SIEMENS Healthineers

xSPECT Quant-based dosimetry following ^{177}Lu PSMA therapy in metastatic prostate cancer

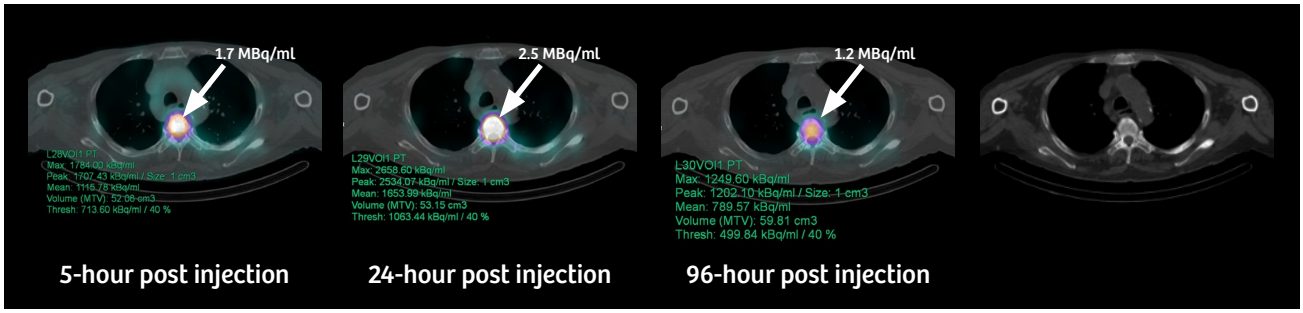
By Michael Hoffman, MD, Associate Professor
Data courtesy of Peter MacCallum Cancer Center, Melbourne, Australia

History

An 82-year-old man with castration-resistant prostate cancer and multiple skeletal metastases demonstrated by ^{68}Ga PSMA PET/CT to be PSMA-avid was referred for ^{177}Lu PSMA[a] therapy. The patient was treated with an intravenous infusion of 8.7 GBq of ^{177}Lu PSMA preceded by amino acid infusion. Five hours following therapeutic administration, the patient underwent a quantitative multi-bed SPECT/CT to image the distribution of ^{177}Lu PSMA within the body. The study was performed on a Symbia Intevo™ 16. Following an initial low-dose CT acquisition (130 kV, 25 eff mAs), a three-bed SPECT/CT study using xSPECT Quant™ was acquired with 60 stops per detector and 10 seconds per stop. The study was reconstructed using xSPECT Quant to quantify ^{177}Lu tracer concentration within the lesions and critical organs. Following the initial SPECT/CT acquisition at 5 hours post-therapy, sequential studies using identical acquisition and reconstruction protocols were performed at 24 hours and again at 96 hours.

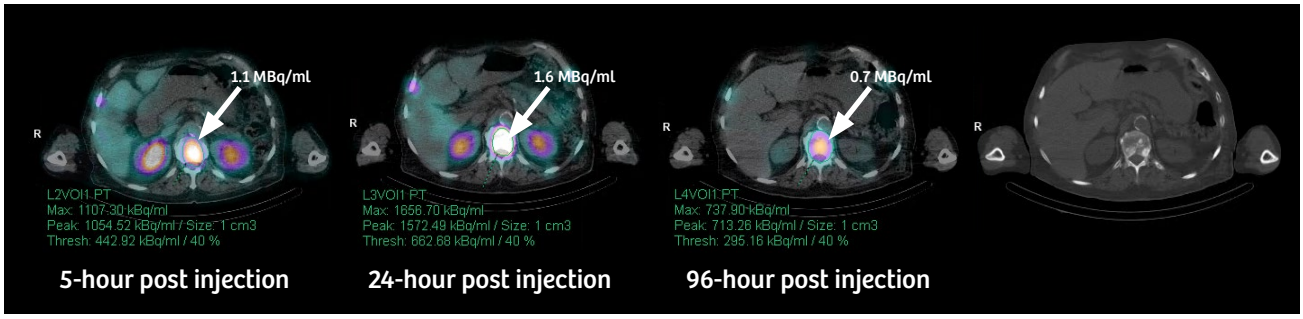
1 MIP images of sequential ^{177}Lu PSMA multi-bed SPECT studies show a progressive increase in tracer uptake within multiple skeletal metastases in the thoracic and lumbar vertebrae, ribs, and pelvis with maximum tracer retention seen 24 hours post injection. The 96-hour image shows slow washout of tracer within the metastases. The 5-hour images show significant renal cortical uptake and tracer retention in the bilateral renal pelvis, but the fast washout at 24-hours followed by a low level of cortical retention at 96 hours suggests good renal clearance of the tracer.

Data courtesy of Peter MacCallum Cancer Center, Melbourne, Australia.



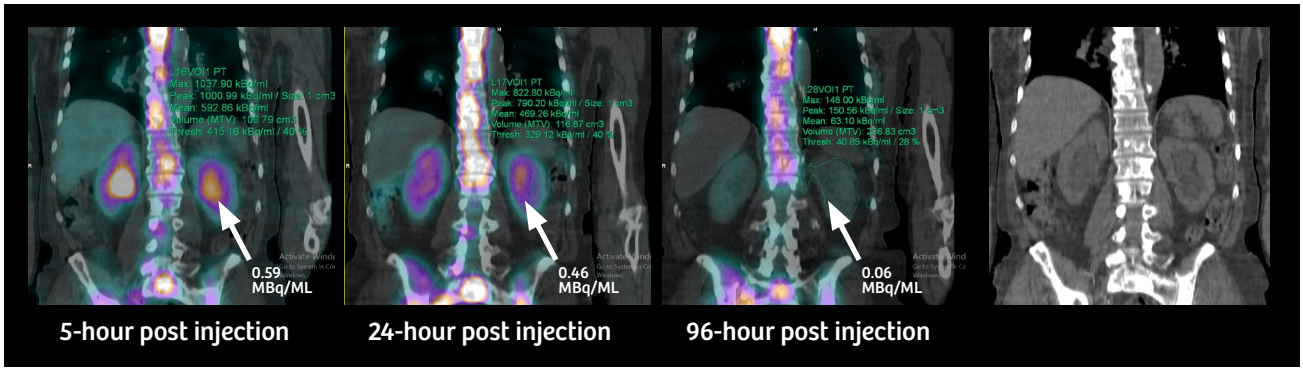
2 Fused images at the level of thoracic vertebral metastases show high initial tracer concentration within ^{177}Lu PSMA-avid metastases with further tracer retention by 24 hours, followed by slow washout. The peak tracer concentration at 24 hours was 2.5 MBq/ml, which decreased by more than 50% at 96 hours. The CT images show significant sclerosis within the metastatic vertebral body.

Data courtesy of Peter MacCallum Cancer Center, Melbourne, Australia.



3 Similar display of maximum tracer concentration in sequential fused images at the level of lumbar vertebral metastases show slightly lower peak concentration as compared to the thoracic vertebrae but with similar increase up to 24 hours with slow clearance. The degree of sclerosis is slightly lower in the lumbar vertebral body as compared to that of the thoracic vertebrae.

Data courtesy of Peter MacCallum Cancer Center, Melbourne, Australia.



4 Coronal-fused images display the maximum tracer concentration in the left kidney along with the renal volume. The peak tracer concentration is 0.59 MBq/ml at 5-hours post injection with fast washout, such that only 10% of the peak concentration is retained in the renal cortex and pelvis after 96 hours. The coronal CT images show normal cortical thickness in both kidneys with normal calyces and pelvis.

Data courtesy of Peter MacCallum Cancer Center, Melbourne, Australia.

Findings

Sequential SPECT/CT images with tracer concentration values in thoracic and lumbar vertebral metastases obtained using xSPECT Quant (as displayed in Figures 1-3) clearly highlight the high initial tracer concentration within the metastases with a gradual increase in concentration up to 24 hours post injection. There was slow washout from the metastases with nearly 50% of tracer retention even at 96 hours post injection. This pattern of initial high uptake and subsequent slow washout within the metastases reflects the potential of high radiation dose delivered by ^{177}Lu PSMA therapy.

The renal uptake appears normal in the initial 5-hour image (Figure 4) with fast washout that left only 10% of the initial concentration at 96 hours. This fast clearance suggests a low residence time of tracer within the renal cortex and a consequently low level of radiation dose to the kidneys. The normal cortical thickness and absence of pelvicalyceal enlargement on CT reflect normal renal morphology and absence of pelvicalyceal stasis or obstruction.

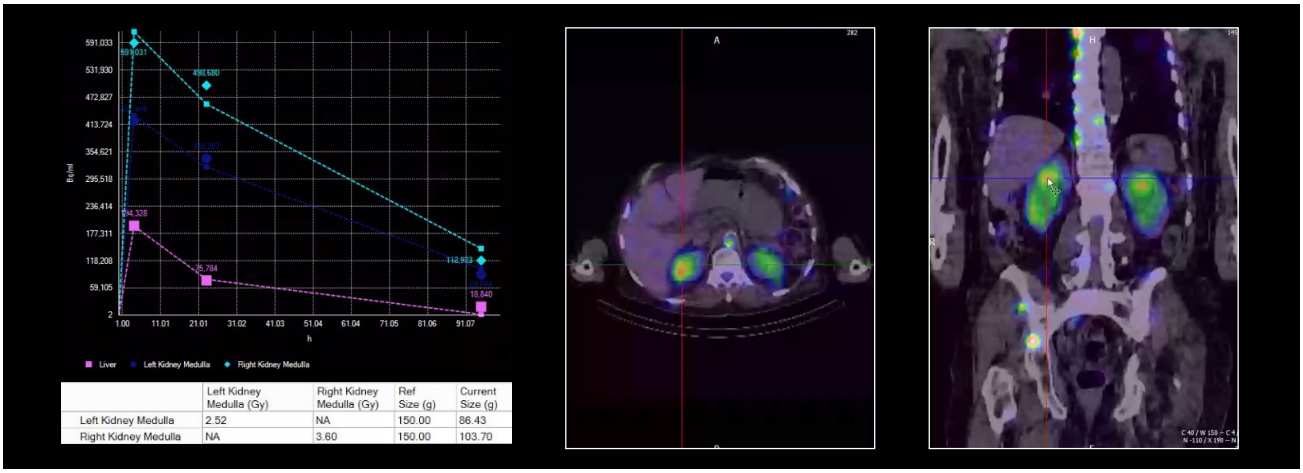
The sequential xSPECT Quant and CT data was fed into Siemens Healthineers' Dosimetry Research Tool (DRT), which enables the automated generation of a volume-of-interest (VOI) that includes the tumor as well as critical organs—such as the kidney, liver, and spleen—SPECT/CT. DRT performs voxel-based dosimetry using absolute tracer concentration values obtained from sequential xSPECT Quant datasets across multiple time points. These time points calculate time-activity curves and tracer residence times within individual voxels as well as within automatically generated VOIs to generate absorbed dose values, dose volume histograms, and absorbed dose maps.

The mean left and right kidney dose (as calculated by the DRT) appears within expected levels. Due to high tracer retention within metastases and the substantial metastatic burden, the circulating tracer available for renal clearance is low and that indicates the potential for low renal cortical dose, also known as a tumor sink effect. This is appropriately reflected in the mean renal dose of 2.52 Gy and 3.6 Gy to the left and right kidneys, respectively.

In view of the low renal dose and the high tracer retention within the metastatic lesions, the delivered tumor dose is expectedly high and multiple therapies would be possible in this patient without undue concern for renal toxicity.

Comments

This study demonstrates 3D dosimetry performed using sequential quantitative SPECT/CT (xSPECT Quant) following therapeutic administration of ^{177}Lu PSMA. In this patient, due to extensive skeletal metastases, the majority of administered tracer is absorbed within PSMA-avid metastases with a low level of circulating ^{177}Lu PSMA available for renal clearance. A low level of renal cortical uptake with fast clearance is reflected on xSPECT Quant data, which shows only 10% of peak renal cortical activity concentration retained after 96 hours. This pattern of low cortical uptake and fast clearance reflects the low overall renal tracer residence time and consequently low levels of renal cortical absorbed dose are expected from dosimetry calculations. This expectation is confirmed by the actual renal cortical dose calculated using



S A time-activity curve of the right and left kidney, derived from research dosimetry software, along with an absorbed dose map with the cursor in the upper right renal cortex, which displays an absorbed dose value of 4.34 Gy. The table of absorbed dose values of the left and right kidney obtained from the DRT shows a mean left renal dose to be 2.52 Gy and a mean right renal dose to be 3.6 Gy.

Data courtesy of Peter MacCallum Cancer Center, Melbourne, Australia.

sequential xSPECT Quant data and DRT, which shows a mean renal dose of 2.52 Gy and 3.6 Gy to the left and right kidneys respectively. The dose map in Figure 5 shows heterogeneity of renal cortical dose with an individual voxel in the right upper renal cortex, which displays an absorbed dose of 4.34 Gy, while the mean right renal cortical dose was 3.6 Gy.

A recent study simulated the effect of an increase in PSMA-avid tumor volume to the tumor and renal dose using the data of 13 patients treated with ^{177}Lu PSMA I&T.[1] According to the simulation, a 10-fold increase in total tumor volume (0.3 L to 3 L) was associated with a reduction of mean renal absorbed dose from 6.5 Gy to 3.7 Gy: a decrease of slightly less than 50%. The conclusion of this study demonstrates that in patients with large PSMA-positive tumor volumes, higher activities can be safely administered to maximize tumor dose without exceeding maximum dose thresholds to critical organs. Dosimetry was performed using sequential planar scintigraphy in the referenced study. In comparison, the present case example utilizes xSPECT Quant with high accuracy of calculated tracer concentration along with dosimetry software, which enables automated segmentation of critical organs. A low level of renal cortical absorbed dose (3.6 Gy to the right kidney) therefore suggests the potential of multiple therapies in order to achieve higher tumor dose without crossing the renal absorbed dose threshold of 23 Gy. Since the patient has normal renal cortical thickness with absence of pelvicalyceal stasis, there is also the possibility of accepting a higher renal cortical dose threshold of 40 Gy, which would enable a significantly higher therapeutic window.

Using sequential quantitative SPECT/CT, based on calibration using a phantom with known concentration of ^{177}Lu to enable conversion of counts to tracer concentration, a study evaluated renal absorbed dose in five patients with metastatic castration-resistant prostate cancer treated with two cycles (approximately 3.6 GBq each cycle) of ^{177}Lu PSMA therapy.[2] A mean renal absorbed dose was 2.2 Gy +/- 0.6 Gy. 3D volumes of the kidney, generated from sequential SPECT/CT images, were used to calculate total tracer concentration and generate time-activity curves for dose estimation using tracer-specific S values. All patients showed overlap of intestinal and liver activity with the kidney on planar images, which was eliminated using SPECT/CT data, therefore the authors categorically recommended utiliizing 3D SPECT/CT-based dosimetry for all ^{177}Lu PSMA studies to avoid this issue with planar scintigraphy. The present case example shows renal dose even lower than the study by Delker et al. with a mean renal cortical dose as low as 0.4 Gy/GBq (right kidney).

Tumor tracer concentration, as shown by xSPECT Quant, was high in the initial study with progressive increase up to 24 hours after injection followed by slow washout with almost 50% of peak tracer concentration retained at 96 hours. This suggests longer tracer residence time within metastatic lesions and consequently higher tumor absorbed dose. Since the present dosimetry study was based on the first therapy, subsequent therapy administrations need to be similarly evaluated using sequential xSPECT Quant studies and dosimetry to determine change in renal and tumor dose with respect to change in overall tumor burden.

Conclusion

Sequential xSPECT Quant studies following therapeutic dose of ^{177}Lu PSMA enables 3D voxel-based dosimetry in a patient with multiple skeletal metastases from prostate cancer, which show normal renal cortical dose with high tumor retention of tracer.

References

1 Begum NJ, Thieme A, Eberhardt N, et al. The effect of total tumor volume on the biologically effective dose to tumor and kidneys for ^{177}Lu-labeled PSMA peptides. *J Nucl Med,* 2018;59:929–933.

2 Delker A, Fendler WP, Kratochwil C, et al. Dosimetry for ^{177}Lu-DKFZ-PSMA-617: a new radiopharmaceutical for the treatment of metastatic prostate cancer. *Eur J Nucl Med Mol Imaging.* 2016;43(1):42-51.

[a] ^{177}Lu PSMA is not currently recognized by the U.S. Food and Drug Administration (FDA) or other regulatory agencies as being safe and effective. Siemens does not make any claims regarding its use.

xSPECT Quant is not commercially available in all countries. Due to regulatory reasons, its future availability cannot be guaranteed. Please contact your local Siemens organization for further details.

The Dosimetry Research Tool is an investigational device. Limited by Federal (or United States) law to investigational use. This device is exclusively for clinical investigations. This investigational device does not fulfill all the essential requirements according to the European Medical Device Directive (93/42/EEC) and its national implementations. It is not commercially available in the European Union, or other countries worldwide.

Examination protocol

Scanner: Symbia Intevo 16

SPECT	
Injected dose	8.7 GBq
Scan acquisition	60 stops at 10 seconds/stop
CT	
Tube voltage	130 kV
Tube current	25 eff mAs
Slice thickness	3 mm

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