# $^{68}$Ga-PSMA PET/CT mapping of early biochemical recurrence after primary surgery in 270 patients: Impact on Salvage Radiotherapy Planning

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**Background/Objectives**: Target volumes for salvage prostate radiotherapy (SRT) are usually drawn in the absence of visibly recurrent disease. However, $^{68}$Ga-PSMA PET/CT detects prostate cancer recurrences with accuracy superior to conventional imaging, at PSA values low enough to impact volume delineations for routine SRT. We conducted this study to i) determine how often volumes based on the Radiation Therapy Oncology Group (RTOG) consensus guidelines cover $^{68}$Ga-PSMA PET/CT defined disease in patients with serum PSA levels <1 ng/ml after radical prostatectomy ii) map the recurrence pattern of early biochemically recurrent prostate cancer after prostatectomy, and iii) assess the potential impact of $^{68}$Ga-PSMA PET/CT on SRT.

**Methods:** This is a post-hoc analysis of an intention to treat population of 270 patients who underwent $^{68}$Ga-PSMA PET/CT in 4 institutions for biochemical recurrence after prostatectomy without prior radiotherapy at PSA<1 ng/mL. RTOG consensus clinical target volumes (consensus CTVs) that included both the prostate bed and pelvic lymph nodes (LN) were contoured on the CT portion of PET/CT by an experienced radiation oncologist blinded to the PET findings. $^{68}$Ga-PSMA PET/CT images were analyzed by an experienced nuclear medicine physician. PSMA avid lesions were compared with the consensus CTVs. PSMA avid lesions not covered by planning volumes based on the consensus CTVs were considered to have a major potential impact on treatment planning.

**Results:** The median PSA at the time of $^{68}$Ga-PSMA PET/CT was 0.48 ± 0.25 (range 0.03-1 ng/ml). 132 of 270 patients (49%) had a positive $^{68}$Ga-PSMA PET/CT study. 52 patients (19% of all patients, 39% of patients with a positive $^{68}$Ga-PSMA PET/CT) had at least one PSMA avid lesion not covered by planning based on the consensus CTVs and would have been inadequately treated using these volumes. 33 patients (12% of all patients, 25% of patients with a positive $^{68}$Ga-PSMA PET/CT) had extra-pelvic PSMA avid lesions and 19 (7% of all patients, 14% of patients with a positive $^{68}$Ga-PSMA PET/CT) had PSMA avid lesions within the pelvis but not covered by consensus CTVs.

**Conclusion:** $^{68}$Ga-PSMA PET to CT would have a major impact on SRT in 52 of 270 (19%) patients with early biochemical recurrence (PSA<1.0 ng/ml) after radical prostatectomy. This impact may justify a randomized imaging trial in a similar patient cohort offered SRT with or without $^{68}$Ga-PSMA PET/CT powered for a clinical outcome. Furthermore, in patients with a positive PSMA-PET, consensus CTVs failed to cover recurrences in 52 of 132 (39%) of patients. 33 (25%) of these 132 patients had M1 disease, a majority of which (66%) were oligometastatic M1a or M1b (1 to 5 extra-pelvic sites). The frequency of oligometastatic patients in this cohort suggests a clinical trial incorporating metastasis-directed therapy is feasible even at low PSA values if patients are imaged with PSMA-PET/CT.

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