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SYNCHRONY – CYBERKNIFE RESPIRATORY COMPENSATION TECHNOLOGY

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Abstract—Studies of organs in the thorax and abdomen have shown that these organs can move as much as 40 mm due to respiratory motion. Without compensation for this motion during the course of external beam radiation therapy, the dose coverage to target may be compromised. On the other hand, if compensation of this motion is by expansion of the margin around the target, a significant volume of normal tissue may be unnecessarily irradiated. In hypofractionated regimens, the issue of respiratory compensation becomes an important factor and is critical in single-fraction extracranial radiosurgery applications. CyberKnife is an image-guided radiosurgery system that consists of a 6-MV LINAC mounted to a robotic arm coupled through a control loop to a digital diagnostic x-ray imaging system. The robotic arm can point the beam anywhere in space with 6 degrees of freedom, without being constrained to a conventional isocenter. The CyberKnife has been recently upgraded with a real-time respiratory tracking and compensation system called Synchrony. Using external markers in conjunction with diagnostic x-ray images, Synchrony helps guide the robotic arm to move the radiation beam in real time such that the beam always remains aligned with the target. With the aid of Synchrony, the tumor motion can be tracked in three-dimensional space, and the motion-induced dosimetric change to target can be minimized with a limited margin. The working principles, advantages, limitations, and our clinical experience with this new technology will be discussed.

Key Words: **Respiratory compensation, Synchrony, CyberKnife, Image-guided radiosurgery, Medical robotics.**

INTRODUCTION

Organs in the thorax and abdomen can move as much as 40 mm with respiration.[1] To protect the critical organs and healthy tissue from high doses of radiation, and maximize the dose conformality to tumor site, it is essential to compensate for respiratory motion during precision radiotherapy and extracranial radiosurgery.

Various types of techniques are used to reduce dose-targeting error. The simplest approach involves minimizing the target motion via breath holding.[2–4] Another common approach is beam gating, where beam is only turned on during a predetermined phase of the respiratory cycle.[5–7] The most direct method is to track the tumor fluoroscopically during treatment. This has been implemented in at least in one facility but the diagnostic x-ray exposure can be higher than acceptable levels.[8–10] An arguably better but also more difficult approach is to allow the patient to breathe freely while a tracking and control system monitors the tumor's position and the position of external markers.[11,12] In this method, tumor position is inferred from the external breathing surrogates. By optically tracking an external signal, which is correlated to tumor motion, large diagnostic x-ray exposure can be avoided. Synchrony™ (Accuray Inc., Sunnyvale, CA) is a respiratory compensation system integrated to CyberKnife® (Accuray Inc.), which uses external markers in conjunction with diagnostic x-ray imaging to compensate for respiratory motion. This article will cover the basics of this new technology used in high-precision radiotherapy and body radiosurgery.

CYBERKNIFE

CyberKnife (CK) is an image-guided radiosurgery system that consists of a 6-MV LINAC mounted to a robotic arm that is coupled through a control loop to a digital diagnostic x-ray imaging system.[13–15] The robotic arm can point the beam anywhere in space with 6 degrees of positioning freedom, without being constrained to a conventional isocenter (Fig. 1). The CyberKnife has been recently upgraded with a real-time respiratory tracking and compensation system called Synchrony, to emphasize the synchronized delivery of the radiation beam with respiratory cycle. Figure 1 depicts the basic components of the CyberKnife with Synchrony (CKS). The main components that make up the CKS are:

- Compact 6-MV X-band LINAC mounted to a robotic arm. The latest-generation LINAC is able to produce a dose rate of 800 monitor units MU/min.

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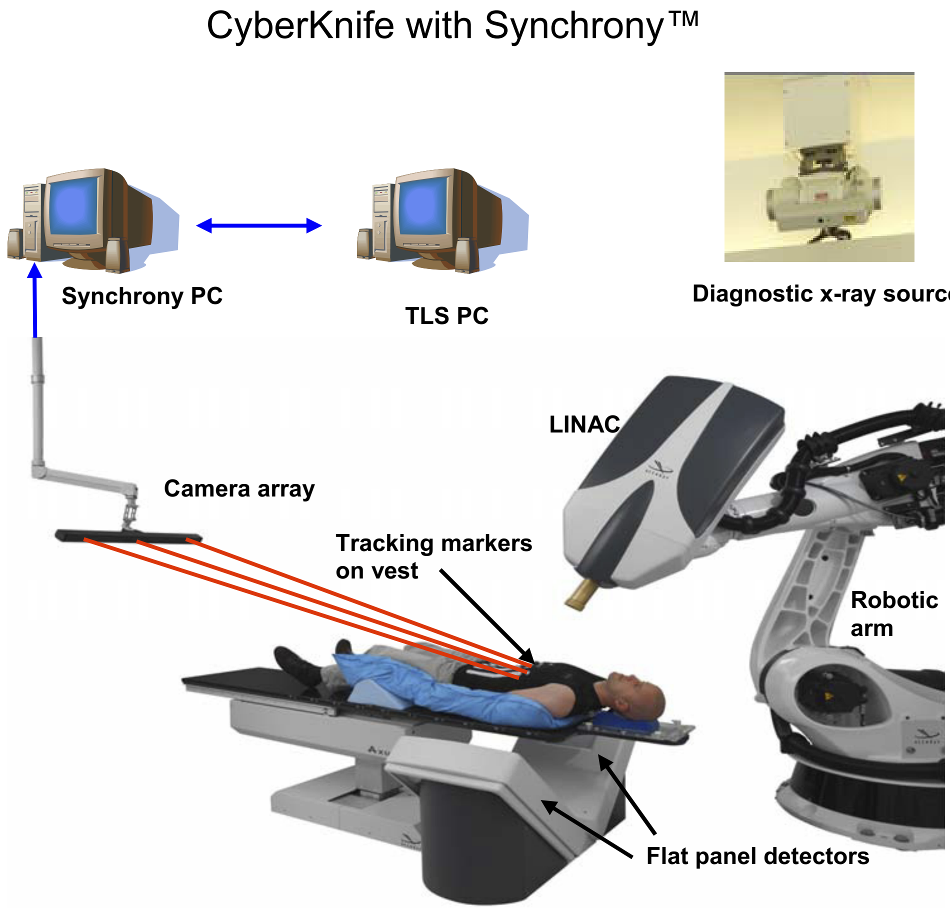

Fig. 1. Main components of the CyberKnife Robotic Radiosurgery System with the Synchrony Respiratory Tracking System are: (1) compact 6-MV X-band LINAC mounted to robotic arm; (2) two orthogonal flat-panel x-ray detectors positioned perpendicular to diagnostic x-ray sources mounted to ceiling; (3) Synchrony tracking vest with LED markers attached; (4) camera array that holds 3 CCD cameras; (5) Synchrony and Target Locating Computers. Image used with permission from Accuray Incorporated.

- Two orthogonal flat-panel amorphous silicon digital x-ray detectors with a resolution of 0.4 mm/pixel. One diagnostic x-ray source for each flat panel detector is mounted to the ceiling such that the diagnostic radiation beam is approximately perpendicular to the surface of the detector.
- Synchrony tracking vest, designed specifically for use with tracking markers, which are light-emitting diodes (LEDs). Three velcro (Velcro Industries, B.V.) tabs on the vest hold the tracking markers in position.
- Synchrony camera array, which holds 3 CCD (charge coupled device) cameras (See Fig. 2). This camera array is mounted to the ceiling and can register the positions of LED markers attached to a patient's vest at a rate of 25 to 40 Hz.
- The Synchrony computer operates the camera array, tracking LED markers, runs the tracking software, and communicates with the rest of CK system, namely, robot controller, target locating system, and console workstation. The target locating system (TLS) is a PC loaded with digital image processing software, which processes the radiographic images from the flat-panel detectors.

HOW SYNCHRONY WORKS

Patient setup and procedures

Prior to treatment, each lung cancer patient was implanted with 2 to 4 gold fiducial markers, which act as radiographic landmarks for the image-guidance system. The lung fiducials are 0.8×5-mm cylindrical gold seeds implanted percutaneously using a 17-gauge needle under computed tomography (CT) guidance. Fiducial markers were implanted in or around the tumor and acted as surrogates for tumor position. After approximately 1 week, patients returned for planning CT and 4D CT study. A GE Lightspeed helical scanner (GE Medical Systems, Milwaukee, WI) was used for planning CT and 4D CT study. For the planning CT, the patient was asked to hold his/her breath naturally at inspiration or expiration, while he/she lay comfortably supine in an alpha cradle or Vac-Lok (MEDTEC, Orange City, IA) bag,

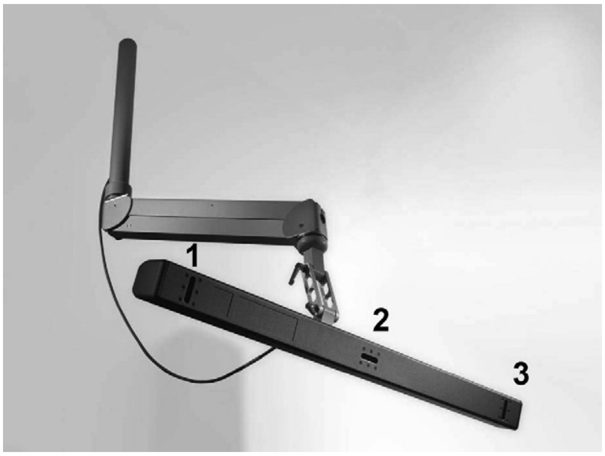

Fig. 2. Synchrony camera array has three 1-dimensional CCD cameras (1, 2, 3), which are capable of determining the positions of LED markers attached to the patient's vest at a rate of 25 to 40 Hz. Image used with permission from Accuray Incorporated.

wearing a custom-fit vest. The vest was form-fitting and highly elastic to ensure that it moved with the patient's chest wall or abdomen. Breath holding during CT scan was necessary to ensure that fiducials were not blurred on the CT images, as this would lead to misidentification of gold fiducial seeds. The 4D CT analyses were needed to determine the amplitude of the tumor motion.[16] If the amplitude was greater than 2 mm in any direction, the patient was considered a candidate for CKS treatment. Those patients whose tumors moved less than 2 mm were treated with the CyberKnife but Synchrony was disabled.

On the day of treatment, the patient was assisted in putting on the custom-fit synchrony tracking vest. The vest had 3 velcro strips that are used to attach 3 LEDs. After putting the vest on, the patient then lay supine on the treatment couch in the same immobilization device that was used during the planning CT scan session. Each patient's immobilization device was custom-made prior to the planning CT scan and the same immobilization device was used on the day of treatment to ensure patient position reproducibility. The 3 tracking LED markers were attached to the patient's chest or abdomen such that these markers were visible to the camera array. The camera array continuously registered the positions of external markers and reported them to the Synchrony computer, a PC with motion-tracking software.

Principles of synchrony

The goal of Synchrony is to track the tumor motion in real-time so that the CyberKnife robot can adjust the radiation beam continuously throughout the treatment to ensure that the beam motion follows the motion of the tumor. If the radiation beam and tumor follow the same trajectory in 3-dimensional space (I/S, A/P, L/R), dosimetrically this is equivalent to a static beam treating a static target, ignoring target rotations and deformations. As a result, a treatment plan can be generated based on static geometry, relative to the radiation beam. At the beginning of treatment, a mathematical model is built, which is then used to determine the tumor position in real time. Two orthogonal diagnostic images are taken at least 8 times at different phases of the respiratory cycle. By registering these images with 2 DRRs (digitally reconstructed radiographs), which are generated from the planning CT, the absolute position of the tumor relative to the fiducials can be determined. To build a reliable model, it is best to image once at the end of inspiration, once at the end of expiration, 3 times at different phases of inspiration, and an additional 3 times at different phases of expiration—a total of 8 images (Fig. 3). Each time a pair of orthogonal images is taken synchronously, they are digitized, positions of internal fiducial markers are registered, and each image is time-stamped. Because the Synchrony camera array continuously records the positions of external markers as a function of time, the positions of external markers corresponding to internal fiducial marker positions registered by the flat-panel de-

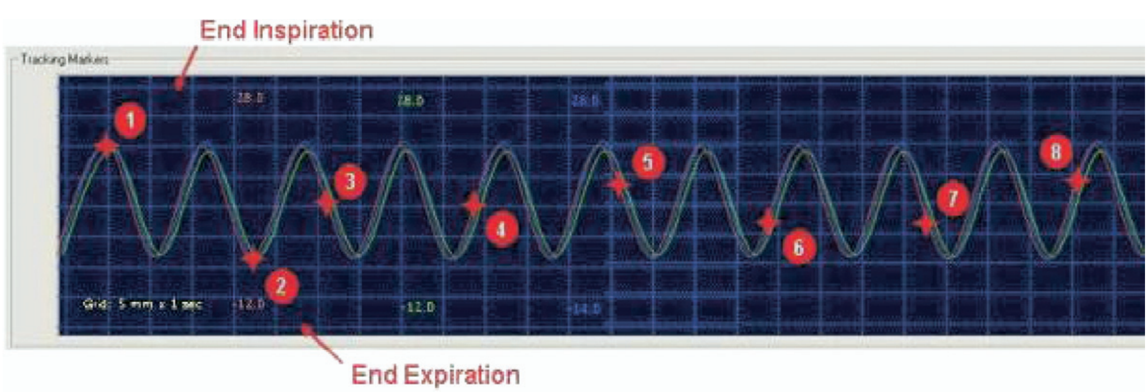

Fig. 3. Patient's breathing cycle as displayed on Synchrony PC monitor in real-time during treatment. To build a reliable correspondence model, 8 diagnostic x-ray images are taken at different phases of respiratory cycle. Four images are taken during inspiratory phase and another 4 during expiratory phase. Image used with permission from Accuray Incorporated.

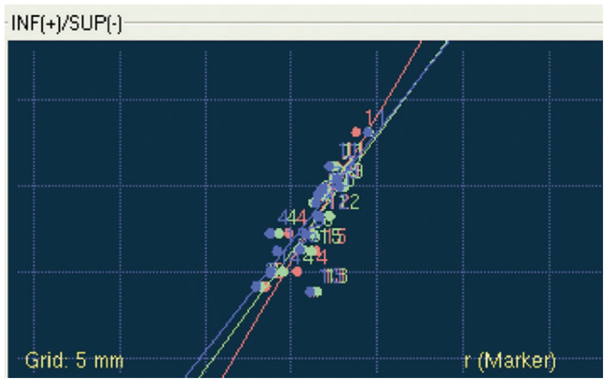

Fig. 4. A plot of internal vs. external marker position for I/S direction. Similar plots for A/P and L/R directions are also computed. Dots in the graph represent the correlation between the internal marker positions extracted from diagnostic x-ray images vs. the corresponding LED positions attached to patient's chest. Each color represents a different LED.

tectors are always known. Review of these dynamics allows us to build a mathematical correspondence model, that can be used to infer internal tumor position from external breathing indicators (LEDs) (Fig. 4). At the beginning of treatment, 8 images are taken to build the correspondence model, using the criteria given above. It is possible that the nature of the patient's respiratory cycle changes throughout the treatment, which may, in turn, cause the correspondence model to change. To account for this potential change, images are taken throughout the treatment typically, every 1 to 2 minutes, and the relationship between the internal markers and external breathing indicators are recomputed. However, Synchrony allows imaging as frequently as approximately every 30 seconds for a typical treatment. The most recent data are then used to update the correspondence model. The model only uses the data from the last 15 images. Once the model has stored 15 images, it starts discarding images taken earlier in the treatment in a first-in-first-out (FIFO) fashion. Thus, the model is based on the patient's current respiratory state, not the initial state, which may have changed during the course of the treatment. If it is believed that the patient's respiratory state has changed at any point during the treatment, the model can be reset, which forces all previous images to be discarded and a new model to be created. If there is a simple correlation between implanted fiducials and external markers, a linear model is built. For complex correlations, a nonlinear model is necessary and needs to be constructed. Models are always 3D, with a separate model for each direction of motion (I/S, A/P, L/R). Currently, Synchrony is the only system in wide clinical use that can track tumor motion in 3 dimensions using real-time feedback from the patient, which does not use continuous fluoroscopy throughout the treatment.[8–10] For some patients, the internal/external marker correlation for inspiration differs from that of expiration. In such a case, a different model is built for each phase of respiratory cycle. The correlation model can be linear for both phases, be linear for one and nonlinear for the other, or can be nonlinear (and different) for both phases. Figure 5 shows the correspondence model parameters reported by the Synchrony computer for the treatment of a lung patient at the beginning and end of the treatment, respectively. Note that at the beginning of the treatment, the model is linear for all directions of motion (Fig. 5A). Here, X, Y, and Z represent the I/S, L/R, and A/P directions of motion, respectively.

However, at the end of the treatment, the correspondence model for the X (I/S) direction is nonlinear and different for inspiratory and expiratory phases of the respiratory cycle (Fig. 5B). The same is true for Z (A/P) axis, whereas for the Y (L/R) direction, the model is still linear. While the correlation error was only 0.796 mm at the beginning of treatment, it increased to 4.749 mm at the end of the treatment (Fig. 5B). Correlation error is the discrepancy between the actual tumor position extracted from radiographic images and the predicted tumor position computed by the correspondence model.

After the correspondence model is built, it can be used to predict the tumor position based on the position of external optical markers. The model computes the position of the tumor at about 25 Hz and sends the new position of the tumor to the robot, which realigns the radiation beam with the current tumor position. In this fashion, radiation beam always remains aligned with moving tumor. Because the tumor position is inferred from external markers, whenever orthogonal images are taken and tumor position is directly determined from the digitized diagnostic images, the predicted position computed from the model can be compared to the actual position of the tumor extracted from the real-time images. The discrepancy between the predicted position

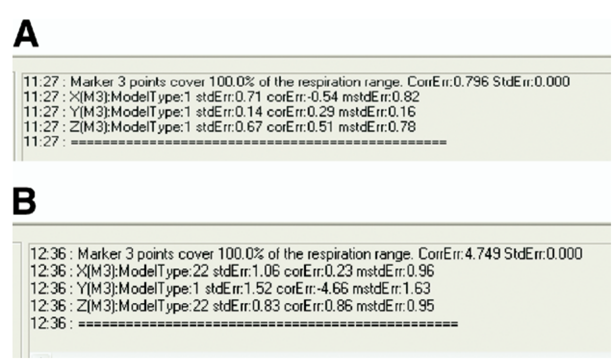

Fig. 5. (A) Modeling parameters displayed at the beginning of treatment. The model was linear (Model Type 1) for all 3 directions (X – I/S, Y – L/R, Z – A/P). Note the correlation error (CorrErr) was only 0.796 mm in the radial direction. (B) Modeling parameters displayed at the end of the treatment. The model for X direction was nonlinear and different (Model Type 22) for inspiratory and expiratory phases. The same applied for Z direction, whereas for Y direction, the model was still linear. Note the correlation error was 4.749 mm.

and the actual position is reported in real time by Synchrony tracking software. If the discrepancy is greater than 5 mm, the radiation beam is turned off automatically and a new correspondence model can be rebuilt. This would constitute building a model exactly in the same manner as was done at the beginning of the treatment by taking 8 images at different phases of the respiratory cycle. The need for a new model can be attributed to changes in the patient's respiratory cycle throughout the treatment. However, if the discrepancy is less than 5 mm, this is simply reported and the actual position of the tumor extracted from live images is used to update the model. By doing so, changes in the patient's respiration can be compensated for to some extent. If the patient's respiration is too irregular or changes too rapidly, the model will have to be reset by discarding all previous images and rebuilding it, as was done at the beginning of the treatment.

TREATMENT PLANNING AND DOSIMETRY

The CyberKnife system uses circular cones only. The diameters of the available cones in millimeters are: 5, 7.5, 10, 12.5, 15, 20, 25, 30, 35, 40, 50, and 60. Depending on the tumor volume, 1 or more cone sizes can be chosen for treatment planning. Typically, only 1 or 2 cone sizes are sufficient to produce an acceptable plan. Larger cones are typically used for extracranial lesions. There are approximately 1200 beam directions available for treatment planning. The treatment planning system is capable of producing single-, multiple-, or non-isocentric plans. Especially for extracranial lesions, which are typically much larger than intracranial tumors, single or multiple-isocentric plans produce poor dose coverage. Because the CK robot has 6-degree-of-freedom maneuverability, it can deliver an array of overlapping beams to be superimposed without an isocenter. Non-isocentric plans, which can be generated using the CK's inverse planning optimization algorithm, typically produce homogeneous dose distributions that closely conform to highly irregular volumes. This unique feature makes CK highly suitable for body radiosurgery applications.

For extracranial treatments, SAD (source-axis distance) can vary between 90 and 100 cm, whereas for intracranial cases, it is typically close to 80 cm. The dose rate for new generation LINAC is 800 MU/min. The typical treatment time for a single-fraction radiosurgical procedure is about 30 to 60 minutes. The 6-MV beam is calibrated to deliver 1 cGy/MU at 80-cm SAD at a depth of 1.5 cm in water for a 60-mm cone. For most treatments, the robot overhead is 20% to 30% of the beam-on time. Robot overhead refers to the total time the robot spends moving the LINAC between beam positions. While the robot moves between beam positions, no radiation is delivered. This time is used efficiently to take and process the digital radiographic images to determine the target position.

Optimization algorithm chooses the optimal beam directions automatically; the treatment planning system does not allow manual selection of beam directions.[13,17,18] Inverse planning is used for the creation of all plans. Because of the robot's great maneuverability, its workspace must be taken into consideration during treatment planning and delivery. The robot's workspace is the total volume within which the robot can maneuver without touching any other object or interfering with any lines of sight for the imaging system.[13,17,18] The planning system accounts for the robot's workspace to ensure that the robotic arm can move through

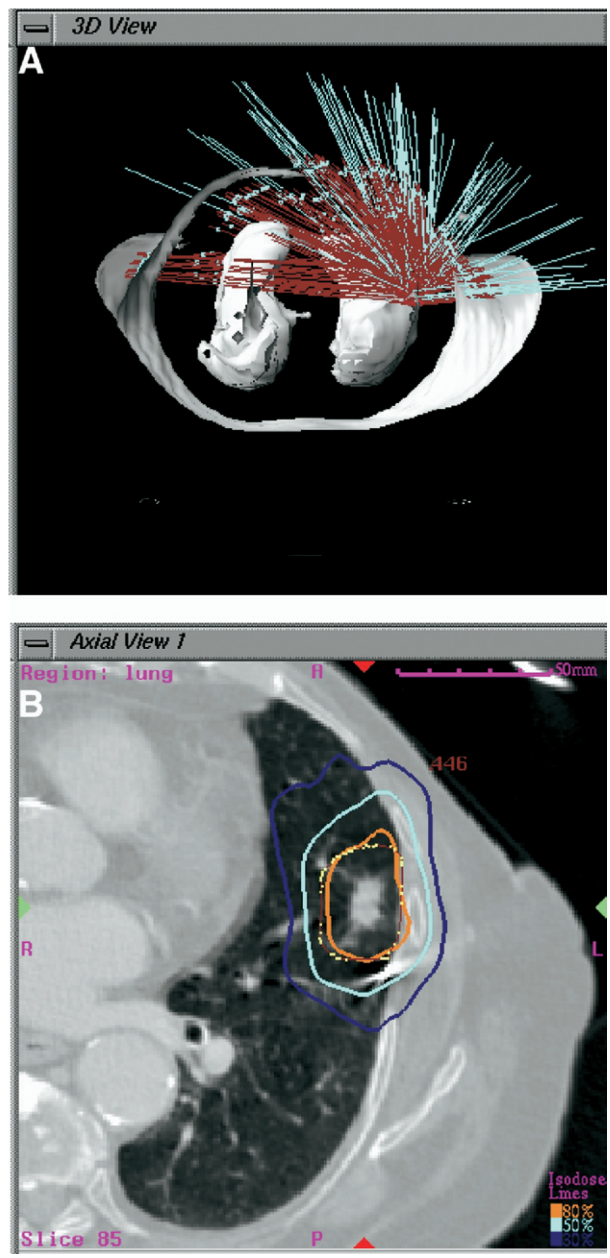

Fig. 6. (A) Beam directions for a synchrony plan of a patient with a tumor at her left lung. Beams with non-zero dose are shown in cyan. (B) A xial view of the synchrony plan (same plan as in Fig. 6A). Tumor is shown in red with yellow dots. Orange represents prescription dose to the 80% isodose line, whereas cyan and blue represent the 50% and 30% isodose lines, respectively.

the entire treatment safely. A typical CK plan has 100 to 150 beams and can be delivered in less than 1 hour. Figure 6A shows the beam directions for a synchrony plan that had 110 beams. All the beams delivering non-zero dose are depicted in cyan. The robot workspace for Synchrony (and all extracranial) treatments occupies an ellipsoidal volume on a coronal plane through the target volume.

All lung patients treated with synchrony are scanned with a CT slice thickness of 1.25 mm. Because the gold-implanted fiducial markers are 5-mm long, they are visible in 1 to 5 consecutive slices, depending on the orientation of the marker. At the beginning of treatment planning, the markers are identified and marked. The fiducial gold seeds act as surrogates for tumor position.

The treatment dose for CyberKnife is typically prescribed to the 80% isodose line and the maximum dose is represented by the 100% isodose line. A plan is considered ideal if 80% of the tumor volume is covered by the prescription dose. In some cases, it may be very difficult to achieve this goal due to the proximity of critical organs and the larger penumbra of the larger cones, which are frequently used for lung treatment. Figure 6B shows an axial view of a synchrony plan, which had 110 beams for a patient with a tumor at her left lung. The orange curve marks the prescription dose of 60 Gy at the 80% isodose line. This isodose line encompasses 83% of the target volume. The tumor is outlined in red with yellow dots. This plan was delivered in 3 fractions over a period of 2 weeks. A 20-mm cone was used because the tumor volume was 14 cc. Only a relatively small volume of the lung received more than 30% of the maximum dose. The 4D CT study for this target showed a motion of 10, 4, and 0 mm in I/S, A/P, and L/R directions, respectively. When the motion of the gold fiducial closest to the target was analyzed, it was found that the marker moved in the same fashion as the tumor within the resolution possible for 4D CT study. This information was considered during patient setup and building of the correspondence model at the beginning of the treatment.

DISCUSSION

To implement radiosurgery successfully to extracranial sites that move with respiration, respiratory motion of the target requires beam compensation. This is especially true for lung tumors, which have been commonly observed to move in excess of a few centimeters.[1] By using real-time feedback from the patient, Synchrony accounts for intra- and inter-fractional variability of respiration. As the correspondence model can be updated as frequently as twice a minute, changes in respiration can be accounted for to some extent by updating the model throughout the treatment. Furthermore, Synchrony's capability to build nonlinear as well as linear correlation models between internal and external markers allows tracking of some targets with complex trajectories. By modeling inspiratory and expiratory phases of respiratory cycle independently, Synchrony can account for hysteresis as well.

However, rotations of the tumor volume and deformations are currently not incorporated into the model. Consequently, for the targets that rotate and/or deform significantly, the tracking accuracy may not be as good as one would like to have. Nevertheless, because every time a set of orthogonal radiographic images are taken, and the position of the tumor determined from these images are compared to the inferred position of the target computed from the correspondence model, it is possible for the operator to determine if the model is not predicting the position of the tumor correctly. If a scenario arises where the model repeatedly fails to infer the tumor position correctly, a clinical decision has to be made to terminate the treatment. The correspondence model may fail if the patient's respiratory cycle is very irregular such as when significant baseline drifts of the breathing pattern are present or the target exhibits high degree of rotational motion about any or all 3 axes (I/S, A/P, L/R). Preparation for careful execution and delivery of treatment requires the following:

1. Run a careful 4D CT analysis of the target before the treatment, record the relevant data, and have it available on the treatment day.
2. Make a careful study of the relative position and orientation of the fiducial markers with respect to the target during 4D CT study and treatment planning.
3. Analyze the first 10 to 20 radiographic images taken at the beginning of the treatment and correlate them to steps (1) and (2).

As of January 2006, 44 lung cancer patients have been treated at our institution using Synchrony with the technique outlined above. The volumes of the lung tumors ranged from 0.5 to 165 cc. Thirty-seven patients were treated in a single fraction with 20 Gy to the 80% isodose line. The remaining 7 patients who had little or no prior radiation treatment and had peripheral lesions received 60 Gy in 3 fractions over a period of 1 to 3 weeks. One patient's tumor exhibited complex motion with large rotations and amplitudes; Synchrony was not able to generate a correspondence model, which could infer the tumor position with less than 5-mm accuracy. In other words, whenever Synchrony tracking software checked the inferred tumor position based on correspondence model vs. the tumor position derived from radiographic images, it frequently reported discrepancies that were larger than 5 mm. It was decided to cancel the treatment.

Proper placement of the fiducial markers in lung has been a challenge. Tracking is most accurate when the markers follow exactly the same trajectory as the tumor in 3D space. Therefore, it is best to implant the markers inside the tumor. It was attempted to implant at least 1 or 2 fiducials inside the tumor whenever possible. In situations where the fiducials were not implanted inside the tumor, there was at least one fiducial very close to the tumor (at most a few millimeters away). In order to treat, at least 1 fiducial need to be in or near the tumor, and at least 2 fiducials are needed to ensure that neither of the 2 fiducials have migrated. The tracking software has the capability to determine whether the internal fiducials have migrated. Whenever these criteria were not met, treatment was postponed until additional fiducial markers were implanted that met the criteria needed to ensure sufficient tracking accuracy.

The complexity of respiration and its variability is well-documented.[19] As discussed in the literature, extended observations have shown that the feasibility of respiratory compensation will not be settled by simple mechanical phantom tests or simplistic assumptions about periodic breathing motion.[20,21] We have, nevertheless, performed the manufacturer-recommended tests for Synchrony using a moving phantom that yielded a dose placement accuracy of 1.1 mm.

Synchrony's unique design with its self-checks for target-tracking accuracy via real-time radiographic imaging can provide an acceptable level of targeting accuracy for selective tumor sites. If the discrepancy between the predicted target position and actual position derived from real-time imaging repeatedly exceeds 5 mm, one can conclude that the correspondence model cannot infer the tumor position for that particular treatment accurately. At this point, a clinical decision can be made as to whether it is preferable to pursue the treatment. Because the system has a tolerance of 5 mm for tracking accuracy, 5-mm margins are typically used for contouring tumor volumes.

Although we have specifically discussed the treatment of lung tumors, the same principles apply to all extracranial treatment sites in which there is motion due to respiration. However, the fiducial implantation technique and the type of fiducials used for soft tissue lesions can be different.

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