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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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Objectives

This study aims to evaluate the impact of SpaceOAR insertion on the efficacy and safety of carbon ion radiotherapy (CIRT) plans for prostate cancer patients. The investigation focuses on how SpaceOAR affects dose distribution to the prostate and surrounding organs during CIRT.

Methods

This retrospective study included 25 prostate cancer patients treated with CIRT after receiving a 10 mL SpaceOAR™ hydrogel injection. Three plans were generated per patient: conventional, rectum-sparing without spacer, and post-SpaceOAR. CT/MRI fusion guided PTV and OAR contouring. Dosimetric metrics (Dmean, Dmax, Dmin, V15–V50) were analyzed. Prostate–rectum separation was measured at three axial levels and grouped by distance to correlate with rectal DVH. Robustness was tested using setup uncertainties (0.5, 0.7 cm) and ±4% density changes, assessing dose constraint compliance. Plan quality was evaluated with ProKnow® scores. Statistical analysis included repeated-measures ANOVA and regression using R (v4.1.3), with significance at $p < 0.05$.

Results

The mean rectal dose (Dmean) decreased significantly from 9.85 Gy(RBE) to 8.58 Gy(RBE) and 3.32 Gy(RBE) across the three plans ($p < 0.001$). V15–V50 indices also declined significantly ($p < 0.001$). Median prostate–rectum separation increased from 0.07 cm to 0.98 cm ($p < 0.001$) at mid-gland. Increased separation correlated negatively with rectal V15–V50, Dmin, and Dmean ($p < 0.05$). Robustness pass rates improved from 40.77% to 60.35% and 83.33% ($p < 0.05$). ProKnow scores rose from 44.05% to 52.81% and 89.03% ($p < 0.001$), corresponding to a total score of 64 points. These results confirm that SpaceOAR hydrogel improves rectal sparing, robustness, and plan quality in CIRT.

Conclusions

The integration of SpaceOAR™ hydrogel enhances the efficacy and precision of CIRT in prostate cancer by improving plan quality, rectal sparing, and robustness to setup uncertainties. Spacer use enables safer dose escalation without increasing rectal toxicity, addressing anatomical limitations in prostate cancer treatment. The study also employs the ProKnow® scoring system for structured, multi-dimensional plan quality assessment, supporting objective strategy comparisons. Spacer insertion aligns with personalized radiotherapy by accommodating individual anatomy and treatment needs. Though limited by its retrospective, single-institution design, the findings support hydrogel spacers as a standard adjunct in CIRT. Future multi-institutional prospective studies are warranted to confirm long-term benefits in tumor control, toxicity reduction, and patient quality of life. Spacer use in CIRT thus represents a practical and effective strategy for advancing safer and more individualized prostate cancer treatment.

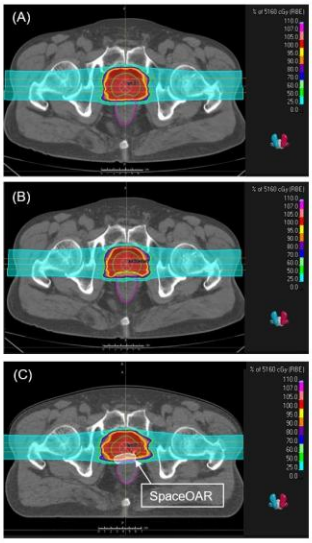

FIGURE 1 Representative dose distribution of carbon ion radiotherapy (CIRT) plans in transverse CT views. (A) Pre-SpaceOAR standard plan. (B) Pre-SpaceOAR rectum protection plan. (C) SpaceOAR insertion plan. The color wash represents dose levels (cGy), highlighting differences in rectal sparing and target coverage across the three planning approaches. These images illustrate the improved rectal sparing achieved with SpaceOAR insertion without compromising target coverage. Abbreviations: cGy, centigray; RBE, relative biological effectiveness; OAR, organ at risk.

TABLE 1 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

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

[2] Pre-SpaceOAR VS Post-SpaceOAR

Abbreviations: DVH, dose-volume histogram; Gy, gray; Dmin, minimum dose; Dmax, maximum dose; Dmean, mean dose; Vx% (e.g., V_{15}–V_{50}%), volume receiving x% or more of the prescribed dose; OAR, organ at risk; SD, standard deviation.

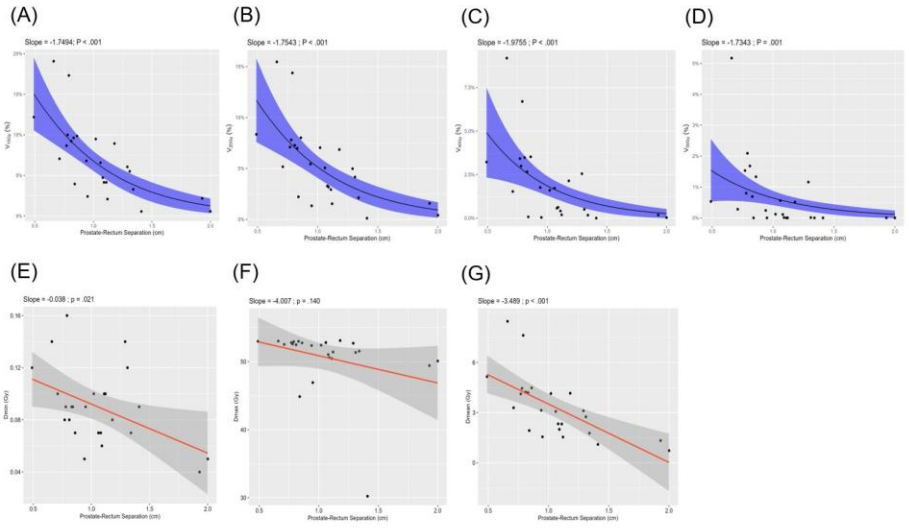

FIGURE 2 Rectum DVH values by Prostate-Rectum separation degree. (A) V_{15Gy} (%), (B) V_{20Gy} (%), (C) V_{40Gy} (%), (D) V_{50Gy} (%), (E) Dmin (Gy), (F) Dmax (Gy) and (G) Dmean (Gy). Abbreviations: Gy, gray; Dmin, minimum dose; Dmax, maximum dose; Dmean, mean dose; Vx% (e.g., V15–V50%), volume receiving x% or more of the prescribed dose; p-value, probability value.

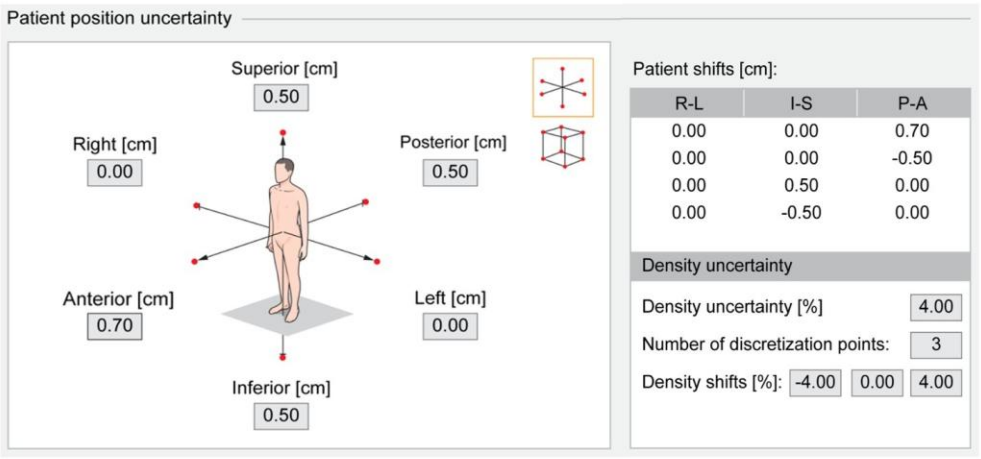

FIGURE 3 Robust evaluation of patient position and density uncertainty in RayStation.

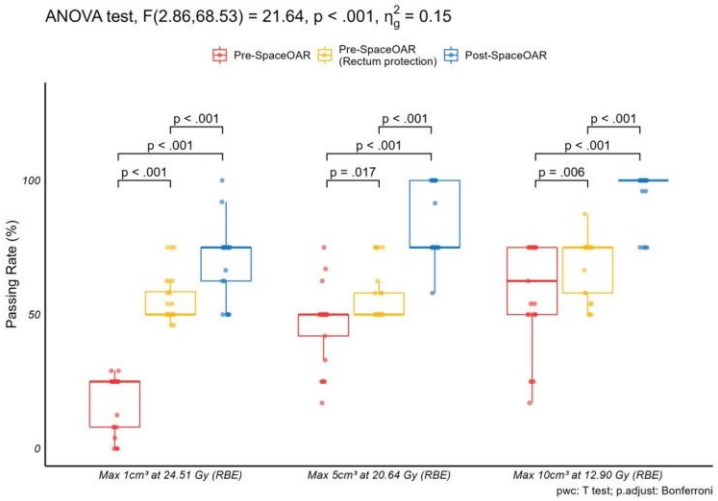

FIGURE 4 Rectum: Robust evaluation passing rate results by criteria. Abbreviations: ANOVA, analysis of variance; cm³, cubic centimeter; Gy, gray; p-value, probability value; RBE, relative biological effectiveness; Max, maximum; OAR, organ at risk.

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

Abbreviations: Gy, gray; PTV, planning target volume.

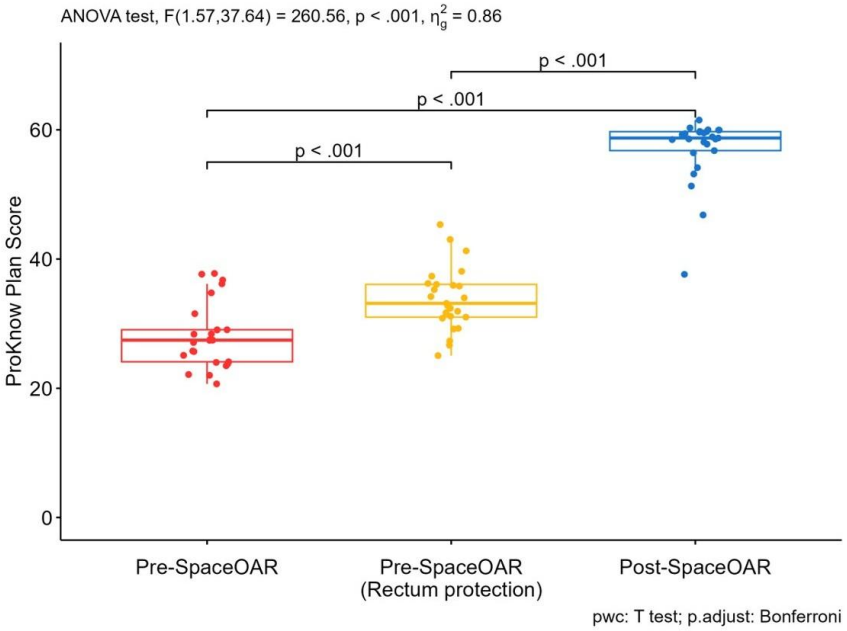

FIGURE 5 Comparison of *p*-values from ProKnow plan evaluation. Abbreviations: ANOVA, analysis of variance; p-value, probability value; OAR, organ at risk.