Can we deliver the dose distribution we plan in HDR-Brachytherapy of Prostate Cancer?

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List of Content

- ERT versus BRT from Dosimetry Point of View

- Treatment Planning and Dose Calculation

- Treatment Delivery

- Treatment Delivery Verification
Modern Radiation Therapy

The Field / Beam:

ERT

BRT

1: Catheter / Needle

3D
Modern Radiation Therapy

Beam Shaping: Plane

Field

Catheter/Needle/Applicator

- MLC
  - 2.5 mm
  - or
  - 5.0 mm
  - or
  - 10.0 mm

ERT

MLC

- 1.0 mm
- 2.5 mm
- 5.0 mm
- 10.0 mm
- ?? mm

BRT

Klinikum Offenbach GmbH

Akademisches Lehrkrankenhaus der Johann Wolfgang Goethe-Universität Frankfurt am Main
Modern Radiation Therapy

Beam Shaping: Plane

BRT: Catheter/Needle

"MLC"

- 1.0 mm
- 2.5 mm
- 5.0 mm
- 10.0 mm
- ?? mm

Raster / Vector Scanning

\[ p^+ / \text{Ions: Raster Scanning} \]
Modern Radiation Therapy

Dosimetric Kernel

ERT  10:1  BRT

Depth Dose

Depth (cm)

Dose Rate Normalized to 1.0 cm

Radial Distance (cm)

- 10 MV
- 18 MV
- 4 MV
- 6 MV

- 20 keV
- 25 keV
- 30 keV
- 40 keV
- 50 keV
- 60 keV
- 70 keV
- 80 keV
- 90 keV
- 100 keV
- 150 keV
- 200 keV
- 300 keV
- 400 keV
- 667 keV
Modern Radiation Therapy

**Dosimetric Kernel**

**ERT**

**BRT**

Dose Rate Normalized to 1.0 cm

Radial Distance (cm)
Modern Radiation Therapy

Dosimetric Kernel

BRT

Dose Rate Normalized to 1.0 cm

Radial Distance (cm)

0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0

- 20 keV
- 25 keV
- 30 keV
- 40 keV
- 50 keV
- 60 keV
- 70 keV
- 80 keV
- 90 keV

100 keV
150 keV
200 keV
300 keV
400 keV
667 keV

Radial Dose Function g(r)

Radial Distance (cm)

0.0 0.2 0.4 0.6 0.8 1.0 1.2 1.4 1.6

0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0

- 20 keV
- 30 keV
- 40 keV
- 50 keV
- 60 keV
- 80 keV
- 100 keV

r^2 = 0.007
Modern Radiation Therapy

Dose Shaping: Intensity Modulation (2D)

“MLC”: Step & Shoot

ERT

BRT

“Bixel/Beamlet/Segment” ↔ Dwell Position

“MU” ↔ Dwell Time
Modern Radiation Therapy

Dose Shaping

ERT

Energy ⇔ Dwell Position (3D)

BRT

"Multi-Spots"

159 MeV Protons

\[ {}^{192}\text{Ir} \ (400 \text{ keV}) \]
Dose Shaping: Intensity Modulation (3D)

MSS: Step & Shoot

\[ F(\{\vec{r}\}, \{t\}) \]

\[ D(\vec{r}) = F(\vec{r}, \{t\}) * K(\vec{r}) \]
Modern Radiation Therapy

The Field / Beam:

Set-Up of the anatomy (Reconstruction) at the 3D-Reference System of the LINAC. Position of Beams and their configuration (MLC-settings) can then be automatically tracked based on integrated technology into the LINAC (electronics, EPID, kV- or MV-CBCT,...)

**Anatomy:** is reconstructed relative to the Imager Coordinate System (DICOM).

**Beams:** Catheters/needles/Applicators have to be placed and reconstructed by user-driven actions relative to DICOM (Anatomy).

ASDPs (MLC) are not tracked automatically but this assumes firstly the reconstruction of the catheters/applicators. **There is no Imaging of ASDPs delivery with respect to anatomy.**
List of Content

- ERT versus BRT from Dosimetry Point of View
- Treatment Planning and Dose Calculation
- Treatment Delivery
- Treatment Delivery Verification
Workflow

Imaging and Anatomy
Definition

Pre-Planning

Imaging and Implantation
and Treatment Plan

Treatment Delivery
The Role of Imaging in Anatomy Definition and related uncertainty effects can be assumed similar to ERT with the following exceptions:

- Image distortion due inserted applicators (e.g. MR and metallic needles, seed artefacts in CT-imaging, ...)

For BRT there exists the following specific issue: Imaging is also used for Identification and Reconstruction of the Catheters/Needles/Applicators (ERT: Beams). Based on their geometry the possible SDPs and required ASDPs are extracted (ERT: MLC settings, beamlets)
Sources of Uncertainties

Imaging, Fusion/Registration, Contouring

Imaging, Fusion/Registration, RTP: “Beam”- Reconstruction

+δVOIs

+δBeams

+δRTP

+δMachine

RTP: Dose Calculation

Treatment Delivery: Machine + Anatomy + “Beams”
e.g. Gynaecological Implants:
- $\approx 5\%$ in $D_{2\text{cm}^3}$ per mm offset for bladder & rectum
- $< 4\%$ per mm offset for CTV $(D_{90}, D_{100})$

Data available limited to gynaecological and prostate implants!
RTP: Dose Calculation

**Beam Data Entry (TG-43)**

- **Source Strength** $S_K$
- **TG-43 Tables**

**Dose Calculation**

Clinic measures $S_K (k=1)$:
- 1.3% for LDR low Energy
- 1.5% for HDR high Energy

Total Dose Calculation TG-43 ($k=1$):
- 4.4% for low Energy
- 3.4% for high Energy

All values for “Best practice” Uncertainties

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A dosimetric uncertainty analysis for photon-emitting brachytherapy sources: Report of AAPM Task Group No. 138 and GEC-ESTRO

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List of Content

- ERT versus BRT from Dosimetry Point of View
- Treatment Planning and Dose Calculation
- Treatment Delivery
- Treatment Delivery Verification
Treatment Delivery:

I. Machine

“MLC” precision of ± 1.0 mm

Complex geometries:
“MLC” accuracy 2.5 – 4.5 mm

Attention: Dose distribution
Depends not only on the position
but also on the orientation (vector) of the sources

By courtesy of University of Vienna
Evaluation of a TG-43 compliant analytical dosimetry model in clinical $^{192}$Ir HDR brachytherapy treatment planning and assessment of the significance of source position and catheter reconstruction uncertainties

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Treatment Delivery:  
I. Machine

Prostate: 16 catheters & 86 ASDPs ("beamlets/segments")

δBeams (Reconstruction)  
Reconstruction uncertainty of 1.0 mm (....) and 2.0 mm (---)

+ δMachine  
"MLC" / source positioning uncertainty of 1.5 mm along catheter

(....) : ≤ 2% up to 200%,  
≤ 5% above 200%

(---) : ≤ 3% up to 150%,  
≤ 9% above 150%

Even in that case, the impact on DVH calculations is ≤ 3%


Slide 22
Treatment Delivery:  
I. Machine

“MU” - dwell time accuracy of ≈ 30 ms

Effect of Rounding: less than 1%

Effect of “MLC” travelling – finite speed of source drive < 1%
Treatment Delivery:
II. Anatomy and Catheters/Applicators

\[ \delta \text{VOIs} + \delta \text{Beams} \]

Between:
- Plan & Delivery
- During Delivery
- Fraction to Fraction (Interfractional: single implant & multiple fractions)

\[ \delta \text{Dose} \]

\[ \text{Delivery} \]
Almost all published data available are based on pre-treatment imaging for the purpose of investigating anatomy & implant changes and thus of potential errors for following workflows (mainly gynaecological and prostate implants):

- Multi-fractions delivery with a single implant
- Multi-implants with single or multi factions delivery per implant
Treatment Delivery

- Multi-fractions delivery with a single implant
Dosimetric effect of interfractional needle displacement in prostate high-dose-rate brachytherapy

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ABSTRACT

PURPOSE: To quantify the dosimetric deviations that would arise from delivering subsequent prostate high-dose-rate fractions with only needle readjustment and no replanning after the first fraction.

METHODS AND MATERIALS: Patients were treated with either two implant sessions (two 9.5-Gy fractions per session) separated by 2–4 weeks or with one implant session and external beam radiotherapy. After needle placement, needle positions were adjusted under CT guidance, after which dosimetric planning was performed before each fraction. To evaluate the consequence of not replanning before the second fraction, we analyzed the dosimetric parameters of 45 consecutive implants (26 patients). Needles with optimized dwell positions from the first fraction were transferred to the needle positions in the second fraction. Needle displacement between fractions was assessed as well as changes in plan metrics.

RESULTS: After adjustment, the mean interfractional needle displacement was 3.5 mm. If replanned, the probability of planning target volume \( D_{90\%} \geq 95\% \) is 100%, prostate \( V_{100\%} \geq 95\% \) is 87%, and urethra \( V_{15\%} \leq 10\% \) is 78%. If treated without replanning, the probability of planning target volume \( D_{90\%} \geq 95\% \) is 82%, prostate \( V_{100\%} \geq 95\% \) is 52%, and urethra \( V_{15\%} \leq 10\% \) is 69%. Even for implants with minimal needle displacement (<3 mm) and minimal prostate volume change (<3 cc), the dosimetric consequence of not replanning the second fraction would result in 46% of cases with a prostate \( V_{100\%} < 95\% \).

CONCLUSION: The dosimetric consequences of not replanning the second fraction for prostate high-dose-rate implants results in significantly inferior plan metrics. © 2012 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords: Prostate, HDR brachytherapy; Needle displacement, Dosimetry
Treatment Delivery

- Multi-fractions delivery with a single implant

**δBeam & δVOI**

Table 3
Mean needle and prostate base displacement evaluated based on the planning CT images (slice thickness of 1.25 mm) for Fraction 2 relative to Fraction 1 after adjustment of catheters.

<table>
<thead>
<tr>
<th>Landmark</th>
<th>Mean needle displacement</th>
<th>Prostate base displacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pubic symphysis</td>
<td>−1.4 to 1.3 cm (0.35 cm)</td>
<td>−1.7 to 1.0 cm (0.36 cm)</td>
</tr>
<tr>
<td>Center of markers</td>
<td>−1.8 to 0.9 cm (0.23 cm)</td>
<td>−1.8 to 0.8 cm (0.23 cm)</td>
</tr>
</tbody>
</table>

Negative values indicate displacement in caudal direction, whereas positive values indicate displacement in cranial direction. Number in parenthesis is the mean of absolute displacement values.

**δDose**

Table 5
Probability of obtaining optimal dosimetric parameters for prostate HDR treatment.

<table>
<thead>
<tr>
<th></th>
<th>PTV</th>
<th>Prostate</th>
<th>Urethra</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$D_{99%}$ ≥ 95%</td>
<td>$V_{100%}$ ≥ 95%</td>
<td>$V_{115%}$ ≤ 10%</td>
</tr>
<tr>
<td>With replanning</td>
<td>100%</td>
<td>87%</td>
<td>78%</td>
</tr>
<tr>
<td>Without replanning</td>
<td>82%</td>
<td>53%</td>
<td>69%</td>
</tr>
</tbody>
</table>

HDR = high dose rate; PTV = planning target volume.

a Prostate $V_{100\%}$ ≥ 92% = 98%.

b Prostate $V_{100\%}$ ≥ 92% = 71%.
RESULTS: After adjustment, the mean interfractional needle displacement was 3.5 mm. If replanned, the probability of planning target volume $D_{90\%} \geq 95\%$ is 100%, prostate $V_{100\%} \geq 95\%$ is 87%, and urethra $V_{115\%} \leq 10\%$ is 78%. If treated without replanning, the probability of planning target volume $D_{90\%} \geq 95\%$ is 82%, prostate $V_{100\%} \geq 95\%$ is 53%, and urethra $V_{115\%} \leq 10\%$ is 69%. Even for implants with minimal needle displacement (<3 mm) and minimal prostate volume change (<3 cc), the dosimetric consequence of not replanning the second fraction would result in 46% of cases with a prostate $V_{100\%} < 95\%$.

Conclusion

In this series, the dosimetric consequences of not replanning the second fraction for prostate HDR implants would result in suboptimal dose distributions. Needle adjustment with planning before each fraction resulted in higher quality dosimetry parameters. The findings of this study justify replanning before consecutive prostate HDR fractions.
Prostate cancer brachytherapy

Justification for inter-fraction correction of catheter movement in fractionated high dose-rate brachytherapy treatment of prostate cancer

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ABSTRACT

Background and purpose: Fractionated high dose-rate (HDR) brachytherapy in the treatment of prostate cancer relies on reproducible catheter positions for each fraction to ensure adequate tumour coverage while minimizing dose to normal tissues. Peri-prostatic oedema may cause caudal displacement of the catheters relative to the prostate gland between fractions. This can be corrected for by changing source dwell positions or by physical re-advancement of catheters before treatment.

Materials and methods: Data for 20 consecutive monotherapy patients receiving three HDR fractions of 10.5 Gy per fraction over 2 days were analysed retrospectively. Pre-treatment CT scans were used to assess the effect of catheter movement between fractions on implant quality, with and without movement correction. Implant quality was evaluated using dosimetric parameters.

Results: Compared to the first fraction (F1) the mean inter-fraction caudal movement relative to the prostate base was 7.0 mm (F2) 6.21 mm (range 0–21 mm) and 3.9 mm (F3) (range 0–25.5 mm). PTV D90% was reduced without movement correction by a mean of 17.8% (F2) and 32.3% (F3), compared with 8.1% and 5.1%, respectively, with catheter movement correction. Dose to 2 cm of the rectum increased by a mean of 0.69% (F2) and 0.76 Gy (F3) compared with an increase of 0.03% and 0.04 Gy, respectively, with correction. The urethra V15 also increased by a mean of 0.56% (F2) and 0.35 Gy (F3) compared with 0.06% and 0.16 Gy, respectively, with correction.

Conclusions: Inter-fraction correction for catheter movement using pre-treatment imaging is critical to maintain the quality of an implant. Without movement correction there is a significant risk of tumour under dosages and normal tissue over dosages. The findings of this study justify additional imaging between fractions in order to carry out correction.

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Treatment Delivery

- Multi-fractions delivery with a single implant

### δBeam

**Mean shift:**
- $f_2 - f_1 = 7.9 \text{ mm}$
- $f_3 - f_1 = 3.9 \text{ mm}$

### δDose

**Table 2**

Mean change in DVH and COIN parameters for all patients relative to fraction 1, values ± standard deviation. Negative values indicate a lower value than that achieved for fraction 1.

| Dosimetric parameter | Fraction 2 | | | Fraction 3 | | |
|----------------------|------------|---|---|------------|---|
|                      | With correction | Without correction | P-value | With correction | Without correction | P-value |
| CTV V100% (%)        | $-3.48 \pm 4.7$ | $-12.61 \pm 9.6$ | 0.000 | $-4.76 \pm 7.4$ | $-15.17 \pm 11.7$ | 0.001 |
| PTV                  | $-4.05 \pm 5.1$ | $-13.07 \pm 9.2$ | 0.000 | $-5.33 \pm 7.8$ | $-15.40 \pm 11.7$ | 0.001 |
|                      | $-5.32 \pm 5.6$ | $-27.7 \pm 22.8$ | 0.000 | $-5.09 \pm 8.3$ | $-32.34 \pm 24.5$ | 0.000 |
| Rectum D2cc (Gy)     | 0.03 ± 0.7 | 0.69 ± 0.9 | 0.000 | 0.04 ± 0.9 | 0.76 ± 1.1 | 0.000 |
|                      | 0.14 ± 0.4 | 0.46 ± 0.8 | 0.001 | 0.22 ± 0.5 | 0.70 ± 1.0 | 0.001 |
| Urethra V12cc (cc)   | 0.06 ± 0.2 | 0.36 ± 0.5 | 0.002 | 0.16 ± 0.4 | 0.39 ± 0.4 | 0.003 |
|                      | $-0.35 \pm 0.4$ | 0.12 ± 0.7 | 0.000 | $-0.27 \pm 0.6$ | 0.27 ± 0.9 | 0.000 |
| COIN index           | $-0.05 \pm 0.1$ | $-0.16 \pm 0.1$ | 0.000 | $-0.05 \pm 0.1$ | $-0.17 \pm 0.1$ | 0.000 |

Fig. 1. Frequency histograms displaying the caudal movement in mm of each catheter at fractions 2 and 3 (326 in total).

Analysis performed using the Wilcoxon signed rank test in SPSS (v16.0 for Windows). P-values < 0.05 were considered significant at the 95% confidence level.
TREATMENT DELIVERY

• Multi-fractions delivery with a single implant

Table 3
Summary of the current relevant literature documenting catheter migration in HDR brachytherapy treatment of prostate cancer.

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of patients</th>
<th>No. fractions over time</th>
<th>Imaging method</th>
<th>Measurements relative to Dosimetric analysis?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim (2007)</td>
<td>10</td>
<td>Two fractions over 24 h</td>
<td>CT scans</td>
<td>Bony and gold seed markers</td>
</tr>
<tr>
<td>Damore (2009)</td>
<td>96</td>
<td>Four fractions over 40 h</td>
<td>X-ray films</td>
<td>Bony markers and tip at first fraction</td>
</tr>
<tr>
<td>Mullokandov (2004)</td>
<td>50</td>
<td>Four fractions over 24–28 h</td>
<td>CT scans (2 mm)</td>
<td>Bony markers, gold seeds and bladder base</td>
</tr>
<tr>
<td>Martinez (2001)</td>
<td>10 analysed</td>
<td>Four fractions over 48 h</td>
<td>X-ray films</td>
<td>Tip at first fraction</td>
</tr>
<tr>
<td>Hoskin (2002)</td>
<td>20</td>
<td>Two fractions over 24–28 h</td>
<td>CT scans (3 mm)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Fig. 4. Graphical interpretation of results in current literature documenting mean caudal catheter migration for prostate HDR brachytherapy. Time is in approximate hours since implant, with two exceptions: Martinez and this study (Saxby) show time in hours since obtaining fraction 1 images and are shown as non-solid symbols.
Prostate cancer brachytherapy

Prostate HDR brachytherapy catheter displacement between planning and treatment delivery

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**K**eYw**o**rds:
HDR prostate brachytherapy
Catheter displacement
Movement

**A**b**s**t**r**act

Background and purpose: HDR brachytherapy is used as a conformal boost for treating prostate cancer. Given the large doses delivered, it is critical that the volume treated matches that planned. Our outpatient protocol comprises two 9 Gy fractions, two weeks apart. We prospectively assessed catheter displacement between CT planning and treatment delivery.

Materials and methods: Three fiducial markers and the catheters were implanted under transrectal ultrasound guidance. Initial marker wires were inserted into reference catheters before CT; marker positions relative to each other and to the marker wires were measured from the CT scout. Measurements were repeated immediately prior to treatment delivery using pelvic X-ray with marker wires in the same reference catheters. Measurements from CT scout and X-ray were compared. For displacements of 5 mm or more, index points were adjusted prior to treatment delivery.

Results: Results are based on 48 implants, in 25 patients. Median time from planning CT to treatment delivery was 294 min (range 81–357 min). Median catheter displacement was 7.5 mm (range 2.9–23.9 mm). 67% of implants had displacement of 5 mm or greater. Displacements were predominantly caudal.

Conclusions: Catheter displacement can occur in the \( \pm 3 \) h between the planning CT scan and treatment. It is recommended that departments performing HDR prostate brachytherapy verify catheter positions immediately prior to treatment delivery.

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Treatment Delivery
• Multi-fractions delivery with a single implant

δ Beam

- Median shift: 7.5 mm [2.9, 23.9]

- Median Δt between CT & delivery: 254 min [81, 367]

Table 2
Occurrence of displacement magnitude.

<table>
<thead>
<tr>
<th>Magnitude (mm)</th>
<th>Number of implants</th>
</tr>
</thead>
<tbody>
<tr>
<td>−3 to −0.1</td>
<td>3</td>
</tr>
<tr>
<td>0 to 4.9</td>
<td>13</td>
</tr>
<tr>
<td>5 to 9.9</td>
<td>18</td>
</tr>
<tr>
<td>10 to 14.9</td>
<td>9</td>
</tr>
<tr>
<td>&gt;15</td>
<td>5</td>
</tr>
</tbody>
</table>

The frequency of occurrence for each group of displacement magnitude is shown here. The number of implants refers to the frequency of occurrence.

Conclusions: Catheter displacement can occur in the 1–3 h between the planning CT scan and treatment. It is recommended that departments performing HDR prostate brachytherapy verify catheter positions immediately prior to treatment delivery.
List of Content

- ERT versus BRT from Dosimetry Point of View
- Treatment Planning and Dose Calculation
- Treatment Delivery
- Treatment Delivery Verification
Treatment Delivery Verification: Off-Line Procedure
CT based – 1 x Implant + 4 x Fractions

Physics Contribution

IN VIVO THERMOLUMINESCENCE DOSIMETRY DOSE VERIFICATION OF TRANSPERINEAL $^{192}$Ir HIGH-DOSE-RATE BRACHYTHERAPY USING CT-BASED PLANNING FOR THE TREATMENT OF PROSTATE CANCER

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Purpose: To evaluate the potential of in vivo thermoluminescence dosimetry to estimate the accuracy of dose delivery in conformal high-dose-rate brachytherapy of prostate cancer.

Methods and Materials: A total of 50 LiF, TLD-100 cylindrical rods were calibrated in the dose range of interest and used as a batch for all fractions. Fourteen dosimeters for every treatment fraction were loaded in a plastic 4F catheter that was fixed in either one of the 6F needles implanted for treatment purposes or in an extra needle implanted after consulting with the patient. The 6F needles were placed either close to the urethra or in the vicinity of the median posterior wall of the prostate. Initial results are presented for 18 treatment fractions in 5 patients and compared to corresponding data calculated using the commercial treatment planning system used for the planning of the treatments based on CT images acquired postimplantation.

Results: The maximum observed mean difference between planned and delivered dose within a single treatment fraction was 8.57% ± 2.61% (root mean square [RMS] errors from 4.03% to 9.73%). Corresponding values obtained after averaging results over all fractions of a patient were 6.88% ± 4.93% (RMS errors from 4.82% to 7.32%). Experimental results of each fraction corresponding to the same patient point were found to agree within experimental uncertainties.

Conclusions: Experimental results indicate that the proposed method is feasible for dose verification purposes and suggest that dose delivery in transperineal high-dose-rate brachytherapy after CT-based planning can be of acceptable accuracy. © 2003 Elsevier Inc.

Brachytherapy, Prostate, In vivo, TLD.
Treatment Delivery Verification: Off-Line Procedure

CT based – 1 x Implant + 4 x Fractions

5 x cases, 18 x Fractions, 14 x TLDs
Treatment Delivery Verification: Off-Line Procedure
CT based – 1 x Implant + 4 x Fractions

5 x cases, 18 x Fractions, 14 x TLDs
Treatment Delivery Verification: Off-Line Procedure
CT based – 1 x Implant + 4 x Fractions

5 x cases, 18 x Fractions, 14 x TLDs

Analysis Example
Treatment Delivery Verification: Off-Line Procedure
CT based – 1 x Implant + 4 x Fractions

Table 2. Comparison of doses measured and calculated in each patient fraction

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Fraction no.</th>
<th>% mean difference</th>
<th>% RMS deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>7.88 ± 4.54</td>
<td>7.45</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>-0.94 ± 8.57</td>
<td>8.07</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>7.16 ± 6.68</td>
<td>9.28</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>7.29 ± 4.02</td>
<td>9.41</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>4.40 ± 7.40</td>
<td>8.32</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>8.57 ± 2.61</td>
<td>8.91</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>7.52 ± 5.11</td>
<td>8.91</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>7.74 ± 3.09</td>
<td>8.25</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>5.10 ± 5.23</td>
<td>7.04</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>4.37 ± 0.98</td>
<td>4.47</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>7.80 ± 3.84</td>
<td>8.57</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>5.68 ± 4.81</td>
<td>7.18</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>3.38 ± 6.49</td>
<td>6.82</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>4.44 ± 4.95</td>
<td>6.33</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>3.50 ± 9.13</td>
<td>9.23</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>-2.43 ± 10.07</td>
<td>9.73</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>-1.98 ± 5.52</td>
<td>5.53</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>-2.69 ± 3.2</td>
<td>4.03</td>
</tr>
</tbody>
</table>

*Abbreviation:* RMS = root mean square.
Treatment Delivery Verification: Off-Line Procedure
CT based – 1 x Implant + 4 x Fractions

Table 3. Comparison of doses measured and calculated in each patient

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>% mean difference</th>
<th>mean SD</th>
<th>%RMS error</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.47 ± 3.80</td>
<td>4.93</td>
<td>6.44</td>
</tr>
<tr>
<td>2</td>
<td>5.61 ± 4.60</td>
<td>5.88</td>
<td>7.07</td>
</tr>
<tr>
<td>3</td>
<td>6.88 ± 2.66</td>
<td>4.01</td>
<td>7.32</td>
</tr>
<tr>
<td>4</td>
<td>4.93 ± 4.93</td>
<td>2.42</td>
<td>6.37</td>
</tr>
<tr>
<td>5</td>
<td>−2.46 ± 5.64</td>
<td>6.90</td>
<td>5.99</td>
</tr>
</tbody>
</table>

*Abbreviations: SD = standard deviation; RMS = root mean square.
*Mean standard deviation.
Treatment Delivery Verification:

Currently common/published/realised 
*CT imaging based Verification* of anatomy and implant geometry before repeated Treatment Delivery for the same Implant

From CT-Imaging to Treatment Delivery there exist in the majority of the cases a patient transportation (*CT-Imaging room ≠ Treatment Room*).

No verification under Treatment Delivery conditions or no verification of dose delivery (except some efforts for a reliable in-vivo dosimetry).
Treatment Delivery Verification:

+δVOIs + δBeams

Between:

- Plan & Delivery
- During Delivery

4D analysis of influence of patient movement and anatomy alteration on the quality of 3D U/S-based prostate HDR brachytherapy treatment delivery

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The Clinical Procedure at Offenbach Clinic

- Pre-Plan
- Needle Implantation
- Treatment Delivery
- Live plan
The Clinical Procedure at Offenbach Clinic: The QA-Tools
The Clinical Procedure at Offenbach Clinic: The QA-Tools

(1) Intraoperative Real Time Treatment Planning System Oncentra Prostate using 2D- and 3D- Ultrasound Imaging. Ultrasound probe remains in place during treatment enabling 2D and 3D verification at any time during the procedure.
The Clinical Procedure at Offenbach Clinic: The QA-Tools

(2) Template-Perineum QA-Tool
(3) Measurement of Free Length of the needles is utilized for both reconstruction purposes (reconstruction of needle tip) and for quality control purposes for checking needle shifts during the treatment procedure.
The mean volume of prostate (PTV) for the 25 cases is **35.8 cm³** with minimum volume of **17.4 cm³** and maximum of **59.6 cm³**.

Average time spent between the clinical (1) and the pre-irradiation (2) 3D acquisition was **51.2 ± 7.1 min***, and between the pre- (2) and post-irradiation (3) acquisition **19.3 ± 2.2 min**.

*as a teaching hospital, we regularly provide the residents training, that increases the time between the clinical set acquisition and irradiation

**irradiation time that depends on the source activity and the prostate volume
Results: Prostate & OARs Movement ➔ \( \delta \text{VOIs} \)

**Prostate**
The prostate movement in the Z direction (DICOM) was equal to 0mm for each of our acquisitions – BASE plane remained unchanged.
The movement in X (horizontal) and Y (vertical) directions was measured compared to the prostate gravity center on the reference plane.

**Urethra**
The shift of urethra was measured on the base, reference and apex plane.

**Rectum and Bladder**
By rectum and bladder, we have not noticed significant movements.
The significance test for the observed differences is always done using the student paired t-test, two sided statistical method. For the paired t-tests the significance level was 0.05.

<table>
<thead>
<tr>
<th>VOI Name</th>
<th>Type</th>
<th>$r_{21}$ [mm]</th>
<th>$r_{31}$ [mm]</th>
<th>$r_{32}$ [mm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>PTV</td>
<td>0.5±0.6</td>
<td>0.6±0.7</td>
<td>0.1±0.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[0.0÷2.1]</td>
<td>[0.0÷2.1]</td>
<td>[0.0÷1.1]</td>
</tr>
<tr>
<td>Urethra</td>
<td>OAR</td>
<td>0.6±0.7</td>
<td>1.1±1.3</td>
<td>0.4±0.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[0.0÷2.7]</td>
<td>[0.0÷5.1]</td>
<td>[0.0÷3.4]</td>
</tr>
<tr>
<td>Reference</td>
<td></td>
<td>0.6±0.7</td>
<td>0.8±0.9</td>
<td>0.3±0.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[0.0÷2.3]</td>
<td>[0.0÷2.9]</td>
<td>[0.0÷1.7]</td>
</tr>
<tr>
<td>Apex</td>
<td></td>
<td>0.6±0.8</td>
<td>0.8±0.9</td>
<td>0.3±0.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[0.0÷3.3]</td>
<td>[0.0÷2.8]</td>
<td>[0.0÷1.7]</td>
</tr>
<tr>
<td>Rectum</td>
<td>OAR</td>
<td>0.3±0.4</td>
<td>0.4±0.4</td>
<td>0.1±0.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[0.0÷1.4]</td>
<td>[0.0÷1.4]</td>
<td>[0.0÷0.6]</td>
</tr>
</tbody>
</table>

*The significance test for the observed differences is always done using the student paired t-test, two sided statistical method. For the paired t-tests the significance level was 0.05.
The shifts of the catheters on **base, reference and apex plane** is measured between the clinical and pre-irradiation; clinical and post-irradiation and pre- and post- irradiation plan.

- In all but one case, is the maximum needle movement **less than 1.5 mm**
Results: Dosimetric Impact

Table VI. Dose-volume parameters for the three time series of planning used in the study. Prescription dose (100\%) is 11.5 Gy.

<table>
<thead>
<tr>
<th>DVH-parameters</th>
<th>Clinical (1)</th>
<th>Preirradiation (2)</th>
<th>Postirradiation (3)</th>
<th>$p_{12}$</th>
<th>$p_{13}$</th>
<th>$p_{23}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(%)</td>
<td>Range (%)</td>
<td>(%)</td>
<td>Range (%)</td>
<td>(%)</td>
<td>Range (%)</td>
</tr>
<tr>
<td>$D_{90}$</td>
<td>103.8 ± 2.1</td>
<td>100.4 : 107.9</td>
<td>102.2 ± 2.1</td>
<td>97.5 : 105.6</td>
<td>101.6 ± 2.7</td>
<td>96.2 : 106.7</td>
</tr>
<tr>
<td>$D_{35}$</td>
<td>96.3 ± 2.7</td>
<td>91.3 : 101.8</td>
<td>94.5 ± 2.7</td>
<td>88.0 : 99.2</td>
<td>94.3 ± 3.4</td>
<td>86.9 : 106.6</td>
</tr>
<tr>
<td>$D_{1cm^3}$</td>
<td>268.3 ± 25.3</td>
<td>219.4 : 306.5</td>
<td>267.1 ± 25.4</td>
<td>215.2 : 308.3</td>
<td>266.7 ± 24.3</td>
<td>218.5 : 312.2</td>
</tr>
<tr>
<td>$V_{100}$</td>
<td>92.9 ± 1.6</td>
<td>90.3 : 96.3</td>
<td>91.8 ± 1.7</td>
<td>88.2 : 94.6</td>
<td>91.5 ± 2.3</td>
<td>87.1 : 95.5</td>
</tr>
<tr>
<td>$V_{150}$</td>
<td>70.1 ± 2.4</td>
<td>66.0 : 73.2</td>
<td>67.5 ± 2.8</td>
<td>62.3 : 72.6</td>
<td>66.8 ± 3.3</td>
<td>60.2 : 73.1</td>
</tr>
<tr>
<td>$V_{200}$</td>
<td>33.3 ± 1.9</td>
<td>27.3 : 35.0</td>
<td>31.4 ± 3.1</td>
<td>23.6 : 39.0</td>
<td>31.1 ± 2.9</td>
<td>24.1 : 37.4</td>
</tr>
</tbody>
</table>

There are only three (of 25) pre-irradiation plans with $D_{90}$ values of 97.5, 97.7 and 97.8 and thus below 100\%. The minimum value for $D_{90}$ for the post-irradiation plan was 96.2\%. There are five (of 25) post-irradiation plans with $D_{90}$ value less than 100\% with values within range of [96.2 to 98.3] \%.
There is much more sense in observing the influence of the *relative shift of catheters with reference to prostate* on the DVH and also radiobiological parameters than the influence of absolute dislocation of needles and/or OARs separately.

The cases that showed large *absolute* prostate and catheter displacements, showed small *relative* displacement and fulfilled the clinical protocol.
Results: Dosimetric Impact \( \delta \text{Dose} \)

<table>
<thead>
<tr>
<th>DVH-parameters</th>
<th>Clinical (1)</th>
<th>Preirradiation (2)</th>
<th>Postirradiation (3)</th>
<th>( p_{12} )</th>
<th>( p_{13} )</th>
<th>( p_{23} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(%)</td>
<td>Range (%)</td>
<td>(%)</td>
<td>Range (%)</td>
<td>(%)</td>
<td>Range (%)</td>
</tr>
<tr>
<td>( D_{90} )</td>
<td>103.8 + 2.1</td>
<td>100.4 : 107.9</td>
<td>102.2 + 2.1</td>
<td>97.5 : 105.6</td>
<td>101.6 + 2.7</td>
<td>96.2 : 106.7</td>
</tr>
<tr>
<td>( D_{95} )</td>
<td>96.3 + 2.7</td>
<td>91.3 : 101.8</td>
<td>94.5 + 2.7</td>
<td>88.0 : 99.2</td>
<td>94.3 + 3.4</td>
<td>86.9 : 100.6</td>
</tr>
<tr>
<td>( D_{1cm^2} )</td>
<td>268.3 + 25.3</td>
<td>219.4 : 306.5</td>
<td>267.1 + 25.4</td>
<td>215.2 : 308.3</td>
<td>266.7 + 24.3</td>
<td>218.5 : 312.2</td>
</tr>
<tr>
<td>( V_{100} )</td>
<td>92.9 + 1.6</td>
<td>90.3 : 96.3</td>
<td>91.8 + 1.7</td>
<td>88.2 : 94.6</td>
<td>91.5 + 2.3</td>
<td>87.1 : 95.5</td>
</tr>
<tr>
<td>( V_{120} )</td>
<td>70.1 + 2.4</td>
<td>66.0 : 73.2</td>
<td>67.5 + 2.8</td>
<td>62.3 : 72.6</td>
<td>66.8 + 3.3</td>
<td>60.2 : 73.1</td>
</tr>
<tr>
<td>( V_{150} )</td>
<td>33.3 + 1.9</td>
<td>27.3 : 35.0</td>
<td>31.4 + 3.1</td>
<td>23.6 : 39.0</td>
<td>31.1 + 2.9</td>
<td>24.1 : 37.4</td>
</tr>
<tr>
<td>( V_{200} )</td>
<td>9.9 + 1.5</td>
<td>7.2 : 12.9</td>
<td>9.5 + 1.6</td>
<td>6.6 : 12.8</td>
<td>9.5 + 2.8</td>
<td>6.5 : 12.6</td>
</tr>
</tbody>
</table>

Urethra

<table>
<thead>
<tr>
<th>DVH-parameters</th>
<th>Clinical (1)</th>
<th>Preirradiation (2)</th>
<th>Postirradiation (3)</th>
<th>( p_{12} )</th>
<th>( p_{13} )</th>
<th>( p_{23} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(%)</td>
<td>Range (%)</td>
<td>(%)</td>
<td>Range (%)</td>
<td>(%)</td>
<td>Range (%)</td>
</tr>
<tr>
<td>( D_{10} )</td>
<td>113.3 + 2.5</td>
<td>104.1 : 114.9</td>
<td>111.2 + 3.3</td>
<td>104.0 : 117.6</td>
<td>110.9 + 3.2</td>
<td>105.8 : 118.3</td>
</tr>
<tr>
<td>( D_{0.1cm^2} )</td>
<td>114.5 + 2.3</td>
<td>107.2 : 116.9</td>
<td>112.4 + 3.2</td>
<td>107.1 : 118.8</td>
<td>112.2 + 3.2</td>
<td>106.7 : 118.8</td>
</tr>
<tr>
<td>( D_{1cm^2} )</td>
<td>98.8 + 7.8</td>
<td>82.4 : 109.2</td>
<td>96.7 + 7.8</td>
<td>78.9 : 107.1</td>
<td>96.3 + 7.5</td>
<td>81.2 : 106.7</td>
</tr>
<tr>
<td>( D_{1} )</td>
<td>117.9 + 2.6</td>
<td>111.0 : 124.3</td>
<td>115.9 + 3.7</td>
<td>109.7 : 123.6</td>
<td>115.7 + 4.0</td>
<td>109.2 : 124.1</td>
</tr>
<tr>
<td>( V_{100} )</td>
<td>58.7 + 9.6</td>
<td>22.4 : 69.0</td>
<td>55.7 + 9.5</td>
<td>22.5 : 68.0</td>
<td>56.6 + 7.5</td>
<td>37.0 : 68.8</td>
</tr>
</tbody>
</table>

Bladder

<table>
<thead>
<tr>
<th>DVH-parameters</th>
<th>Clinical (1)</th>
<th>Preirradiation (2)</th>
<th>Postirradiation (3)</th>
<th>( p_{12} )</th>
<th>( p_{13} )</th>
<th>( p_{23} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(%)</td>
<td>Range (%)</td>
<td>(%)</td>
<td>Range (%)</td>
<td>(%)</td>
<td>Range (%)</td>
</tr>
<tr>
<td>( D_{10} )</td>
<td>49.5 + 7.9</td>
<td>28.9 : 62.7</td>
<td>52.7 + 8.3</td>
<td>30.8 : 67.6</td>
<td>52.3 + 8.5</td>
<td>35.7 : 67.9</td>
</tr>
<tr>
<td>( D_{0.1cm^2} )</td>
<td>66.4 + 11.5</td>
<td>37.9 : 79.9</td>
<td>65.2 + 11.1</td>
<td>37.3 : 79.3</td>
<td>63.6 + 10.8</td>
<td>36.8 : 76.0</td>
</tr>
<tr>
<td>( D_{2cm^2} )</td>
<td>48.1 + 9.7</td>
<td>29.0 : 64.8</td>
<td>44.8 + 10.9</td>
<td>24.8 : 64.4</td>
<td>43.1 + 11.0</td>
<td>20.4 : 60.6</td>
</tr>
<tr>
<td>( D_{1} )</td>
<td>64.5 + 10.4</td>
<td>36.7 : 75.8</td>
<td>65.1 + 10.5</td>
<td>37.0 : 76.9</td>
<td>64.0 + 10.3</td>
<td>38.9 : 77.6</td>
</tr>
</tbody>
</table>

Rectum

<table>
<thead>
<tr>
<th>DVH-parameters</th>
<th>Clinical (1)</th>
<th>Preirradiation (2)</th>
<th>Postirradiation (3)</th>
<th>( p_{12} )</th>
<th>( p_{13} )</th>
<th>( p_{23} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(%)</td>
<td>Range (%)</td>
<td>(%)</td>
<td>Range (%)</td>
<td>(%)</td>
<td>Range (%)</td>
</tr>
<tr>
<td>( D_{10} )</td>
<td>56.2 + 5.2</td>
<td>48.6 : 69.9</td>
<td>56.4 + 6.3</td>
<td>48.3 : 76.6</td>
<td>56.7 + 5.2</td>
<td>49.2 : 68.0</td>
</tr>
<tr>
<td>( D_{0.1cm^2} )</td>
<td>76.9 + 2.9</td>
<td>69.3 : 79.7</td>
<td>76.0 + 3.7</td>
<td>69.0 : 83.3</td>
<td>77.0 + 3.4</td>
<td>70.0 : 86.7</td>
</tr>
<tr>
<td>( D_{2cm^2} )</td>
<td>58.9 + 4.6</td>
<td>51.0 : 66.0</td>
<td>58.2 + 4.8</td>
<td>49.6 : 65.7</td>
<td>58.8 + 4.7</td>
<td>50.5 : 68.6</td>
</tr>
<tr>
<td>( D_{1} )</td>
<td>73.7 + 3.0</td>
<td>66.2 : 78.6</td>
<td>72.9 + 3.2</td>
<td>65.9 : 77.0</td>
<td>73.8 + 3.1</td>
<td>66.7 : 82.2</td>
</tr>
</tbody>
</table>
Results: Dosimetric Impact → δDose

Table VII. COIN, COIN coefficients, and EI for clinical, preirradiation, and postirradiation plans.

<table>
<thead>
<tr>
<th>COIN-parameters</th>
<th>Clinical (1) (%)</th>
<th>Preirradiation (2) (%)</th>
<th>Postirradiation (3) (%)</th>
<th>$p_{12}$</th>
<th>$p_{13}$</th>
<th>$p_{23}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$c_1$</td>
<td>0.93 ± 0.02</td>
<td>0.90 : 0.96</td>
<td>0.92 ± 0.02</td>
<td>0.88 : 0.95</td>
<td>0.92 : 0.02</td>
<td>0.87 : 0.95</td>
</tr>
<tr>
<td>$c_2$</td>
<td>0.95 ± 0.03</td>
<td>0.89 : 1.00</td>
<td>0.93 ± 0.03</td>
<td>0.89 : 0.99</td>
<td>0.93 ± 0.03</td>
<td>0.89 : 0.98</td>
</tr>
<tr>
<td>$c_3$</td>
<td>1.00 ± 0.00</td>
<td>0.99 : 1.00</td>
<td>1.00 ± 0.00</td>
<td>0.99 : 1.00</td>
<td>1.00 ± 0.00</td>
<td>0.99 : 1.00</td>
</tr>
<tr>
<td>COIN</td>
<td>0.88 ± 0.03</td>
<td>0.83 : 0.94</td>
<td>0.86 ± 0.02</td>
<td>0.80 : 0.90</td>
<td>0.85 ± 0.04</td>
<td>0.78 : 0.91</td>
</tr>
<tr>
<td>EI</td>
<td>0.05 ± 0.03</td>
<td>0.00 : 0.11</td>
<td>0.07 ± 0.03</td>
<td>0.01 : 0.12</td>
<td>0.07 ± 0.03</td>
<td>0.02 : 0.12</td>
</tr>
</tbody>
</table>

Note: Percentage of the prescribed dose: 11.5 Gy.

The COIN values for all pre-irradiation plans remain above 0.8. For 1 of 25 post-irradiation plans the COIN drops below 0.8 with values 0.78
The radiobiological quantities $P_+$ and $\bar{D}$ were employed to evaluate the effectiveness of the examined dose distributions. $P_+$ is the probability of complication-free tumor control and can be approximated by:

$$P_+ = P_B - P_I$$

where $P_B$ and $P_I$ are the total probability of tumor control and injury, respectively and $\bar{D}$ is the biologically effective uniform dose, which is the dose that causes the same tumor control or normal tissue complication probability as the actual dose distribution, $\tilde{D}$ given to the patient and it can be iteratively determined from:

$$P(\tilde{D}) \equiv P(\bar{D})$$
II.G. Radiobiological treatment plan evaluation

The probability of tissue response, \( P \), of a region of interest that is irradiated uniformly with a dose, \( D \), is determined by the expression

\[
P = \exp \{- \exp[\gamma e - \frac{D}{D_{50}} (\gamma e - \ln(\ln 2))]\},
\]

where \( D_{50} \) is the dose which gives a 50\% response and \( \gamma \) is the maximum normalized dose-response gradient. The dose-response parameters presented in Table IV were used in this study.\(^7\)\(^{15-18}\) The \( \alpha/\beta \) was assumed to be three for prostate and normal tissues.\(^7\) For all the targets and OARs, the mean, maximum and minimum dose values are reported. Furthermore, the scalar quantities \( P_+ \) and \( \bar{D} \) were also calculated. \( P_+ \) is the probability of complication-free tumor control and can be approximated by\(^19\)

\[
P_+ = P_B - P_I,
\]

where \( P_B \) and \( P_I \) are the total probability of tumor control and injury, respectively, and \( \bar{D} \) is the biologically effective uniform dose,\(^20\) which is the dose that causes the same tumor control or normal tissue complication probability as the actual dose distribution, \( \bar{D} \) given to the patient and it can be iteratively determined from

\[
P(\bar{D}) \equiv P(\bar{D}) \Rightarrow \bar{D} = D_{50} \frac{e\gamma - \ln(-\ln(P(\bar{D})))}{e\gamma - \ln(\ln(2))}.
\]
Summary of the model parameter values for the examined prostate cancer cases. $D_{50}$ is the 50% response dose, $\gamma$ is the maximum normalized value of the dose-response gradient and $s$ is the relative seriality, which characterizes the volume dependence of the organ.

<table>
<thead>
<tr>
<th>Radiobiological Model</th>
<th>$D_{50}$ (Gy)</th>
<th>$\gamma$</th>
<th>$s$</th>
<th>$\alpha/\beta$</th>
<th>Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>70.0</td>
<td>4.0</td>
<td>—</td>
<td>3.0</td>
<td>Control</td>
</tr>
<tr>
<td>Urethra (U)</td>
<td>120.0</td>
<td>3.0</td>
<td>0.03</td>
<td>3.0</td>
<td>Stenosis</td>
</tr>
<tr>
<td>Bladder (B)</td>
<td>80.0</td>
<td>3.0</td>
<td>0.3</td>
<td>3.0</td>
<td>Symptomatic contracture, volume loss Proctitis, necrosis, fistula, stenosis</td>
</tr>
<tr>
<td>Rectum (R)</td>
<td>80.0</td>
<td>2.2</td>
<td>0.7</td>
<td>3.0</td>
<td></td>
</tr>
</tbody>
</table>
The average DVHs of the prostate gland (red), urethra (black), bladder (pink) and rectum (blue) are presented for the three HDR treatment plans, namely 1: after implantation (clinical acquisition) (solid), 2: just before starting the treatment execution (pre-irradiation acquisition) (dashed) and 3: just after finishing the treatment delivery (post-irradiation acquisition) (dotted-dashed). Here, the total dose of 34.5 Gy delivered by three fractions of 11.5 Gy is considered to be the total prescription dose (100%).
Fig. 11. The average curves of the total tumor control probability, $P_B$ (green); total normal tissue complication probability, $P_I$ (red); and complication-free tumor control probability, $P_+$ (black) are presented for the three series of HDR treatment plans, namely, (1) after implantation (clinical acquisition) (solid), (2) just before starting the treatment execution (preirradiation acquisition) (dashed), and (3) just after finishing the treatment delivery (postirradiation acquisition) (dotted-dashed), regarding different prescription doses. The solid and dashed vertical lines indicate the radiobiological dose levels of the clinically prescribed dose distributions, respectively. The probability values are calculated using Eqs. (A2)-(A4) and are based on the DVHs of Fig. 9. Here, the total dose of 34.5 Gy delivered by three fractions of 11.5 Gy is considered to be the total prescription dose (100%).
The measured mean shift of anatomy and needles (“beams”) is as low as 1.0mm.

For high modulated plans as those in HDR brachytherapy such small shifts result in dosimetric changes which are in general lower than 5%.

These results demonstrate that quality assurance procedures have to be clinically implemented to guarantee anatomy and implant stability of the order of “1mm”.

This can only be realized without any manipulation of the implant and anatomy as done, for example, in the case of removing the US-probe before treatment delivery (Presentation by Dr. Milickovic on Monday)!
The Clinical Procedure at Offenbach Clinic: The QA-Tools
Treatment Delivery Verification:
An open Issue ...

Currently double check (4 x eyes) !!!!
Treatment Delivery Verification:

The dose-fluence pattern incident verification, that will enable the real 3D-dose reconstruction (analogue to on-line fluence measurement in ERT), assumes the on-line “Beamlets” & “MU” Tracking: source dwell positions & dwell times.

Advance in-vivo dosimetry systems could partly support this.

Currently we have to build on:

- Anatomy Reconstruction & Tracking
- Catheter Reconstruction & Tracking

Under delivery conditions / during delivery!

OCTAVIUS® III by PTW Freiburg, Germany

ERT
CLINICAL UNCERTAINTY ANALYSES FOR BRACHYTHERAPY

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Running title: Clinical uncertainty analyses for brachytherapy

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HDR $^{192}$Ir temporary brachytherapy implants for prostate (Monotherapy or Boost)

In this example, the relative dosimetric uncertainties are considered with the respect to the $D_{90}$ and $V_{150}$ dose-volume parameters for the prostate/PTV.

<table>
<thead>
<tr>
<th>Category</th>
<th>Optimum level</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source strength</td>
<td>2%</td>
<td>PSDL traceable calibrations</td>
</tr>
<tr>
<td>Treatment planning</td>
<td>3%</td>
<td>Reference data with the appropriate bin width is used</td>
</tr>
<tr>
<td>Medium dosimetric corrections</td>
<td>1%</td>
<td>Full scatter conditions in the pelvic region and for the prostate location are assumed.</td>
</tr>
<tr>
<td>US-based Treatment planning and delivery</td>
<td>2%</td>
<td>Assuming usage of dedicated catheter reconstruction tools (catheter free-length measurement based methods) for an accurate (0.7 mm) reconstruction of catheter tip and 1.0 mm source positioning accuracy by the afterloader for straight catheters and transfer tubes.</td>
</tr>
<tr>
<td>Catheter reconstruction and source positioning accuracy</td>
<td>2%</td>
<td>US QA performed according to AAPM TG-128.</td>
</tr>
<tr>
<td>Changes of catheter geometry relative to anatomy between intraoperative treatment planning and intraoperative treatment delivery</td>
<td>2%</td>
<td>Assuming that new image acquisition and treatment plan calculation is done always before each fraction. It is also required that no manipulation of the implant and anatomy occurs, as it is the case when removing/manipulating the US-probe or moving the patient from the operation table before treatment delivery.</td>
</tr>
<tr>
<td>Total dosimetric uncertainty</td>
<td>5%</td>
<td>For treatment delivery without patient movement and changes in the lithotomy setup and with the US probe at the position of the acquisition (transversal plane at the base plane).</td>
</tr>
</tbody>
</table>
Reproducibility of Treatment Delivery: What does it mean for the individual patient or individual implant?

52 consequent patients with a total of 117 plans and treatment deliveries. Only Live Plans (Treatment Plans delivered are considered).

- Mean PTV of \((38.9 \pm 16)\) cm\(^3\)
- Range 15 – 97 cm\(^3\)
## Prostate (PTV = CTV 1):

- $D_{90} \geq 100\%$
- $V_{100} \geq 90\%$
- $V_{150} \leq 35\%$

## Urethra:

- $D_{10} \leq 115\%$
- $V_{115\%} \leq 10\%$
- $D_{0.1\text{cm}^3} \leq 120\%$

## Rectum & Bladder

- $D_{10} \leq 75\%$
- $V_{75\%} \leq 10\%$
- $D_{0.1\text{cm}^3} \leq 80\%$
How we contour

Since the last 7 years
We contour also bladder.
Thus urethra stops cranially where bladder begins.
Reproducibility of Treatment Delivery

I. PTV (38.9 ± 16) cm³

\[ \text{N=117} \]

\[
\begin{align*}
D_{90} &= (102.5 \pm 2.0)\% \\
V_{100} &= (92.0 \pm 1.6)\% \\
V_{150} &= (29.1 \pm 3.2)\%
\end{align*}
\]

Prostate (PTV = CTV 1):

\[
\begin{align*}
D_{90} &\geq 100\% \\
V_{100} &\geq 90\% \\
V_{150} &\leq 35\%
\end{align*}
\]
Reproducibility of Treatment Delivery

II. Urethra (17.2 ± 3.2) cm³

\[ D_{10} = (112.9 \pm 1.6)\% \]
\[ D_{0.1\text{cm}^3} = (114.0 \pm 1.3)\% \]
\[ D_{1.0\text{cm}^3} = (98.4 \pm 13.2)\% \]
\[ V_{100} = (63.9 \pm 9.2)\% \]

Urethra:
\[ D_{10} \leq 115\% \]
\[ V_{115} \leq 10\% \]
\[ D_{0.1\text{cm}^3} \leq 120\% \]
Reproducibility of Treatment Delivery

III. Rectum (33.8 ± 9.6) cm³

- $D_{10} = (52.5 ± 4.8)\%$
- $D_{0.1cm^3} = (74.9 ± 2.7)\%$
- $D_{2.0cm^3} = (58.1 ± 5.3)\%$

Rectum
- $D_{10} \leq 75\%$
- $V_{75} \leq 10\%$
- $D_{0.1cm^3} \leq 80\%$

N=117
Reproducibility of Treatment Delivery

IV. Bladder $(28.6 \pm 13.4)$ cm$^3$

- $D_{10} = (50.5 \pm 8.2)\%$
- $D_{0.1cm^3} = (73.8 \pm 4.9)\%$
- $D_{2.0cm^3} = (53.6 \pm 5.7)\%$

- $N=117$

- Bladder
  - $D_{10} \leq 75\%$
  - $V_{75} \leq 10\%$
  - $D_{0.1cm^3} \leq 80\%$
Conclusions

Can we deliver the dose distribution we plan?

- Currently we do not have a “close-loop” System (Technology) clinically routinely available to answer this for the different localisations (similar to kV-, MV-CBCT in ERT, Industry)

- We do have data supporting and proving the YES-Answer under specific conditions and scenarios (in the enormous diversity of methods & clinical workflows)

- We definitively need site-specific guidelines (procedures and action levels) for Treatment Delivery Verification in modern Brachytherapy!
Thank you very much for your Attention!