



# Prostate-Specific Antigen Kinetics after Carbon-Ion Radiotherapy in Patients with Localized Prostate Cancer: Single Center Preliminary Experience in Japan

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## Abstract

Currently, Carbon-Ion Radiation Therapy (CIRT) is regarded as one of the effective therapeutic options for patients with localized Prostate Cancer (PC); however, Prostate-Specific Antigen (PSA) kinetics following CIRT have not been well documented. This study included a total of 116 patients with low or intermediate-risk localized PC who underwent CIRT with a prescription dose of 51.6 Gy in 12 fractions over 3 weeks, and characterized post-treatment changes in PSA values in these patients. PSA values 1 and 2 years after CIRT in these patients were reduced by 69 and 77%, respectively, relative to baseline values at diagnosis, and only 1 (0.86%) of the 116 was diagnosed with PSA failure. Collectively, these findings indicate that CIRT as monotherapy could efficaciously control PSA values in the majority patients with low or intermediate-risk localized PC.

**Keywords:** Carbon-ion radiation therapy; Localized prostate cancer; PSA kinetics

## Introduction

Carbon-Ion Radiation Therapy (CIRT) has been shown to provide several promising advantages over conventional Radiation Therapy (RT) with X-rays [1]. For example, CIRT has an estimated threefold higher Relative Biological Effectiveness (RBE) than X-rays, while an effective dose distribution of CIRT, known as the “Bragg peak”, can be created by releasing the majority of energies in the target tissues [1]. Considering these features, it is theoretically possible to permit dose escalation for target organs with less toxicity in normal tissues. In fact, CIRT has recently been recognized as one of the most useful advanced modalities for the treatment of localized Prostate Cancer (PC) [2,3]; however, CIRT is currently performed in a limited number of centers in the world, and, thus, detailed assessments of clinical outcomes after CIRT for localized PC remain insufficient.

Prostate-Specific Antigen (PSA) has been widely accepted as a reliable biomarker precisely reflecting the status of PC [4]. However, it is sometimes difficult to interpret changes in PSA levels during the surveillance of PC patients following RT, since there are some patients with fluctuating and temporally increasing PSA levels, a phenomenon called the PSA bounce, in addition to curative or failure cases [5]. Furthermore, it is not well-documented whether PSA kinetics in localized PC patients after CIRT is similar to that after conventional RT.

## Material and Methods

This study included a total of 116 consecutive patients who were diagnosed with either low or intermediate-risk localized PC according to the National Comprehensive Cancer Network guideline and were subsequently treated with CIRT as monotherapy between October 2018 and May 2020 at Osaka Heavy Ion Therapy Center. In this series, two gold markers were initially implanted into the prostate to facilitate accurate position verification, and a prescription dose of 51.6 Gy in 12 fractions over 3 weeks was delivered with parallel-opposed lateral fields. As a rule, PSA levels were measured before and every 3 months after the initiation of CIRT in all patients.

## Results

The median age and PSA at diagnosis in the 116 patients were 68 years and 5.8 ng/mL, respectively, while 56 (48.3%) and 60 (51.7%) were judged to have Gleason score 6 and 7 diseases, respectively. Figure 1A presents time-dependent changes in PSA values relative to base-line values

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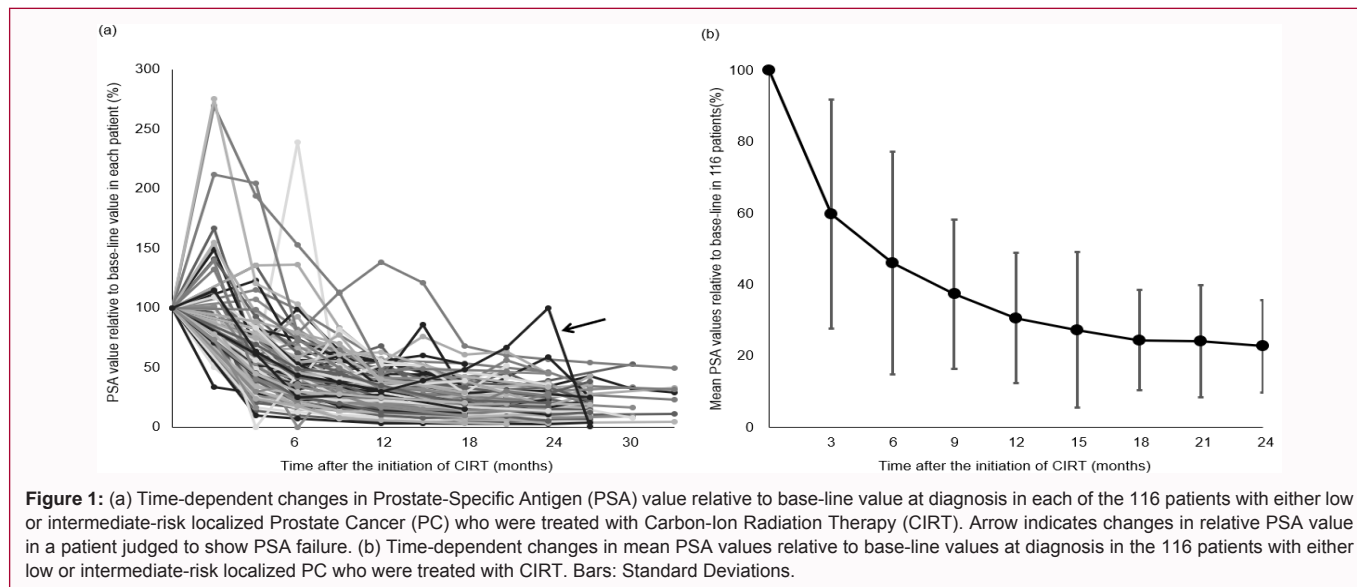
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at diagnosis. Only 1 (0.86%) of the 116 patients was judged to show PSA failure, and then received androgen deprivation therapy. As shown in Figure 1B, PSA values 1 and 2 years after the initiation of CIRT in the 116 patients were reduced by 69 and 77%, respectively, compared with those at diagnosis.

## Discussion

During the observation period of this series, 115 of the 116 patients with low or intermediate-risk localized PC showed favorable PSA response to CIRT. Although long-term observation will be further required to draw a definitive conclusion on the prognostic issue, these findings strongly suggest that CIRT as monotherapy could effectively control PSA values in the majority of low or intermediate-risk localized PC patients.

In the first report with respect to PSA kinetics after CIRT for localized PC from Gunma University Heavy Ion Medical Center, PSA failure was observed in 8 (6.1%) of 131 patients [6]. It is of interest to explore causes of the different incidences of post-treatment PSA failure between the above first report and our present findings. There are several different conditions between these 2 studies, such as dosing schedules and follow-up periods, which could affect the different outcomes. At our institution, however, the margins of beam-specific Planning Target Volume (bsPTV) were determined based on the findings of intra- and inter-fractional target motions assessed by gold markers, and treatment plans according to bsPTV were applied to each PC patient [7]; therefore, such fiducial marker-based position verification and a compensation of target changes by bsPTV treatment plans may contribute to accurately realize optimal dose distribution in the prostate and its surrounding tissues, which may have an association with favorable post-CIRT PSA kinetics.

## Conclusion

In conclusion, we performed CIRT in a total of 116 patients with low or intermediate-risk localized PC at Osaka Heavy Ion Therapy

Center, and retrospective assessments of post-treatment PSA kinetics in these patients revealed that PSA failure was detected in only 1 of the 116 patients. Although it is necessary to confirm the present findings by a prospective study with a larger sample size, achievement of a favorable PSA response to CIRT in the majority of patients suggest the usefulness of our treatment plans according to bsPTV determined by gold markers.

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