Radiation Dosimetry and Radiobiological Efficiency in Personalized Targeted Radionuclide Therapy

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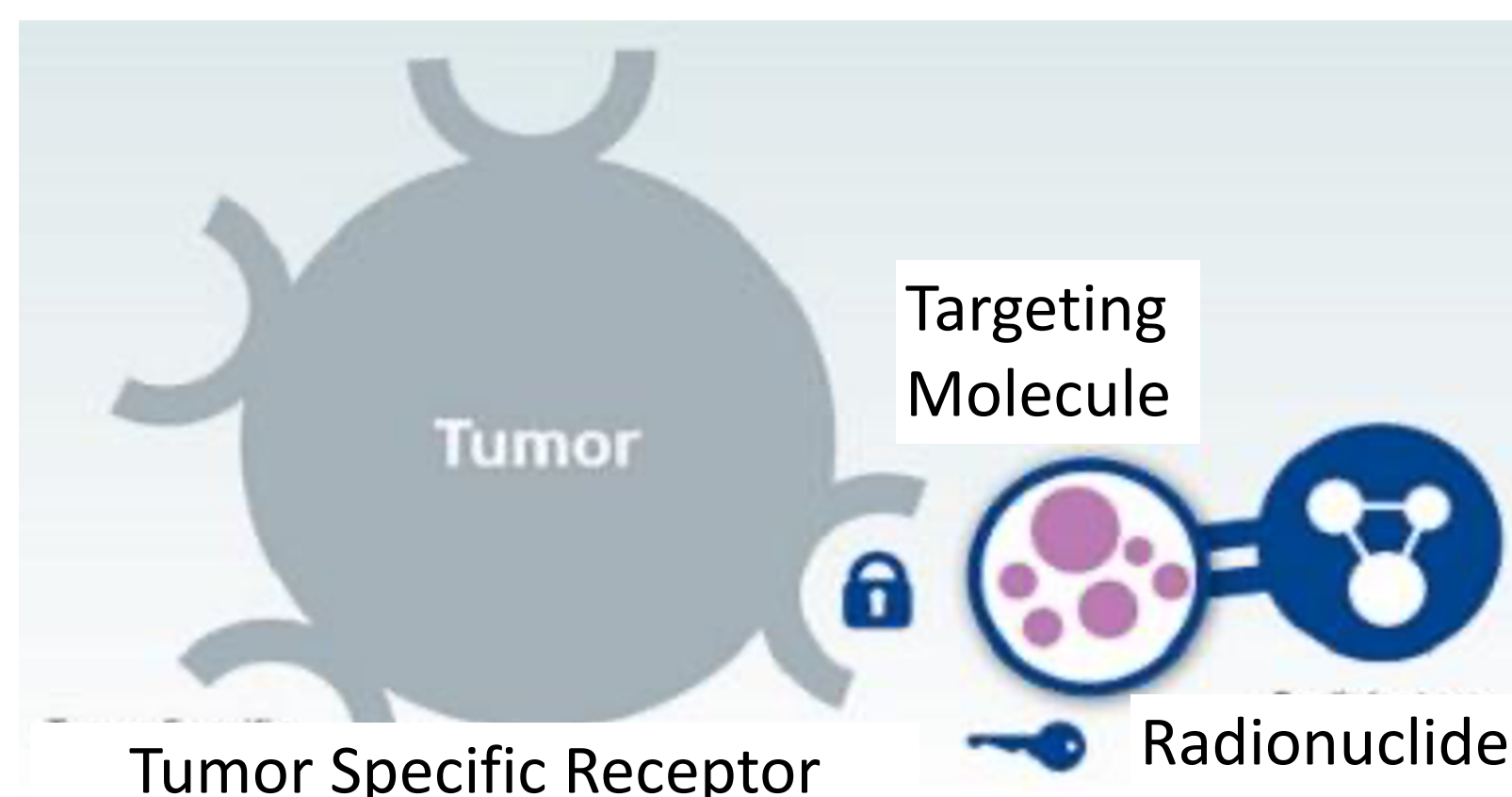[2] Champalimaud Centre for the Unknown, Fundação Champalimaud, Lisboa, Portugal

Introduction

- Cancer caused more than 10 million deaths worldwide in 2018.
- WHO predicts this number will grow to almost 40 million in 2040 [1].
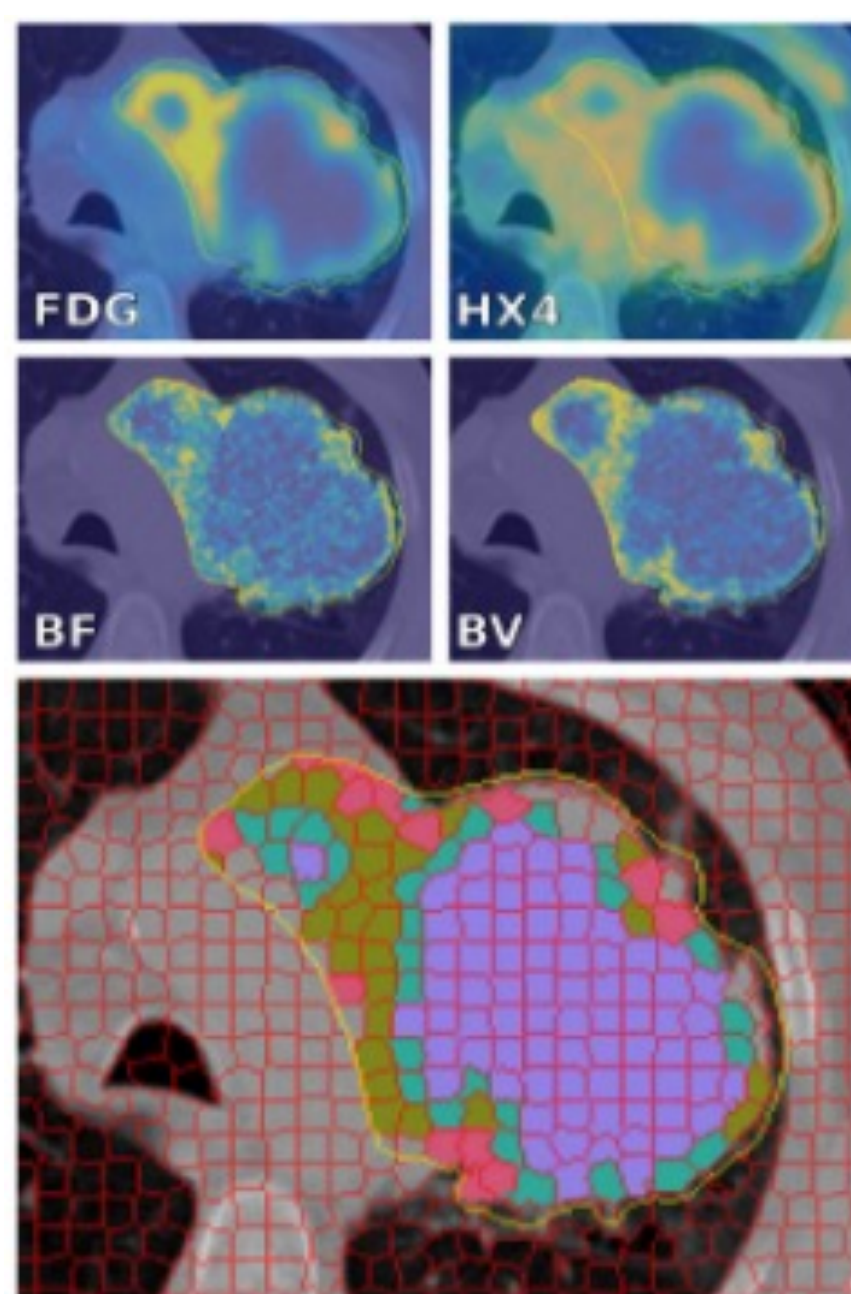
❖ Targeted Radionuclide Therapy (TRT)

- Targeted Radionuclide Therapy (TRT) is a cancer treatment modality that uses a molecule labeled with a radionuclide to deliver damaging ionizing radiation to tumors [2].
- TRT presents several advantages, such as:

Tumor cell specificity.

More localized tumor irradiation.

❖ Tumor Heterogeneity

- Tumor sub-volumes (or phenotypes) can be distinguished within the same tumor mass [3,4].

  Many times not considered in clinical practice!

- Nonuniform activity distribution may occur at the organ, voxel, cellular and sub-cellular levels [5].
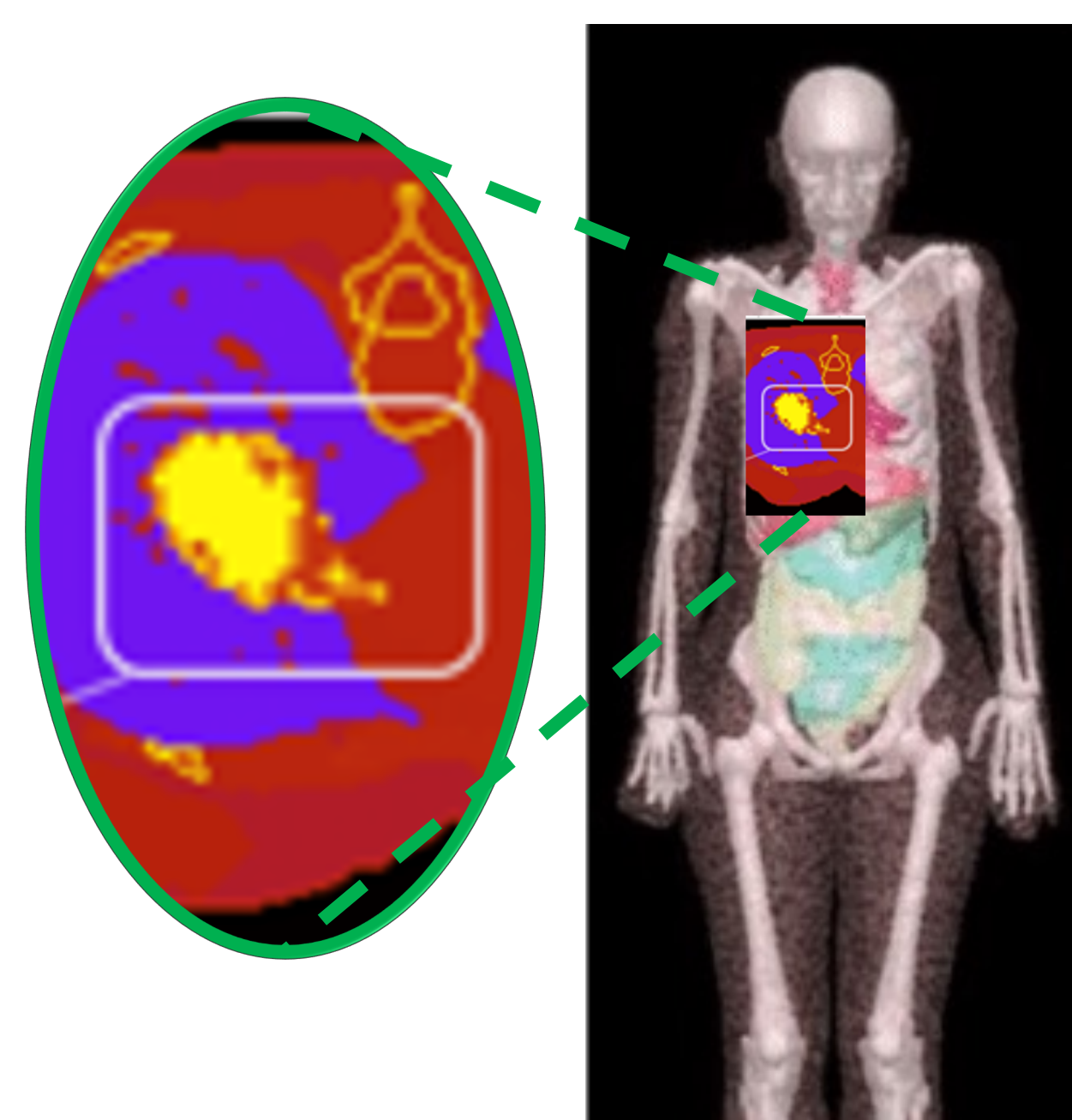
  May compromise therapy efficiency!

❖ Main Aim of the Study

Assess dosimetric and radiobiological efficiency of TRT directed to the tumor phenotype

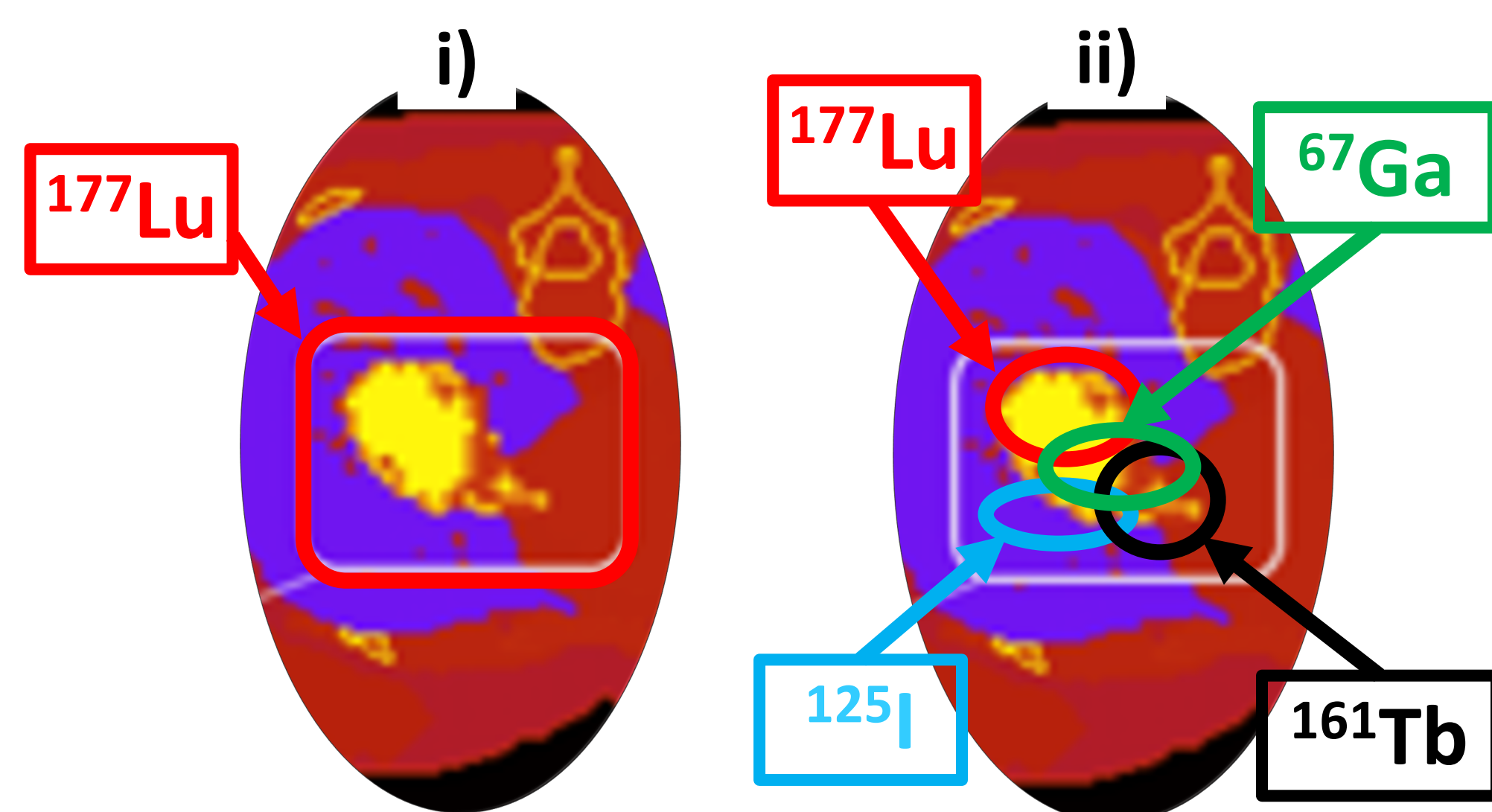## Part 1: MC Simulations with Tumor Model

- Tumor model divided in four phenotypes developed.
- Tumor model inserted in the right lung of reference computational phantom [6].
- Monte Carlo (MC) simulations performed to calculate:
  - **S-value** (absorbed dose per cumulated activity);
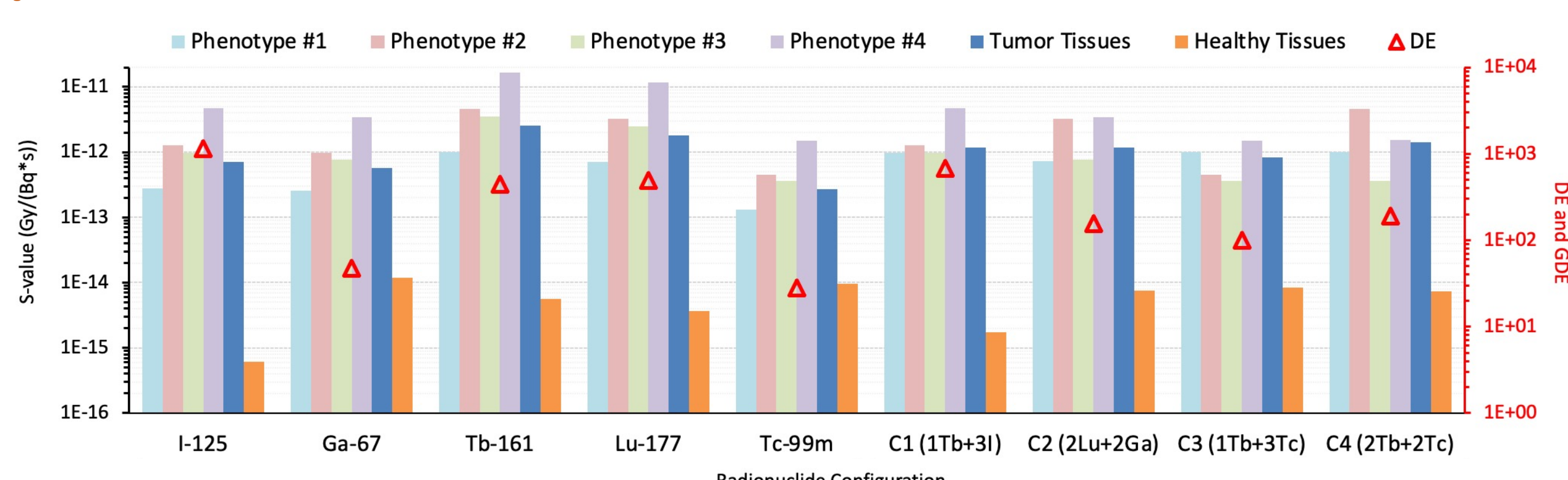 - **Dosimetric Efficiency (DE).**

$$DE = \frac{S - value\ (tumor\ tissue)}{S - value\ (healthy\ tissues)}$$

❖ 2 irradiation scenarios considered:

i) **Current Practice** – all four tumor phenotypes irradiated by one radionuclide

ii) **Ideal** – each tumor phenotype irradiated by a different radionuclide

❖ Results:

Irradiating the tumor with a mix of radionuclides enhances absorbed dose in tumor tissues and improves dosimetric efficiency!

Part 2: Clinical Image Analysis

- PET-CT (Positron Emission Tomography - Computed Tomography) images images acquired at the Nuclear Medicine-Radiopharmacology Department - Champalimaud Foundation.
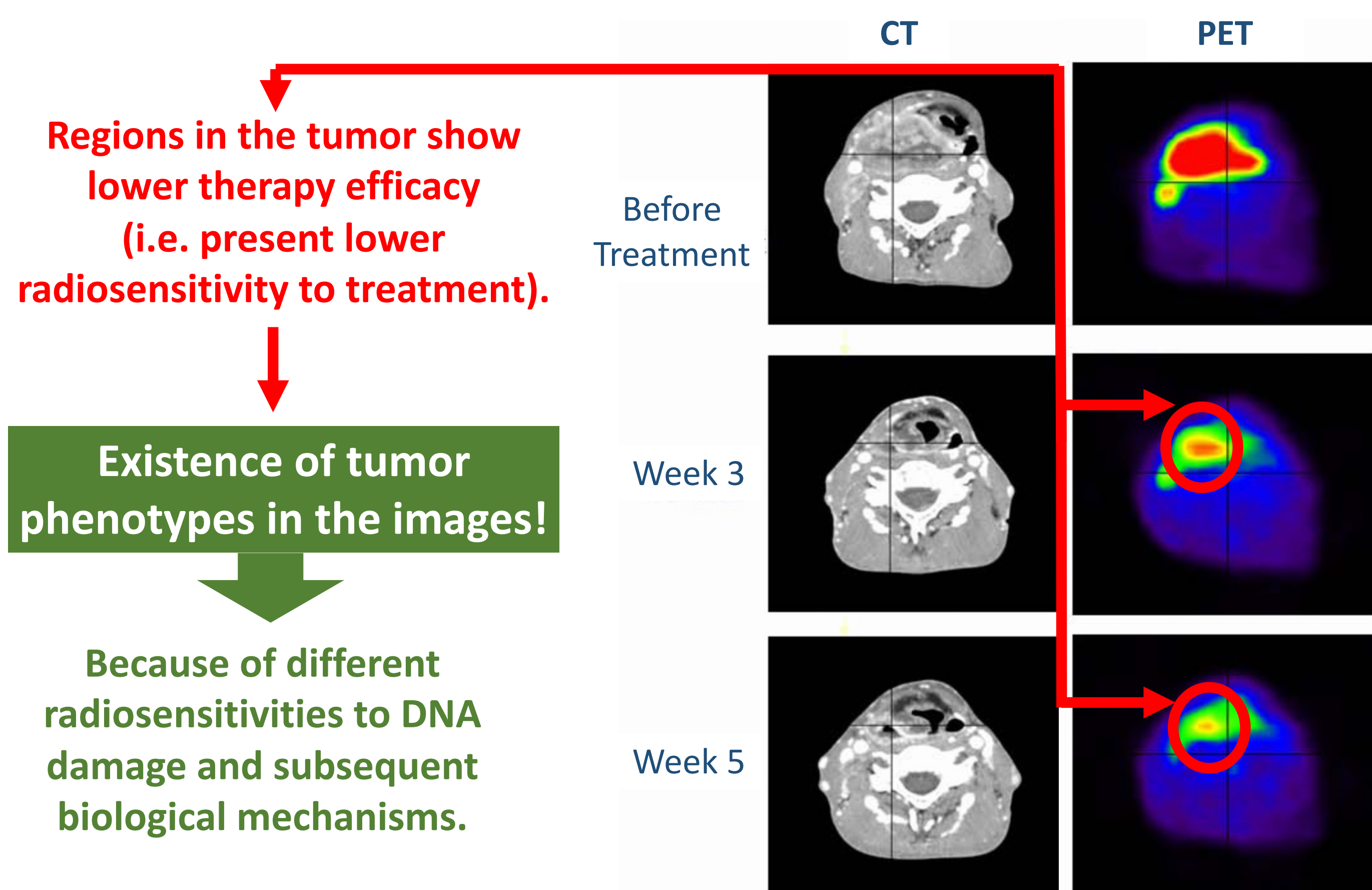
  Images show anatomical and functional information before and after treatment.

- ^{68}Ga images are used when treating patients with neuroendocrine tumors with ^{177}Lu.

❖ How are phenotypes identified using clinical images?

- Calculation of therapy efficacy:

$$Therapy\ Efficacy = \frac{Voxel\ Intensity_{before\ treatment}}{Voxel\ Intensity_{after\ treatment}}$$

- Voxel intensity is a surrogate for radionuclide activity.

Regions in the tumor show lower therapy efficacy (i.e. present lower radiosensitivity to treatment).

Existence of tumor phenotypes in the images!

Because of different radiosensitivities to DNA damage and subsequent biological mechanisms.

Example of PET-CT images acquired before and after treatment [7].

Conclusion

- Irradiating a heterogenous tumor using a phenotype directed strategy and various radionuclides …

  - **Maximize damage to tumor;**
  - **Minimize damage to healthy tissue.**

Increase Therapy efficacy and success rate → **Personalized Therapy**

Future Work: Radiobiological Efficiency

- Development of a patient-specific computational phantom from segmented clinical images.

  Assessment of dosimetric and radiobiological efficiency of personalized TRT

- Radiobiological assays

  → Dose-cell survival curves for several cell lines

    → Cell lines represent tumor phenotypes

❖ Nanodosimetry (DNA damage calculation)

- Usage of a radiobiological model combined with parameters estimated using MC simulations.
- Quantity to measure biological response:

  Relative Biological Effectiveness (RBE)

❖ Main Aim:

Calculate RBE for different tumor phenotypes

References

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