Simultaneous ThermoBrachytherapy can improve OAR sparing in prostate HDR Brachytherapy

Total Hotspot Volume	bi-obj BRIGHT				tri-obj BRIGHT + metric 1			tri-obj BRIGHT + metric 2		
	<=∞	<=1.0	<=0.5	<=0.0	<=1	<=0.5	<=0.0	<=1.0	<=0.5	<=0.0
P01	0.46	0.46	0.46	0.00	0.47	0.47	-0.12	0.44	0.44	0.42
P02	0.53	0.53	0.15	N/A	0.54	0.42	N/A	0.43	0.41	0.32
P03	0.44	0.45	0.45	0.27	0.46	0.46	0.31	0.44	0.42	0.41
P04	0.00	N/A	N/A	N/A	-0.12	-0.43	N/A	-0.16	N/A	N/A
P05	0.34	0.32	0.32	0.32	0.31	0.31	0.31	0.29	0.28	0.28
P06	0.41	0.38	-0.01	N/A	0.40	0.39	N/A	0.37	0.36	0.31
P07	0.10	0.02	-0.43	N/A	0.08	0.07	-0.22	0.05	0.04	-0.11
P08	0.50	N/A	N/A	N/A	0.43	0.38	-0.23	0.44	0.37	N/A
P09	0.44	0.11	N/A	N/A	0.43	0.38	N/A	0.41	0.40	0.36
P10	0.41	0.40	0.39	-0.26	0.42	0.41	0.36	0.39	0.39	0.37
P11	0.34	0.34	0.34	N/A	0.36	0.35	0.27	0.32	0.32	0.31
# golden corner	11	9	6	3	10	10	4	10	10	8
# worsening	-	3	6	10	2	5	10	10	10	11

GC + no worsening
GC + worsening
No GC + no worsening
No GC + worsening
No plans

Table 1: Summary of the resulting best LCI-value plan given positive LSI-value (LCI values of the blue diamond plans in Figure 1) of treatment planning results (median of 5 runs, to mitigate randomness in BRIGHT) in bi-objective BRIGHT and both versions of tri-objective BRIGHT, given multiple upper bounds on maximum total HS volume (e.g., ≤ 0.5 mL) in the TPs. *Abbreviations: <=X, for plans with HS upper bound X; P01, patient 1, GC = golden corner.* A positive LCI-value means that all clinical aims are satisfied. If no plans had been produced that satisfy the total HS volume upper bound for a patient, then N/A is reported. If the reported median is significantly worse (Mann–Whitney U test, p-value = 0.05) than the found unconstrainted (total HS volume <= ∞) bi-objective BRIGHT value, it is considered as a worsening. In the bottom row the number of patients is reported for which the GC has been reached (# golden corner) and for which number of patients there was a worsening in best LCI value given a positive LSI value (# worsening). For patient 4 and 8, bi-objective BRIGHT resulted in GC treatment plans with a total HS volume of at least 2 mL and 1.5 mL, respectively. Due to unfavourable implant geometry for patient 4, tri-objective BRIGHT was not able to create GC treatment plans with HV <= 1 mL.

OC-0276 Simultaneous ThermoBrachytherapy can improve OAR sparing in prostate HDR Brachytherapy

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Purpose or Objective

Thermotherapy is a known sensitizer to radiation (Horsman MR, Overgaard J.; Clin. Oncol.; 2007) and is known to lower the α/β of tumors (Datta NR, Bodis S.; Radiother. Oncol.; 2019). The thermal enhancement ratio (TER) of the radiation dose is, however, known to be dependent on the time interval between the radiation and thermal dose delivery, with the highest TER for simultaneous application of the two modalities. Simultaneous ThermoBrachytherapy (STBT) is defined as HDR-BT with simultaneous interstitial thermotherapy assuming the same equivalent dose (EQD) to the target by sensitization and lower physical BT dose (Androulakis I, et al.; Int. J. Hyperth. 2021). In this study we investigated what OAR dose reduction can be expected when HDR-BT only is replaced by STBT in low and intermediate risk prostate cancer (PCa).

Materials and Methods

The effect of the combined TBT treatment was quantified using the temperature dependent LQ model (Van Leeuwen CM, et al.; Int. J. Hyperth. 2017). We compared the physical HDR-BT fraction dose delivered to 10 previously irradiated PCa patients with a STBT treatment. In the original treatment consisting of 2 fractions, the prescribed dose was D_p = 13.5 Gy per fraction. For the TBT simulations we assumed 85% of the original HDR-BT dose and added an EQD-optimized simultaneous thermal dose fraction of 1h with a maximum temperature constraint of 47 °C, using the same dose objectives and constraints (Fig. 1). For all tissues we assumed an α/β = 3 Gy. For the target, the temperature dependence of α (α_{43}/α_{37}) and β (β_{43}/β_{37}) was based on PC-3 and DU-145 PCa cell line data (Pajonk F, et al.; Cancer Res.; 2005). As there is limited thermoradiotherapeutic data available on healthy tissues, we investigated α_{43}/α_{37} and β_{43}/β_{37} ranging from 1 to the value assigned to PCa . We evaluated the target coverage ($V_{100\%}$), as well as the urethra $D_{0.1cc}$, rectum D_{1cc}, and bladder D_{1cc}, accounting for the variability due to different α_{43}/α_{37} and β_{43}/β_{37} values. Differences in dose-volume metrics were evaluated for statistical significance using a paired sampled Wilcoxon signed rank test with $p < 0.001$.

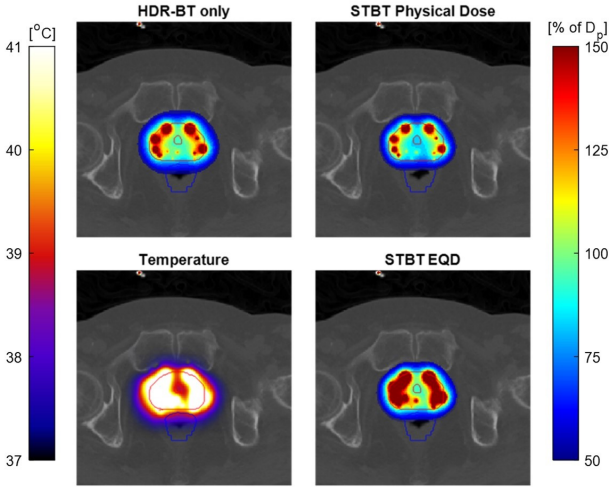

Fig. 1 – Dose and temperature distributions in a single plan. Top left; The physical dose distribution of the original HDR-BT only plan delivered to the patient. Top right; The reduced physical dose (85%) as used for the Simultaneous ThermoBrachytherapy (STBT) plan. Bottom left; The optimized temperature distribution for the STBT treatment. Bottom right; The STBT thermally sensitized equivalent dose (EQD) resulting from the temperature distribution and the reduced physical dose distribution, assuming equal sensitization (α_{43}/α_{37}= 2.4; β_{43}/β_{37}=6.8) of target and healthy tissue. The outer red line, inner red line and blue line represent the target, urethra and rectum outline respectively. For temperature values the colorscale on the left is used, and for dose values the colorscale on the right is used, where dose values are expressed in percentage of the prescribed dose (D_p).

Results

The target objective was reached, with no significant difference in $V_{100\%}$ between the HDR-BT only and STBT plan (0.1%±0.3%). For the OAR, the dose reduction was significant in all cases. For the scenario of equal sensitization of healthy and PCa tissue, the reductions in the urethra $D_{0.1cc}$, rectum D_{1cc}, and bladder D_{1cc}, were 2.2%±2.3%, 2.7%±2.5%, and 4.7%±2.5%, respectively (Fig. 2). For the scenario of no sensitization of healthy tissue, the reductions were 16.7%±0.1%, 10.7%±0.6%, and 10.8%±0.7%, respectively (Fig. 2).

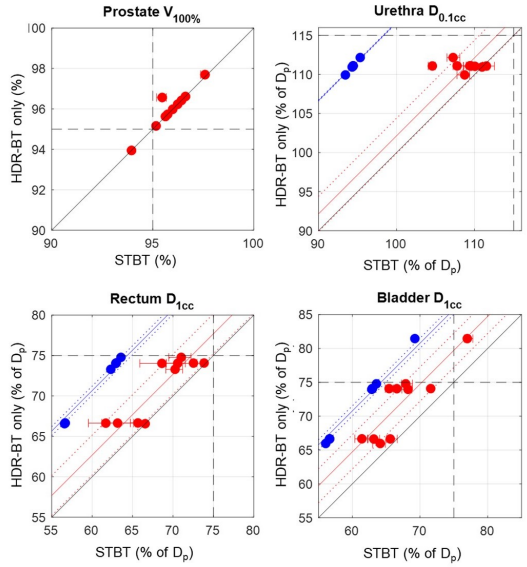

Fig. 2 – Comparison of plan parameters in the original HDR-BT only plan and the calculated Simultaneous ThermoBrachytherapy (STBT) plan for the 10 patients studied. The red dots and lines are assuming equal sensitization of target and healthy tissue. The blue dots and line are assuming no sensitization of healthy tissue. The uncertainty bars per patient represent the uncertainty in sensitization, resulting from the different sensitization factors for PC-3 (α_{43}/α_{37}= 2.4; β_{43}/β_{37}=6.8) and DU-145 (α_{43}/α_{37}= 0.8; β_{43}/β_{37}=1.8) cell lines. The straight and dotted lines represent the average values and standard deviation, respectively, for all patients. The dashed horizontal and vertical lines represent the dose objectives and constraints. Everything above the diagonal indicates a lower value for the STBT plan. Target V100% is expressed in percent of total volume and the dose metrics for the OAR are expressed in percent of the prescribed dose (D_p).

Conclusion

Our calculations indicate that STBT has the potential to reach the same target coverage with a significantly lower dose to the OAR in monotherapy for low and intermediate risk PCa. For a final conclusion including clinical relevance, more information on the temperature dependence of α and ß for normal tissue is needed.