Possible Causes for the Reduced Efficacy of US Based Image Guided Treatment of Prostate Cancer with External Beam Radiation Therapy

F. Van den Heuvel Ph.D.¹

Dept of Experimental Radiotherapy, University of Leuven, Leuven, Belgium

AAPM 2010 Philadelphia, 2010
Outline

1. Introduction
2. The Heisenberg Principle
3. Intra–fractional Motion
   - Reconstruction
   - Link the position to a time
   - Patient data
   - Results
4. Ultrasound calibration
5. Conclusions
Introduction

At the end of the 1990s Ultrasound was a popular way to correct inter fractional prostate movement before external radiation therapy.

1. Absolutely no ionizing radiation.
2. Excellent soft tissue contrast.
3. Relatively cheap.

This presentation tries to evaluate its use, why it failed to reach a larger audience and learn lessons to help in future applications of Ultrasound in the treatment of diseases.
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The first implementation

- A well known device was the BAT-ultrasound.
- Standard off-the-shelf ultrasound probe.
- Indexed arm.
- Registration interface for CT and Ultrasound.
The BAT™ Ultrasound

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The Heisenberg Principle

Intra-fractional Motion Reconstruction

Link the position to a time

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Ultrasound calibration

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The BAT™ Ultrasound

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A good idea

- First presentation at AAPM 1997 Milwaukee
- WE-D5-10 The Use of Position Sensing, Ultrasound Imaging, and Dose Distribution Information for Improving Treatment Room Setup Accuracy - R. Campbell, M. Carol, B. Curran, R. Huber, R. Nash, W. Richard, B. Rosen
The first results

**Figure**: Sagittal plane plot of shifts detected using ultrasound positioning
The first results

- More and larger errors than expected were seen!
  - More prostate movement than expected.
  - Errors have large systematic component.
  - Have we been treating our patients wrongly up to that point in time?
  - But we have good clinical results.
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More vendors joined the fray

What is SonArray?

High-Precision Image Guided Patient Positioning System

- Extracranial lesions
  - 3D Stereotactic
    - Prostate
    - Spine
    - All sites

- Intracranial lesions
  - Stereotactic CT
  - All Indications
  - Functional Targets

Figure: Zmed, camera based positioning
More vendors joined the fray

**How Does it Work?**
3D-Ultrasound Acquisition

200+ images acquired in ~10 s

**Figure:** Zmed, camera based positioning, 3D capabilities
Ultrasound for therapy

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Figure: Updated

BAT SXi – Functionality and Features

Alignment Procedure

Volumetric, increased accuracy, increased throughput, user-friendly.
A first objective appraisal

- A comparison of daily CT localization to a daily ultrasound-based system in prostate cancer

- Ultrasound-based stereotactic guidance of precision conformal external beam radiation therapy in clinically localized prostate cancer
  idd. in Urology 55 (1), 2000
A first objective appraisal

Figure: From the first article (educational use all rights IJORBP)
A first objective appraisal

Figure: Let’s get the data in a different format
A first objective appraisal

Figure: A Bland–Altman plot teaches us a little bit more
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- Good correlation between the two systems exists.
- In the sagittal plane a systematic difference occurs.
- Reasons according to the authors:
  - Finite slice thickness of the CT information
  - Transfer of patient from CT to Ultrasound suite.
- In the second article CT and US taken immediately after each other.
- The problems seemed to disappear.
- Conclusions by the authors: Good system (editorial).
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Clinical appraisal

Does a system like this improve the treatment of the patients in the clinic?

Two groups investigating this:

1. Evaluation of ultrasound-based prostate localization for image-guided radiotherapy

Clinical appraisal

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Clinical appraisal

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Clinical appraisal

- Does a system like this improve the treatment of the patients in the clinic?
- Two groups investigating this:
  1. Evaluation of ultrasound-based prostate localization for image-guided radiotherapy
  2. Independent verification of ultrasound based image-guided radiation treatment, using electronic portal imaging and implanted gold markers.
Table 1. Numeric analysis of 92 alignments

<table>
<thead>
<tr>
<th>Direction</th>
<th>Marker (mm)</th>
<th>BAT (mm)</th>
<th>Directed difference (mm)</th>
<th>Absolute difference (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP (CU)</td>
<td>-0.9 ± 3.9</td>
<td>-0.7 ± 5.2</td>
<td>0.2 ± 3.7</td>
<td>2.7 ± 2.5</td>
</tr>
<tr>
<td>SI (CO)</td>
<td>0.1 ± 3.9</td>
<td>2.7 ± 4.5</td>
<td>2.7 ± 3.9</td>
<td>3.7 ± 2.9</td>
</tr>
<tr>
<td>Lateral (CR)</td>
<td>0.2 ± 3.4</td>
<td>1.8 ± 3.9</td>
<td>1.6 ± 3.1</td>
<td>2.7 ± 2.1</td>
</tr>
</tbody>
</table>

Abbreviations: CU = couch up; SI = superoinferior; CO = couch out; CR = couch right.
Data presented as average ± SD couch shifts for all three directions.
Couch moves according to marker information compared with those according to the BAT system.

**Figure:** In patient treatments, the systematic shifts again are important
Figure: In patient treatments, the systematic shifts again are important
**Introduction**

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**Figure:** In patient treatments, the systematic shifts again are important

<table>
<thead>
<tr>
<th></th>
<th>( \Sigma_{\text{base}} )</th>
<th>( \sigma_{\text{base}} )</th>
<th>( \Sigma_{\text{US}} )</th>
<th>( \sigma_{\text{US}} )</th>
<th>Margin (base)</th>
<th>Margin (US)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC</td>
<td>5.05</td>
<td>1.13</td>
<td>6.67</td>
<td>1.26</td>
<td>10.39</td>
<td>14.56</td>
</tr>
<tr>
<td>LL</td>
<td>3.04</td>
<td>0.82</td>
<td>2.74</td>
<td>1.17</td>
<td>5.17</td>
<td>4.67</td>
</tr>
<tr>
<td>AP</td>
<td>5.04</td>
<td>1.49</td>
<td>3.68</td>
<td>0.78</td>
<td>10.64</td>
<td>6.75</td>
</tr>
</tbody>
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Possible Explanations

- The Heisenberg Principle
- Intra fractional motion
- The human body is different from a calibration phantom
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Possible Explanations

- The Heisenberg Principle
- Intra fractional motion
- The human body is different from a calibration phantom
Due to the measurement the system that is being measured is affected reducing the possible accuracy of the measurements.

- Pressure of the transducer changes the position
- The natural relaxation of the prostate is interrupted
Assessing Intrafractional motion

- Does the prostate move significantly between measurement and treatment?
- Does the prostate move significantly during the treatment?
Figure: Subsequent images for IMRT treatment of the prostate after Intensity map subtraction and display enhancement. The horizontal lines are due to a slight misalignment of the MLC leafs in the open image with respect to the treatment image.
Automated marker detection

**Figure:** After MEK filter as proposed by Nederveen et al. We use the a priori knowledge of the 3D configuration of the markers to select the best candidates.
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**Reconstruct**

**Figure:** Combining the projection line by determining the point of the closest distance of the projection lines of point candidates
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Figure: Marker Match, at \( T = T_0 \) we lose the information on patient movement
**Figure:** After marker match and analysis the patient is shifted. This part can take some time. After that can start the treatment and an image can be obtained, the image obtained after the first field is given has a time stamp $T_1$. 
Figure: Images obtained during treatment. Combination of images provides positional information at times $T_2$, $T_3$, $T_4$, and $T_5$. The timing information is provided by the computer that tags each image with a time stamp.
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The Heisenberg Principle

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Application to patients

- 27 patients
- A total of 4475 images converted and analyzed
- Detection efficiency of >99% (statistics from 16 patients).
- Time stamps from 101 to 1821 seconds (mean 325 seconds)
  - Rpo : 101 to 1647 (mean 229)
  - Rao : 143 to 1697 (mean 280)
  - Ant : 200 to 1741 (mean 327)
  - Lao : 242 to 1778 (mean 374)
  - Lpo : 299 to 1821 (mean 428)
Reporting data

- We obtain positional data for the prostate at 4 points (5 if we count the original marker match setting)
- We can use the usual data like mean, standard deviation etc.
- Alternatively we can use single quantity to represent the complete picture for all patients.
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Results

Margins needed to treat the target as proposed by van Herk and Stroom:

\[ M = 2.5\Sigma + 0.7\sigma \]  

Not a complete picture as this is only valid for the position of the target with interfractional movement. A misalignment in only one of the fields does not have the same value as for the complete treatment.

The numbers obtained are an upper limit!
Results

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Results — Problems

What happens if there is movement in between the fields?

- Is the reconstruction still OK?
- A phantom containing 4 seeds in a clinical configuration was moved along a straight line in the sagittal plane. This in between every field of a 5 IMRT treatment
- Reconstructing the position of the Center of Mass of the seeds and compared to the ground truth.
Results — Problems

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Caveats Movement between fields

Figure: What happens if there is movement in between the fields
A proposal by Kotte et al. (IJROBP 2007) is to assume that the movement of the projection ray is minimal between two fields and that there is a minimal path between the two projection rays.

- This assumption allows an analytical solution to the problem, but not a correct solution.
- We applied the same methodology, with the difference that we did not assume that the motion between all projection rays should be equal.
- The solution can be found by numerical means.
- This also allows to provide data at an additional point as we can assume motion between the original marker match and the first field.
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Results

![Graph showing margins required to accommodate intrafraction motion](image)

**Figure:** Images obtained during treatment. Combination of images provides positional information at times $T_2$, $T_3$, $T_4$, and $T_5$. The timing information is provided by the computer that tags each image with a time stamp.

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Link the position to a time

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Conclusions
Conclusions

- We have shown that it is possible to obtain in treatment information.
- The data obtained are in tune with other intra-fractional measurements.
- The time between the different images is important. This is definitely the case in the original setup. A fast kV-MV image pair is therefore the best way to obtain correct positioning information.
- The future
Movie loop of MRI of prostate over one hour, Ghilezan et al. IJROBP
Can we solve it by treating faster?

Poisson Model:

\[ f(k, \lambda t) = \frac{e^{-\lambda t} (\lambda t)^k}{k!} \]

\[ \lambda = 0.1/\text{min}^* \]

\[ P_{\text{shift}} = 1 - f(0, \lambda t) \]

<table>
<thead>
<tr>
<th>Imaging Acquisition</th>
<th>Image Analysis and adaptation</th>
<th>Treatment delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>15% stability gain</td>
</tr>
<tr>
<td>Imaging Acquisition</td>
<td>Image Analysis and adaptation</td>
<td>Treatment delivery</td>
</tr>
<tr>
<td></td>
<td></td>
<td>40% stability gain</td>
</tr>
</tbody>
</table>

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Study shows that the software implementation is a major factor in the timely delivery of the treatment, more so than the difference between RapidArc and regular IMRT treatment. Cfr. timing study j. Verstraete.
Finally some ultrasound physics

Based on the work of D. Fontanarosa (Maastro, Maastricht, The Netherlands)
Time of Flight

**Figure**: In US imaging distances and positions are given by the time of flight of the US pulses
Figure: TOF depends on the Speed of Sound (SOS). The assumed SOS is 1540 m/s
Figure: SOS is a property of the material crossed
Influence of SOS on distances

Figure: $d_1 = c_1 t_1$  

$d_2 = c_1 t_1 + c_2(t_2 - t_1)$ etc…
An example

Figure: 14.6cm total path length
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An example

(a) 3cm fat 1460m/s

(b) 3cm bladder 1520m/s
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An example

(c) 3cm muscle 1590m/s
(d) 3cm prostate 1529m/s

Figure: =14.32cm or 3mm error
Correcting for SOS variations

- We do not know which tissues are crossed a priori.
- SOS change over time
- Local SOS mapping? → need US tomography
- Not really an issue in radiology, but definitely in therapy
SOS dependence

SOS depends on many parameters and is difficult to measure absolutely in human tissues:

- Temperature
- Pressure
- Elasticity
- Variable composition, Water, protein content
- How to characterize tumor
SOS dependence

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How to characterize tumor
SOS depends on many parameters and is difficult to measure absolutely in human tissues:

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SOS dependence

Quantitatively, SOS is a function of compressibility $K$ and density $\rho$

$$c = \frac{1}{\sqrt{K\rho}}$$ (2)
Empirical results of SOS a.f.o. tissue type

Figure:
Figure: $c = 1.12\rho + 0.391\text{m/s} \pm 0.02$
Conclusions

- It is possible to generate corrected US images starting from the CT information
- Caveat: What with changes in the CT?
- Deformable registration in an iterative way?
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Final Conclusions

1. **Speed is important**
   - Speed of treatment start
   - Speed of sound

2. **Measuring accurately with US is more difficult than it seems**

3. **CT information allows to correct**

4. **HIFU (High intensity Focussed US) is a newer modality**

5. **Do we need planning systems and/or more physics involvement in HIFU planning?**
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