3D surface imaging for image guidance in Stereotactic body RT and deep inspiration breath hold RT for left-sided breast cancer

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The Netherlands Cancer Institute - Antoni van Leeuwenhoek hospital
Disclosure

Research collaboration with:
- Elekta Oncology Systems
- VisionRT
- RaySearch Laboratories

Our department licenses software to:
- Elekta Oncology Systems
- Precision X-Ray Inc.
- Xstrahl Ltd.
Acknowledgements

Tanja Alderliesten
Anja Betgen
Rutger Heddes
Joeri Honnef
Corine van Vliet-Vroegindeweiij
Peter Remeijer
Lung SBRT Surveillance
Introduction

SBRT @ NKI-AVL

• 3 fractions of 18 Gy
• Immobilization:
  • Arm supports
  • Knee supports
• 4D-CBCT-guided correction protocol
• Initially non-coplanar IMRT, now VMAT
SBRT Lung: Pre-Alignment
SBRT Lung: Tumor Aligned
Residual Error after Correction

3 consecutive fractions
Intra-fraction Variability

3 consecutive fractions
Time is a significant predictor for both 3D vectors in a linear regression model (p<0.001)
Aim

Validate the use of a 3D surface imaging system for monitoring intrafraction motion in frameless SBRT of lung cancer by comparison with CBCT
Material and Methods

- Speckle projector
- Data camera
- Data camera

3D surface imaging system

Beam on/off detection*

* Black Cat Systems, Westminster, USA
Materials and Methods

- Correction protocol
  - Alignment to room lasers
    - (4D-)CBCT
    - Registration CBCT – Planning CT
      - Local rigid tumor alignment
  - Couch shift
    - (4D-)CBCT for verification
      - Treatment delivery
    - (4D-)CBCT to assess intrafraction variability

3D surfaces were captured during CBCT acquisition
Registrations

- Local rigid registration
  - Correlation ratio as cost function
- ROI
  - Clipbox: bony anatomy
  - Tumor mask (GTV + 5 mm)
  - Surface mask (side treated lung)

---

Materials and Methods

- **Data**

<table>
<thead>
<tr>
<th></th>
<th>Surface vs. CBCT clipbox</th>
<th>Surface vs. CBCT tumor</th>
<th>Surface vs. CBCT surface</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>41</td>
<td>41</td>
<td>32</td>
</tr>
<tr>
<td>Males</td>
<td>34</td>
<td>34</td>
<td>20</td>
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</tbody>
</table>

**CBCT: surface was not always in field of view**
Materials and Methods

- **Bland and Altman analysis – Measuring agreement**
  - Differences in Intrafraction Motion
    - Estimated bias: Mean
    - Random fluctuations: Standard deviation (SD)
  - 95% limits of agreement
    - Mean ± 1.96xSD

*Also known as a Tukey mean-difference plot*
• ROC analysis
  – Binary classifier system (predict: tumor movement ≥ threshold)
  – Point: sensitivity / specificity pair corresponding to threshold
Results

M, Σ, σ

<table>
<thead>
<tr>
<th>Δ intrafraction motion (mm)</th>
<th>Surface vs. CBCT clipbox</th>
<th>Surface vs. CBCT tumor</th>
<th>Surface vs. CBCT surface</th>
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<tbody>
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<td>3D</td>
<td>3D</td>
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<td>Females</td>
<td>M 1.7</td>
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<td>0.2</td>
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<tr>
<td></td>
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<tr>
<td></td>
<td>σ 2.4</td>
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<td>1.9</td>
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<tr>
<td>Males</td>
<td>M 1.9</td>
<td>1.3</td>
<td>0.5</td>
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<tr>
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<td></td>
<td>σ 3.1</td>
<td>3.4</td>
<td>4.0</td>
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</table>
Results

- Bland and Altman analysis

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<th>Δ intrafraction motion (mm)</th>
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<tr>
<td></td>
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<td>3D</td>
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<tr>
<td>Females</td>
<td></td>
<td></td>
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<tr>
<td>Mean</td>
<td>1.8</td>
<td>0.9</td>
<td>0.3</td>
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<tr>
<td>SD</td>
<td>2.6</td>
<td>2.6</td>
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<td>-3.7</td>
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<tr>
<td>Mean+1.96xSD</td>
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<td>4.3</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean</td>
<td>2.4</td>
<td>1.8</td>
<td>0.4</td>
</tr>
<tr>
<td>SD</td>
<td>3.8</td>
<td>4.1</td>
<td>4.1</td>
</tr>
<tr>
<td>Mean-1.96xSD</td>
<td>-5.1</td>
<td>-6.3</td>
<td>-7.5</td>
</tr>
<tr>
<td>Mean+1.96xSD</td>
<td>9.8</td>
<td>9.8</td>
<td>8.4</td>
</tr>
</tbody>
</table>

Results females more promising than results males
Results

- Bland and Altman plots (Females)

CBCT clipbox, CBCT tumor: discrepancy tends to increase with increasing intrafraction motion
Results

- ROC analysis (Females)

### Surface vs. CBCT tumor

<table>
<thead>
<tr>
<th>Threshold (mm)</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<th>7</th>
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<td>9</td>
<td>7</td>
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<td>3</td>
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<td>3</td>
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<td>34</td>
<td>38</td>
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<table>
<thead>
<tr>
<th></th>
<th>FPR</th>
<th>TPR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 mm</td>
<td>0.75</td>
<td>0.79</td>
</tr>
<tr>
<td>3 mm</td>
<td>0.42</td>
<td>0.68</td>
</tr>
<tr>
<td>4 mm</td>
<td>0.31</td>
<td>0.75</td>
</tr>
<tr>
<td>5 mm</td>
<td>0.25</td>
<td>0.60</td>
</tr>
<tr>
<td>6 mm</td>
<td>0.18</td>
<td>0.50</td>
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<td>7 mm</td>
<td>0.15</td>
<td>0.00</td>
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<tr>
<td>8 mm</td>
<td>0.07</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Threshold 4 mm promising prediction model?

### Intrafraction motion - CBCT tumor

<table>
<thead>
<tr>
<th>(mm)</th>
<th>LR</th>
<th>CC</th>
<th>AP</th>
<th>3D</th>
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<tbody>
<tr>
<td>average</td>
<td>0.4</td>
<td>1.3</td>
<td>-0.8</td>
<td>3.1</td>
</tr>
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<td>min</td>
<td>-4.5</td>
<td>-1.1</td>
<td>-5.7</td>
<td>0.4</td>
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<tr>
<td>max</td>
<td>4.7</td>
<td>6.0</td>
<td>4.8</td>
<td>7.7</td>
</tr>
</tbody>
</table>

Alderliesten et al. R&O, 2012
Workflow SBRT Surveillance

1. Align patient to treatment isoc
2. Acquire CBCT scan
3. Register & correct
4. Acquire validation CBCT and simultaneous surface image
5. Determine correction difference and adjust surface isoc
6. Monitor Surface with 4 mm threshold
Introduction

Left-sided breast cancer radiation

- Increased risk for long term heart disease
To decrease the irradiated heart volume

- Voluntary deep inspiration breath hold (DIBH)
During inspiration*:
- Lung volume is increased
- Breast is moved craniocaudally
- Heart is moved caudally

Setup verification (DIBH)
  • CBCT (half scan protocol: 30 sec, arc of 200°)
  • Rigid registration CBCT – planning CT

Dose delivery
  • Lateral fields (DIBH)
  • Medial fields (DIBH)

Monitoring depth breath hold
  • kV fluoroscopy (IMRT segments)
  • MV fluoroscopy EPID (open fields)
Introduction

Disadvantages

- 2D
- Additional imaging dose
- kV source and kV imaging panel at 90 degrees to treatment line
- Monitoring with EPID not possible during IMRT segments
Purpose

Investigate the applicability of a 3D surface imaging system for image guidance in DIBH RT for left-sided breast cancer by comparison with CBCT
Purpose

Patient movement outside tolerance for 1 second
Materials and Methods

Patients (n=20)

- Left-sided breast cancer
- Breast conserving therapy
  - BCS
  - DIBH RT in treatment
    - WBI, n=1
    - SEQ, n=2
    - SIB, n=17
Registration

- Planning CT surface – captured 3D surface
  - Iterative closest point algorithm*
  - ROI defined on reference surface

Registration

• Planning CT– CBCT
  • Local rigid registration
    – Cost function: correlation ratio*
  • ROI defined on planning CT scan
    – Surface left side

Mean residual registration error (RRE)

- RMS distance between
  - planning CT surface (reference)
  - registered CBCT / AlignRT (target) surface

\[
\text{RRE} = \sqrt{\frac{1}{k} \sum_{i=0}^{k-1} \left| p_i^r - T(p_i^t) \right|^2}
\]

Where

- \( p_i^r \) denotes a point in the reference surface
- \( T(p_i^t) \) denotes a point in the transformed target surface
- \( k \) the number of points

- Mean residual setup error after setup correction and shape changes
Mean residual registration error (RRE)

- CBCT surface segmentation (thresholding and smoothing)*

* Honnef, J. et al. ESTRO, 2010
Bland and Altman analysis – Measuring agreement

• Difference between setup errors
  • Estimated bias:
    Mean
  • Random fluctuations:
    Standard deviation (SD)

• 95% limits of agreement
  • Mean±1.96xSD
ROC analysis

- Binary classifier system (predict: movement ≥ threshold)
- Point: sensitivity / specificity pair corresponding to threshold
# Results

## RRE

<table>
<thead>
<tr>
<th></th>
<th>AlignRT – Planning CT</th>
<th>CBCT – Planning CT</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>ROI: both sides</td>
<td>ROI: left side</td>
</tr>
<tr>
<td>RRE (cm)</td>
<td>nr of points</td>
<td>RRE (cm)</td>
</tr>
<tr>
<td>min</td>
<td>0.05</td>
<td>0.03</td>
</tr>
<tr>
<td>max</td>
<td>0.82</td>
<td>0.44</td>
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<tr>
<td>mean</td>
<td>0.23</td>
<td>0.19</td>
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<tr>
<td>stdev</td>
<td>0.13</td>
<td>0.09</td>
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</tbody>
</table>
Results

### RRE

<table>
<thead>
<tr>
<th></th>
<th>AlignRT – Planning CT</th>
<th>CBCT – Planning CT</th>
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<tr>
<td>ROI: both sides</td>
<td>RRE (cm)</td>
<td>nr of points</td>
</tr>
<tr>
<td>min</td>
<td>0.05</td>
<td>92</td>
</tr>
<tr>
<td>max</td>
<td>0.82</td>
<td>526</td>
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<tr>
<td>mean</td>
<td>0.23</td>
<td>230</td>
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<tr>
<td>stdev</td>
<td>0.13</td>
<td>92</td>
</tr>
</tbody>
</table>

- Wilcoxon signed ranks test
  - AlignRT [ROI: left side] < CBCT < AlignRT [ROI: both sides]  \( p<0.001 \)

- No time trends were observed for the RRE values
Results

Bland and Altman analysis

ROI: both sides

ROI: left side
## Results

**Bland and Altman analysis**

<table>
<thead>
<tr>
<th>ROI</th>
<th>cm</th>
<th>LR</th>
<th>CC</th>
<th>AP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both sides</td>
<td>m</td>
<td>0.02</td>
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<tr>
<td></td>
<td>sd</td>
<td>0.31</td>
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<tr>
<td></td>
<td>m-1.96xsd</td>
<td>-0.59</td>
<td>-0.66</td>
<td>-0.57</td>
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<tr>
<td></td>
<td>m+1.96xsd</td>
<td>0.63</td>
<td>0.50</td>
<td>0.29</td>
</tr>
<tr>
<td>Left side</td>
<td>m</td>
<td>0.07</td>
<td>-0.01</td>
<td>-0.15</td>
</tr>
<tr>
<td></td>
<td>sd</td>
<td>0.21</td>
<td>0.21</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>m-1.96xsd</td>
<td>-0.34</td>
<td>-0.42</td>
<td>-0.52</td>
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<tr>
<td></td>
<td>m+1.96xsd</td>
<td>0.48</td>
<td>0.39</td>
<td>0.23</td>
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</table>

ROI left side tighter limits of agreement than ROI both sides
## Results

### ROC analysis (3D movement >= Threshold)

**AlignRT surface (ROI: left side) vs CBCT surface**

<table>
<thead>
<tr>
<th>Threshold (mm)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
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<td>43</td>
<td>47</td>
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</tr>
<tr>
<td>FP</td>
<td>1</td>
<td>6</td>
<td>11</td>
<td>6</td>
<td>23</td>
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<tr>
<td>TP</td>
<td>375</td>
<td>261</td>
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<td>314</td>
<td>272</td>
<td>222</td>
<td>171</td>
<td>143</td>
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<td>43</td>
<td>58</td>
<td>92</td>
<td>130</td>
<td>172</td>
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<tr>
<td>FPR</td>
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<td>0.60</td>
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<td>0.19</td>
<td>0.13</td>
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<td>TPR</td>
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<td>0.98</td>
<td>0.96</td>
<td>0.95</td>
<td>0.91</td>
<td>0.84</td>
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**Graphs**

- **3D Setup Error (mm)**
  - Equation: \( y = 0.84x + 0.92 \)
  - \( R^2 = 0.74 \)

- **True Positive Rate vs False Positive Rate**

---

---
## Results

### ROC analysis (3D movement \(\geq\) Threshold)

<table>
<thead>
<tr>
<th>Threshold (mm)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<th>7</th>
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<td>43</td>
<td>58</td>
<td>92</td>
<td>130</td>
<td>172</td>
</tr>
</tbody>
</table>

### Performance Metrics

- **FPR (False Positive Rate)**
  - Threshold 4-8 mm: promising prediction model?

- **TPR (True Positive Rate)**
  - Threshold 4-8 mm: promising prediction model?

### Graphs

- **3D Setup Error (mm)**

- **True Positive Rate vs False Positive Rate**

Alderliesten et al. IJROBP, 2013
Statistics on Discrepancies

M, Σ, σ in cm and $R^2$

<table>
<thead>
<tr>
<th>ROI</th>
<th>LR</th>
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<th>AP</th>
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<tbody>
<tr>
<td>Both sides</td>
<td>M</td>
<td>0.04</td>
<td>-0.07</td>
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<tr>
<td></td>
<td>Σ</td>
<td>0.29</td>
<td>0.23</td>
</tr>
<tr>
<td></td>
<td>σ</td>
<td>0.14</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>$R^2$</td>
<td>0.33</td>
<td>0.79</td>
</tr>
<tr>
<td>Left side</td>
<td>M</td>
<td>0.08</td>
<td>-0.01</td>
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<td>Σ</td>
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<td>σ</td>
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<td>$R^2$</td>
<td>0.70</td>
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Is the Surface an adequate surrogate for the Tumor Bed?

- 20 breast cancer patients
- Three registration methods:
  - Bony anatomy
  - Breast surface
  - Tumor bed
- Compare residual geometric uncertainties
Boost position variability – Surrogate accuracy

<table>
<thead>
<tr>
<th></th>
<th>No-correction</th>
<th>Bone</th>
<th>Surface</th>
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<tbody>
<tr>
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<td>AP</td>
</tr>
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<td>−3.1</td>
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<tr>
<td>Σ (mm)</td>
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<tr>
<td>σ (mm)</td>
<td>2.6</td>
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</tr>
<tr>
<td>Margin</td>
<td>8.3</td>
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<td>7.7</td>
</tr>
</tbody>
</table>

Margin = 2.5Σ + 0.3σ

Topolnjak et al. IJROBP 2008
Relative Surface surrogate benefit

Topolnjak et al. IJROBP 2008
Is the Surface Correlated with the Heart Correlation

- **LR**
  - Equation: $y = 0.60x - 0.12$
  - $R = 0.56$, $R^2 = 0.31$

- **AP**
  - Equation: $y = 0.60x - 0.09$
  - $R = 0.68$, $R^2 = 0.47$

- **CC**
  - Equation: $y = 0.39x - 0.04$
  - $R = 0.62$, $R^2 = 0.38$

- **Planning CT - CBCT**
  - Equation: $y = 0.60x - 0.12$
  - $R = 0.56$, $R^2 = 0.31$
Workflow Breath-hold Monitor

- Align patient to treatment isoc
- Acquire validation CBCT and simultaneous surface image
- Register & correct
  - Determine correction difference and adjust surface isoc
  - Online / Offline
- Monitor Surface
  - PRV margin for the Heart
Conclusions

- Surface imaging promising for SBRT surveillance and breath-hold monitoring
- Male thorax is challenging
- Better integration with other imaging technology for internal anatomy required