Case Report

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First Southeast Asian Experience of Terbium-161 PSMA Therapy for Metastatic Castration-Resistant Prostate Cancer (mCRPC): Quantitative Imaging and Dosimetric Approach

Metastatik Kastrasyona Dirençli Prostat Kanseri (mCRPC) için Terbiyum-161 PSMA Tedavisinin Güneydoğu Asya'daki İlk Deneyimi: Kantitatif Görüntüleme ve Dozimetrik Yaklaşım

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Abstract

Prostate-specific membrane antigen (PSMA)-targeted radionuclide therapy has become an established treatment option for metastatic castration-resistant prostate cancer. Although lutetium-177 (^{177}Lu) PSMA therapy has shown promising clinical benefits, terbium-161 (^{161}Tb) PSMA is an emerging theranostic agent offering potential advantages due to its combination of beta and Auger electron emissions. This work presents the first documented case in Thailand and Southeast Asia of a patient treated at Ramathibodi Hospital with ^{161}Tb-PSMA following progression on ^{177}Lu-PSMA therapy. This report describes the clinical application of this novel radiopharmaceutical, the implementation of quantitative imaging protocols, single photon emission computed tomography/computed tomography calibration processes, and absorbed dose estimations from voxel-based dosimetry that contributed to individualised treatment planning.

Keywords: Prostate cancer, terbium-161 PSMA, lutetium-177 PSMA, theranostics, SPECT calibration, dosimetry, auger electrons

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Öz

Prostat spesifik membran antijeni (PSMA) hedefli radyonüklid tedavisi, metastatik kastrasyona dirençli prostat kanseri için yerleşik bir tedavi seçeneği haline gelmiştir. Lutetyum-177 (^{177}Lu) PSMA tedavisi umut verici klinik faydalar göstermiş olsa da, beta ve Auger elektron emisyonlarının birleşimi sayesinde potansiyel avantajlar sunan terbiyum-161 (^{161}Tb) PSMA, gelişmekte olan bir teranostik ajandır. Bu çalışma, ^{177}Lu-PSMA tedavisi sonrasında progresyon gelişen ve Ramathibodi Hastanesi'nde ^{161}Tb-PSMA ile tedavi edilen bir hastaya ait, Tayland ve Güneydoğu Asya'daki ilk belgelenmiş olguyu sunmaktadır. Bu rapor, söz konusu yeni radyofarmasötiğin klinik uygulamasını, kantitatif görüntüleme protokollerinin hayata geçirilmesini, tek foton emisyon bilgisayarlı tomografi/bilgisayarlı tomografi kalibrasyon süreçlerini ve bireyselleştirilmiş tedavi planlamasına katkı sağlayan voksel tabanlı dozimetriye dayalı soğurulan doz hesaplamalarını tanımlamaktadır.

Anahtar kelimeler: Prostat kanseri, terbiyum-161 PSMA, lutetyum-177 PSMA, teranostik, SPECT kalibrasyonu, dozimetri, auger elektronları

Introduction

Metastatic castration-resistant prostate cancer (mCRPC) remains a major clinical challenge, characterised by progression despite androgen deprivation therapy (ADT) and the use of second-line systemic treatments (1,2). Theranostic approaches targeting the prostate-specific membrane antigen (PSMA) with radiolabelled compounds, such as lutetium-177 (^{177}Lu)-PSMA, have demonstrated significant therapeutic benefits. However, a subset of patients ultimately develops resistance or progresses despite multiple cycles of ^{177}Lu-PSMA therapy (3).

Terbium-161 (^{161}Tb)-PSMA is a novel radionuclide offering theoretical advantages over ^{177}Lu-PSMA, including higher linear energy transfer and the emission of conversion and Auger electrons, which may enhance therapeutic efficacy, particularly in small-volume or micro-metastatic disease. However, clinical data on ^{161}Tb-PSMA therapy remain extremely limited, especially in Southeast Asia (1,4,5).

This report presents the first clinical application of ^{161}Tb-PSMA therapy in Thailand and Southeast Asia, providing early insights into integrating quantitative single photon emission computed tomography (SPECT) imaging and the voxel-based absorbed dose estimation in the therapeutic process.

Case Report

A 68-year-old male was initially diagnosed with locally advanced prostate cancer in 2006 and received pelvic external beam radiation therapy combined with brachytherapy, followed by ADT. In 2017, a solitary PSMA-avid mediastinal nodal metastasis was detected and managed with stereotactic body radiation therapy (SBRT). However, disease recurrence was observed in 2019, prompting the initiation of ^{177}Lu-PSMA radioligand therapy. The patient subsequently underwent 13 cycles of ^{177}Lu-PSMA therapy (administered at 150-200 mCi per cycle), with treatment continuing until June 2024. During the first 10 cycles of ^{177}Lu-PSMA therapy, metastatic disease was confined to lymph node and pulmonary involvement, without evidence of skeletal metastases.

In parallel, systemic chemotherapy was introduced, docetaxel in 2022 and cabazitaxel in 2024, the latter completed in December 2024. Interval development of bone oligo-metastases at the lumbar, vertebra and left iliac bone was identified on 11th post-therapy ^{177}Lu-PSMA imaging in March 2024. These two skeletal lesions were treated with SBRT. However, subsequent imaging after the 12th and 13th cycles of ^{177}Lu-PSMA demonstrated progression of bone metastases, indicating treatment resistance. Consequently, second-line chemotherapy with cabazitaxel was initiated.

Despite these interventions, disease progression was noted under the mCRPC setting. Galium-68 PSMA positron emission tomography combined with computed tomography scan in January 2025 demonstrated further disease progression with multiple PSMA-avid bone metastases, in addition to widespread involvement of the supraclavicular and mediastinal lymph nodes, pulmonary parenchyma, and skeletal system, along with rising prostate-specific antigen (PSA) levels. The most symptomatic lesion was located in the right femur, where the patient reported nocturnal pain with a numeric rating scale score of 5 out of 10. Analgesic management included tramadol and non-steroidal anti-inflammatory drugs (NSAIDs).

Given the exhausted therapeutic options and persistent disease activity, the patient was selected for treatment with ^{161}Tb-PSMA, which commenced in February 2025. Pre-treatment imaging confirmed extensive PSMA-avid lesions without any contraindications to therapy. Baseline laboratory investigations, including renal and hematologic parameters, were within acceptable limits and monitored closely throughout the treatment process.

Written informed consent was obtained from the patient for the publication of this short communication and any accompanying images. All identifiable information has been anonymised to protect the patient's privacy.

Radiopharmaceutical Preparation and Administration

^{161}Tb was obtained from TerThera BV, Germany, and prepared at Bangkok Hospital. Radiolabelling with PSMA-I&T ligand was performed using a protocol adapted from ^{177}Lu-PSMA procedures, with modifications to minimise radiolysis (6). The process was carried out under good manufacturing practice quality-controlled conditions. Radiochemical purity assessed by instant thin layer chromatography was 99.7% (acceptance criterion ≥95%), with an R_f value of 0.8 confirming radiochemical identity. Quality control testing demonstrated acceptable pH 4.5 (normal range 4.5-5.5), low bacterial endotoxin levels (<5.0 EU/mL), and satisfactory filter integrity, indicating adequate product stability prior to administration. Following completion of quality control, the radiopharmaceutical was transported to Ramathibodi Hospital. A total activity of 6283 MBq (169.81 mCi) of ^{161}Tb-PSMA was administered intravenously to the patient.

SPECT Calibration

Since ^{161}Tb is not included in the standard isotope libraries of most commercially available SPECT/computed tomography (CT) systems, a customised calibration protocol was established to enable accurate quantitative imaging. All imaging procedures were conducted using a dual-head hybrid SPECT/CT scanner (GE Discovery 870 DR, GE Healthcare, MI, USA) equipped with a Low-Energy High-Resolution collimator at Ramathibodi Hospital. Energy window settings were optimised for ^{161}Tb detection. The primary photopeak was centred at 74.6 keV with a ±10% energy window, and the lower and upper scatter correction windows were set at 63 keV±6% and 88 keV±6%.

Intrinsic calibration of the SPECT system was performed using both a point source and a flood source of ^{161}Tb. A small-volume point source was prepared to assess energy peak alignment and system sensitivity, while a flood source of ^{161}Tb was used to evaluate detector uniformity across the field of view. These steps ensured that calibration conditions closely matched the specific emission characteristics of ^{161}Tb.

An extrinsic flood calibration was also conducted to correct potential system nonuniformities introduced by the collimator-detector assembly. For quantitative SPECT, planar system sensitivity was determined by imaging a petri dish filled with a known activity of ^{161}Tb solution, containing approximately 37 MBq (1 mCi), following the NEMA NU1-2012 protocol. Activity measurements were verified with a radionuclide activity calibrator to ensure precise sensitivity calculations.

Post-therapeutic Imaging Protocol

Post-therapeutic quantitative SPECT/CT imaging was performed following administration of ^{161}Tb-PSMA, using acquisition settings based on the calibration previously described. SPECT/CT imaging was conducted at 2 hours, 24 hours, and 96 hours post administration.

SPECT acquisition was performed with 10 seconds per frame across all imaging sessions using a matrix size of 128 × 128 pixels, and the view angle was set at 3 degrees, 60 projections per detector, for a total of 180 projections. For this patient, four overlapping bed positions were acquired per session, with each bed position requiring approximately 15 minutes of scan time. A low-dose CT scan was performed for attenuation correction and anatomical localisation.

Quantitative SPECT image reconstruction was performed with the assistance of the MIM Software technical team and the local GE Healthcare support staff. Reconstruction was performed using an Ordered Subset Expectation Maximisation algorithm with 4 iterations and 10 subsets and applying corrections for attenuation and scatter. No post-reconstruction filtering was applied to preserve the voxel-level quantitative accuracy required for dosimetric analysis. Voxel activity concentrations were calibrated based on the planar sensitivity measurements previously established during system calibration.

Absorbed Dose Calculation

Voxel-based absorbed dose calculations were performed using the Hermes Medical Solutions software, under a research collaboration agreement between the institution and Hermes Medical Solutions (Hermia, Sweden). The absorbed dose analysis utilised the Voxel Dosimetry module, version 3.1.

Organ and tumour segmentations were generated using the software's automatic AI-based segmentation tools to facilitate consistent and efficient volume delineation. Absorbed dose calculations were performed using a Monte Carlo simulation method integrated within the Voxel Dosimetry workflow.

Discussion

Post-therapeutic quantitative SPECT/CT imaging following ^{161}Tb-PSMA therapy (6283 MBq or 169.81 mCi) enabled voxel-based dosimetry using AI-assisted segmentation (Figure 1). The absorbed dose distribution effectively targeted PSMA-avid lesions while maintaining acceptable radiation exposure to normal organs. This favourable tumor-to-organ dose distribution is consistent with recently

reported multicentre clinical experience with ^{161}Tb-PSMA, which demonstrated safe organ dosimetry and promising antitumor activity even in patients refractory to prior ^{177}Lu-PSMA therapy (7).

The mean absorbed dose to the kidneys was 1.83 Gy, with 1.97 Gy delivered to the left kidney and 1.69 Gy to the right kidney, both remaining well below established renal tolerance thresholds. Other organs received relatively low absorbed doses, including 0.48 Gy to the liver and 0.63 Gy to the spleen. Lung doses were asymmetrical, with 3.61 Gy to the left lung corresponding to metastatic involvement and 0.49 Gy to the right lung. Skeletal lesions exhibited the highest absorbed doses, with the lesion in the left femur receiving 6.51 Gy and the lumbar spine lesion 5.23 Gy, as summarised in Figure 2, which includes the AI-assisted organ segmentation. Comparable organ absorbed doses and higher lesion doses have been reported in multicentre studies, supporting the therapeutic selectivity of ^{161}Tb-PSMA while maintaining organ safety margins (7).

An intra-patient comparison of renal dosimetry was undertaken between the 12th treatment cycle with ^{177}Lu-PSMA in March 2024 and the 14th cycle with ^{161}Tb-PSMA in February 2025, as illustrated in Table 1. For the ^{177}Lu-PSMA cycle, dosimetry was performed using a single time-point (STP) based on the Hänscheid approach, with quantitative SPECT/CT imaging obtained approximately 48 hours post-administration. The mean kidney absorbed dose was 1.84 Gy, corresponding to a dose-per-activity ratio of 0.22 mGy/MBq. In contrast, the ^{161}Tb-PSMA therapy incorporated a multiple time-point imaging protocol, as STP models for ^{161}Tb-PSMA are not yet established. Despite methodological differences, the mean kidney absorbed dose during the ^{161}Tb-PSMA cycle remained comparable at 1.83 Gy. However, the mean absorbed dose per administered activity was slightly higher at 0.29 mGy/MBq.

This observation aligns with published dosimetric data showing that ^{161}Tb-PSMA may deliver similar macroscopic organ doses to ^{177}Lu-PSMA while potentially providing enhanced microscopic dose deposition due to the emission of short-range Auger electrons (7). The modest increase in dose-per-activity in the present case may also reflect differences in disease burden and radiopharmaceutical kinetics, as the patient demonstrated more advanced disease progression at the time of ^{161}Tb-PSMA therapy. Previous studies suggest that ^{161}Tb-PSMA may be particularly effective in heterogeneous or micrometastatic disease, although current macrodosimetry approaches may underestimate its true biologic impact (7). Given the evolving metastatic landscape between treatment cycles, lesion-specific absorbed doses were not directly compared.

From a clinical perspective, biochemical response after ^{161}Tb-PSMA therapy was limited. Serum PSA increased

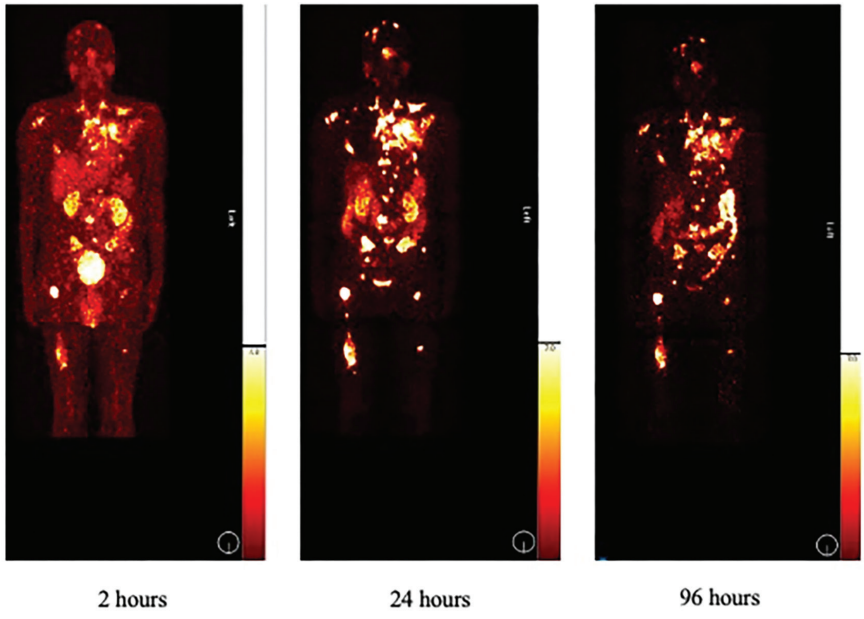
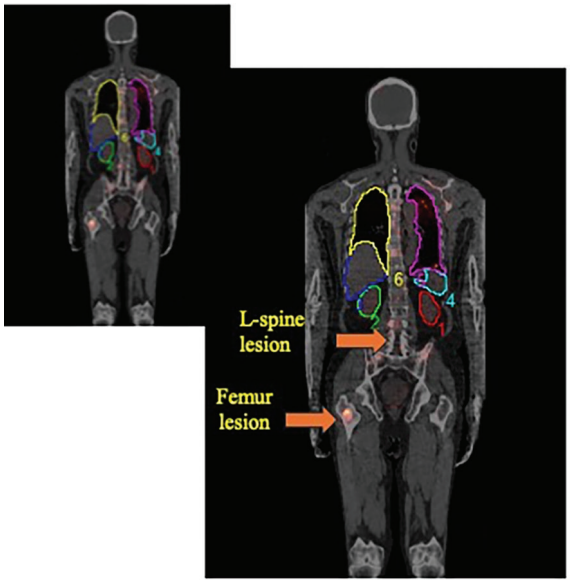


Figure 1. Quantitative SPECT/CT imaging maximum intensity projection at 2 hours (left), 24 hours (middle), and 96 hours (right) post-administration of ^{161}Tb-PSMA

^{161}Tb-PSMA: Terbium-161-prostate-specific membrane antigen, SPECT/CT: Single photon emission computed tomography/computed tomography



Organ	Absorbed Dose (Gy)
Lt. Kidney	1.97
Rt. Kidney	1.69
Mean Kidneys (volume average)	1.83
Liver	0.48
Spleen	0.63
Lt. Lung	3.61
Rt. Lung	0.49
Lesion Femur	6.51
Lesion L-Spine	5.23

Figure 2. (Left) Coronal fused SPECT/CT image at 24 hours post-treatment showing AI-assisted organ segmentation used for voxel-based dosimetry analysis. Organs segmented include the left lung (yellow), right lung (pink), left kidney (green), right kidney (cyan), spleen (red), and liver (blue). Selected skeletal metastases, including a lumbar spine lesion and a left femoral lesion, are annotated. (right) Absorbed dose to organs at risk and lesion from ^{161}Tb-PSMA
SPECT/CT: Single photon emission computed tomography/computed tomography, ^{161}Tb-PSMA: Terbium-161-prostate-specific membrane antigen

Table 1. Intra-patient of renal dosimetry between the 12th treatment cycle with ^{177}Lu-PSMA in March 2024 and the 14th cycle with ^{161}Tb-PSMA in February 2025

	^{177}Lu-PSMA	^{161}Tb-PSMA
Treatment cycle	12th	14th
Time	Mar 2024	Feb 2025
Treatment activity (MBq)	8103 (219 mCi)	6283 (170 mCi)
Dosimetry software and method	Hermes 3.1 singlet time-point dosimetry at 48 h (hanscheid method)	Hermes 3.1 multiple time-point dosimetry
Mean kidneys (Gy)	1.84	1.83
Mean kidneys per administered activity (mGy/MBq)	0.22	0.29

^{177}Lu-PSMA: Lutetium-177-prostate-specific membrane antigen, ^{161}Tb-PSMA: Terbium-161-prostate-specific membrane antigen

from 918 ng/mL prior to treatment to 978 ng/mL at early post-therapy assessment, consistent with advanced disease burden and possible delayed or absent biochemical response in this heavily pretreated setting. In contrast, a marked symptomatic improvement was observed. The patient's pain, previously rated as 5 out of 10 at the right thigh, improved substantially after ^{161}Tb-PSMA therapy, with a post-treatment pain score of 0-1 out of 10, allowing discontinuation of tramadol and NSAID analgesics.

Regarding treatment-related toxicity, ^{161}Tb-PSMA was generally well tolerated. The patient experienced transient fatigue and malaise during the first week after therapy, which resolved spontaneously. Xerostomia was not newly observed and was attributed to cumulative prior ^{177}Lu-PSMA treatments, for which the patient continued to use artificial saliva.

Laboratory monitoring demonstrated stable renal function and hematologic parameters following ^{161}Tb-PSMA administration. Serum creatinine showed a mild increase from 1.25 mg/dL before therapy to 1.31 mg/dL after therapy, without clinical evidence of nephrotoxicity. Hematologic indices remained stable, with haematocrit changing from 29.0% to 28.9% and platelet count decreasing from 185000/μL to 159000/μL, without clinically significant cytopenia. These findings are consistent with previously reported safety profiles of ^{161}Tb-PSMA therapy (7).

Conclusion

This case represents the first reported clinical application of ^{161}Tb-PSMA therapy in Thailand and Southeast Asia. Quantitative SPECT/CT-based voxel dosimetry demonstrated effective lesion targeting and favourable absorbed dose distribution, with acceptable radiation exposure to normal organs. A comparative intra-patient analysis revealed that the renal absorbed dose per administered activity was slightly higher for ^{161}Tb-PSMA than for ^{177}Lu-PSMA, likely reflecting differences in diseases burden and biodistribution. Although an early biochemical response was not observed, ^{161}Tb-PSMA therapy resulted in marked symptomatic improvement with substantial pain relief and reduced analgesic requirements, while maintaining a favourable safety profile without clinically significant renal or hematologic toxicity. These findings support the role of quantitative imaging, dosimetry and suggest that ^{161}Tb-PSMA may offer a safe and clinically meaningful palliative option in heavily pretreated patients with mCRPC after ^{177}Lu-PSMA therapy.

Ethics

Informed Consent: Written informed consent was obtained from the patient for the publication of this short communication and any accompanying images. All identifiable information has been anonymised to protect the patient's privacy.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: T.A., B.K., W.C., K.C., Concept: T.A., K.C., Design: K.C., Data Collection or Processing: S.A., P.C., P.P., T.T., B.K., W.C., Analysis or Interpretation: S.A., W.C., K.C., Literature Search: K.K., W.C., K.C., Writing: K.C.

Conflict of Interest: No conflicts of interest were declared by the authors.

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Availability of Data and Material

The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request.

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