Does Breathing Motion Change Weeks to Years after Treatment?

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SUMMARY

4DCT has been the exclusive method for providing breathing-sorted CT imaging for radiation therapy since the early 2000s. 4DCT is limited in its ability to provide artifact-free images for irregular breathing patients, as well as alternative image outputs and quantitative precision and accuracy metrics. Model-based CT, specifically 5DCT, named for its use of the three spatial coordinates and the breathing amplitude and rate, has provided an alternative to 4DCT and has been conducted more than 300 times for patients with lung or other thoracic cancers.

One of the critical questions for model-based CT regards the stability of the model parameters. If the parameters are stable for only a few seconds to minutes, then the process data are limited to generating images for treatment planning, but the motion character and magnitude may be sufficiently different on the day of treatment as to limit its utility. If the model parameters are stable over a period of weeks, especially if they do not change during treatment, then the information available from the treatment plan can be used to support the treatment delivery methods, including breathing motion mitigation strategies and CBCT imaging.

Regardless of short-term stability, the motion model parameters will change over time, due to changes in lung elasticity, ventilation, or disease state. This change should be, on average, gradual and consistent between patients. Therefore, an analysis of the change in model-based parameters is warranted.

KEY POINTS

3 Tested Model Change Metrics

17 Patients 22 Comparisons

2/3 Metrics Showed Significant Parameter Change in Time

Not Same Patient Analysis Showed Poor Correlation

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INTRODUCTION

Our group has developed a process that models human breathing as a function of breathing amplitude and rate[1]. The current process uses 25 fast-helical free-breathing CT scans acquired simultaneous to a breathing surrogate. The surrogate is correlated against the imaged diaphragm dome position such that the amplitude A and rate $\dot{A}$ correspond to the diaphragm craniocaudal position and speed, respectively. The motion model is a linear combination of voxel-specific parameters such that the position of any voxel (specifically within the lungs) is

$$\vec{X} = \vec{X_0} + \vec{\alpha}A + \vec{\beta}\dot{A}$$

$\vec{\alpha}$ and $\vec{\beta}$ describe the motion as functions of breathing depth and rate, corresponding to the motion due to lung filling and hysteresis, respectively, and the model is termed 5DCT to reflect the three spatial coordinates, amplitude and rate. The motion model is used clinically to create a replacement for the commercial 10-phase 4DCT images that represent the motion envelope of the CT session with limited image artifacts and precision and accuracy metrics that allow clinicians to tailor margins according to not only tumor motion, but its measurement uncertainties (Figure 1). Future applications that are being developed to leverage the model are automated treatment planning, dose accumulation, and improved cone-beam CT. The potential for these future applications depends on how stable the model parameters are for each patient. The more stable they are, the smaller the clinical impact is of their change. This study describes an analysis of repeated 5DCT scans, mostly from patients undergoing subsequent treatment courses, to identify if, and by how much, the model parameters change.

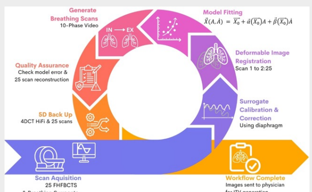

Fig. 1. 5DCT clinical workflow describing the steps from image acquisition to the transfer of images for contouring. In this work, we are concerned primarily with the generation and stability of the motion model data, specifically the value of $|\vec{\alpha}|$ as acquired for the same patient on multiple CT Simulation sessions.

METHODS & MATERIALS

Patients & data

22 model comparison of 17 patients. Each had a complete 5DCT session. Two of these patients were scanned repeatedly for a research study, while the remaining were rescanned as part of followup radiation therapy treatments.

Alignment

To allow for a direct comparison, the fractions were aligned using manually selected spine landmarks and an additional rotation using the sternum. The earliest scan exhalation image (image deformed by the motion model to represent exhalation) was compared against the later exhalation images and the diaphragm position shift used to modify the later scans to the same breathing amplitude (defined by the diaphragm dome position). A deformable image registration (deedsBCV) was then conducted to align the tissues.

Model Comparison

The model comparison was limited to the $\vec{\alpha}$ parameter, specifically the magnitude $|\vec{\alpha}|$. The histogram of the $|\vec{\alpha}|$ parameters of each 5DCT were compared and tested to determine how similar they were. Tests included the Wasserstein-1 distance, the Kolmogorov-Smirnov statistic, and the Jensen-Shannon Divergence.

Wasserstein-1 distance: Measures the total "work" required to move to transform one distribution to another. Units are of alpha (mm/mm), value of zero means exact match.

Kolmogorov-Smirnov (KS) statistic: Maximum absolute difference between two cumulative distribution functions. Dimensionless and bounded by [0,1], where 0 indicates identical distributions.

Jensen-Shannon (JS) Divergence: Measures how much "information" is lost when one distribution is approximated by the other, evaluated symmetrically and dimensionless. Bounded by [0,1].

The three comparison metrics were conducted for all patient reference simulations and followup simulations and evaluated as a function of time between fractions. To calibrate the variation of these metrics, comparisons were also made between the reference simulations and the collection of 221 patients and the 7 patients with the closest lung volumes (via the lung mask) were selected to compare.

Evaluation Parameter Calibration

One important question regarding the use of these evaluation tools is what values correspond to general inter-patient variability and what values to inter-fraction variability? To evaluate this, we compared each of the 17 reference distributions to the remaining 204 patient scans and for each reference distribution, finding the 5 scans with the closest lung volume as defined by a lung mask. The comparison metrics were computed for each of these 5 scans and the median, 25th percentile and 75th percentile values logged.

RESULTS

Examples comparing $|\vec{\alpha}|$ for patients with similar and dissimilar results are shown in Figure 2.

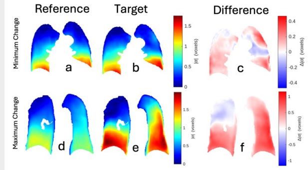

Fig. 2. Coronal views of the $|\vec{\alpha}|$ distribution for two patients, two 5DCT simulation sessions each. The reference session is the earliest CT simulation and the target a later session. Shown are the pair of scans with the smallest (0.043) and largest (0.341) values of the Kolmogorov-Smirnov statistic, respectively, showing the range of similarity and dissimilarity of the $|\vec{\alpha}|$ model parameters. The right-most column (c, f) show the differences between the reference and target $|\vec{\alpha}|$ distributions.

The analysis of the three model comparison metrics are shown in Figure 3 as functions of time between scans. The values for the patients themselves are shown in blue, and the not-same patient values shown in gray, along with the 25th to 75th percentile range. Note that in each case, the inter-patient values were greater than the intra-patient values, indicating that the model parameters were stable between CT imaging sessions.

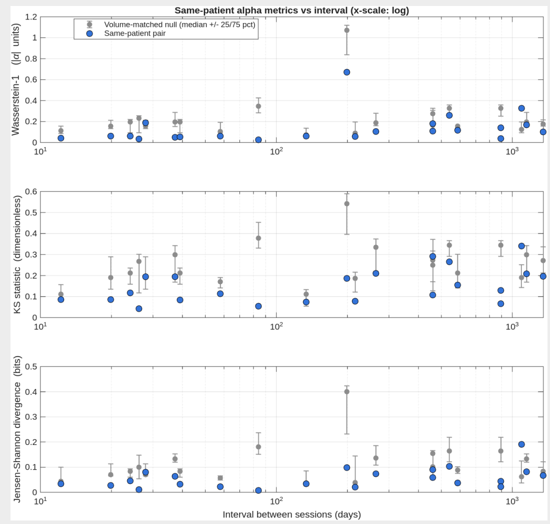

Fig. 3. Analysis of the three similarity evaluation metrics as a function of the amount of time between fractions (log scale). Blue indicates intra-patient analysis and gray not-same patient analysis.

The three parameters each demonstrated a trend as a function of time between CT sessions, so this was evaluated for all 3 parameters (Fig 4).

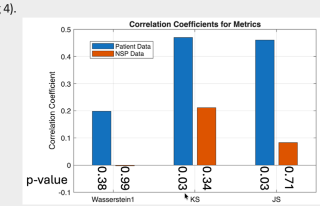

Fig. 4. Correlation coefficients of trend of parameters with respect to time for intra-patient (blue) and inter-patient (red, Not Same Patient) showing that the KS and JS parameters provided moderately large correlation coefficients that were statistically significant for the same patient but not significant for NSP.

These validate that comparing against the not-same patients shows no temporal trend.

Finally, the inter-patient and intra-patient data were compared to determine if the inter-patient parameters were statistically significantly greater than the intra-patient parameters. Fig 4 also shows that the intra-patient comparison is not correlated.

DISCUSSION

This analysis showed that the 5DCT parameter $|\vec{\alpha}|$ is relatively stable, as demonstrated by comparing against similar-lung volume patients, although it does change slowly with time. This implies that the motion model has some level of stability, which can help in terms of relying on it for treatment planning, dose accumulation, and model-based cone-beam CT imaging.

CONCLUSIONS

The 5DCT motion model, specifically $|\vec{\alpha}|$ the component that describes motion as a function of breathing amplitude, has been shown to be relatively stable in time, with gradual systematic changes.

Future work: Correlate the changes with changes in lung function, disease, and radiation burden.

REFERENCES

1. Low DA, et al. Novel breathing motion model for radiotherapy. Int J Radiat Oncol Biol Phys 2005;63(3):921–929.

CONFLICTS

Dr. Low and Dr. Moghanaki are founders of Respirati, a company dedicated to the commercialization of model-based CT.