Comparative Analysis of Radiation Therapy Plans Before and After Biodegradable Hydrogel (SpaceOAR) Injection for Reducing Rectal Toxicity in Prostate Cancer Patients Undergoing Carbon Ion Radiotherapy

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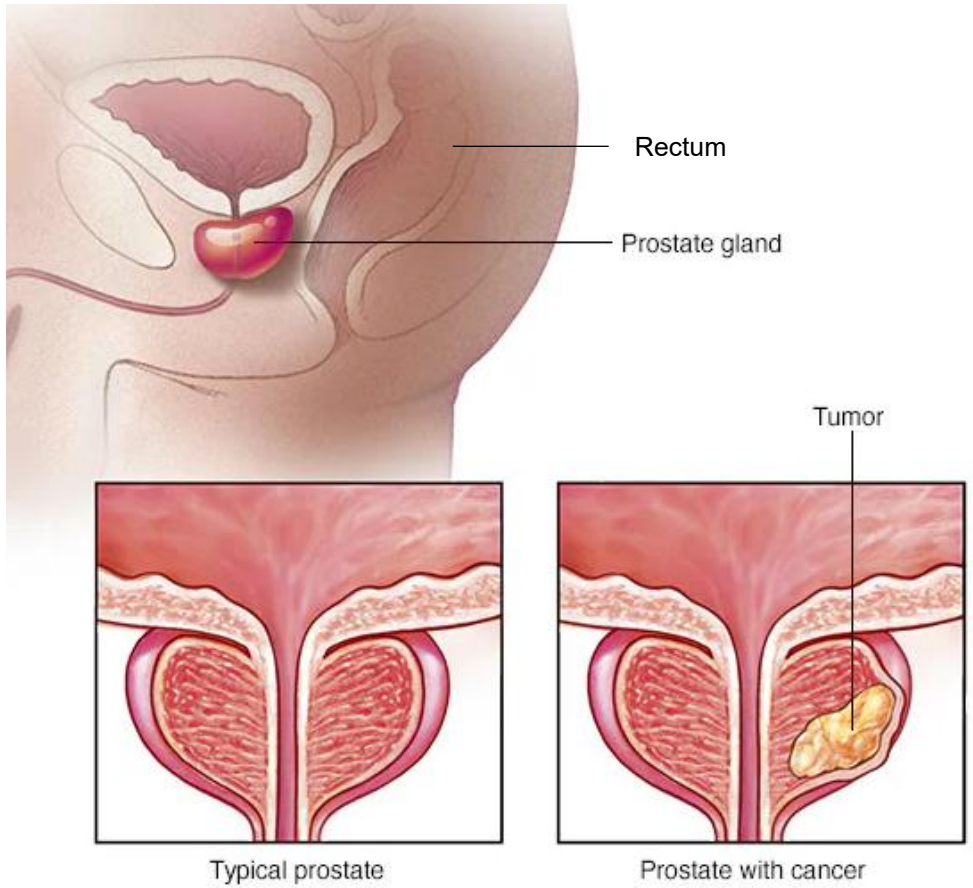
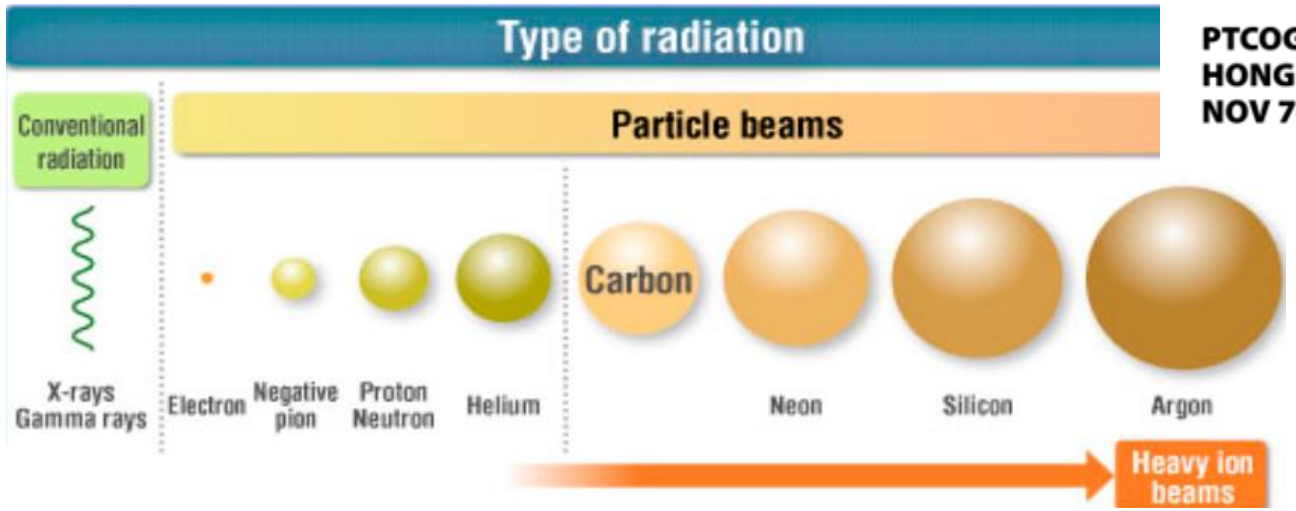
Presenter: Hyun Jin Kim

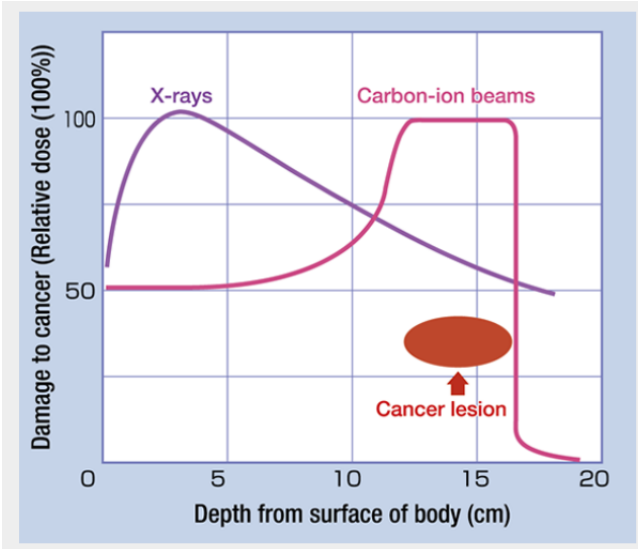
Background

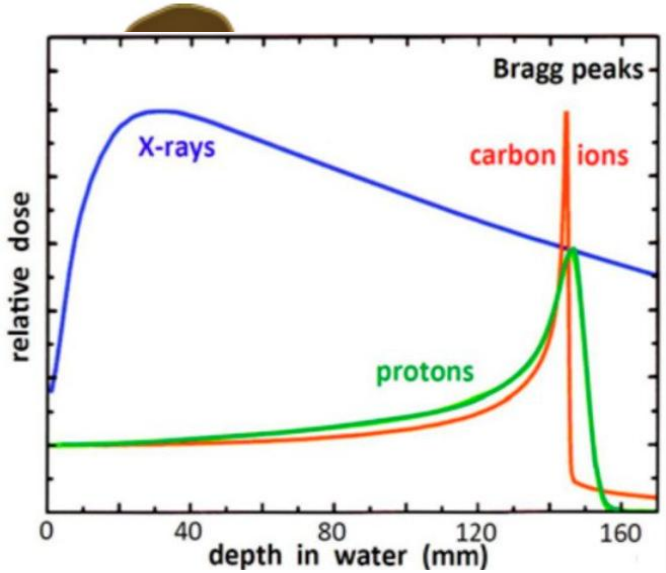
Prostate Cancer

- 2nd most common cancer
  - ✓ 5th in male mortality (2018)
  - ✓ Incidence nearly doubling by 2040









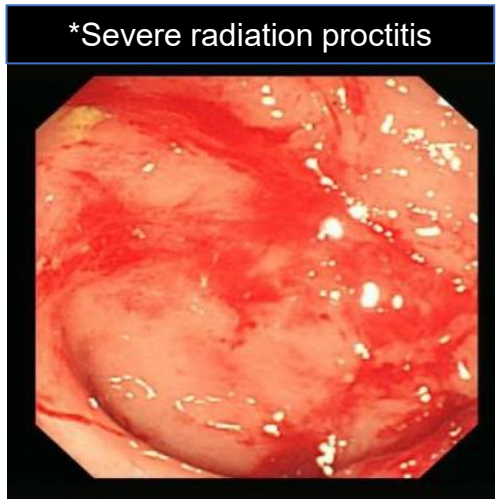
➢ **Carbon Ion Radiotherapy (CIRT)** increasingly used for prostate cancer
Bragg peak / Superior cancer cell killing / Shorter Treatment Duration

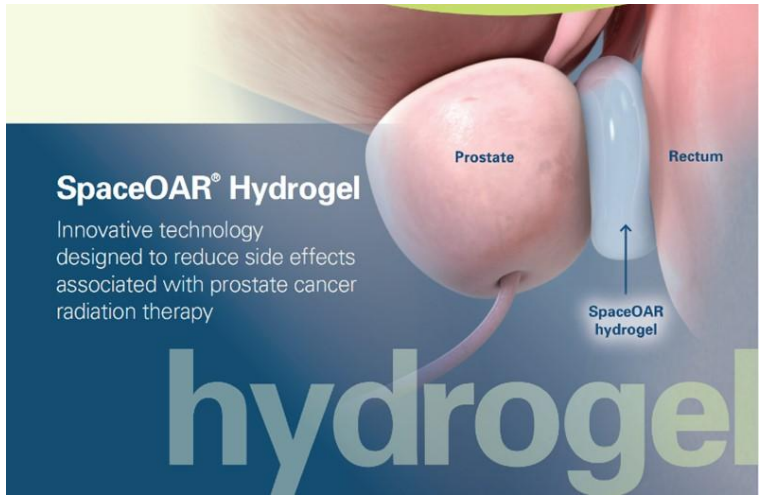
✓ ***Key challenge: Rectal toxicity***

Background

➢ SpaceOAR™ hydrogel

Creates prostate–rectum separation → **reduces rectal dose**





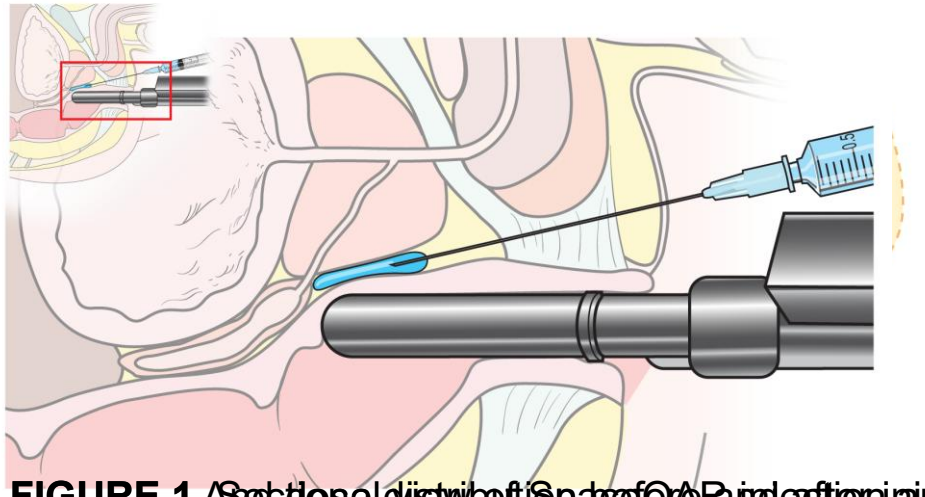


FIGURE 1 Sectional view of SpaceOAR injection and dose distribution

Clinical Investigation

Hydrogel Spacer Prospective Multicenter Randomized Controlled Pivotal Trial: Dosimetric and Clinical Effects of Perirectal Spacer Application in Men Undergoing Prostate Image Guided Intensity Modulated Radiation Therapy

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Clinical Investigation

Continued Benefit to Rectal Separation for Prostate Radiation Therapy: Final Results of a Phase III Trial

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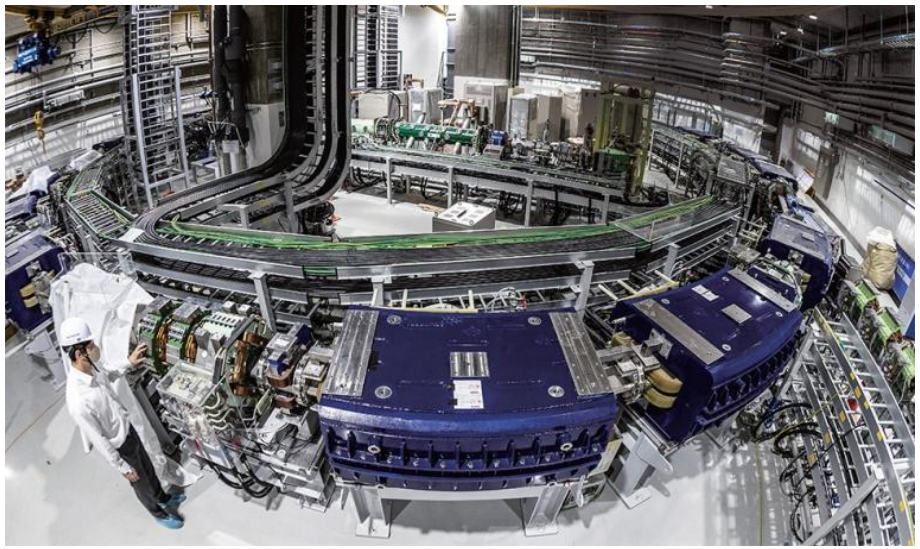
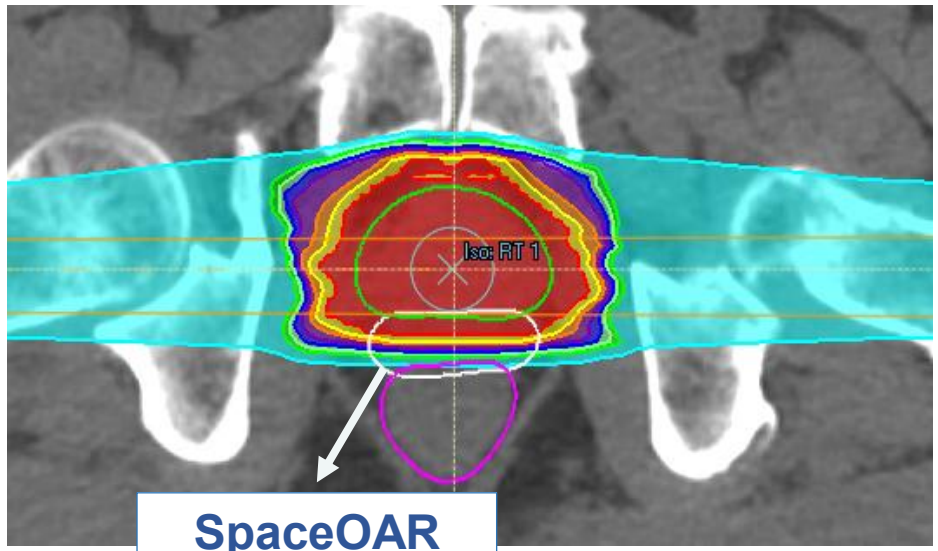
Objectives

- A comparative analysis of CIRT plans for prostate cancer before and after SpaceOAR insertion is conducted, as the combination of CIRT with perirectal spacers has not been extensively studied.

① Confirm the safety and efficacy of combining CIRT with SpaceOAR.
② Assess how SpaceOAR affects dose distribution to the prostate and surrounding organs.
③ Quantify the dose reduction and evaluate the overall impact on treatment plan robustness and efficacy.





**IRB-approved* *retrospective study (Severance Hospital, No. 4-2024-0862)*

Methods

[Patient Cohort]

- ✓ 25 prostate cancer patients
- ✓ Primary tumors treated with definitive RT.
- ✓ Hydrogel injection followed by CIRT
- ✓ Both have pre- and post-carbon ion therapy CT and MRI

[Exclusion criteria]

- ✓ Prostate volume > 80 cm^3
- ✓ Previous surgery or RT
- ✓ Metastatic disease
- ✓ Androgen deprivation therapy
- ✓ Significant CT scan timing or prostate volume changes

Carbon planning and details

- Three treatment plans
  - ① Conventional
  - ② Rectum-protection (no spacer)
  - ③ Post-SpaceOAR

- ✓ Fusion imaging (T2-MRI / CT) used for target and SpaceOAR delineation
- ✓ 51.6 Gy / 12 fx (4.3 Gy/fx)
- ✓ Fixed-beam room (couch 0°/180) alternating bilateral ports
- ✓ TPS: RayStation (version 11B)
- ✓ RBE calculated using the modified Microdosimetric Kinetic Model (mMKM)

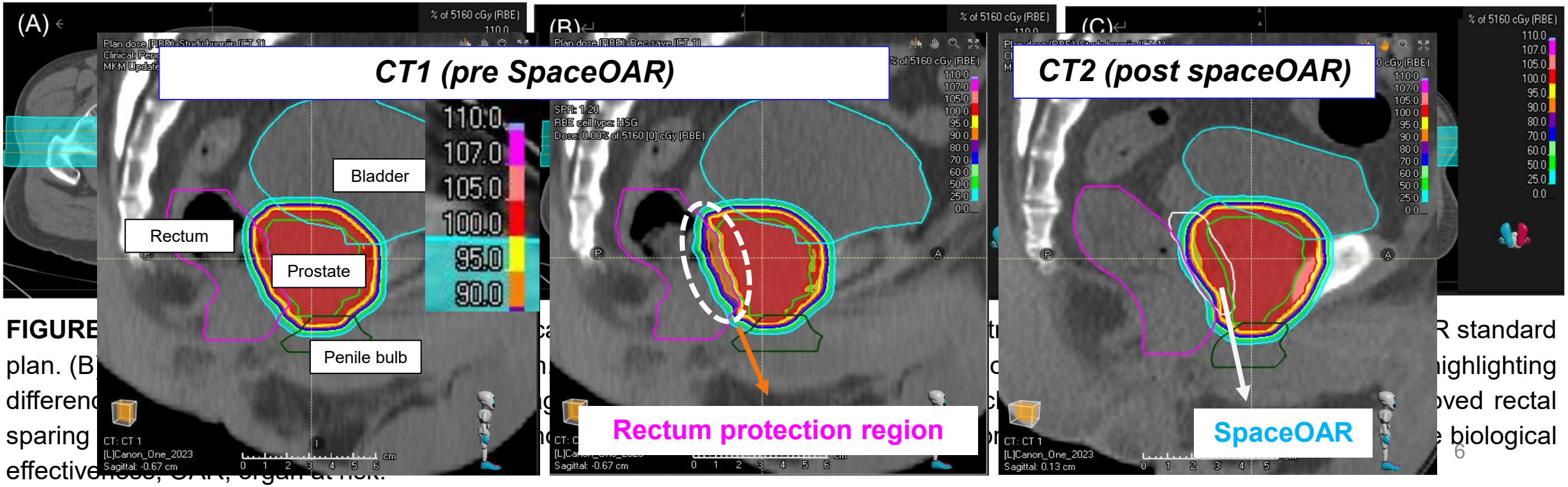


FIGURE R standard plan. (B ighlighting differenc oved rectal sparing e biological effectiveness, OAR, organ at risk.

Evaluation - Prostate-Rectum Separation and Rectal DVH Analysis

- Measured before and after SpaceOAR insertion with CT/MRI fusion
  - ✓ Patients grouped by separation distance (0-5 mm, 5-10 mm, etc.).

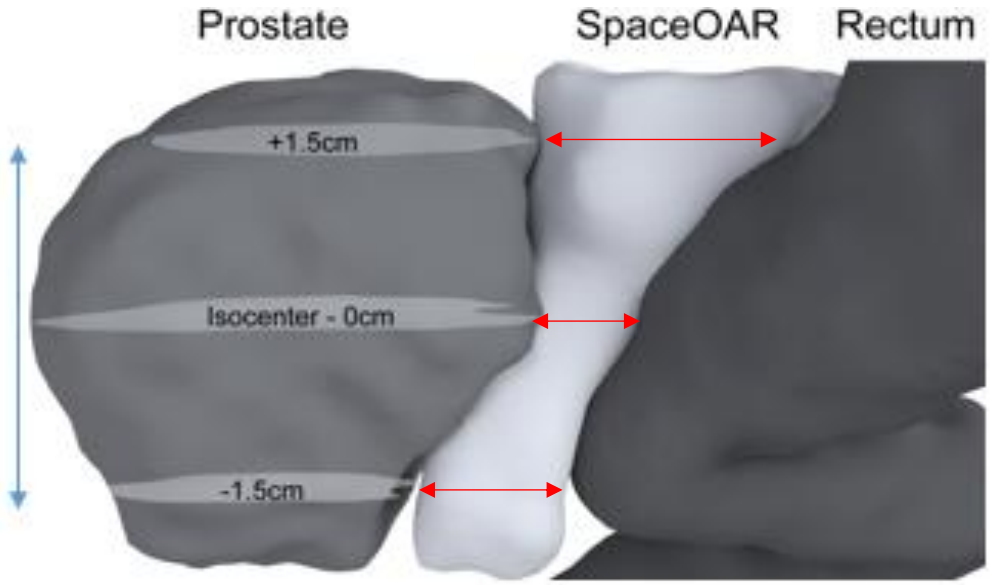


FIGURE 3 Illustration of different prostate levels in the sagittal plane. The isocenter at 0 cm represents the center of the prostate. The +1.5 cm point is located 1.5 cm superior to the 0 cm, while the -1.5 cm point is 1.5 cm inferior to the 0 cm.

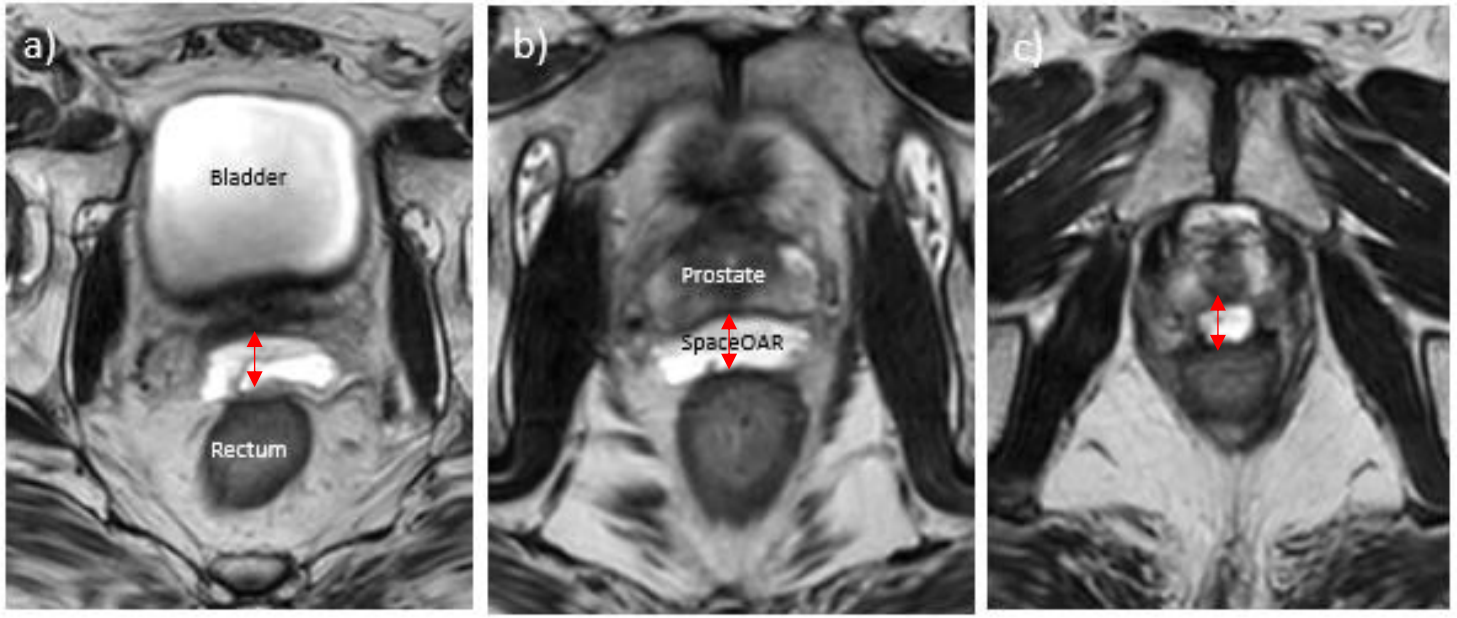


FIGURE 4 Transverse view of the T2 magnetic resonance image (T2- MRI). a) +1.5 cm from the center of the prostate, b) Center of the prostate, c) -1.5 cm from the center of the prostate.

- Rectal DVH: Dose analysis by prostate–rectum distance

Evaluation - Robust evaluation of treatment plans

- Robust evaluation: 12 scenarios considering uncertainties; setup error, range uncertainty

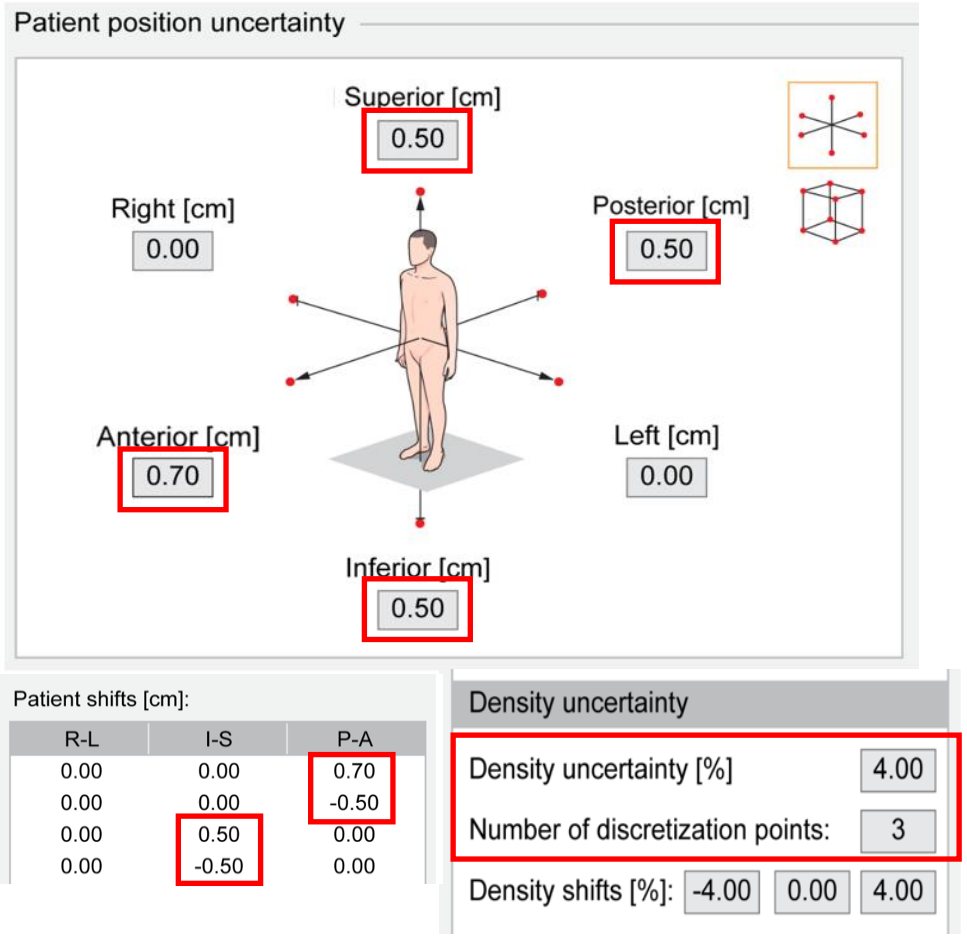


FIGURE 5 Robust evaluation of patient position and density uncertainty in RayStation.

TABLE 1 Dosimetric Criteria for Treatment Plans

Organ	Dosimetric Criteria
Prostate	At least 49.02 Gy (RBE) covering 99.9% of the volume At least 49.02 Gy (RBE) covering 100.0% of the volume
Rectum	Maximum 1.00 cm^3 volume at 49.02 Gy (RBE) Maximum 5.00 cm^3 volume at 41.28 Gy (RBE) Maximum 10.00 cm^3 volume at 25.80 Gy (RBE)
Bladder	Volume receiving 44.89 Gy (RBE) < 25% Volume receiving 28.38 Gy (RBE) < 45%
Penile bulb	Dose to a 0.03 cm^3 volume

95% of the prescribed dose (51.60 Gy)

95% of the prescribed dose (51.60 Gy)
80%....
50%...

✓ **Passing rate**: ratio of passed cases among 12 scenarios.

Evaluation - ProKnow scoring

TABLE 2 Plan metrics collected for each prostate carbon ion therapy radiation treatment plan.
(Total points 64, 8 plans used to produce per-metric and composite plan scores)

No	Metric description	Minimum requirement	Ideal	Interval	Weight
1	Volume (%) of Bladder covered by 44.89 (Gy)	10	25	5	1
2	Volume (%) of Bladder covered by 28.38 (Gy)	15	45	10	1
3	Dose (Gy) covering 99.90 (%) of the Prostate	49.02	51.6	PTV coverage 1~2% difference	1
4	Dose (Gy) covering 100.00 (%) of the Prostate	49.02	51.6	PTV coverage 1~2% difference	1
5	Volume (cc) of the Rectum covered by 49.02 (Gy)	0.4	1	0.2	2
6	Volume (cc) of the Rectum covered by 41.28 (Gy)	2	5	1	2
7	Volume (cc) of the Rectum covered by 25.80 (Gy)	1	10	3	2
8	Dose (Gy) covering 0.03 (cc) of the Penile bulb	20	50	10	1

Elekta ProKnow®

- ProKnow®(Elekta) used to assess treatment plans for prostate, rectum, bladder, and penile bulb.
- Scores ranged from *'Ideal'* to *'Unacceptable'*, with composite scores for comparison.

Prostate-Rectum Separation Results

TABLE 3 Patient cases based on Prostate-Rectum separation.

Prostate-Rectum Separation	Patient Cases
0-5 mm	1
5-10 mm	11
10-15 mm	11
>15 mm	2

Note: Patient cases are organized according to the degree of separation between the prostate and the rectum.
The degree of separation was determined as the mean of the separation distances measured at the 0 cm, +1.5 cm, and -1.5 cm positions within the prostate.

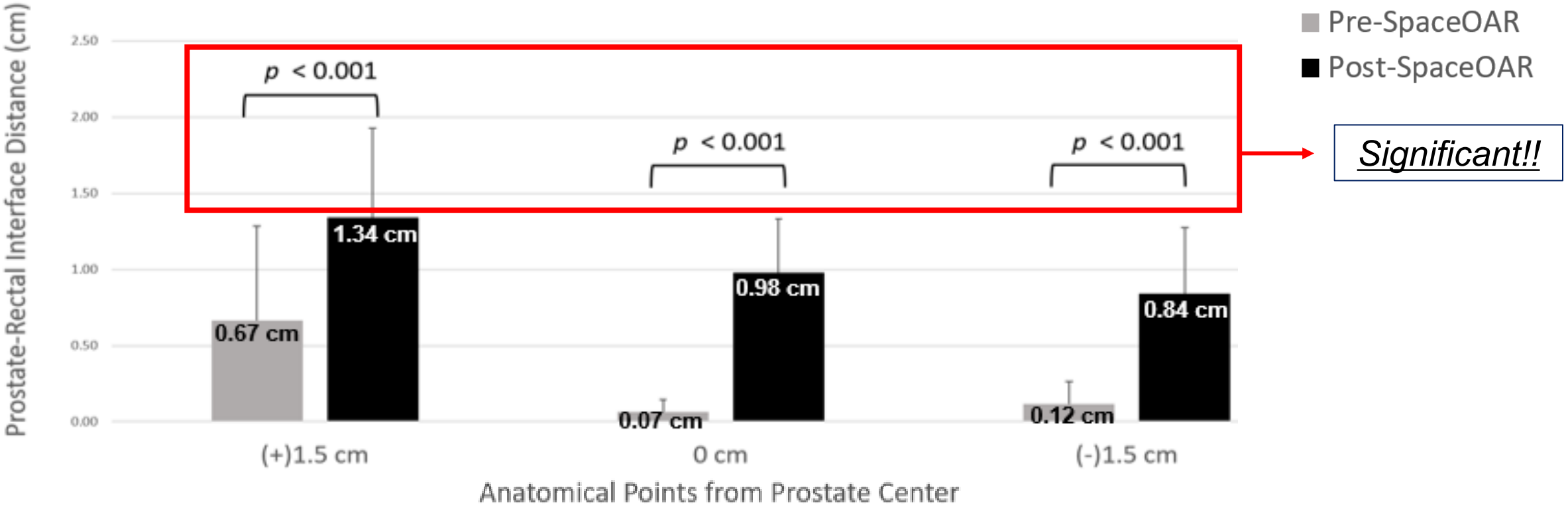
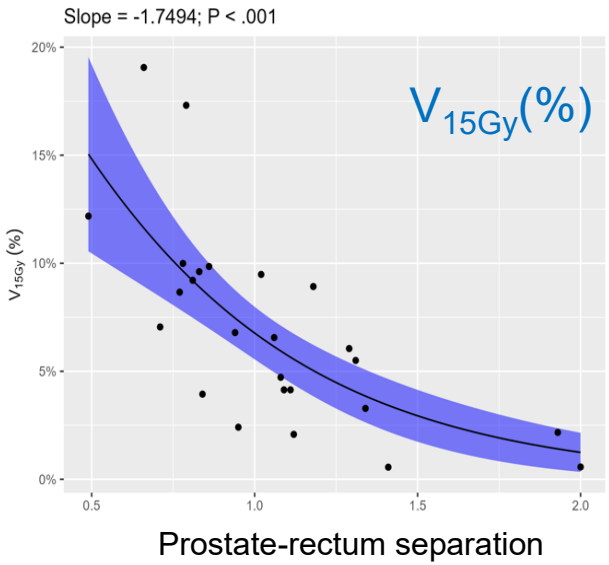
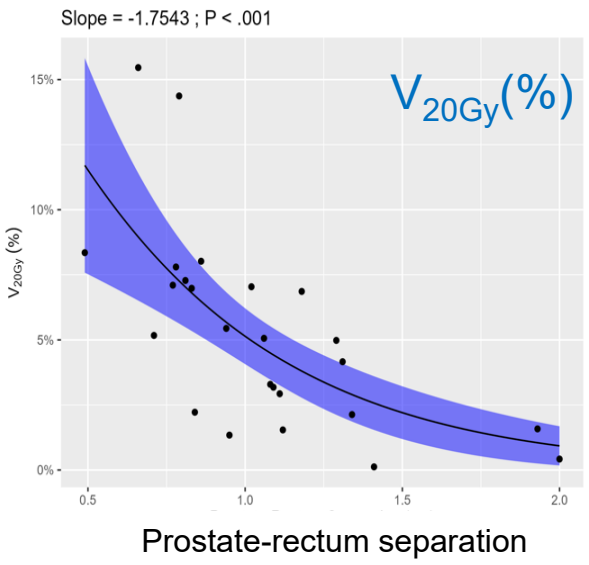
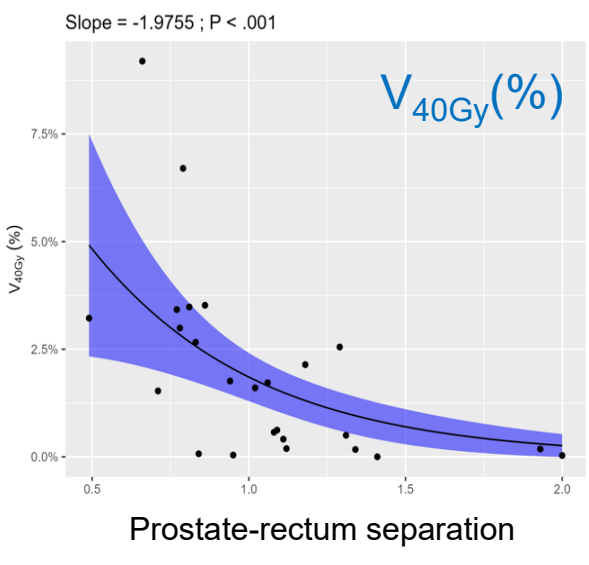


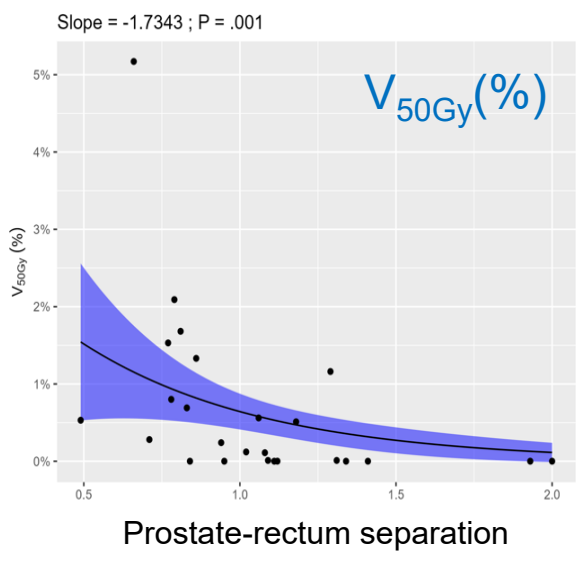
FIGURE 6 Prostate-rectum separation before and after injection of SpaceOAR at difference levels of the prostate.

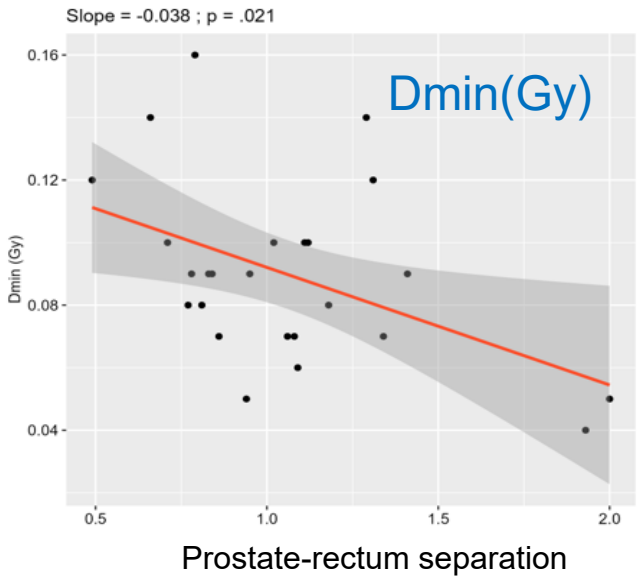
Rectum DVH values by Prostate-Rectum separation degree

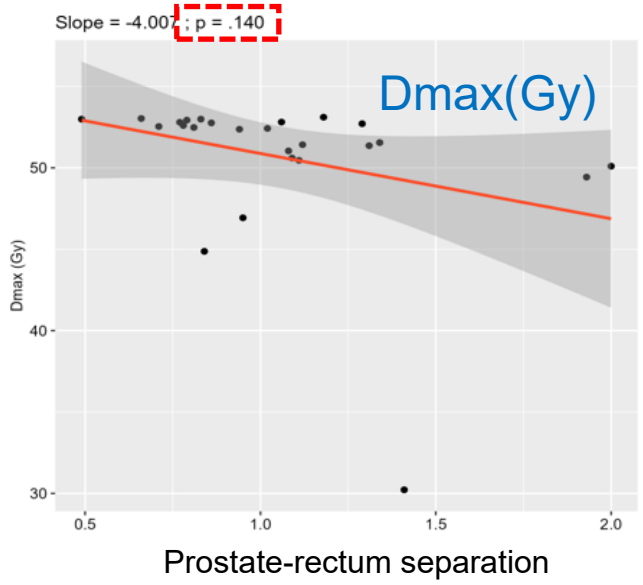


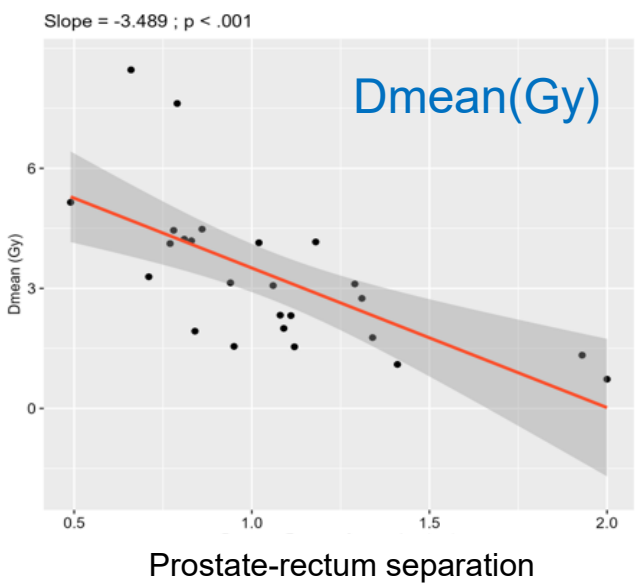












- As prostate-rectum separation increased, rectal dose (V15~50, Dmin, Dmean) *significantly decreased*.

FIGURE 8 Rectum DVH values by Prostate-Rectum separation degree

Comparison of Dosimetric Indices among Three Plans

TABLE 4 Mean DVH Values Pre-SpaceOAR, Pre-SpaceOAR with Rectum Protection, and Post-SpaceOAR

		Prostate			Rectum										Penile bulb									
		Dmin (Gy)	Dmax (Gy)	Dmean (Gy)	Dmin (Gy)	Dmax (Gy)	Dmean (Gy)	V_{15} (%)	V_{20} (%)	V_{25} (%)	V_{30} (%)	V_{35} (%)	V_{40} (%)	V_{45} (%)	V_{50} (%)	Dmin (Gy)	Dmax (Gy)	Dmean (Gy)	V_{15} (%)	V_{20} (%)	V_{25} (%)	V_{30} (%)	V_{35} (%)	V_{40} (%)	V_{45} (%)	V_{50} (%)
Pre-Space OAR	Mean	51.46	52.30	51.91	0.08	52.83	9.85	21.60	19.17	17.32	15.67	13.98	12.24	10.61	7.85	2.88	51.31	16.06	37.73	29.93	28.86	27.28	20.46	19.35	18.08	11.12
	SD*	0.12	0.47	0.11	0.03	0.39	1.77	4.09	3.70	3.31	2.95	2.72	2.37	2.03	1.61	11.03	7.08	7.02	16.81	13.93	13.84	13.26	10.91	10.10	9.58	7.08
Pre-Space OAR (Rectum Protection)	Mean	46.54	53.86	52.67	0.08	50.81	8.58	20.27	17.66	15.52	13.49	11.35	9.12	6.35	0.06	0.46	52.64	19.72	45.28	37.97	35.84	33.81	28.23	24.97	23.19	15.52
	SD*	3.58	2.70	1.56	0.03	0.82	1.80	4.54	3.92	3.43	3.21	2.68	2.77	2.28	0.06	0.20	1.04	7.32	16.61	15.74	14.28	13.95	13.40	11.75	11.29	9.23
	p-value[1]	<0.001	0.025	0.071	0.013	<0.001	<0.001	0.015	0.006	0.003	0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.060	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Post-Space OAR	Mean	51.47	52.26	51.90	0.09	50.66	3.32	6.97	5.31	4.34	3.57	2.67	1.97	1.46	0.67	0.41	53.73	16.98	37.38	33.65	29.50	25.41	23.16	20.01	15.93	12.50
	SD*	0.09	0.07	0.02	0.03	4.70	1.88	4.65	3.84	3.50	3.25	2.65	2.22	1.91	1.12	0.18	2.91	6.82	16.26	14.12	13.66	13.11	11.49	10.59	10.27	8.45
	p-value[2]	>0.999	>0.999	>0.999	0.339	0.086	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.981	0.411	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Expanded range

[1] Pre-SpaceOAR VS Pre-SpaceOAR (Rectum Protection)

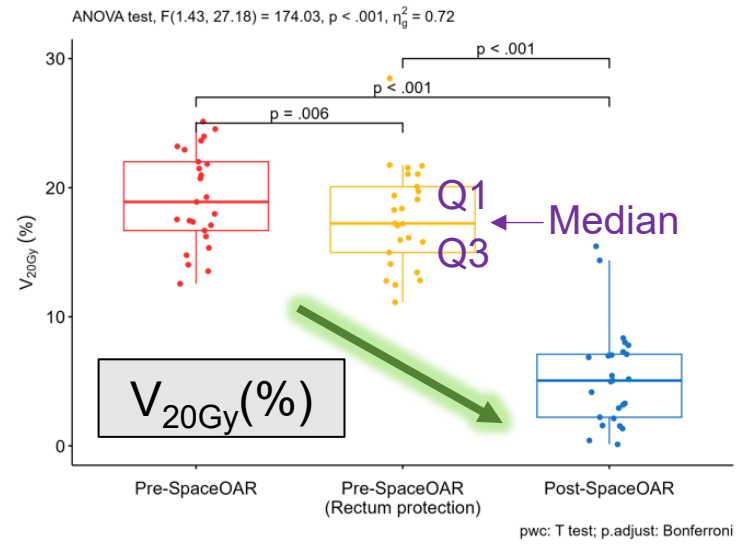
[2] Pre-SpaceOAR VS Post-SpaceOAR

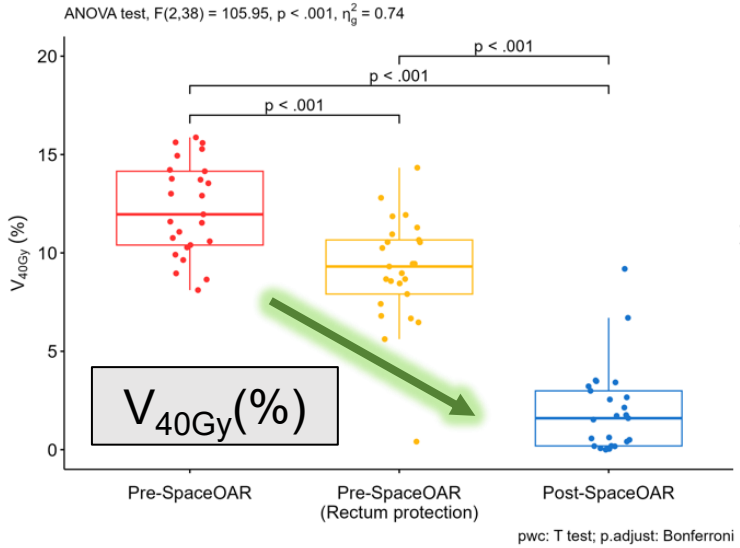
→ Most of the significant but inconsistent changes.

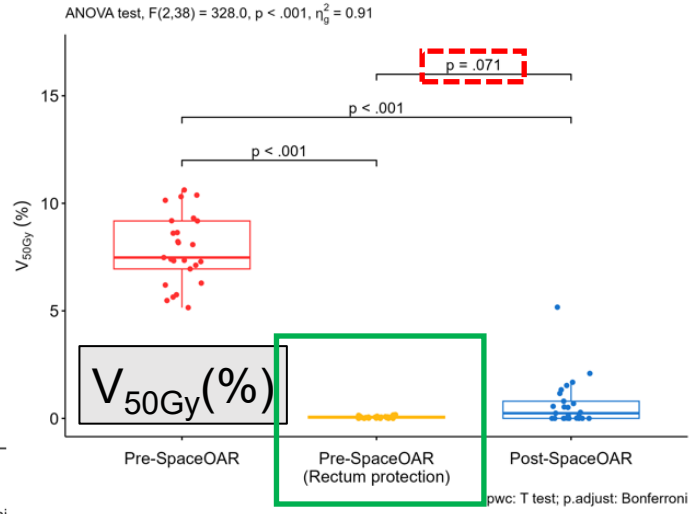
p < 0.05: statistically significant

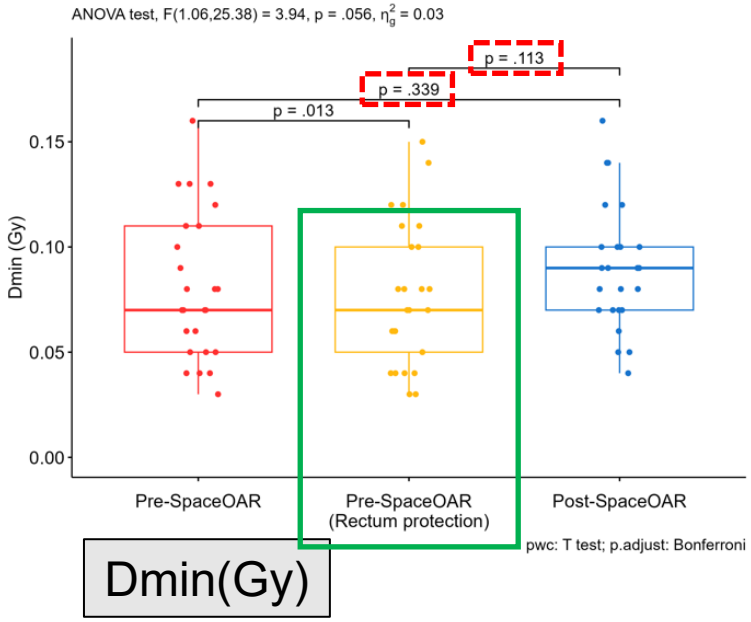
Result

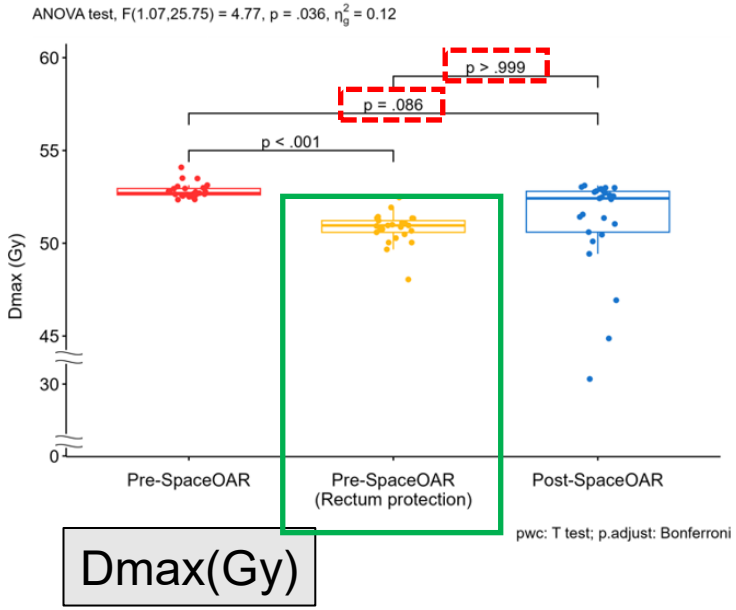
Comparison of Dosimetric Indices among Three Plans

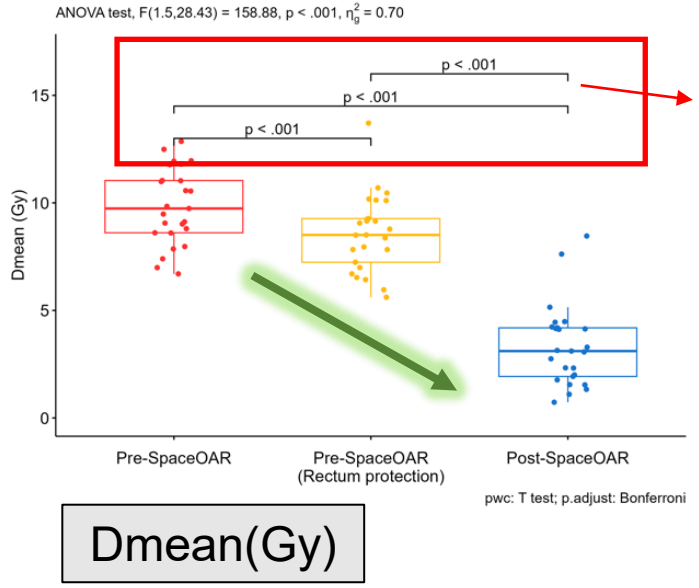












Significant!!

FIGURE 7 Rectal dosimetric outcomes for Pre-spaceOAR (Standard Plan), Pre-spaceOAR (Rectum Protection Plan), and Post-spaceOAR

Result

Robust evaluation

TABLE 5 Robust evaluation passing rates for anatomical organs.

Anatomical Sites	Pre-SpaceOAR		Pre-SpaceOAR (Rectum Protection)		Post-SpaceOAR	
	Mean	SD	Mean	SD	Mean	SD
Prostate	40.06	44.10	0.00	0.00	37.81	39.07
Rectum	40.77	22.58	60.35	11.98	83.33	15.71
Bladder	100.00	0.00	100.00	0.00	100.00	0.00

Note: Mean and standard deviation (SD) values are represented as percentages (%).

- ✓ **Post-SpaceOAR** passing rates were significantly higher than both **pre-SpaceOAR** and **pre-SpaceOAR with rectal protection.**

($p < 0.05$ for all comparisons)

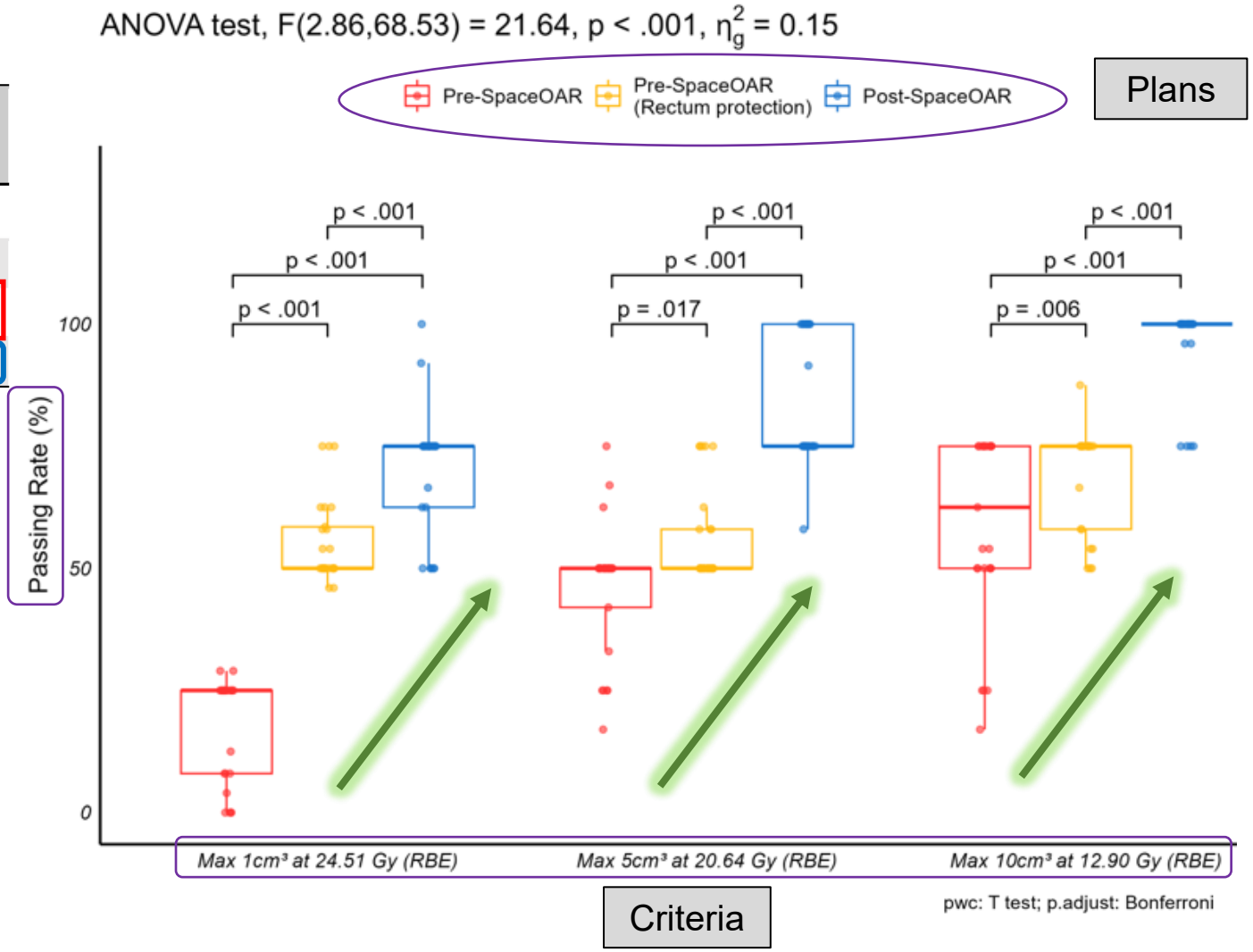
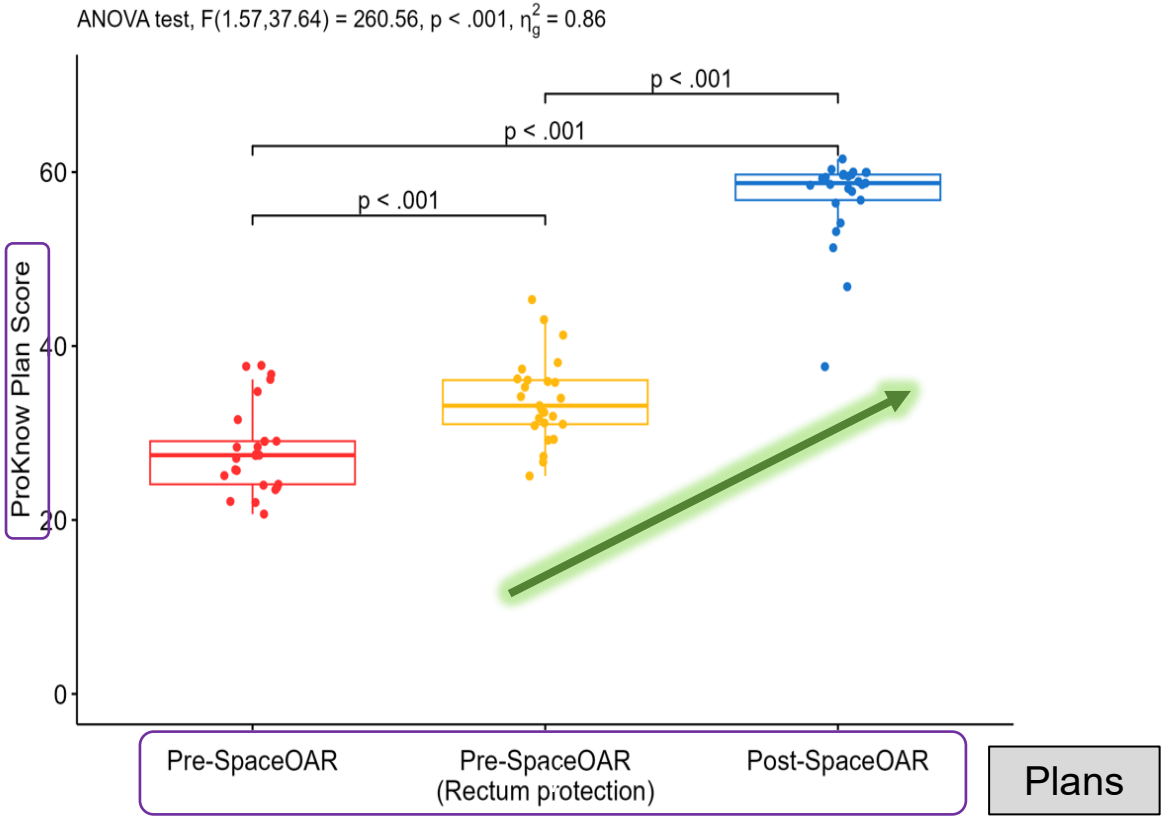


FIGURE 9 Rectum: Robust evaluation passing rate results by criteria.

ProKnow scoring

TABLE 6 Comparative Analysis of Plan Scores Pre-SpaceOAR, Rectum Protection, and Post-SpaceOAR Injection.

	Pre-SpaceOAR	%		Pre-SpaceOAR (Rectum Protection)	%		Post- SpaceOAR	%
Mean	28.19	44.05%	<	33.80	52.81%	<	56.98	89.03%
SD	5.03	7.86%		4.89	7.64%		5.19	8.11%



*$p < 0.05$ for all comparisons

FIGURE 10 Comparison of *p*-values from ProKnow plan evaluation

Discussion & Conclusion

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- CIRT & SpaceOAR
  - ✓ This is **one of the first studies to evaluate the combined effect of SpaceOAR and CIRT for prostate cancer,** compared to prior studies focused on photon-based RT.

- Various evaluating methods.
  - ✓ Robust evaluation,,ProKnow scoring…

- ***Limitations:*** small sample size, retrospective, single-institution, no toxicity evaluation

- ***Conclusions:*** Strong evidence supports the routine use of SpaceOAR in CIRT for prostate cancer, with potential for it to become a standard treatment pending additional prospective studies and validation. !

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Thank you for Listening !

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