ICDA-4

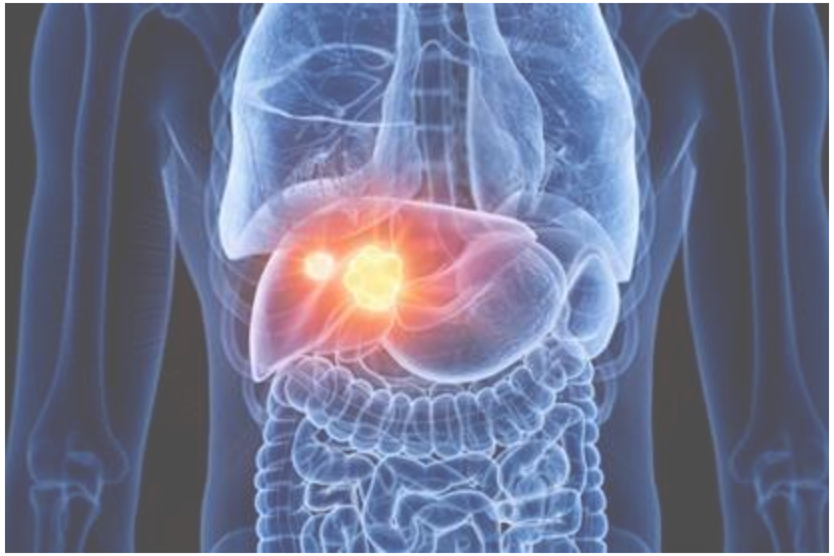
4th International Conference on Dosimetry and its Applications

TÉCNICO LISBOA

C2TN

Fundação Champalimaud

Data Science Pipeline for Development of Patient-Specific Phantoms and S-value Calculation in Radiopharmaceutical Therapy



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INTRODUCTION

- Radiopharmaceutical Therapy (RPT) is a cancer treatment modality that uses:

Targeting molecule + Radionuclide → To deliver damaging ionizing radiation (IR) to tumor cells.

- RPT presents advantages such as:
  - More localized tumor irradiation (including metastases)
  - Higher tumor cell specificity.

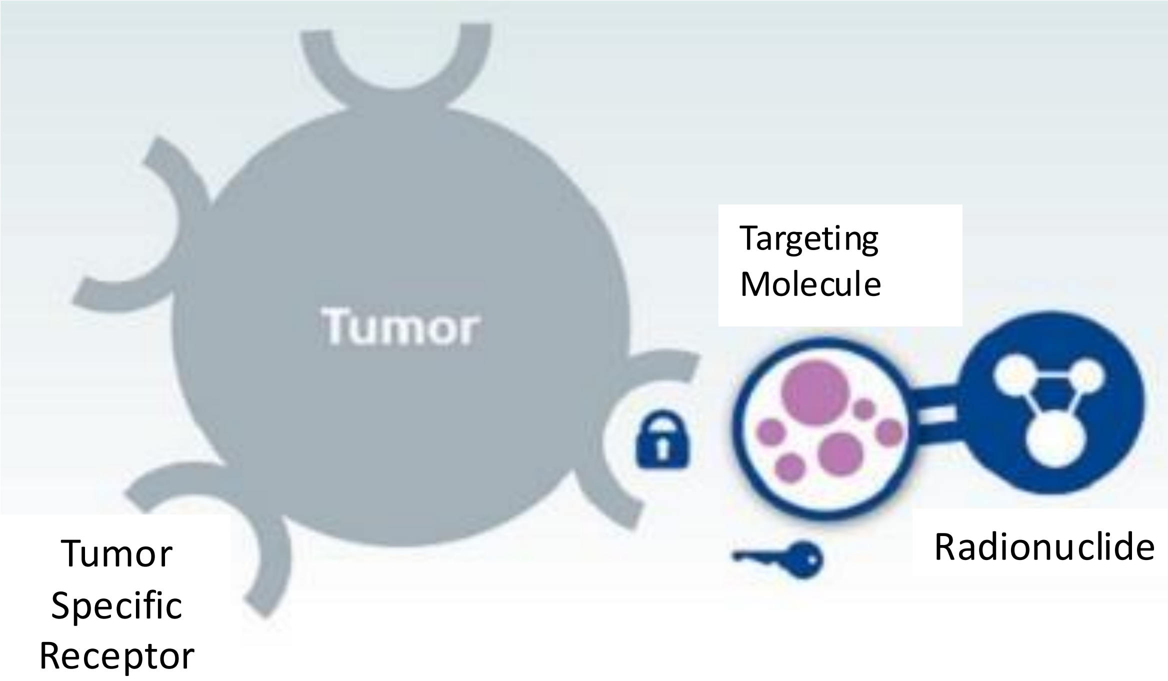

Fig. 1 – Cell schematic of Radiopharmaceutical Therapy.

Sgouros G et al. Nat Rev Drug Discov 2020;19:589–608. | Gudkov S et al. Int J Mol Sci 2015;17(1):33. | https://*ccr.cancer.gov/news/article/clinical-trial-will-investigate-targeted-radionuclide-therapy-for-inoperable-rare-tumors*. Accessed on: 27/08/2022.

INTRODUCTION

- Tumors and patients often display heterogeneity at the time of diagnosis.
- Often overlooked during treatment planning in RPT.

Use of functional and anatomical imaging to identify tumor phenotypes (i.e. sub-volumes) inside a tumor mass.

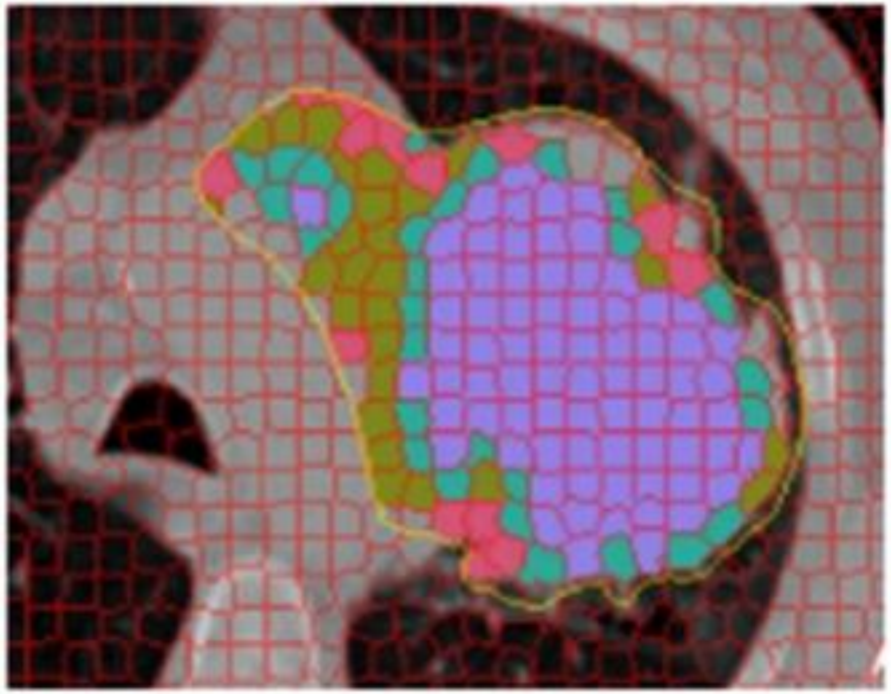

Fig. 2 – Identification of tumor phenotypes based on radiomics methods, such as CT number, hypoxia and vascularity [Even et al. 2017].

- Different tumor phenotypes may exhibit different resistance/sensitivity to the same therapy.

Lee G et al. Korean Journal of Radiology 2020. 21(2):159-171. | Even AJ et al. Radiotherapy and Oncology 2017. 125(3):379-84. | Bentzen SM et al. Semin Radiat Oncol 2011;21:101–10. | Ma L et al. Radiology and Oncology 2019. 53(1):6-14. | Bodei L et al. Eur J Nucl Med Mol Imaging 2023.

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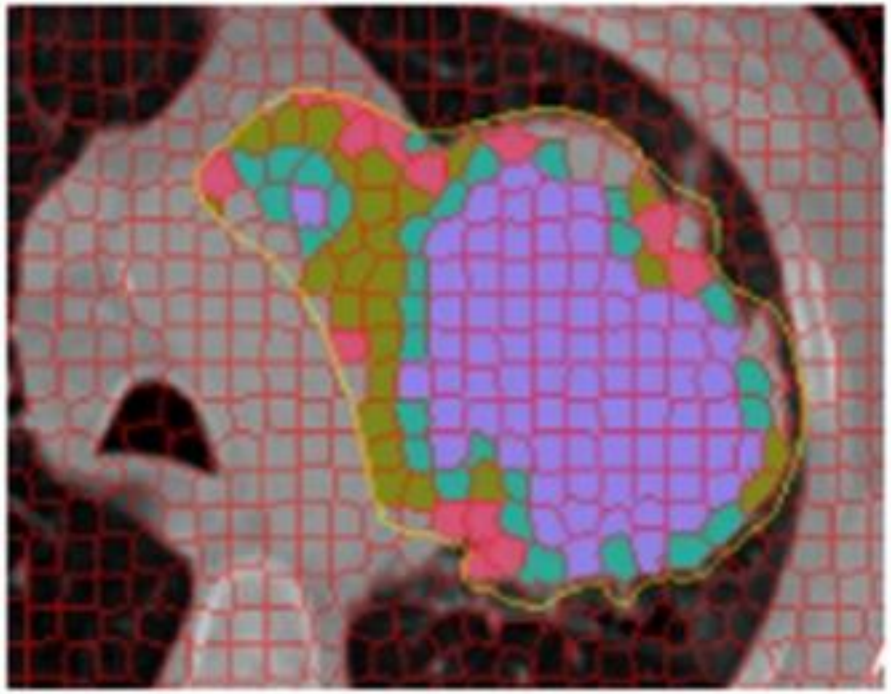

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- Different tumor phenotypes may exhibit different resistance/sensitivity to the same therapy.

Improved Individual Dosimetry → tailor the radiation-absorbed dose to the individual, to maximize efficacy of tumor treatment, while minimizing healthy tissue toxicity

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PURPOSE

MAIN AIM:

- Develop a Patient-Specific Phantom (PSP) and perform dosimetric calculations by comparing results with the ICRP reference adult female voxel phantom (ICRP-AF).

SECONDARY AIMS:

- Segment clinical functional and anatomical images.
- Develop a Data Science pipeline able to streamline the development of PSP for Monte Carlo (MC) simulation.
- Create PSP from acquired clinical images.
- Validate the created PSP, by performing MC simulations and comparing dosimetric results with the ICRP-AF. → e.g. SAF, S-value

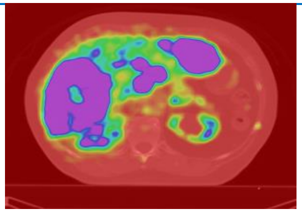
METHODS

- RPT with ^{177}Lu-DOTATATE of neuroendocrine tumor in the liver.

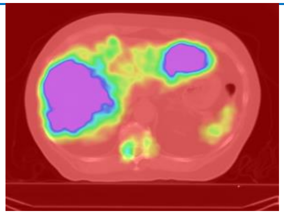
Image Acquisition and Segmentation

EXAMPLE OF TREATMENT (1 CYCLE):

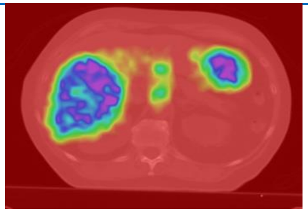
- Pre-treatment: PET-CT using ^{68}Ga-DOTANOC



- 24h post–treatment: SPECT + CT using ^{177}Lu-DOTATATE



- 168h post-treatment: SPECT using ^{177}Lu-DOTATATE



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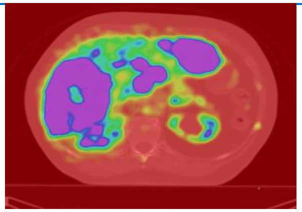

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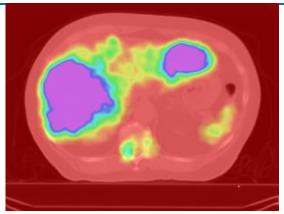

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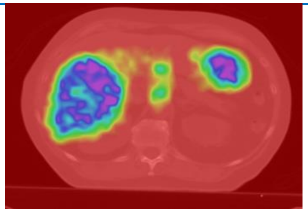
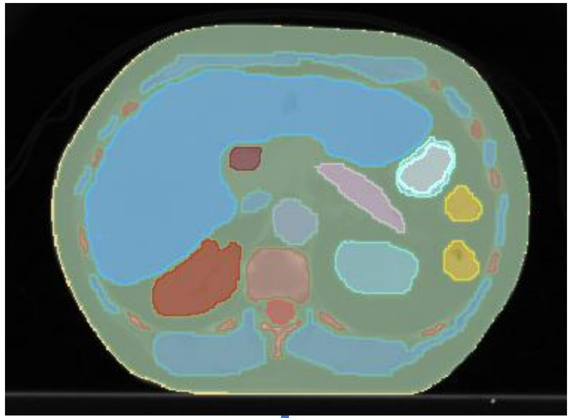


WORK FLOW:

Segment pre-treatment CT in Pinnacle TPS



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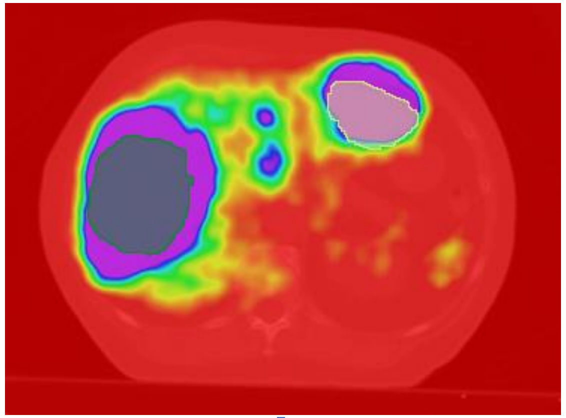
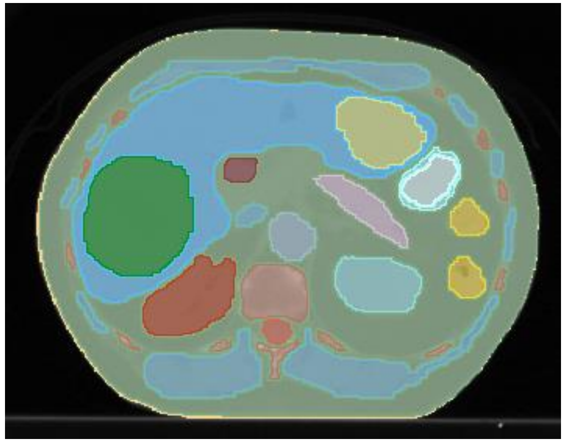


Combined full segmentation



Imported into Slicer and exported as labelmap (.nrrd)

METHODS

Data Analytics/Science Pipeline

- Pipeline developed using Python, employing data science libraries/modules.
- Pipeline analyzes image data and produces voxel phantom file for Monte Carlo (MC) dosimetric calculations using the peanEasy2020/PENELOPE2018 program.
- Specific Absorbed Fractions (SAF) and S-value calculated in ICRP-AF and segmented phantom (MARIA).

Spyder

5.4.3

METHODS

Data Analytics/Science Pipeline

Summary Workflow Diagram For Patient-specific Phantom (PSP) Generation Pipeline:

1. Load used input and set up variables

- Read organ NRRD data and organlist file.
- Crop 3D array to delete CT dead space (e.g. air, machine equipment) around the patient.
- Load CT file and read calibration curve. Crop phantom read from CT file.

2. Calculate PSP statistical info from various sources using pandas

- Calculate mass density for each singular voxel.
- Create dataframes and perform statistical analysis (e.g. nº voxels, volume, mass, mean/median density, voxel bounding box, center of mass) for each segmented structure, using pandas.
- Data integrity checks: correct negative densities, deviations to ICRP reference values and set air density to ICRP reference value
- Create phantoms: ‘phantom_avgden’ and ‘phantom_ctden’

3. Create output files for MC simulation and visualization

- Data Visualization: Generate and save 2D plots of the phantoms along the three anatomical planes (axial, sagittal, coronal).
- Write files for simulation with PENELOPE: ‘phantom_avgden.vox’ and ‘phantom_ctden.vox’
- Output ‘report.out’ containing execution information and statistics.

Spyder

5.4.3

RESULTS AND DISCUSSION

ICRP-AF SAF Comparison with Literature

- SAF(Liver<-Liver), SAF(Stomach W.<–Liver), SAF(Lungs<-Liver) calculated and compared to literature (10, 50, 100 keV).
- Photons → **6.2%**
- Electrons → **2.3%**

L Hadid et al 2010 Phys. Med. Biol. 55 3631

Table 1 – Organ mass in ICRP-AF and MARIA and relative difference [ICRP, 2009. ICRP Publication 110. Ann. ICRP 39 (2)].

Organ	Mass (kg) ICRP-AF	Mass (kg) MARIA	Relative Difference (%)
Lung	0.941	0.835	11%
Breast, glandular	0.200	0.054	73%
Liver	1.400	3.019	116%
Spleen	0.130	0.089	32%
Stomach	0.140	0.096	32%
Kidneys	0.275	0.395	44%
Bladder	0.040	0.043	7%

MEAN RELATIVE DIFFERENCE: **44%**

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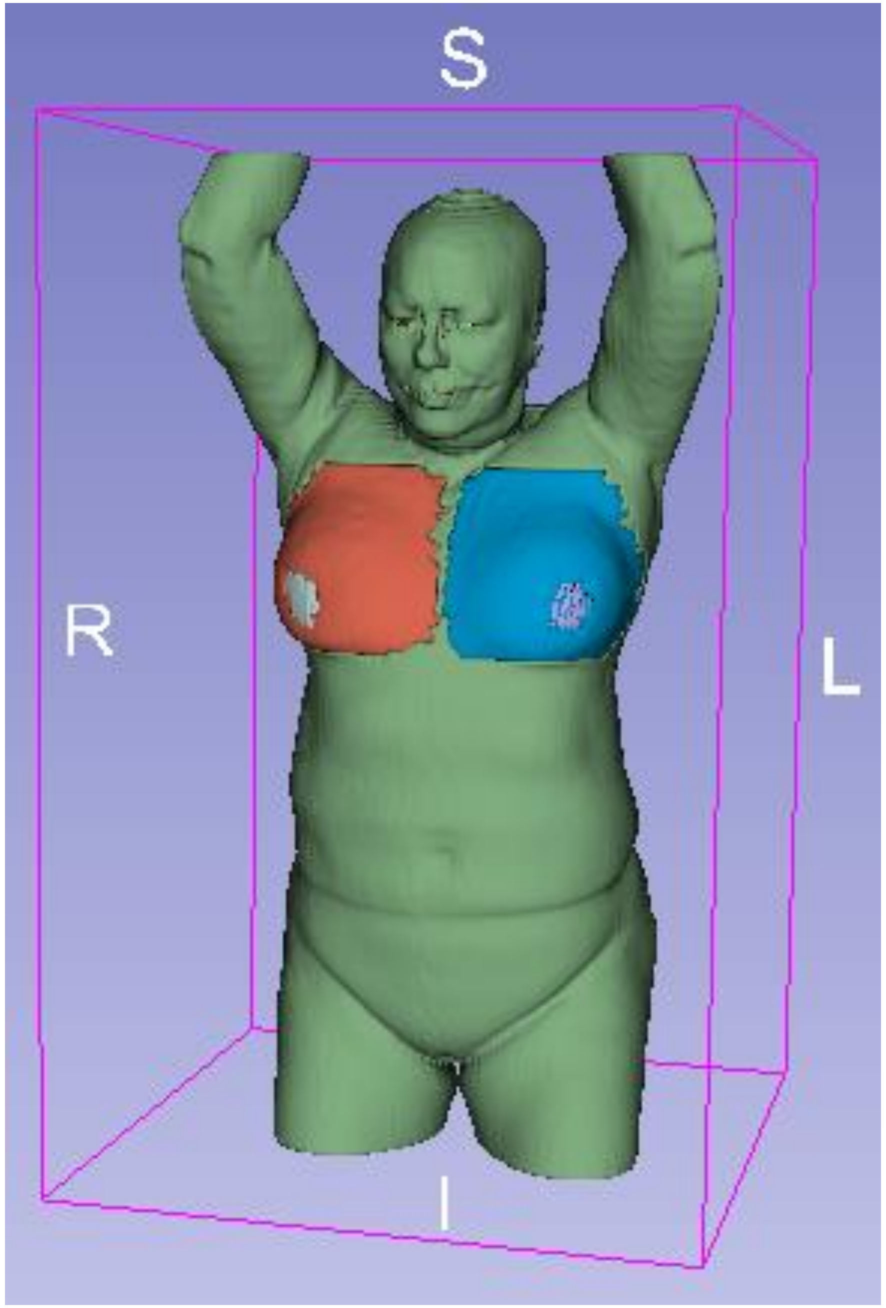

Fig. 3 - Patient-specific Phantom segmented from clinical images (obtained in Slicer).

RESULTS AND DISCUSSION

$$Relative\ Difference\ (\%) = \frac{SAF_{\mathrm{ICRP-AF.}} - SAF_{MARIA}}{SAF_{\mathrm{ICRP-AF.}}} \times 100$$

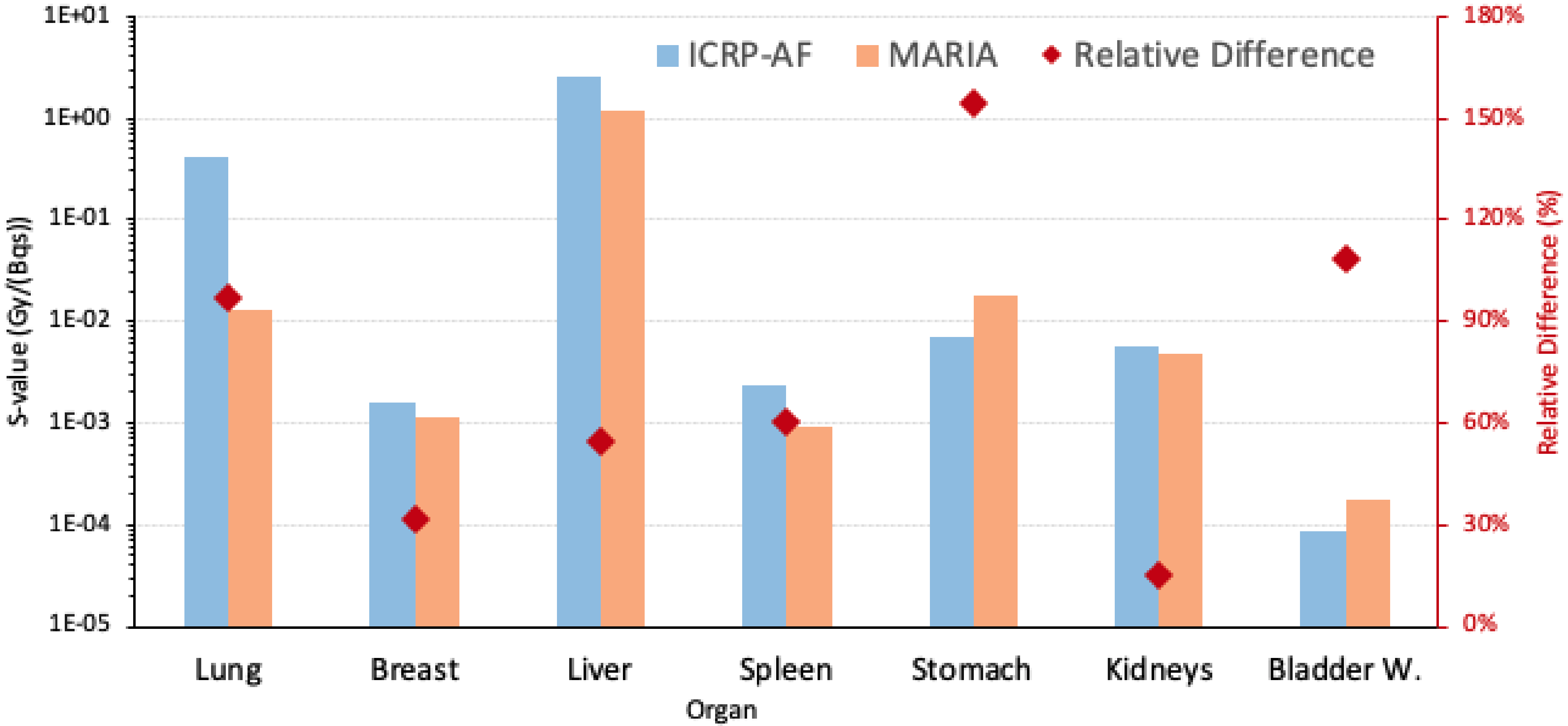

Fig. 4 – S-value in the Lung, Breast, Liver, Spleen, Stomach, Kidneys and Bladder Wall, with Liver as source organ, calculated in the ICRP-AF, MARIA and their relative difference. The emissions of ^{177}Lu were considered, namely beta, internal conversion and auger electrons, as well as X-ray and gamma photons.

S-value mean relative difference: **74%**

- As expected, the differences obtained between the two phantoms reflect the unequal patient individual anatomy, e.g. MARIA has much higher liver mass than ICRP-AF.

CONCLUSION

- The PSP created (MARIA) is considered validated, by comparison of calculated S-values to ICRP-AF.
- The developed Pipeline is efficient, versatile and user-friendly, able to work with any CT image or labelmap.

  Home PC → Pipeline runs in ~ 7 min for 25 million voxel phantom ➡ Efficient for research!

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Tumor Heterogeneity

Interpatient Variability

Heterogenous radiopharmaceutical distribution in tumor

Unpredictable Therapeutic Index and Clinical Outcome

Commitment to

Image-based

Personalized Dosimetry

Thank you for your attention!

ACKNOWLEDGEMENTS

- Fundação para a Ciência e Tecnologia (FCT) and European Social Fund for PhD grant no. 2020.05908.BD.

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- Authors and Institutions:

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SUMPPLEMENTARY SLIDES

^{177}Lu emissions [ICRP Publication nº 109, 2007]

Emitted Particle	Energy (eV)	Yield (/nt)
Beta	133300	1
IC	87370	0.1548
Auger	1014	1.117
X-ray	2576	1.374
Gamma	175000	0.1803

FUTURE WORK

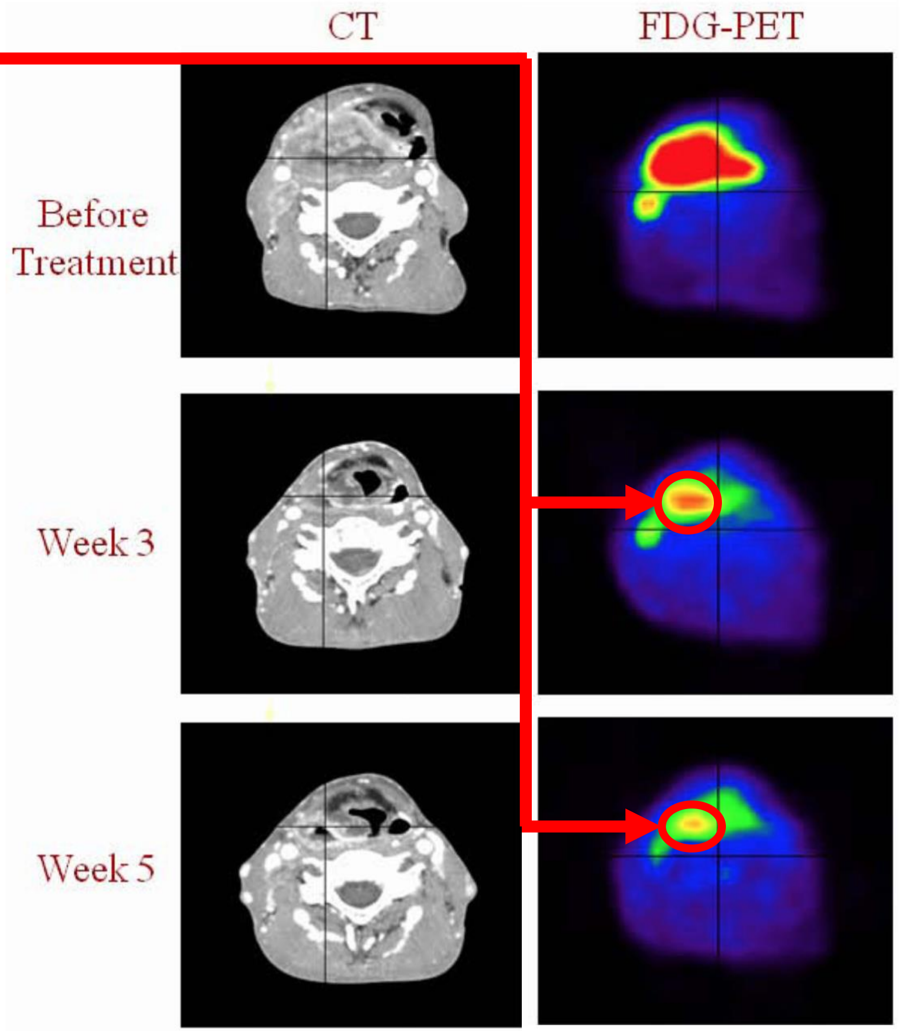
Segmentation of clinical PET-CT images.

$$\textbf{Therapeutic Index (TI)} = \frac{\textit{Voxel Intensity}_{before\ treatment}}{\textit{Voxel Intensity}_{after\ treatment}}$$

- Patient-specific Voxel Phantom: MC simulations using PENELOPE

Identification of tumor areas depicting TI inhomogeneities (i.e. phenotypes).

Correlate dose in tumor phenotypes to therapy outcome observed in clinical images



Example of PET-CT images acquired before and after treatment. Bentzen SM et al. Semin Radiat Oncol 2011;21:101–10.

METHODS

- Pre-treatment CT images and 24h post-treatment SPECT images segmented using state-of-the-art specialized software, i.e. Pinnacle TPS and Slicer, respectively.
- Automatic, semi-automatic and manual segmentation methods employed.

MC Simulations

- Pipeline developed using data science methods to create simulation voxel phantom.
- MC simulations performed using penEasy2020/PENELOPE2018.
- Specific Absorbed Fractions (SAF) andS-value calculated in ICRP-AF and segmented phantom (MARIA).

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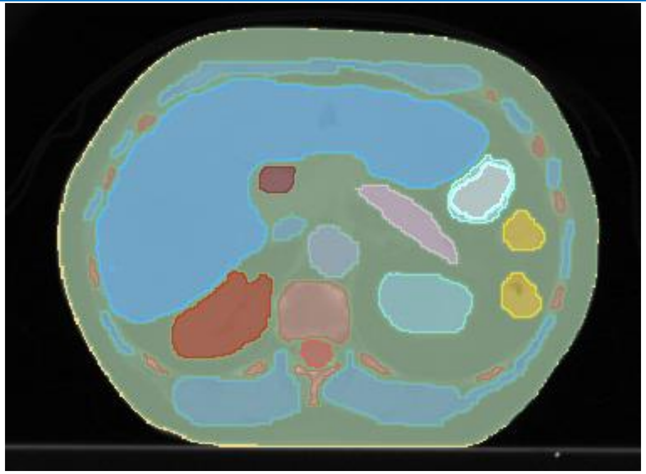

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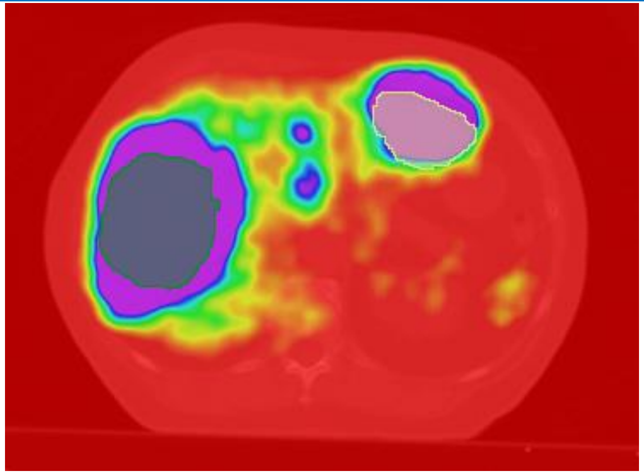

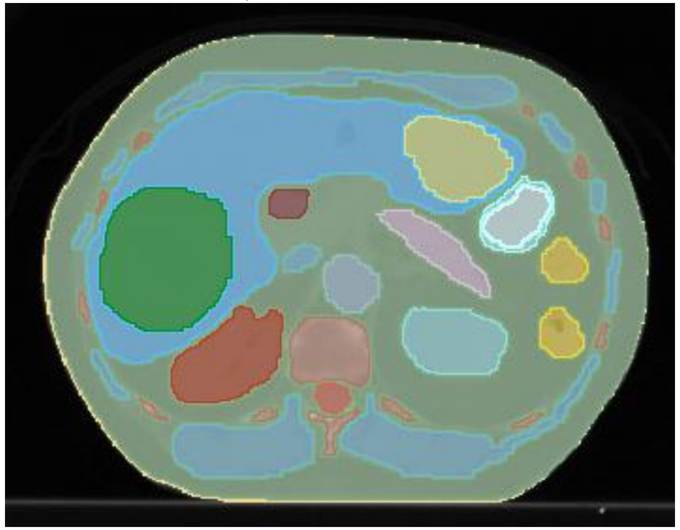

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