Towards artificial intelligence-based automated treatment planning in clinical practice: a prospective study of the first clinical experiences in high-dose-rate prostate brachytherapy

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Towards artificial intelligence-based automated treatment planning in clinical practice: A prospective study of the first clinical experiences in high-dose-rate prostate brachytherapy

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ABSTRACT

PURPOSE: This prospective study evaluates our first clinical experiences with the novel "BRachytherapy via artificial Intelligent GOMEA-Heuristic based Treatment planning" (BRIGHT) applied to high-dose-rate prostate brachytherapy.

METHODS AND MATERIALS: Between March 2020 and October 2021, 14 prostate cancer patients were treated in our center with a 15Gy HDR-brachytherapy boost. BRIGHT was used for bi-objective treatment plan optimization and selection of the most desirable plans from a coverage-sparing trade-off curve. Selected BRIGHT plans were imported into the commercial treatment planning system Oncentra Brachy . In Oncentra Brachy a dose distribution comparison was performed for clinical plan choice, followed by manual fine-tuning of the preferred BRIGHT plan when deemed necessary.

The reasons for plan selection, clinical plan choice, and fine-tuning, as well as process speed were monitored. For each patient, the dose-volume parameters of the (fine-tuned) clinical plan were evaluated.

RESULTS: In all patients, BRIGHT provided solutions satisfying all protocol values for coverage and sparing. In four patients not all dose-volume criteria of the clinical plan were satisfied after manual fine-tuning. Detailed information on tumour coverage, dose-distribution, dwell time pattern, and insight provided by the patient-specific trade-off curve, were used for clinical plan choice. Median time spent on treatment planning was 42 min, consisting of 16 min plan optimization and selection, and 26 min undesirable process steps.

CONCLUSIONS: BRIGHT is implemented in our clinic and provides automated prostate high-dose-rate brachytherapy planning with trade-off based plan selection. Based on our experience, additional optimization aims need to be implemented to further improve direct clinical applicability of treatment plans and process efficiency.

Keywords: AI-based plan optimization; Trade-off; Clinical experience; HDR; Prostate brachytherapy

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Introduction

Interstitial high-dose-rate (HDR) brachytherapy is an established and evolving treatment technique for prostate cancer (1–3). Good results for both dosimetry and tumour control with no excess toxicity, can be achieved with a treatment plan that has a desirable trade-off between coverage of the target and sparing of the organs at risk (OARs).

Because many potential solutions for a treatment plan exist, manual treatment planning for HDR brachytherapy is complex and time consuming. Therefore, various techniques for dwell time optimization have been considered over the years, particularly from mathematical optimization literature, resulting in a single optimized plan (4–14). This does however not reflect the inherent trade-off nature between coverage and sparing in radiotherapy in general.

Alternatively, evolutionary algorithms (EAs) have been investigated too (15,16). EAs are a form of artificial intelligence (AI), considered to be the state-of-the-art for multi-objective optimization (17). It maintains a population of potential solutions (i.e., treatment plans), and gradually improves the quality of this population through variation and selection. The optimization of a multi-objective problem with an EA results in an approximation set of (near) Pareto optimal solutions, where each solution has a different coverage-sparing trade-off in each of the respective objectives (18,19).

In a retrospective study the Multi-Objective Real-Valued Gene-pool Optimal Mixing Evolutionary Algorithm (MO-RV-GOMEA (19)) was used to automatically generate a large set of plans with different trade-offs for 18 prostate cancer patients (20). In this modern model-based EAs as much as possible problem specific brachytherapy information was integrated. Moreover, an optimization model was used in which the clinically evaluated dose-volume parameters were optimized directly, resulting in the EA optimizing directly what the medical expert would like to accomplish. In this blinded observer study it was found that these MO-RV-GOMEA plans were preferred over the clinical plan in 98% of the cases (20). The ability to compare multiple plans was considered insightful and highly appreciated by the observers.

Also was shown that with a specialized implementation for a graphics processing unit, MO-RV-GOMEA plans optimized using 20 000 dose-calculation points could be obtained within 30 s (21).

The aforementioned studies suggest that higher plan quality can be achieved in reduced treatment planning time when the described algorithms were applied. However, these studies were only simulating clinical practice or were tested retrospectively. Furthermore, it is not known if a clinically optimal solution is achieved or how to navigate the set of trade-off solutions in order to determine the preferred solution.

Thereby, AI based treatment planning is an increasingly studied topic in radiotherapy, but gaining experience and prospective evaluation in clinical practice still needed to be done, especially in the field of brachytherapy.

In March 2020, we clinically introduced the use of MO-RV-GOMEA under the name "**BR**achytherapy via artificial **I**ntelligent **G**OMEA- **H**euristic based **T**reatment planning" (BRIGHT). The aim of the use of BRIGHT is to overcome a time-consuming and complex plan optimization process, by automatically creating a set of high-quality treatment plans from which the physician can choose the preferred plan per patient.

The purpose of this study was to prospectively investigate whether the BRIGHT approach we developed fulfils the expectations in clinical practice, evaluated in terms of resulting dose-volume parameters, process speed, reasons for plan selection and clinical plan choice, and additional needs for further improvement of AI in clinical practice.

Methods and materials

Patient cohort and treatment characteristics

Between March 2020 and October 2021 14 prostate cancer patients were treated in our centre with a single-dose HDR-brachytherapy boost of 15 Gy prescribed on the target volume approximately a week after volumetric-modulated arc therapy with a dose schedule of 12×3 Gy to the prostate and base of the seminal vesicles with a 7 mm margin. Patient specific characteristics are shown in Supplementary table A.1.

Catheter insertion was performed in the operating room under general anaesthesia using real-time transrectal ultrasound. Simultaneously, Oncentra Prostate (Elekta Brachy, Veenendaal, The Netherlands) was used for preplanning for optimal needle placement. After completing the catheter insertion, the patient recovered before magnetic resonance imaging (MRI). For definitive treatment planning a three orthogonal pelvic T2-weighted turbo spin echo MRI (Ingenia 3T Philips Healthcare, Best, the Netherlands) scan was made, with a resolution of 0.52×0.52 mm, and a slice thickness of 3.0 mm with a 0.3 mm gap. Catheter reconstruction and delineation of the PTVs (prostate and base of the seminal vesicles with 0 mm margin) and the OARs (bladder, urethra, and rectum) on the MRI-scan was done in Oncentra Brachy (OB) (Elekta Brachy, Veenendaal, The Netherlands). After treatment planning, the approved plan was delivered using a Flexitron afterloader (Elekta Brachy, Veenendaal, The Netherlands) with an Ir-192 radioactive source.

Plan optimization using BRIGHT

For plan optimization we used a bi-objective planning model (18,21,22) directly based on our clinical protocol. In this bi-objective model the original 11 planning criteria (Table 1) were grouped into one coverage objective and one sparing objective by returning the least satisfied

Table 1
Overview of the coverage and sparing planning criteria and resulting dose-volume parameters, and recalculated normalized least coverage index (LCI) and normalized least sparing index (LSI) of the approved clinical treatment plan for each patient (P01−P14)

Dose-volume parameter	CRITERION	P01	P02	P03	P04	P05	P06	P07	P08	P09	P10	P11	P12	P13	P14
Target coverage															
Prostate V100%	**> 95%**	97.2	94.8	95.6	91.4	96.3	98.4	95.0	97.9	98.2	99.7	99.1	96.8	97.3	95.2
Base seminal vesicles V11GY	**> 95%**	98.0	99.2	99.6	74.8	99.6	100.6	99.1	45.6	100.1	99.9	99.5	100.0	82.3	100.0
Prostate D90%	**> 15Gy**	16.8	16.6	16.3	13.2	16.4	17.0	16.0	16.5	17.2	16.8	17.1	16.4	16.5	15.5
Organ-at-risk sparing															
Prostate V150%	**< 40%**	39.3	42.6	23.2	29.3	29.3	37.5	26.5	28.5	36.2	26.2	34.1	29.5	31.0	23.6
Prostate V200%	**< 15%**	14.5	15.2	8.0	12.2	11.6	13.2	10.9	10.3	12.4	9.1	12.6	12.2	10.3	9.5
Bladder D1 cm^3	**< 13Gy**	12.7	12.6	10.8	9.0	12.9	12.9	11.8	12.4	12.7	11.9	13.0	12.1	11.8	11.6
Bladder D2 cm^3	**< 12Gy**	11.7	11.0	9.6	8.2	11.3	11.8	9.8	10.6	11.7	10.8	11.8	10.9	10.8	10.3
Rectum D1 cm^3	**< 11Gy**	10.6	9.9	9.5	7.8	10.5	10.0	8.4	10.8	10.7	9.9	10.7	10.7	10.5	8.7
Rectum D2 cm^3	**< 9.5Gy**	9.3	8.3	8.5	6.9	9.5	8.7	7.2	9.3	9.7	8.6	9.4	9.6	9.6	7.7
Urethra D30%	**< 16.5Gy**	16.2	15.8	15.9	13.5	16.4	16.7	16.4	16.3	16.4	16.3	16.7	16.3	16.9	15.4
Urethra D0.1 cm^3	**< 18Gy**	17.8	17.8	17.1	14.5	17.9	17.3	18.0	17.3	9.7	16.9	17.2	17.3	18.4	16.0
Normalized LCI	**> 0**	0.41	-0.04	0.11	-4.05	0.26	0.44	0.00	-9.88	0.49	0.40	0.46	0.30	-2.54	0.03
Normalized LSI	**> 0**	0.01	-0.06	0.03	0.18	0.01	-0.01	0.00	0.01	-0.02	0.01	-0.01	-0.01	-0.02	0.07

Orange colour denotes the dose-volume parameter was nearly satisfied. Red denotes exceeding the dose-volume parameter criterion > 2.0 Gy or > 2.0%.

criterion in each group, referred to as the Least Coverage Index (LCI) and Least Sparing Index (LSI), respectively.

The bi-objective model was configured as follows:

$$LCI(t) = \min *\{\delta_c(V_{100\%}^{prostate}),\ \delta_c(D_{90\%}^{prostate}),\ \delta_c(V_{11Gy}^{vesicles})\} \quad (1)$$

$$LSI(t) = \min *\{\delta_s(V_{150\%}^{prostate}), \delta_s(V_{200\%}^{prostate}), \delta_s(D_{1cm3}^{bladder}), \delta_s(D_{2cm3}^{bladder}), \delta_s(D_{1cm3}^{rectum}), \delta_s(D_{2cm3}^{rectum}),\ \delta_s(D_{30\%}^{urethra}), \delta_s(D_{0.1cm3}^{urethra})\} \quad (2)$$

$$\delta_s(D_v^o) = D_v^{o,aim} - D_v^o \quad (3)$$

$$\delta_c(V_d^o) = V_d^o - V_d^{o,aim} \quad (4)$$

Eqs. 1 to 4 shows how the LCI and LSI are calculated for a given treatment plan **t**. Here, $\delta(V_d^o)$ or $\delta(D_v^o)$ indicate, as a percentage, how close a volume or dose parameter criterion, is from being satisfied according to the aim as specified in the clinical protocol, denoted $D_v^{o,aim}$ and $V_d^{o,aim}$. A positive value indicates that it is satisfied, whereas a negative value indicates that it is not satisfied.

As a consequence, when the LCI or LSI is positive, all coverage or sparing constraints are satisfied, respectively. Moreover, min* is an approximation of the minimum operator, while giving a very small weight to values that are not the minimum.

In short, the LCI was constructed by combining the three coverage criteria, in a worst-case manner: prostate V100%, prostate D90% and base seminal vesicles V11Gy. As example, an LCI of 2.0 means that the worst target coverage is 2.0% or 2.0Gy more than its planning criterion and the other targets have a higher coverage.

The LSI was constructed in a similar worst-case approach from the eight sparing criteria: prostate V150%, prostate V200%, bladder D1 cm^3, bladder D2 cm^3, rectum D1 cm^3, rectum D2 cm^3, urethra D30%, and urethra D0.1 cm^3. For instance an LSI of 2.5 means that the worst spared OAR is spared 2.5% or 2.5 Gy more than its planning criterion, and all other OARs are spared even more.

Within BRIGHT, this biobjective model was optimized with the EA MO-RV-GOMEA. The result of a multi-objective EA is a set of solutions that each has a different trade-off with regard to the objectives. A run in the BRIGHT software generates a large set of up to 1000 treatment plans, each with a different LCI/LSI trade-offs. For a more detailed explanation of the method please refer to the study of Bouter *et al.*(21)

In order to make a meaningful comparison between dose-volume parameters with different units and different ranges, we scaled calculated dose-volume parameters relative to their protocol planning aim. We refer to this as normalized LCI and LSI (23). For the calculation of these normalized values, δ_s^{norm} and δ_c^{norm}, as specified in Eqs. 5 to 8, were used instead of δ_s and δ_c, respectively. Here, $V^{o,tot}$ specifies the total volume of organ o, and $D^{o,max}$ specifies the highest desirable dose for organ o (here: 130%). For plans that satisfy all dose-volume criteria the values for the normalized LCI and LSI are larger than zero and this area was defined as the 'golden corner'.

$$\delta_s^{norm}(D_v^o) = (D_v^{o,aim} - D_v^o) \ / \ D_v^{o,aim} \quad (5)$$

$$\delta_s^{norm}(V_v^o) = (V_d^{o,aim} - V_d^o) \ / \ V_d^{o,aim} \quad (6)$$

$$\delta_c^{norm}\left(D_v^o\right) = \left(D_v^o - D_v^{o,aim}\right) \;/\; \left(D^{o,max} - D_v^{o,aim}\right) \quad (7)$$

$$\delta_c^{norm}\left(V_d^o\right) = \left(V_d^o - V_d^{o,aim}\right) \;/\; \left(V^{o,tot} - V_d^{o,aim}\right) \quad (8)$$

Although great care was taken to ensure dose calculation in BRIGHT deviates as little as possible from that in OB, the dose-volume parameters calculated in OB were used for evaluation of the resulting dose-volume parameters of the clinically used plan. From these parameters, the normalized LCI and LSI of the clinically used plan were recalculated for evaluation.

Workflow implementation of BRIGHT

The BRIGHT software was in-house developed by Amsterdam UMC and CWI and a new treatment plan optimization workflow was introduced for clinical use. The implemented BRIGHT workflow is schematically shown in Fig. 1a. During the treatment planning process the Radiotherapy Technologists (RTT), Radiation Oncologist (RO), and Medical Physicist Expert (MPE) were involved.

The treatment planning started in OB with the generation of a basic treatment plan consisting of (1) a structure set of at least the planning target volumes (PTVs) and the OARs, (2) a reconstruction of the implanted catheters, and (3) activated dwell positions inside the PTVs with a maximum of 3mm margin beyond the PTVs, excluding the volume of the urethra with an 1mm margin. The DICOM structure set and DICOM plan were exported to BRIGHT to start bi-objective treatment plan optimization. After optimization, the approximation set of Pareto optimal solutions was visualized as a coverage-sparing "trade-off curve" (Fig. 1b). The RO navigated through this trade-off curve, together with the RTT and MPE. Primary procedure was to select five plans from the "trade-off curve" in the BRIGHT graphical user interface.

The selected BRIGHT plans with optimized dwell times were saved as DICOM RTPLAN and imported in OB to ensure clinically validated dose-calculation. In OB the selected BRIGHT plans were compared to each other by evaluating dose-volume parameters and the dose distributions, after which the preferred BRIGHT plan for the patient was chosen. If necessary, patient specific manual fine-tuning of the preferred BRIGHT plan was subsequently performed by the RTT together with the RO and MPE based on detailed information regarding for example, tumour coverage, and (undesirable) dwell time pattern. Finally, plan approval was performed by the RO, referred to as the clinical plan.

Monitoring and prospective evaluation of BRIGHT in clinical practice

As BRIGHT is in-house developed software, validation and in-house clinical implementation of BRIGHT was performed according to the Medical Device Regulation (24). This included documentation of general safety and performance (technical and functional) requirements of the software, test reports, a user manual, and validation of clinical value. Furthermore, multidisciplinary prospective risk-analysis and user training were performed and documented.

Post-implementation clinical follow-up is needed to ensure reliable and consistent quality, safety, and performance. A first evaluation was done after three patients, a second evaluation after the subsequent four patients, and a third evaluation was done after the subsequent seven patients. The results of these evaluations are described in this paper and were included in the clinical follow-up and Plan-Do-Check-Act (PDCA-)cycle documentation.

AI-based treatment planning was a novel procedure in clinical HDR brachytherapy with which we had no extensive clinical experience. In order to prospectively investigate whether the BRIGHT workflow we developed fulfils the expectations in our clinic, questionnaires were used to capture plan selection criteria and process parameters.

Per patient the following plan selection aspects were monitored during the treatment planning process:

1. Number of plans selected in BRIGHT;
2. The reason(s) why the subset of plans were selected in BRIGHT to evaluate in OB;
3. The reason(s) for clinical plan choice in OB out of the selected BRIGHT plans;
4. Way of (possibly attempting) fine-tuning the preferred BRIGHT plan in OB and reason why this was needed;
5. If and how the available patient-specific clinical information was used for plan selection in BRIGHT as well as for clinical plan choice.

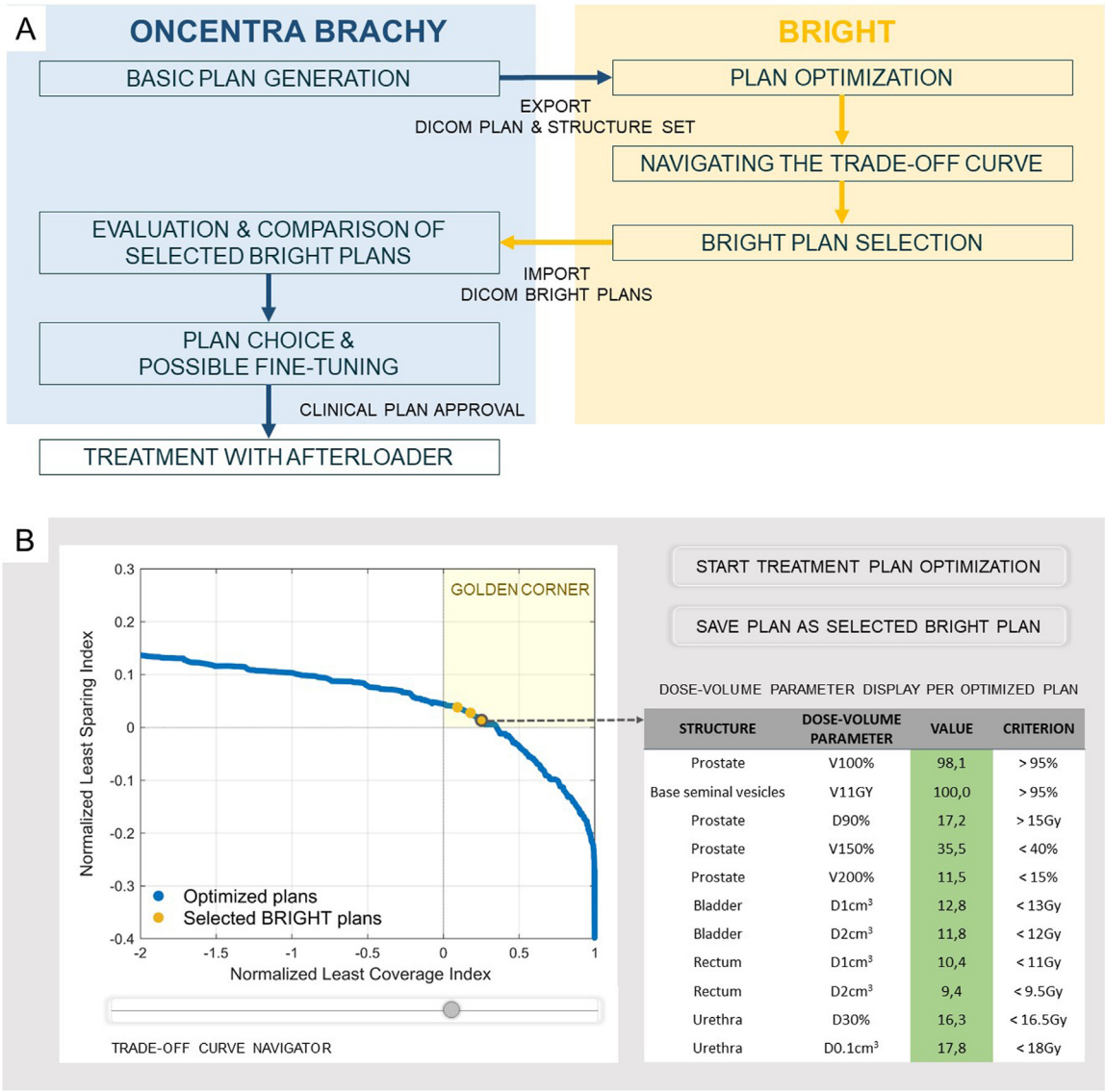
Time spent on the following process steps was monitored:

1. Navigating through the set of plans generated by BRIGHT and selecting a subset of plans for further inspection;
2. Importing the selected BRIGHT plans into OB and performing 3D dose calculation;
3. Evaluation of the selected BRIGHT plans in OB and choosing the clinical plan to treat the patient with, out of the selected BRIGHT plans;
4. Possibly attempting fine-tuning of the preferred BRIGHT plan, until actual clinical plan approval.

Results

Plan selection and clinical plan choice

Figure 2 shows the calculated trade-off curves with the selected and preferred BRIGHT plan(s), and the clinically used plan of all patients. As shown in this figure, multiple



STRUCTURE	DOSE-VOLUME PARAMETER	VALUE	CRITERION
Prostate	V100%	98,1	> 95%
Base seminal vesicles	V11GY	100,0	> 95%
Prostate	D90%	17,2	> 15Gy
Prostate	V150%	35,5	< 40%
Prostate	V200%	11,5	< 15%
Bladder	D1cm³	12,8	< 13Gy
Bladder	D2cm³	11,8	< 12Gy
Rectum	D1cm³	10,4	< 11Gy
Rectum	D2cm³	9,4	< 9.5Gy
Urethra	D30%	16,3	< 16.5Gy
Urethra	D0.1cm³	17,8	< 18Gy

Fig. 1. (a) Schematic representation of implemented clinical workflow using BRIGHT. (b) Example of BRIGHT's graphical user interface (GUI) with the approximation set of (near) Pareto optimal solutions (trade-off plans) insightfully visualized as a coverage-sparing "trade-off curve" from which a BRIGHT plan can be selected based on dose-volume parameters and LCI/LCI. With the trade-off curve navigator bar one can slide over all trade-off plans and evaluate the corresponding dose-volume parameters displayed in the table to make a BRIGHT plan selection. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

BRIGHT plans could be selected in the golden corner for all cases.

After the first evaluation meeting it was determined that five plans had no additional clinical value for plan comparison and caused unnecessary process delay. Therefore, it was decided to select three BRIGHT plans, unless a specific case required otherwise. Based on the second and third evaluation, the selection process remained unchanged, and additional training of the procedure was provided for the RTTs.

The patient-specific trade-off curve was used for navigation of the optimized set of possible treatment plans. Moreover, it provided insight whether it was possible at all to achieve a plan with both good coverage of the targets and sparing of the OARs. Furthermore, the choice between either good OAR sparing or high target coverage was made based on dose distribution comparison in OB and detailed patient information. For example, in eight cases the tumour location was used for clinical plan choice and reason for manual fine-tuning.

In 13 patients time was spent on manual fine-tuning of the preferred BRIGHT plan before clinical plan approval. In nine of these cases small manual fine-tuning was performed to reduce large dwell times that caused undesired large high-dose sub-volumes ("hotspots") in the target, local optimization for a specific OAR, and

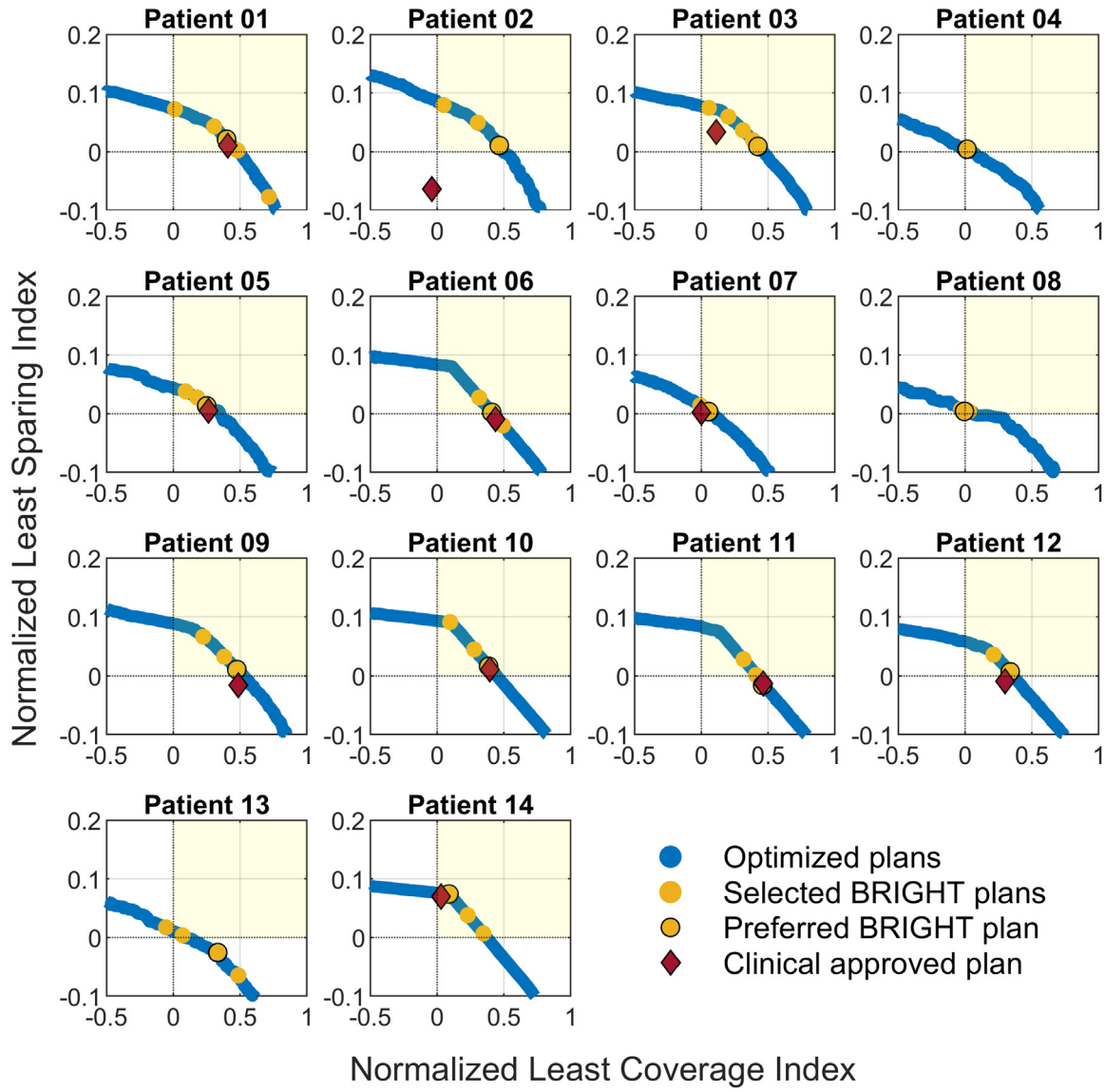


Fig. 2. Set of possible treatment plans (visualized as trade-off curves) found per patient. Yellow circles represent selected BRIGHT plans in the BRIGHT interface, based on dose-volume parameters. In Oncentra Brachy the selected BRIGHT plans were evaluated and compared, from which the preferred BRIGHT plan was chosen. A dark red diamond represents the clinically approved plan used for treatment, including the possible manual fine-tuning of the preferred BRIGHT plan. The clinical plans for patients 4, 8, and 13 are not visualized due to the violation of target coverage criteria after necessary manual adjustments, resulting in a normalized least coverage index (LCI) of respectively -4.05, -9.88, and -2.45, which falls outside the figure range. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

activation of extra dwell positions for better coverage of the target(s).

In four patients, significant manual adjustments were performed to the preferred BRIGHT plan, resulting in not achieving all desired dose-volume protocol values in the clinical plan. The reasons for this were as follows:

During the quality check of the selected BRIGHT plans for patient 2, it was found that a catheter was incorrectly reconstructed in OB. This was corrected in OB followed by manual optimization of the dwell positions and dwell weights in the surrounding catheters – the plan was not re-optimized in BRIGHT due to time pressure – resulting in a 0.2% lower Prostate V100% and respectively a 2.6% and 0.2% higher prostate V150% and V200%, than the desired values in the clinical protocol.

Patient 4 previously received primary rectum irradiation and therefore the focus for this patient was on even higher sparing of the rectum and bladder than the planning aim in the clinical protocol which BRIGHT used for optimization. At the end, the decision was made to lower the prescription dose to the target from 15 Gy to 13 Gy.

Table 2
Results of captured time taken (in min) per process step per patient

Patient ID	1. Plan selection in BRIGHT	2. Import of selected BRIGHT plans to OB	3. Plan evaluation and clinical plan choice in OB	4. Manual fine-tuning and plan approval in OB	Netto time plan selection and clinical plan choice
P01	0:04	0:18	0:34	0:02	0:38
P02	0:03	0:25	0:08	0:26	0:11
P03	0:03	0:16	0:10	0:22	0:13
P04	0:04	0:01	0:01	0:28	0:05
P05	0:04	0:09	0:02	0:35	0:06
P06	0:03	0:10	0:16	0:04	0:19
P07	0:02	0:15	0:17	0:04	0:19
P08	0:01	0:07	0:05	0:38	0:06
P09	0:07	0:18	0:15	0:15	0:22
P10	0:07	0:12	0:02	0:07	0:09
P11	0:05	0:13	0:12	-	0:17
P12	0:03	0:09	0:05	0:17	0:08
P13	0:04	0:10	0:07	0:10	0:11
P14	0:08	0:09	0:07	0:14	0:15
Median	0:04	0:11	0:07	0:15	0:12
IQR	0:03-0:04	0:09-0:15	0:05-0:14	0:07-0:26	0:08-0:18

The netto time plan selection represents the time that includes the selection of BRIGHT plans from the trade-off curve (step 1) and the subsequent evaluation of these plans in Oncentra Brachy resulting in the selection of the preferred BRIGHT plan for the patient at hand (step 3). Per process step the median time (min) and inter-quartile-range (IQR) was calculated. For patient 11 data is missing for step 4 due to separate clinical work of the radiation oncologist.

In patients 8 and 13 the base of the seminal vesicles was suboptimal implanted to achieve good coverage. Since no seminal vesicle invasion was present in these patients, it was decided to accept a reduced dose in favour of OAR sparing and undesirable high-dose to surrounding healthy tissue.

The main reason(s) for plan selection in BRIGHT and clinical plan choice in OB, the necessary fine-tuning, and used patient-specific information are shown in Supplementary Table A.2.

Reached dose-volume parameters and dose distributions

Table 1 summarizes the dose-volume parameters and normalized LCI and LSI values of the approved clinical treatment plan for each patient. In ten patients, all dose-volume criteria of the clinical plan were satisfied within a range of 0.2 Gy.

The necessary manual adjustments in patient 2, 4, 8, and 13 resulted in lower LCI/LSI values of the clinical plan than the original preferred BRIGHT plan (Fig 2), resulting in a clinical plan outside the desired 'golden corner'. In patient 3 and 7 the clinical plan fell inside the golden corner, but below the trade-off curve. For all other patients the dose-volume parameters remained roughly unchanged after fine-tuning (within a normalized LSI of -0.02).

As an example, Fig 3 shows dose distributions of three clinical plans: with a suboptimal implant (patient 8), chosen for highest coverage (patient 11) and highest sparing (patient 14) plan.

Figure 4 shows examples of the difference in dose distribution, dose-volume parameters and LCI/LSI for 3 patients where manual adjustments were needed:

In patient 3 dose to normal tissue was decreased, resulting in a clinical plan inside the golden corner, but below the trade-off curve. In patient 5 extra dwell positions were activated to increase dose to the base seminal vesicles, resulting in minor changes in dose-volume parameters and the LCI/LSI were unchanged. In patient 13 significant changes were made: Hot-spots in the base seminal vesicles, as a result of a sub-optimal implant geometry, were reduced and dose at the GTV location was increased, resulting in significant changes of dose-volume parameters of the target.

Process speed

The time per process step per patient can be found in Table 2. The optimization in BRIGHT took only 5 min. The median time spent on navigating the trade-off curve and selecting plans in BRIGHT was 4 min (interquartile range (IQR), 3-4 min). Most time was spent on the BRIGHT plan import into OB (a median delay of the entire process of 11 min). The median time spent on the subsequent evaluation and comparison of the dose distributions of the selected BRIGHT plans and selecting the best plan for each patient was 7 min (IQR 5−14 min). Finally, the median time spent on manual fine-tuning in OB was 15 min (IQR 7−26 min).

This results in a median time spent on treatment planning of 42 min (IQR 39-56 min) through the currently necessary but undesirable import-export process steps and manual fine tuning. Potentially this median time could at

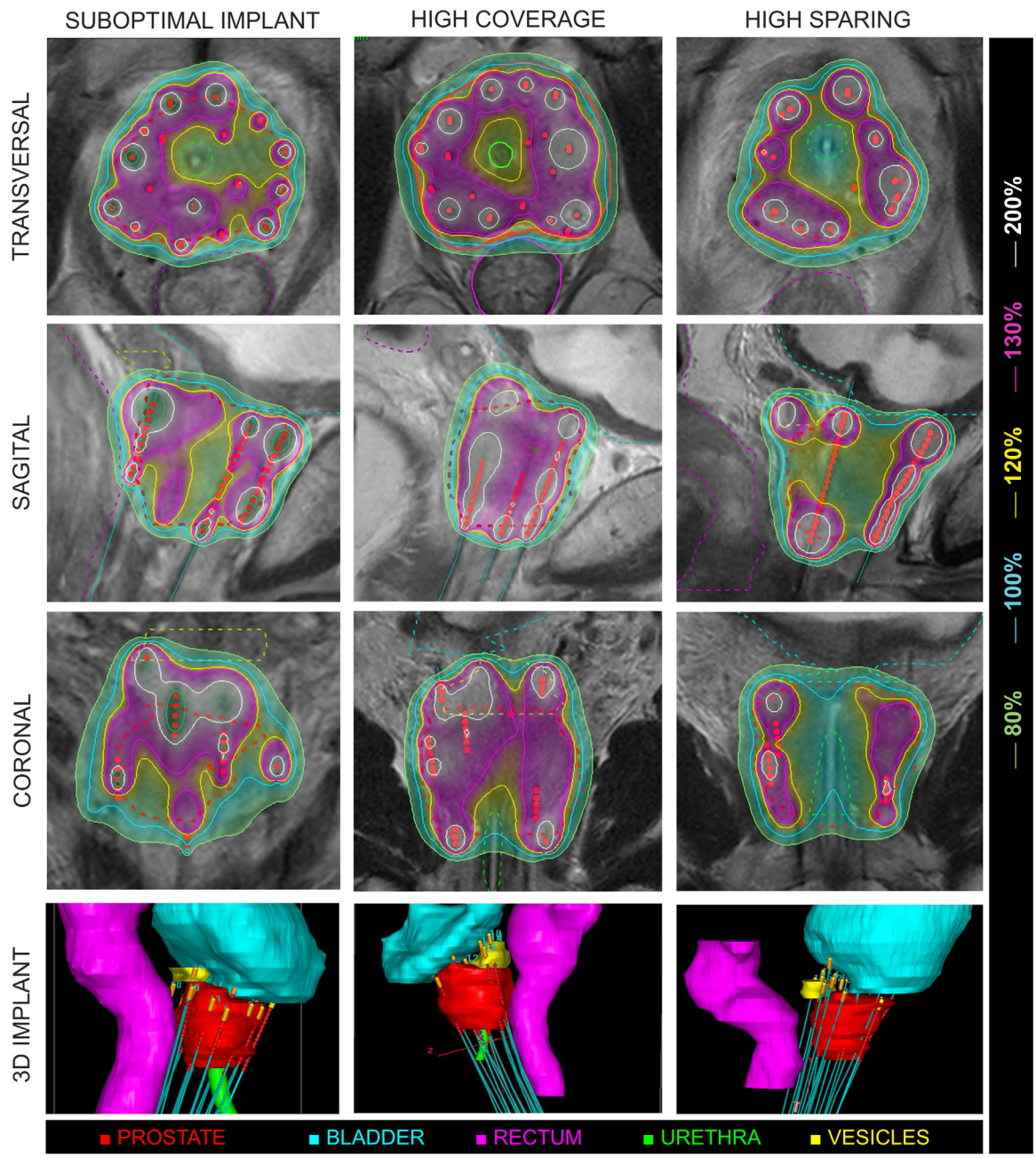


Fig. 3. Three examples of dose distributions of clinically approved plans with different selection reasons: coverage-sparing trade-off due to a suboptimal implant (patient 8), high coverage (patient 11), and high sparing (patient 14). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

least be reduced to 16 min for plan optimization and plan selection.

Discussion

This prospective study presents the first clinical experience at our centre with AI-based treatment planning applied for HDR prostate brachytherapy. The results show that a key added value of BRIGHT is that it enables inspection of the automatically generated trade-off curve to gain insight in what was feasible for the individual patient. For all patients, BRIGHT optimized plans that surpass the planning aims for the dose-volume criteria in the protocol could be selected for the clinical treatment planning process. All patients were treated as intended.

Previous studies showed superiority of automated treatment plans over manual optimized HDR-brachytherapy treatment plans and conducted research on user interaction using these automated planning approaches (11,12,25,26).

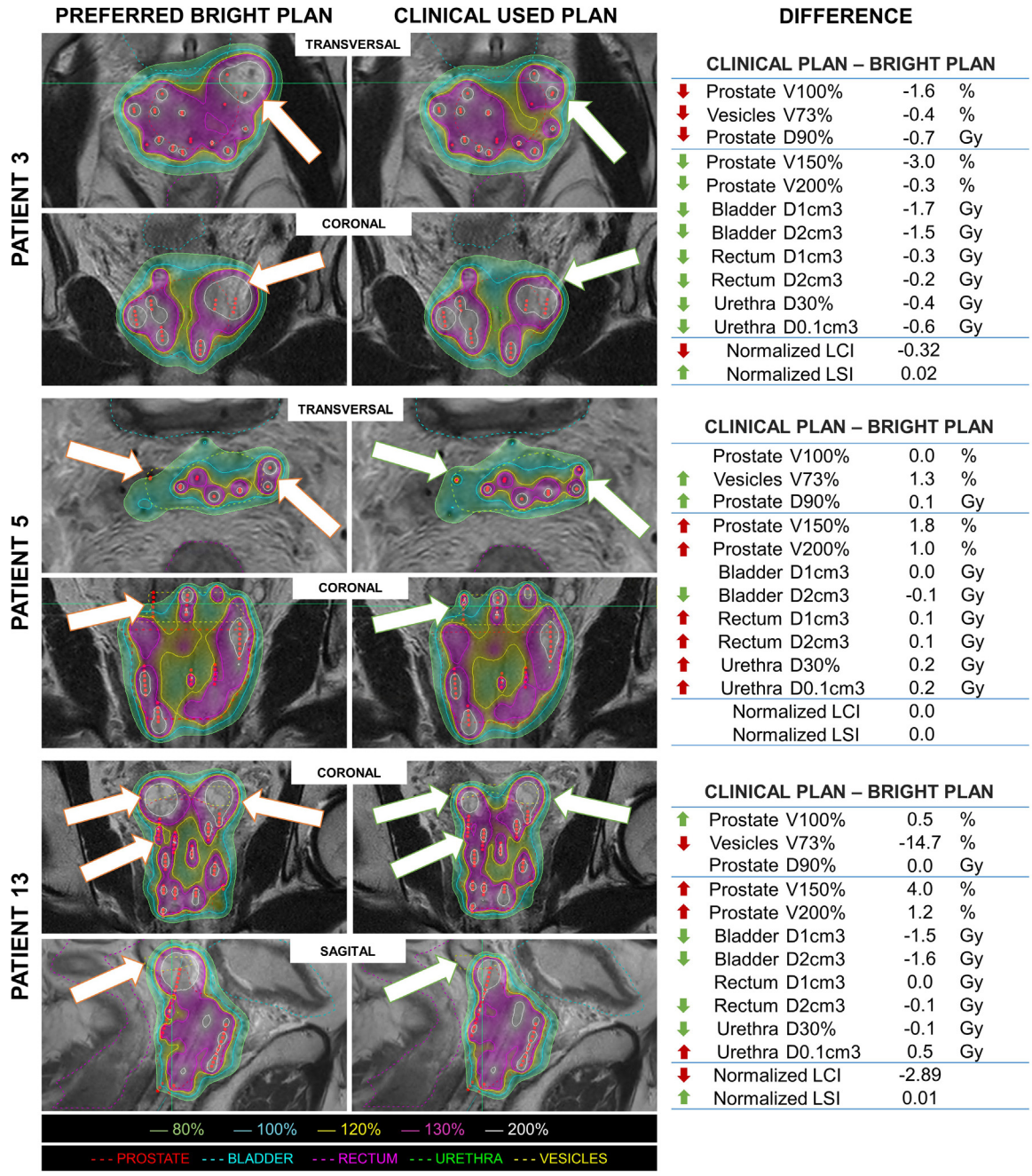


Fig. 4. Three examples of differences in dose distributions and dose-volume parameters of the originally preferred BRIGHT plan (left) and the clinically approved plan (right) after manual fine tuning. White arrows indicates where fine-tuning was done to decrease dose to surrounding tissue or increase dose to the targets. The right panel summarizes the differences in dose-volume parameters and normalized least coverage index (LCI) and normalized least sparing index (LSI) between the clinical used plan (including the manual fine-tuning) and the preferred BRIGHT plan (without manual fine-tuning). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

The use of our new approach (BRIGHT) differs from these studies since these were retrospective and thereby in our prospective study, time pressure was present in clinical practice. Furthermore, these works described a simulation of the clinical workflow, and do not report experiences in clinical practice for HDR brachytherapy, in terms of reasons for plan selection and/or tuning of specific weights, nor in process speed other than automatic plan optimization time.

In this study we aimed to investigate the expectations of the BRIGHT approach in clinical practice and report this experience.

The retrospective observer study from our group (20) concluded that fast and insightful navigation of MO-

GOMEA plans was of interest for clinical implementation of bi-objective treatment planning. This expectation was fulfilled in clinical practice using BRIGHT: BRIGHT has the ability to combine automatic generation of a set of high-quality solutions in a short time-span and offers plan selection based on sparing versus coverage from a trade-off curve of possible plans. This introduces a new way of plan selection and decision making in clinical practice for brachytherapy.

Furthermore, the advantage and distinctiveness of BRIGHT with respect to other solutions described in literature (4,6,11,12,14,25,26), is the fast generation of a set of Pareto-optimal plans that can be explored. Showing multiple solutions and giving the user the flexibility to choose a treatment plan, created confidence that the best trade-off between coverage and sparing could be made and the best plan has actually been chosen. In this way, AI-based treatment planning adds value to the way the RO can use his/her domain expertise to select the best treatment plan for each individual patient.

As shown in our results, the preferred BRIGHT plans satisfied all dose-volume criteria, which is consistent with the results of the retrospective study of the non-BRIGHT workflow (20). However, in 13 cases the preferred BRIGHT plan was fine-tuned manually. It was not unexpected that in six of these cases the resulting clinical plans were no longer on the trade-off curve, since the physician makes use of patient-specific information, experience and general knowledge that was not, or cannot be, captured by dose-volume criteria. In addition, in patients 2, 4, 8, and 13 the RO revised the protocol values to patient-specific values, among others to overcome suboptimal implant geometry.

The retrospective observer study (20) did not provide adjustments of preferred plans, since the question was ‘choose the best plan’ out of five preselected plans, but showed that almost all BRIGHT plans were superior to non-BRIGHT plans.

The evaluation of plan selection criteria and reasons for manual fine-tuning in this study taught us which additional (dose-volume) criteria are deemed of importance, such as aims for gross-tumour-volume, contiguous high-dose sub-volumes (“hotspots”), and high-dose regions in close proximity to OARs.

The current formulation as dose-volume criteria do not provide spatial information and two adjacent plans on the trade-off curve could be very different in dose distributions. Since for example, GTV location was an important criterion, we suggest to delineate GTV volumes when deemed necessary and possible, and subsequently register the clinically evaluated corresponding dose-volume parameters. The same is true for example in areas to spare in case of reirradiation and other physician specific desires that need to be indicated beforehand.

Furthermore, further research is needed to investigate if forms of parameterized approximations sets in the decision space (27) could be used, aiming to improve the navigability of the trade-off-curve to make it even more intuitive and faster for plan selection based on patient specific information such as urinary problems or re-irradiation.

Preliminary results of ongoing research showed that dwell-time-gradient restriction and/or a third optimization objective are possible solutions to reduce undesirable hotspots with minimal impact on resulting dose-volume parameters (28).

If these new acquired criteria are implemented, we believe we can reduce the need for manual adjustments.

A limitation of our study is that the time taken for clinical plan choice in OB and additional fine-tuning until clinical plan approval was sometimes difficult to capture separately.

While the new treatment planning workflow with BRIGHT worked well, avoidable process delays were present such as BRIGHT plan import into OB, resulting in a median time spent on treatment planning of 42 min. The captured time taken for only plan selection, a median of 12 min (IQR 8−18 min), shows the potential of BRIGHT when integrated in a commercial treatment planning system in which unnecessary user interactions (i.e., export and import of DICOM data) can be further reduced. Potentially the median total time spent on plan optimization and plan selection could then be reduced to 16 min. Although the non-BRIGHT workflow was not within the scope of this study, our results show a slight improvement over the historical data of the observer study (20), which showed that five recorded planning sessions in our clinic lasted for a median of 33 min (range: 9−48) from the first modification until the last modification. In contrast to our study, time taken for plan approval and plan QA was not included in this historical data.

Most importantly, there might be a shift in the use of time. With BRIGHT, time can be spent on carefully choosing the desired plan, instead of adjusting one plan iteratively without having any indication one has actually arrived at the best possible plan for that patient and what alternatives are.

Finally, it is known that using the same optimization methodology, implants can also be optimized in a pre-planning phase (29). Including this extension in the clinical use of BRIGHT might help to prevent suboptimal implants.

Conclusion

This prospective study shows that, the use of bi-objective, AI-based plan optimization for HDR prostate brachytherapy is feasible in clinical practice and of added value. At the same time, our first clinical experience has provided additional information about how the methodology could be further improved from a clinical perspective. This creates confidence for further application of our method in the field of brachytherapy.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.brachy.2022.11.013.

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