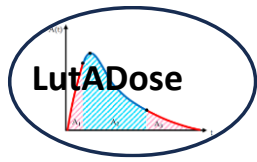


LutADose

Personalized dosimetry to improve the clinical outcome of prostate cancer patients treated with $^{177}\text{Lu}/^{225}\text{Ac}$ -PSMA targeted therapies

General objective



Increase the **clinical applicability** of tumour and organ **dosimetry** during $^{177}\text{Lu}/^{225}\text{Ac}$ -PSMA **therapy** to allow individualized treatment schemes and move away from a 'one fits all' approach.

=> better **balance** between maximizing tumor kill and minimizing toxicity to organs at risk

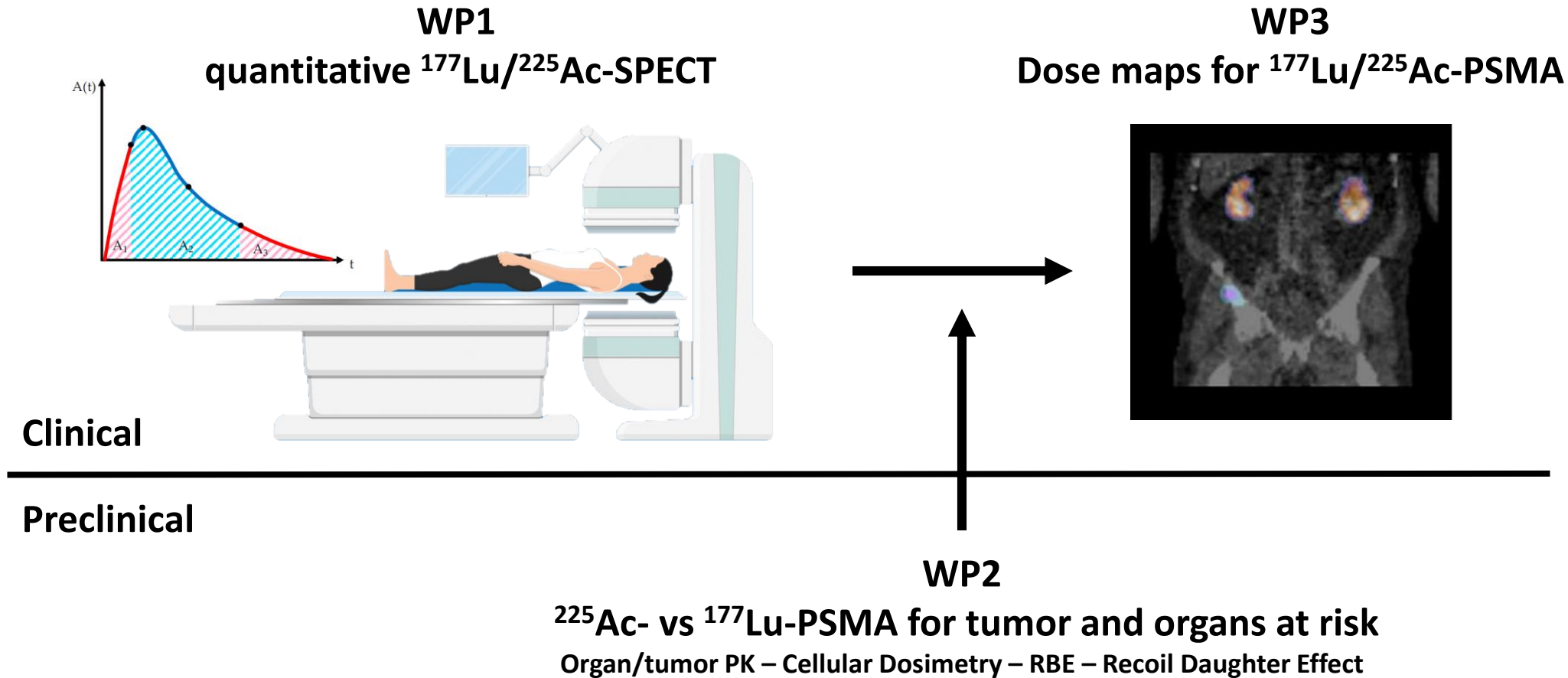
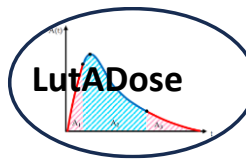
<> current clinical therapeutic schemes with **fixed activities**, resulting in a conservative tendency to **undertreat** patients and to sacrifice efficacy for safety

Clinical impact

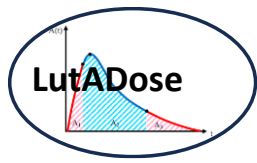
prostate cancer second most frequent malignancy worldwide with **> 1.4 million** new diagnoses in 2020 (incidence rate: 30.7 per 100,000 males)

10-20% develop castration-resistant prostate cancer (CRPC) within five years and more than 80% evolve to metastatic disease (mCRPC)

Workpackages



WP1 ^{177}Lu - and ^{225}Ac -SPECT imaging



State-of-the-art SPECT-CT systems



WB SPECT-CT 1 hour

600k euro / large install base

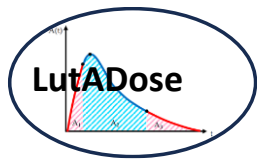
Compact CZT-based 3D SPECT-CT system
with integrated collimation



WB SPECT-CT 20 min

1.2M euro / limited install base

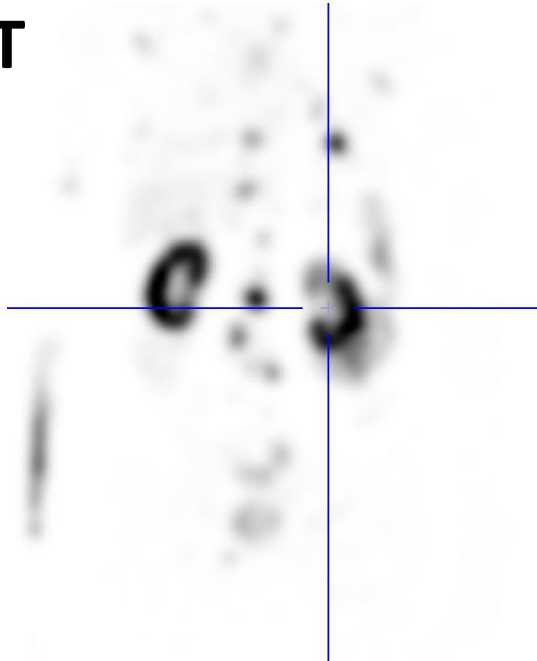
WP1 ^{177}Lu - and ^{225}Ac -SPECT imaging



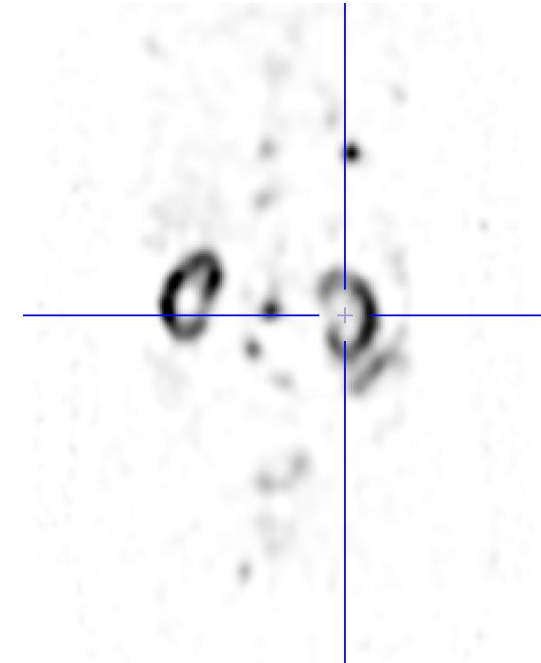
State-of-the-art SPECT-CT systems

Compact CZT-based 3D SPECT-CT system
with integrated collimation

^{177}Lu -SPECT



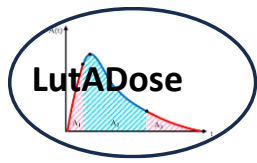
Deep Learning



WB SPECT-CT 1 hour
600k euro / large install base

WB SPECT-CT 20 min
1.2M euro / limited install base

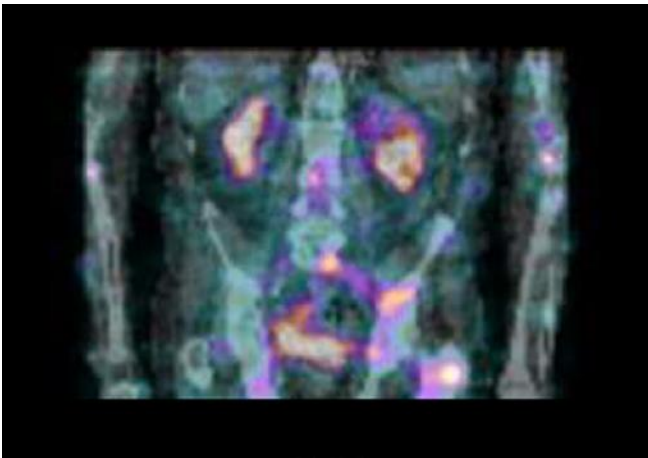
WP1 ^{177}Lu - and ^{225}Ac -SPECT imaging



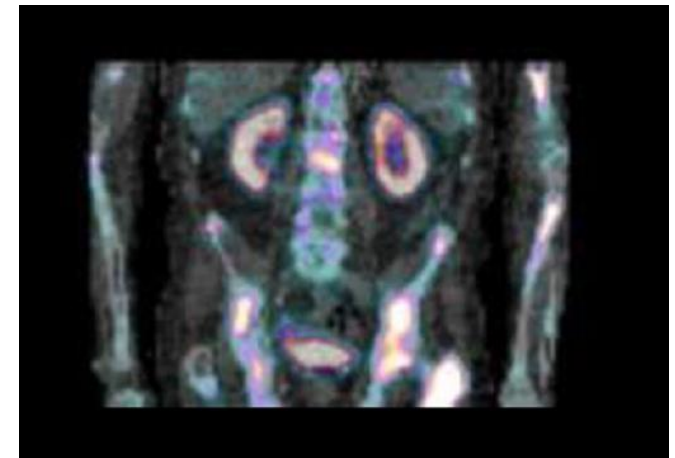
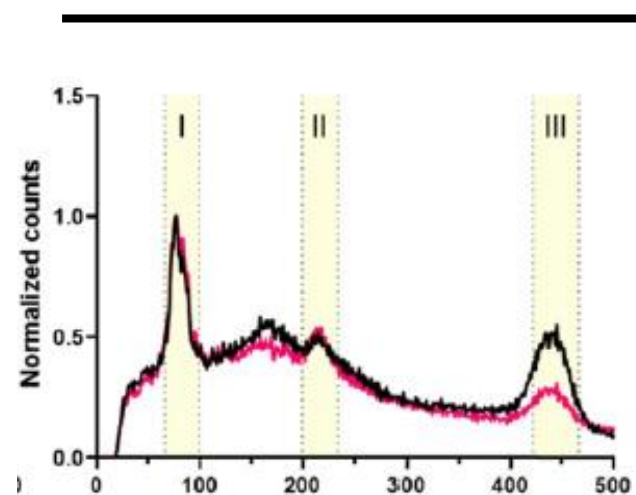
low therapeutic activities (4–8 MBq)

Low amount of γ -emissions

^{225}Ac -SPECT

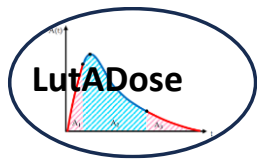


spectral reconstruction



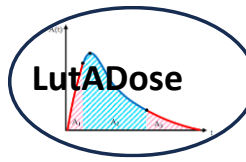
comparable image quality
to ^{177}Lu -SPECT

WP1 ^{177}Lu - and ^{225}Ac -SPECT imaging

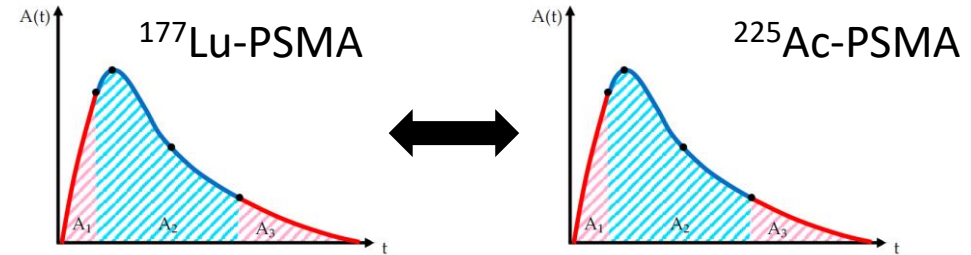


- Extending the EANM/EARL accreditation program for quantitative using 3D CZT ^{177}Lu -SPECT
- Evaluation of 3D CZT SPECT for quantitative ^{225}Ac -SPECT
- Multi-organ CT-based segmentation of organs at risk and SPECT/CT-based segmentation of tumour lesions
- Quantitative ^{177}Lu - and ^{225}Ac -SPECT imaging of the salivary glands

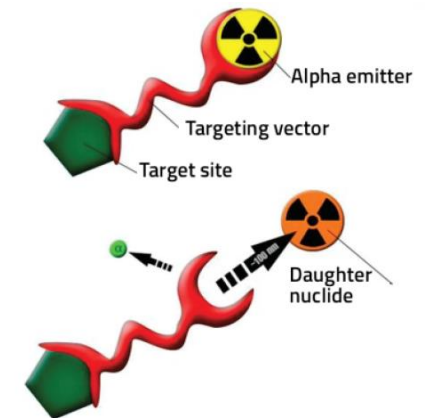
WP2 therapeutic and radiotoxic effects of ^{225}Ac - vs ^{177}Lu -PSMA



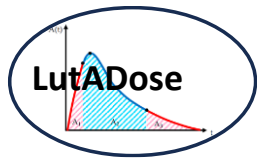
- ^{177}Lu -PSMA kinetics as a surrogate for ^{225}Ac -PSMA kinetics in tumor and major OARs



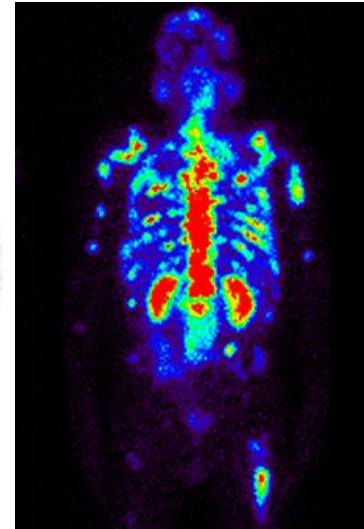
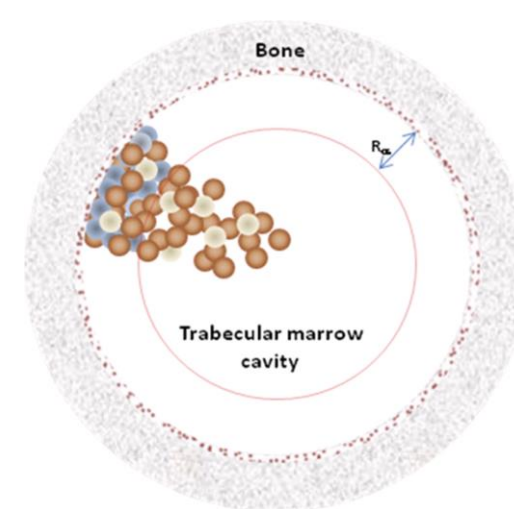
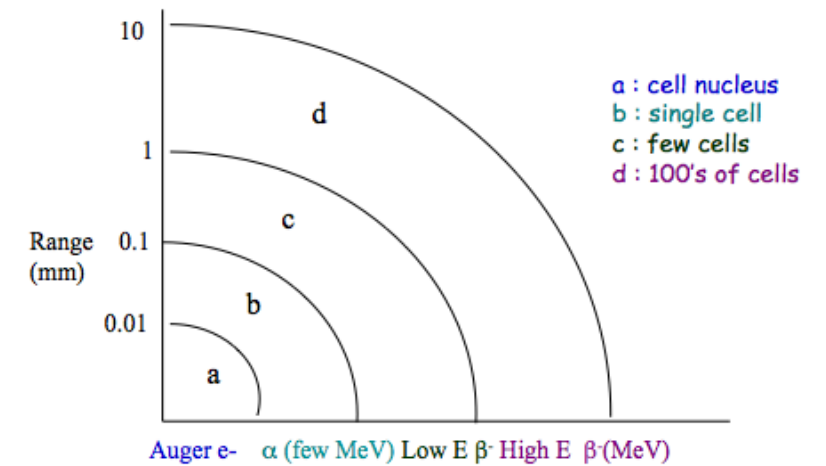
- revisit RBE of ^{225}Ac - vs ^{177}Lu -PSMA for tumor and salivary glands to better predict differences in efficacy and radiotoxic effects
- Evaluate the recoil daughter effect for ^{225}Ac -PSMA, with potential renal toxicity caused by redistribution of free ^{213}Bi



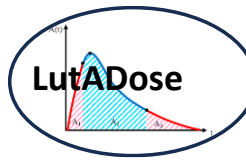
WP3 ^{225}Ac -PSMA absorbed dose estimates to tumor and OARs



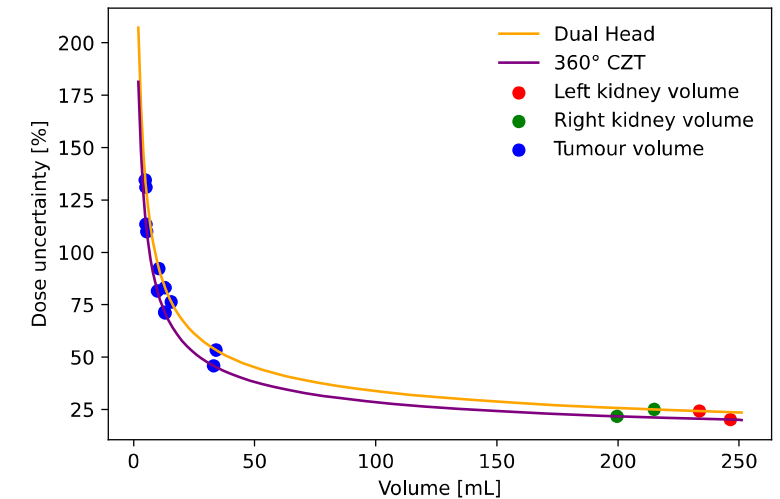
- Small scale dosimetry for salivary glands and bone marrow
- Translating ^{177}Lu - to ^{225}Ac -PSMA absorbed doses for salivary glands and tumor lesions



WP3 ^{225}Ac -PSMA absorbed dose estimates to tumor and OARs



- Small scale dosimetry for salivary glands and bone marrow
- Translating ^{177}Lu - to ^{225}Ac -PSMA absorbed doses for salivary glands and tumor lesions
- Uncertainty analysis of ^{225}Ac -PSMA dose estimates for tumoral lesions and salivary glands
- Clinical evaluation of revised RBE values for tumor and salivary glands during ^{225}Ac -PSMA therapy
- Guidelines for quantitative ^{225}Ac -SPECT



Partners & EU projects



KU Leuven (KUL)
Belgian Nuclear Research Centre (SCK CEN)



Erasmus Medical Centre, Rotterdam (EMC)

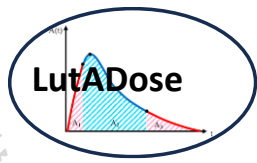
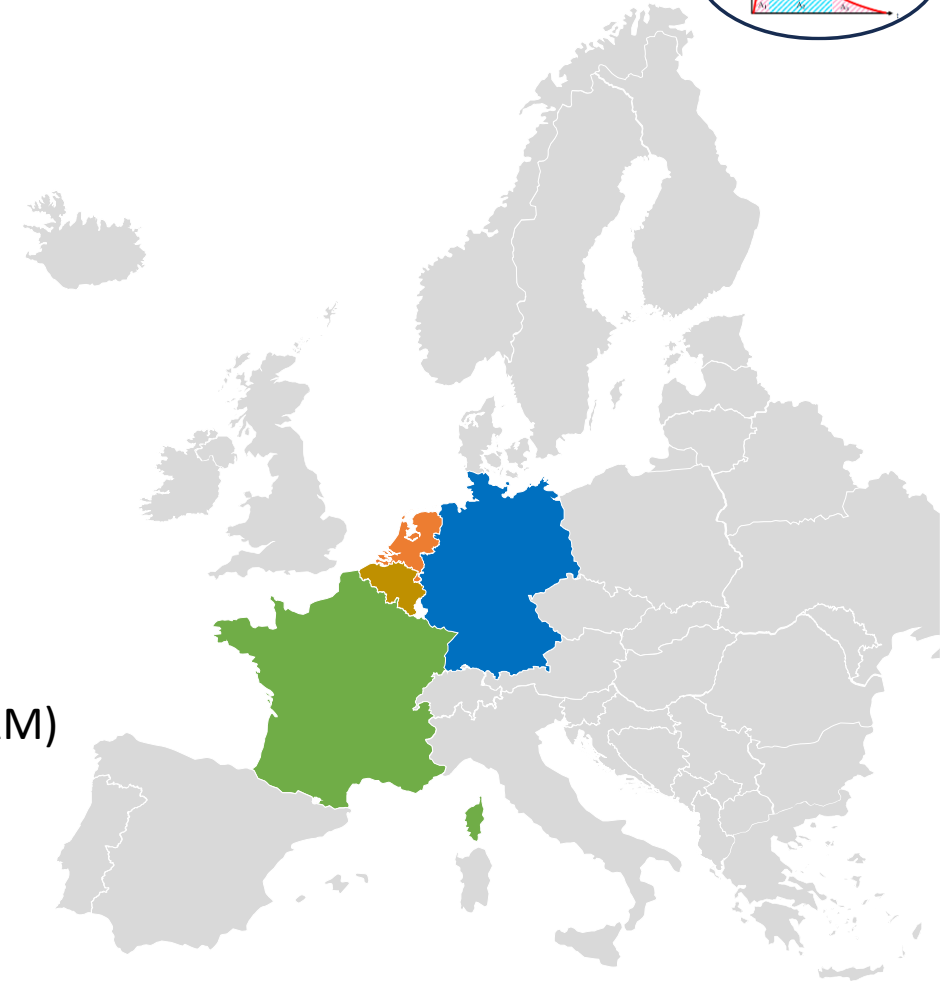


Ludwig Maximilian University Hospital, Munich (LMU)



Institut National de la Sante et de la Recherche Medicale, Brest (INSERM)

- AlphaMET, EURAMET-funded European project on Metrology for emerging targeted alpha therapies (2023-26)
- RATIONALE (Radionuclide theragnostics for personalised medicine – 2023-27)
- EANM/EARL European accreditation program on Quantitative ^{177}Lu -SPECT



Planning

	2024				2025				2026				2027			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
WP1 Quantitative ^{177}Lu - and ^{225}Ac SPECT																
WP1.1 Low count quantitative ^{177}Lu -SPECT	KUL, EMC, LMU, INSERM															
WP1.2 EANM/EARL accreditation for 3D CZT ^{177}Lu -SPECT	KUL, EMC															
WP1.3 Quantitative 3D CZT ^{225}Ac - SPECT			KUL, EMC													
WP1.4 Spectral reconstruction for quantitative ^{225}Ac -SPECT					LMU, KUL, EMC											
WP1.5 ^{177}Lu - and ^{225}Ac -SPECT imaging of the salivary glands									LMU, EMC, KUL							
WP1.6 SPECT/CT based segmentation of tumor and organs at risk									INSERM, KUL, LMU, EMC							
WP2 ^{225}Ac - vs ^{177}Lu -PRLT for tumor and organs at risk																
WP2.1 Tumor and organ pharmacokinetics of ^{225}Ac - vs ^{177}Lu -PSMA	SCK CEN, EMC															
WP2.2 Cellular dosimetry for ^{225}Ac - vs ^{177}Lu -PSMA					INSERM, SCK CEN, EMC											
WP2.3 Revisiting the RBE of ^{225}Ac - vs ^{177}Lu -PSMA									EMC, SCK CEN							
WP2.4 Recoil daughter effect for ^{225}Ac -PSMA					SCK CEN, EMC											
WP3 Tumor and organ absorbed dose for ^{225}Ac -PRLT																
WP3.1 Small scale dosimetry for ^{225}Ac -PRLT	EMC, SCK CEN, INSERM, LMU															
WP3.2 Translating ^{177}Lu -- to ^{225}Ac -PRLT absorbed doses					LMU, SCK CEN											
WP3.3 Uncertainty analysis of ^{225}Ac -PRLT dose estimates									KUL, LMU, EMC, INSERM, SCK CEN							
WP3.4 Clinical evaluation of revised RBE values for ^{225}Ac -PRLT													LMU, EMC, KUL			
WP3.5 Guidelines for quantitative ^{225}Ac -SPECT in a clinical setting															LMU, EMC, KUL, INSERM	

3.25 PhD students (156 PM) + supervision by senior researchers (55 PM) => 1/3 ratio