Robustness of IPSA optimized high-dose-rate prostate brachytherapy treatment plans to catheter displacements

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Abstract

\textbf{Purpose:} Inverse planning simulated annealing (IPSA) optimized brachytherapy treatment plans are characterized with large isolated dwell times at the first or last dwell position of each catheter. The potential of catheter shifts relative to the target and organs at risk in these plans may lead to a more significant change in delivered dose to the volumes of interest relative to plans with more uniform dwell times.

\textbf{Material and methods:} This study aims to determine if the Nucletron Oncentra dwell time deviation constraint (DTDC) parameter can be optimized to improve the robustness of high-dose-rate (HDR) prostate brachytherapy plans to catheter displacements. A set of 10 clinically acceptable prostate plans were re-optimized with a DTDC parameter of 0 and 0.4. For each plan, catheter displacements of 3, 7, and 14 mm were retrospectively applied and the change in dose volume histogram (DVH) indices and conformity indices analyzed.

\textbf{Results:} The robustness of clinically acceptable prostate plans to catheter displacements in the caudal direction was found to be dependent on the DTDC parameter. A DTDC value of 0 improves the robustness of planning target volume (PTV) coverage to catheter displacements, whereas a DTDC value of 0.4 improves the robustness of the plans to changes in hotspots.

\textbf{Conclusions:} The results indicate that if used in conjunction with a pre-treatment catheter displacement correction protocol and a tolerance of 3 mm, a DTDC value of 0.4 may produce clinically superior plans. However, the effect of the DTDC parameter in plan robustness was not observed to be as strong as initially suspected.

\textbf{Key words:} brachytherapy, catheter displacement, DTDC, IPSA, prostate cancer.
the target and organs at risk may lead to a more significant change in delivered dose to the volumes of interest relative to plans with more uniform dwell times. Recently, the Nucletron Oncentra TPS has added the dwell time deviation constraint (DTDC) parameter to the IPSA optimization process. This parameter constrains the allowable dwell times in the optimization process and can be set to a value between 0 and 1 in increments of 0.1. A value of 0 corresponds to completely unrestricted dwell times and a value of 1 results in homogeneous dwell times [9].

The displacement of catheters relative to the target and organs at risk during the time between imaging and patient treatment has been reported by a number of groups [10,11,12,13]. The displacements have predominantly been reported along the patient longitudinal axis and in the caudal direction [10] primarily due to acute edema between the prostate and perineal skin [14]. Previous work from our group [11] demonstrated a median catheter displacement of 7.5 mm in caudal direction (range 2.9-23.9 mm) in the time from planning CT to treatment (approximately 1-3 hours). Tiong et al. [10] have reported significant adverse effects on the tumor control probability for catheter displacements larger than 3 mm, including underdosage of the target and overdosage to critical structures. Due to these findings, our department has implemented a clinical protocol, in which internal catheter positions are verified and corrected immediately prior to treatment delivery with a tolerance of 3 mm.

This study aims to determine if the DTDC parameter can be optimized to improve the robustness of HDR prostate brachytherapy plans to catheter displacements relative to patient anatomy. A set of 10 clinically acceptable prostate plans were re-optimized with a DTDC parameter of 0 and 0.4. The values of 0 and 0.4 were chosen to reflect the change that is currently occurring in our clinical protocol. For each plan, catheter displacements of 3, 7, and 14 mm were retrospectively applied, and the change in DVH indices and conformity indices analyzed.

**Material and methods**

**Initial plans**

A set of 10 clinical prostate HDR brachytherapy plans were chosen for analysis. These CT plans were created between 2012 and 2015 on the Nucletron Oncentra Brachytherapy TPS (v4.3, Nucletron B.V., Veenendaal, The Netherlands). The prostate planning target volume (PTV), urethra, and rectum were all contoured by the same radiation oncologist at the time of treatment. Prostate volumes varied between 25.1 and 59.4 cm³ and the number of catheters used was between 14 and 24. All patients received 2 fractions of 9.5 Gy with 2 weeks between fractions. Catheter insertion (using Oncosmart, ProGuide Sharp Needle, 6F, Nucletron B.V., Veenendaal, The Netherlands), CT scan, planning, and treatment were all performed on the same day, and the mean time between the planning CT and treatment was 182 minutes.

**IPSA optimization and DTDC**

Each plan was optimized using the IPSA algorithm using the parameters outlined in Table 1. As per clinical protocol, plans were initially optimized with the DTDC parameter set to 0. The plans were then re-optimized with the DTDC parameter set to 0.4 and all other parameters kept constant. The dwell time characteristics of each plan were then compared using the plan modulation index (M), as defined by Smith et al. [9]. The plan modulation index is defined as the maximum deviation of dwell time from the average dwell time for each catheter, normalized to the maximum dwell time for the treatment plan, averaged over all catheters in the plan.

**Catheter displacements**

Catheter displacements in the caudal direction were then simulated for each plan. Offsets of 3, 7, and 14 mm were performed. Displacements of this magnitude were chosen as they corresponded to clinically relevant catheter displacements, as found in a previous study by our group [11]. Our center has implemented a clinical protocol, in which catheter displacements ≥ 3 mm are corrected for, immediately prior to treatment by altering the indexer length at the treatment console. Implanting the catheters past the prostate base into the bladder allowed for extra dwell positions beyond the prostate in the event of a caudal shift. Physical re-insertion was not performed.

**Plan analysis**

All patient plans were assessed by evaluating dose volume histogram (DVH) indices and dose quality indices. Dose volume histogram indices used for plan evaluation are outlined in Table 2. Furthermore, a normal tissue (NT) contour was created by adding a 2 mm margin around the PTV and subtracting this expanded contour from the external contour, e.g. NT = Body − (PTV + 2 mm). These parameters were automatically calculated by the

### Table 1. Inverse planning simulated annealing (IPSA) optimization parameters used for patient plan optimization

| ROI          | Usage | Surface | Volume |
|--------------|-------|---------|--------|
|              | Weight| Min (cGy)| Max (cGy) | Weight| Min (cGy)| Max (cGy)| Weight |
| Prostate     | 100   | 950     | 1425   | 100  | 100   | 100   | 950     | 30    |
| Rectum       | Organ | 665     | 50     | 50   | 475   | 50    |
| Urethra      | Organ | 120     | 950    | 998  | 50    | 950   | 998     | 50    |

*PTV – planning target volume*
TPS and are highly dependent on the size of the histogram bin used for calculation [8]. Because of this, a conformity index (CI), a dose inhomogeneity index (DHI), and an overdose volume index (ODI) were also calculated for each plan.

The CI used in this study is the one introduced by van’t Riet et al. [15] and is shown in Equation 1:

\[
CI = \frac{V_{T,\text{ref}}}{V_T} \times \frac{V_T}{V_{\text{ref}}} \quad (1),
\]

where \(V_{T,\text{ref}}\) is the volume of the PTV receiving a dose greater than or equal to the 100\% isodose, \(V_T\) is the volume of the PTV, and \(V_{\text{ref}}\) is the volume of the 100\% isodose. The DHI parameter gives an indication of the homogeneity of the dose within the PTV, which was first introduced by Wu et al. [16] and is shown in Equation 2:

\[
DHI = \frac{V_{T,\text{ref}} - V_{T,1.5\text{ref}}}{V_{T,\text{ref}}} \quad (2),
\]

where \(V_{T,1.5\text{ref}}\) is the volume of the PTV receiving a dose greater than or equal to the 150\% isodose, and \(V_{T,\text{ref}}\) is as described above. Finally, the ODI parameter [17] indicates the amount of high dose (greater than 200\%) within the PTV:

\[
ODI = \frac{V_{T,\text{2ref}}}{V_{T,\text{ref}}} \quad (3),
\]

where \(V_{T,\text{2ref}}\) is the volume of the PTV receiving a dose greater than or equal to the 200\% isodose.

The change in DVH and dose quality indices was then calculated as a function of catheter displacement for both DTDC values of 0 and 0.4. The change in these indices with increasing catheter displacement gives an indication of the robustness of the plans to changes in catheter position relative to the targets and organs at risk between planning CT and treatment. Statistical significance between the DTDC values was verified using a paired \(t\)-test with \(\alpha = 0.05\) (corresponding to a 5\% significance level).

**Results**

**Initial clinical plans**

Initial clinical prostate plans IPSA optimized with a DTDC value of 0 produced a large spread of dwell times, relative to those plans optimized with a DTDC value of 0.4. The plan modulation index (M) for each plan variant is given in Table 3 along with the total dwell time, normalized to the air kerma strength of the source. The average M for the 0 DTDC case (± 1 SD) was equal to 0.44 ± 0.07, whereas for the 0.4 DTDC case \(M = 0.20\) ± 0.06. The effect of increasing the DTDC parameter is to limit the maximum dwell time in any catheter; this is reflected by the decreasing value of M, as more homogeneous dwell time distribution is created within each catheter position relative to the planning target volume.

| Table 2. Clinically acceptable dose volume histogram (DVH) indices |
|---|---|---|---|
| Volume type | Dose (%) | Dose (cGy) | Volume (%) |
| PTV | 100 | 950 | ≥ 90 |
| PTV | 150 | 1425 | < 30 |
| PTV | 200 | 1900 | < 15 |
| Rectum | 70 | 665 | 0 |
| Urethra | 120 | 1140 | 0 |

\(\text{PTV} – \) planning target volume

| Table 3. Plan modulation index (M) and normalized total dwell time (cGy/cm²) |
|---|---|---|---|
| Patient | Plan modulation index (M) | Normalized total dwell time (cGy/cm²) |
| | DTDC 0 | DTDC 0.4 | DTDC 0 | DTDC 0.4 |
| 1 | 0.48 | 0.09 | 8.32 × 10⁻⁶ | 7.73 × 10⁻⁶ |
| 2 | 0.34 | 0.23 | 2.75 × 10⁻⁶ | 2.55 × 10⁻⁶ |
| 3 | 0.43 | 0.25 | 2.57 × 10⁻⁶ | 2.33 × 10⁻⁶ |
| 4 | 0.41 | 0.23 | 10.44 × 10⁻⁶ | 9.82 × 10⁻⁶ |
| 5 | 0.57 | 0.17 | 15.27 × 10⁻⁶ | 14.32 × 10⁻⁶ |
| 6 | 0.43 | 0.18 | 12.45 × 10⁻⁶ | 12.34 × 10⁻⁶ |
| 7 | 0.42 | 0.24 | 6.32 × 10⁻⁶ | 6.12 × 10⁻⁶ |
| 8 | 0.48 | 0.19 | 8.72 × 10⁻⁶ | 8.29 × 10⁻⁶ |
| 9 | 0.40 | 0.21 | 8.37 × 10⁻⁶ | 7.80 × 10⁻⁶ |
| 10 | 0.44 | 0.20 | 7.27 × 10⁻⁶ | 6.80 × 10⁻⁶ |

| DTDC – dwell time deviation constraint |

| Table 4. Initial dose volume histogram (DVH) and dose indices before catheter displacement |
|---|---|---|---|---|
| Parameter | DTDC 0 | DTDC 0.4 | \(p\) |
| PTV \(V_{100}\%\) | 92.9 ± 1.9\% | 93.4 ± 1.7\% | ≤ 0.2620 |
| PTV \(V_{150}\%\) | 18.9 ± 3.6\% | 23.0 ± 3.7\% | ≤ 0.0001 |
| PTV \(V_{200}\%\) | 7.5 ± 1.6\% | 9.0 ± 1.4\% | ≤ 0.0002 |
| Rectum \(V_{70}\%\) | 0.1 ± 0.1\% | 0.1 ± 0.1\% | ≤ 0.3498 |
| Urethra \(V_{120}\%\) | 10.4 ± 5.6\% | 5.9 ± 5.9\% | ≤ 0.0421 |
| NT \(V_{100}\%\) | 11.0 ± 3.0 cc | 5.7 ± 1.9 cc | ≤ 0.0001 |
| NT \(V_{150}\%\) | 3.3 ± 1.4 cc | 1.2 ± 0.7 cc | ≤ 0.0001 |
| NT \(V_{200}\%\) | 1.5 ± 0.2 cc | 0.5 ± 0.3 cc | ≤ 0.0018 |
| CI | 0.691 ± 0.046 | 0.748 ± 0.042 | ≤ 0.0002 |
| DHI | 0.204 ± 0.039 | 0.246 ± 0.038 | ≤ 0.0001 |
| ODI | 0.081 ± 0.018 | 0.097 ± 0.014 | ≤ 0.0004 |

\(\text{PTV} – \) planning target volume, \(\text{NT} – \) normal tissue, \(\text{CI} – \) conformity index, \(\text{DHI} – \) dose inhomogeneity index, \(\text{ODI} – \) overdose index, \(V_{100}\%, V_{150}\%, V_{200}\%\) – volume of relevant structure receiving 100\%, 150\%, 200\% of the prescribed isodose, respectively, \(\text{DTDC} – \) dwell time deviation constraint
Effect of catheter displacements

The effect of catheter displacements on DVH and dose quality indices are shown in Tables 5, 6, and 7 for catheter shifts of 3, 7, and 14 mm, respectively. Overall, a DTDC value of 0 improves the robustness of PTV coverage to catheter displacements relative to a DTDC value of 0.4. This is reflected in the smaller changes in PTV $V_{100\%}$ and CI (Figure 1) and CI (Figure 2) for all three catheter displacement values. The dwell positions moving out of the PTV in the DTDC 0 plans have smaller weights relative to those in the DTDC 0.4 plans, resulting in smaller changes in PTV $V_{100\%}$ and CI with catheter displacements.

Conversely, a DTDC value of 0.4 improves the robustness of the plans to changes in hotspots, reflected by statistically significant differences in changes to PTV $V_{150\%}$, PTV $V_{200\%}$ (Figure 3), DHI, and ODI (Figure 4) compared to plans optimized with a DTDC value of 0 for catheter displacements up to 14 mm. This behavior can be explained by considering that the isolated dwell times at the end of the catheters often exist just outside the PTV.

Table 5. Change in dose volume histogram (DVH) and dose indices for a 3 mm catheter displacement

| Parameter     | DTDC 0       | DTDC 0.4      | p            |
|---------------|--------------|---------------|--------------|
| PTV $V_{100\%}$ | $0.788 \pm 0.751\%$ | $-1.299 \pm 0.916\%$ | $\leq 0.0001$ |
| PTV $V_{150\%}$ | $1.786 \pm 1.540\%$ | $0.146 \pm 0.537\%$ | $\leq 0.0009$ |
| PTV $V_{200\%}$ | $1.051 \pm 0.829\%$ | $-0.034 \pm 0.183\%$ | $\leq 0.0021$ |
| Rectum $V_{70\%}$ | $0.078 \pm 0.081\%$ | $0.080 \pm 0.090\%$ | $\leq 0.8905$ |
| Urethra $V_{120\%}$ | $-5.628 \pm 4.878\%$ | $-4.019 \pm 5.047\%$ | $\leq 0.0088$ |
| NT $V_{100\%}$ | $-1.042 \pm 1.314\%$ | $1.314 \pm 1.661\%$ | $\leq 0.0454$ |
| NT $V_{150\%}$ | $-1.033 \pm 0.893\%$ | $0.468 \pm 0.504\%$ | $\leq 0.0001$ |
| NT $V_{200\%}$ | $-0.568 \pm 0.674\%$ | $0.171 \pm 0.318\%$ | $\leq 0.0052$ |
| CI            | $0.002 \pm 0.017$ | $-0.024 \pm 0.022$ | $\leq 0.0011$ |
| DHI           | $0.017 \pm 0.005$ | $0.005 \pm 0.006$ | $\leq 0.0033$ |
| ODI           | $0.011 \pm 0.008$ | $0.001 \pm 0.002$ | $\leq 0.0035$ |

Table 6. Change in dose volume histogram (DVH) and dose indices for a 7 mm catheter displacement

| Parameter     | DTDC 0       | DTDC 0.4      | p            |
|---------------|--------------|---------------|--------------|
| PTV $V_{100\%}$ | $-2.803 \pm 2.516\%$ | $-8.99 \pm 2.283\%$ | $\leq 0.0001$ |
| PTV $V_{150\%}$ | $2.199 \pm 2.670\%$ | $-1.626 \pm 1.158\%$ | $\leq 0.0002$ |
| PTV $V_{200\%}$ | $1.255 \pm 1.260\%$ | $-0.689 \pm 0.427\%$ | $\leq 0.0008$ |
| Rectum $V_{70\%}$ | $0.271 \pm 0.324\%$ | $0.265 \pm 0.324\%$ | $\leq 0.7793$ |
| Urethra $V_{120\%}$ | $-6.461 \pm 5.879\%$ | $-4.333 \pm 6.804\%$ | $\leq 0.0205$ |
| NT $V_{100\%}$ | $1.072 \pm 3.121\%$ | $4.381 \pm 1.996\%$ | $\leq 0.0189$ |
| NT $V_{150\%}$ | $-0.399 \pm 1.639\%$ | $1.507 \pm 0.753\%$ | $\leq 0.0041$ |
| NT $V_{200\%}$ | $-0.471 \pm 0.940\%$ | $0.641 \pm 0.517\%$ | $\leq 0.0014$ |
| CI            | $-0.046 \pm 0.044$ | $-0.136 \pm 0.046$ | $\leq 0.0005$ |
| DHI           | $0.029 \pm 0.024$ | $0.011 \pm 0.016$ | $\leq 0.0007$ |
| ODI           | $0.016 \pm 0.012$ | $0.002 \pm 0.004$ | $\leq 0.0020$ |

Table 7. Change in dose volume histogram (DVH) and dose indices for a 14 mm catheter displacement

| Parameter     | DTDC 0       | DTDC 0.4      | p            |
|---------------|--------------|---------------|--------------|
| PTV $V_{100\%}$ | $-18.69 \pm 5.197\%$ | $-25.74 \pm 5.313\%$ | $\leq 0.0003$ |
| PTV $V_{150\%}$ | $0.522 \pm 3.343\%$ | $-3.589 \pm 2.063\%$ | $\leq 0.0001$ |
| PTV $V_{200\%}$ | $0.566 \pm 1.455\%$ | $-1.628 \pm 0.786\%$ | $\leq 0.0005$ |
| Rectum $V_{70\%}$ | $0.690 \pm 0.917\%$ | $0.665 \pm 0.956\%$ | $\leq 0.4049$ |
| Urethra $V_{120\%}$ | $-4.657 \pm 7.543\%$ | $-0.592 \pm 10.624\%$ | $\leq 0.0523$ |
| NT $V_{100\%}$ | $8.928 \pm 4.198\%$ | $13.495 \pm 2.333\%$ | $\leq 0.0002$ |
| NT $V_{150\%}$ | $1.582 \pm 1.210\%$ | $3.981 \pm 1.197\%$ | $\leq 0.0008$ |
| NT $V_{200\%}$ | $0.453 \pm 0.786\%$ | $1.756 \pm 0.747\%$ | $\leq 0.0036$ |
| CI            | $-0.251 \pm 0.072$ | $-0.352 \pm 0.064$ | $\leq 0.0003$ |
| DHI           | $0.056 \pm 0.040$ | $0.041 \pm 0.039$ | $\leq 0.0013$ |
| ODI           | $0.027 \pm 0.018$ | $0.013 \pm 0.010$ | $\leq 0.0043$ |
Therefore a catheter shift is implemented. Therefore, the V\textsubscript{150\%} and V\textsubscript{200\%} volumes are surrounding these dwell positions and, as a catheter shift is implemented, they move further away from the PTV and into healthy tissue.

For a catheter displacement of 3 mm, plans optimized with a DTDC value of 0.4 were found to be more robust in terms of NT V\textsubscript{100\%}, NT V\textsubscript{150\%}, and NT V\textsubscript{200\%}. Conversely, for larger catheter shifts of 7 and 14 mm, the plans optimized with DTDC 0 were more robust. This is due to the fact that for a catheter shift of 3 mm, one of the large isolated dwell positions in the DTDC 0 plans moves into the normal tissue. However, for larger shifts, subsequent dwell positions moving into the normal tissue have significantly smaller dwell times compared to those in the DTDC 0.4 plans, resulting in smaller changes in NT V\textsubscript{100\%}, NT V\textsubscript{150\%}, and NT V\textsubscript{200\%}.

The urethra V\textsubscript{120\%} was more sensitive to catheter displacements than the rectum V\textsubscript{70\%} for both values of DTDC. A DTDC value of 0.4 improved the robustness of the plans to changes in urethra V\textsubscript{120\%} compared to plans optimized with a DTDC value of 0, with statistically significant differences for catheter displacements of 3 and 7 mm. There was also no statistically significant difference found between DTDC values for the rectum V\textsubscript{70\%}.

Discussion
As expected, the plan modulation index (M) was observed to decrease with an increased value of DTDC. The calculated values of M = 0.44 ± 0.07 (DTDC = 0) and M = 0.20 ± 0.06 (DTDC = 0.4) are in close agreement with those found in a previous study by Smith et al. [9]. The in-
Conclusions

The results of this study indicate that the robustness of clinically acceptable prostate plans to catheter displacements in the caudal direction are dependent on the DTDC parameter. A DTDC value of 0.4 improves the robustness to normal tissue compared to DTDC = 0. Whereas a DTDC value of 0.4 improves the robustness of the plans to changes in hotspots to a DTDC value of 0.4. A DTDC value of 0.4 were found to be more robust in terms of catheter displacements in the cranial direction occurred for only 3 of 48 cases, with the remainder occurring in the caudal direction. One limitation of this study is that catheter displacements were only considered along the cranial direction. One recent advance in the field of HDR prostate brachytherapy has been the use of 3D trans-rectal ultrasound (TRUS) based treatment planning [18]. The use of this technique has been shown to significantly reduce the time between imaging and treatment compared to CT based treatment planning. Milickovic et al. [18] have shown that for an average time between imaging and treatment of 51.2 minutes, the average needle displacement was found to be 1 mm. This displacement is small relative to those noted in other studies [11,14], and is likely due to the reduction in time between imaging and treatment. Therefore, one current initiative of our group is to reduce the time between imaging and treatment, and the introduction of 3D TRUS based planning is being investigated.

A previous study by our group [11] has shown that catheter displacements in the cranial direction occurred for only 3 of 48 cases, with the remainder occurring in the caudal direction. One limitation of this study is that catheter displacements were only considered along the longitudinal axis in the cranial direction. Catheter shifts in the lateral and anterior-posterior directions due to edema were also not considered.

A further limitation is that only two values of DTDC were considered. Preliminary calculations showed that small changes in DTDC, e.g. from 0.2-0.4 do not significantly affect the robustness of the plans to catheter displacements. Furthermore, values of 0 and 0.4 were chosen to reflect the change that is currently occurring in our clinical protocol. Historically, plans have been optimized using a DTDC value of 0; however previous studies [9] have shown that a DTDC value of 0.4 gives plan modulation equivalent to graphical optimization without significantly compromising plan quality.

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Disclosure

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