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Respiratory Motion Prediction for Tumor Following Radiotherapy by using Time-variant Seasonal Autoregressive Techniques

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Abstract— **We develop a new prediction method of respiratory motion for accurate dynamic radiotherapy, called tumor following radiotherapy. The method is based on a time-variant seasonal autoregressive (TVSAR) model and extended to further capture time-variant and complex nature of various respiratory patterns. The extended TVSAR can represent not only the conventional quasi-periodical nature, but also the residual components, which cannot be expressed by the quasi-periodical model. Then, the residuals are adaptively predicted by using another autoregressive model. The proposed method was tested on** 105 **clinical data sets of tumor motion. The average errors were** 1.28 ± 0.87 **mm and** 1.75 ± 1.13 **mm for** 0.5 **s and** 1.0 **s ahead prediction, respectively. The results demonstrate that the proposed method can outperform the state-of-the-art prediction methods.**

I. Introduction

In radiotherapy, continuous irradiation only to the target volume can achieve high therapeutic effects and avoid the adverse effects, resulting in a favorable outcome [1]. However, any static positioning to the target, even it is highly accurate, can be affected badly by intra-fractional internal organ motions, such as respiratory motion of lung.

Real-time image-guided radiation therapy (IGRT) can achieve accurate and continuous irradiation to a moving target and requires at least the following two techniques:

- Real-time measurement of the target tumor motion
- Real-time beam positioning to follow the motion

The techniques have been equipped to most modern radiotherapy machines, such as kV X-ray fluoroscopic imaging system for measurement and multi-leaf collimator and/or moving couch for beam positioning, respectively. However, in those techniques currently available, there is a delay up to several hundred milliseconds between motion observation and beam positioning [2]. The delay of several hundred milliseconds can naturally distance the center of the target volume from the isocenter of the irradiation.

In this case, tumor motion prediction can be useful for compensating the delay and thus several prediction methods for tumor motion have been proposed [3]. Nevertheless, any prediction method sufficient for clinical use has not been developed yet due to the complex and time-varying nature involved in respiratory motion.

Periodicity found in respiratory motion is useful to predict the target motion because it ensures that the past pattern observed will repeatedly arise at the periods ahead future in general. A problem here is that the respiratory motion is not purely periodical, rather quasi-periodical in which intervals between each respiratory cycles are not constant, but time-variant. Therefore, the pure periodic model is not sufficient for accurate prediction of the respiratory motion. To adapt to the quasi-periodical nature can thus be a main challenge in the respiratory motion prediction.

A time-variant seasonal autoregressive (TVSAR) model-based method is one of the state-of-the-art methods for such complex lung tumor motion prediction [4]. The TVSAR was developed to express the quasi-periodical nature by adapting to the fluctuated periodicity and can predict a regular breathing position at most 1 s ahead future within 1 mm accuracy on average. On the other hand, the TVSAR does not take into account other variations involved in respiratory motion such as baseline shift, amplitude change, and so on [5].

In this paper, the TVSAR model-based method is extended to adapt to such various respiratory motions by using a new residual component model that is unable to be represented by the conventional TVSAR model. The method was evaluated by using several clinical data sets of lung tumor motion.

II. Respiratory motion of lung tumor

Lung tumor moves with patients' breathing and the motion has complex nonlinear and time-varying characteristics. As an example, Fig. 1 shows a three-dimensional respiratory motion of lung tumor. The example is taken from a clinical data set obtained at George town University Hospital by using Cyberknife Synchrony system [5]. The sampling frequency was 26 Hz approximately.

In general, a lung tumor motion involves a periodical component because breathing is composed of repetition of inspiration and expiration. Fig. 2 provides power spectrum density of the superior-inferior motion shown in the top of Fig. 1. The dominant frequency corresponding to the respiratory cycle can be found at 0.30 Hz approximately in this example. This means that the tumor motion has a periodical component induced by the 3.3 s respiratory cycle in average. Recalling that the breathing period is time-variant, short-time Fourier transform (STFT), instead of the

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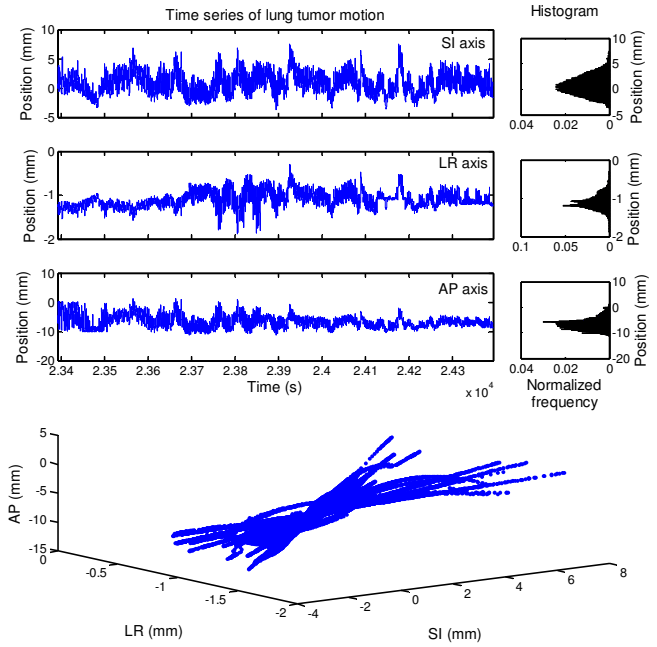

Fig. 1. An example of complex lung tumor motion [5] composed of time-variant periodical motion with amplitude change, base line shift, etc. SI: superior-inferior axis, LR: left-right axis, and AP: antero-posterior axis.

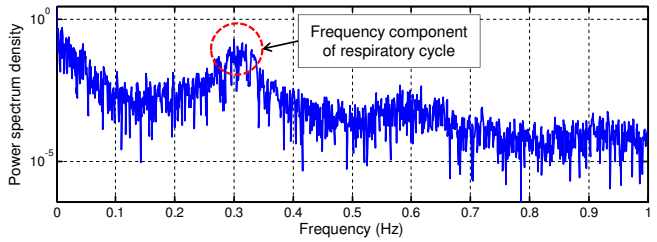

Fig. 2. Power spectrum of SI tumor motion shown in Fig. 1. The dominant frequency of the respiratory cycle is 0.3 Hz approximately.

normal long-time Fourier transform, was performed on the superior-inferior motion. The time-variation of the frequency spectrum is shown in Fig. 3. The dominant frequency at each time is depicted as a black dashed line. The line indicates that the respiratory cycle fluctuates with time. The range of the fluctuation was from 0.29 to 0.40 Hz in this example.

III. Methods

A. Prediction methods

Let $\{y(t)\} = \{y(1), y(2), \ldots, y(t), \ldots, y(T)\}$ be one-dimensional target time series of length T. Here $y(t)$ is a coordinate of lung tumor motion at discrete time t.

1) Seasonal autoregressive (SAR) model: Let us first define the SAR model that is fundamental to the TVSAR model and its extension proposed in this paper.

The N-th SAR model is given as

$$y(t) = \epsilon(t) + \sum_{n=1}^{N} \Phi_n \cdot y(t - n \cdot s) \qquad (1)$$

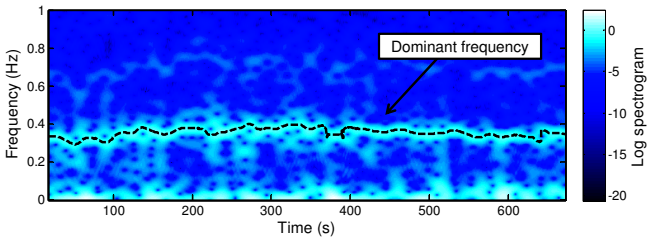

Fig. 3. Time-frequency analysis of SI motion shown in Fig. 1 (top). The black dashed line depicts the dominant frequency of the respiratory cycle at each time.

where $\epsilon(t) \sim \mathcal{N}(0, \sigma^2)$ is a Gaussian noise, $\Phi_n, n = 1, 2, \ldots, N$ are SAR coefficients, and s is the period of the target time series $\{y(t)\}$. Then, the SAR model-based equation for h-sample ahead prediction can be given by substituting $t + h$ for t:

$$\hat{y}(t + h|t) = \sum_{n=1}^{N} \hat{\Phi}_n \cdot y(t + h - n \cdot s) \qquad (2)$$

Here $\hat{y}(t+h|t)$ denotes h-sample ahead prediction of $y(t+h)$ predicted at time t and $\hat{\Phi}_n$ is an estimate of Φ_n.

The general SAR model can predict periodical time series with a constant period s, but the SAR model does not take into account the time-variation of the periodical nature involved in lung tumor motion $\{y(t)\}$. This limitation often affects badly on the prediction accuracy.

2) TVSAR model: To overcome the limitation of the general SAR model, TVSAR introduced a time-varying and irregular interval, instead of a constant period s.

The prediction equation of the N-th TVSAR is given as

$$\hat{y}(t + h|t) = \sum_{n=1}^{N} \hat{\Phi}_n \cdot y(t + h - \hat{r}_n(t + h|t)). \qquad (3)$$

where $r_n(t|t) > 0$ are called reference intervals for indicating the past observed values at a corresponding phase, ideally the same phase, to the current value $y(t)$. $\hat{r}_n(t+h|t) > 0$ are intervals predicted at time t for indicating the corresponding phase to the future value $y(t + h)$. For simplicity, the order and coefficients below are fixed as $N = 2$ and $\hat{\Phi}_n = 1/N$, respectively.

The reference intervals $r_n(t|t)$ are important for adapting the model to the fluctuation of the target periodical nature, but unknown in general. A correlation analysis based method is then used to estimate such intervals that can indicate the corresponding values.

The estimation procedure is as follows.

1) At time t, calculate a correlation function of lag $k = 0, 1, 2, \ldots$ given by

$$C(t, k) = \frac{1}{w} \sum_{j=0}^{w-1} \frac{y(t - j) - \mu_t}{\sigma_t} \frac{y(t - k - j) - \mu_{t-k}}{\sigma_{t-k}} \qquad (4)$$

where μ_t and σ_t are the sample mean and variance of a subset time series with length w described as $[y(t - w + 1), y(t - w + 2), \ldots, y(t)]$.

2) The n-th reference interval is estimated as the lag k of the n-th local maximum of the correlation function $C(t,k)$ as

$$\hat{r}_n(t|t) = \arg\max_k C(t,k) \tag{5}$$

where search range is set as $r_n(t-1|t-1) - w/2 < k < r_n(t-1|t-1) + w/2$ for n.

3) Update the subset length by $w = \lfloor a \cdot \hat{r}_1(t|t) + 0.5 \rfloor$. Here a is a coefficient to adapt the length based on $\hat{r}_1(t|t)$ and was empirically set as 0.5 to use a subset of an approximate half length of the latest wave.

The initial reference intervals used for the estimation procedure were given as

$$\hat{r}_n(t_s|t_s) = n \times \hat{s}. \tag{6}$$

Here $t_s > w$ is a start time for prediction and $\hat{s}$ is a period estimated by using the values initially available, i.e., $\{y(t)\}, 1 \le t \le t_s$. In this study, $\hat{s}$ was given as the interval between lag 0 and the first local maximum of the autocorrelation function of $\{y(t)\}, 1 \le t \le t_s$. The zero-order hold technique was used to predict reference intervals at h-sample future required in the prediction equation (3).

$$\hat{r}_n(t+h|t) = \hat{r}_n(t|t). \tag{7}$$

3) TVSAR with adaptive residual prediction (Proposed): The TVSAR model-based method can predict the quasi-periodical component in tumor motion, but does not take into account the other components such as the baseline shift and amplitude change. This is a limitation of the conventional TVSAR prediction for such tumor motion. To improve the prediction accuracy, the residual error of the TVSAR prediction is considered in the proposed method.

The TVSAR prediction can be separated into the predicted N-quasi periodical components as follows.

$$\hat{y}_n(t+h|t) = y(t+h-\hat{r}_n(t+h|t)), n = 1,2,\ldots,N \tag{8}$$

where $\hat{y}_n(t+h|t)$ are prediction values of the quasi-periodical components.

If the target motion involves the other, not quasi-periodical, components, there still remains N-seasonal residuals between the actual values $y(t+h)$ and the predicted quasi components $\hat{y}_n(t+h|t)$ at each time t.

The N-seasonal residuals can be written by

$$z_n(t+h|t) = \frac{1}{\left(\sum_{n=1}^{N} \Phi_n\right)} y(t+h) - \hat{y}_n(t+h|t). \tag{9}$$

Note that the residuals for $h > 0$ are unknown future values, but the past residuals can be obtained for $h \le 0$ at each time t. If we can build an appropriate model with sufficient accuracy for residuals by using the past ones, then it is expected that the prediction accuracy of the TVSAR method can be improved by predicting those residuals using the model.

To predict the residuals, we assumed that each residual can be expressed by the M_n-th autoregressive model. Therefore, the residuals are modeled by using the residuals obtained for $h \ge 0$. The residual model is given as

$$z_n(t+h|t) = \epsilon_n(t) + \sum_{m=1}^{M_n} \phi_{m,n} z_n(t+h-m|t) \tag{10}$$

where $\phi_{m,n}, m = 1,2,\ldots,M_n$ are the AR coefficients.

To build the residual models, the coefficients $\phi_{m,n}$ are adaptively estimated by using the Burg's algorithm [6] and the order M_n is determined based on Akaike information criterion [7] at each time t. Data length for building the residual models is given as $L = \lfloor b \cdot \hat{r}_1(t|t) + 0.5 \rfloor$.Here b is a coefficient and was empirically set as 1.5 in this study.

Then, once the order $\hat{M}_n$ and the coefficients $\hat{\phi}_{m,n}$ are estimated, the N residuals can be iteratively predicted. The prediction equation of the residual is as follows.

$$\hat{z}_n(t+h|t) = \sum_{m=1}^{\hat{M}_n} \hat{\phi}_{m,n} \hat{z}_n(t+h-m|t). \tag{11}$$

The residual prediction can improve the accuracy and this is a core contribution of the proposed method compared to the conventional TVSAR.

The final form of the proposed prediction equation is given as follows.

$$\hat{y}(t+h|t) = \sum_{n=1}^{N} \hat{\Phi}_n \left\{ \hat{z}_n(t+h|t) + \hat{y}_n(t+h|t) \right\} \tag{12}$$

It may be worth to mention that the idea to model the residual component as an AR process is not new and has been used in a general SAR model [6], but the residual modeling in the proposed TVSAR is different from the SAR model because only one AR model is used in the SAR, while specific AR models are individually built for corresponding seasonal components in the proposed model. In this sense, the proposed TVSAR is more general than the SAR.

4) Other prediction methods for comparison: For prediction benchmark, zero-order hold (ZOH) and first-order hold (FOH) were tested. Prediction equations of ZOH and FOH are given as follows.

- ZOH: $\hat{y}(t+h|t) = y(t)$
- FOH: $\hat{y}(t+h|t) = y(t) + (y(t) - y(t-1))h$

Note that ZOH corresponds to the case that the delay in the radiotherapy system is not compensated.

B. Data sets

The lung tumor motion data sets of 105 treatment fractions for 30 patients were used for the performance evaluation. An example of the motion has been shown in Fig. 1. More details of the data sets are described in Suh et al. [5].

C. Prediction performance index

For evaluating the prediction performance, we have adopted the root mean square error (RMSE) given as

$$\text{RMSE}(h) = \sqrt{\frac{1}{T} \sum_{t=1}^{T} e(t+h|t)^2} \tag{13}$$

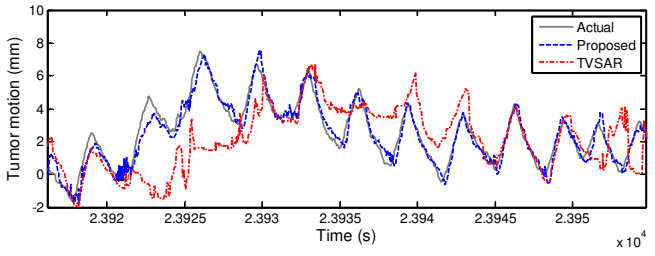

Fig. 4. An prediction example of tumor motion for 7 samples forward future (approximately 0.27 s ahead).

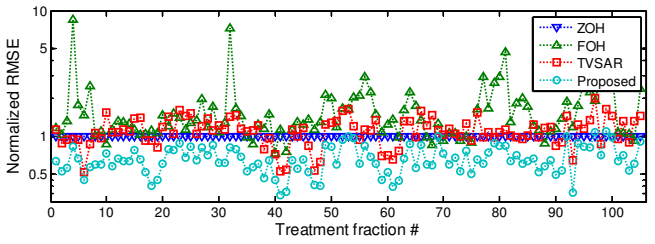

Fig. 5. RMSEs normalized by using each of RMSE values of ZOH for 105 data sets at prediction horizon 0.5 s.

Here $e(t+h|t)$ is the Euclidean distance between the three-dimensional actual and predicted values.

IV. EXPERIMENTAL RESULTS

Fig. 4 shows an example of 7 samples (approximately 0.27 s) forward predictions by the proposed and conventional TVSARs. As is clear from this figure, the proposed method can trace the actual values accurately. On the other hand, due to the lack of the other components except for quasi-periodical one, the conventional prediction is not fitted to the actuals at the regions involving a trend and/or amplitude variation. The example suggests an advantage of the proposed residual prediction as expected.

Fig. 5 shows RMSEs normalized by RMSE values of ZOH for 105 data sets at 13 samples (0.5 s) ahead. According to this figure, normalized RMSEs of the proposed method are almost less than 1 and other normalized RMSEs. Thus the proposed method is superior to the other methods and the superiority is robust to data variation.

Fig. 6 shows the RMSE, averaged over all the 105 data sets, as a function of prediction horizon. As is clear from the figure, the least averaged RMSE is achieved by the proposed method for all the prediction horizons tested. The RMSEs of the proposed method for 0.5 s and 1.0 s ahead predictions were 1.28 ± 0.87 mm and 1.75 ± 1.13 mm, respectively. Only the proposed method achieved the RMSE less than 2 mm.

On the other hand, TVSAR showed RMSE of 2.13 ± 1.49 mm for 0.5 s prediction horizon. This is larger than RMSE of ZOH at the same horizon. The TVSAR prediction is thus not suitable for this data sets at least for short prediction horizons. The difference between the performances of the proposed and conventional TVSARs indicates that the proposed method is superior to the conventional one. Also, the higher performance for many clinical data suggests that the proposed method can be used to predict a wide variety of respiratory motions.

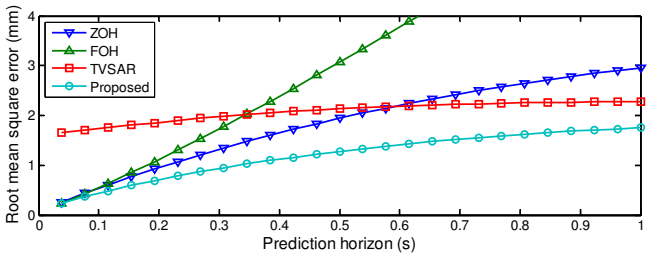

Fig. 6. The average of root mean squared error (RMSE) as a function of prediction horizon for 105 data sets.

V. CONCLUSIONS

In this paper, a new TVSAR model with adaptive residual prediction was proposed for respiratory tumor motion prediction. The performance evaluation using 105 clinical data sets has demonstrated that the proposed method can achieve the best prediction accuracy among the methods tested, including the conventional TVSAR. Since the conventional TVSAR had shown the state-of-the-art performance for several clinical data sets, we may thus conclude that the proposed method can be superior to the state-of-the-art prediction and help the continuous and accurate irradiation to the moving tumor.

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