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Carbon Ion Radiotherapy for Primary Sarcoma of the Prostate and Urethra: Efficacy and Safety

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# **Objectives**

Sarcomas of the prostate and urethra are extremely rare malignancies with poor prognosis, posing significant clinical challenges due to their unpredictable behavior and the lack of standardized treatments. This study aimed to evaluate the safety and efficacy of carbon-ion radiotherapy (CIRT) as a potential therapeutic option for these tumors.

#### Methods

Adult patients with histologically confirmed, localized (cN0M0) primary sarcoma of the prostate or urethra who received upfront CIRT at our institute were prospectively analyzed. CIRT was delivered using two parallel-opposed lateral fields in the supine position, with a total dose of 70.4 Gy (relative biological effectiveness, RBE) in 16 fractions to the gross tumor volume (GTV). All patients underwent urinary catheterization during treatment. No concurrent chemotherapy or fiducial markers were used. Tumor response was assessed by MRI at three months post-treatment using RECIST criteria. Acute toxicity, defined as the highest-grade event within 90 days post-CIRT, was graded using the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.

### Results

Between May 2023 and December 2024, three patients (two males with prostate sarcoma and one female with urethral sarcoma) were treated with upfront CIRT. Characteristics of the patients were shown in Table 1. Dysuria was the most common presenting symptom. Pre-treatment tumor sizes were 7.3 cm, 6.8 cm, and 2.5 cm, which decreased to 5.5 cm, 5.3 cm, and 2.5 cm, respectively, at three months post-CIRT (Figure 1). Two patients (Cases 1 and 2) demonstrated marked tumor regression with resolution of diffusion restriction on MRI, consistent with a partial response. The third patient (Case 3) exhibited stable tumor size but demonstrated poor contrast enhancement and absence of diffusion restriction. Notably, the tumor in Case 1 continued to decrease in size over the one-year follow-up period (Figure 2). Histopathological analysis of the transurethral resection specimen at one year revealed necrotic granulation tissue, indicative of a pathological response. Two of three patients experienced grade 1 dysuria at the end of CIRT, which resolved within few weeks. No grade ≥3 genitourinary or gastrointestinal toxicity was observed.

#### **Conclusions**

This study presents the first report of CIRT in patients with primary sarcoma of the prostate and urethra, demonstrating favorable tolerability and significant tumor volume reduction.

Table 1. Clinicopathological characteristics of patients with primary sarcoma of the prostate or urethra

	Case 1	Case 2	Case 3
Characteristics			
Age at diagnosis (years)	79	83	27
Gender	Male	Male	Female
ECOG	1	1	0
Tumor location	Prostate	Prostate	Bladder neck & Urethra
Bladder invasion	yes	yes	yes
Rectal invasion	no	no	no
Tumor volume (ml)	382.6	135.0	22.7
Diagnostic modality	TURP	TURP	TURBT
Histology	Leiomyosarcoma	Stromal sarcoma	Spindle cell sarcoma
Tumor necrosis	present	absent	absent
Initial PSA (ng/ml)	0.34	0.54	NA
Presenting symptoms			
Urinary retention	present	present	absent
Hydroureteronephrosis	present	absent	absent
Dysuria	present	present	present
Hematuria	present	absent	absent
Change in bowel habits	present	absent	absent
CIRT treatment planning			
Dose	70.4Gy(RBE) in 16 fractions 70.4Gy(RBE) in 16 fractions 70.4Gy(RBE) in 16 fraction		
GTV V95 (%)	98.41	96.93	99.99
Rectum V56Gy (cc)	7.95	0.02	0.0
Bladder V45Gy (%)	65.1	23.9	22.0
Acute toxicity			
Dysuria	None	Grade 1	Grade 1
Hematuria	Grade 1 (painless urethral discharge)	None	None
Proctitis	None	None	None
Fatigue	Grade 1	None	None

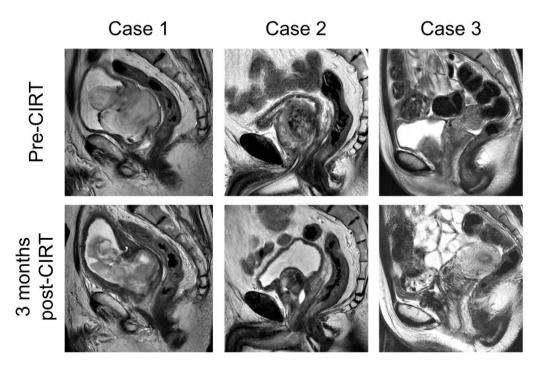
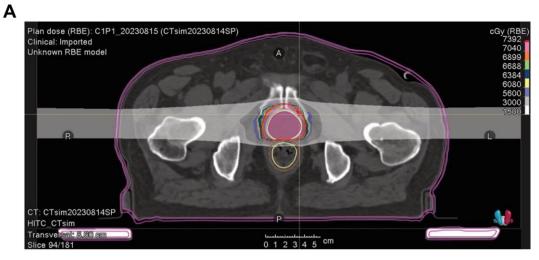


Figure 1. Sagittal MRI of the tumor before and three months after carbon-ion radiotherapy (CIRT).



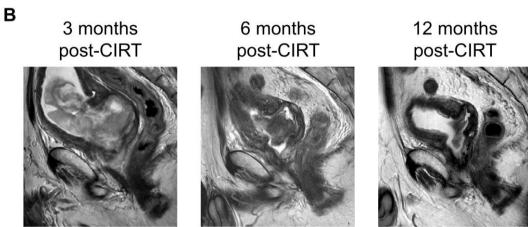


Figure 2. (A) Treatment planning of Case 1. (B) Tumor size reduction in Case 1.