MATERIALS AND METHODS

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

PSMA I&T and its lutetium complexes were synthesized according to a previously published protocol (1). 7.4 GBq 177Lu-PSMA-I&T was synthesized using a constant amount of 190 ± 10 µg precursor. ^{177}Lu-PSMA-I&T was administered in compliance with The German Medicinal Products Act, AMG §13 2b, and in accordance with the responsible regulatory body (Government of Oberbayern). 30–60 min before administration of ^{177}Lu-PSMA-I&T a 5-HT3 antagonist (granisetron), corticosteroid (dexamethasone) and amino-acid infusion (2.5%Arginin/Lysine) was started based on the recommendations for PRRT (2). Decrease in renal absorbed dose by amino acid infusion before ^{177}Lu-PSMA-I&T therapy has not been proven yet. Salivary glands were cooled and saliva production was stimulated by candies. 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. Directly after the application of ^{177}Lu-PSMA-I&T and before each whole-body scintigraphy a measurement with a probe counter (ISOMED 2101, MED, Nuklear-Medizintechnik Dresden, Dresden, Germany) was performed. These measurements were used to determine the remaining amount of activity in the body at each time point. Whole-body scintigraphy was performed at least between 30-120 minutes, 24 hours and 6-8 days after administration of ^{177}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. Each scan was obtained at a speed of 12cm/min on a dual-headed SYMBIA T6 (Siemens Medical Solutions, Erlangen, Germany) equipped with 9.5mm NaI(Tl) crystals and medium-energy low-penetration collimators. A 20% and a 12% energy window were placed around the 208 keV and 113 keV peak of ^{177}Lu, respectively. The

image matrix contained 1024×256 pixels, with pixel size of 2.4×2.4mm^2.

Image Analysis.

For tumor dosimetry only lesions showing no overlap with high physiological uptake or other lesions positive on scintigraphy were chosen. Background ROIs were drawn outside the body. An extracorporeal background ROI was drawn and its content was scaled according to the size of the individual organ or lesion ROI and subtracted. For estimation of the background activity from soft tissue, a ROI on the thigh was used. The content of this (tissue) background ROI was appropriately scaled and subtracted from the counts in the kidney ROI only. It was not necessary to use it for the liver due to its size and the fact that there is no accumulating tissue in front or behind it. Neither was the ROI subtracted from the different glands since there is only minimal uptake in overlapping tissue. Calibration factors were calculated based on the whole-body ROI in the first scan and the measurements performed with the probe counter in order to normalize the number of counts to the administered activity. If the uptake in the normal organs overlapped with physiological uptake in healthy tissue or lesions, this uptake was included in the ROI. For the kidneys, the first whole-body scan, with no visible uptake in the intestine, was used to correct the following scans showing overlap of uptake in the intestine. The self-attenuation correction was neglected, because it had no relevant influence on the tumor, kidneys and glands due to their size. The liver turned out to be no organ at risk and therefore self-attenuation was not considered. There was no scatter correction used. Count rates for each ROI were extracted using the open-source DICOM software OsiriX (version 5.1, 64-bit, Pixmeo, Geneva, Switzerland) and the geometric mean for each ROI was calculated. 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. The same tumor lesions were chosen as analyzed in post-therapeutic whole-body scintigraphy. Finally, organ and tumor doses for each cycle were calculated using OLINDA/EXM (2), the time-integrated activity coefficients were calculated

using the EXM module using a mono- or bi-exponential function. By visual inspection and depending on the individual data set the time-activity-curves were fitted with a mono- or bi-exponential function. Therefore it was necessary to deviate from the European Association of Nuclear Medicine guidelines due to the limited number of data points that could be acquired. In all cases, data measured at least 6 days after injection were included in the fitting procedure, ensuring an adequate description of the exponential tail of the time-activity curve. The absorbed doses for tumor lesions and salivary glands were calculated using the density sphere model.

For tumor lesions SUVmax and SUVmean with 50% of maximum isocontour were calculated in corresponding pre- and post-therapeutic PET-datasets using a dedicated workstation (Syngo MMWP, Siemens Healthcare, Erlangen, Germany). To estimate the volume of a lesion a volume-of-interest with a 20-50% of SUVmax isocontour adjusting the volume-of-interest optimal to the anatomical configuration of the lesion was drawn. 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).

References:

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