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Original paper

Dose optimization and endorectal balloon for internal pudendal arteries sparing in prostate SBRT

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ABSTRACT

Purpose: Vessel-sparing radiotherapy has shown promising results in preserving erectile function (EF). Using an endorectal balloon (ERB) may help to reduce the dose to the internal pudendal arteries (IPA) by pushing the prostate forward. We tested this hypothesis and evaluated the limits of IPA dose optimization in prostate cancer patients simulated with and without ERB.

Materials and methods: Twelve patients with localized disease were simulated both with and without ERB. IPA were delineated on every CT after MRI registration. Planning target volumes (PTV) were planned to receive 36.25 Gy in 5 fractions with a VMAT technique. Twenty-four *initial* plans were generated using a knowledge-based planning software without any specific constraints for IPA. Additional stepwise optimization was performed until stabilization of the IPA dose or trespassing of PTV homogeneity limits.

Results: Without optimization, the median mean IPA dose (D_{mean}) was lower with ERB than without (10.5 *vs.* 12.8 Gy, $p = 0.023$). After optimization, the IPA D_{mean} dropped significantly (from 11.1 to 4.8 Gy) without impairing the PTV dose homogeneity and the organs at risk dose constraints. The comparison of the best-optimized plans with and without ERB showed an optimal sparing of IPA using ERB (28% mean dose reduction, $p = 0.006$; median D_{mean} of 4.1 Gy *vs.* 5.7 Gy with and without ERB, respectively).

Conclusion: IPA dose sparing is feasible without compromising dose prescription and constraints. ERB significantly reduced the dose on IPA compared to plans generated without ERB. As no specific constraints are available for vessel-sparing SBRT, optimal IPA dose reduction should be recommended to maximize EF preservation.

1. Introduction

Erectile dysfunction (ED) is one of the most common long-term side effect of curative radiotherapy (RT) in prostate cancer patients [1]. Although the underlying mechanism of ED after RT is not yet well established, it is strongly suspected that radiation induced vascular damage play a major role [2–4]. Sparing the internal pudendal arteries (IPA) with modern RT techniques may then potentially help to preserve erectile function (EF) in men treated with RT for localized prostate cancer [5,6]. Vessel-sparing techniques using intensity modulated RT aim to reduce the dose to the penile bulb, the corpora cavernosa, and the IPA [7–9]. Compared to historical RT and nerve-sparing prostatectomy, high tumor control rates while achieving optimal EF preservation have been reported [7].

Stereotactic body radiotherapy (SBRT) for localized prostate cancer is an emerging treatment technique providing excellent clinical results regarding tumor control and toxicity rates [10,11]. Since IPA dose reduction appears to be critical for EF preservation, treatment planning optimization becomes crucial while waiting for dose constraint guidelines, unavailable so far.

Several publications have reported on the use of endorectal balloons (ERB) for dose sparing of the rectal and anal walls, as well as for position reproducibility and prostate immobilization [12–17]. To our knowledge, however, no studies have assessed so far the influence of ERB on IPA dose sparing, apart from preliminary conference results of our research group [18]. Based on the hypothesis that ERB may help to optimize the dose distribution to the IPA, we aimed to compare dosimetric results on twelve prostate cancer patients simulated both with

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and without ERB before definitive SBRT. Furthermore, we aimed to evaluate the maximum IPA dose reduction that can be achieved with systematic optimization, without impairing the dose distribution received by the planning target volume (PTV) and the remaining organs at risk (OaR).

2. Materials and methods

The computed tomography (CT) datasets of twelve prostate cancer patients were used in this study. For every patient, two simulation CTs with 2-mm thickness axial slices were acquired: the first with an ERB inflated with air (100 ml) and the second without ERB. All patients were simulated with an empty rectum and a full bladder following an institutional protocol. For contouring purposes, the CTs were rigidly registered with T2-weighted sequences of a pelvic MRI (with or without ERB) using the imaging module of the treatment planning system (TPS) Eclipse (v.13.6, Varian Medical Systems, Palo Alto, USA). Each patient underwent two MRI exams, a diagnostic MRI without ERB, and an MRI with ERB in the planning position, with flat table top and RT dedicated immobilization devices. The PTV encompassed the prostate and the proximal part of the seminal vesicles with a 5-mm isotropic expansion, except posteriorly where a 3-mm margin was used. Contouring the OaR on the 24 planning CTs was performed following the male pelvis normal tissue contouring guidelines of the RTOG [19]. The rectal wall (RW) was defined using a 3-mm and 5-mm thickness section for patients simulated with and without ERB, respectively. A 5-mm thick section was extracted from the bladder to create the bladder wall (BW). IPA were contoured with the MRI as previously described [7,8]. No planning risk volume was added around the IPA.

A dose of 36.25 Gy in 5 fractions was prescribed to the PTV, while dose constraint limits on OaR were: $V_{100\%} = V_{36.25Gy} < 5\%$, $V_{90\%} = V_{32.63Gy} < 10\%$ and $V_{80\%} = V_{29Gy} < 20\%$ for the RW, $V_{100\%} = V_{36.25Gy} < 15\%$, $V_{90\%} = V_{32.63Gy} < 20\%$, and $V_{50\%} = V_{18.13Gy} < 50\%$ for the BW, and $D_{2\%} < 50\% = 18.13$ Gy for the femoral heads (FH). All plans were created in Eclipse using the Photon Optimizer and the Analytical Anisotropic Algorithm (v.13.6). Treatment was planned to be delivered with two full volumetric modulated arcs (VMAT), with 10 FFF photon beams, using a TrueBeam linear accelerator (Varian Medical System) mounted with a Millenium™ MLC, with leaves of 5 mm width in the central region. Collimator angles were 30 and 330°. For all plans in the study, plan normalization was fixed such that the 95% isodose prescription line (34.44 Gy) covered 98% of the PTV.

For every patient, a pair of *initial* plans (with and without ERB) was created using the knowledge-based planning software RapidPlan™ (RP) (Varian Medical Systems). RP aims to create the best possible plan using previous knowledge such as dose and patient anatomy extracted from data of previously treated patients, and is used in our institution on a routine basis for prostate treatment planning. The prostate RP database, created using about 60 SBRT plans (with and without ERB), is used to generate dose volume histogram (DVH) and optimization constraints for PTV, RW, BW, and FH. No IPA dose constraints were introduced to generate the 24 *initial* plans. We did not introduce a dose constraint for the penile bulb (PB).

For the present modelling effort a series of stepwise optimization runs were launched adding an optimization constraint on the mean IPA dose (D_{mean}). This constraint was assigned a constant weight and a dose value 2 Gy lower than the one obtained with the *initial* plans. The IPA doses of these new plans were extracted and the optimization process was repeated until one of the following criteria was met: 1) PTV $D_{2\%}$, reached or exceeded the limit of 107% of the prescribed dose (38.79 Gy), or 2) IPA D_{mean} stabilized or increased compared to the previous optimization results (stabilization was defined by a decrease inferior to 0.25 Gy). The 24 plans obtained at the end of this process (satisfying PTV $D_{2\%} \leq 38.79$ Gy and with the lowest IPA D_{mean}) were called *best* plans. In total, three to six runs per CT were computed. We extracted from those plans DVH data for the PTV, IPA, RW, BW, FH and the PB, as well as the volume encompassed by the 95% isodose band and the needed number of monitor units (MU).

Qualitative and quantitative analyses of the change in geometry induced by the ERB were performed. The influence of the ERB on IPA dose distribution (when no dose constraints were applied) was evaluated by investigating the differences between the *initial* plans with and without ERB. IPA D_{mean} and maximal doses ($D_{2\%}$) were compared, as well as the PTV dose homogeneity and the OaR dose distribution. Prescription isodose target conformality was evaluated using the Dice index (DI) defined as $DI = 2 \cdot (V_{PTV} \cap V_{prescription}) / (V_{prescription} + V_{PTV})$, where $V_{prescription}$ is the volume of the 95% isodose and V_{PTV} is the PTV volume.

Next, we determined to what extent IPA D_{mean} and $D_{2\%}$ could be decreased with the optimization process by comparing our *best* plans to the *initial* plans. The effects of IPA dose optimization on PTV homogeneity, prescription isodose conformality, OaR sparing, and estimated MU were also investigated. Last, the difference between the *best* plans with and without the ERB was evaluated to assess the potential role of ERB in optimally sparing the IPA.

Statistical analyses were performed with the SPSS software (v.24, IBM, Chicago, USA) and significance levels for the difference between datasets (plans with *vs.* without ERB and *initial vs*. *best* plans) were determined using the non-parametric related-samples *Wilcoxon signed-rank* test, with *p*-values ≤ 0.05 considered as statistically significant.

3. Results

The IPA volume was similar in the two CT datasets, with or without ERB: median IPA volume with ERB: 4.75 cm^3 (range, 3.80–7.20) and without: 4.95 cm^3 (range, 3.80–7.00) ($p = 0.721$). The median PTV was slightly larger with ERB: median 99.0 cm^3 (range, 70.5–262.8) than without ERB: median 95.00 cm^3 (range 60.9–247.6) ($p = 0.028$). A qualitative inspection of the IPA and PTV contours on the CTs revealed that the IPA position in the pelvis did not change in a systematic way with ERB, whereas the PTV was always shifted anteriorly. The later determined an increase in the median distance between the geometric barycentre of the PTV and the IPA from 3.3 cm (range, 2.6–4.1) to 4.6 cm (range, 3.8–5.0) without and with ERB, respectively ($p = 0.002$). We observed, however, only a moderate correlation between individual PTV-to-IPA barycentre distances and IPA D_{mean} (coefficient of determination of the linear regression, $r^2 = 0.34$).

The analysis of the *initial* plans obtained with RP and no IPA dose constraints showed that the median IPA D_{mean} was 18% lower with ERB than without ERB (10.5 *vs.* 12.8 Gy, respectively, $p = 0.023$) (Table 1 and Fig. 1b). The median IPA $D_{2\%}$ was also lower though not statistically significant. As for the PTV, the median $D_{2\%}$ was slightly higher (0.5 Gy) for plans with ERB, while differences in DI were not significant. The doses to the OaR were similar regardless of the use of ERB except for a small increase in the BW $V_{100\%}$ with ERB.

For all patients and all CTs (with and without ERB) the optimization strategy led to a progressive decrease of dose to the IPA and a controlled increase in PTV inhomogeneity (Fig. 2). The optimization process was stopped when the limit of $D_{2\%} \geq 38.79$ Gy (107%) was reached (PTV prescription limit). However, for one patient, this limit was exceeded in the *initial* plan with ERB though further optimization led to a *best* plan with a lower PTV $D_{2\%}$ and a lower IPA D_{mean}. Moreover, our analysis revealed that DI slightly decreased in plans with a better sparing of the IPA ($p = 0.012$). When considering all CTs, we observed that the median IPA D_{mean} decreased by 57%, from 11.1 to 4.8 Gy ($p < 0.001$). With ERB, the median D_{mean} to the IPA was reduced by 61% (from 10.5 to 4.1 Gy, $p = 0.002$) whereas, without ERB, the median D_{mean} decreased by 55% (from 12.8 to 5.7 Gy, $p = 0.002$) (Table 1 and Fig. 1). IPA $D_{2\%}$ was also reduced consequently by the optimization process with (17.6 to 8.1 Gy) or without ERB (20.8 to 9.3 Gy), $p = 0.002$, in both cases.

As for OaR, the RW dose remained constant through the

Table 1
Medians and ranges of dosimetric parameters for initial and best plans, with or without ERB.

	Initial plans			Best plans			Intial *vs.* best plans *p*-value	
	With ERB	Without ERB	*p*-value	With ERB	Without ERB	*p*-value	With ERB	Without ERB
PTV								
$D_{2\%}$ (Gy)	37.0 [36.7–39.1]	36.5 [36.1–38.2]	0.004	38.1 [37.5–39.0]	38.4 [36.9–38.8]	0.306	0.003	0.002
DI	0.947 [0.909–0.961]	0.955 [0.905–0.963]	0.117	0.937 [0.907–0.960]	0.940 [0.901–0.959]	0.875	0.010	0.012
IPA								
D_{mean} (Gy)	10.5 [6.6–18.9]	12.8 [7.7–20.2]	0.023	4.1 [3.2–6.6]	5.7 [3.2–9.9]	0.006	0.002	0.002
$D_{2\%}$ (Gy)	17.6 [12.6–32.2]	20.8 [12.9–34.3]	0.071	8.1 [4.7–21.0]	9.3 [5.4–28.0]	0.071	0.002	0.002
RW								
$V_{100\%}$ (%)	0.3 [0.0–10.0]	0.3 [0.0–7.7]	0.480	1.4 [0.4–9.6]	1.5 [0.1–7.9]	0.855	0.008	0.034
$V_{90\%}$ (%)	10.7 [6.7–21.7]	10.7 [6.1–21.0]	0.391	10.6 [6.6–21.8]	10.2 [5.5–21.1]	0.312	0.157	0.120
$V_{80\%}$ (%)	13.7 [8.9–27]	14.3 [8.8–25.7]	0.964	13.4 [8.7–27.2]	13.8 [8.4–25.3]	0.681	0.157	0.111
BW								
$V_{100\%}$ (%)	2.6 [0.0–7.7]	0.4 [0.0–6.8]	0.027	7.2 [1.7–15.4]	6.6 [0.5–16.1]	0.028	0.003	0.005
$V_{90\%}$ (%)	14.2 [7.3–25.2]	12.4 [6.9–28.8]	0.166	14.5 [7.3–25.3]	12.6 [6.9–30.5]	0.172	0.083	0.590
$V_{50\%}$ (%)	26.4 [12.8–45.3]	23.2 [12.6–49]	0.153	26.3 [13.0–44.5]	23.2 [12.3–50.4]	0.080	1.000	0.763
FH								
$D_{2\%}$ (Gy)	16.7 [13.6–18.5]	16.0 [13.4–17.3]	0.050	17.9 [16.9–20.8]	17.3 [14.8–20.1]	0.091	0.002	0.002
PB								
D_{mean} (Gy)	3.7 [1.4–29.7]	2.9 [1.6–22.3]	0.388	3.5 [1.4–27.4]	2.8 [1.8–19.5]	0.530	0.012	0.117
$D_{2\%}$ (Gy)	7.4 [2.6–36.7]	5.3 [3.7–36.3]	0.480	6.8 [2.6–38.2]	5.1 [3.6–38.3]	0.583	0.155	0.158
MU								
Number	2450 [2177–2593]	2271 [2115–2539]	0.034	2388 [2044–2582]	2318 [1956–2638]	0.530	0.182	0.530

Abbreviations: endorectal balloon (ERB), planning target volume (PTV), internal pudendal arteries (IPA), rectal wall (RW), bladder wall (BW), femoral head (FH), penile bulb (PB) and monitor units (MU). *P*-values characterize the significance level of differences between plans with and without ERB, and between initial and best plans.

optimization process except for a minor increase in $V_{100\%}$ (Table 1). All *best* plans fulfilled the dose constraint of $V_{100\%} < 5\%$ (except for one patient for whom the *initial* plans with and without ERB were beyond this limit). Similarly, the BW dose did not significantly change from *initial* to *best* plans except for a small increase in $V_{100\%}$, even though the dose limit of $V_{100\%} < 15\%$ was exceeded in one patient only (15.4% with ERB and 16.1% without ERB). The median $D_{2\%}$ for the FH increased by 7–8% from *initial* to *best* plans but remained inside acceptable limits, while we observed a minor decrease in the PB D_{mean} in the plans with ERB. The number of MU per plan did not significantly increase along the optimization process (Table 1).

Finally, the present analysis showed that when comparing *best* plans with and without ERB the median IPA D_{mean} was reduced by 28% with ERB ($p = 0.006$) and the median $D_{2\%}$ by 13% (not significant) (Table 1). In contrast, the dose distributions for the PTV and OaR were similar.

4. Discussion

In this study, we investigated to what extent the IPA dose can be reduced in a prostate SBRT setting by a systematic optimization procedure. In addition, we assessed whether the use of an ERB can help to further improve vessel sparing. Our data shows that, regardless of the use of the ERB, it is possible to markedly reduce the dose to the IPA (both D_{mean} and $D_{2\%}$) with optimization without compromising the PTV homogeneity and OaR sparing. This dose reduction was larger in patients simulated with ERB. The IPA D_{mean} was lower with than without ERB, especially when comparing the *best* plans (4.1 *vs.* 5.7 Gy, respectively) and regardless of a minor increase in the PTV volume with ERB.

The differences in D_{mean} to the IPA with or without ERB were linked

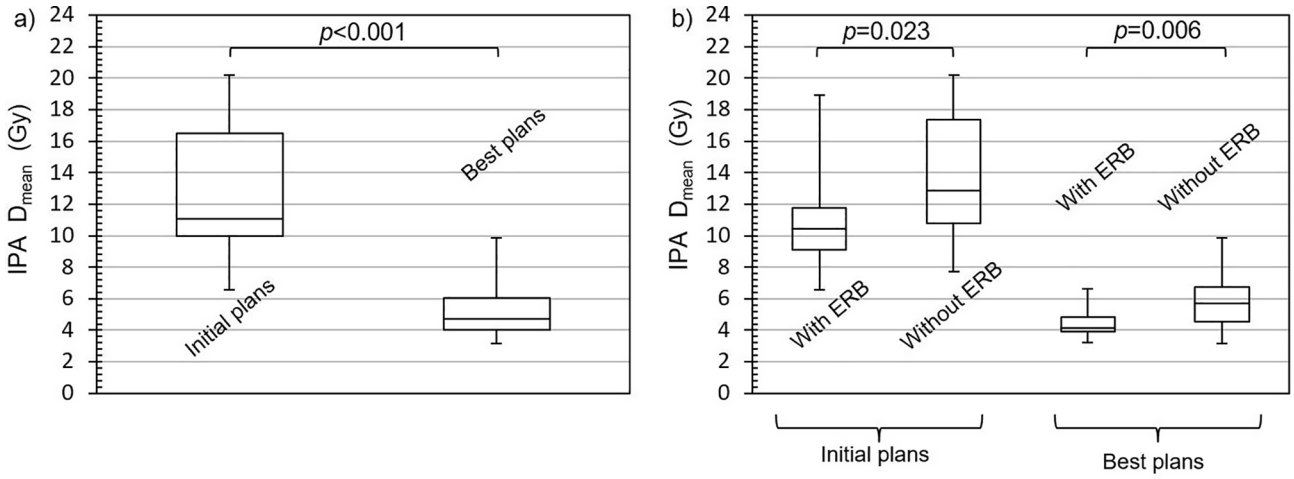

Fig. 1. Box-and-whisker plots (showing median, max, min, first, and third quartile) of D_{mean} received by the internal pudendal arteries (IPA): (a) data for all plans, with and without endorectal balloon (ERB), before and after optimization, (b) data stratified in two groups, with and without ERB.

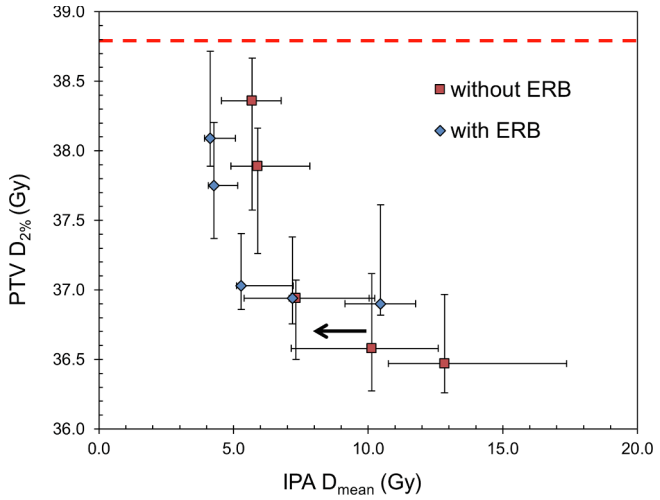

Fig. 2. Plots of median PTV $D_{2\%}$ *vs.* median IPA D_{mean} for the successive plans of the twelve patients, showing the optimization process for IPA (direction is indicated by the arrow) and the PTV with and without endorectal balloon (ERB). The horizontal dashed red line indicates the dose constraint limit $D_{2\%}$ = 107% at which the optimization was stopped. The lower and upper error bars correspond to the 1st and 3rd quartiles of the distributions, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

to changes in anatomy induced by ERB which caused the median distance between the IPA and the PTV barycentre to increase by 39% (from 4.6 to 3.3 cm). We believe that the weak correlation between individual PTV-to-IPA barycentre distances and IPA D_{mean} was most likely linked to the large IPA anatomical differences among patients as discussed by Lee et al. [8].

It is not yet known what dose parameters the IPA are sensitive to. Research groups studying vessel-sparing RT generally aim at an IPA dose reduction as low as reasonably achievable [7]. In our study, both D_{mean} and $D_{2\%}$ were decreased by 57% with the optimization process, while only D_{mean} was significantly reduced with ERB when comparing plans with and without ERB. It seems reasonable to assume that for structures with small cross-section diameters (*e.g.*, < 5–6 mm) such as IPA, dose-volume-effect parameters be likely unreliable, except possibly for D_{mean}. Therefore, the use of ERB could still improve EF preservation after SBRT by helping decreasing the IPA D_{mean}. In addition, ERB were shown to decrease intra-fraction motion of the prostate during prostate RT treatment [17]. In contrast with our results, some studies have also shown that using an ERB allows for a better sparing of the RW [12–14].

Notwithstanding the reduced group of patients in this study, the number of cases was consistent with cohorts used in similar dosimetric studies [12,14]. In addition, the fact that each patient underwent a pair of CTs, with and without an ERB, allowed for a proper evaluation of the potential benefit of ERB. The *initial* plans were generated with a knowledge-based planning method. We did choose this approach to ensure a certain level of homogeneity and to reduce the potential bias induced by creating all plans by a single planner [20–22]. Since plans with and without ERB were used to create the RP database, the quality of the results should not necessarily depend on the presence of the ERB.

Various studies have included IPA dose sparing in treatment planning of prostate RT [6–9]. However, they have not used a systematic optimization strategy such as ours, nor clear criteria to stop the optimization process. The optimization method in this study aimed to gradually reduce the IPA dose while keeping all other dose constraints constant. This procedure is similar to *Pareto's* optimal front determination [23,24]. Such optimization could have been performed with a dedicated multicriteria optimization software which is faster and less biased than manual planning [25]. Our department is not equipped with such software thus the present optimization procedure should be viewed as an alternative, even though it does not guarantee that the actual *Pareto* front is reached. Plots of the PTV $D_{2\%}$ *vs.* IPA D_{mean} represent a sampling of the *Pareto* front for these two plan properties and allow comparison between treatment modalities with and without ERB. Our results (Fig. 2) indicated that if we prioritize an optimal PTV homogeneity, the modality without ERB yielded a better trade-off, whereas if the IPA sparing was privileged ERB plans offered a better compromise.

The analysis also showed that the IPA dose distribution optimization correlated with a slight decreased of the DI, reflecting the fact that the prescription dose to the PTV was less well-fitted. However, all plans were considered clinically acceptable. A dose reduction of 55% to the IPA median $D_{2\%}$ value was obtained with optimized plans without ERB which can be compared to the results by McLaughlin et al. [6]. In their study, they compared 5 patients assessing the $D_{5\%}$ received by the IPA on CT-based and on MRI/CT-based treatment plans, respectively. A mean dose decrease of 39% was estimated with 3D conformal RT for MRI/CT-based plans probably less optimal for sparing critical structures such as IPA than our treatment plans with VMAT.

In this study, we focussed our interest on IPA disregarding sparing other structures such as the penile bulb, the neuro-vascular bundles, or the corpora cavernosa, also considered to be potentially involved with EF [26–29]. Recent studies have suggested that a hydrogel spacer between the rectum and the prostate may help to reduce the dose to the penile bulb which may translate in better 5-year EF preservation compared to patients treated without a spacer [30,31]. In the present study, however, the penile bulb dose parameters such as D_{mean} and $D_{2\%}$ were not significantly different between plans regardless of the use of ERB.

Our study was performed in the context of an SBRT dose prescription of 36.25 Gy in 5 fractions, even though our results can be extrapolated to other fractionation schemes. Since dose constraints on IPA are not yet known and it is unclear whether the decrease in dose achieved by our method is clinically significant, an essential point with our approach, besides keeping the PTV dosimetry according to prescription, was to check that OaR dose constraints were respected. Our results showed that the toll to pay in order to reduce the IPA D_{mean} and $D_{2\%}$ by 57% was a slight increase in $V_{100\%}$ for the RW and BW and the $D_{2\%}$ for the FH. All these parameters, however, remained within dose constraints and were clinically acceptable. Finally, IPA sparing is not expected to affect SBRT target coverage during treatment delivery since PTV margins were not modified, and PTV coverage was not reduced in plans with optimal IPA sparing (all plans in the study were normalized such that 98% of the PTV was covered by 95% of the prescription dose).

5. Conclusion

Regardless of ERB, an optimal IPA dose reduction can be implemented with SBRT for prostate cancer without compromising the PTV homogeneity and OaR dose constraints. ERB for prostate SBRT significantly reduced the dose on IPA compared to plans generated without ERB. As no specific dose constraints are available for vessel-sparing SBRT, optimal IPA dose reduction should be recommended. Clinical studies assessing EF effects *vs.* dose to the IPA should be undertaken to confirm or reject this hypothesis.

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Conflict of interest

The authors have no relevant conflicts of interest to disclose

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