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CORRELATION OF EXTERNAL MARKERS AND FUNCTIONAL TARGETS FOR RESPIRATION COMPENSATION IN RADIOTHERAPY

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***Abstract*:** The goal of radiation therapy is to give as intensive treatment dose as possible to the exact location of a tumor (target) and at the same time minimising a potential harm to the healthy tissues. Advances in the computer-based control have enabled planning and providing accurate treatments. However, current technology does not allow compensating for respiratory motion in the lungs and abdomen area. As the target moves due to respiratory motion, healthy tissues are affected. This paper presents a work-in-progress, which aims at developing algorithmic techniques for estimating correlation of external markers and functional targets. These techniques will enable tracking tumours during radiotherapy sessions an dynamically adjusting for respiratory movements.

***Keywords*:** respiratory radiotherapy, respiratory tumor motion, correlation, regression

1. Introduction

The goal of the radiation therapy is to give as much dose as possible to the target volume of tissue and avoid giving any dose to a normal tissue. Advances of the computer-based control allow planning and performing accurate plans and treatments [1, 2, 3] however motion compensation during treatment remains a considerable problem. Different techniques to cope with such problem are analyzed in [4]. General solution can be defined as follows [5]: determine position of tumor, predict its motion to overcome time delays, reposition the beam, adapt dosimetry.

An important step in respiratory motion compensation is predicting a functional target position from an internal marker, because usually, during radiotherapy it is not possible to track tumor in real-time. There have been several attempts to analyze internal/external correlation [6,7,8,9], where Pearson correlation and Gaussian filters, Fourier transformation and cross-correlation, linear interpolation and partial-least squares (PLS) are used. The results are promising, all techniques produce similar results, but there is a lot of space for improvement as well, because motion includes both slow, quasi-static change due to circulation, muscle fatigue and faster periodic change due to respiration, as well, as stochastic component [5].

This paper described our work-in-progress on on analysis of correlation between a functional target and external markers, obtained using MRT. The signals are represented as 2D time series in the sagittal and axial planes. Our goal is to develop algorithmic techniques for a practical application task - dynamic shifting of a patient using a robotic-couch (e.g. Elekta HexaPOD evo RT). For predicting the position of a functional target we use the he ordinary least squares linear regression that takes the signals from external markers as inputs.

A linear regression model is preferred, since it is simple, fast and produces easily interpretable results, which is essential in medical applications.

The remainder of the paper is organized as follows. In section 2 data collection, problem formulation and used methods are presented. Section 3 discusses experimental results. In section 3 concluding remarks and future plans are provided.

2. Methods and Materials

3.1. Respiratory Motion Data Collection

Respiratory motion data was collected with MRT Achieva XR (Philips Medical Systems) (with a 16-channel SENSE XR Torso coil). Data of 8 different persons was collected. Three external markers placed in different positions were used. Records were produced in DICOM. Time series from the records were extracted using in-house tools, where several (6-10) points-of-interest (POI) instead of tumors were tracked. Duration of the records varies from 300 to 500 frames, i.e. 150 - 400 sec. Overall, 87 signal-pairs were obtained. Some signals are useless, because either target or marker do not move (6).

In Table 1 and Fig. 1 summary on signals is provided.

Table 1 Signals summary (we ignore immobile objects)

Direction	Min (non 0)	Max	SD
P0 *x*	25.9	30	0.97
P0 *y*	74.8	75.5	0.18
P1 *x*	23.7	24.7	0.24
P1 *y*	48.4	48.6	0.05
P2 *x*	23.8	24.8	0.22
P2 *y*	20.9	21.4	0.11
P3 *x*	45.7	50.7	1.21
P3 *y*	56.8	61.8	1.42
P4 *x*	35.1	37.8	0.62
P4 *y*	34.3	40.4	1.53
P5 *x*	29.2	29.8	0.12
P5 *y*	27.3	31.5	1.16
P6 *x*	41.8	46.8	0.88
P6 *y*	29.3	34	1.5
P7 *x*	44.5	46	0.33
P7 *y*	36.5	43.3	1.7
P8 *x*	50.6	53.8	0.74
P8 *y*	29.9	38	2.02
P9 *x*	42.5	46.2	0.64
P9 *y*	24.9	30.5	1.45

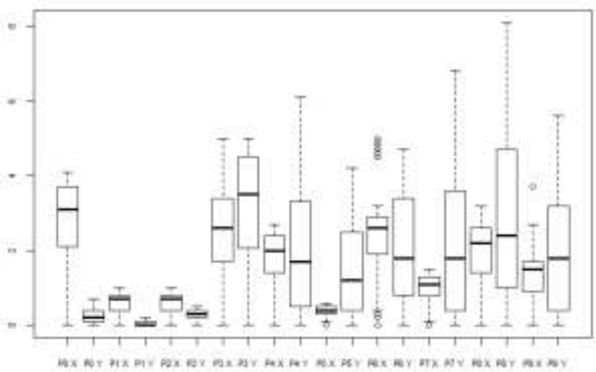

Fig. 1 Signals boxplot

Collected signals analysis shows that maximum range of targets is higher than of external markers, i.e. functional targets move more. Moreover, markers move more in x (anterior-posterior) direction and targets move more in y (superior inferior) direction. In this case lateral direction was not observed. When anterior-posterior and lateral directions were observed (superior inferior direction was ignored) targets and markers move more in anterior posterior direction.

Observed amplitudes are lower, than presented in literature or other experiments. It could be due to the fact, that during MRT a coil is placed on the abdomen/breast of the patient, in such a way partially immobilizing her.

Each signal was transformed using formulas:

$$\tilde{x}_{ij} = x_{ij} - \min(x_{i1}, x_{i2}, \ldots, x_{in}) \quad (1)$$

$$\tilde{y}_{ij} = y_{ij} - \min(y_{i1}, y_{i2}, \ldots, y_{in}) \quad (2)$$

where $P_i = \{p_{i1}, p_{i2}, \ldots, p_{in}\}$ is a signal of n observations and $p_{ij} = \{x_{ij}, y_{ij}\}$. After transformation signal minimu P_i is equal to zero and maximum is equal to $\max(P_i) - \min(P_i)$.

3.2. Problem Formulation

Let us have n observation of two signals $M = \{m_1, m_2, \ldots, m_n\}$ and $T = \{t_1, t_2, \ldots, t_n\}$, where $m_i = (x_i^m, y_i^m)$ is a vector indicating the position of an external marker at time i and $t_i = (x_i^t, y_i^t)$ is a vector indicating the position of the target at time i. Our goal is to find a functional relationship $T = \mathrm{F}(M)$ between the signals, separately for each component:

$$x^t = \mathrm{F}_1(x^m), \quad (3)$$

$$y^t = \mathrm{F}_2(y^m), \quad (4)$$

Functions $\mathrm{F}_1, \mathrm{F}_2$ by agreement has the same form of the formula, but different parameters values.

3.3. Loss Function

For evaluating the performance of a model we suggest using the mean absolute error (MAE), i.e. the average distance from the predicted position to the true position of the tumor. Let us have a testing dataset of n records. $t_i = (x_i^t, y_i^t)$ is the true position of the tumor at time i and $\hat{t}_i = (\hat{x}_i^t, \hat{y}_i^t)$ is the corresponding prediction, then mean absolute error is defined as follows

$$MAE = \frac{\sum_{i=1}^{n} \sqrt{(\hat{x}_i^t - x_i^t)^2 + (\hat{y}_i^t - y_i^t)^2}}{n}. \quad (5)$$

3.3. Correlation

We start with correlation analysis of external markers and functional targets, using Pearson correlation coefficient. Correlation coefficient between variables $x = \{x_1, x_2, \ldots, x_n\}$ and $y = \{y_1, y_2, \ldots, y_n\}$ is calculated using formula:

$$r_{xy} = \frac{\sum_{i=1}^{n} (x_i - \bar{x}) \sum_{i=1}^{n} (y_i - \bar{y})}{n \sigma_x \sigma_y}, \quad (6)$$

where $\bar{x}, \bar{y}$ are averages of x and y, σ_x, σ_y are standard deviations of x and y, n - sample size.

Coefficient values are between -1 and 1. The closer the absolute value of r_{xy} gets to 1, the stronger linear relationship between the variables is, see Table 2.

Table 2 Correlation results interpretation

r_{xy}	Strength of relationship
-1 to -0.5 or 0.5 to 1	Strong
-0.5 to -0.3 or 0.3 to 0.5	Medium
-0.3 to -0.1	Weak
-0.1 to 0.1	None or very weak

3.3. Linear regression

Linear regression assumes, that two two variables are systematically linked by a linear relationship. The general form of a linear regression is:

$$y = \beta_0 + \beta_1 x + \varepsilon, \tag{7}$$

where y is predicted variable, β_0, β_1 are model parameters and ε is random error. Usually, least squares are used to estimate the values of β_0 and β_1.

4. Experimental Results

3.3. Correlation

We calculated Pearson correlation coeficient for each signals pair, see Table 3 for some results.

Table 3 Correlation matrix

	P0 x	P0 y	P1 x	P1 y	P2 x	P2 y
P3 x	0.05	-0.06	0.07	-0.07	0.06	0.03
P3 y	-0.33	0.37	-0.33	0.26	-0.3	-0.24
P4 x	0.98	-0.91	0.97	-0.82	0.93	0.89
P4 y	-0.99	0.93	-0.98	0.85	-0.94	-0.89
P5 x	0.77	-0.64	0.79	-0.65	0.9	0.85
P5 y	-0.97	0.88	-0.95	0.82	-0.96	-0.91
P6 x	0.41	-0.4	0.42	-0.4	0.41	0.39
P6 y	-0.72	0.72	-0.74	0.64	-0.73	-0.66
P7 x	0.92	-0.91	0.92	-0.79	0.84	0.79
P7 y	-0.99	0.93	-0.97	0.84	-0.93	-0.88
P8 x	0.97	-0.91	0.96	-0.82	0.91	0.86
P8 y	-0.97	0.91	-0.96	0.83	-0.92	-0.88
P9 x	-0.09	0.04	-0.05	0.03	-0.01	-0.06
P9 y	-0.79	0.78	-0.8	0.7	-0.79	-0.73

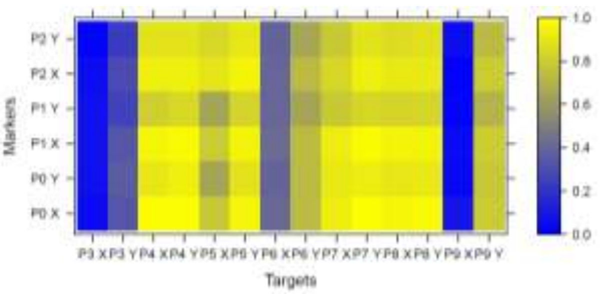

Fig. 2 Example of correlation heatmap

We use heatmaps where blue color indicates weak correlation and yellow - strong (see Fig. 2), to simplify correlation results analysis.

Correlation analysis shows, that most of the signals are linked by strong or medium relationships. The strongest correlation was observed between target P4 and marker P0. The weakest relationship was found between targets P3, P9 and all external markers due to the failed detection of P3 and P9. Despite the fact that correlation between target P6 and all external markers is quite strong this target detection was also failed. Overall data correlation varies from 0.001 to 0.991 with average equal to 0.492.

3.3. Prediction of Functional Target Position

Based on the correlation analysis results linear model was chosen. Model training/test set was split 50:50. We analyzed internal signals motion dependence on each external signal motion. Each functional target coordinate was predicted separately based on the assumption that position of each coordinate of the internal point only depends on the position of the corresponding coordinate of the external marker.

Analysis of results shows that in cases where x is lateral direction and y is anterior posterior, beter results were obtained by predicting y (anterior posterior) direction. When lateral direction was ignored, prediction of anterior posterior direction was more successful than superior inferior. It leads to the conclusion that better prediction results are obtained using markers with a greater range of movement.

Prediction accuracy also depends on the external marker position. Analyzing anterior posterior and lateral directions greater accuracy was obtained using external markers from position P1, and better results from anterior posterior and superior inferior were obtaibed using external markers from position P0.

Part of the results are provided in Table 1.

Table 4 Prediction Error for Selected Models

Model	MAE, mm	p-value		R^2	
		x	y	x	y
P4~P0	0.55	0	0	0.96	0.89
P4~P1	0.79	0	0	0.93	0.74
P4~P2	0.89	0	0	0.87	0.81
P5~P0	0.51	0	0	0.53	0.81
P5~P1	0.61	0	0	0.55	0.7
P5~P2	0.61	0	0.03	0.72	0.86
P7~P0	0.62	0	0	0.82	0.88
P7~P1	0.87	0	0	0.83	0.72
P7~P2	0.95	0	0	0.66	0.8
P8~P0	0.85	0.13	0	0.94	0.85
P8~P1	1.04	0.03	0	0.91	0.68
P8~P2	1.1	0	0	0.85	0.77
Overall average (all models)	1.1				
Minimal error	3.4				
Maximal error	0.26				

Results show, that the range of error is ~0.5 mm. The minimum error is observed for P5~P0 relation, see Fig. 3 and Fig. 4. It differs from the expected results based on correlation analysis: it was expected that best results will be in case of P4~P0, see Fig. 5 and Fig. 6.

Difference between the expected and actual results was observed due to the nature of evaluation criterion: MAE is an average distance from the predicted position to the true position of the internal point, i.e. prediction accuracy depends on the signal motion range. Results in Table 1 show that regression models are characterized by relatively high values of the coefficient of determination. However, p-values of Durbin-Watson test indicate that we are faced with the problem of autocorrelation, therefore of R^2 may be overrated.

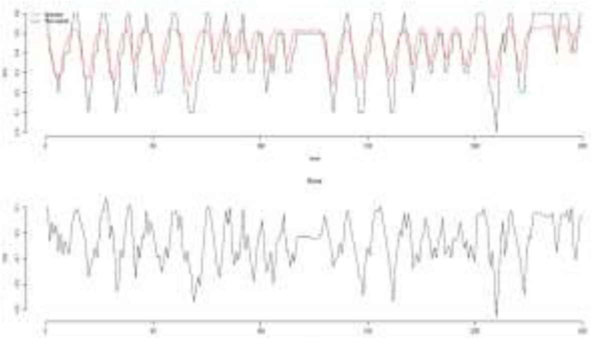

Fig. 3 Forecast and error term of *x* from relation P5~P0

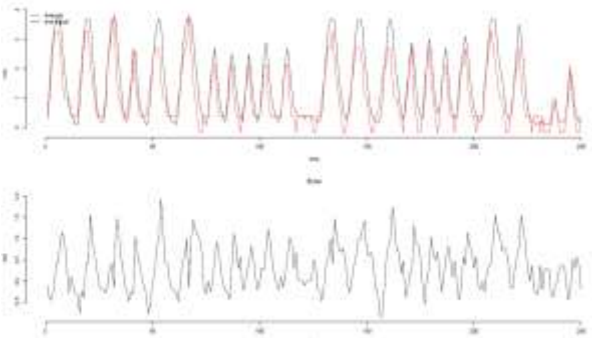

Fig. 4 Forecast and error term of *y* from relation P5~P0

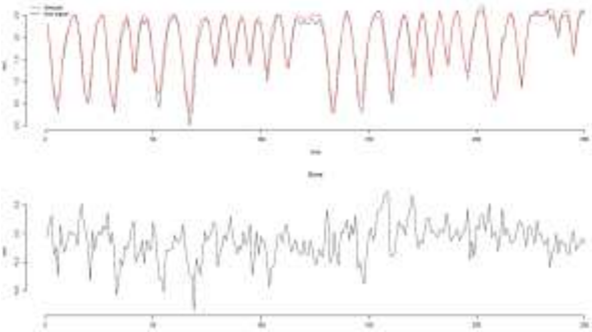

Fig. 5 Forecast and error term of *x* from releation P4~P0

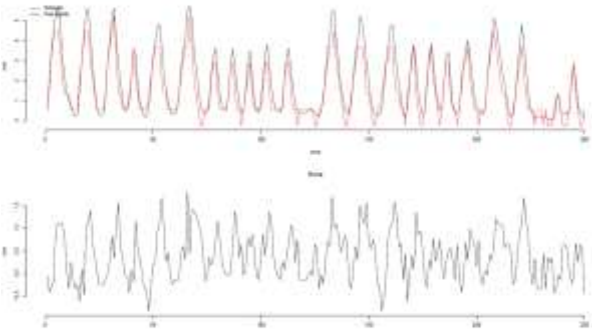

Fig. 6 Forecast and error term of *y* from relation P4~P0

4. Conclusions

Signals analysis shows that functional targets move more than external markers. Also, signals movement range depends on their directions: markers move more in anterior-posterior direction; targets - in superior inferior direction, if this direction is ignored, then in anterior-posterior. Experimental results show that in most cases even linear regression can predict motion of internal target with quite good accuracy. Better result are obtained using markers with a greater range of movement and position P0 if lateral direction is ignored, otherwise P1. Loss function (MAE) is sensitive to the range, therefore we will have to use other quality measures as well and regression residuals are auto-correlated, therefore future plans include experiments with more complex regression cases, multi-dimensional prediction and methods for solving the problem of residuals autocorrelation. Furthermore, we are planning to analyze respiratory motion prediction and design cases of an overall system radiation therapy system with respiratory motion compensation.

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