the dataset assembled for the patient setup simulation at pretreatment setup of radiation treatment can be optimal.

Table 1. Possible patient displacements as rotation and translation.

Rotation[degree]	Torsion[degree]	Translation[mm]
0	0	0
± 3	± 3	± 15
± 6	± 6	± 30
± 9	± 9	± 45

While in the previous method, the data set was assembled by body detection system, nine external markers were put into nine region of the surface of the body to covere body and assembled data. Also all of the markers coincide with a reference point. Since between nine external markers were put onto the surface of body and the reference point is a correlation, the models were able to estimate patient roto-translational displacement, and the couch is then correctly re-positioned by using controllable servomotors according to predictive model output. It is a drawback that the predictive models' accuracy is highly dependent on the quality and quantity of database required for models' configuration. Moreover, for experimental validation of the models, the data set integrated from XCAT phantom was extended to four real patient. For this aim, the fixed point was assumed at near middle loin (T6), and the fixed point was used to fixing the geometry of the phantom and real patient. Also, for the extension dataset from phantom to real patient, two corrected parameters must be calculated. These two corrected parameters include: 1) the distance between external markers put on the surface of patients and phantom and 2) the coefficient of the rotation-torsion parameters in the new position of the each markers. Figure 2 shows the extension dataset from phantom to real patient.

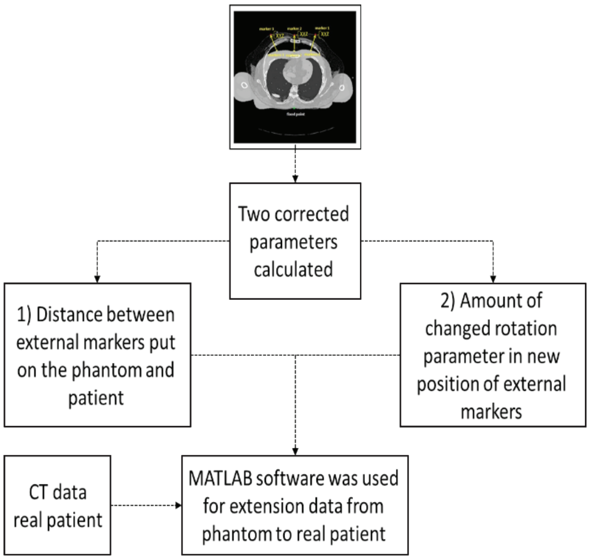

Figure 2. Extension of external motion data from phantom surface (yellow dots as markers) to surface body of real patient (red dots as markers). Green dot represents fixed point. Flowchart was shown typical extension from XCAT phantom to a patient.

The CT data information of four real patients used in this work are shown in Table 2.

Table 2. Patients CT data information.

Patient	Image dimension	Pixel dimension [mm]
Patient one	512*512*169	0.97*0.97*2
Patient two	512*512*170	0.87*0.87*2
Patient three	512*512*187	0.78*0.78*2
Patient four	512*512*161	1.17*1.17*2

Since due to between the pair's dataset which included the nine external markers and position of patient coach is a correlation, the prediction models were proposed. While the configuration of predictive model was based on correlation coefficient or non-deterministic approach between input and output data, a non-linear relationship between pairs dataset made a predictive model that able to predict missing information. Therefore, the un-couched positions of patients can be predicted by only external markers during treatment. In this study, the four intelligent models were used to align un-couched position of patient. In the following page, these models were introduced.

2.1. ANN Prediction Model

In this study, the Artificial Neural Network (ANN) with three-layer type of Perceptron was used. While artificial neural network is a computational tool based on the properties of biological neural systems, neural network as non-linear method is robust to realize the complex relationships through imperfect or missing information [20]. Also the structure of the ANN model was included: six neurons in first layer, seven neurons in second layer, and four neurons in third layer with pure line transfer function. Although the transfer function and number of neurons were determined based on a trial and error method, the ANN model during the train dataset used Levenberg-Marquardt learning algorithm. Moreover, any information about the ANN model is shown in Table 3.

Table 3. The structure of the artificial neural network (ANN) model.

Feature	Type/Count
Type of Network	Feed-Forward Back Propagation
Number of Layers	3
Number of Neurons In Layer 1	6
Number of Neurons In Layer 2	7
Number of Neurons In Layer 3	4
Number of Inputs	27
Number of Outputs	4
Transfer Function of First Layer	Pure Line
Transfer Function of Second Layer	Pure Line
Transfer Function of third Layer	Pure line
Back Propagation Network Training Function	Gradient Descent
Back Propagation Weight/Bias Learning Function	Gradient Descent

2.1.ANFIS Prediction Model

Although the theory of fuzzy logic provides a mathematical strength to capture the non-statistical uncertainties associated with human cognitive processes, a fuzzy neural network or Neuro-fuzzy system is learning a machine that tunes the parameters of a fuzzy system exploiting approximation techniques from neural networks [15]. The ANFIS model used in this study consisted of seven membership functions which parts of the membership function have replaced type-3 ANFIS with two rule. Since for learning the ANFIS model, the Sugeno's type of the fuzzy inference systems was used [15], the type of ANFIS model and number of membership function were determined based on a trial and error method. Also any information about the ANFIS model was shown in Table 4.

Table 4. The structure of the adaptive neuro fuzzy interference system (ANFIS) model.

Parameter	Type
And Method	Product of Elements
OR Method	Probabilistic OR
Implication Method	Product of Elements
Aggregation Method	Sum of Elements
Defuzzification Method	Weighted Average
Input Membership Function	Gaussian

It shoud be noted that both neural networks and adaptive neuro fuzzy inference system work are similar in some ways. They can be applied as a solution to a problem [20]. In this study, the block box of the models was used. Also in pre-treatment step, the 90% and 10% of all the dataset respectively was used for training and evaluation performance of the models.

2.1.3. ANFIS Prediction Model with Two Inputs Selection Models

The ANFIS and ANN models have been used for re-alignment and continuous tracking, but some time the correlation models have needed updating during treatment. In this case, while the models must be renewed, the time of the radiotherapy was increased. In this study for decreasing run-time of the update models, the input selection models based on the correlation coefficient were proposed. The input selection models have been used to select some inputs that have been more efficiently than others. Among the mathematical correlation models, two categories of models that included canonical correlation analysis (CCA) [16] and principal component analysis (PCA) [19] were proposed to selecting inputs. The canonical correlation analysis (CCA) has found a linear combinations between the input and output data that have maximum correlation with each other. While the selected data has done by 98% correlation coefficient between input and output data, these selected data has applied to the ANFIS model for predicting un-couched position of the patient.

The second method used to input selection is the principle component analysis (PCA). Moreover the PCA is a statistical procedure to convert a set of observations correlated variables into a set of uncorrected variables, the equations based on coefficient inputs were returned. While this equation was sorted based on maximum variance, each variable of the equation was an expression of the correlation coefficient between input data with all the outputs data [19]. In this study, the first equation, covered 70% of the variance, the PCA input selection model was used. Since the first equation covered the maximum coefficient variables, it used as an input selection of the ANFIS model to predicate un-couched patient position. Figure 3 shows performances of the models.

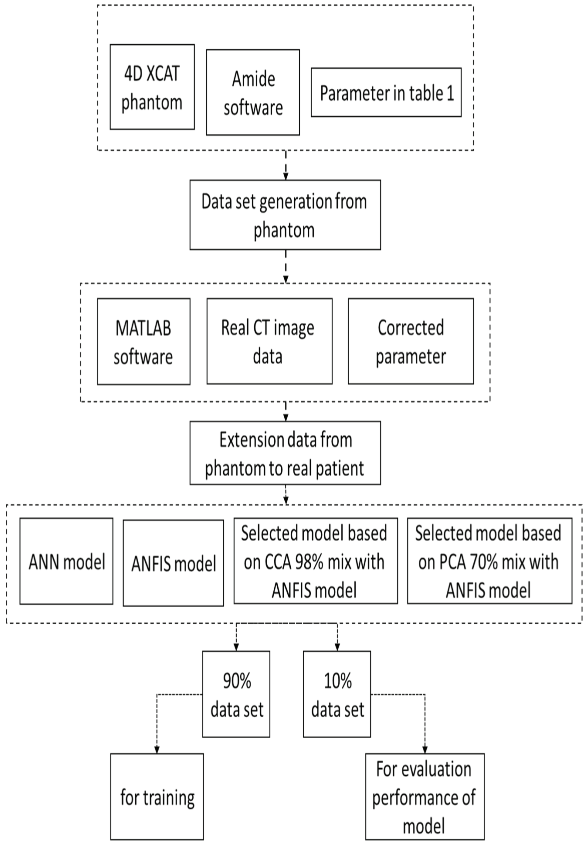

Figure 3. Workflow of model configuration, performance.

3. Results

Root Mean Square Error (RMSE) was expressed to test and evaluate the performance of intelligent models between benchmarked output and model output according the following metric:

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

Where, N is the number of predicted samples, A_i is the i_{th} actual output in the dataset, and P_i is the i_{th} predicted output by the model. Also the Duncan statistical test followed by F-test was used to show that the intelligent models have the same performance accuracy. The F-test is any statistical test which has an F-test distribution under the null hypothesis. It is most often used when comparing statistical models that have been fitted to a data set, in order to identify the model that best fits the population from which the data were sampled. Exact "F-tests" mainly arises when the models have been fitted to the data using least squares [24].

Figure 4 shows RMSE between four intelligent models (ANN model with all markers, ANFIS model with all markers, input selection based on canonical correlation analysis [98% CCA] mixed the ANFIS model and principal component analysis [70% PCA] mixed the ANFIS model). In Figure 4, the results for four real patients to estimat un-couched position of the patient are shown.

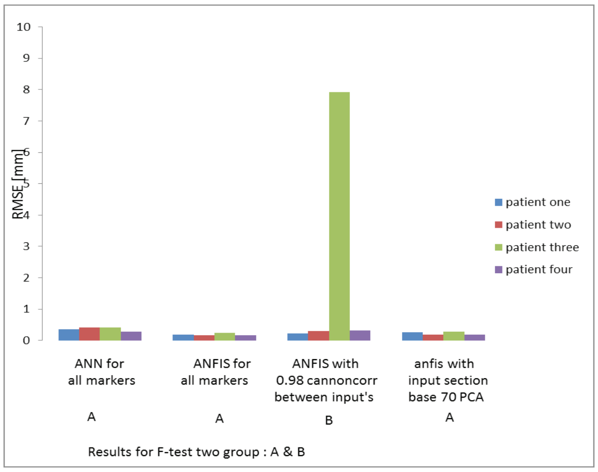

Figure 4. RMSE of four intelligent correlation models at four patients and comparison with together.

Since the RMSEs represent the uncertainty errors of four intelligent models to re-align four cases, the RMSE rang performance accuracy is different for each patient uniquely in a case by case basis. Table 5 shows an average of RMSE between four intelligent models output and our patient group over a course of radiation treatment of each case.

4. Discussion

In this study, the patient geometrical set-up was comprehensively simulated by using the 4D XCAT anthropomorphic phantom. This phantom used NURBS-based Cardiac-Torso methods with Spline-based model to access 4D modeling of breathing and heartbeat motions. This validated phantom has been widely utilized at several research activities ranging from nuclear medicine to radiation treatment of moving tumors [32-34]. Since then, this phantom simulating different dynamic organs with detailed information and also breathing motion issues are not exactly the same as real patient body due to phantom simplification, some concerns may raise during phantom performance. Moreover, the AMIDE software, the medical dada examination, was also utilized to capture surface body motion information by means of external markers located at chest and motion extraction of patient couch pre-defined as reference point. All of the possible roto-translation displacements that may have happened at initial patient position before re-aligning by operator were taken into account. The patient displacements were proposed based on Table 1, then gathered data were saved in the text files. Although an experimental validation of the models is required, the fixed point is assumed at near middle loin (T6) to extension data set from phantom to real patient. Also four real patients are considered to further investigation and testing real clinically application.

Table 5. Average RMSE of un-couched four intelligent models over patients group.

Patient number	RMSE [mm] ANN all markers	RMSE [mm] ANFIS all markers	RMSE [mm] ANFIS model 0.98 CCA	RMSE[mm] ANFIS model 0.70 PCA
Patient 1	0.35875	0.1926	0.2307	0.2737
Patient 2	0.41435	0.1716	0.29705	0.1872
Patient 3	0.41095	0.25245	7.9174	0.2807
Patient 4	0.29185	0.17535	0.3242	0.1911

By determining patient displacement, the patient set-up can be done at each fraction during a course of radiation treatment. In the previous study of the patient setup, while a correlation model has been utilized to estimate patient displacement and monitoring motion body surface was used to extract the position of the patient during treatment, a predictive model based on training data set has been used for re-alignment and patient setup. In this study, the four models based on a non-deterministic correlation model were proposed for re-alignment and patient setup. In fact, our proposed models were used to assess the process of simulation procedure in patient geometrical set-up. Four intelligent models have been proved as commercially available method to finding out complex relationship among high variable database rather than other conventional mathematical methods. It should be considered that correlation models are only a part of patient setup process, all of the possible roto-translation change that may have happened during patient setup was simulated with 7360 separate data point using position information of three external markers at each data point. When the patient displacements were predicted by our models, a corrective process happened by patient couch motion to re-align tumor volume against therapeutic irradiation beam.

For estimating un-couch patient position, the correlation model must be learned and configured by training database, and the models are ready to estimate un-couch patient position. The paired database are synchronized before using at training step. Also the training database include: 1) external markers motion located at chest representing body surface motion and 2) patient treatment couch position.

While in Figure 4, the ANFIS model with all markers can predict un-couched position of the patient, Table 5 shows the same results for four patients. This indicated that the ANFIS model is able to re-align patient position with less error. It should be noted that the RMSE rang performance accuracy is different for each patient uniquely in a case by case basis. Patient setup depends on rotation (roll, pitch and tilt) and translation (shift on x and y directions) parameters. Each of them has a unique effect on patient alignment. In this study, the role of each parameter was taken into account. Since external markers motion data required as input for patient displacement estimation may be captured at any desired time during respiratory cycle, the amount of this data may have an effect on intelligent models performance. To assess this issue, external markers data were captured at five breathing phases between exhalation-inhalation peaks and patient setup was done separately using models. Final results show that the best patient alignment happened at the exhalation phase where all organs are almost fixed with least motions.

One concerning issue considered in this work was configuring an optimum models with less uncertainty error in displacement prediction. Model configuration highly depends on the quality and quantity of training dataset as illustrated before. Both of these features were considered and the results shown in Figure 4 and Table 5 which represent that the best performance is achieved when training dataset is perfect. As an example, average errors reduction for all patients was improved from 5.26 mm to less than 1.5 mm. Also, for statistical analysis, the F-test was proposed. The F-test is a statistical test which has been the test distribution under the null hypothesis. It is most often used when comparing statistical models which need the models fitted to a data set, and in order to identify the model that best fits the population from which the data were sampled. By using F-test, the four intelligent models were divided into two groups A & B. While the A group contain ANN model with all markers, ANFIS model with all markers, and ANFIS model with 70% PCA, the B group only contains ANFIS model with 98% CCA. Also between two groups, a significant difference exists which indicated that the A group of models has more accuracy than the B group. Moreover, in group A, the ANFIS model with all markers with 0.198 mm error is the best model.

In this study for patient setup, a comprehensive simulation study was performed on flexible phantom (XCAT phantom). The 4DCT image of the XCAT phantom was combined with AMIDE software to develop new data set that includes all possible positions of the patient. For experimental validation, the 4DCT data of phantom were developed to four real patients. Then, the non-deterministic correlation models were also proposed to estimate patient displacement, and all of the models by using the database obtained by phantom at the pre-treatment step were trained. Moreover, the effect of different parameters on models performance in error reduction were done ranging from training data preparation for models construction to the type and number of models input for patient misalignment estimation. After analyzing the results, the ANFIS and ANN models are able to correctly align tumor volume against irradiation beam with less uncertainty error. Future studies may be needed assessing to find an optimal location of the external markers assessing intelligent models abilities in combination with image registration techniques at patient setup improvement.

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