Radiation dosimetry for $^{177}$Lu-PSMA-I&T in metastatic castration-resistant prostate cancer: Absorbed dose in normal organs and tumor lesions

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ABSTRACT

Purpose: Prostate-specific membrane antigen (PSMA) targeted radioligand therapy (RLT) is increasingly used in metastatic castration-resistant prostate cancer (mCRPC). We aimed to estimate the absorbed doses for normal organs and tumor lesions using $^{177}$Lu-PSMA-I&T in patients undergoing up to four cycles RLT. Results were compared to pre-therapeutic $^{68}$Ga-PSMA-HBED-CC positron-emission-tomography (PET).

Methods: A total of 34 cycles in 18 patients were analyzed retrospectively. In 15 patients the first, in 9 the second, in 5 the third and in 5 the fourth cycle was analyzed, respectively. Whole-body scintigraphy was performed at least between 30-120 minutes, 24 hours and 6-8 days after administration. Regions of interest (ROIs) covering the whole body, organs and up to 4 tumor lesions were drawn. Organ and tumor masses were derived from pre-therapeutic $^{68}$Ga-PSMA-HBED-CC PET/Computed tomography (CT). Absorbed doses for individual cycles were calculated using OLINDA/EXM. Standardized-uptake-values (SUV) from pre-therapeutic PET were compared to absorbed doses and to change of SUV.

Results: Mean whole body effective dose for all cycles was 0.06±0.03 Sv/GBq. The mean absorbed organ doses were 0.72±0.21 Gy/GBq for the kidneys, 0.12±0.06 Gy/GBq for liver, 0.55±0.14 Gy/GBq for parotid, 0.64±0.40 Gy/GBq for the submandibular and 3.8±1.4 Gy/GBq for lacrimal glands. Absorbed organ doses were relatively constant when among the four different cycles.
cycles. Tumor lesions received a mean absorbed dose per cycle of 3.2±2.6 Gy/GBq (range 0.22-12 Gy/GBq). Doses to tumor lesions gradually decreased with 3.5±2.9 Gy/GBq for the first, 3.3±2.5 Gy/GBq for the second, 2.7±2.3 Gy/GBq for the third and 2.4±2.2 Gy/GBq for the fourth cycle. SUVs of pre-therapeutic PET moderately correlated with absorbed dose (r=0.44, p<0.001 for SUVmax, r=0.43, p<0.001 for SUVmean) and moderately correlated with the change of SUV (ΔSUV; r=0.478, p<0.001 for SUVmax, r=0.50, p<0.001 for SUVmean).

**Conclusions:** Organ and tumor absorbed doses for $^{177}$Lu-PSMA-I&T are comparable to recent reports and complement these with information on an excellent correlation between the four therapy cycles. With the kidneys representing the critical organ, a cumulative activity of 40 GBq $^{177}$Lu-PSMA-I&T appears to be safe and justifiable. The correlation between pre-therapeutic SUV and absorbed tumor dose emphasizes the need for PSMA-ligand PET-imaging for patient selection.

**Running title:** Radiation dosimetry for 177Lu-PSMA I&T
INTRODUCTION

Prostate cancer (PC) is the second most common cancer in men worldwide (1). About 30% of men experience biochemical recurrence often followed by progression to mCRPC. Despite several treatment options for these patients more than 250,000 men are still dying from PC worldwide each year (1). Most recently PSMA is gaining significant interest as a target for imaging as well as radionuclide therapy (2,3). Its expression correlates with the malignancy of the disease, being further increased in mCRPC (4). A variety of PSMA-ligands for RLT have been developed in recent years (for an overview, see (5)). Several studies using $^{131}$I or $^{177}$Lu labelled PSMA-ligands for RLT reported reductions in tumor volume and serum prostate-specific antigen (PSA) levels (3,6–10). For the assessment of a new radiopharmaceutical dosimetry is essential to aim for the optimal therapeutic response with limited side effects. Beside the high and specific uptake of PSMA-ligands in prostate cancer tissue, different normal organs (e.g. kidney, salivary glands, proximal intestine) exhibit tracer accumulation. Recently published studies using the theranostic DOTA-conjugated PSMA-ligand $^{177}$Lu-PSMA-DKFZ-617 reporting both results for post-therapeutic dosimetry (9,11,12) as well as for pre-therapeutic dosimetry (13).

DOTAGA-(I-y)fk(Sub-KuE) termed PSMA-I&T for imaging and therapy is another PSMA-ligand (6). It also allows using $^{68}$Ga and $^{177}$Lu-labelled compounds as “theranostic twins”. Our initial experiences in antitumor effect and side effects in heavily pre-treated patients using this
agent have been published recently (10). Similar results on clinical efficacy were reported by Baum et al. with additionally data on dosimetry (7). In peptide receptor radionuclide therapy (PRRT) for neuroendocrine tumors high tumor uptake in pre-therapeutic PET and high tumor-absorbed dose are regarded to be predictive of the therapeutic success (14). The standardized uptake value (SUV) may serve as indicator for later-achieved absorbed dose (15–17). Presumably also in mCRPC decision for or against RLT may be influenced and eventually potentially based on pre-therapeutic PET.

Thus, the purpose of this study was to estimate the absorbed doses for $^{177}$Lu-PSMA-I&T in normal organs and in tumor lesions in a considerable number of patients with mCRPC undergoing up to four cycles with a reference activity of 7.4 GBq. In addition, we aimed to investigate the relationship of pre-therapeutic SUV of $^{68}$Ga-PSMA HEBD-CC PET and subsequently achieved tumor-absorbed dose and tumor response by PET.

**MATERIALS AND METHODS**

Patients And $^{68}$Ga-PSMA-HEBD-CC PET/CT.

Between January 2015 and March 2016, 18 patients (Table 1) with mCRPC and PSMA-avid lesions on pre-therapeutic PET underwent a total of 34 cycles $^{177}$Lu-PSMA-I&T (n=15 for first, n=9 for second, n=5 for third, n=5 for fourth cycle) using a reference activity of 7.4 GBq.
combined with a dedicated protocol for post-therapy dosimetry. The institutional review board of
the Technische Universität München approved this study and all subjects signed a written informed
consent.

\(^{177}\text{Lu-PSMA-I&T RLT And Post-therapy Scintigraphy.}\)

Mean applied activity for all cycles was 7.3±0.30 GBq (range: 6.47-7.83), 7.3±0.32 GBq
(range: 6.47-7.78) for the first cycle, 7.3±0.34 GBq (range: 6.47-7.73), for the second cycle,
7.5±0.22 GBq (range: 7.30-7.83) for the third cycle, and 7.3±0.24 GBq (range: 6.95-7.60) for the
fourth cycle. Whole-body scintigraphy was performed at least between 30-120 minutes, 24 hours
and 6-8 days after administration of \(^{177}\text{Lu-PSMA I&T}.\) In some cycles (n=8) patients also
underwent whole-body scintigraphy 48 and 72 hour after the tracer injection (p.i.). In detail, 26
cycles were analyzed with 3, 2 cycles with 4 and 6 cycles with 5 post-therapy scintigraphies,
respectively. Details on the synthesis, application and post-therapy scintigraphy of \(^{177}\text{Lu-PSMA-}
\text{I&T is given in supplemental “Material and Methods”}.\)

Image Analysis.

Individual patient absorbed doses for whole body, kidneys, liver, parotid, submandibular
glands and lacrimal glands were estimated based on the Medical Internal Radiation Dose scheme
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and as recommended in the European Association of Nuclear Medicine Dosimetry Committee Guidelines (18,19). Regions of interest (ROIs) on whole body, kidneys, liver, parotid glands, submandibular glands and lacrimal glands and up to 4 tumor lesions were delineated manually on the anterior and posterior whole-body images at 24 hours p.i. by two experienced nuclear medicine physicians and then manually relocated on the previous and subsequent scans (Figure 1). The volume of normal organs and tumor lesions were calculated using the CT-dataset of the corresponding pre-therapeutic $^{68}$Ga-PSMA-HBED-CC PET/CT. A total of 93 representative lesions were analyzed (74 bone, 8 lymph node, 8 liver, 3 lung metastases; the assignment to the different cycles is shown in Table 2). Details on the ROIs for scintigraphy as well as volume calculation in CT is given in supplemental “Material and Methods”.

Statistical Analysis.

All continuous data reported are expressed as mean, standard deviation and range. Two-sample t tests were used to evaluate differences between individual groups. Correlations between SUVs, change of SUV between pre- and post-therapeutic PET ($\Delta$SUV) and absorbed dose in tumor lesions were assessed using Spearman’s rank correlation coefficient. A significance level of $\alpha=5\%$ was used. Statistical analyses were conducted using MedCalc (version 13.2.0, 2014; MedCalc, Ostend, Belgium).
RESULTS

Qualitative $^{177}$Lu-PSMA-I&T Distribution On Post-therapeutic Scintigraphy.

Physiological uptake was seen in lacrimal, parotid and submandibular glands, kidneys, small intestine and less pronounced in liver and spleen. Uptake in excess of background was also seen for multiple tumor lesions with progressive accumulation up to 24-48 h after injection (Figure 1). Delayed whole-body images (up to 6-8 days post-therapy) exhibited long-term retention of $^{177}$Lu-PSMA-I&T in the metastases with nearly no residual uptake in normal organs.

Dosimetry For Normal Organs.

The mean whole body effective dose for all cycles was 0.41± 0.18 Sv (0.06 Sv/GBq). Mean absorbed organ doses were 5.3±1.6 Gy (0.72 Gy/GBq) for the kidneys, 0.89±0.42 Gy (0.12 Gy/GBq) for the liver, 4.0±1.1 Gy (0.55 Gy/GBq) for parotid glands, 4.8±2.8 Gy (0.64 Gy/GBq) for submandibular glands, 27±10 Gy (3.8 Gy/GBq) for lacrimal glands. The values (mean, standard deviation and ranges) for the corresponding absorbed doses per GBq are presented in Table 1. No substantial difference for absorbed doses of normal organs were observed when comparing them with respect to cycle number (Table 1 and Figure 2). The mean organ masses underlying these absorbed dose estimates were liver 1595±307g (range 1165-2373), kidneys
153±29.9g (range: 88.4–218.7), parotid gland 19.1±5.7g (range: 8.0–35.6), submandibular gland 8.2±1.9g (range: 4.2–14.3), lacrimal gland 0.45±0.12g (range: 0.25–0.78). For paired organs masses from both sides were summed.

Dosimetry For Tumor Lesions.

In total, all lesions received a mean dose per cycle of 23±20 Gy (3.3 Gy/GBq). Mean absorbed dose for bone, lymph node, liver, and lung metastases were 26±20 Gy (3.4 Gy/GBq), 24±16 Gy (3.2 Gy/GBq), 8.5±4.7 Gy (1.28 Gy/GBq), and 13±7.4 Gy (1.7 Gy/GBq). The values (mean, standard deviation and range) for the corresponding absorbed doses per GBq are presented in Table 2. Figure 2 shows the mean absorbed dose in all tumor lesions with respect to the specific therapy cycle. Figure 3 shows a representative example of a patient with a histologically proven lung metastasis and multiple bone metastases. There is a clear trend towards a lower absorbed dose with an increasing number of the cycle. Mean absorbed dose per lesion was 26±21 Gy (3.5 Gy/GBq) for the first, 24±19 Gy (3.3 Gy/GBq) for the second, 20±18 Gy (2.7 Gy/GBq) for the third and 18±17 Gy (2.4 Gy/GBq) for the fourth cycle. A similar trend can be seen for the subgroup of bone metastases. No reliable comparison is possible for lymph node, liver and lung metastases due to a low sample number.
Correlation Of SUV And Absorbed Doses In Tumor Lesions.

The mean SUVmax and mean SUVmean of all lesions in pre-therapeutic PET were 22±14 (range: 3.5-64.8) and 15±10 (range: 2.4-46.8), respectively (supplementary Table 2). Mean change in SUV (ΔSUV) was 4.8±8.2 (range: -7.2-34.8) for SUVmax and 3.3±5.7 (range -4.8-24.1) for SUVmean. SUVmax and SUVmean moderately correlated with absorbed dose for all lesions (r=0.442, p<0.001 and r=0.433, p<0.001, respectively; supplementary Table 2, supplementary Figure 1). Change of SUVmax and SUVmean (ΔSUV) for all lesions showed a moderate and highly statistical significantly correlation to the pretherapeutic SUV (r=0.468, p<0.001 for SUVmax, r=0.498, p<0.001 for SUVmean, supplementary table 3). No correlation could be found between the change of SUVmax and SUVmean (ΔSUV) for all lesions and the absorbed dose (r=0.163, p=0.129 for SUVmax, r=0.153, p=0.154 for SUVmean, supplementary table 4). Details for both correlation on the subgroups of bone and soft-tissue lesions are shown in supplementary tables 2, 3 and 4.

DISCUSSION

We present data for radiation dosimetry for normal organs and tumor lesions using $^{177}$Lu-PSMA-I&T RLT in 18 patients and a total of 34 cycles. Our results for normal organs are comparable to a recent clinical work on the safety and efficacy on $^{177}$Lu-PSMA-I&T including
results on dosimetry (7) and data reported for $^{177}$Lu-PSMA-DKFZ-617 (9,11,12). The kidneys are one of the critical organs with a mean absorbed dose of 0.72 Gy/GBq as well as glandular tissue with high PSMA-ligand uptake (lacrimal: 3.8 Gy/GBq, parotid: 0.55 Gy/GBq and submandibular gland: 0.64 Gy/GBq). The long-term retention in tumor lesions resulted in a high mean absorbed tumor dose of 3.2 Gy/GBq with a maximum of 12 Gy/GBq. In addition, high pre-therapeutic SUV of a tumor lesion on PET may serve as rough indicator for a high absorbed dose emphasizing the importance of pre-therapeutic PSMA-PET imaging for patient selection.

Data on the dosimetry are essential during the evaluation of new radiopharmaceuticals for radionuclide therapy to assess the risk of potential toxicity and response probability. There are common radiation tolerance limits as guiding values derived from external beam radiation therapy. Thus, to some extent dose escalation studies can be omitted and dosing of new radiopharmaceuticals can be based on dosimetry. Qualitative judgement of the distribution of $^{177}$Lu-PSMA-I&T showed physiological tracer uptake in the abdominal organs, especially the kidneys as well as the lacrimal and salivery glands (20). Besides the high number of patients and total number of cycles included a further strength of this study is the availability of a late (6-8 days p.i.) time-point for post-therapeutic scintigraphy. Baum et al also included late scintigraphy for their $^{177}$Lu-PSMA-I&T dosimetry, however only up to five days post injection (7). For $^{177}$Lu-

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PSMA-DKFZ-617 it has been shown that (mainly) over-estimation of doses is present when omitting the late time point (mean 9.8% for whole body, 22.0% for kidney, 19.4% for salivary glands, 10.6% lacrimal glands) (12).

In several radio-receptor therapies the kidney is regarded as the dose limiting organ (21). Our results for kidneys (mean 0.72 Gy/GBq) are well comparable to a recent publication using the same radiopharmaceutical (kidney: median 0.8 Gy/GBq) (7). For $^{177}$Lu-PSMA-DKFZ-617 three recent reports state mean absorbed doses between 0.53 and 0.75 Gy/GBq for kidneys (9,11,12). These values are relatively comparable to that for the treatment of neuroendocrine tumors (for $^{177}$Lu-DOTATATE e.g. 0.6 Gy/GBq in (22)).

Whole body absorbed dose determined in our study (mean 0.06 Sv/GBq, median 0.03 Sv/Gy)) was slightly different to findings by Baum et al. (7) (median 0.02 Gy/GBq) with only a higher maximum range. This is potentially based on a higher overall tumor burden in our patient cohort (median PSA 354.5 ng/ml) as compared to Baum et al. (median PSA 43.2 ng/ml). As 15 of 18 patients in our study demonstrated with extensive bone involvement, red marrow cross-doses might have been high. However therapy induced myelosupression was not noted on clinical follow-up.

Other organs at risk are salivary and lacrimal glands. For parotid and submandibular
glands the organ doses (mean 0.55 and 0.64 Gy/GBq) derived from our study are lower than in the recent report for $^{177}$Lu-PSMA-I&T (median 1.3 Gy/GBq) (7) and to the published data for $^{177}$Lu-PSMA-DKFZ-617 (mean 0.72-1.4 Gy/GBq) (9,11,12). The main reason is most likely variations of the volumes used for dose estimation. For salivary glands e.g. Hohberg et al. (12) used 85g based on International Commission on Radiological-Protection 23 data while Delker et al. (11) used 38g based in individual organ masses. Due to the high intra-individual size variation, we also aimed to use individual values based on CT-images with a mean volume for both sides of 54g. In addition, further variation is possible due to different tracer distribution, different time-points of post-therapy scintigraphy and different overall tumor burden. Finally the effect of cooling of salivary glands and post-therapeutic stimulation of saliva production is still unclear. Currently data are too sparse to estimate the potential benefit of the latter.

For the lacrimal glands potential discrepancies are even more pronounced when performing dosimetry due to their small size on the lacrimal glands. So far only Hohberg et al. evaluated the organ dose for lacrimal glands using $^{177}$Lu-PSMA-DKFZ-617 with a mean of 2.8 Gy/GBq. Our calculations resulted in a mean organ dose of 3.8 Gy/GBq. However, we most likely underestimated the size of the lacrimal glands (mean of 0.8g) in CT compared to Hohberg et al. using a mass assumption of 1.4g based on MR-data (12). With a mean underestimation of volumes in our calculation (~42%) both results are quite comparable. However, despite the relatively high
absorbed doses for salivary and lacrimal glands in clinical practice they do not represent critical organs at risk. In our experience despite the application of up to 30 GBq $^{177}$Lu-PSMA-I&T so far only sporadic cases of reversible xerostomia and no considerable complaints on dry eyes were noted ($^{10}$). E.g. Hey et al. using external beam radiation therapy reported that a dose to the parotid glands below 26 Gy allows complete recovery of pre-therapeutic salivary flow rates ($^{23}$).

The absorbed doses (esp. for the critical organs) showed an excellent correlation between the four therapy cycles. Delker et al. reported an overall Persons´s rho of 0.97 when comparing the first and second cycle in 5 patients using $^{177}$Lu-PSMA-DKFZ-617 ($^{11}$). Similar results have been found for PRRT using up to 5 cycles ($^{24}$). This might allow the prediction of the absorbed dose of the following therapy cycle with sufficient accuracy and the possibility of potential adaptation of the activity for the next cycle.

Our results for absorbed dose on tumor lesions (mean 3.2 Gy/GBq) are comparable with data by Delker et al. ($^{11}$) and Kratochwil et al. ($^{9}$) for $^{177}$Lu-PSMA-DKFZ-617 and with Baum et al. ($^{7}$) for $^{177}$Lu-PSMA I&T. In addition, we also analyzed and observed that the absorbed dose on the tumor is decreasing with the cycle number (Figure 2, Table 2). In PRRT this has also been reported for the use of $^{177}$Lu-Ocreotate ($^{25}$). Compared to leukemia, most lymphomas and germ cell tumors epithelial tumors like neuroendocrine tumors and PC are only moderately radiosensitive and require a significantly higher dose of radiation. The reason for a decreasing
absorbed dose remains unclear. Potential explanation could be prior therapy effect with reduced target expression (in later cycles predominantly patients were included with reasonable prior response). An indirect sign for this is the considerable drop of the PSA-value in these patients indicating therapy response with potential decreased presence of the target in the next cycle.

The highly significant and moderate correlation between pre-therapeutic SUV and absorbed dose of $^{177}$Lu-PSMA-I&T (SUVmax: $\kappa=0.44$, SUVmean: $\kappa=0.43$) stresses the importance of pre-therapeutic PET-imaging. Similar results are known for PRRT (17). Our initial data are a preliminary basis for estimating therapeutic efficacy (or feasibility) of PSMA-RLT. The highly significant moderate correlation between pre-therapeutic SUV and change of SUV ($\Delta$SUV) fits into the concept that with a higher target expression a higher molecular response can be expected. Nevertheless, the missing correlation between absorbed dose and change of SUV ($\Delta$SUV) indicates that besides target expression other factors of tumor biology are present for determination of therapy response. In addition, it has to be taken into account that more sophisticated approaches exist which can be used to predict the therapeutic biodistribution. E.g. Hardiansyah et al. recently presented a so-called physiologically based pharmacokinetic model which aims for individualization of treatment planned and integrates a variety of patient specific data (e.g., weight, tumor volume, and glomerular filtration rate) (26).

With the kidneys being the relevant critical organ our data indicate that in average a
cumulative activity of 40 GBq $^{177}$Lu-PSMA-I&T is safe when taken 28 Gy (50% probability of developing severe late kidney damage within 5 years) as dose limit (27). With respect to the average life expectancy of mCRPC patients this approach seems to be justifiable. This would allow at least five cycles using 7.4 GBq $^{177}$Lu-PSMA-I&T (standard activity at our institution) achieving relevant absorbed doses on tumor lesions and offering the possibility of several cycles for midterm tumor control. These findings are in line with data presented by Kabaskal et al. using pre-therapeutic dosimetry for $^{177}$Lu-PSMA-DKFZ-617 and who calculated a maximum activity of 30 GBq to achieve 23 Gy kidney dose (13). Nevertheless these absorbed dose limits are based on the conventionally fractionated external beam therapy and cannot necessarily be directly applied to low dose-rate radiation (28). Patients without risk factors for kidney disease might tolerate a renal biological equivalent dose up to 40 Gy, based on experience in NET (29).

There are several limitations of our study. First, the different peptides used for PET on one hand (PSMA-HBED-CC) and therapy on the other (PSMA I&T) is noteworthy. Second, one principal bias of dosimetry studies is the selection of tumor lesions that show better delineation from the surrounding healthy tissue and thus a relatively high absorbed dose. Numerous factors can impair the accuracy of PET and planar dosimetry and can lead to decreased correlation of the two modalities. Overlay in planar scintigraphy can lead to an overestimation of dose (11,20).
with physiological uptake and tumor uptake. Potential additional errors can occur both for volumetric assessment and measurement of SUV for the tumor lesions. We tried to minimize this error, by adjusting a volume-of-interest using information from PET best to the anatomical configuration of the lesions. However, especially for bone lesions, the anatomical delineation can be difficult. On the other hand SUVmax (as compared to SUVmean) is a highly reproducible metric with small expected error for quantification is in the range of up to 10% \((30,31)\). Third, we have not applied any sophisticated model in this study to aim for individual treatment planning. Fourth, it has to be stressed that the data comparing absorbed doses in different treatment cycles are not only based on the same patients.

#### Conclusion

Organ and tumor absorbed doses for \(^{177}\text{Lu-PSMA-I&T}\) for RLT are comparable to recent reports using the same ligand as well as \(^{177}\text{Lu-PSMA-DKFZ-617}\). The kidneys represent the critical organ with a mean absorbed dose of 0.72 Gy/GBq. Kidney absorbed dose is relatively similar across different studies and is constant across several cycles in the same patient. Using established dose limits from radiation oncology up to 40 GBq \(^{177}\text{Lu-PSMA-I&T}\) appear feasible with limited risk of radiation induced side-effects on normal organs given the average life
expectancy for mCRPC patients. The preliminary correlation between pre-therapeutic SUV and absorbed tumor dose emphasizes the need for initial PSMA-ligand PET-imaging for appropriate patient selection. Nevertheless, more data needs to be collected from larger series to confirm and validate these initial findings.
References


Figure Legends

Figure. 1: $^{177}$Lu-PSMA-I&T whole body scintigraphy images obtained at 2 h, 20 h, 43 h, 69 h and 165 h after administration. ROIs were drawn on the liver, kidneys, parotid glands, submandibular glands, lacrimal glands, and lesions in the right humerus, the thoracic vertebrae and the right femur.
Figure. 2: Absorbed doses for normal organs and tumors at respective cycle.
Figure. 3: A 64-yar old patient with metastasis in lung (Black arrow) and bone (White arrows).

A: Absorbed dose for lung metastasis for 1st, 2nd and 3rd cycle were 20.9 Gy, 9.7 Gy and 6.9 Gy, respectively. B. SUVmax and SUVmean on pre-therapeutic PET at each cycle were 21.2, 9.9 and 3.7, and 13.8, 6.6 and 2.5 respectively.
Table 1. Effective dose for whole body in Sv/GBq and absorbed doses for normal organs in Gy/GBq.

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#: Absorbed doses for paired organs is presented as an average between right and left side
*median value: 0.03 Sv/GBq (for comparison with Baum et al.)
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<td>0.22-12.03</td>
<td>1.63-3.76</td>
<td>0.85-2.59</td>
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<tr>
<td>2nd cycle</td>
<td>n</td>
<td>26</td>
<td>3.3±2.5</td>
<td>21</td>
<td>3.4±2.4</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>0.70-8.46</td>
<td>1.03-9.59</td>
<td>1.98-8.46</td>
<td>0.70-1.17</td>
</tr>
<tr>
<td>3rd cycle</td>
<td>n</td>
<td>14</td>
<td>2.7±2.3</td>
<td>10</td>
<td>3.2±2.5</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>0.94-7.99</td>
<td>1.11-7.99</td>
<td>18.87</td>
<td>0.47-1.42</td>
</tr>
<tr>
<td>4th cycle</td>
<td>n</td>
<td>12</td>
<td>2.4±2.2</td>
<td>10</td>
<td>2.7±2.3</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>0.74-7.60</td>
<td>1.04-7.60</td>
<td></td>
<td>0.74-1.51</td>
</tr>
</tbody>
</table>
Radiation dosimetry for $^{177}$Lu-PSMA-I\&T in metastatic castration-resistant prostate cancer: Absorbed dose in normal organs and tumor lesions


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