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Tumor and organ dosimetry from sequential quantitative SPECT/CT following a single dose of albumin-bound ^{177}Lu PSMA-ALB-56 in 3 patients with metastatic prostate cancer

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Data and images courtesy of Center for Nuclear Medicine & PET/CT Positronmed, Santiago, Chile

Background

Lutetium 177 (^{177}Lu)-PSMA therapy is increasingly being adopted for patients with metastatic prostate cancer. Although therapy results have been encouraging, there is still room for optimization, particularly regarding tracer uptake and absorbed dose to the salivary glands. The concept of using a small molecular weight albumin-binding entity attached to the PSMA ligand to enhance the blood-circulation time was the basis for development of ^{177}Lu-PSMA-ALB-56[a], which is a PSMA radioligand with higher tumor accumulation compared to other established PSMA ligands with relatively low background retention.

Ten patients with metastatic castration resistant prostate cancer (mCRPC) were treated with a single dose of approximately 3.3 GBq (89.1 mCi) of ^{177}Lu-PSMA-ALB-56 followed by sequential quantitative SPECT/CT acquisition at 1.5 hours, 6 hours, 24 hours, and 48 hours as well as 7 days following therapy administration in order to calculate tracer time activity curves (TACs) for tumor and critical organs for dosimetry evaluation. Quantitative SPECT/CT-based dosimetry for 3 such patients is highlighted in this clinical case review.

History

Whole-body (WB) SPECT/CT scans were acquired (3 bed positions from the top of the head to the upper thighs: 90 projections and 25 seconds per projection) on a Symbia™ SPECT/CT at approximately 1.5 hours, 6 hours, 24 hours, 48 hours, and at 7 days post-therapy administration with a ^{177}Lu reference standard of approximately 10 MBq within the field of view (FOV).

A medium-energy low-penetration (MELP) collimator was used with an acquisition of 3 energy windows with the peak window width of 20% centered around the 208 keV energy peak and 2 adjacent corresponding lower- and upper-scatter energy windows of 10% width.

All SPECT images were co-registered to the CT images. Volumes of interest (VOIs) were generated around the kidneys (left and right), liver, spleen, salivary glands (left and right parotid and submandibular glands), and up to 5 tumor lesions per patient with segmentation performed with either the SPECT or CT image.

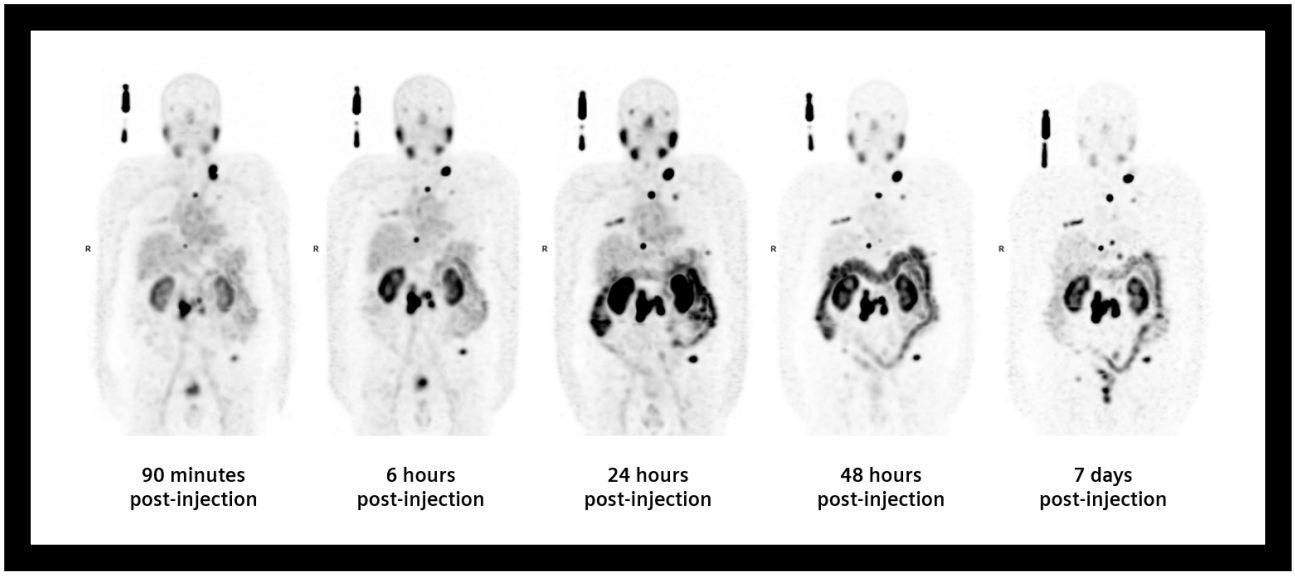
Total counts within VOIs obtained from sequential SPECT/CT images were converted to Bq/ml using phantom study derived calibration factor. TACs were generated from all VOIs. All TACs were fitted depending on the degree of correlation to a mono- or bi-exponential function. The cumulated activity for each source organ and tumor was determined by calculating the area under the curve of the fitted TAC. The normalized cumulated activity or residence time was calculated for all source organs and tumors as the cumulated activity divided by the administered activity. The absorbed organ doses and effective dose calculations were performed using OLINDA/EXM 1.1® software. Tumors were assumed to be spherical, and their volumes were calculated with sphere diameters based on the average of the 2 longest diameters in the axial view on contrast-enhanced CT images. Additionally, tumor masses were calculated with either a density of 1.06 g/cm^3 for soft-tissue lesions or 1.92 g/cm^3 (same as cortical bone) for bone lesions.

Findings

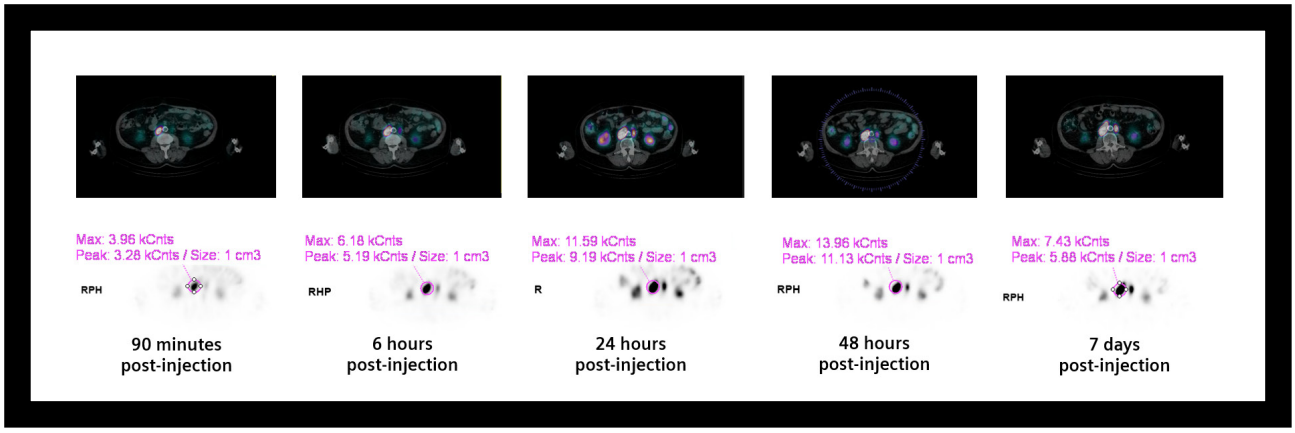
Patient 1

An approximately 70-year-old male was referred with large para-aortic lymph node metastases along with left supraclavicular node metastases. Small focal bone metastases are also visualized in the sternum, right transverse process of the T7 vertebra, and the left iliac crest. All nodal and bone metastases show high ^{177}Lu-PSMA-ALB-56 uptake in sequential SPECT/CT images.

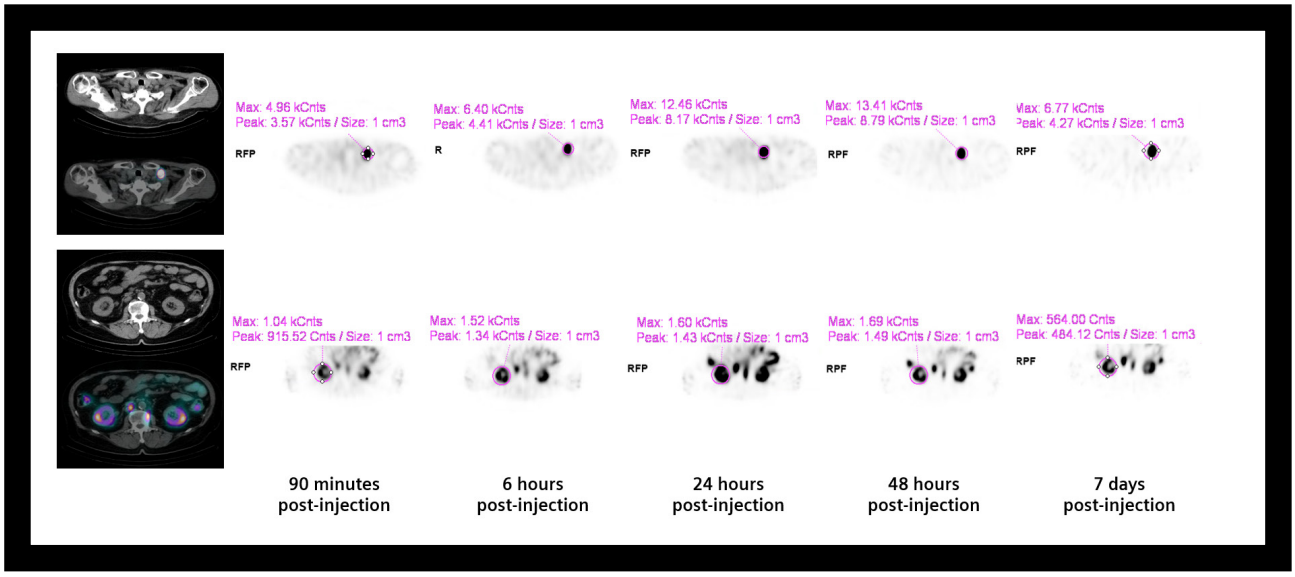
Tracer concentrations and volumes derived from sequential SPECT/CT data were used to generate TACs for subsequent dosimetry calculations. Calculated average absorbed dose to the para-aortic nodal metastases was 69.8 Gy/GBq while that to the



1 **Sequential multi-bed SPECT maximum intensity projection (MIP) images acquired at 90 minutes, 6 hours, 24 hours, 48 hours, and at 7 days post-injection of 3.3 GBq of ^{177}Lu-PSMA-ALB-56 show initially high uptake with progressive increase in tracer retention in para-aortic and supraclavicular lymph node metastases as well as in bone metastases in the sternum, thoracic vertebra, and left ilium. The tracer concentration within the metastases peaks at 48 hours post-administration. Renal cortex and salivary glands show progressive increase in uptake, with the peak reached at 24 hours post-injection, with slow washout.**



2 **Sequential axial SPECT/CT and SPECT images at the level of abdominal para-aortic nodal metastases show increased uptake with progressive increase in tracer concentration within the lymph node lesion with maximum concentration reached at 48 hours. Images show maximum voxel counts within VOI around lymph node metastases.**



3 **Sequential SPECT images show progressive increase in tracer concentration up to 48 hours post-administration in the left supraclavicular lymph node metastases as well as the bilateral renal cortex. Lymph node metastases show slower washout as compared to renal cortex.**

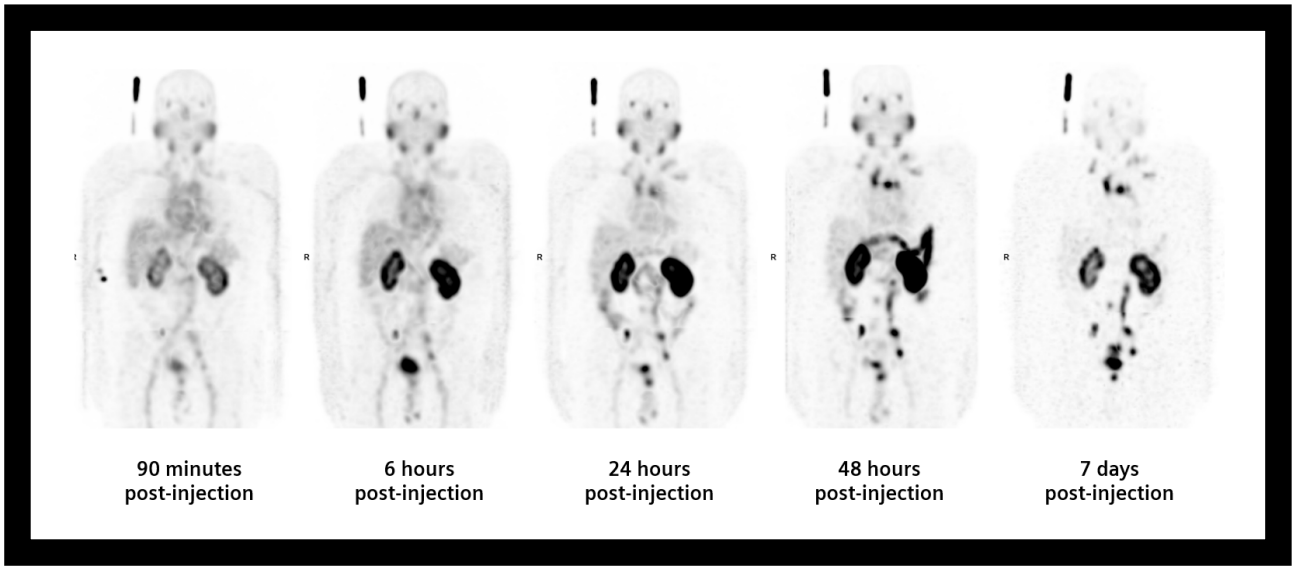
supraclavicular metastases was 23.6 Gy/GBq. Average absorbed dose to bilateral renal cortex was 2.43 Gy/GBq. For an administered dose of 3.3 GBq, the absorbed dose to the largest tumor lesion (para-aortic nodal mass) was approximately 230 Gy, which is extremely high for a single therapy cycle.[1] Renal cortical dose was calculated to be approximately 8 Gy. Among salivary glands, the left parotid gland received a high absorbed dose of 0.72Gy/GBq while the right parotid gland received 0.63 Gy/GBq. Bone marrow dose was higher than expected (0.30 Gy/GBq) with marrow dose predicted to be approximately 1 Gy for a single therapy cycle. In view of the 2 Gy cumulative bone marrow dose limitation threshold,[2] the high marrow dose estimation is a cause for concern and close hematological monitoring during subsequent therapy cycles.

Follow-up evaluation of serum PSA shows a 15% decrease after 10 weeks after therapy administration. There was no significant renal or bone marrow toxicity.

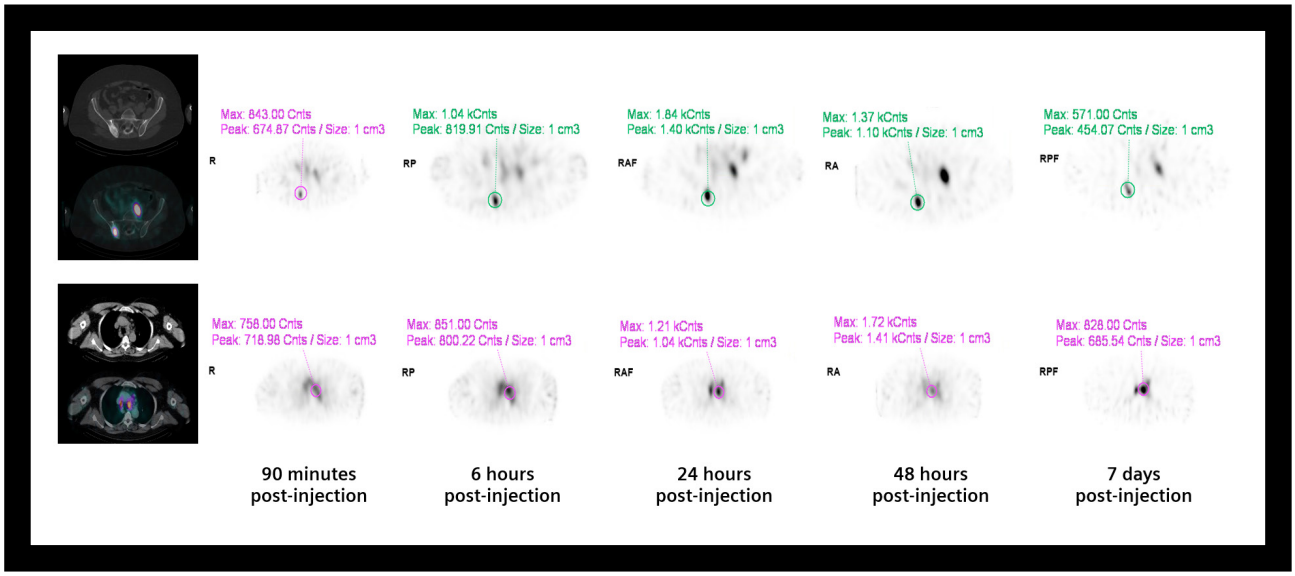
Patient 2

An approximately 60-year-old male with mCRPC with pelvic bone metastases along with mediastinal lymph node metastases underwent ^{177}Lu-PSMA-ALB-56 therapy. Following administration of 3.4 GBq (91.8 mCi) of ^{177}Lu PSMA-ALB-56, sequential multi-bed SPECT/CT was performed at 90 minutes, 6 hours, 24 hours, 48 hours, and 7 days.

Dosimetry results show the bone metastases in the right ileum received an absorbed dose of 0.42 Gy/GBq (1.38 Gy for a single therapy cycle of 3.3 GBq), which is low for a 3.3 GBq therapy; however, the low retention of tracer within bone metastases on the 7-day image correlates well with the calculated absorbed dose. The mediastinal nodal metastases received a high dose of 9.52 Gy/GBq, which resulted in a predicted absorbed dose of 31.4 Gy for a 3.3 GBq therapy dose. The average renal cortical absorbed dose was 2.95 Gy/Gbq (9.7 Gy for single therapy cycle), which was higher than expected, suggesting the risk of crossing the 23 Gy renal absorbed dose limit within 3 cycles,

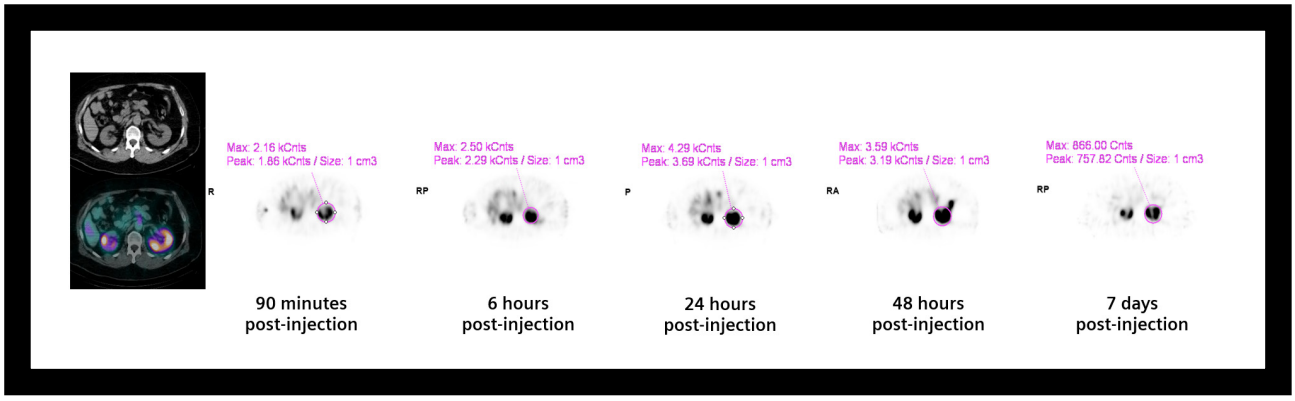


4 **WB MIP of multibed sequential SPECT shows progressive increase in uptake in the right pelvic bone metastases as well as mediastinal metastases, especially the para-tracheal lymph node metastases. Lesions show peak uptake at 48 hours with slow washout. Kidneys show gradual increase in cortical retention with maximum uptake at 24 hours but slow washout with significant cortical retention after 7 days along with significant tracer stasis in the dilated ureter.**



5 **Axial SPECT images through pelvic bone and para-tracheal mediastinal metastases show progressive increase in tracer concentration with peak reached at 48 hours and a slow subsequent washout.**

assuming similar renal cortical doses in subsequent therapies. Renal dose can vary significantly compared to the initial cycle since the tumor burden may decrease with higher tracer clearance through the kidneys leading to higher renal dose. Average bone marrow dose was calculated to be 0.24 Gy/GBq (0.8 Gy for single therapy cycle), which was higher than expected considering the presence of a single bone metastasis. Salivary gland doses were moderate. The left parotid gland received an absorbed dose of 0.77 Gy/GBq while the right parotid gland received 0.64 Gy/GBq.



6 **Axial SPECT images at the level of the kidneys show progressive cortical retention peaking at 24 hours with slow washout.**

Patient 3

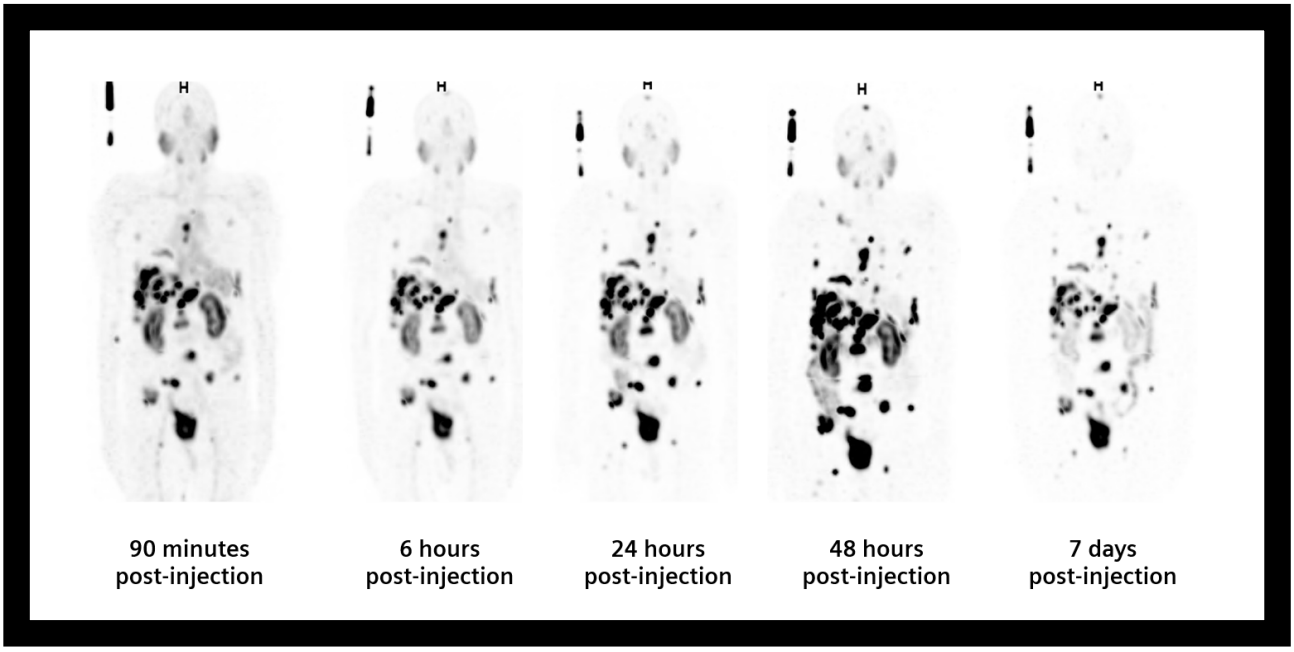
An approximately 75-year-old male with mCRPC with multiple bone and liver metastases was administered 3.6 GBq (97.2 mCi) of ^{177}Lu PSMA-ALB-56. Sequential quantitative SPECT/CT was acquired based on the acquisition protocol followed in the preceding cases.

Dosimetry results show the average renal cortical absorbed dose of 2.09 Gy/GBq (6.8 Gy for the single therapy cycle). This was slightly higher than expected with implication that 2 more therapies would lead to the maximum allowed cumulative renal dose of 23 Gy,[3] assuming a similar cortical dose for subsequent therapies. The largest bone metastases in the lumbar vertebrae received an absorbed dose of 8.14 Gy/GBq (26.8 Gy for the single therapy cycle) while the slightly smaller thoracic vertebral metastases received 6.97 Gy/GBq. Average bone marrow dose was calculated to be 0.27Gy/GBq (0.89 Gy for single therapy), which was quite high, reflecting the presence of multiple bone metastases impacting the dose to functioning marrow. Salivary gland doses were also significantly higher than expected as both the left and right parotid glands received an absorbed dose of approximately 0.80 Gy/GBq.

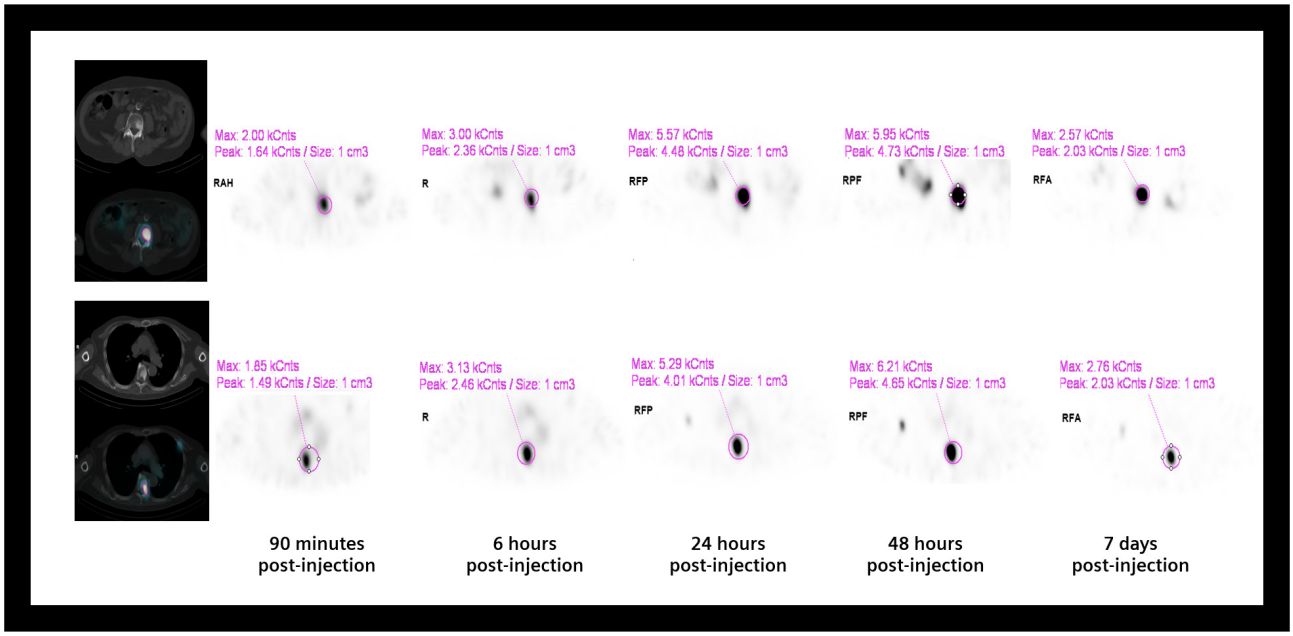
Discussion

The clinical cases discussed here are part of 10 cases representing the first clinical application of ^{177}Lu PSMA-ALB-56, which is a modified PSMA ligand with the aim of increasing the accumulation in tumor lesions. The cases demonstrate that the use of ^{177}Lu PSMA-ALB-56 successfully achieved a 1.4 to 2.3-fold higher absorbed dose to tumor lesions (6.64 Gy/GBq on average) as compared with published values for ^{177}Lu-PSMA-617 (3.87 Gy/GBq). The lesions considered for dosimetry among these patients were all larger than 1.5 ml in volume in order to reduce partial-volume effects. Of the 10 cases treated with a single therapy cycle of ^{177}Lu PSMA-ALB-56, the mean absorbed kidney dose of 2.55+/- 0.93 Gy/GBq was about 3.3 times higher than that reported for ^{177}Lu PSMA-617 (0.60-0.88 Gy/GBq), resulting in a mean tumor to kidney dose ratio of 3.3, which is lower than the reported dose ratio of 5.1 for ^{177}Lu PSMA-617.[4]

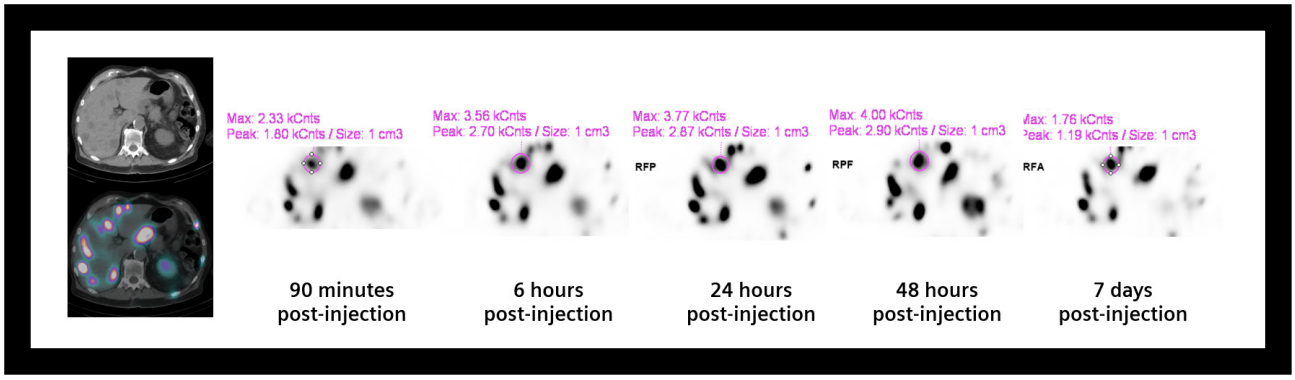
The higher renal dose highlights the need for measures like amino-acid infusion and diuresis to reduce renal toxicity. Follow-up of these 10 patients after 1 cycle of approximately 3.3 GBq of ^{177}Lu-PSMA-ALB-56 demonstrated a decrease in serum PSA values in 78% of patients with greater than 50% reduction in 44% of the patients. This observation is comparable to previous studies showing 77% of patients having a decrease in serum PSA after a single cycle of 7.5 GBq of ^{177}Lu PSMA-617.[5] The efficacy observed for ^{177}Lu PSMA-ALB-56, administered at approximately 45% less activity was thus comparable to that of ^{177}Lu PSMA-617.



7 Multibed sequential SPECT MIP images following administration of a therapy dose of ^{177}Lu PSMA-ALB-56 show progressive increase of tracer uptake in multiple skeletal and liver metastases. Tracer uptake intensity peaks at 48 hours post-therapy administration with slow washout. Renal cortex shows high initial uptake with normal washout with minimal renal cortical retention after 7 days. The salivary glands show high initial uptake but with progressive decrease in tracer concentration.



8 Quantitative SPECT images at the level of two vertebral body metastases involving the thoracic and lumbar spine show high initial uptake of ^{177}Lu PSMA-ALB-56 with progressive increase in tracer concentration reaching peak at 48 hours with slow washout with almost 40% of peak tracer concentration retained within the lesions even after 7 days following therapy administration. This suggests high absorbed dose within skeletal lesions.



9 **Sequential SPECT/CT images at the level of liver metastases show progressive increase in uptake within liver metastases reaching its peak at 48 hours with slow washout with more than 40% of peak tracer concentration retained within large liver metastases 7 days after therapy.**

Conclusion

Quantitative SPECT/CT is key to obtaining accurate TACs for subsequent dosimetry. Symbia SPECT/CT enabled multibed SPECT/CT acquisitions with accurate CT attenuation correction and scatter correction along with collimator detector response modeling to obtain SPECT/CT data that could be used to obtain quantitative information on tracer concentration in Bq/ml. Quantitative multibed WB SPECT/CT data could be used in commercially available dosimetry software for accurate absorbed dose calculation. Considering the higher tumor absorbed dose possibility with ^{177}Lu PSMA-ALB-56, there is potential of improving radionuclide therapy of metastatic prostate cancer using such radioligands, although higher renal and salivary dose considerations need to be considered. In such situations, accurate dosimetry using sequential SPECT/CT is of key importance for improving therapeutic outcomes while avoiding toxicity.

Examination protocol

Scanner: Symbia SPECT/CT

Therapy	
Injected dose	3.3 GBq (89.1 mCi) ^{177}Lu-PSMA-ALB-56

SPECT	
Post-injection delay	90 minutes, 6 hours, 24 hours, 48 hours, 7 days
Acquisition	90 projections, 25 seconds per projection
Image reconstruction	3DOSEM

CT	
Tube voltage	130 kV
Tube current	59 ref mAs
Slice collimation	2 x 4 mm
Slice thickness	5 mm

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References

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[a] The tracer used in this case is a research pharmaceutical. It is neither recognized to be safe and effective by the FDA nor commercially available in the United States or in other countries worldwide. Its future availability cannot be guaranteed. Please contact your local Siemens Healthineers organization for further details.

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