Correlation and prediction uncertainties in the CyberKnife Synchrony respiratory tracking system

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(Received 14 June 2010; revised 26 April 2011; accepted for publication 9 May 2011; published 22 June 2011)

Purpose: The CyberKnife uses an online prediction model to improve radiation delivery when treating lung tumors. This study evaluates the prediction model used by the CyberKnife radiation therapy system in terms of treatment margins about the gross tumor volume (GTV).

Methods: From the data log files produced by the CyberKnife synchrony model, the uncertainty in radiation delivery can be calculated. Modeler points indicate the tracked position of the tumor and Predictor points predict the position about 115 ms in the future. The discrepancy between Predictor points and their corresponding Modeler points was analyzed for 100 treatment model data sets from 23 de-identified lung patients. The treatment margins were determined in each anatomic direction to cover an arbitrary volume of the GTV, derived from the Modeler points, when the radiation is targeted at the Predictor points. Each treatment model had about 30 min of motion data, of which about 10 min constituted treatment time; only these 10 min were used in the analysis. The frequencies of margin sizes were analyzed and truncated Gaussian normal functions were fit to each direction's distribution. The standard deviation of each Gaussian distribution was then used to describe the necessary margin expansions in each signed dimension in order to achieve the desired coverage. In this study, 95% modeler point coverage was compared to 99% modeler coverage. Two other error sources were investigated: the correlation error and the targeting error. These were added to the prediction error to give an aggregate error for the CyberKnife during treatment of lung tumors.

Results: Considering the magnitude of 2σ from the mean of the Gaussian in each signed dimension, the margin expansions needed for 95% modeler point coverage were 1.2 mm in the lateral (LAT) direction and 1.7 mm in the anterior-posterior (AP) direction. For the superior-inferior (SI) direction, the fit was poor; but empirically, the expansions were 3.5 mm. For 99% modeler point coverage, the AP margin was 3.6 mm and the lateral margin was 2.9 mm. The SI margins for 99% modeler point coverage were highly variable. The aggregate error at 95% was 6.9 mm in the SI direction, 4.6 mm in the AP direction, and 3.5 in the lateral direction.

Conclusions: The Predictor points follow the Modeler points closely. Margins were found in each clinical direction that would provide 95% modeler point coverage for 95% of the models reviewed in this study. Similar margins were found in two clinical directions for 99% modeler point coverage in 95% of models. These results can offer guidance in the selection of CTV margins for treatment with the CyberKnife. © 2011 American Association of Physicists in Medicine.

[DOI: 10.1118/1.3596527]

Key words: lung cancer, respiratory motion, CyberKnife, prediction model

I. INTRODUCTION

Radiation therapy is the preferred treatment for cancer patients who cannot undergo surgical resection, which is the best option for lung cancer patients.^{1,2} One immense challenge for radiation treatment is to compensate for tumor motion induced by patient respiration, which is especially pronounced in lung and abdominal tumors. This motion can occur in all anatomic directions and inhibits the accurate delivery of radiation.³ It is

reported that 42.9% of motion is in the superior–inferior direction (SI), 30.5% is in the anterior–posterior direction (AP), and 26.6% is in the lateral direction (LAT).³ The International Commission on Radiation Units and Measurements (ICRU) recommends that margins be added to the tumor position to compensate for the geometric uncertainties brought about by this motion and tumor rotations.^{4,5}

In the absence of real-time tracking and adjustments, the margin expansions can be large enough to require a dose

reduction in order to spare normal tissue.⁶ For gantry based Stereotactic radiosurgery (SRS), margins can be as high as 2 cm in order to ensure adequate dosage to the tumor.^{7,8} A reduction in margin can reduce lung toxicity, which has been reported with TD_{5/5} limits of 15 Gy to 50% and 20 Gy to 35%.⁹ Various clinical practices have been employed using image tracking to reduce the margin needed for effective radiation delivery. One study showed that 10–13 mm margins are necessary for 95% isodose coverage when considering systematic error and random error of a tracking system.⁴ Another study recommended 8.2 mm margins when accounting for systematic error.³

SRS offers the potential for high accuracy and sub-centimeter margins.^{1,3} The CyberKnife® Robotic Radiosurgery System (Accuray, Incorporated, Sunnyvale, CA) is one such option. This system includes the Synchrony® Respiratory Tracking System (SRTS), a hybrid tracking system for lung tumors^{10,11} with which to make real-time adjustments with changes in the tumor position.^{1,2} The CyberKnife has a 6 MV linear accelerator mounted on a frameless robotic arm, and is often used for hypofractionated lung treatments;^{1,2,12–20} it is also used for stereotactic brain radiosurgery^{21–24} and prostate radiosurgery.^{25,26}

Using the CyberKnife Synchrony system, margin expansion has been reduced by 44%, decreasing the normal tissue complication probability from 2.5 to 0.1%.⁶ Furthermore, skin sparing and reduced incidents of pneumonitis have been attributed to the CyberKnife's delivering of dose from many nodes (>50).¹⁹ In addition, the CyberKnife generates conformal, nonisocentric plans¹² and has the benefit of a 100% duty cycle, unlike gated treatments.^{6,11,12,27,28}

The CyberKnife Synchrony system can compensate inconsistent breathing motion with reduced treatment margins, especially with compensation for end-of-exhale baseline shift.²⁹ CyberKnife users have reported using margins as large as 8 mm (Ref. 17) and as small as 2 mm (Ref. 6); common margins are 3–5 mm.^{1,7,8} At CyberKnife of Indianapolis, 7 mm margins are used in the SI direction and 5 mm margins are used in the AP and LAT directions; for some patients with tumors in the lung apex, 5 mm margins are used in the SI direction as well.

Previous studies have not taken into account directionally specific errors and the varied margins needed to compensate for this. This paper presents a synopsis of the errors inherent to treatment with the CyberKnife and offers a clinically viable algorithm for determining the necessary margin size needed to compensate for these errors.

II. METHODS AND MATERIALS

II.A. Data source

Data sets for 100 treatment models of 23 de-identified lung patients, previously treated at CyberKnife of Indianapolis using the Synchrony model, were investigated. During treatment, the patient wears a tightly fitting vest that has three infrared light emitting diodes (LEDs) on its anterior. If an LED is out of phase with the others, it can be deactivated, but at least one LED is needed to run the Synchrony system.

Additionally, a pair of orthogonal x-rays tubes image the patient to monitor the location and orientation of several seeds implanted in or near the tumor.^{10,19,20,26,30} Three flash-point cameras continually track the external LEDs and the data are recorded at a frequency of 26 Hz. X-rays are taken by the operators (usually radiation therapist) using the CyberKnife control panel on an approximately per-beam basis, depending on user settings and treatment plan details. The time intervals between two adjacent x-rays may vary between 10 and 50 s.^{10,11,20} This tracking data is fed into the SRTS.

A correlation function is generated to relate the position signals of the LEDs to the internal fiducial locations. The built-in CyberKnife correlation function is either linear, quadratic, or dual-quadratic²⁸ and has the LEDs positions as the domain and the internal fiducial positions as the range. The most recent 15 data points from the periodic x-rays are used to verify the continued accuracy of the correlation model.^{11,20} If the discrepancy between the position given by the model and the position indicated by the x-ray exceeds 5 mm, the CyberKnife Synchrony treatment would stop. It is possible to have more than one Synchrony model for a treatment fraction. This could be due to (1) a CyberKnife synchrony system breakdown, (2) the patient asking for a break, and (3) the patient taking a “big” breath or coughing, etc., during the CyberKnife Synchrony treatment.^{11,20}

The other component of the SRTS is the prediction model, which is needed to overcome the 115 ms latency between tumor recognition and the completion of any beam adjustments.^{12,20,28} At the onset of treatment, about 2 s of tracking data is collected as seed data for the prediction model. During treatment, the CyberKnife generates five data log files,²⁰ they are:

- The *Modeler.log* file contains the output of the correlation model (modeler points), giving the estimated tumor position at a given time.
- The *Predictor.log* file contains the output of the prediction algorithm (predictor points) and the corresponding modeler points.
- The *ModelPoints.log* file contains the correlation error relating the modeler points to the x-ray registration of tumor position.
- The *ERSiData.log* file contains information about the location and status of the linear accelerator. A treatment session consists of irradiation from many nodes¹⁹ and treatment is interrupted during the repositioning from one node to another.²⁰ The *ERSiData.log* file was used to identify the times when radiation was being delivered, which amounted to about 10 min per session.
- The *Markers.log* file records the location of the external markers but is not used in this study.

In addition to the tracking data, the following data were acquired for each tumor from a single treatment planning image per tumor: the lung lobe containing the tumor [i.e., right upper lobe (RUL), right middle lobe (RML), right lower lobe (RLL), left upper lobe (LUL), or left lower lobe (LLL)]; the volume of the gross tumor volume (GTV) in cubic millimeters; the attachment status of the tumor (i.e.,

either free or attached to a fixed structure); the perpendicular distance from the tumor to the apex of the lung and to the base of the lung; the perpendicular distance from the tumor to the spinal cord and to the lateral wall of the lung; the perpendicular distance from the tumor the anterior of the lung and to the posterior of the lung; and the distance from the tumor to the aorta, if the tumor was not located superior to the aortic arch.

II.B. Data preparation and sources of error

The CyberKnife system records data in two concentric coordinate systems. The patient, or imaging system, is based on a patient in the supine position and has $+X$ in the inferior direction, $+Y$ in the left direction, and $+Z$ in the anterior direction. The CyberKnife robot operates in a coordinate system that is a rotation of the patient system about the Z axis such that $+X$ is in the direction of the robot base, which is at 45° between $-X$ and Y in the Patient coordinate system (whether it is on the left or the right is specific to the facility; the robot base at CyberKnife of Indianapolis is on the $+Y$ side). All data in this study were transformed into the patient system using a rotation matrix

$$\mathbf{P}_p = \begin{bmatrix} \cos 135^\circ & -\sin 125^\circ \\ \sin 135^\circ & \cos 135^\circ \end{bmatrix} \cdot \mathbf{P}_c$$

where $\mathbf{P}_p$ is the tumor position in the patient coordinate system and $\mathbf{P}_c$ is the tumor position in the robot coordinate system.

II.C. Impacting factors for margin expansion

There are three impacting factors for margin expansion during treatment delivery with the CyberKnife Synchrony model: (i) the targeting accuracy of the CyberKnife, which is the discrepancy between intended target and where the CyberKnife actually delivers radiation; (ii) the correlation error, which is the discrepancy between the position given by the correlation function and the position indicated in the x-ray images; and (iii) the prediction error, which is the discrepancy between the position given by the prediction model and the corresponding position indicated by the correlation function.

Investigations of total error in CyberKnife treatments have shown it to be 0.7–5 mm.^{2,6–8,11,16,20} By analyzing the CyberKnife log files, the correlation error and prediction error were able to be understood in terms of margin expansion.

II.C.1. Margin expansion for targeting error

Previous investigations discovered that the mechanical inaccuracy is 0.1 mm and the maximum position uncertainty is 0.3 mm.³¹ In the monthly quality assurance protocols at CyberKnife of Indianapolis, a single point is irradiated from many nodes (>100) and the spread of the dose delivery is evaluated; this has shown a 0.5 mm targeting error.

II.C.2. Margin expansion for correlation error

It has been reported that the correlation error can be 0.3–2.5 mm and correlated with motion amplitude.^{20,28} In our

analysis, the correlation error was extracted from the Model-Points.log file and considered over the course of a treatment session. The mean, minimum, maximum, and standard deviation of the correlation error for each session were determined. To ensure 95% modeler point coverage, two standard deviations from the mean in each anatomical direction were used; however, if the minimum or maximum were less deviant than two standard deviations, they were used instead. The mean of these values were calculated to describe the correlation errors over all patients

II.C.3. Margin expansion for prediction error

Previous studies have reported the root mean square error of the prediction model as 1.5 ± 0.8 mm (Ref. 10) and the standard deviation as up to 2.9 mm.²⁰ In our study, the prediction error was derived by comparing the predictor position with the modeler position 115 ms in the future. For each data pair of modeler (M) and predictor (P) points, the difference was calculated as the vector triple $(\Delta x, \Delta y, \Delta z)$ by $\bar{M} - \bar{P}$. Under assumption of a rigid tumor, this triplet gives the required margins in each dimension necessary to cover that modeler point when treatment is targeted at the predictor point.

In a scatter plot of all triples $(\Delta x, \Delta y, \Delta z)$ for a treatment model, a box enclosing points would indicate the margins necessary to cover all those points along each signed axis. Clinically, it is desirable to select margins that cover a certain percentage of data points ($p\%$). As tumor motion is in 3D space, the 3D margin should be considered simultaneously. Simply choosing margins that cover $p\%$ in any one dimension is insufficient. As shown in Fig. 1, a data point that is enclosed by a margin covering $p\%$ in the X dimension can be outside of the margin covering $p\%$ in the Y dimension. Thus, a two-step process was designed to calculate the margin that covers $p\%$ of data points.

First, margins were initially set individually to cover $p\%$ of data points along each axis. These margins could cover, at most, $p\%$ of data points, but, in practice, cover less. Second, the margins were then expanded in a way to include additional points, bringing total coverage up to $p\%$. The cost function of adding new points to the box is minimizing the added volume with the margin expansion. For each margin direction (superior, inferior, left, right, anterior, and posterior), the area of the face is calculated. This quantity is multiplied by the distance to the next closest point in that direction outside the

FIG. 1. Individual and composite margins show data points included in one dimension's margin may fall outside another (unfilled data points).

FIG. 2. Example of margin expansion to next closest data point. After the first iteration of this example, the $-x$ margin is expanded.

margin to give the additional volume covered by an expansion that includes that next closest point. The margin expansions in all six directions are compared and the one that adds the least volume to the total coverage is accepted. This process is repeated until $p\%$ of points are covered (Fig. 2).

The distribution of margin expansions for all treatment models in each anatomic direction at a particular level of

TABLE I. Summary of Correlation error analysis as the smaller of $x \pm 2a$ and the maximum error.

Direction	Correlation error (mm)
Superior	2.4
Inferior	2.9
Posterior	2.4
Anterior	1.8
Right	1.8
Left	1.7

overall coverage was considered and truncated Gaussian normal functions were fit to them via the maximum-likelihood method implemented by R statistical software.^{32–34} In fitting a truncated Gaussian, the data are not presumed to represent the entire distribution, but rather a function is matched such that the relative densities of the data in the known regions are maintained. This is in line with previous research showing the compensated residuals of Synchrony to be normally distributed.¹¹

FIG. 3. Charts showing correlation errors for each treatment model as $\mu \pm 2\sigma$ ($\square$) and minimum/maximum errors ($\blacklozenge$). The alternating groups of filled and unfilled diamonds indicate the models from individual patients (i.e., the first four data points are from the first patient, the next four from second patient, and the next from a third patient, etc.). The arrows in (a) indicate unique tumor situations, see Sec. IV below. The data points exceeding the graphical bounds in (a) are, from left to right, 10.0, 8.3, 8.7, 10.8, -8.1 , 8.2, and 8.8; the data point in (b) is 8.4.

TABLE II. Summary of margins expansions for 95 and 99% coverage in each anatomic direction.

Direction	95% Coverage		99% Coverage	
	Mean (mm)	Standard Deviation (mm)	Mean (mm)	Standard Deviation (mm)
Superior	-1.27	1.36	-2.76	2.93
Inferior	1.31	1.36	2.92	3.35
Posterior	-0.52	0.46	-1.23	0.78
Anterior	0.50	0.39	1.21	1.05
Right	-0.66	0.49	-1.44	1.04
Left	0.70	0.86	1.49	1.32

Optimization errors required shedding extreme points from some datasets to fit a Gaussian. The goodness of fit was evaluated by calculating the average absolute prediction error when comparing the population of histogram bins of size 0.5 mm with the frequency predicted by the Gaussian over the same range for all models included in the Gaussian fitting. Additionally, the expectation value of the Gaussian curve in was calculated over the range of fitting and compared to the mean margin expansion. Two standard deviations from the mean in the appropriate signed direction were considered for each anatomic direction as an estimate of the margin expansion necessary to provide the desired coverage in 95% of models. For this study, the margins for 95% modeler point coverage and 99% modeler point coverage were compared.

II.D. Correlating margin expansion with tumor characteristics

The prediction error margin expansions were compared to the tumor location data acquired from the treatment planning images. The relationships between margin size in each direction and various location measurements were investigated.

III. RESULTS

III.A. Correlation error

The correlation error was found to differ in matching anatomic directions by no more than 1 mm. In 30% of cases, the minimum or maximum correlation error was used instead of two standard deviations from the mean. Table I shows the

TABLE III. Parameters of the Gaussian normal distributions for 95% coverage fit by the fitdistr function in R statistical software.

Direction	Mean (mm)	Standard Deviation (mm)	Data points excluded from fitting (of 100) (%)	Average error	Difference in means (mm)
Superior	0.42	1.10	21	2.9	1.03
Inferior	0.05	0.77	29	3.6	1.01
Posterior	-0.14	0.76	0	3.8	0.20
Anterior	0.22	0.67	1	5.8	0.27
Right	-0.21	0.51	1	3.4	0.28
Left	-0.08	0.66	0	13.9	0.31

(a) Superior Direction

(b) Right Direction

Fig. 4. Fitted Gaussian normal functions overlaying margin expansion histograms (0.5 mm bins, normalized for density) for 95% coverage.

aggregate correlation error in each anatomical direction. Figure 3 shows the aggregate correlation error for each model built during treatment fractions in the superior/inferior and lateral directions.

III.B. Results for margin expansion based on prediction error only

The margin expansion method was used to generate margins for 95 and 99% modeler point coverage levels for the prediction algorithm. These results are summarized in Table II.

A Shapiro-Wilk test performed on the distribution of margins for 95% coverage revealed normality when considering margins less than 2 mm (average p -value of 0.12). However,

TABLE IV. Parameters of the Gaussian normal distributions for 99% coverage fit by the fitdistr function in R statistical software.

Direction	Mean (mm)	Standard Deviation (mm)	Data points excluded from fitting (of 100)	Average error (%)	Difference in means (mm)
Posterior	-0.45	1.59	0	2.3	0.40
Anterior	0.35	1.60	1	4.2	0.62
Right	-0.63	1.13	1	3.4	0.56
Left	0.06	1.41	1	4.2	0.66

FIG. 5. Charts showing margin expansions about Predictor points necessary for 95% ($\square$) coverage and 99% ($\blacklozenge$) coverage of Modeler points for each treatment model. The alternating groups of filled and unfilled diamonds indicate the models from individual patients (i.e., the first four data points are from the first patient, the next four from second patient, and the next from a third patient, etc.).

this normality was compromised as the range was broadened, particularly for margins in the SI direction. The parameters of the fitted distributions are given in Table III; two of the functions are plotted overlaying histograms of the data in Fig. 4.

Considering 2σ from the mean of the Gaussian in each signed dimension, the margin expansion showed consistency in given directions (e.g., anterior margins agreed with posterior margins). In the LAT direction, margins expansions of 1.2 mm were found to be needed to achieve 95% modeler point coverage for 95% of data sets. In the anterior/posterior direction, 1.7 mm margins were necessary. The fitted curves in the SI indicate a need for 1.7 mm margins, however, due to the exclusion of a large number of points, this does not match an empirical calculation; a 3.5 mm margin is necessary for this.

For 99% modeler point coverage, only the distributions for LAT and AP motion could be fit by algorithms used in

the R software. These fittings indicated 2.9 mm margins are needed to compensate for lateral motion and 1.6 mm margins are needed to compensate for AP motion. For SI motion, the increase in margin size from 95% modeler point coverage to 99% modeler point coverage was inconsistent, ranging from almost no increase to more than a 16 mm increase; for this reason, no Gaussian distribution could be fit. The parameters of the fitted distributions are given in Table IV. Figure 5 shows a comparison of margin expansions for 95 and 99% modeler point coverage in the SI and LAT directions for each model.

III.C. Margin expansion from combined error

Combining the correlation and prediction errors with the considerations for delivery error, a total margin can be

TABLE V. Estimate of total margin expansion for 95% modeler point coverage in millimeters.

Direction	Correlation	Prediction	Targeting	Total
Superior	2.4	3.5	0.5	6.4
Inferior	2.9	3.5	0.5	6.9
Posterior	2.4	1.7	0.5	4.6
Anterior	1.8	1.6	0.5	3.9
Right	1.8	1.2	0.5	3.5
Left	1.7	1.2	0.5	3.4

TABLE VI. Estimate of total margin expansion for 99% modeler point coverage in millimeters. Estimates could not be made for margin contribution in the SI direction (see Sec. III B above).

Direction	Correlation	Prediction	Targeting	Total
Superior	2.4	N/A	0.5	>2.9
Inferior	2.9	N/A	0.5	>3.4
Posterior	2.4	3.7	0.5	6.6
Anterior	1.8	3.6	0.5	5.9
Right	1.8	2.9	0.5	5.2
Left	1.7	2.7	0.5	4.9

FIG. 6. Histogram of total margin expansions from all treatment models normalized for density with bins of 2 mm showing the frequency of each margin size in each anatomic direction.

estimated that will provide 95% modeler point coverage. This is summarized in Table V. Table VI presents similar data for 99% modeler point coverage.

Considering individual patient treatment models, a range of margins was found in each anatomic direction. These distributions are shown in Fig. 6.

Comparing these results to the margins in place at CyberKnife of Indianapolis (SI: 7 mm, AP/LAT: 5 mm), 73% of models were adequately covered in the SI direction, 87% were adequately covered in the LAT direction, and 75% were adequately covered in the AP direction.

III.D. Results of correlating margin expansion with tumor geometric characteristics

Comparisons of prediction error margin expansion with tumors' geometric location yielded some quantitative results. Scatter plots of SI margin expansion versus distance from lung apex and distance from the midsagittal plane were enclosed by linear envelopes (Figs. 7 and 8). A similar plot relating the AP position of the tumors is presented in Fig. 9. The approximate positions of each tumor are shown in Fig. 10.

IV. DISCUSSION

One point that deserves discussion is the difference in methods used to calculate the prediction margins and corre-

FIG. 7. SI margin expansion versus distance to midsagittal plane measured perpendicularly. The enclosing lines are $y = 0.045x + 0.5$ and $y = -0.05x - 0.5$.

FIG. 8. SI margin expansion versus distance to lung apex measured perpendicularly. The enclosing lines are $y = 0.04x + 1$ and $y = -0.03x - 1$.

lation margins. Ninety five percent modeler point coverage was able to be precisely obtained using the algorithm for the prediction margin because the collection of data points was at such a high frequency and the total number of points considered was $>10,000$. When analyzing the correlation error, much fewer points were available (<30) and they were not collected at a constant frequency throughout a treatment model. For this reason, the correlation error points were considered as a sample set when calculating the correlation error for a treatment model. The consistency of the correlation error could be evaluated by collecting internal positioning data at a higher rate, enabling more frequent comparisons; the trade-off for this would be higher patient dose from x-rays. Two patients of interest are indicated by arrows in Fig. 3(a). The first patient (filled diamond markers) has two different tumors, each treated with four fractions. The second patient (unfilled diamond markers) has a tumor uniquely located when compared to the tumor locations in all other patients. This patient's tumor is attached to the posterior wall directly adjacent to a vertebral process.

While there was considerable variation in the prediction error-based margin expansions for the SI direction, when considering a particular tumor over all of its treatment models, there was more consistency. For 95% modeler point coverage, the standard deviation of margin expansions in the SI

FIG. 9. SI margin expansion versus fractional AP distance. Margin expansion increases as tumors are more centrally located in the chest cavity. The fractional AP position is the quotient of the distance from the anterior chest wall to the tumor and the distance from the anterior chest wall to the posterior chest wall, i.e., 0 is adjacent to the anterior chest wall and 1 is adjacent to the posterior chest wall.

FIG. 10. Approximate position of tumors. (a) Axial, (b) coronal, and (c) sagittal slices of generic anatomy showing approximate positions of each tumor. The numbering corresponds with the patient grouping sequence in Figs. 3 and 5. N.B. exact location information was not available for the ninth and sixteenth patients; however, they are both in the lower lobe of the left lung.

direction was 1.36 (for both superior and inferior margins); when considering the standard deviation of individual patients, the average was 0.37 (for both superior and inferior margins). Over all directions, the standard deviation ranged from 0.39 to 1.36 with a median of 0.67; on a per patient basis, the average standard deviation ranges from 0.16 to 0.55 with a median of 0.30. For 99% modeler point coverage, the standard deviation of margin expansions in the SI direction was 2.93 for superior and 3.35 for inferior; when considering the standard deviation of individual patients, the average was 0.91 for superior and 1.28 for inferior. Over all directions, the standard deviation ranged from 0.98 to 3.35 with a median of 1.19; on a per patient basis, the average standard deviation ranges from 0.40 to 1.28 with a median of 0.70. The large uncertainties in margins at the 99% modeler point coverage level suggest factors such as spiked noise and outliers.

Strong correlations between tumor characteristics such as location and size with margin expansion were not found, but the enclosing envelopes can offer some guidance in margin selection. Upper-bounds on prediction error can be estimated and general trends can be inferred, such as lower, more peripheral tumors tended to require larger margins. This is shown in Figs. 7–9. With a larger sample size, adequate populations could be built for a given parameter set, which may enable a complete marginal analysis.

This study has resulted in general recommendations of margin expansions, but patient specific margins would be more practical as many of the margin expansion are the maximum expansion, which is not always needed. Since consistency for a patient throughout treatment was observed, one way of obtaining patient specific margins would be to have a dry-run treatment session prior to treatment planning. Following that session, the log files could be analyzed to determine margins specific to that patient. Another possibility would be to incorporate monitoring into each treatment session. Treatment planning could be done using known errors inherent to the particular machine, and then a period of monitoring could occur prior to radiation delivery. The data from this period could be analyzed to inform the system of patient specific errors and the treatment plan could be expanded to

include these additional margins. However, a comparison of prediction margins from 1 min of monitoring to a retrospective calculation only yielded correlations with R^2 values ranging from 0.2 to 0.6.

Some research has been done into the stability of fiducial positions and organ shape, neither of which are recognized by the automatic x-ray registration. Imura has reported that implanted fiducials are stable for 2 weeks and others have reported the fiducial positions to be robust.^{7,11,17,30,35} Lu has reported that if tracking is perfect, a 3 mm margin is needed to compensate for organ deformation to ensure 95% isodose coverage.³⁶ The Lu study consisted of 12 lung tumors analyzed retrospectively by applying 0, 3, and 5 mm margins to an end of inspiration phase CT scan based on an end of expiration phase dose plan. Three millimeter margins gave $97.1 \pm 1.6\%$ coverage. This expansion was not included in the current study due to the small sample size and because it did not consider organ positioning throughout treatment. Further investigation with a larger sample may reveal location dependent organ deformation.

V. CONCLUSION

A study was done that compared Predictor points and the Modeler points of the CyberKnife Synchrony model. It was found that margin expansion can be an effective tool to generate 95% modeler point coverage. A statistical analysis led to the finding of margins that would provide 95% modeler point coverage for 95% of the models reviewed in this study. Due to spiked noise and outliers, achieving 99% modeler point coverage using margin expansion was found to be an inconsistent process. Several recommendations were made to obtain patient specific margins for use in treatment planning. Future investigations into the correlation error and organ deformation will enable more precision calculations of margin expansion.

VI. CONFLICTS OF INTEREST

Bryce Lord, D. O. is the radiation oncologist at CyberKnife of Indianapolis and Yuenian Zhang, Ph.D. is the physicist at CyberKnife of Indianapolis.

ACKNOWLEDGMENTS

The authors would like to thank Alex Li of Accuray Inc. for his technical assistance.

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