

Robotic Tumor Tracking Techniques in Radiation Therapy

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Abstract

Precise and accurate dose delivery is critically important in external beam radiation therapy. In many cases target-volumes are stationary, but the problem arises when the tumors move significantly. Respiratory and cardiac motions have been found to displace and deform tumors in the lung, pancreas, liver, breast, and other organs. Because of this, radiation oncologists must expand the margin around tumor for radiation therapy. Consequently, a large volume of healthy tissue is irradiated, and critical organs adjacent to the tumor are sometimes difficult to spare. Implementation of the robotic tumor tracking techniques can potentially improve the quality of patient treatment by reducing unnecessary radiation dose to healthy normal tissues and critical structures and thereby lowering the toxicity level and increasing survival. Moreover, unlike gating, robotic tracking and dynamic delivery of radiation dose would be faster and efficacious.

Keywords: Robotic tumor tracking; Real-time tracking; Radiation therapy; Robotic couch; Multi-leaf collimator

Background and Introduction

Using the traditional treatment techniques, radiation oncologists have to contend with variations in tumor position during the treatment by treating a margin of healthy tissue around the tumor. Significant tumor motion, which can be up to 5 cm, has been induced mostly by cardiac and respiratory motion [1-6]. To accommodate this undesired movement and other errors; physicians incorporate a large margin around the tumor to delineate Planning Target Volume (PTV), so that the cancerous Clinical Target Volume (CTV) receives the prescribed radiation dose under any scenario during treatment session. Consequently, a large volume of healthy tissue is included in the PTV and sometimes it is difficult to spare critical organs adjacent to the tumor.

Therefore, it is extremely important to irradiate only the target-volume and minimize the healthy tissue irradiation by compensating for tumor movement and deformation. Major factors contributing to the overall geometric error and consequently inaccurate and/or undesired delivery of radiation dose are: 1) inter- and intra observer variations in Gross Tumor Volume (GTV) definition, 2) motion artifacts (respiratory and cardiac) on the CT images used to define targets and surrounding structures, 3) motion during dose delivery due to respiration and heartbeat, 4) variations caused by changing organ volumes (e.g. bladder filling during setup and treatment), tumor growth or shrinkage, tissue swelling, and 5) patient setup error (typically 3-5 mm with 1 mm standard deviation) [6]. Of these factors, respiratory motion is the major cause of target movement in and around the thorax. That is, there are significant motion problems for tumors in the lung, breast, esophagus, liver and kidney. But, due to the lack of appropriate tools, it is common practice to encompass the CTV with a PTV margin that allows for these variations. However, large PTV margins will result in the irradiation of the surrounding normal tissues and critical structures.

Methods

Tumor tracking techniques and robotic applications

There are various techniques that are currently available for monitoring and ultimately controlling or compensating respiratory motion during radiation therapy. These methods are: slow CT scanning, inhale and exhale breath-hold CT imaging, or 4D CT/respiration-

correlated CT, gating using an external respiration signal, gating using internal fiducial markers. Breath-holding methods, like deep-inspiration breath-hold, active-breathing control, self-held breath-hold without respiratory monitoring, can be used. Also, forced shallow breathing with abdominal compression is a commonly used approach. Finally, it is possible to employ real-time tumor tracking to compensate for tumor movement.

However, none of these methods is perfect; different methods have different types of drawbacks. For example, imaging and planning cannot be done in real-time (in a strict sense) and it requires good correlation between 4D CT and respiratory motion; the respiratory gating technique suffers from severely truncated duty-cycle of radiation delivery; breath-hold method requires the patient to be trained (uncomfortable, particularly for patients with compromised pulmonary capacity), hypo-oxygenation due to breath-hold may reduce the effectiveness of the killing of cancerous cells; shallow-breathing with abdominal compression approach is uncomfortable for the patient and may affect tumor oxygenation. Although robotic real-time tracking promises better results, it is more involved because of its rudimentary stage of development. Moreover, none of the studies or developed systems so far investigated the deformation of the target-volume during respiration.

Recently, several research groups are investigating various aspects of tumor tracking and developing tools to deliver precise dose to moving target-volumes [5-18]. Generally, commonly practiced methods for compensating target/tumor motion can be structured as: (i) breath-hold techniques, (ii) gating techniques, and (iii) Active Tracking and Dynamic Delivery (ATDD). The ATDD is the most effective technique,

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but it is the most challenging one. The ATDD can be accomplished in three different ways: (1) using the multi-leaf collimator (MLC), (2) using the treatment couch, and (3) using the MLC and the couch simultaneously. However, each of them has its own unique limitations.

For instance, MLC gating technique using internal fiducials requires kilovoltage x-ray which delivers unwanted radiation dose to the patient, and additionally gating suffers from severely low duty-cycle (only 30%-50%) and IMRT efficiency (only 20%-50%); all these lead to a 4- to 15-fold increase in delivery time over conventional treatment [6]. Therefore, it is of tremendous clinical interest, if the radiation beam can be delivered with higher duty-cycle (or almost continuously) while compensating for the target movement without exposing the patient to kilovoltage x-ray. CyberKnife Robotic Radiosurgery System, which is a 6MV linear accelerator mounted on a six degree-of-freedom (DOF) Keller und Knappich Augsburg (KUKA) industrial robot, is the only product in the market for so-called real-time tracking during beam delivery. However, this system has significantly long time delay (about 200 ms) between acquisition of tumor coordinates and repositioning to the linear accelerator. This delay is in addition to image acquisition, read-out, and processing times. The CyberKnife-KUKA robot with linear accelerator end-effector is suited for radiation therapy to anybody sites. Its field size is restricted to limited geometry (12 discrete circular fields ranging from 5 mm to 60 mm in diameter), workspace is limited and the radiation therapy community has not yet fully embraced the idea of using an industrial articulated robotic manipulator.

On the other hand, repositioning to an MLC aperture incurs a time delay on the order of 100 to 200 ms or more [6]. Movement of the MLC is restricted to back and forth in one direction with limited displacement. This means that moving shapes in a direction that is perpendicular to the direction of leaf motion requires a complex opening and closing pattern for the leaves. Although the commercially available HexaPOD robotic couch is capable of positioning the patient with high accuracy compared to other conventional couches [15], currently it does not have provision for compensating the tumor movement due to respiratory and cardiac motion. Another group has recently investigated the feasibility of using the treatment couch (HexaPOD and Dynatrac) for intra-fraction motion tracking [14]. Their study concluded that the achievable speed was not always enough to counter respiration-induced tumor motion in the realm of clinically relevant motion amplitudes. Such a robotic system which is subjected to a large load and operating at moderate frequency with small amplitude requires not only robust electro-mechanical design but also stable closed-loop dynamic control that can produce high degree of repeatability and accuracy with varying external perturbations. However, the idea of coordinated tracking of tumor using a robotic couch and tracking MLC presented in [16,17,18] can be very effective for any types of motions of the tumor. In this methodology, the high frequency low amplitude part of the tumor motion is allocated to the MLC or MLC bank and the low frequency part is allocated to the robotic couch.

Furthermore, image guided radiation therapy (IGRT) for the treatment of cancer has become a reality with the availability of imaging capabilities in the radiation treatment room with the patient in the actual treatment position, where volume images can be acquired on a daily basis. Commercially available in-room image devices now include CT/Volumetric CT and MRI. It is reasonable to expect even more sophisticated functional imaging modalities, e.g. PET, available for the patient in treatment position in the future. These images can potentially guide radiation therapy in the following two aspects. Firstly, the direct reference of the images obtained with the patient

in the treatment position to the treatment machine coordinates can substantially reduce the geometric uncertainty of internal structures. With the additional real time tracking and adjustment capabilities, more precise radiation will then be delivered with prescribed dose to target volume while sparing nearby critical structures, taking advantage of the latest available technology in radiation therapy: intensity modulated radiation therapy (IMRT). Secondly, with the images available on a more frequent basis, analysis will yield tumor response during radiation treatments in the initial stages that will allow adjustment of treatment techniques (fraction size, radiation modality, radiation treatment plan modification, etc.). However, due to the lack of proper commercial software tools, not all the potentials of the imaging systems are being utilized. Essential software tools are needed to take full advantage of IGRT equipment in use.

For accurate and efficient adjustments, tools that allow registration of internal structures between image sets are mandatory. Since internal structures are expected to deform, registration technique that incorporates deformation has to be employed. To evaluate tumor size variation during radiation therapy treatment courses, one needs efficient and accurate tools that define structures with/without human intervention. Other general essential tools are image manipulation capabilities that include appropriate image filtering for maximum information rendering. If radiation therapy treatment plan modification is deemed necessary, tools have to be included for the ability to create radiation treatment plans with full dosimetric calculation capability using the real-time acquired geometry.

As mentioned above, recent technical advances in radiotherapy offer the potential of more control of the radiation dose distribution. Three-dimensional conformal radiation (3D-CRT) makes it possible to restrict dose to the tumor region, reducing undesired dose to nearby critical structures. The relatively recent introduction of intensity modulated radiation therapy (IMRT) further expands the capability of dose shape control, with the ability to achieve irregular dose avoidance of critical structures. These technologies make it possible to deliver more radiation dose to tumor for better treatment outcome, while reducing the side-effects of radiation treatment.

However, in order to benefit from these latest technologies, better real-time information of the tumor geometry with respect to other nearby critical structures is imperative. Tumor shape and relative location are changing during day-to-day radiotherapy which can extend through weeks or months. Radiation treatments have to be adjusted to these changes [19]. Image guided radiation therapy (IGRT) has been the focus of much research in recent years. The essential components of this technique are accurate and efficient imaging equipment for frequent image acquisition, and the associated image analysis methods and tools to guide radiation treatment adjustment.

With the advent of more advanced technologies and decrease in manufacturing costs, it is reasonable to expect functional imaging capabilities in the treatment room. These images (PET, SPECT, etc.) have higher correlation with tumor locations [20,21].

In order to achieve wide-spread use of these latest technologies, sufficiently powerful efficient strategies and tools have to be coupled with this new hardware. IGRT has very limited implementation, currently used for anatomical localization during radiation dose delivery, mainly due to the lack of strategies and tools for image analysis and/or for adjusting treatments when image analysis indicates the need for change. A fully integrated package that includes image analysis methods and radiation treatment adjustment tools is very much in

demand if the new imaging capabilities described above are to be truly helpful. Given the current situation where the imaging systems are becoming widely available, there is a need to develop appropriate tools for using this technology.

Thus, there is an urgent need for developing a hybrid system which efficiently exploits the great advantages of state-of-the-art technologies including 4D imaging, 6DOF patient support, predictive modeling, adaptive control and real-time tracking and dynamic radiation dose delivery considering tumor movement and deformation caused by physiological movements.

The latest reported research in the field of tumor tracking included fluoroscopic tumor tracking, error analysis using probability theory, prediction filter investigation and development of the different tracking algorithms. In [22] the accuracy of two-dimensional projection imaging methods in three-dimensional tumor motion monitoring was investigated. The geometric uncertainties were investigated as well. In [23] a method that can track a deforming lung tumor in fluoroscopic video using active shape models was presented. A fluoroscopic tumor tracking for image-guided lung cancer radiotherapy was proposed in [24]. In [25] authors performed 4D targeting error analysis represented by a motion probability density function. In the article, the statistical fluctuations of tumor trajectory were described. In [26], the evaluation of the use of multi dimensional linear adaptive filters and support vector regression to predict the motion of lung tumors tracked at 30 Hz was performed. Since the frequencies of the cardiac cycle and respiratory cycle are about 3 Hz and 0.3 Hz, respectively, any tracking sampling rate more than 15 Hz should be adequate. In order to predict tumor motion during irregular breathing cycle, in [27] a novel adaptive acceleration-enhanced normalized least mean squares prediction filter with a breathing acceleration prediction was proposed. The performances of the filter were compared with both artificial neural network and AE-nLMS filters. Authors in article [28] proposed an algorithm that utilizes the on-board portal imager of the treatment machine for tracking lung tumors. The general framework of correlation-based tumor position estimation that could be applicable to various imaging configurations, where instant 3D target positions cannot be measured, was introduced in [29]. In [30] the authors have developed algorithms for direct tumor tracking in rotational cone-beam projections and for reconstruction of phase-binned 3D tumor trajectories. This work shows the feasibility of a direct tumor tracking technique for rotational images. A dynamics-based robotic approach to tumor motion prediction and tracking was described in [31]. The proposed system was evaluated using 4D-CT real patient data.

With advancement of the technology, it is now feasible to infer the tumor position from surrogate breathing motion signal from external markers [32-35]. However, in this approach two main issues need to be addressed: (1) the 3D model should strongly correlate the internal tumor motion to the external signal, and (2) time delay in computing the location of the marker and correspondingly the tumor location in task-space should be minimized, i.e. shortening the prediction time. The external breathing signal can be measured using infrared cameras and markers. A recent study showed a significant improvement of the adaptive capabilities of respiratory motion prediction filtering [36-38] using artificial neural network [39]. Other predictive filters have been used as well, such as Kalman Filter (KF) and Extended Kalman Filter (EKF) [40]. 4D real-time position of the tumor can also be measured by using implantable radiofrequency (RF) transponders that can be tracked electromagnetically from outside of the patient [41-42]. Recently, the researchers have reported that the

Calypso® System can be used with similar capability to fluoroscopy for localizing the tumor but without any added dose to the patient, [43]. Investigation whether patients could tolerate the motion of the robotic couch that compensates for breathing-induced tumor motion has been recently investigated [44]. The authors have concluded that most patients could tolerate compensatory couch motion and that motion sickness should not pose the problem in the implementation of different tumor tracking methods.

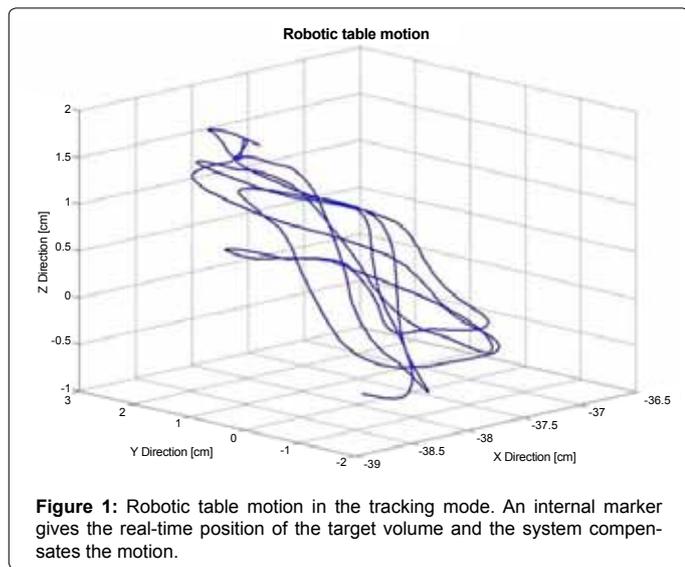
Results

Real-time robotic tracking strategy

During the ATDD using robotic treatment couch, the two general tumor motion compensation strategies can be implemented. The first is the tumor tracking without knowing the tumor position in advance, and the second one is the adaptive tracking mode, when the trajectory is known before the treatment starts. For the tumor tracking the controller should be placed in the position tracking mode to support changing the target volumes of an absolute position move during the treatment. The movement of target-volume (internal organ/tumor) can be measured either using (1) surrogate breathing motion signals from external markers, (2) implanted electromagnetic transponders, or X-Site Lung used for Cyber Knife system. The latest tracking system is based on difference in contrast of tumor and the surrounding tissues in lung. In the former case a robust 3D model correlating the tumor motion and the external marker's signal should be implemented. In the later case, the coordinates of the tumor volume should be periodically extracted from the direct measurement of the transponder's position. A closed-loop dynamic control of the robotic couch should be employed to continuously reposition the patient reciprocally to the tumor motion so that the treatment beam always finds the target-volume stationary. The tracking strategy sometimes includes the mutual tracking. That option is useful in the case when there are two targets (i.e. lung tumor and moving lymph nodes). The controller will then calculate a new trajectory based upon the new target position and the acceleration, deceleration, and speed parameters that have been set. The control system has to update the position information at the appropriate rate. The controller generates a profiled point every other sample, and interpolates one sample between each profiled point. Based on the tumor velocity and position, the controller will either continue in the direction it is heading, change the direction it is moving, or decelerate to a stop. The position tracking mode is suitable in the case when the internal markers give the real-time position during the motion compensation and tracking and that kind of system is able to generate robotic couch trajectory on the fly. The simulation of the robotic table position when the tumor position is not known in advance is given in Figure 1.

The adaptive contour mode allows the user to generate custom profiles by updating the reference position at a specific time rate or to have predefined tumor trajectory. This approach was analyzed in [18]. To obtain real patient data 4D-computer tomography (CT) image technique could be used. 4D-CT device is able to acquire images during ten phases of breathing cycle and to calculate tumor centroid displacement for each of the ten phases with respect to the treatment isocenter Figure 1.

Once, the 3D position and orientation of the target-volume is defined in the task-space (or Cartesian coordinates), the inverse kinematics solution for the robotic couch can be obtained by using suitable inverse transformations. This transformation yields the joint-space reference coordinates for the robotic system and accordingly commands can



be sent to the actuators to position and orient the couch in reverse direction of the target-volume movement to compensate the unwanted motion of the target so that for the treatment beam the target appears to be stationary. The change in shape of the target-volume in addition to the rigid-body movement of the tumor must be incorporated in the dosimetric planning so that the system can be adjusted accordingly to deliver accurate dose to the tumor. This may require the radiation beam field shaping. The potential undesired displacement or change of the shape of the target-volume (or organ) will be analyzed in the one of the following parts.

Prediction of respiratory and tumor motion

The presence of system latency (time delay) requires that the tumor position be predicted in advance, so that the beam can be synchronized to arrive at the actual position of the tumor once the adjustment has been made. This is necessary regardless of the method by which the tumor position is determined and applies to both beam gating and real-time tracking systems. The problem is complicated by the fact that a typical human breathing cycle, while nominally periodic, has significant cycle-to-cycle fluctuations in displacement, as well as longer-term fluctuations in both displacement and frequency [5]. However, these fluctuations are not purely random [7], which means that it should be possible to predict the character of a particular breath from the observed characteristics of its predecessors. This is the basis for time series prediction by an adaptive filter. Researchers have analyzed breathing prediction using a variety of adaptive filters and have found that the tumor position can be predicted quite accurately even in the presence of a 200 ms system delay, but accuracy degrades rapidly with longer delay intervals [36-39].

Commonly used technique for the respiratory and tumor motion prediction is adaptive filtering. An adaptive filter is able to self-adjust its transfer function according to the optimization rule. Since the trajectory of a respiratory motion is unlikely to be represented by a uniform transfer function even if the respiration is normal, the adaptive filters are more suitable comparing to the non-adaptive filters. Among the adaptive filters, Normalized Least Mean Square (nLMS) and Artificial Neural Network (ANN) filters are frequently used for the prediction. Standard procedure for the development the nLMS, ANN, and Acceleration-enhanced (AE) filters incorporates: training, verification, parameters selection and performance test, [27, 31].

Adaptive nLMS filter is one of the members in adaptive LMS filters family. LMS is an algorithm where iterative procedures are employed to make successive corrections to the weight vector towards the negative direction of the gradient vector. Eventually, minimal mean square error will be achieved. Basic challenge of these filters is choice of the learning rate in order to ensure output stability. Similarly to the adaptive LMS filters, the adaptive ANN filters need to have weights and bias adapted in order to minimize the error between the desired and the outputs Figure 2.

Two AE filters have been developed recently, [27]. One filter adapts the previous respiration positions to the current positions while the other filter adapts the previous respiration velocities to the current velocities. The velocities are derived from the change of the adapted positions, and the accelerations of the respiratory motion are derived from the change of the adapted velocities. This method uses the acceleration to give further correction to the adapted position. After training, the filters use current positions and velocities to predict future positions. In this work, the velocities are always predicted by the adaptive nLMS filter because it responds to abrupt changes of the signals better than ANN filter. The positions are predicted by the adaptive nLMS filter in AE-nLMS filter, and in AE-ANN filter they are predicted by the ANN filter.

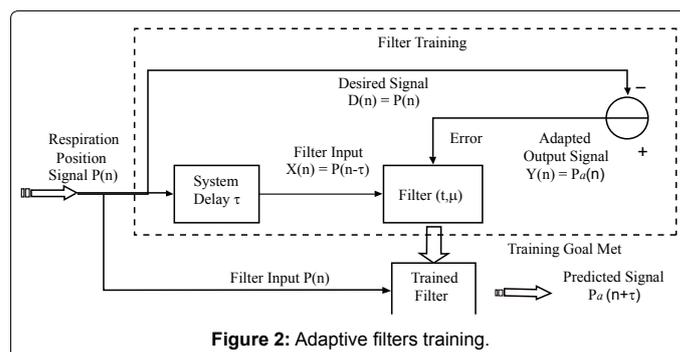
For a certain tap number and learning rate, adaptive nLMS and adaptive ANN filters are trained according to the schematic shown in Figure 2.

AE prediction algorithm can be implemented into the prediction module (PM) of treatment couch robotic system to eliminate the time delays. PM of the tracking system is capable to predict 3D tumor motion in for both regular and irregular cycle. Change of the amplitude in each cycle of the normal respiration induced motion is much smaller than that of the irregular respiration induced motion. First 20 seconds is the training period for the PM. The time range from 20th and 40th second is the verification period. Consequently, PM is ready for the simulations after 40s. The test (or simulation) period is from 40-60s. For the specific case, as in [31], average errors for prediction module in X, Y and Z directions were, respectively, -0.0092 mm, 0.021 mm and 0.012 mm. RMS errors for prediction module in X, Y and Z direction were, respectively, 0.267 mm, 0.450 mm and 0.039 mm.

Discussion

Clinical and dosimetric justification of tumor tracking

The influence of the tumor tracking technique to the treatment outcome was analyzed in [45-46]. The purpose of the dosimetry studies was to investigate clinical benefits of tumor tracking and to evaluate changes of treatment volumes when proposed tumor tracking technique is applied. The study includes the evaluation of dosimetric



advantages of tumor motion tracking and the irradiation of normal lung and spinal cord. The dosimetric evaluation of tumor tracking was carried out on randomly selected ten patients who were scanned using 4D-CT technique.

It was observed that during respiratory cycle a tumor volume was changed by up to 20 cm³ depending on tumor size, location, and patient specific breathing pattern. The 3D tumor displacement for all investigated patients were more than 10 mm. Using the active tracking technique it was found that for average tumor motion of 1.5cm the irradiated planning target volume (PTV) was 20-30% less which indicate significant amount of healthy tissue could be spared. The average maximum dose was 110% of PD and the mean dose was 103.6% of PD. It was observed that average lung volumes that received 5, 13, 20 and 30 Gy, with tracking technique were about 17.4%, 19.3%, 18.3% and 22.7% lower than the volumes without tracking, respectively. It was concluded that approximately 20% of healthy lung received 4-8 Gy less dose when the tumor tracking technique was used. Spinal cord was the most important critical organ for the studied lung cases. Dose to the 5% of spinal cord (D5) with tracking technique was 17.5% lower compared to that of without tracking. D5 of the spinal cord received approximately 0.5-11 Gy less dose when tumor tracking technique was used; wide variations were observed due to differences in prescribed dose, tumor location and size.

In [47] it was reported that prostate cancer patients treated with reduced margins and tumor tracking had less radiotherapy-related morbidity than their counterparts treated with conventional margins. Highly contoured intensity-modulated radiotherapy shows promise as a successful strategy for reducing morbidity in prostate cancer treatment.

However, application of the tracking techniques could be challenge when there are two or more independent tumors which move relatively to each other in irregular pattern. The following part is our dosimetry study where of relative motion of the primary tumors and lymph nodes for the 4D lung patients. It is known that one third of the lung cancer patients have disease that has been spread to lymph nodes (www.radiologyinfo.org). The dosimetric data for three patients diagnosed with lung cancer and secondary malignancy on the lymph nodes has been analyzed. Eleven plans were generated for each patient using XiO Treatment Planning System (TPS): ten for the different phases of breathing cycle and one for the average intensity projection study set. The prescription for all plans was 70Gy in 35 fractions to the PTVs. For the plans where tracking was introduced we analyzed coverage of the combined PTV (D99, D95, D50, maximum and mean dose) as well as coverage of the lymph nodes. The influence of the relative motions between the primary and secondary tumors to the tumor dose was also analyzed. It was observed that a significant amount of the healthy tissue was spared when tumor tracking was applied. The PTV for tracked plans was approximately 37% less comparing to the clinically used plan generated on the average phase. Furthermore, average V20 was 4% less for phase-plans. The average relative motions between lung tumor and lymph nodes were 8.6 mm and 15 mm for the first and second patient. Coverage of the primary target-volumes for the clinically used plans were D99=69.64Gy, D95=70.69Gy, D50=73.36Gy, MaxD=75.49Gy, MeanD=73.25Gy. Presented data leads to conclusions regarding the significant advantage of tracking techniques applied to the primary tumor. However, analyzing lymph node coverage for relative motion of 8.6 mm, it was observed that local hotspots were up to 3Gy higher (about 2.8%) compared to the original plan. Average coverage of the lymph nodes was: D99, 11Gy less (15.84%), D95, 5.77Gy less, D50 about the same. The mean dose was 0.5Gy less (0.5%). For relative motion

between primary tumor and lymph nodes of 15mm coverage was 8% lower then the previous case. To apply tumor tracking techniques for patients with developed primary and secondary cancer one should be aware that coverage of the secondary tumors could be compromised if only primary tumor was tracked, especially when tumor motion amplitude increases.

Another issue for the tumor tracking could be influence of the tracking error to the tumor coverage. Total compensation of the motion of thoracic tumors during irradiation may not be possible due to errors in prediction and tracking techniques. The dosimetric effects of the residual motions, i.e. errors in 4D tumor tracking, have been presented in the following section, for the robotic tracking technique proposed in [48,31].

4D-CT images of five patients are used to determine the trajectory of the tumor motion. Four patients are randomly selected and one patient with unusually large tumor motion (more than 4 cm in each direction) is selected as an extreme case. The clinical plans are used for comparison. All the dosimetric plans are generated using the XiO TPS. In 4D tumor tracking and motion compensation approach, the CTV is tracked accurately, with the maximum error of 1 mm. Since the internal margin (IM) is compensated by tracking, the PTV contains only the CTV and Set-up Margin (SM). To simulate the residual motion, the isocenter of the beams is shifted from the isocenter of the clinical plan by an amount equivalent to the residual motion of the prediction. The range of the tumor motion is within 2 cm in each direction, and the respiration cycle is about 4-5 sec. The phase-wise study shows that the average differences in the D99 of the PTV and CTV are about 1.37% and 0.21%, respectively. Even in the extreme case (the respiration cycle is only 3 s, and the amplitudes of tumor motion in the X, Y, and Z directions are 4.1 cm, 5.2 cm, and 4.2 cm, respectively), the difference in the D99 of the CTV is 0.9%. This case, however, is very unlikely to occur. In all other cases, the differences are less than 0.2%. This study also reveals that the discrepancy in the delivered doses caused by the predictions is insignificant for most of the anatomical structures. For example, the average change in the V20 is 0.04%, while the average changes in the D5 of the spinal cord and carina are 0 Gy and 0.14 Gy, respectively. The dosimetric effects of the residual motion in prediction are negligible for the tracking proposed in [31]. Even in the extreme case, these effects can be lessened by increasing the PTV margin by a small amount. However, this may not be a case for other tracking systems.

Conclusion

Based on the clinical investigation, the importance of the efforts for developing the robotic tracking techniques is understandable. Implementation of real-time tracking techniques can minimize irradiation to health tissues and improve sparing of critical organs. Consequently, quality of patient treatment potentially can be improved. Adaptive control for ATDD can be a good choice because of the variability in the payload on the system, i.e., the weight of the patient. One of the main challenges is to synchronize the respiratory motion with the robotic couch and/or IMRT delivery (or 3D conformal radiotherapy) considering the target-volume deformation in addition to target movement. With the implementation of tracking techniques, it would be possible to administer radiation dose to the tumor faster and efficaciously than the conventional methods like gating. With the advancement of the technology it is possible to assume that all tumor tracking techniques move toward real-time tracking approach. The tracking and active dose delivery should compensate tumor motion in all directions (especially, superior-inferior, lateral and anterior-

posterior directions). Tumor deformations may be automatically detected and the dose delivery systems should be able to administer dose more precisely using adaptive plans on the daily basis. Due to the better tumor position detection, it is conceivable that dose regimens can be greatly improved.

References

- Shirato H, Suzuki K, Sharp GC, Fujita K, Onimaru R, et al. (2006) Speed and amplitude of lung tumor motion detected in four-dimensional setup and in tumor-tracking radiotherapy. *Int J Radiat Oncol Biol Phys* 64: 1229–1236.
- Chen QS, Weinhaus MS, Deibel FC, Ciezki JP, Macklis RM (2001) Fluoroscopic study of tumor motion due to breathing. Facilitating precise radiation therapy for lung cancer patients. *Med Phys* 28: 1850–1856.
- Barnes EA, Murray BR, Robinson DM, Underwood LJ, Hanson J, et al. (2001) Dosimetric evaluation of lung tumor immobilization using breath hold at deep inspiration. *Int J Radiat Oncol Biol Phys* 50: 1091–1098.
- Erridge SC, Seppenwoolde Y, Muller SH, van Herk M, De Jaeger K, et al. (2003) Portal imaging to assess set-up errors, tumor motion and tumor shrinkage during conformal radiotherapy of non-small cell lung cancer. *Radiother Oncol* 66: 75–85.
- Ozhasoglu C, Murphy MJ (2002) Issues in respiratory motion compensation during external-beam radiotherapy. *Int J Radiat Oncol Biol Phys* 52: 1389–1399.
- Keall PJ, Mageras GS, Balter JM, Emery RS, Forster KM, et al. (2006) The management of respiratory motion in radiation oncology report of AAPM Task Group 76. *Med Phys* 33: 3874–3900.
- Benchetrit G (2000) Breathing pattern in humans: diversity and individuality. *Respir Physiol* 122: 123–129.
- Vedam SS, Keall PJ, Docef A, Todor DA, Kini VR, et al. (2004) Predicting respiratory motion for four-dimensional radiotherapy. *Med Phys* 31: 2274–2283.
- Sharp GC, Jiang SB, Shimizu S, Shirato H (2004) Prediction of respiratory tumor motion for real-time image-guided radiotherapy. *Phys Med Biol* 49: 425–440.
- Schweikard A, Glosser G, Bodduluri M, Murphy MJ, Adler JR (2000) Robotic motion compensation for respiratory movement during radiosurgery. *Comput Aided Surg* 5: 263–277.
- Kamino Y, Takayama K, Kokubo M, Narita Y, Hirai E, et al. (2006) Development of a four-dimensional image-guided radiotherapy system with a gimbaled x-ray head. *Int J Radiat Oncol Biol Phys* 66: 271–278.
- D'Souza W, McAvoyn TJ (2006) Analysis of the treatment couch and control system dynamics for respiration-induced motion compensation. *Med Phys* 33: 4701–4701.
- Keall PJ, Cattell H, Pokhrel D, Dieterich S, Wong KH, et al. (2006) Geometric accuracy of a real-time target tracking system with dynamic multileaf collimator tracking system. *Int J Radiat Oncol Biol Phys* 65: 1579–1584.
- D'Souza W, Naqvi SA, Yu CX (2005) Real-time intra-fraction-motion tracking using the treatment couch: a feasibility study. *Phys Med Biol* 50: 4021–4033.
- Chung H, Jin H, Palta J, Kim S (2006) Mechanical Accuracy of a Robotic Couch. *Med Phys* 33: 6.
- Podder TK, Buzurovic I, Hu Y, Galvin JM, Yan Yu (2007) Partial transmission high-speed continuous tracking multi-leaf collimator for 4D adaptive radiation therapy. In the IEEE Int Conf on Bioninformatics and Bioengineering (BIBE) 1108–1112.
- Podder TK, Buzurovic I, Galvin JM, Yu Y (2008) Dynamics-based decentralized control of robotic couch and multi-leaf collimators for tracking tumor motion. In the IEEE Int Conf on Robotics and Automation (ICRA) 2496–2502.
- Podder TK, Buzurovic I, Yu Y (2007) Coordinated dynamics-based control of robotic couch and MLC-bank for feedforward radiation therapy. *Int J of Computer Assisted Radiology and Surgery* 2: S49–52.
- Ling CC, Humm J, Larson S, Amols H, Fuks Z, et al. (2000) Towards multidimensional radiotherapy (MD-CRT): Biological imaging and biological conformality. *Int J Radiat Oncol Biol Phys* 47: 551–560.
- Ellis RJ, Kim EY, Conant R, Sodee DB, Spirnak JP, et al. (2001) Radioimmunoguided imaging of prostate cancer foci with histopathological correlation. *Int J Radiat Oncol Biol Phys* 49: 1281–1286.
- Suh Y, Dieterich S, Keall PJ (2007) Geometric uncertainty of 2D projection imaging in monitoring 3D tumor motion. *Phys Med Biol* 52: 3439–3454.
- Xu Q, Hamilton RJ, Schowengerdt RA, Jiang SB (2007) A deformable lung tumor tracking method in fluoroscopic video using active shape models: a feasibility study. *Phys Med Biol* 52: 5277–5293.
- Lin T, Cerviño LI, Tang X, Vasconcelos N, Jiang SB (2009) Fluoroscopic tumor tracking for image-guided lung cancer radiotherapy. *Phys Med Biol* 54: 981–992.
- Riaz N, Shanker S, Wiersma R, Gudmundsson O, Mao W, et al. (2009) Predicting respiratory tumor motion with multi-dimensional adaptive filters and support vector regression. *Phys Med Biol* 54: 5735–5748.
- Riboldi M, Sharp GC, Baroni G, Chen GT (2009) Four-dimensional targeting error analysis in image-guided radiotherapy. *Phys Med Biol* 54: 5995–6008.
- Huang K, Buzurovic I, Yu Y, Podder TK (2010) A Comparative Study of a Novel AE-nLMS Filter and Two Traditional Filters in Predicting Respiration Induced Motion of the Tumor. *Proc of 2010 IEEE Int Conf on Bioinformatics and Bioengineering (BIBE)* 281–282.
- Rottmann J, Aristophanous M, Chen A, Court L, Berbeco R (2010) A multi-region algorithm for marker less beam's-eye view lung tumor tracking. *Phys Med Biol* 55: 5585–5598.
- Cho B, Poulsen PR, Keall PJ (2010) Real-time tumor tracking using sequential kV imaging combined with respiratory monitoring: a general framework applicable to commonly used IGRT systems. *Phys Med Biol* 55: 3299–3316.
- Lewis JH, Li R, Watkins WT, Lawson JD, Segars WP, et al. (2010) Markerless lung tumor tracking and trajectory reconstruction using rotational cone-beam projections: a feasibility study. *Phys Med Biol* 55: 2505–2522.
- Buzurovic I, Huang K, Yu Y, Podder TK (2011) A Robotic Approach to 4D Real-time Tumor Tracking for Radiotherapy. *Phys Med Biol* 56: 1299–1318.
- Ahn S, Yi B, Suh Y, Kim J, Lee S, et al. (2004) A feasibility study on the prediction of tumour location in the lung from skin motion. *Br J Radiol* 77: 588–596.
- Hoisak JD, Sixel KE, Tirona R, Cheung PC, Pignol JP (2004) Correlation of lung tumor motion with external surrogate indicators of respiration. *Int J Radiat Oncol Biol Phys* 60: 1298–1306.
- Tsunashima Y, Sakae T, Shioyama Y, Kagei K, Terunuma T, et al. (2004) Correlation between the respiratory waveform measured using a respiratory sensor and 3D tumor motion in gated radiotherapy. *Int J Radiat Oncol Biol Phys* 60: 951–958.
- Schweikard A, Glosser G, Bodduluri M, Murphy MJ, Adler JR (2000) Robotic motion compensation for respiratory movement during radiosurgery. *Comput Aided Surg* 5: 263–277.
- Murphy MJ, Jalden J, Isaksson M (2002) Adaptive Filtering To Predict Lung Tumor Breathing Motion during Image-Guided Radiation Therapy. *Computer-Assisted Radiology and Surgery* 539–544.
- Sharp GC, Jiang SB, Shimizu S, Shirato H (2004) Prediction of respiratory tumor motion for real-time image-guided radiotherapy. *Phys Med Biol* 49: 425–440.
- Vedam SS, Keall PJ, Docef A, Todor DA, Kini VR, et al. (2004) Predicting respiratory motion for four-dimensional radiotherapy. *Med Phys* 31: 2274–2283.
- Vedam S, Murphy M, Docef A, George R, Keall P (2005) Long-term prediction of respiratory motion with artificial neural network based adaptive filtering techniques. *Med Phys* 32: 1925.
- Yan KG, Podder T, Xiao D, Yu Y, Liu TI, et al. (2006) Online Parameter Estimation for Surgical Needle Steering Model. *Med Image Comput Comput Assist Interv* 321–329.
- Seiler PG, Blattmann H, Kirsch S, Muench RK, Schilling C (2000) A novel tracking technique for the continuous precise measurement of tumour positions in conformal radiotherapy. *Phys Med Biol* 45: 103–110.
- Balter JM, Wright JN, Newell LJ, Friemel B, Dimmer S, et al. (2005) Accuracy of a wireless localization system for radiotherapy. *Int J Radiat Oncol Biol Phys* 61: 933–937.
- Malinowski K, Parikh P, Santanam L, Lechleiter K, Hubenschmidt J, et al.

- (2006) Concurrent Tracking and Fluoroscopic Imaging of Implantable Wireless Electromagnetic Transponders. *Med Phys* 33: 2162.
43. Sweeney RA, Arnold W, Steixner E, Nevinny-Stickel M, Lukas P (2009) Compensating for Tumor Motion by a 6-Degree-of-Freedom Treatment Couch: Is Patient Tolerance an Issue?. *Int J Radiat Oncol Biol Phys* 74: 168-171.
44. Buzurovic I, Werner-Wasik M, Biswas T, Galvin J, Dicker A, et al. (2010) Dosimetric Advantages of Active Tracking and Dynamic Delivery. *Med Phys* 37: 3191.
45. Buzurovic I, Huang K, Werner-Wasik M, Biswas T, Dicker AP, et al. (2010) Dosimetric Evaluation of Tumor Tracking in 4D Radiotherapy. *Int J Radiat Oncol Biol Phys Suppl* 78: S689.
46. Sandler HM, Liu PY, Dunn RL, Khan DC, Tropper SE, et al. (2010) Reduction in Patient-reported Acute Morbidity in Prostate Cancer Patients Treated With 81-Gy Intensity-modulated Radiotherapy Using Reduced Planning Target Volume Margins and Electromagnetic Tracking: Assessing the Impact of Margin Reduction Study. *Urology* 75: 1004-1008.
47. Buzurovic I, Huang K, Yu Y, Podder TK (2010) Tumor Motion Prediction and Tracking in Adaptive Radiotherapy. In the Proc of 2010 IEEE Int Conf on Bioinformatics and Bioengineering (BIBE) 273-278.