Respiratory management in lung and esophageal cancers

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Treatment Planning - Goals

Deliver maximum dose to the tumor (Increase cure rate)
Reduce dose to the surrounding normal structures (reduce complications)
Target Volumes

ICRU50

• GTV - Gross Target Volume
• CTV - Clinical Target Volume
• PTV - Planning Target Volume

ICRU62

• ICRU Report 62
  • internal target volumes (ITVs) and planning organ at risk
  • volumes (PRVs) in order to account for geometric uncertainties
  • reliable ITVs and PRVs require detailed data on tumor and organ mobility, which are currently largely unavailable.
Organ Motion

- **Interfraction**
  - motion occurs between fractions and primarily is related to changes in patient localization

- **Intrafraction**
  - motion occurs during fractions and primarily is related to respiration
Importance of reducing the CTV to PTV margin

- Conventional: Increases dose to normal tissues, limiting factor for dose escalation
- Accounting motion: CTV – PTV margin reduced
All tumor motion is complex

- Some motion is mostly Anterior / Posterior
- Some motion is mostly Superior / Inferior
- All tumor motion is Complex
PROBLEMS OF RESPIRATORY MOTION DURING RADIOTHERAPY

- If respiratory motion is not accounted
- artifacts during image acquisition
- commonly seen with thoracic CT images
Treatment-planning limitations

- margins need to be large enough to ensure coverage of the target for most of the treatment delivery

- artifacts observed in CT images in which respiratory motion has not been accounted for, the magnitude of margin to allow for respiratory motion is difficult to quantify, particularly for individual patients in whom a wide range of tumor motion is complex
Radiation-delivery limitations

Radiation delivery in the presence of intrafraction organ motion causes an averaging or blurring of the static dose distribution over the path of the motion while inter-fraction motion causes a shift of the dose distribution.
Techniques to treat mobile tumors

Static Tumor

Moving Tumor
No margin

Moving Tumor
with margin

Moving Tumor
Gating
Techniques to treat mobile tumors

Moving Tumor Tracking with CyberKnife

Moving Tumor Tracking with DMLC

Deforming Tumor Tracking with DMLC
a clinical process guide for managing respiratory motion

Respiratory motion management

- If target motion >5 mm – RMM technology is appropriate
- also appropriate when the procedure will increase normal tissue sparing
<table>
<thead>
<tr>
<th>Observer</th>
<th>SI</th>
<th>AP</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barnes: (Ref. 74) Lower lobe</td>
<td>18.5 (9–32)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Middle, upper lobe</td>
<td>7.5 (2–11)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chen (Ref. 73)</td>
<td>(0–50)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ekberg (Ref. 22)</td>
<td>3.9 (0–12)</td>
<td>2.4 (0–5)</td>
<td>2.4 (0–5)</td>
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<td>Engelsman: (Ref. 24)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Middle/upper lobe</td>
<td>(2–6)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lower lobe</td>
<td>(2–9)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Erridge (Ref. 104)</td>
<td>12.5 (6–34)</td>
<td>9.4 (5–22)</td>
<td>7.3 (3–12)</td>
</tr>
<tr>
<td>Ross: (Ref. 60) Upper lobe</td>
<td>-</td>
<td>1 (0–5)</td>
<td>1 (0–3)</td>
</tr>
<tr>
<td>Middle lobe</td>
<td>-</td>
<td>0</td>
<td>9 (0–16)</td>
</tr>
<tr>
<td>Lower lobe</td>
<td>-</td>
<td>1 (0–4)</td>
<td>10.5 (0–13)</td>
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<tr>
<td>Grills (Ref. 80)</td>
<td>(2–30)</td>
<td>(0–10)</td>
<td>(0–6)</td>
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<td>Hanley (Ref. 61)</td>
<td>12 (1–20)</td>
<td>5 (0–13)</td>
<td>1 (0–1)</td>
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<tr>
<td>Murphy (Ref. 77)</td>
<td>7 (2–15)</td>
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<td>-</td>
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<td>Plathow: (Ref. 65) Lower lobe</td>
<td>9.5 (4.5–16.4)</td>
<td>6.1 (2.5–9.8)</td>
<td>6.0 (2.9–9.8)</td>
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<tr>
<td>Middle lobe</td>
<td>7.2 (4.3–10.2)</td>
<td>4.3 (1.9–7.5)</td>
<td>4.3 (1.5–7.1)</td>
</tr>
<tr>
<td>Upper lobe</td>
<td>4.3 (2.6–7.1)</td>
<td>2.8 (1.2–5.1)</td>
<td>3.4 (1.3–5.3)</td>
</tr>
<tr>
<td>Seppenwoolde (Ref. 50)</td>
<td>5.8 (0–25)</td>
<td>2.5 (0–8)</td>
<td>1.5 (0–3)</td>
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<td>Shimizu (Ref. 75)</td>
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<td>6.4 (2–24)</td>
<td>-</td>
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<td>Sixel (Ref. 79)</td>
<td>(0–13)</td>
<td>(0–5)</td>
<td>(0–4)</td>
</tr>
<tr>
<td>Stevens (Ref. 49)</td>
<td>4.5 (0–22)</td>
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</table>
TABLE II. Abdominal motion data. The mean range of motion and the (minimum-maximum) ranges in millimeters for each site and each cohort of subjects. The motion is in the superior-inferior (SI) direction.

<table>
<thead>
<tr>
<th>Site</th>
<th>Observer</th>
<th>Breathing mode</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Shallow</td>
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<tr>
<td>Pancreas</td>
<td>Suramo (Ref. 57)</td>
<td>20 (10–30)</td>
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<tr>
<td></td>
<td>Bryan (Ref. 59)</td>
<td>20 (0–35)</td>
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<tr>
<td>Liver</td>
<td>Weiss (Ref. 66)</td>
<td>13±5</td>
</tr>
<tr>
<td></td>
<td>Harauz (Ref. 67)</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Suramo (Ref. 57)</td>
<td>25 (10–40)</td>
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<tr>
<td></td>
<td>Davies (Ref. 58)</td>
<td>10 (5–17)</td>
</tr>
<tr>
<td>Kidney</td>
<td>Suramo (Ref. 57)</td>
<td>19 (10–40)</td>
</tr>
<tr>
<td></td>
<td>Davies (Ref. 58)</td>
<td>11 (5–16)</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>Wade (Ref. 68)</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Korin (Ref. 64)</td>
<td>13</td>
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<tr>
<td></td>
<td>Davies (Ref. 58)</td>
<td>12 (7–28)</td>
</tr>
<tr>
<td></td>
<td>Weiss (Ref. 66)</td>
<td>13±5</td>
</tr>
<tr>
<td></td>
<td>Giraud (Ref. 63)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Ford (Ref. 76)</td>
<td>20 (13–31)</td>
</tr>
<tr>
<td>Organ/source</td>
<td>Respiratory signal</td>
<td>$N$ patients (measurements)</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Diaphragm SI fluoroscopy</td>
<td>Abdominal displacement</td>
<td>5 (60)</td>
</tr>
<tr>
<td>Tumor and diaphragm, fluoroscopy</td>
<td>Abdominal displacement</td>
<td>43</td>
</tr>
<tr>
<td>Tumor, SI fluoroscopy</td>
<td>Spirometry and abdominal displacement</td>
<td>11 (23)</td>
</tr>
<tr>
<td>Tumor, 3D biplane radiography</td>
<td>Abdominal displacement</td>
<td>26</td>
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<tr>
<td>Lung vessels, cine MRI</td>
<td>Abdominal displacement</td>
<td>4</td>
</tr>
<tr>
<td>Lung tumor, respiration-correlated CT</td>
<td>Abdominal displacement</td>
<td>9 where tumor SI motion $&gt;5$ mm</td>
</tr>
<tr>
<td>Lung tumor, SI respiration-correlated CT</td>
<td>Diaphragm position</td>
<td>12</td>
</tr>
</tbody>
</table>
Respiratory motion management methods

- Motion-encompassing methods
- respiratory gated techniques
- breath-hold techniques
- forced shallow-breathing methods
- respiration-synchronized techniques
Motion-encompassing methods

- Technique that include entire range of tumor motion
  - slow CT
  - inhalation and exhalation breath-hold CT
  - four-dimensional 4D or respiration-correlated CT

RT,IRCH, AIIMS
Slow CT

- peripheral lung tumors
- CT is operated very slowly, and/or multiple CT scans are averaged such that, on average, multiple respiration phases are recorded per slice
- yields a tumor-encompassing volume, with the limitation that the respiratory motion will change between imaging and treatment, and, thus, additional margins are required to account for these variations.

**Disadvantage**
- loss of resolution due to motion blurring, which potentially leads to larger observer errors in tumor and normal organ delineation

- recommended only for lung tumors (mediastinum or the chest wall)
Inhalation and exhalation breath-hold CT

- acquire both inhalation and exhalation gated or breath-hold CT scans
- relies on the patient’s ability to hold his or her breath reproducibly.
- require image fusion and extra contouring.
- For lung tumors, MIP tool can be used to obtain the tumor-motion encompassing volume,
- Advantage over slow scanning method
  - Blurring caused by the motion present during FB is significantly reduced
4D-CT / Respiration-correlated CT

- determines the mean tumor position, tumor range of motion for treatment planning
- can be used to reconstruct inhalation, exhalation, and slow CT Scans
- The MIP tool can be used for obtaining the tumor-motion-encompassing target volume
- Another motion-encompassing method is to derive a single set out of the 4D CT scan where the tumor is close to its time-averaged position. In that case, the expected dose blurring effect of respiration can be accounted for in the CTVPTV margin
QUASAR Respiratory motion motion phantom
Respiratory gating methods

- involves the administration of radiation during both imaging and treatment delivery within a particular portion of the patient’s breathing cycle, commonly referred to as the “gate”

- Displacement gating
  - relative position between two extremes of breathing motion, namely, inhalation and exhalation.
  - the radiation beam is activated whenever the respiration signal is within a pre-set window of relative positions.

- Phase gating
  - respiration signal that must satisfy periodicity criteria
  - the radiation beam is activated when the phase of the respiration signal is within a pre-set phase window.
Respiratory gating methods ...contd..

- Gating using an external respiration signal
  - Real-time Position Management system
  - ExacTrac Gating/Novalis Gating.

- Gating using internal fiducial markers
  - Fiducials 2 mm diameter gold spheres are implanted in or near the tumor using a percutaneous or bronchoscopic implanting technique
  - Fiducial position is tracked in all three dimensions several times a second using a pair of stereotactic kilovoltage x-ray imaging

- Gated IMRT
Varian RPM Gating System
Prospective CT Image Acquisition

Inhalation

Exhalation

CT Scan

Axial scan trigger, 1st couch position

Scan

Axial scan trigger, 2nd couch position

Scan

Axial scan trigger, 3rd couch position

Scan
Retrospective 4D CT Image Acquisition

“Image acquired” signal to RPM system

X-ray on

1st couch position

2nd couch position

3rd couch position

(Ford 2003, Vedam 2003)
Breath-hold methods

- Deep-inspiration breath hold
- Active-breathing control
- Self-held breath hold without respiratory monitoring
- Breath hold in combination with IMRT
Deep Inspiration breath-hold

The patient is asked to take a deep breath and then hold the respiration for a fixed time depending upon on the patient comfortability
Impact of different breathing conditions on the dose to surrounding normal structures in tangential field breast radiotherapy


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ABSTRACT

Cardiac toxicity is an important concern in tangential field breast radiotherapy. In this study, the impact of three different breathing conditions on the dose to surrounding normal structures such as heart, ipsilateral lung, liver and contralateral breast has been assessed. Thirteen patients with early breast cancer who underwent conservative surgery (nine left-sided and four right-sided breast cancer patients) were selected in this study. Spiral CT scans were performed for all the three breathing conditions, viz., deep inspiration breath-hold (DIBH), normal breathing phase (NB) and deep expiration breath-hold (DEBH). Conventional tangential fields were placed on the 3D-CT dataset, and the parameters such as V30 (volume covered by dose >30 GY) for heart, V20 (volume covered by dose >20 GY) for ipsilateral lung and V50 (volume receiving >50% of the prescription dose) for heart and liver were studied. The average reduction in cardiac dose due to DIBH was 64% (range: 26.5-100%) and 74% (range: 37-100%) as compared to NB and DEBH respectively. For right breast cancer, DIBH resulted in excellent liver sparing. Our results indicate that in patients with breast cancer, delivering radiation in deep inspiration breath-hold condition can considerably reduce the dose to the surrounding normal structures, particularly heart and liver.

Key words: Breast cancer, cardiac dose, organ motion
Active Breathing Co-ordinator

A propriety device from Elekta used for holding the respiration for a given time
**Active Breathing Co-ordinator**

Digital spirometer

Balloon valve

Mouthpiece

prevents airflow to and from the patient
Respiratory tracing with ABC
**Procedure**

- Patient is trained for 30 - 45 minutes
- Maximum inspiratory capacity
  - ABC spirometer
- Usually breath-hold threshold level is set at 75 - 80% of IC value for mDIBH
- mDIBH level
  - Chosen as a balance between internal organ displacement and patient comfort
- CT scans
  - Free breathing
  - DIBH
Forced shallow breathing with abdominal compression

- originally developed for stereotactic irradiation of small lung and liver lesions

- the patient is immobilized and positioned using the stereotactic body frame SBF, consisting of a rigid frame with an attached “vacuum pillow” that is custom fitted to each patient.
Real-time tumor-tracking methods

- reposition the radiation beam dynamically so as to follow the tumor’s changing position
- eliminate the need for a tumor-motion margin in the dose distribution

Four steps

- Identify the tumor position in real time
- anticipate the tumor motion to allow for time delays in the response of the beam-positioning system
- reposition the beam
- adapt the dosimetry to allow for changing lung volume and critical structure locations during the breathing cycle.
Advantage of gated radiotherapy

The risk of toxicity is reduced with respiration-gated radiotherapy as compared not gated SRT in lung cancer

*Underberg et al* Benefit of respiration-gated stereotactic radiotherapy for stage I lung cancer: an analysis of 4DCT datasets. IJRO BP 2005
Comparison between rate of pneumonitis at different levels of mean lung dose

Rate Pulmonary Toxicity (%) vs Mean Lung Dose (Gy)

- Oetzel (66)
- Kwa (400)
- Graham (99)
- Hernando (201)
- Yorke (49)
Respiratory motion in oesophageal cancer

- Distal tumors were found to have significantly greater SI and AP motion than proximal or mid-esophageal tumors.

- Margins of 1.5 cm SI, 0.75 cm AP, and 0.75 cm LR would account for respiratory tumor motion of >95% of esophageal primary tumors in the dataset.

- Patel et al., Implications of respiratory motion as measured by four-dimensional computed tomography for radiation treatment planning of esophageal cancer. IJROBP 2009
Oesophageal cancers

- Conformal radiotherapy with respiratory gating for esophageal cancer decreases the irradiated dose to OAR

- DIBH technique should be used when irradiation is performed using the spirometric system

- In Tidal Volume, the inspiration phase is the most favourable and should be chosen for irradiation with a free breathing gating system

Recommended clinical process for respiratory motion during the radiotherapy

- recommended 5 mm motion-limit criterion value may be reduced for special procedures, such as SBRT

- may be reduced in the future as other errors in radiotherapy, such as target delineation and setup error, are reduced, with respiratory motion thereby becoming the accuracy limiting factor.
Conclusion

- The management of respiratory motion in radiation oncology is an evolving field.

- IGRT provides a solution for combating organ motion in radiotherapy.

- Delivering higher dose to tumor and less dose to normal tissue.

- Limited clinical studies, needs to be studied further.

- IGRT – the future of radiotherapy.