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Personalized Multi-Timepoint Voxel-Level Dosimetry in Patients with Metastatic Castration-Resistant Prostate Cancer Treated with 177Lu-PSMA-617 Therapy

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Published 01/26/2026

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Categories: Radiation Oncology
Keywords: dosimetry, pluvicto, radiation oncology, radiopharmaceutical therapy

How to cite this abstract
Basree M (January 26, 2026) Personalized Multi-Timepoint Voxel-Level Dosimetry in Patients with Metastatic Castration-Resistant Prostate Cancer Treated with 177Lu-PSMA-617 Therapy. Cureus 18(1): a1608

Abstract

Purpose: Radiopharmaceutical therapy (RPT) has grown rapidly, though standard dosing across agents (e.g., 200 mCi) remains unchanged. Prior studies have shown correlations between absorbed dose, toxicity, and treatment response. We evaluated patient-specific dosimetry, its relationship to outcomes, and potential for treatment personalization using voxel-level dose parameters.

Methods: Nineteen patients were included in this series, treated between July 2023 and May 2025, who had evaluable post-cycle 1 dosimetry and received at least 1 cycle of therapy.Voxel-level Monte Carlo dosimetry was performed using the Torch RPT dosimetry platform (Voximetry). SPECT/CT imaging was acquired at three timepoints following the first treatment cycle: 3 ± 2 hours, 24 ± 4 hours, and 96 ± 24 hours. Mean absorbed doses from cycle 1 were extrapolated across six cycles to approximate cumulative dose. Institutional organ-at-risk (OAR) constraints were defined as kidney mean dose (D_mean) < 24 Gy and salivary gland D_mean < 20 Gy for a full course of therapy. After cycle 1 dosimetry, physicians could continue therapy as planned, delay subsequent cycles, reduce injected activity by 20%, or discontinue treatment. Descriptive statistics summarized the findings.

Results: Reasons for obtaining patient dosimetry included prior external beam radiotherapy (n=11; 57.9%), bone marrow toxicity concerns (n=9; 47.4%), kidney dysfunction (n=6; 31.6%), prior RPT (n=2; 10.3%), or a combination of these (n=7; 36.8%). Compared with VISION phase III trial data, mean absorbed doses to key OARs (heart, kidneys, liver, lungs, salivary glands, spleen) were not substantially different. Assuming consistent dosimetry across six cycles, cumulative mean kidney and salivary gland doses were 17.7 Gy (range, 5.8-27.5) and 15.9 Gy (range, 3.0-32.2), respectively. Other OAR mean doses included bowel bag 7.9 Gy (range, 0.4-20.8) and bone marrow 9.4 Gy (range, 1.2-24.3). Tumor volumes received a mean absorbed dose of 91.3 Gy (range, 9.6-273.4). Personalized dosimetry, combined with clinical context, guided safe continuation of Pluvicto in most patients (n=13; 68.4%), while a smaller number of patients were recommended to discontinue treatment early (n=5; 26.3%) or delay cycle administration (n=1; 5.3%). Based on kidney dose limits after cycle 1, 15/19 patients (79.0%) could have safely received a seventh cycle; similarly, based on salivary gland limits, 8/15 patients (53.3%) could have received an additional cycle.

Conclusion: Multi-timepoint voxel-level dosimetry is feasible and provides actionable data to personalize RPT. Our institutional experience demonstrates the potential to safely extend therapy in select patients. Future work will focus on workflow optimization, standardized tumor segmentation, and integration of dosimetry as a clinical decision-support tool.