LUNG SBRT WITH THE CYBERKNIFE® SYSTEM

REPORT ORGANIZATION

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Background
Worldwide, lung cancer is the most common cancer in terms of both incidence and mortality, with 1.61 million new cases and 1.38 million deaths in 2008 (1). External beam radiotherapy (EBRT) has long been an accepted treatment modality for lung cancer, particularly for patients who are inoperable or refuse surgery. However, work within the last five years (2, 3) has suggested that replacing the standard EBRT lung treatment regimen of thirty 2Gy fractions with a hypofractionated regimen called Stereotactic Body Radiotherapy (SBRT) giving approximately the same total dose, but split over five or fewer fractions, has a beneficial effect both on local control and overall survival.

One of the challenges associated with delivery of such a hypofractionated regimen is that critical structure and normal tissue tolerances may be exceeded if a typical EBRT treatment plan is used, thus potentially leading to an unacceptable level of complications. Hence it is necessary to find methods to make the treatment dose distribution more conformal to the target and to minimize normal tissue exposure in order to be able to deliver the treatment safely.

For traditional gantry-based radiation delivery systems, the standard approach (4) for SBRT is to generate an Internal Target Volume (ITV), which encompasses the entire range of motion of the Clinical Target Volume (CTV) during respiration. A set-up margin is added to the ITV to form a Planning Target Volume (PTV) which accounts for additional geometric uncertainties such as initial set-up inaccuracy. This approach, however, comes with the drawback of large volumes of normal tissue exposed to the prescription dose, especially in cases where the tumor undergoes a large excursion during breathing.

CyberKnife Solutions for Lung SBRT
Using the CyberKnife System, hypofractionated lung treatments are delivered in such a way that accuracy and conformality are maximized (5,6,7,8). Tumors can be tracked using radiopaque markers implanted in or near the treatment target. The marker implantation, if done percutaneously, carries with it a risk of pneumothorax (9), and hence fiducial-free tracking alternatives are clinically desirable. Versions of Xsight® Lung Tracking, a fiducial-free tracking method, have been available for several years, but it is not applicable for all lung tumors and it can be challenging to identify prospectively the cases in which it will be applicable.

The Lung Optimized Treatment feature for the CyberKnife System provides a range of tracking modes to offer a fiducial-free treatment option for all lung tumors, and a simulation workflow allowing the optimal tracking mode to be selected prior to treatment planning. In cases where the target can be seen well enough to be tracked in at least one of the X-ray projections, by tracking and moving the treatment beams to compensate for some or all components of the respiratory motion of the target, less normal tissue is exposed to radiation than with traditional gantry-based systems. For targets in which full, accurate motion compensation, and hence reduced margins, is vital, bronchoscopic fiducial implantation remains a viable alternative, particularly when treating lesions close to the mediastinum.

The following features are included in the Lung Optimized Treatment package:

- Simulation Application, which is a workflow-based application that facilitates the choice of optimal tracking mode for each patient
- 1-View A and 1-View B tracking modes, which track targets that are visible in only one X-ray image
- 0-View tracking mode, which treats an ITV using Xsight Spine tracking for patient alignment

Objectives
The goal of this paper is to illustrate the clinical workflow associated with Lung SBRT on the CyberKnife System, in particular the decision making process involved in making a selection of the correct tracking mode for each patient.

We also analyze retrospective data from lung treatment plans for which fiducials were implanted, and use the fiducial positions as a ground truth to determine the location of the treatment target. We examine the effect of changing breathing pattern, and intra- and inter-fraction target drift, on the accuracy with which the planned ITV describes the treatment time motion trace of the target as determined by the fiducial positions. We also use fiducials, in a larger set of retrospective data, as a gold standard by which we evaluate the in-plane tracking accuracy of our direct target tracking algorithm. The outcome of this analysis is thus a quantitative accuracy evaluation for 0-View, 1-View, and Xsight Lung tracking.
II. CYBERKNIFE® SYSTEM FEATURES ENABLING LUNG SBRT TREATMENT

CyberKnife® Radiosurgery

The CyberKnife System is markedly different from gantry-based systems and is designed to deliver radiosurgery, generally using 1–5 treatment fractions, to targets located anywhere in the body (9). Two technical requirements for radiosurgery are that the dose distribution should be highly conformal to the target volume, with steep dose gradients in all directions away from the target volume, and treatment beams should be aligned and delivered with high accuracy to the target volume throughout every treatment fraction. High conformity and steep dose gradients in all directions are achieved through the combination of a robotic manipulator, which enables routine use of a large number of non-isocentric, non-coplanar beams that are individually targeted at unique points within the patient without the need to reposition the patient for each beam (Figure 1); multileaf collimation, which enables multiple beam sizes and shapes to be combined within each treatment such that a complex dose distribution can be constructed from a set of independently targeted and sized beams; and powerful plan optimization algorithms, which select optimal beam weights, beam directions and leaf apertures. High accuracy is achieved using two high-resolution kV X-ray projections coupled with tracking algorithms and an optical tracking system to allow the radiation beams to be offset to account for respiratory target motion, and to detect and correct for patient movement during the treatment fraction.

Figure 1: Beam geometry for a CyberKnife lung SBRT plan. The CyberKnife System can generate sharp dose gradients to maximize conformity and protect nearby critical structures, by means of many non-coplanar, non-isocentric beams and the use of target motion compensation without moving the patient.

CyberKnife Imaging Geometry

The CyberKnife imaging geometry consists of two ceiling-mounted kV X-ray sources and floor-mounted detectors arranged such that the source-to-detector axes for the two images are orthogonal, and both axes lie in the axial plane of the patient (Figure 2).

Using this imaging system, it is possible to perform rapid and accurate setup and intra-treatment correction for gross patient motion using cranial skeletal features (10) for cranial cases, spinal skeletal features (11) for spinal cases, or fiducial markers (12) for soft tissue treatments such as prostate and liver, by means of robotic beam alignment rather than couch or patient motion.

Figure 2: The arrangement of X-ray sources and detectors for the CyberKnife® System.
The Synchrony® Respiratory Tracking System
In addition to accurate setup and intra-treatment correction for gross patient movement, the CyberKnife® System has the ability to monitor and correct for respiratory motion of the treatment target. The Synchrony® Respiratory Tracking System consists of a camera in the treatment room that monitors the motion of visible markers attached to a vest worn by the patient (Figure 3). Using a correlation model relating the markers with the position of the treatment target as determined by periodic X-ray image pairs, the system offsets the treatment beam to follow the motion of the target, with a system specification, measured by means of an end-to-end test in a phantom with simulated respiratory target motion, of 0.95 mm accuracy. The correlation model is augmented by a prediction model to take account of the time lag between correlation and the robot reaching the desired position, which is 115 milliseconds. The correlation model is built before the beginning of treatment, and is continually updated as X-ray images are taken during treatment, so that changes in the patient’s breathing pattern during radiation delivery are accounted for. It should be noted that with the Synchrony System the beam is continuously on and tracks the motion of the target, in contrast to gating approaches where the beam is static and must be switched off for part of the respiratory cycle where the target goes outside the gating “window”.

For more detailed information regarding the Synchrony System, a recent CyberKnife overview (13) contains references to multiple clinical and technical studies.

Figure 3: The Synchrony tracking camera, the vest with optical markers attached, and the Synchrony System in action, moving the treatment beam according to respiratory motion of the target.

Xsight® Lung Tracking
For lung cases where the target is clearly visible in both X-ray images, the 3D position of the target may be directly localized (Figure 4) using the Xsight® Lung Tracking algorithm without the need for fiducials, and the treatment beam moved in real time to follow the target motion. In such cases, targets that move with respiration may be treated without the need either for implanted fiducials or for an ITV expansion to account for the motion range. All versions of the Xsight Lung algorithm use an algorithm that matches tumor patterns from a Digitally Reconstructed Radiograph (DRR), i.e., a projection through the CT to simulate an X-ray image, to the corresponding live images. The most recent version of the algorithm, introduced in CyberKnife version 9.6, improves on the earlier versions of the algorithm with the following additional features:

- Tumor Region DRR. The algorithm uses Tumor Region DRRs in addition to standard, full-content DRRs generated from the entire CT image. Tumor Region DRRs are generated by projecting only the subset of the CT image in the vicinity of the tracking target. By simultaneously using Tumor Region DRRs and full-content DRRs, the algorithm preferentially matches those portions of the target region that occur in both the Tumor Region and full-content DRRs, ignoring occlusions from distal structures projected onto the target region.
II. CYBERKNIFE® SYSTEM FEATURES ENABLING LUNG SBRT TREATMENT (CONTINUED)

- Robust Local Similarity Measure. By using a new advanced local similarity measure, the Xsight Lung algorithm becomes robust to intensity differences between DRR and live x-ray images caused by different x-ray parameters, scatter and noise. Using the new similarity measure, the Xsight Lung algorithm is able to correctly match patterns even with significant intensity pattern differences.

- Preferred Projection. When this mode is enabled, the Xsight Lung algorithm takes advantage of the CyberKnife® System shared geometry constraint to restrict the search to solutions with the same Inferior-Superior coordinates in both x-ray images.

- Improved Uncertainty Metric. The latest Xsight Lung algorithm provides a more accurate estimate of the uncertainty of the found solution. The uncertainty metric takes into account several factors, including the maximum of the similarity map, amount of other local optima within a tracking range, distance from the expected location and the size of the tumor.

Lung Optimized Treatment
The goal of the Lung Optimized Treatment package is to provide a fiducial-free treatment option for all lung tumors. We introduce and describe a new tracking mode, 1-View Tracking, together with a new use for an existing tracking mode, 0-View Tracking, and use retrospective clinical data to determine the in-plane and out-of-plane accuracy. The combined feature set of Xsight Lung Tracking with the Lung Optimized Treatment package (1-View Tracking, 0-View Tracking, and the Simulation Application) is designed to give the user a simple workflow to evaluate the optimal tracking mode for each patient, generate a treatment plan using that tracking mode and deliver the treatment with optimal accuracy.
III. CYBERKNIFE® SYSTEM PLANNING OPTIONS FOR LUNG SBRT

Planning for Xsight® Lung Tracking
The planning process for Xsight Lung Tracking is fundamentally similar to that for tumors that do not move with respiration, because the real-time target motion compensation of the CyberKnife® System means that there is no need to take into account the motion range of the target during planning.

In Figure 5 we show a GTV (red line) and corresponding PTV expansion (orange line) for a lung tumor. Given that the 3D motion of the tumor is tracked, this would be a fairly typical GTV to PTV expansion (8,14) for a CyberKnife lung treatment, and it should be noted that there is no ITV margin required because of the real-time tracking. The CTV is not shown.

Planning for 1-View Lung Tracking
For some lung cases, the size, shape, and position of the target is such that it can be seen and tracked in one of the orthogonal X-ray images, but not the other. This situation most frequently occurs when the target is superimposed on other X-ray attenuating structures such as the heart or spine in one of the projections. In Figure 6 we show an example of the PTV expansion necessary for such a case. In this example, we assume that the target can be tracked in the projection whose axis runs from the patient’s anterior left to posterior right. Hence all motion is tracked and compensated, except for motion in the axis of the projection. We thus divide position and motion into two parts: in-plane position and motion refers to the motion normal to the source-detector axis (motion visible in one imager); out-of-plane position and motion refers to the motion along the source-detector axis (motion not visible in either imager). The Synchrony® System receives as input a 3D target position determined from the in-plane tracked location and a static out-of-plane offset. A Synchrony model is then built in the usual way, but only in-plane motion of the target is tracked, so out-of-plane motion must be accommodated using an ITV. Figure 6 shows a “projection ITV” created using CTVs delineated in both the exhale and inhale phases of respiration. The motion for the projection ITV is determined by taking the component of the overall motion vector in the axis of the projection.
Planning for 0-View Lung Tracking

In a minority of cases, the location and size of the tumor is such that it cannot be seen well enough to be tracked in either of the orthogonal X-ray images. This situation occurs most commonly with small and/or diffuse tumors that show faintly in the X-ray projections, and those located near the mediastinum that tend to be blocked by large, dense structures such as the heart and cardiac blood vessels. In such cases, if the necessary margin expansions are clinically acceptable, 0-View Tracking may be used. For 0-View Tracking, the patient is aligned using spinal skeletal structures with rotational and translation corrections in a manner identical to that in an Xsight® Spine treatment. A treatment plan is created to treat a full ITV using CTVs delineated in the exhale and inhale phases of respiration. The ITV is expanded into a PTV with margins specified in the three patient cardinal directions. During treatment, the global patient alignment is corrected in the same manner as for an Xsight Spine treatment; the treatment beams are aimed at the ITV using the offset between the spine alignment center and the ITV location defined by the treatment plan. It should be noted that the Synchrony® System is not used for 0-view, because the beams are not moved to account for respiratory target motion.

Figure 6: Example GTV/CTV exhale (cyan line), GTV/CTV inhale (yellow line), projection ITV (orange line), and projection PTV (magenta line) for a lung tumor treated with 1-view tracking.

Figure 7: Comparison of projection ITV (orange shaded area) for 1-View tracking with full ITV (blue shaded area) for 0-View tracking. For 1-View tracking, the position of the CTV at inhale is projected onto the imaging axis going through the center of CTV exhale; only the component of motion along the imaging axis is used to create the projection ITV, and the Xsight Lung algorithm operates to determine target position in the imaging plane. For 0-View tracking, the full excursion of the CTV is used to create the ITV.

1 Xsight Spine Tracking is a tracking mode that identifies and tracks skeletal spine structures in the live X-ray images. Using Xsight Spine, six-degree-of-freedom patient alignment and motion compensation can be achieved without the need for implanted fiducials.
The Simulation Application feature of the Lung Optimized Treatment package is intended to allow the user to determine a tracking mode for each patient, such that the maximum amount of motion tracking is applied, but the user maintains confidence that the treatment delivery will be able to proceed successfully without tracking failure. With this in mind, the workflow is divided into five primary steps.

**Simulation Plan**

The first step is designed to provide the necessary inputs so that an imaging simulation may be performed. The default workflow is to load two CT scans of the patient, one taken in the exhale and one in the inhale phase of respiration. The user then performs an approximate delineation of the visible mass of the target in each CT scan, and defines the spine tracking volume (an approximately cylindrical volume enclosing the bones of the spine). The plan is then saved as a simulation plan, without any beams or dose attached.

**Simulation Application**

Once the simulation plan has been created and saved, the next step is to bring the patient into the treatment room and perform a simulation. In this context, by "simulation", we mean acquiring a set of X-ray images of the patient, and attempting to locate the treatment target in the X-ray images on the basis of the information given by the simulation plan. The results of this simulation are used to determine the optimal tracking mode for each patient. The simulation is performed by means of the Simulation Application. The application is workflow-based, and the user interface is designed to divide the simulation process into a series of steps:

![Example GTV/CTV exhale (cyan line), GTV/CTV inhale (yellow line), ITV (orange line), and PTV (magenta line) for a lung tumor treated using 0-View Tracking.](image-url)
IV. WORKFLOW FOR LUNG OPTIMIZED TREATMENT

1. Spine alignment. This is identical to the patient alignment procedure for Xsight® Spine and Xsight Lung treatments. Gross patient alignment (rotation and translation) is performed by comparing X-ray images of the patient’s spine with DRRs (Digitally Reconstructed Radiographs) produced from the primary CT.

2. Lung alignment. Using the known offset from the planning CTs between the spine alignment center and the center of the motion range of the tracked target, a couch shift is performed in order to bring the lung target into the field of view of the imaging system.

3. X-ray technique refinement. The user views histograms of live images from each of the two X-ray projections, and adjusts the X-ray parameters (energy, current, and exposure time) until the histograms show a satisfactory spread of values instead of being “bunched” at one end of the intensity scale.

4. Data set collection. A data set is a collection of eight to twelve X-ray images designed to maximally span the respiratory cycle. The system automatically performs repeated X-ray acquisitions until twelve images are acquired, or seven out of eight respiratory bins are filled.

5. Offset specification. The user moves a target overlay onto the position of the target in two of the X-ray images for each projection. These offsets are interpolated and extrapolated into the other images to provide the center of the search area for subsequent target location attempts. The user may optionally declare the target to be invisible in one or both images, in which case no target location attempts will be performed in the images for which the target cannot be seen.

6. Correlation. The system uses the image correlation algorithm to attempt to locate the target in each of the X-ray projection images. For cases in which the system declares that it has a successful target match, the user must review the match and declare it to be correct, incorrect, or uncertain.

7. Review. The user sees the correlation results and parameters corresponding to each data set acquired during the simulation process, together with an estimate given by the system of the optimal tracking mode (Xsight Lung, 1-View, 0-View, or undefined) on the basis of each data set.

In addition, there is a manual workflow available where the user performs alignment, imaging, and correlation without the division into steps shown above. In this case, the user determines the optimal tracking mode based on the simulation results.

Simulation Review
An application is provided on the CyberKnife® Data Management System (CDMS) that allows subsequent review of simulation activities and results, in addition to production of reports. The goal of this application is to provide all decision makers (physicians, physicists, and therapists) with the information necessary to reach an informed decision about which tracking mode is optimal for each patient.

Treatment Planning
Once the simulation has been completed and a decision made about the tracking mode to be used, the user may create a treatment plan on the basis of the simulation plan. The tracking contours and CT volumes belonging to the simulation plan are inherited from the simulation plan. The clinical contours (GTV and CTV in both respiratory phases and critical structures) are delineated, and the desired tracking mode is selected. There are tools provided in the MultiPlan® Treatment Planning System that allow ITV and PTV creation for 1-View and 0-View tracking modes; for PTV creation the user supplies in-plane and out-of-plane margins in mm for 1-View tracking, and margins in the three cardinal patient directions for 0-View tracking. Once all contours have been created, the treatment planning process is then identical to that for other CyberKnife treatments.

Treatment Delivery
From the treatment delivery perspective, the only new tracking mode is 1-View Tracking. Xsight Lung treatments are delivered as with existing CyberKnife technology, and 0-View treatments appear identical to Xsight Spine treatments in terms of the tracking technology used. During delivery of a 1-View treatment, both X-ray projections acquire images approximately centered on the treatment target. However, correlations are only attempted in the projection being used for tracking.
Figure 9: Examining and confirming correlation results during simulation. The user must provide input with respect to each correlation deemed successful by the system. The possible user choices are confirm success (shown by green check marks), reject (shown by red cross), and uncertain (shown by eye icon with red cross).

Figure 10: Review of results for a simulation data set. In addition to algorithm parameters and X-ray techniques used for spine alignment and lung tracking, the percentage of successful correlations is displayed for each view, and for both views combined. A suggested optimal tracking mode, as determined by the system on the basis of the correlation success percentages, is displayed at the right of the results row.
V. ANALYSIS METHODS AND RESULTS

Methods
In this section we describe the methodology used to evaluate the in-plane tracking accuracy of our direct target tracking algorithms. The outcome of this analysis is thus a quantitative accuracy evaluation for 0-View, 1-View, and Xsight Lung tracking.

- We analyze retrospective data from lung treatment plans for which fiducials were implanted, and use the fiducial positions as a ground truth to determine the location of the treatment target.
- We examine the effect of changing breathing pattern, and intra- and inter-fraction target drift, on the accuracy with which the planned ITV describes the treatment time motion trace of the target as determined by the fiducial positions.

The goal of the error analysis is to provide four different metrics:

1. The Xsight Lung 3D tracking accuracy, which is the 3D distance between the target centroid location predicted by fiducials and that predicted by the Xsight Lung tracking algorithm.
2. The 1-View in-plane tracking accuracy, which is the 2D distance, projected back to isocenter, between the in-plane position of the target centroid localized by the tracking algorithm and the in-plane position of the target centroid predicted by the locations of implanted fiducials.
3. The 1-View out-of-plane alignment accuracy, which is the amount of extension of the ITV center line, if any, required in order to include the projection of the target centroid onto the ITV center line.
4. The 0-View overall target alignment accuracy, which is the distance of the target centroid from its closest point on the ITV center line.

A detailed description of the methods and formulae used for the error analysis is provided in Appendix A.

Results
For 1-View out-of-plane accuracy and 0-View overall accuracy, we analyzed a total of 29 cases collected from three clinical sites; two of these sites (11 and 7 cases) provided treatment plans using biphasic CT, and the third site (11 cases) used only a single CT. For Xsight Lung 3D tracking accuracy and 1-View in-plane tracking accuracy, a total of 100 cases were analyzed; of these, 81 (81%) yielded sufficient visibility of the target in at least one projection image to allow comparison of fiducial tracking with direct target tracking. Of these 100 cases, 64 (64%) yielded sufficient visibility of the target in both projection images to allow derivation of the 3D tracking error. We define “sufficient visibility” to mean that at least 75% of image pairs (or images in the case of 1-View) returned a successful correlation. A correlation was deemed successful when the confidence metric was greater than 60% in both views (the single view being used for 1-View) and there was no more than 4mm error in each image plane (the single image plane for 1-View) relative to the fiducial ground truth.

Xsight® Lung 3D tracking error (2-view tracking)

Table 1: Results of Xsight Lung 3D tracking error analysis

<table>
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<tr>
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<th>RMS error (mm)</th>
<th>Mean 95% error (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>X (mm)</td>
<td>Y (mm)</td>
<td>Z (mm)</td>
<td>0.82 ±0.51</td>
<td>0.86 ±0.43</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.97 ±0.49</td>
<td>1.61 ±0.64</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.43 ±0.87</td>
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</table>

In Table I, we give for Xsight Lung Tracking the mean absolute error with standard deviation for the X (left-right), Y (anterior-posterior) and Z (inferior-superior) directions, in addition to 3D RMS total error (RMS over the individual X-ray images for each case, mean and standard deviation over cases) and 95% error (95% over the individual X-ray images for each case, mean and standard deviation over cases).
1-View in-plane tracking error and out of plane alignment error

In Table 2, we give for 1-View Tracking the RMS in-plane error (RMS over the individual X-ray images for each case, mean and standard deviation over cases) and 95% in-plane error (95% over the individual X-ray images for each case, mean and standard deviation over cases).

<table>
<thead>
<tr>
<th>RMS distance (mm)</th>
<th>Mean 95% error (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.39 ± 0.63</td>
<td>2.20 ± 0.91</td>
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</table>

Table 2: Results of 1-View in-plane tracking error analysis

In Table 3 above, we show the results of the 1-View out of plane alignment analysis. The first column gives the mean and standard deviation of the RMS distance in mm along the source-detector axis of the target position from the centroid of the projected ITV (root mean square over individual X-ray images for each case, mean and standard deviation over cases). The second column gives the mean and standard deviation of the 95% expansion, i.e., the mean size of the projected ITV to projected PTV margin expansion in mm along the source-detector axis that would be necessary to encompass 95% of the target positions (95% value over individual X-ray images for each case, mean and standard deviation over cases). The results appear to be somewhat consistent between the sites, with no clear bias seen due to single or biphasic CT being used for the analysis.

<table>
<thead>
<tr>
<th>Site 1 (biphasic CT)</th>
<th>RMS distance (mm)</th>
<th>Mean 95% expansion (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.90 ± 2.89</td>
<td>5.02 ± 5.51</td>
</tr>
<tr>
<td>Site 2 (biphasic CT)</td>
<td>3.03 ± 2.30</td>
<td>3.20 ± 2.50</td>
</tr>
<tr>
<td>Site 3 (Single CT)</td>
<td>3.53 ± 2.30</td>
<td>4.68 ± 4.02</td>
</tr>
<tr>
<td>Total</td>
<td>3.55 ± 2.52</td>
<td>4.45 ± 4.37</td>
</tr>
</tbody>
</table>

Table 3: Results of 1-View out of plane alignment analysis

0-View overall target alignment error

In Tables 4 and 5 above, we show the results of the 0-View overall target alignment analysis. Table 4 gives the mean RMS error (RMS of errors from individual X-ray images in each case, mean and standard deviation over cases) both in components and overall vector distance. Table 5 gives the mean 95% error (95% error from individual X-ray images in each case, mean and standard deviation over cases) both in components and overall vector distance.

<table>
<thead>
<tr>
<th>Site 1 (biphasic CT)</th>
<th>Inf-sup RMS Error (mm)</th>
<th>Ant-Post Overall (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left-Right</td>
<td>Ant-Post</td>
</tr>
<tr>
<td>Site 1 (biphasic CT)</td>
<td>4.48 ± 4.85</td>
<td>3.41 ± 3.08</td>
</tr>
<tr>
<td>Site 2 (biphasic CT)</td>
<td>3.56 ± 3.56</td>
<td>2.54 ± 1.64</td>
</tr>
<tr>
<td>Site 3 (Single CT)</td>
<td>4.29 ± 2.26</td>
<td>2.62 ± 1.40</td>
</tr>
<tr>
<td>Total</td>
<td>4.19 ± 3.16</td>
<td>2.90 ± 2.20</td>
</tr>
</tbody>
</table>

Table 4: RMS Error from 0-View overall target alignment analysis

<table>
<thead>
<tr>
<th>Site 1 (biphasic CT)</th>
<th>Inf-sup 95% Error (mm)</th>
<th>Ant-Post Overall (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left-Right</td>
<td>Ant-Post</td>
</tr>
<tr>
<td>Site 1 (biphasic CT)</td>
<td>7.61 ± 7.58</td>
<td>6.32 ± 7.28</td>
</tr>
<tr>
<td>Site 2 (biphasic CT)</td>
<td>5.40 ± 4.25</td>
<td>3.73 ± 1.92</td>
</tr>
<tr>
<td>Site 3 (Single CT)</td>
<td>8.15 ± 4.46</td>
<td>4.52 ± 2.30</td>
</tr>
<tr>
<td>Total</td>
<td>7.28 ± 5.72</td>
<td>5.01 ± 4.77</td>
</tr>
</tbody>
</table>

Table 5: 95% Error from 0-View overall target alignment analysis
VI. DISCUSSION

V. DISCUSSION

We see that when all target motion is tracked, as is the case with Xsight Lung tracking (2-view tracking), the errors are quite small. The average RMS tracking error for Xsight Lung was $1.61 \pm 0.64$ mm, with a 95% value of $2.43 \pm 0.87$ mm (see Table 1). In addition our results show that 64/100 test cases had sufficient visibility of the tumor in both images for this tracking mode to be possible.

The tumor was found to have sufficient visibility in at least one image for the 1-View method to be possible in 81/100 cases. In this case, the tracking error for Xsight Lung within the tracking plane (the in-plane error) is shown in Table 2 to have an RMS value of $1.39 \pm 0.63$mm, with a 95% value of $2.20 \pm 0.91$ mm. The out of plane alignment errors, as shown in Table 3, were larger than the in-plane tracking errors as expected. In this untracked direction, the RMS error value was $3.55 \pm 2.52$ mm, with a 95% value of $4.45 \pm 4.37$ mm.

0-View tracking was found to be the only possible option in the remaining 19/100 cases, because there was insufficient tumor visibility in both images. In this case the target alignment errors are larger than the two previous methods as expected. These results are shown in Tables 4 and 5. The RMS alignment error was $6.50 \pm 4.10$ mm, and the 95% value was $11.18 \pm 7.13$ mm. It is important to recognize that the treatment data on which both the 0-View and the 1-View out of plane target alignment analysis was based on using implanted fiducial markers for target tracking, with the addition of an initial spine alignment that was vital for this study but was not used for the treatment itself. It is possible that in some cases there was gross patient movement between the spine alignment step and the fiducial-based treatment. This effect would cause the values we report for 0-View target alignment error and 1-View out of plane alignment error to be artificially increased – when 0-View and 1-View tracking modes are used clinically, the spine alignment is an initial step that is used for treatment, and clinical users ensure that there is no gross patient movement between spine alignment and treatment (in the case of 0-View, the spine alignment is also periodically checked and automatically corrected during treatment).

There are several published papers (15, 16, 17, 18) discussing the phenomena of intra- and inter-fraction ITV drift, and comparing the alignment transformation given by direct alignment on the ITV using a pre-treatment cone-beam CT or planar MV portal imaging with the transformation given by alignment using bony structures. These studies can be compared with our results for 0-View target alignment, since the basic alignment process is similar. Sonke (18) notes that the earlier studies typically used portal imaging for manual bony structure alignment, and this could be an explanation for the larger ITV alignment errors given (e.g., Purdie (16) gives an average of 6.8mm) when compared to Sonke’s average error of 4.1mm using a semi-automatic rigid registration algorithm to match the treatment cone-beam CT to the planning CT.

However, our analysis gives a value closer to that of Purdie, with 6.5mm 0-View target alignment error on average. Considering the possibility that our results were artificially increased because of gross patient motions explained above, our results are likely to fall somewhere between the values predicted by Sonke and Purdie. It is worthy of note that the 95% values reported for 0-View alignment error are quite large, which is fundamentally in agreement with, although slightly lower than Purdie (16) who gave a 90% value of 13.9 mm for overall ITV alignment error.

VII. CONCLUSIONS

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We have used retrospective clinical data from lung patients treated with implanted fiducials to analyze the in-plane and 3D accuracy of the Xsight® Lung algorithm, and also to quantify the effects of intra-fraction and inter-fraction ITV drift. When Xsight Lung Tracking was possible (64/100 cases in this study) the 3D RMS tracking algorithm error is just $1.66$mm averaged over the population, with an average 95% error of $2.44$mm.

In agreement with existing studies (15, 16, 17, 18), we have found that when direct tumor tracking is replaced with spine alignment and a fixed offset from the spine to the tumor then the overall ITV alignment error between planning and treatment can be significant, with a 3D RMS error averaged over the population of $6.5$mm and 95% error of more than 10mm. However, when the tumor is tracked in one projection X-ray image, as was possible in 81 of 100 test cases in this study, there is then only one axis of uncertainty, and the alignment error is markedly reduced, giving a 3D RMS error of $3.6$mm and 95% value of $4.5$mm on average in the untracked direction.
VII. CONCLUSIONS

(reducing to 1.4mm and 2.2mm respectively in the tracked directions). For this reason, we hypothesize that 1-View tracking may be an attractive alternative in many cases when compared to systems that provide alignment on the ITV using a pre-treatment volumetric image (cone beam or 4D CT), when these systems must still treat the entire ITV which must encompass a range of motion >10mm in many cases.

As with any radiation treatment, it is important that appropriate margins are applied to the CTV to account for internal motion and set-up uncertainties. In this case, the data presented in Tables 1-5 should provide useful input data to whichever margin recipe is considered appropriate, as a function of tracking method and margin direction. It should be noted that this data should be combined with other uncertainties in the treatment delivery procedure, such as those demonstrated by End-to-End test, to arrive at the appropriate margin.

In comparing 0-View tracking to gantry-based systems, it is clear that the gantry-based approach gives the advantage of direct alignment on the target, but the CyberKnife® System performs periodic correction for intra-fraction patient motion, unlike competing systems. Also, it should be reiterated that for some cases, particularly tumors near the mediastinum, accuracy is of utmost importance in order to be able to treat with sufficient dose to achieve local control but without introducing complications due to overdose to critical structures. In these cases, the CyberKnife technology with bronchoscopic fiducial placement and full motion compensation may be the only clinically viable method of treatment. Fiducial placement and full 3D motion tracking remains an option for any patient, and the Simulation procedure is a valuable tool that can be used together with the clinical details of each case to guide this decision.

Finally, retrospective analysis on 100 patients has revealed that with the most current version of the Xsight Lung algorithm, 64% of the cases examined could undergo successful target tracking in both views, and 81% of the cases could undergo successful in-plane target tracking in at least one of the views. These results support the hypothesis that for a significant majority of patients treated, 2-View or 1-View tracking will be successful, hence allowing a treatment that takes advantage of the motion tracking and compensation ability that is unique to the CyberKnife System without the need for fiducial implantation.

REFERENCES

**Xsight Lung 3D Tracking Accuracy**

For those cases in which the treatment target could be located in both X-ray images, the following procedure was employed to derive the 3D tracking accuracy:

1. Localize the fiducials in the planning CT. Take the centroid of the fiducial positions to give $F_{CT}$.
2. Delineate the GTV in the planning CT. Take the centroid of the GTV, as determined by the MultiPlan® Treatment Planning System to give $GTV_{CT}$.
3. Calculate the offset between the GTV and fiducial centroids as $offset_{CT}$.
4. For each X-ray image taken during treatment, localize the fiducials and find the fiducial centroid in each image to give 2D positions $F_A$ and $F_B$.
5. Combine the positions $F_A$ and $F_B$ to give the 3D position of the fiducial centroid $F$.
6. Derive the estimated position of the target $T=F+ offset_{CT}$.
7. Use the target localization algorithm in the two images to give two estimated target positions $L_A$ and $L_B$.
8. Combine the estimated target positions $L_A$ and $L_B$ to give a 3D target position $L$.
9. Record the 3D tracking accuracy as the magnitude of the vector $T - L$.

**1-View In-Plane Tracking Accuracy**

The following procedure was used to determine 1-View in-plane tracking accuracy:

1. Localize the fiducials in the planning CT. Take the centroid of the fiducial positions to give $F_{CT}$.
2. Delineate the GTV in the planning CT. Take the centroid of the GTV, as determined by the MultiPlan® Treatment Planning System to give $GTV_{CT}$.
3. Calculate the offset between the GTV and fiducial centroids as $offset_{CT}$.
4. For each X-ray image taken during treatment, localize the fiducials and find the fiducial centroid in each image to give 2D positions $F_A$ and $F_B$.
5. Combine the positions $F_A$ and $F_B$ to give the 3D position of the fiducial centroid $F$.
6. Derive the estimated position of the target $T=F+ offset_{CT}$.
7. Project $T$ into the two images to give 2D the positions $T_A$ and $T_B$.
8. Use the target localization algorithm in the two images to give two estimated target positions $L_A$ and $L_B$.
9. Derive the 2D error vectors in each image, $E_A = L_A - T_A$ and $E_B = L_B - T_B$.
10. Scale the error vectors back to the the imaging plane. If $D_A$ and $D_B$ are the distances from sources A and B to detectors A and B respectively, and $I_A$ and $I_B$ the distances from sources A and B to the imaging isocenter, then the reported errors are $E_A^* = \frac{I_A}{D_A} E_A$ and $E_B^* = \frac{I_B}{D_B} E_B$.

**1-View Out of Plane Alignment Accuracy**

In order to calculate 1-View out of plane alignment accuracy, we used the following steps (the example given is for 1-View tracking in which the untracked direction is the source-detector axis of image A: Figure 11):

1. Record the CT position of the spine alignment center.
2. Record the positions $P_1$ and $P_2$ of the fiducial centroid in the primary and secondary (exhale and inhale) CT volumes. For cases with only a single CT, we instead use the positions of the fiducial centroid in exhale and inhale phase while the respiratory model is being built at the start of the first fraction.
3. Project the positions $P_1$ and $P_2$ onto the source-detector axis to give points $P_1A$ and $P_2A$.
4. For each pair of live images, localize the fiducial centroid and derive its 3D position.
5. Use the spine alignment plan and subsequent couch shift to render the fiducial centroid into the CT coordinate system, giving position $P_{sA}$.
6. Project the position $P_{sA}$ onto the source-detector axis to give point $TA$.
7. Measure the distance $\epsilon_A$ from $TA$ to $\frac{1}{2} (PA_1 + PA_2)$.
8. The metric of interest is $\epsilon_A$, relative to $\frac{1}{2} (PA_1 + PA_2)$, i.e., how much expansion, if any, would be necessary along the source-detector axis to include point $TA$. 

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**APPENDIX A: DERIVATION OF TRACKING ACCURACY RESULTS**
**0-View Overall Target Alignment Accuracy**

We employed a similar approach to the 1-View out of plane error analysis in order to determine the effect of inter- and intra-fraction drift and change in breathing pattern on the alignment of the planning ITV with the target position during treatment. We used the following steps (Figure 12):

1. Record the CT position of the spine alignment center.
2. Record the positions $P_1$ and $P_2$ of the fiducial centroid in the primary and secondary (exhale and inhale) CT volumes. For cases with only a single CT, we instead use the positions of the fiducial centroid in exhale and inhale phase while the respiratory model is being built at the start of the first fraction.
3. For each pair of live images, localize the fiducial centroid and derive its 3D position.
4. Use the spine alignment plan and subsequent couch shift to render the fiducial centroid into the CT coordinate system, giving position $P_{fid}$.
5. Measure the distance $\varepsilon_0$ from $P_{fid}$ to the closest point to $P_{fid}$ on the line segment joining $P_1$ and $P_2$.
6. The metric of interest is $\varepsilon_0$ and also the components in the patient cardinal directions of the vector giving rise to $\varepsilon_0$. These components determine how much expansion in each of the cardinal directions would be necessary to include point $P_{fid}$.

![Figure 11: Out of plane error estimation for 1-View tracking](image1)

![Figure 12: Estimation of 0-View overall target alignment error](image2)

The information provided in this report is intended for background and educational purposes only as it relates to the CyberKnife System. The information contained herein is not intended, nor should it be construed, as advocating the acquisition or purchase of a CyberKnife System. Please direct any questions or comments to the contact information below.