Chapter-9

Magnitude of shift of tumor position as a function of moderated deep inspiration breath hold: an analysis of pooled data of lung patients with active breath control in image guided radiotherapy.

9.1. Introduction:

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9.1. Introduction:

Respiratory motion studies have tracked the movement of the tumor, the host organ, radiographic fiducial markers imbedded at the tumor site, radioactive tracers targeting the tumor, and surrogate organs, such as the diaphragm, which are assumed to correlate with the tumor.

To reduce the target margin error due to the respiratory motion various respiratory motion control treatment techniques including gating, \cite{1-3} breath holding \cite{4} or active breathing control (ABC) \cite{5,6} are used in radiotherapy. A precise breathing monitor system is needed for such techniques. The most commonly used systems are:

The Spirometer to measure the change in the lung volume, measurement of the surface of the abdomen by tracking a reflective marker on the chest with a fixed camera \cite{2,7-10} or by measuring the distance from a fixed point to the surface of the abdomen using a laser-based distance sensor \cite{1} and by tracking internal markers using x-ray \cite{11-15} or internal sensors using magnetic fields \cite{16}.

Stereotactic radiotherapy (SRT) in the treatment of lung tumors has been shown to have good results and low morbidity \cite{17-18} and has been supported by various methods using immobilization devices \cite{19} or coordinating systems for respiratory motion. To reduce respiratory motion during IGRT for lung or liver tumors and improve feasibility for IGRT in elderly patients or patients with pulmonary dysfunction we used deep inspiration breath-hold method. Reproducibility of organ position, especially diaphragmatic motion is verified in healthy volunteers by others. \cite{20} However, the diaphragm position does not necessarily reflect the lung tumour position directly, especially for tumors in the lower lobe, due to the complexity of tumour motion in a clinical setting. \cite{21} Because of this from June 2007, we
have used the 2D-2D match analysis of bone landmarks method in IGRT for lung tumours clinically and directly verified the interbreath-hold reproducibility of tumour position using CT scans before the treatment.

9.2. Methods and Materials

9.2.1. Active Breathe control System

It consists of Patient respiratory system, which again consists of mouthpiece, transducer turbine, ballon valve coupler etc, Mirror support system, patient control switch, RS-232 cable, control computer and PC extender system transmitter [Figure-1].

Figure-1: Active breathe control system

9.2.2. Patient background

Eight patients with lung cancer are treated with RT on study from March 2007 to Jan 2008 [Table-1]. All tumours are delivered 5 Gy per fraction at the isocenter, and the total dose is 50 GY with ten fractions, with a Deep inspiration breath-hold method using spirometer-based monitoring. The median age is 62 years (range from 47 years to 82 years). Five patients are male and three are female. Six patients are diagnosed with primary lung cancers and two patients had double primary lung cancers. The median tumour volume is 69 cc (ranging 10.33 cc to 149.13 cc). Tumor location is as follows: Two tumors in the right
upper lobe (RUL), two tumors in the right middle lobe (RML), four tumors in the right lower lobe (RLL), two tumors in the left upper lobe (LUL). All tumors are peripheral lung tumors and are not adjacent to other organs, such as the chest wall or heart.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Gender</th>
<th>Tumor size (CC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>53</td>
<td>M</td>
<td>52.61</td>
</tr>
<tr>
<td>2</td>
<td>65</td>
<td>F</td>
<td>118.49</td>
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<tr>
<td>3</td>
<td>69</td>
<td>M</td>
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</tr>
<tr>
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<td>70</td>
<td>M</td>
<td>35.77</td>
</tr>
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<td>5</td>
<td>55</td>
<td>M</td>
<td>115.7</td>
</tr>
<tr>
<td>6</td>
<td>47</td>
<td>F</td>
<td>10.33</td>
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<td>7</td>
<td>82</td>
<td>M</td>
<td>19.01</td>
</tr>
<tr>
<td>8</td>
<td>55</td>
<td>F</td>
<td>51.03</td>
</tr>
</tbody>
</table>

Table-1: Patients underwent IGRT with ABC

9.2.3. The deep inspiration breath-hold method using spirometer-based monitoring in Active breath control system

Here we described the procedure of the Active breath control method using a spirometer.

A reproducible state of maximum breath-hold (deep-inspiration breath-hold [DIBH]) is advantageous for treating thoracic tumors, because it significantly reduces respiratory tumor motion and changes internal anatomy in a way that often protects critical normal tissues. The pneumotach spirometer is a differential pressure transducer that measures air flow; a computer program integrates the signal to obtain the volume of air breathed in and out, which is displayed and recorded as a function of time. To monitor the respiratory
phase and breath-holding phase, the patient breathed through a mouthpiece connected to a pneumotachometer. The other end of the pneumotachometer is attached to a spirometer to assist the breath hold. A nose clip is used to prevent nasal breathing and ensure that the patient breathed through the mouthpiece. For patient set-up, we used All in One (AIO) (POCL, USA) immobilization system [Figure-2].

![Patient with AIO immobilization. A mouthpiece connected to the spirometer for mDIBH](image)

Figure-2: Patient with AIO immobilization. A mouthpiece connected to the spirometer for mDIBH

The workstation shows the spirometry signal, yielded the respiratory tidal volume of the patient and is able to display a flow–time curve which can show the state of inspiration, expiration and breath-hold [Figure-3]. Patients are familiarized with the procedure before the treatment with training sessions. Threshold limit is taken as 80% of the maximum value of the deep inspiration. On an average 20 seconds are taken as time duration for to hold the breath.
9.2.4. CT scan procedure

The largest intra-fraction motion observed is respiratory motion. CT scans (Somatom, Siemens, USA) are performed at the breath-holding (the Moderated deep inspiration) phase. Set-up is also performed at the treatment position. Images are acquired with moderate deep inspiration breath hold (mDIBH) and are sent to three-dimensional (3D) Treatment planning system (CMS XIO Planning system, USA). Slice thickness and interval are 2 mm and 2 mm, respectively.

9.2.5. Target delineation and data analysis:

Target delineation is performed on a 3D treatment planning system. Physician delineated the target volume on the axial CT slices using lung CT window settings. Pleural indentations are included within the target. MRI and PET CT are used for delineation.

9.2.6. Shift verification:

Digital Reconstructed radiographs from planning system are used to compare the images taken from iView-GT for tumor position and potential motion during ABC in treatment room using 2D-2D matching tool for the bony landmark [Figure-4]. Daily patient position can be corrected based on accurate 4-D data at the time of radiation delivery. Portal images
are taken five times with the same threshold that we used for scanning during one treatment delivery.

Figure-4: Comparison of DRR’S from TPS to iViewGT

This procedure is chosen to measure the reproducibility that can eliminate any external set-up errors, and thus all tumour displacement would be a measure of internal motion only. The deviation is measured and displayed in graph as shown in [Figure-5 to Figure-11].

During an ABC procedure, a specifically designed device is utilized to reproducibly apply the same breath-holding level for each session. After a predefined volume of air (threshold volume) has passed through the spirometer, a small balloon valve will inflate and occlude the tube, applying an assisted breath hold (BH). The system is configurable to each individual patient or procedure, with variable threshold levels and BH durations possible. For the same value of Threshold, the shifts in x, y and z directions of target are noticed and tabulated. This is done with the help of AP and lateral DRR's comparison with 4D-CT DRR's using 2D-2D match tool in iView-GT. The treatment table is moved to match DRR’S and began treatment delivery.
9.3. Results: A total of 80 fractions of radiation are delivered using ABC breath holds. Our study pertains to 40 observations taken @ 5 mDIBH per patient in one of the treatment fractions. Intrafraction motion of the tumor is observed on DRR during ABC breath holds upto 3.2 mm. The maximum shifts in x, y and z directions are 3 mm, 3.2 mm and 2.9 mm respectively, indicating a change of tumor position over the course of treatment with breath holds at the same phase of the respiratory cycle (mDIBH) with same value of threshold.

9.4. Discussion

Good reproducibility of the tumour position has been reported in all kinds of breath-hold methods. Cheung et al\textsuperscript{25} reported that the interfraction reproducibility of the tumour position with the active breath control (ABC) device, which temporary immobilizes the patient's breathing, and the average displacement of the GTV center is 0.3 mm (±1.8 mm), 1.2 mm (±2.3 mm), and 1.1 mm (±3.5 mm) in LR, AP and CC directions, respectively.

According to Cheung PC et al, the average (+/- standard deviation) displacement of GTV centers with ABC breath hold applied is 0.3 mm (+/- 1.8 mm), 1.2 mm (+/- 2.3 mm), and 1.1 mm (+/- 3.5 mm) in the lateral direction, anterior-posterior direction, and superior-inferior direction, respectively\textsuperscript{26}.

The DIBH manoeuver is found to be highly reproducible, with intra breath-hold reproducibility of 1.0 (+/- 0.9) mm and inter breath-hold reproducibility of 2.5 (+/- 1.6) mm, as determined from diaphragm position. Patients are able to perform 10-13 breath-holds in one session, with comfortable breath-hold duration of 12-16 s\textsuperscript{27}.

In our study, the shift in the tumor position is 3.2 mm, 3.0 mm and 2.9 mm in CC, LR and AP directions respectively by using the moderated deep inspiration technique by matching
bony anatomy from TPS to iViewGT threw DRR’s. These results are similar to the results of other reports with breath-hold methods. Seppenwoolde et al \textsuperscript{21} demonstrated that the trajectory of the tumour during inhalation is different from the trajectory during exhalation, i.e. hysteresis, by analyzing the 3D motion of lung tumours during radiotherapy using a real-time tumour tracking system, and suggested the complexity of tumour motion, especially that of tumours in the lower lobe. Our study suggested that our method would be effective for temporary immobilization of respiratory motion in the lower lobe and in the upper lobe.

We have to pay more attention to the patient training sessions and monitoring of respiratory motion during treatment. The advantage of our method is feasibility in many patients and adaptability by many institutions because patients are able to hold their breath more comfortably at the deep-inspiration phase. One more advantage of this study is a single time CT with ABC is sufficient instead of taking CT scans 4 to 5 times to study the intrafraction movement of the tumor. In our experience, this method is very much feasible for elderly patients also.

We calculated geometric uncertainties of the tumour position from our results. There have been many reports focused on the geometric uncertainties of the set-up \textsuperscript{28-31}; however, there are few reports focused on the geometric uncertainties of internal organs or tumour motion. Stoom et al \textsuperscript{22} calculated the geometric uncertainties of lung cancer patients. In this study, systematic deviations are 2 mm, 3 mm and 3 mm in LR, AP and CC directions, respectively, and random deviations are 4 mm, 5 mm and 5 mm in LR, AP and CC directions, respectively [Table-2]. However, it is considered meaningful to have obtained the reproducibility of the tumour position (x, y, z, vectors) as well as systematic and
random motion deviations by our breath-hold method, and we believe that the internal margin of the interbreath-hold reproducibility of lung tumour position would be within almost 5 mm in vector for the treatment planning of IGRT or SRT due to the relatively good reproducibility of our method.

<table>
<thead>
<tr>
<th>S.NO</th>
<th>Threshold</th>
<th>Volume of air Inhalation(Liters)</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5</td>
<td>1.75</td>
<td>13.2</td>
<td>-7.6</td>
<td>2.7</td>
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<tr>
<td>2</td>
<td>1.5</td>
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<td>12.6</td>
<td>-3.5</td>
<td>3</td>
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<tr>
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<td>1.9</td>
<td>11.6</td>
<td>-4.6</td>
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</tr>
<tr>
<td>4</td>
<td>1.5</td>
<td>2</td>
<td>12.6</td>
<td>-4.8</td>
<td>5.6</td>
</tr>
</tbody>
</table>

Table-2: Deviations in X, Y and Z directions for patient-1.

9.5. Conclusion: Even though we are using very sophisticated instruments like active breathe control systems for to control the moving targets there is still some interfraction variations in the position of the tumor. Daily tumor targeting of lung cancers are feasible with the help of DRR’s from planning system when compared with DRR’S from iView-GT. Much accuracy needed when we go for hypo fractionation. Due to these reasons we studied the intrafraction variations by using mDIBH in a single fraction for 5 times on eight patients. In our study we have taken the DRR’S of the bony anatomy as reference. We compared the DRR’s from the TPS to the DRR’s from the iViewGT in selected gating phase. Our data demonstrate good intrafraction reproducibility of lung tumor position using ABC with same value of threshold limit.

Patient cannot inhale same amount of air every time even though the threshold value is kept
the same. As the volume of inhalation is different for each duration the maximum shift observed is less than 4mm. For maximum difference of inhaling volume there is a need for observing the shift. The results that are obtained are closer with other author's results that compared TPS Data to the iViewGT data by using soft tissues, external markers and internal permanent markers. If this shift is less than permissible level we can continue treatment other wise new session of mDIBH should start. Also 5mm margin has to give while contouring itself for compensating the magnitude of the shift of tumor position with respect to mDIBH. This procedure is going to give us better and more accurate treatment. Finally we can conclude that, the moderated deep inspiration breath-hold method with a spirometer is feasible, with relatively good reproducibility of the tumor position for Image guided radiotherapy in lung cancers.

![Graph showing shifts with respect to volume of air inhalation in AP DRR](image)

**Figure-5:** Shift with respect to volume of air inhalation in AP DRR (Patient-1)
Figure-6: Shift with respect to volume of air inhalation in Lat DRR (patient-1).

Figure-7: Shift with respect to volume of air inhalation in Lat DRR (patient-2).

Figure-8: Shift with respect to volume of air inhalation in Lat DRR (patient-3).
Figure-9: Shift with respect to volume of air inhalation in Lat DRR (patient-4)

Figure-10: Shift with respect to volume of air inhalation in AP DRR (patient-5)

Figure-11: Shift with respect to volume of air inhalation in Lat DRR (patient-6)
9.6. References:


