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## Kidney dosimetry

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Targeted radionuclide therapies with small molecules, like peptides, labeled with beta-emitting radionuclides have been reported to be potentially radiotoxic to the kidneys<sup>1</sup>. Quick clearance of these compounds through the urinary tract creates a higher radiation dose to the kidneys. Radiation dosimetry is capable of predicting the probability of renal impairment. The injected activity can be tailored for a safe kidney dose in each individual patient.

**Patient-averaged dose:** The MIRD schema dosimetry was originally designed for use with diagnostic radio-pharmaceuticals at a dose level (< 1 Gy) without any risk for kidney impairment. The geometry of the MIRD-schema kidney is an ellipsoid with a homogenous activity distribution. The only patient-specificity in this approach is introduced by the kidney kinetics, measured with planar imaging or quantitative SPECT imaging of the kidneys at several time points throughout the kidney clearance transit time<sup>2</sup>. A little more patient-specificity can be achieved by adjusting the MIRD kidney volume for gender and age. Usually patient-averaged MIRD kidney doses are used, as no clear relationship between dose and renal toxicity is found with this method.

**Non-uniform kidney dose:** For therapeutic radionuclides more sophisticated dose models are needed that correct for inhomogeneous activity distributions. A multi-region kidney model was introduced in MIRD pamphlet 19 which allows sub-organ dosimetry for cortex, medullae and pelvis inside the MIRD kidney geometry<sup>3</sup>. The standard man/woman and children's renal MIRD-19 dose factors for each kidney segment can be corrected for its actual volume derived from CT-imaging<sup>4</sup>. The heterogeneity of dose distributions can be visualized by dose volume histograms, when the renal kinetics is studied voxel-wise instead of per kidney or segment ROI.

**Dose-effect models for renal radiation toxicity:** Radiobiological models describing the dose-effect relationship for radiation induced kidney damage are based on external beam experience. The linear quadratic model is needed to compare the dose given with radionuclide therapy to the reference conditions of fractionated beam radiotherapy. For the long-ranged beta-emitter <sup>90</sup>Y there is now evidence that renal damage by <sup>90</sup>Y-DOTA-octreotide follows the radiotherapy standards, when corrected for the exponential dose rate and fractionation by the LQ model<sup>4,5</sup>. Shorter ranged radiation by low energy beta emitters, as <sup>177</sup>Lu, or Auger emitters, like <sup>111</sup>In shows a dose distribution very unfamiliar to radiotherapy-based radiobiology. Interpretation of the dose volume histograms for these nuclides is still cumbersome. Autoradiographs of excised kidneys show a heterogeneity in the renal uptake of peptides below the resolution of SPECT and PET. Uptake in the cortex by tubular cells along this microscopic pattern creates a homogenous dose distribution in the cortex with <sup>90</sup>Y, but very local dose deposition by <sup>177</sup>Lu and <sup>111</sup>In<sup>6</sup>. This can explain the lower incidence of renal impairment seen with these nuclides in comparison to <sup>90</sup>Y at comparable doses.

**Conclusion:** Patient-tailored dosimetry for kidney dose in peptide receptor radionuclide therapy is becoming feasible; both dose as toxicity threshold models are identified, but the whole procedure is very resource demanding, comparable to radiotherapy treatment planning.

### References

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