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Single-fraction PSMA-PET- and Multiparametric MRI-guided Focal SBRT for Prostate Cancer Local Recurrences

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Abstract
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Abstract

Objectives:

The treatment of localized and locally advanced prostate cancer (PCa) usually consists of radical prostatectomy (RPE), external beam radiotherapy (EBRT), or a combination of both with the potential use of androgen deprivation therapy (ADT) as well as active surveillance in selected patients. Still, a considerable proportion of treated patients will suffer from a local relapse. However, with the recent advances in the field of stereotactic body radiation therapy (SBRT) and functional imaging with prostate-specific membrane antigen positron emission tomography (PSMA-PET), new treatment options in the recurrence setting arise. To the best of our knowledge, available evidence and reports are strictly limited to fractionated SBRT, without any dedicated data on single-fraction SBRT in conjunction with PSMA-PET and multiparametric magnetic resonance imaging (mpMRI). Moreover, previously reported irradiations usually target the whole prostate or prostate bed and not specifically the local recurrence. The objective of this analysis was to describe and to assess the efficacy and safety of single-fraction PSMA-PET- and mpMRI-guided SBRT for the focused treatment of localized PCa recurrences in intensively pre-treated patients.

Methods:

Patients with PSMA-PET positive PCa local recurrences treated with focal single-fraction SBRT between June 2016 and December 2020 were included. Treated recurrences must have been identified and localized by a PSMA-PET-CT or PSMA-PET-MRI and mpMRI. All treatments were delivered with a CyberKnife® radiosurgery system (Accuray Inc., Sunnyvale, CA, USA). Patients with previous and current distant metastasis were excluded. Identification for new tumor growth (recurrences or metastatic spread) after SBRT was based on increasing prostate-specific antigen (PSA) levels and subsequent PSMA-PET imaging.

Results:

Sixty-four patients were identified. Patients received various treatments before SBRT (31 patients with RPE, 18 EBRT and RPE, five EBRT alone, and the remaining ten received other combinations of local therapies). In patients with previous EBRT, all patients were treated in an area previously irradiated. The majority of patients had a Gleason score of 7 (62%) or higher (17%) at first diagnosis. The median follow-up and the time from first diagnosis to SBRT were 21.6 months and 7.9 years, respectively. All patients received a single-fraction treatment with a median prescription dose and isodose line of 21 Gy and 65%, respectively. The median planning target volume (PTV) was 2.8 cubic centimeters. At the time of SBRT, six patients received ADT (9%). The median pretreatment PSA of 1.47 ng/ml declined to 0.66, 0.57, 0.47, 0.42, and 0.43 ng/ml after the first five follow-up ($p = 0.03$). A total of three local recurrences, i.e., new tumor growth inside the PTV, were detected throughout the follow-up. The progression-free survival (PFS) after 1-, 2-, and 3-years were 85.3%, 65.9%, and 51.2%. The majority of disease progression (23/29 recurrences) occurred locoregionally, i.e., inside the prostate or pelvic lymph nodes. In the multivariable Cox proportional hazards model for PFS, only the International Society of Urological Pathology (ISUP) grade group 5 was associated with progression ($HR = 39.7$, $p = 0.01$). The rates of newly started ADT after 1-, 2-, and 3-years were 1.8%, 7.3%, and 22.7%. The mean and median time to starting a new ADT were 21.3 and 23.3 months, respectively. Four of six patients with ADT at the time of SBRT were able to stop ADT during the available follow-up. Grade 1 or 2 toxicities occurred in six patients (9%), and no high-grade (⩾ grade 3) toxicity was observed.

Conclusion(s):

While the available SBRT data for PCa local recurrences usually describe outcomes for fractionated treatments and non-focal irradiation, the findings of this first analysis of single-fraction, PSMA-PET- and mpMRI-guided focal SBRT are encouraging. Such treatment appears to be a safe, efficient, and time-saving therapy even in intensively pre-treated patients. Recurrence-directed treatments can delay the use of ADT and could avoid prostate bed irradiation in selected patients. Prospective work is required to validate the observed results.