

# Kidney dosimetry for $^{177}\text{Lu}$ -DOTA-octreotate

## Mark Konijnenberg

Radiology & Nuclear Medicine dept.

- Erasmus MC, Rotterdam
- Radboud UMC, Nijmegen

The Netherlands

[m.konijnenberg@erasmusmc.nl](mailto:m.konijnenberg@erasmusmc.nl)

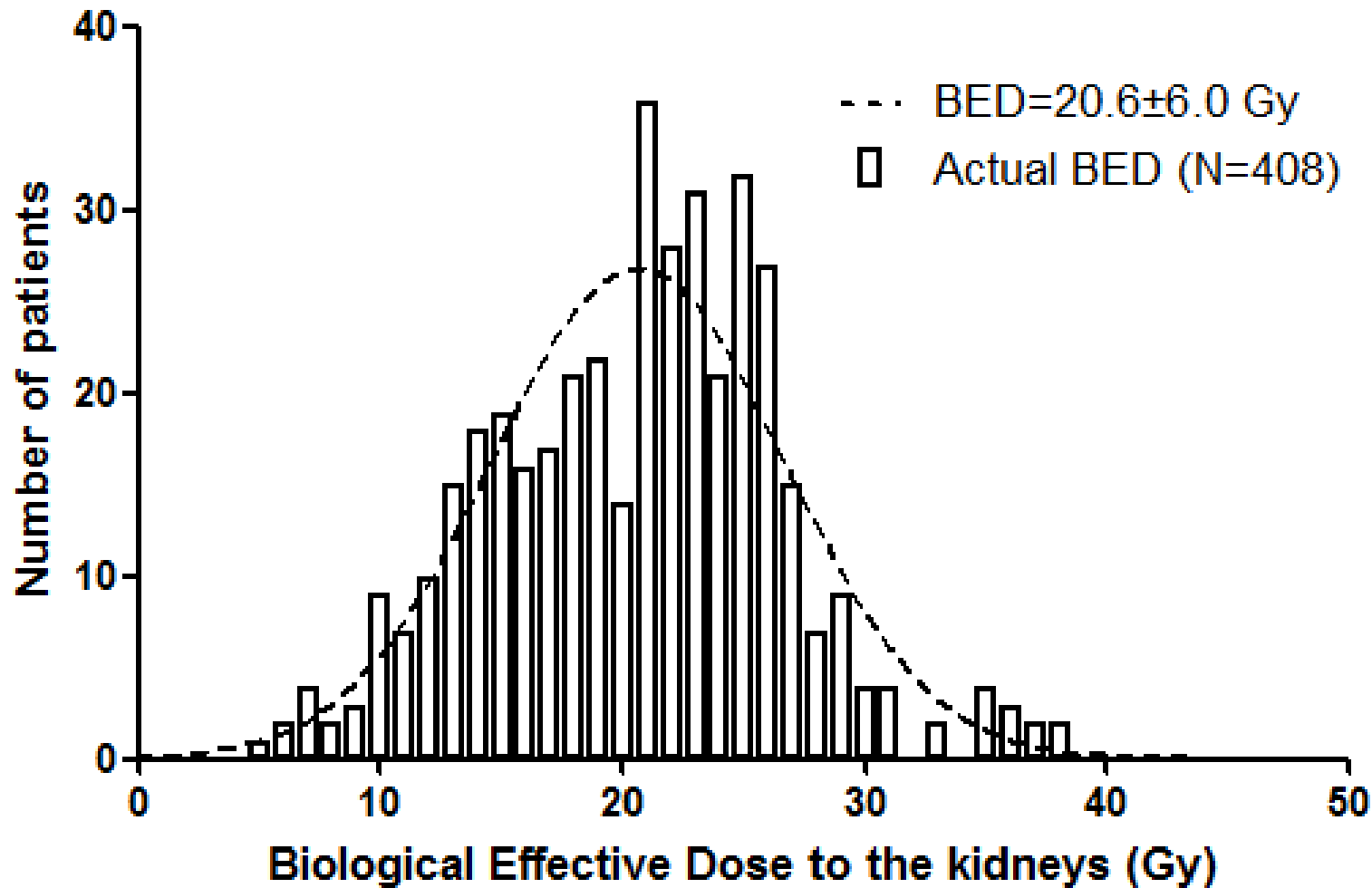
Workshop on Radiopharmaceutical  
Therapy (RPT) Normal Tissue Effects in  
the Clinic (TEC) RPT-TEC-2022

SEPTEMBER 24 - 29, 2022

**Erasmus MC**  
University Medical Center Rotterdam



# BED kidneys 4 x 7.4 GBq <sup>177</sup>Lu-DOTA-octreotate

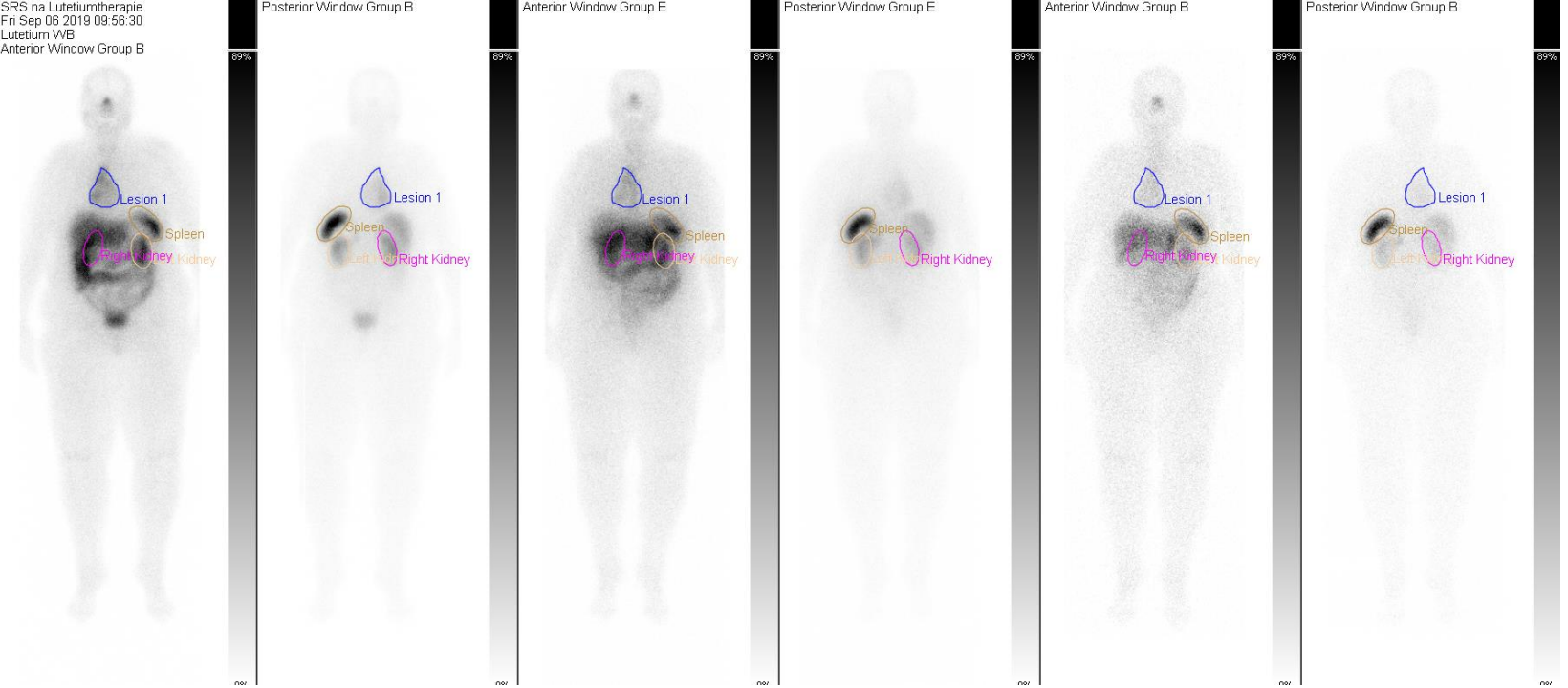
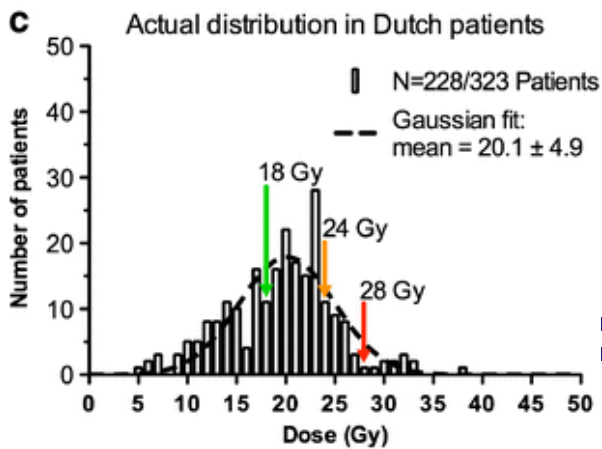
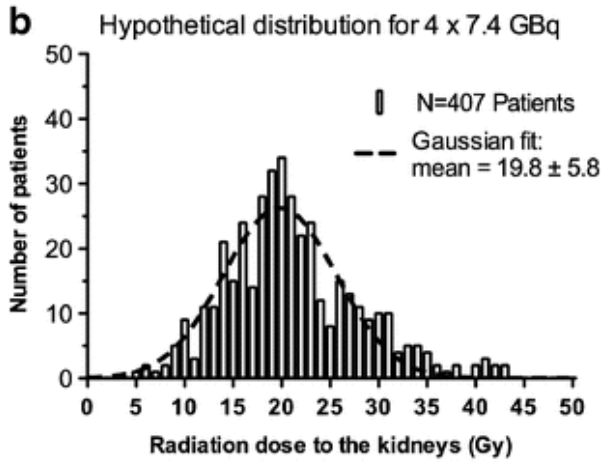
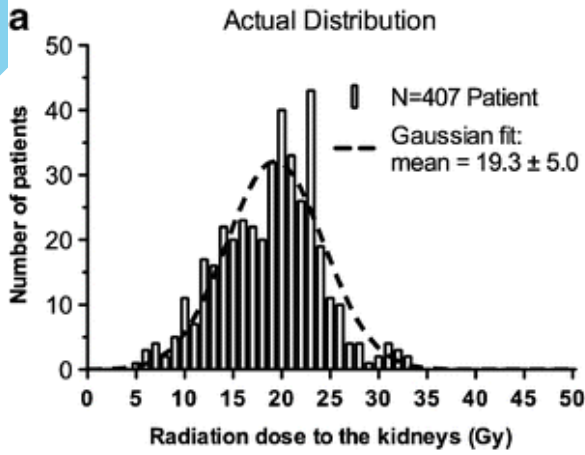


- 615 patients included from 2000 – 2007
  - 408 kidney dosimetry
- Kidney protection by mixed AA infusion
- Mean BED
  - $21 \pm 6$  Gy (5 – 38)
- Mean effective half-life
  - $T_{\text{eff}} = 61 \pm 12$  h

H Bergsma et al.  
Eur J Nucl Med Mol Imaging.  
2016;43:1802-11.

# Radiation dose to the kidneys

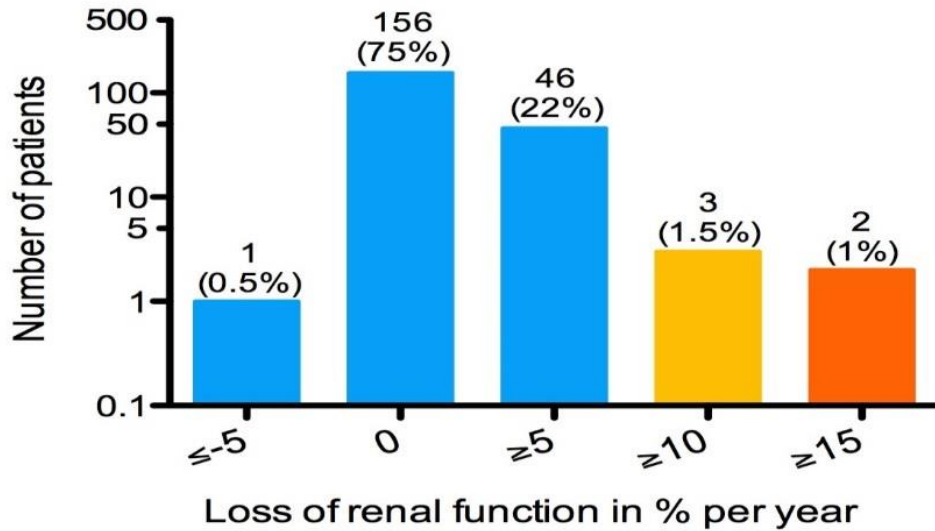
SRS na Lutetiumtherapie  
 Fri Sep 06 2019 09:56:30  
 Lutetium WB  
 Anterior Window Group B



- 615 patients included from 2000 – 2007
  - 554 patients on-protocol
  - 407 kidney dosimetry (74%)
  - Maximum 23 Gy (408 patients) or 4 x 7.4 GBq (146)
  - 323 Dutch patients with
- Dosimetry based on planar imaging at 24, 72-96 and 168 h
  - Fixed kidney mass (female 275 g / male 310 g)
  - Ratio reality/phantom: 0.95 (range 0.49 – 1.71)

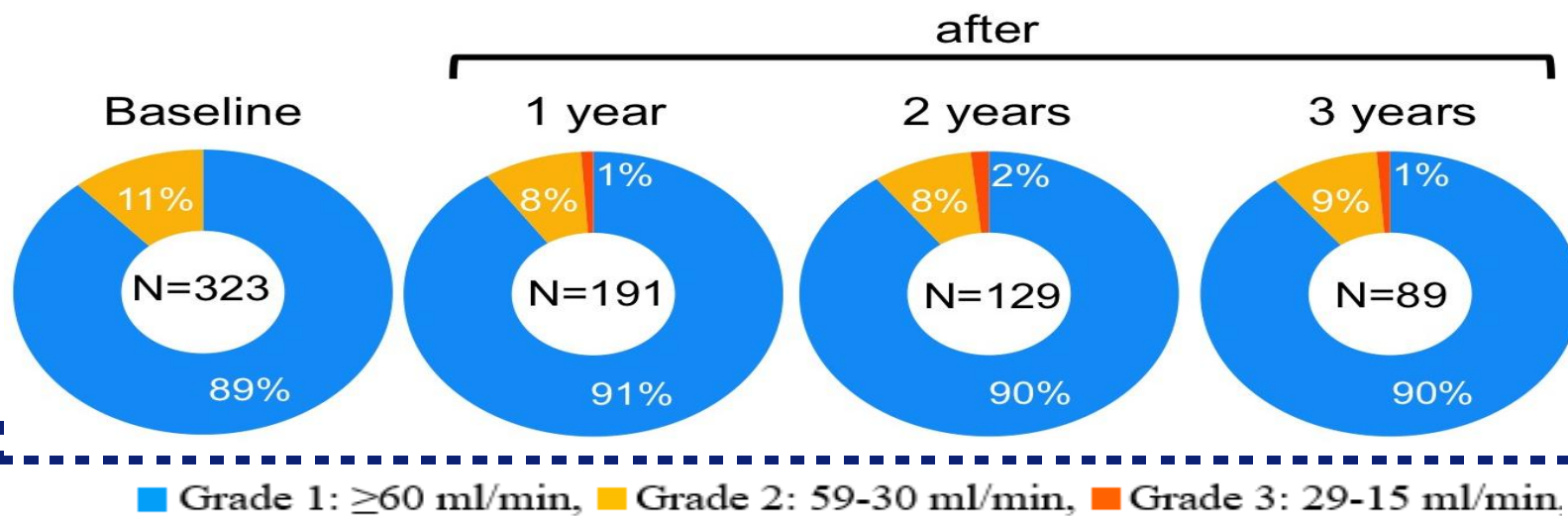
# Nephrotoxicity observed at Erasmus MC after 4 x 7.4 GBq <sup>177</sup>Lu-DOTA-Octreotate ... no tox, no evidence

Annual loss of renal function in 208 patients



Reason lost to follow-up

Reason lost to follow-up	After 1 year	After 2 years	After 3 years
Progressive disease	43	47	56
Death	8	9	12
Follow-up elsewhere (patient request)	18	23	32
Complications (e.g. bleeding, infection, ileus, dyspnoea)	11	13	19
Bone marrow suppression	4	7	9
Liver failure	2	2	2
Other therapy	23	28	40
Octreoscan-negative lesions during follow-up	2	2	3
Retreatment with <sup>177</sup> Lu-DOTATATE	3	37	51
Kidney failure (see text)	0	0	1
Total number of patients	114	168	225



## Erasmus MC

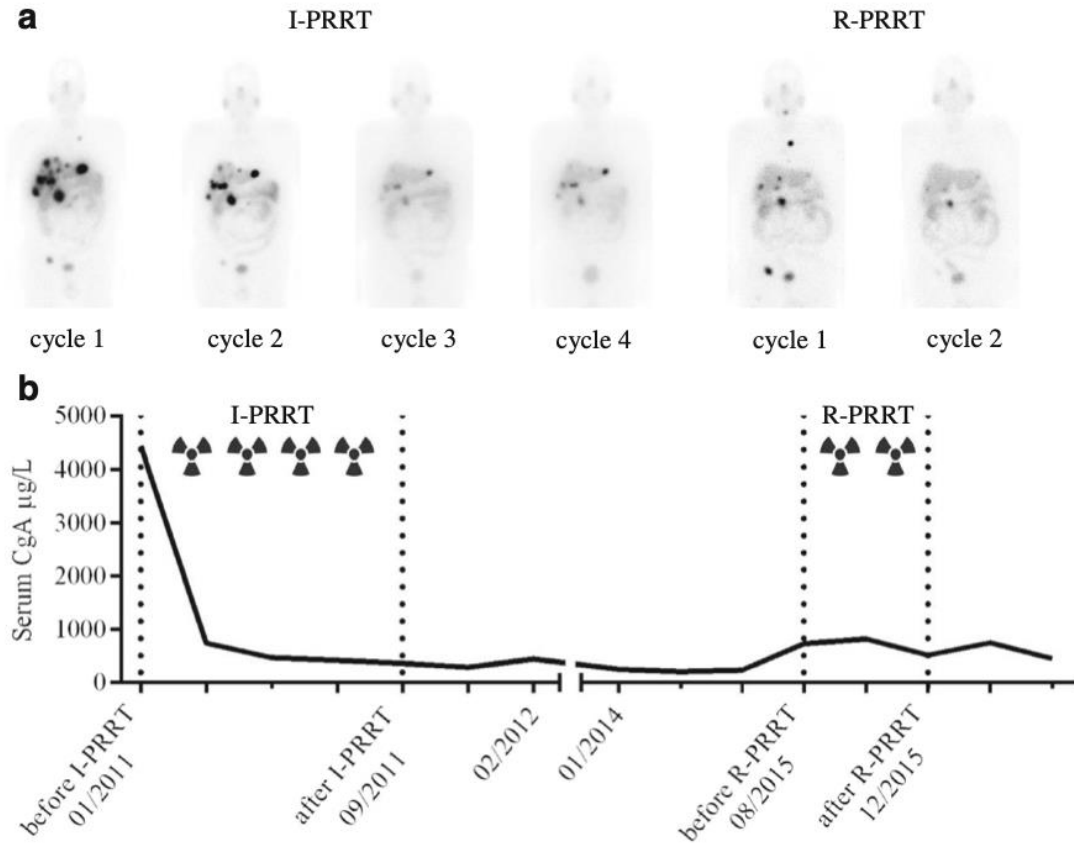
- 323 patients
- 228 dose < 23 Gy
- 191 ≥ 1 y f.u.

H Bergsma et al., Eur J Nucl Med Mol Imaging (2016) 43:1802–1811

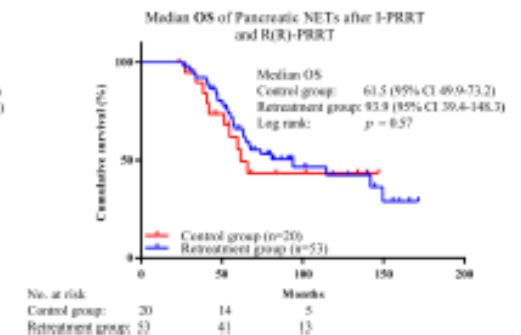
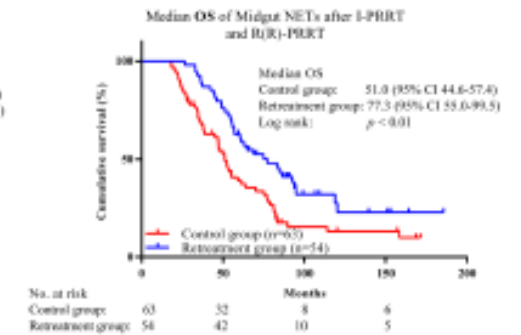
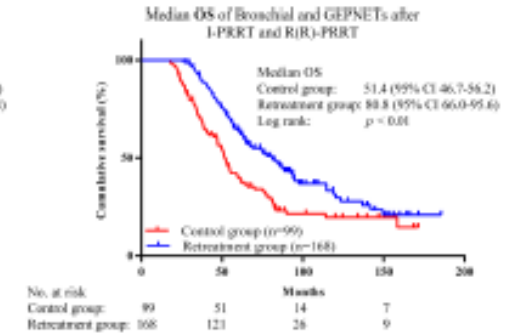
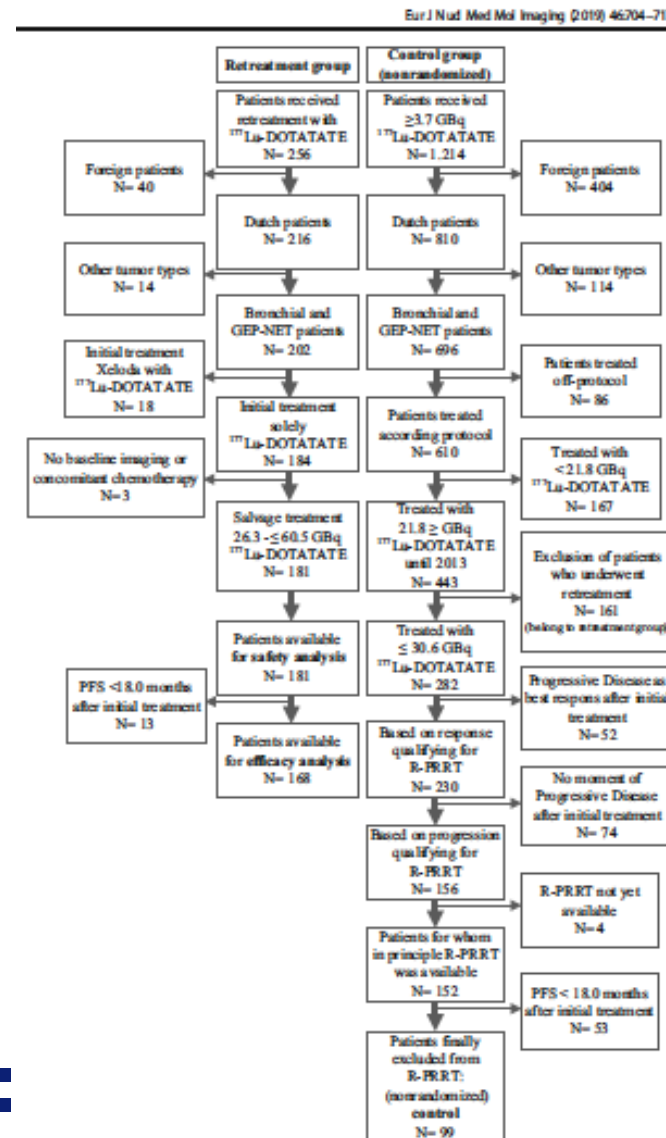
Erasmus MC



# Re-treatment PRRT up to 44 – 60 GBq, without renal toxicity



WA van der Zwan et al., EJNMMI (2019) 46:704–717

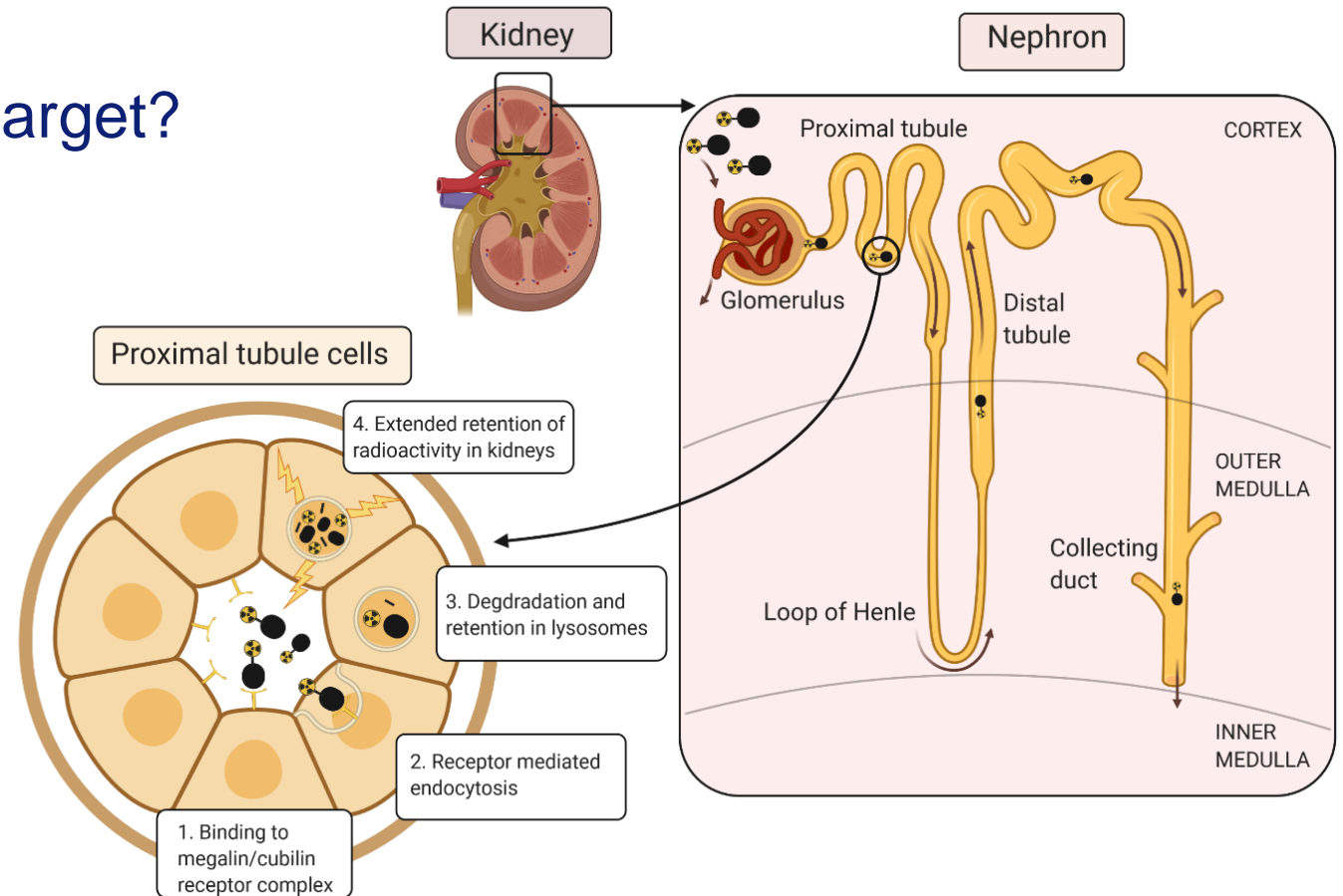


Erasmus MC

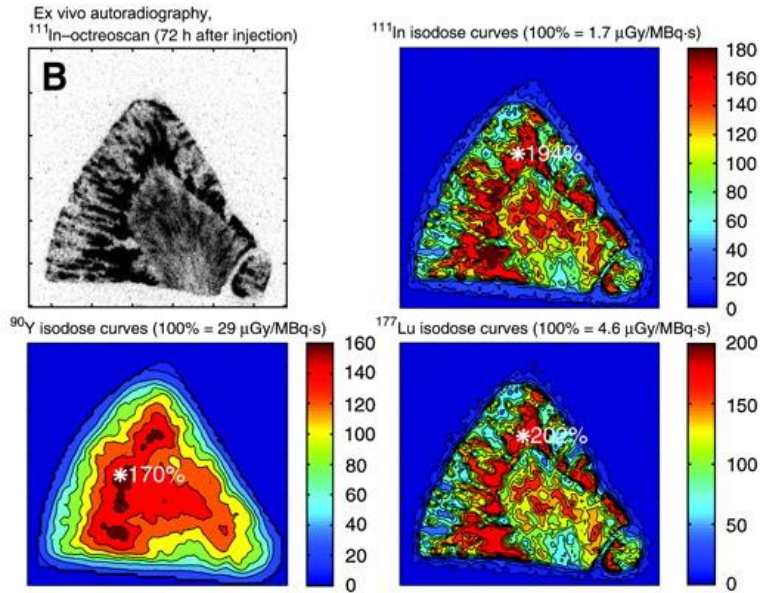


# How meaningful is a mean absorbed kidney dose ?

- Internal dosimetry
  - Whole organ or specific target?
- Specific uptake
  - Functional sub-units
  - Metabolic cancer cells
- Range of particles emitted
  - High energy beta-emitters
  - Low energy beta-emitters
  - Auger-electron emitters
  - Alpha-particle emitters



# Non-uniform kidney activity uptake



M Konijnenberg et al. JNM 2007

- **Beta-emitters**
- *Homogeneous dose distribution with  $^{90}\text{Y}$*
- *Max range 11 mm*
- *Non-uniform dose distribution with  $^{177}\text{Lu}$*
- *Max range 2 mm*

- **Alpha-emitters**
- **Small scale dosimetry model for nephron**
  - Proximal tubuli uptake
  - Dose  $\frac{\text{Cortex}}{\text{Glomerulus}} 4.5$

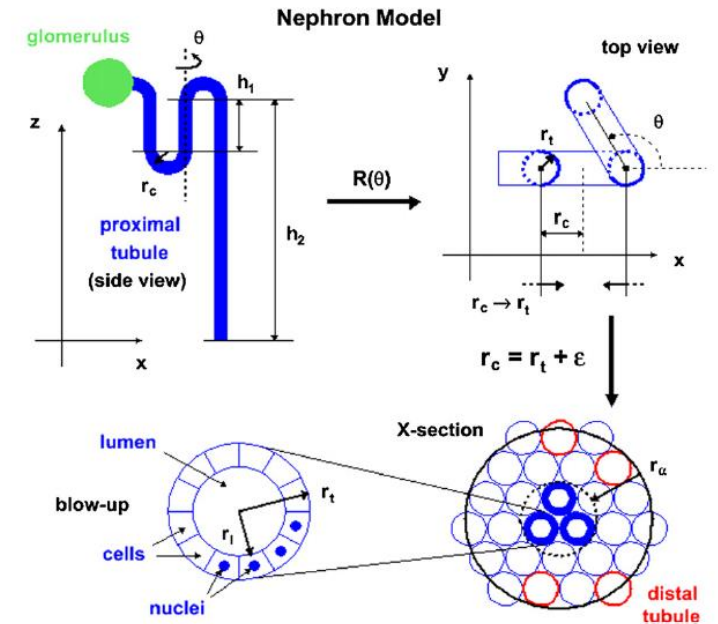
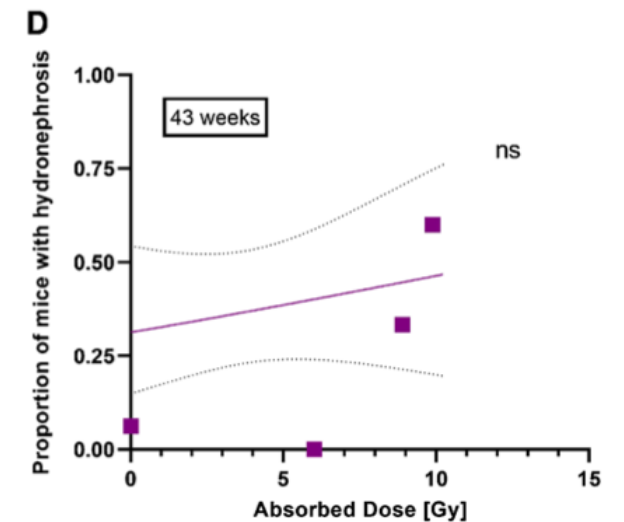
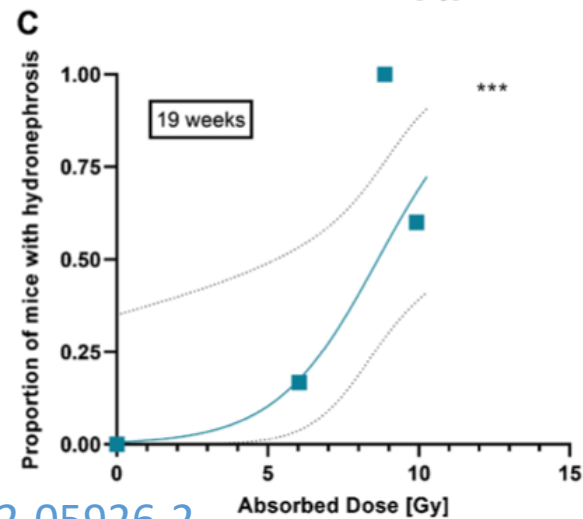
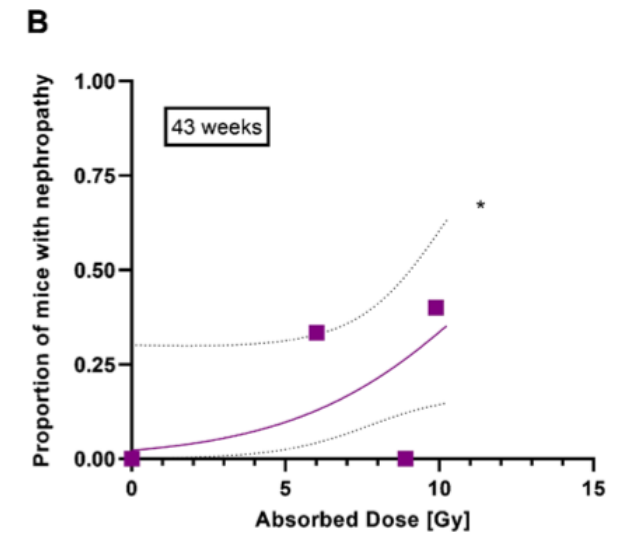
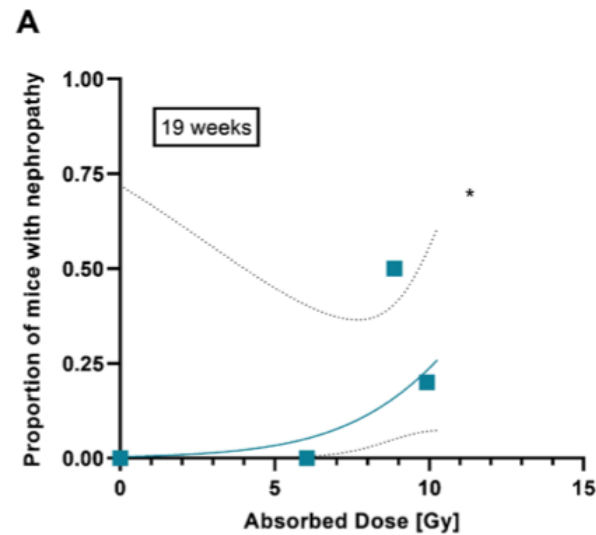
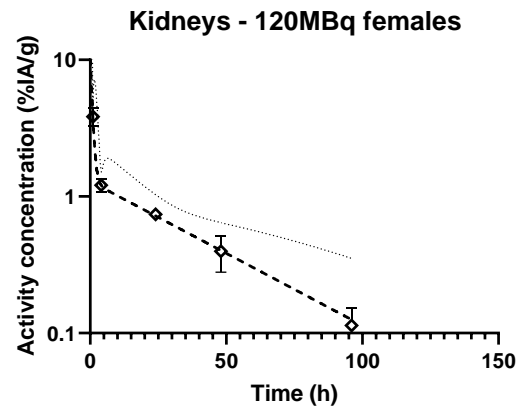
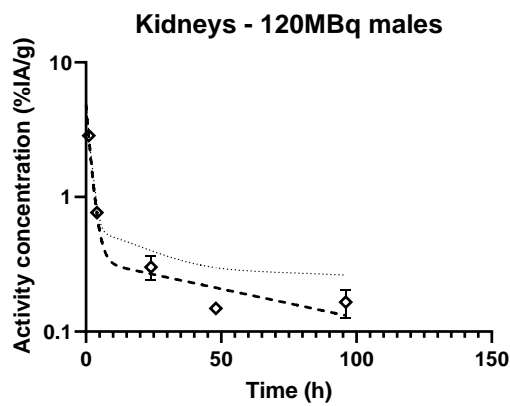
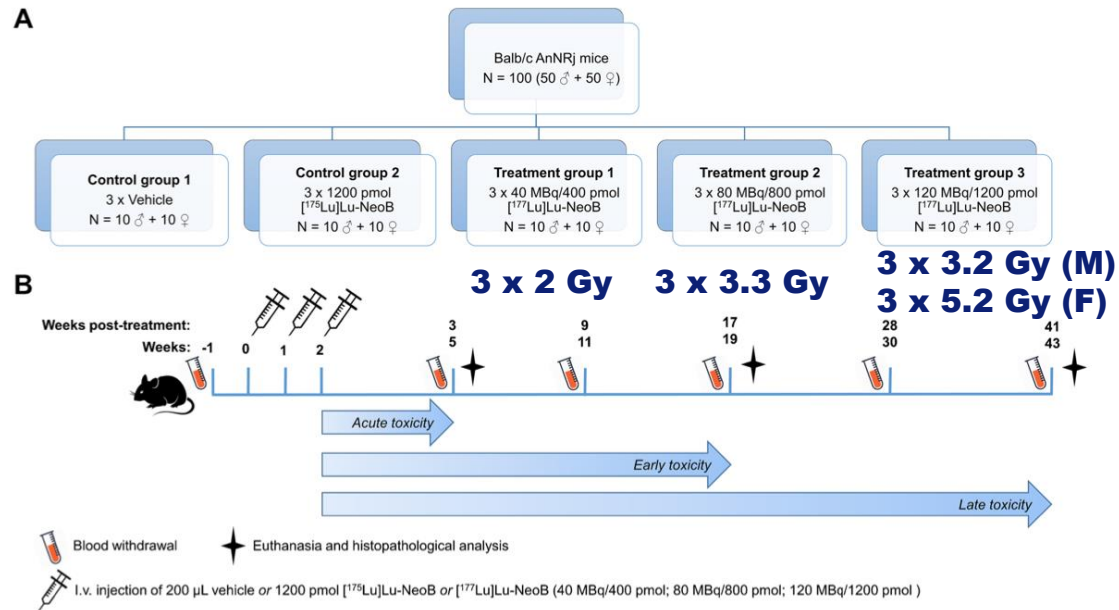


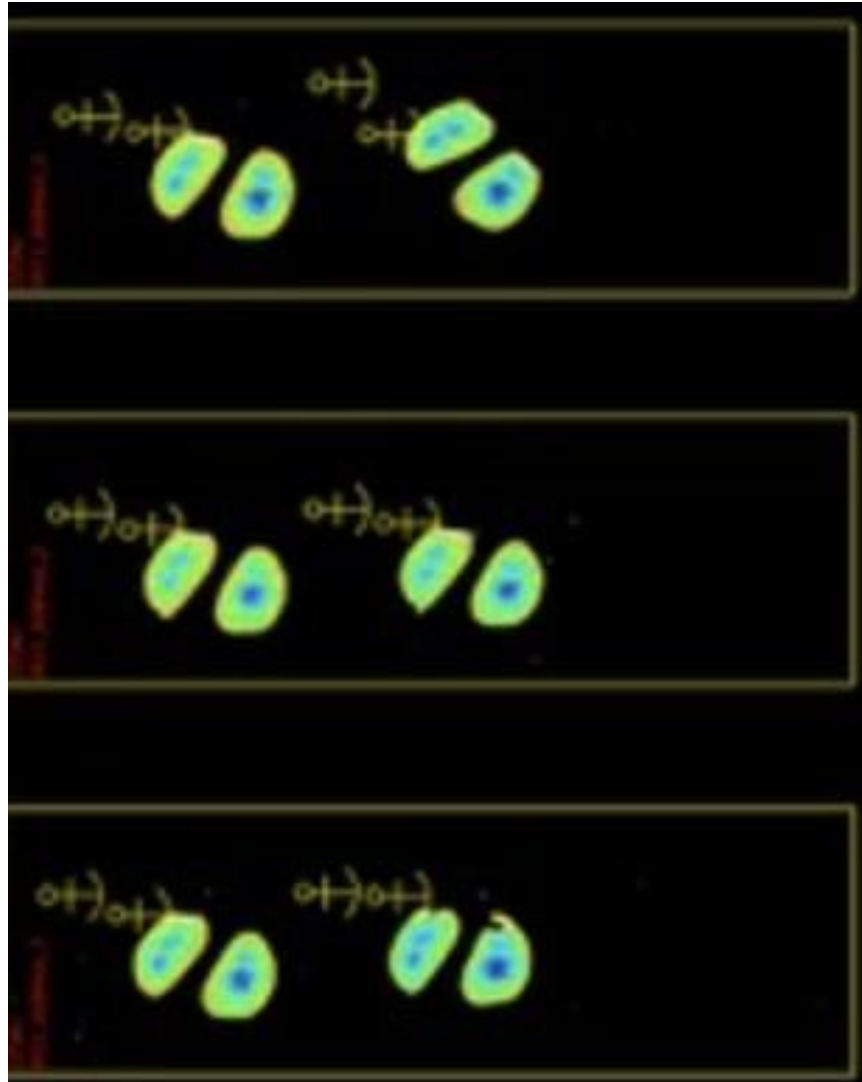
Figure 1. Idealized geometrical nephron model. The parameters shown are those used for the simulation:  $r_t$  is the proximal tubule radius,  $r_l$  is the lumen radius as measured by histology. The  $\epsilon$  value is taken to be  $1 \mu\text{m}$  and corresponds to interstitial space,  $h_1$  and  $h_2$  represent the scale of the proximal tubule length.

# Kidney toxicity in pre-clinical setting $^{177}\text{Lu}$ -NEOB





# Autoradiography kidneys 24 h post injection



- Specific uptake in cortex
- Need higher resolution

# Conclusion

- Large number of  $^{177}\text{Lu}$ -DOAT-octreotate patients with kidney dosimetry (N=408)
  - Planar imaging 3 time-points
  - No patient-specific kidney volume
  - Total dose  $19 \pm 5$  Gy  $\Rightarrow$  BED =  $21 \pm 6$  Gy  $\Rightarrow$
- No kidney toxicity in > 1 year follow-up on 4 x 7.4 GBq
- No kidney toxicity after salvage therapy up to 8 x 7.4 GBq
- Inhomogeneous uptake in kidney cortex (tubular reabsorption)
- Pre clinical toxicity assessment
  - Hydronephrosis at 19 weeks threshold 5 Gy