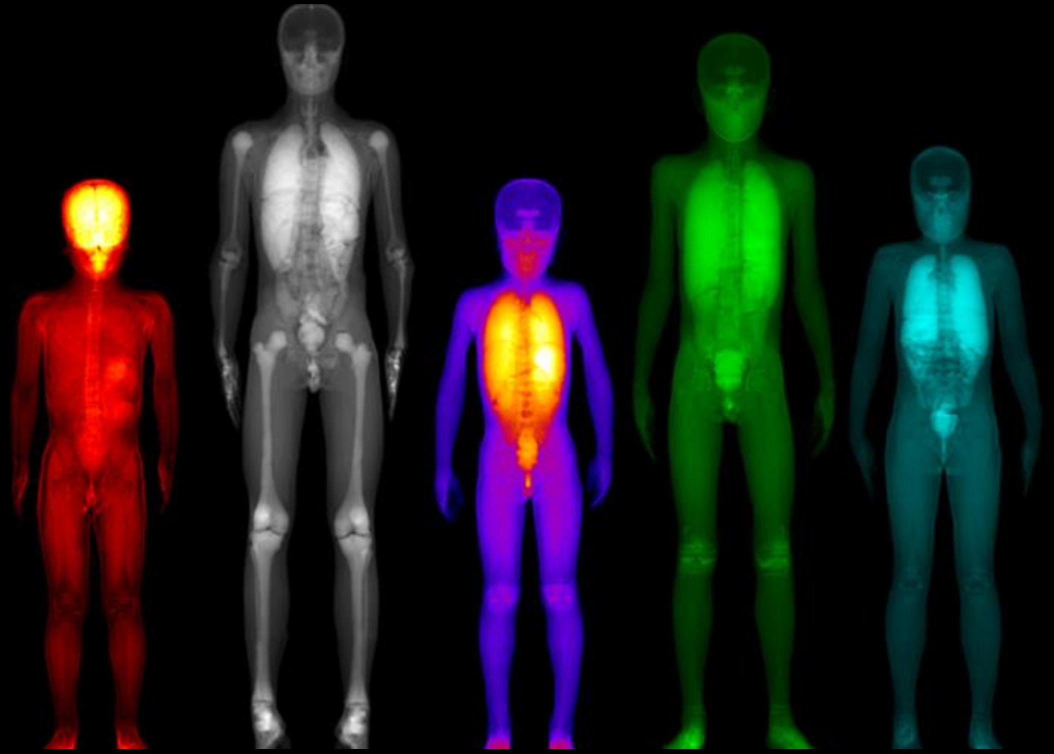
# The role of HPC technologies today

PediDose
A pediatric simulated dosimetry platform for clinical use

BIOEMTECH



**Panagiotis Papadimitroulas**
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Project Director & Co-Founder
BIOEMTECH

EURO Greece

4 EuroHPC

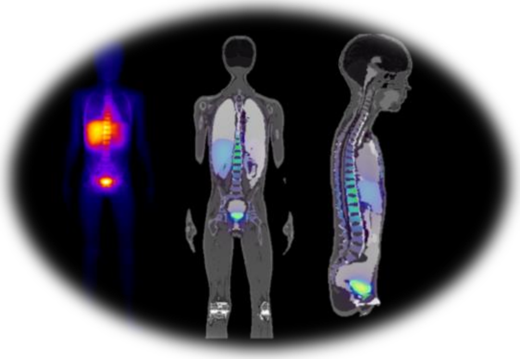
**EuroCC@Greece / HPC training for consultants of the EEN**
*Athens, 17.06.2022*

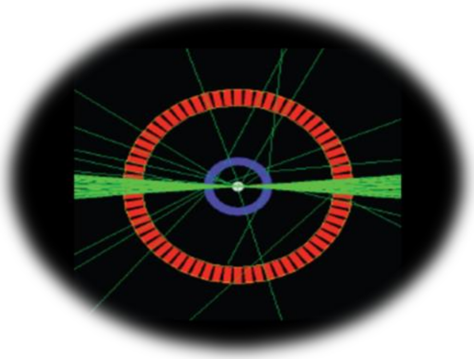
# Background (a bit of history…)

BIOEMTECH

- 2003-2009: BSc in Applied Physics (NTUA)
- 2009-2011: MSc in Medical Physics (UPAT)
- 2011-2015: PhD in Medical Physics (UPAT)
- 2013-Today: Co-founder & Project Director (BIOEMTECH)

*Evaluation of Diagnostic, Therapeutic and Dosimetry Protocols in Nuclear Medicine, with the Development of Computational Models and the Use of Monte Carlo Simulations*



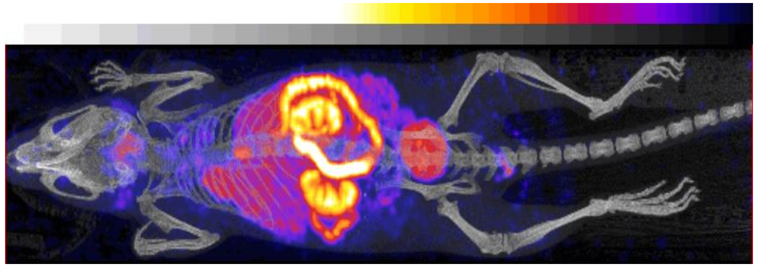


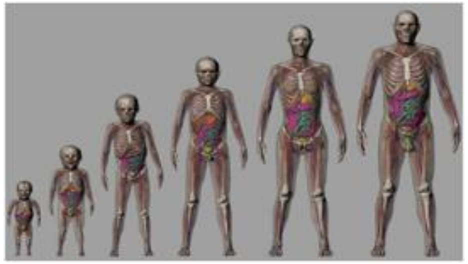
# BIOEMTECH activities

**BIOEMTECH** develops and offers innovative solutions in pharmaceutical, medical physics and biotechnology research.

We focus on **molecular imaging, dosimetry & biomedical engineering**:

- ✓ Design and construction of low-cost benchtop imaging devices
- ✓ Performance of preclinical imaging services in our imaging platform
- ✓ Computational solutions using MC simulations & AI techniques





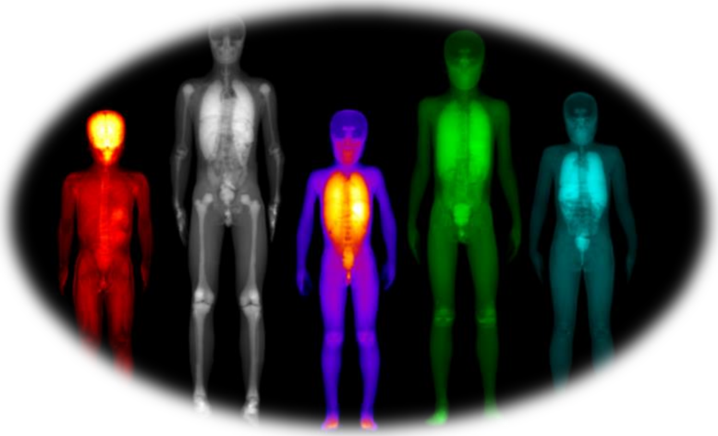
# PediDose - Overview

Call: FF4EuroHPC Call-1

Start date: June 2021

Duration: 15 months

- **BIOEMTECH** (Domain expert & End-user) – Coordinator
  SME in the field of Biotechnology
- **IKNOWHOW** (End-user)
  SME in the field of Medical Software
- **GRNET** (HPC expert)
  Greek National Infrastructures for Research and Technology



* **YOTTA** (HPC provider) – Subcontractor

# The problem…

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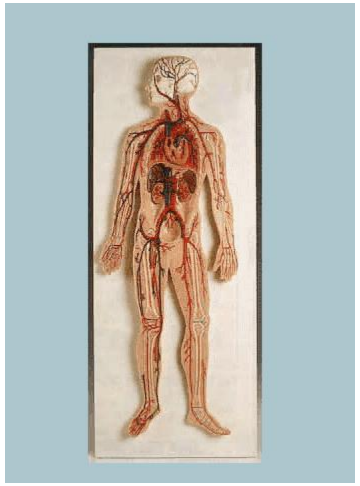
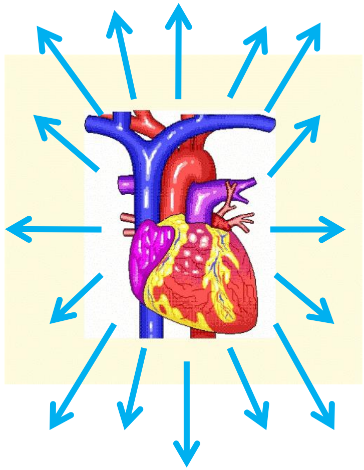
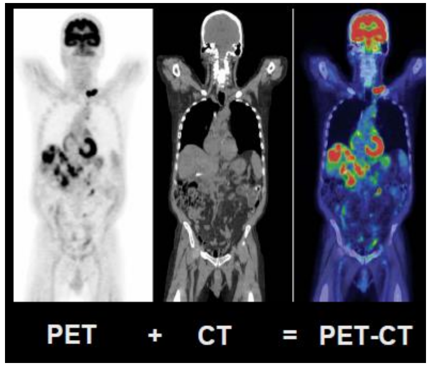
- ✓ Nuclear Medicine procedures involve radioactivity.
- ✓ Ionizing radiation deposits energy in human body.
- ✓ Absorbed dose from ionizing radiation can lead to cancer.
- ✓ Pediatric patients are higher radiosensitive than  adults.
- ✓ No way to measure the absorbed dose in each organ of the body(internal dosimetry).
- ✓ Estimations are based on the acquired images.
- ✓ Pre-calculations with MC simulations based on standard models.
- ✓ Optimization of pediatric dosimetry based on personalized patient’s characteristics







# Current solution…

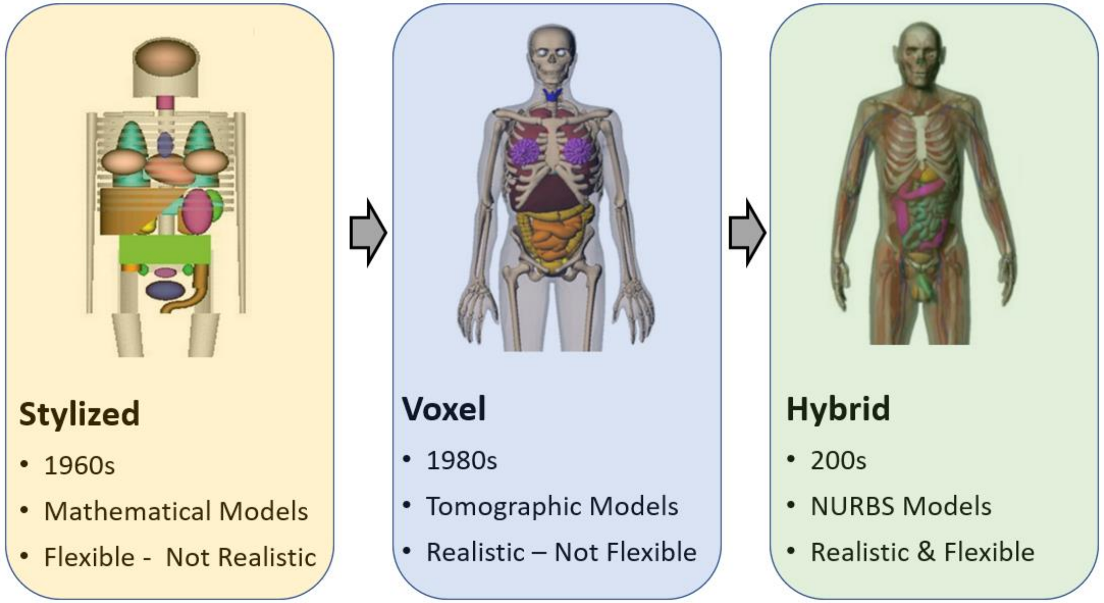
**“Monte Carlo method is a statistical approach to solve deterministic problems and define a specified system using random number generators”**

## Current Solution

✓ >40 years MC techniques are applied in Medical Physics.

✓ MC simulations serve as ground truth for dosimetry.

✓ Calculations of doses per organ from a specific adult phantom (rescaling for pediatrics)



# Our idea…

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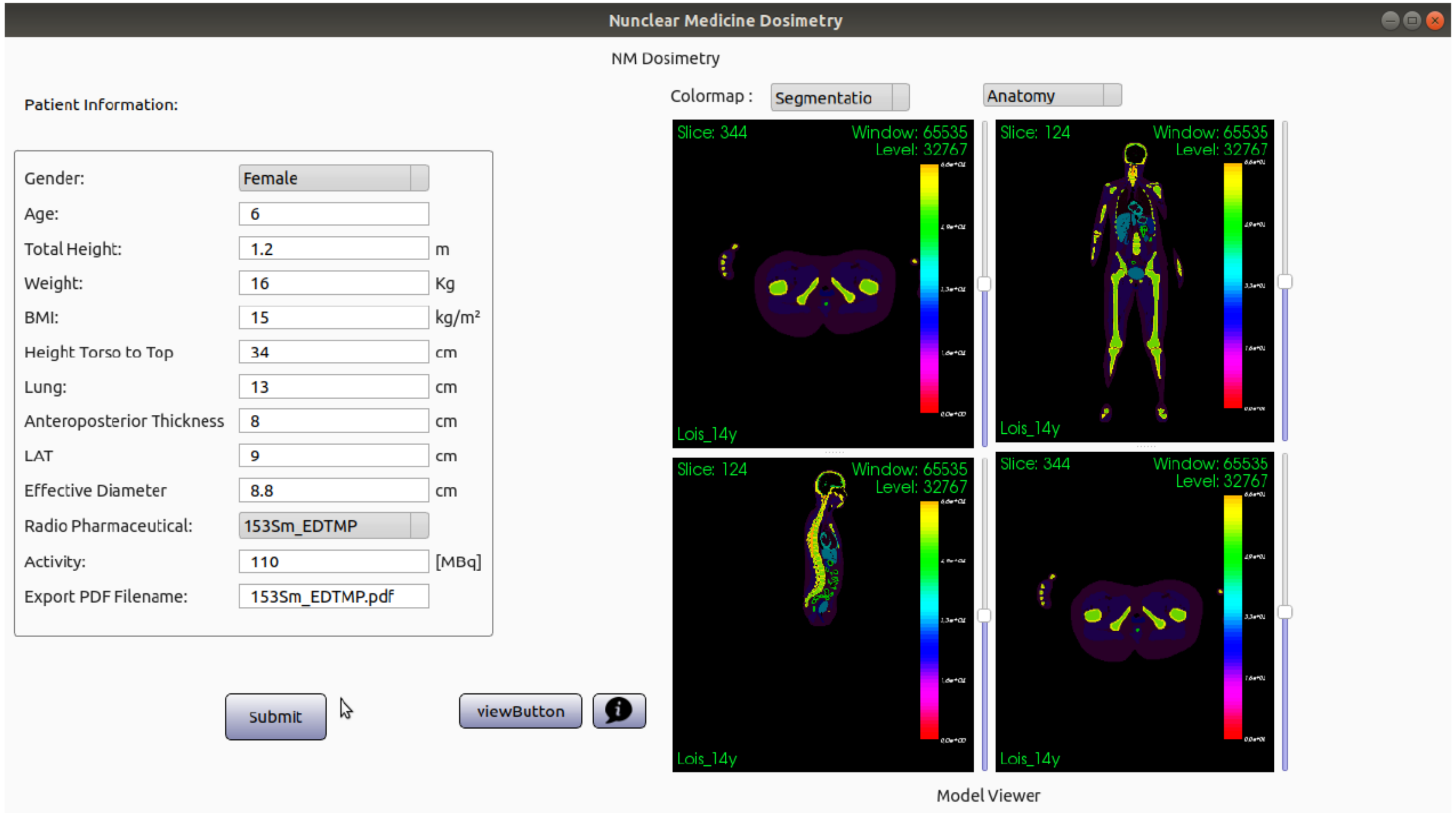
- Develop a new product – clinical software tool – assist clinicians
- Personalized pediatric dosimetry prediction
- Based on a dosimetry methodology previously developed (H2020-MSCA-RISE ERROR project



# Business Opportunity

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- ✓ **BIOEMTECH** currently has 3 preclinical imaging devices (HW department).
- ✓ Extend and grow in medical SW market.
- ✓ Exploit expertise and create product based on developed methodologies
- ✓ Autonomous SW Department within the company.
- ✓ **IKH** enhances its medical SW, going beyond imaging to dosimetry.
- ✓ No current solution for personalized internal dosimetry (only rough estimations exist).
- ✓ Exploiting AI will provide a competitive advantage to existed dosimetry tools (OLINDA/EXM, RadCalc etc).

# Experiment Approach & Expected Outcome

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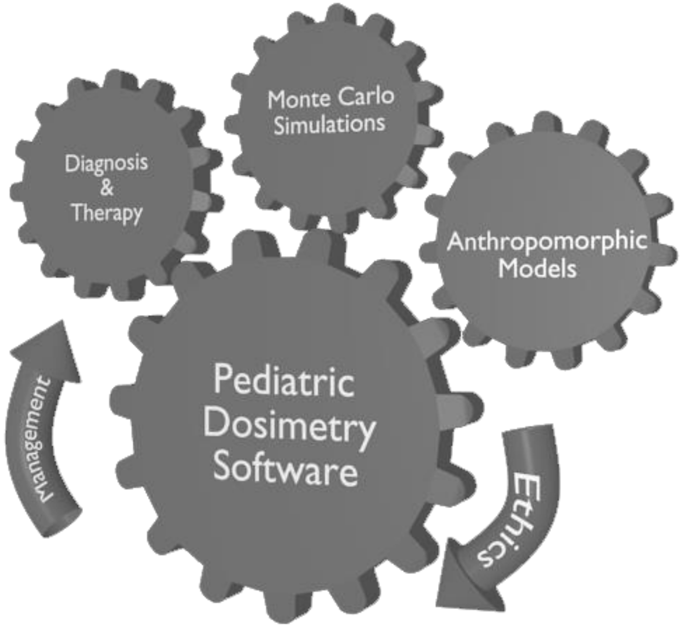
## Goal

To exploit advanced computational techniques (MC simulations, anthropomorphic computational phantoms and AI techniques) for the development of a realistic, simulated dosimetry database.

## Outcome

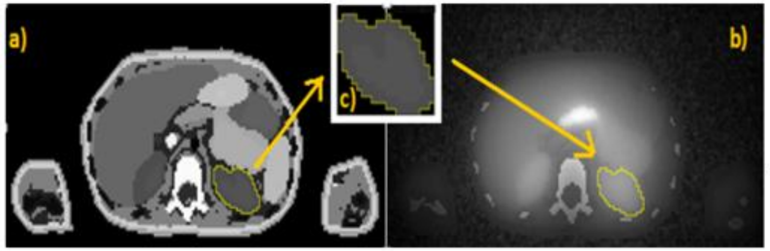
A novel software product (decision support) that will offer clinicians the possibility to assess internal dosimetry and optimize Nuclear Medical (NM) imaging clinical protocols in terms of personalized dosimetry.

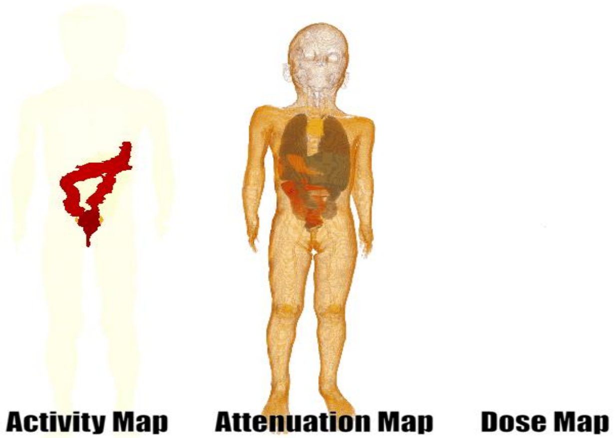


# Experiment Approach (I)

- Use of data for the biodistribution of specific radiopharmaceuticals
- Population of computational pediatric models
- Dosimetry MC simulations
- Creation of the simulated database
- ML techniques for prediction model

- Software development
- Clinical evaluation of the product
- Commercialization



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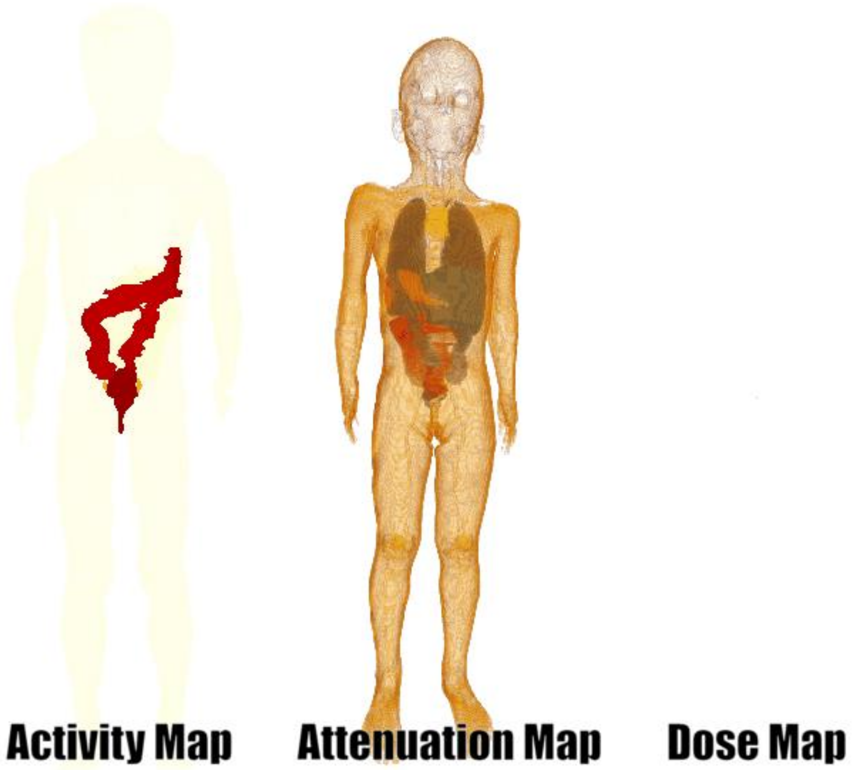
- <u>Large number & Intensive simulations:</u>
  - There is ~28 pediatric models (2-15 years old)
  - Test at least 5 most common radiopharmaceuticals
  - To have an accurate dosimetry assessment, 4 time points will be used for each radiopharmaceutical.

  **~500 different simulations**.




- <u>Machine Learning training models:</u>
  - Training of the models will be tested in HPC to investigate their speed up

# Experiment Approach (II)

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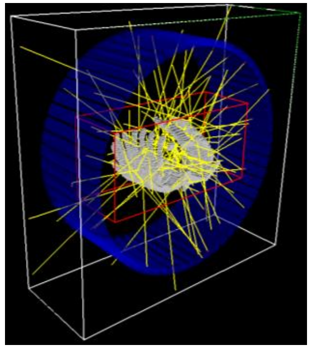
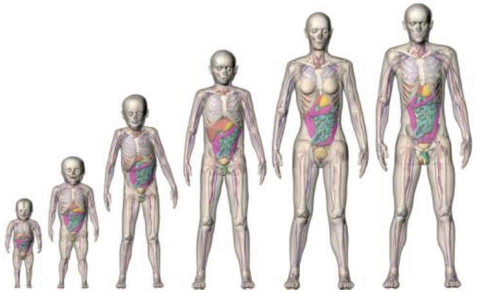
## All the appropriate tools and technology exist

- ✓ MC tools well validated (high accuracy)

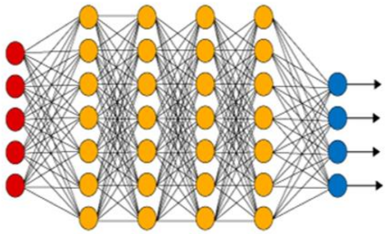


- ✓ Advanced computational anthropomorphic models



- ✓ HPC resources (highly demanding in computational time)

- ✓ AI techniques for prediction models



# Experiment Approach (III)

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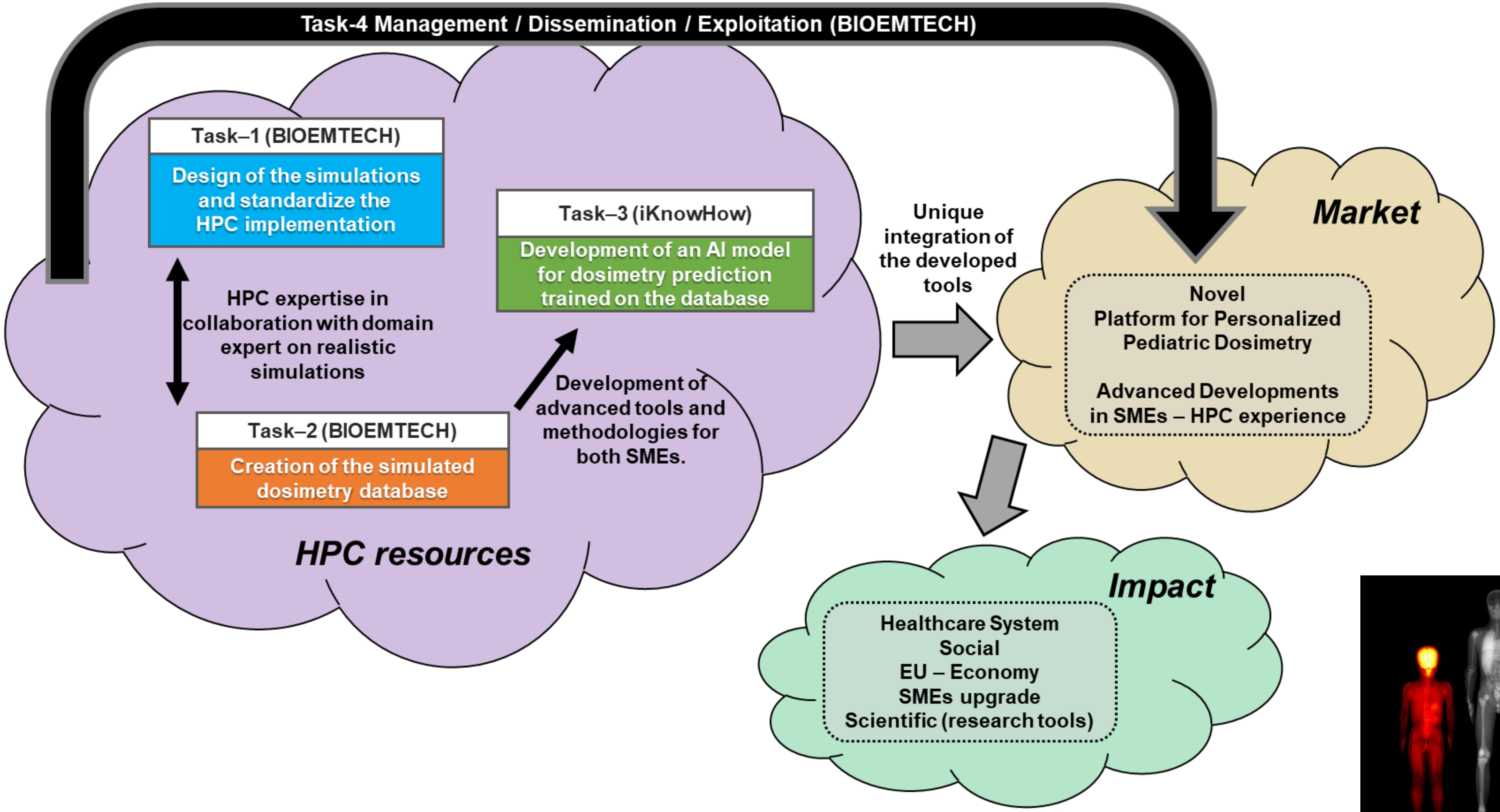


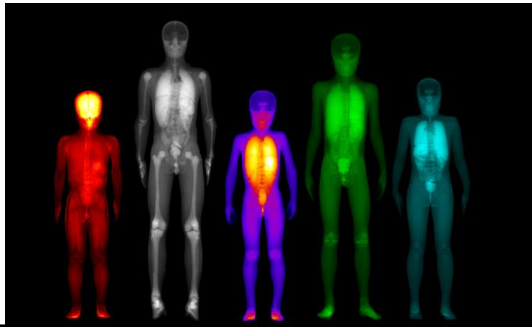

# Main Achievements

- ✓ Standardized & benchmarked the execution of GATE MC simulations in the HPC
- ✓ Completed all the simulations (5 radiopharmaceuticals for a set of 28 pediatric computational models).
- ✓ Creation of the database, incorporating the completed simulated datasets.
- ✓ ML predictive models were developed, estimating the absorbed doses for each new patient.
- ✓ Dissemination activities:
  Presentations, video, poster, logo, conference participation, social media

# Simulated Dosimetry .db

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## “Creation of the simulated Database”

| No. (#) | Age (y) | Gender | Weight (Kg) | Torso to top (cm) | Total height (m) | BMI (kg/m²) | Lung (cm) |
|---|---|---|---|---|---|---|---|
| Phantom-01 | 14 | Male | 50.4 | 91.8 | 1.7 | 17.6 | 11.3 |
| Phantom-02 | 5 | Female | 17.7 | 62.5 | 1.09 | 14.9 | 8.6 |
| Phantom-03 | 6 | Male | 18.6 | 66.4 | 1.16 | 13.8 | 8.3 |
| Phantom-04 | 8 | Female | 29.64 | 74 | 1.36 | 16 | 9.2 |
| Phantom-05 | 8 | Male | 25.6 | 79.6 | 1.37 | 13.6 | 9.6 |
| Phantom-06 | 11 | Female | 34 | 83.3 | 1.49 | 15.3 | 9.6 |
| Phantom-07 | 17.2 | Male | 86.2 | 49.7 | 1.83 | 25.7 | 12.6 |
| Phantom-08 | 15 | Male | 58 | 46.6 | 1.66 | 21 | 11.2 |
| Phantom-09 | 2.1 | Female | 12.2 | 24.2 | 0.86 | 16.5 | 7.1 |
| Phantom-10 | 2.8 | Female | 14.9 | 28 | 0.92 | 17.6 | 7.7 |
| Phantom-11 | 3.3 | Female | 13.8 | 28.1 | 0.93 | 16 | 7.2 |
| Phantom-12 | 5 | Female | 19.9 | 32 | 1.13 | 15.6 | 8.7 |
| Phantom-13 | 5.2 | Female | 15.3 | 30.8 | 1.07 | 13.4 | 7.4 |
| Phantom-14 | 13.8 | Male | 67.4 | 45.8 | 1.79 | 21 | 12 |
| Phantom-15 | 9.8 | Female | 40.7 | 35 | 1.27 | 25.2 | 9.6 |
| Phantom-16 | 10 | Female | 33 | 37 | 1.39 | 17.1 | 10 |

| | | Dose Rates (Gy/Mbq/sec) – Tc-99m | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Phantoms | Time(h) | Target organs of interest | | | | | | | | | | | | | |
| Phantom 1 | | Brain | Bladder | Urethra | Heart | Blood | Kidneys | Liver | Lungs | Salivary | Eyes | Intestines | Intestines’ Air | Pancreas | Spleen |
| Phantom 1 | 0 | 1.05E-10 | 1.30E-10 | 3.87E-10 | 1.51E-10 | 1.65E-10 | 1.14E-09 | 2.67E-10 | 1.35E-10 | 1.03E-10 | 9.28E-11 | 1.92E-10 | 8.24E-11 | 3.36E-10 | 3.19E-10 |
| Phantom 1 | 1.42 | 1.01E-10 | 1.92E-10 | 2.95E-10 | 1.29E-10 | 1.42E-10 | 7.85E-10 | 1.96E-10 | 1.38E-10 | 1.15E-10 | 1.12E-10 | 1.58E-10 | 7.00E-11 | 2.47E-10 | 2.33E-10 |
| Phantom 1 | 4.11 | 1.02E-10 | 2.75E-10 | 1.91E-10 | 1.14E-10 | 1.24E-10 | 3.35E-10 | 1.26E-10 | 1.42E-10 | 1.26E-10 | 1.27E-10 | 1.31E-10 | 6.11E-11 | 1.53E-10 | 1.40E-10 |
| Phantom 1 | 20.2 | 1.06E-10 | 1.50E-10 | 1.32E-10 | 1.13E-10 | 1.18E-10 | 1.38E-10 | 1.02E-10 | 1.46E-10 | 1.33E-10 | 1.33E-10 | 1.11E-10 | 5.11E-11 | 1.18E-10 | 1.04E-10 |
| | | | | | | | | | | | | | | | |
| Phantom 2 | 0 | 2.56E-10 | 2.87E-10 | 2.80E-10 | 3.17E-10 | 3.35E-10 | 2.11E-09 | 5.19E-10 | | 2.88E-10 | 2.79E-10 | 4.05E-10 | 2.35E-10 | 5.47E-10 | 5.24E-10 |
| Phantom 2 | 1.42 | 2.66E-10 | 4.80E-10 | 3.10E-10 | 2.90E-10 | 3.06E-10 | 1.48E-09 | 4.06E-10 | | 3.51E-10 | 3.91E-10 | 3.39E-10 | 1.98E-10 | 4.18E-10 | 4.32E-10 |
| Phantom 2 | 4.11 | 2.81E-10 | 7.44E-10 | 4.00E-10 | 2.72E-10 | 2.85E-10 | 6.83E-10 | 2.92E-10 | | 3.97E-10 | 4.60E-10 | 2.80E-10 | 1.55E-10 | 2.93E-10 | 3.24E-10 |
| Phantom 2 | 20.2 | 2.93E-10 | 3.15E-10 | 2.75E-10 | 2.72E-10 | 2.80E-10 | 3.28E-10 | 2.53E-10 | | 4.15E-10 | 4.83E-10 | 2.39E-10 | 1.34E-10 | 2.49E-10 | 2.83E-10 |
| | | | | | | | | | | | | | | | |
| Phantom 3 | 0 | 2.44E-10 | 2.50E-10 | 5.68E-10 | 2.75E-10 | 3.32E-10 | 1.86E-09 | 4.52E-10 | 2.70E-10 | 2.77E-10 | 2.49E-10 | 4.21E-10 | 2.31E-10 | 6.46E-10 | 5.11E-10 |
| Phantom 3 | 1.42 | 2.60E-10 | 4.15E-10 | 4.80E-10 | 2.31E-10 | 3.08E-10 | 1.31E-09 | 3.40E-10 | 2.81E-10 | 3.46E-10 | 3.37E-10 | 3.41E-10 | 1.95E-10 | 4.80E-10 | 3.87E-10 |
| Phantom 3 | 4.11 | 2.77E-10 | 6.54E-10 | 4.10E-10 | 2.07E-10 | 2.83E-10 | 5.99E-10 | 2.39E-10 | 2.93E-10 | 3.94E-10 | 3.94E-10 | 2.64E-10 | 1.57E-10 | 3.05E-10 | 2.57E-10 |
| Phantom 3 | 20.2 | 2.89E-10 | 2.50E-10 | 2.65E-10 | 2.07E-10 | 2.72E-10 | 2.87E-10 | 2.06E-10 | 2.99E-10 | 4.13E-10 | 4.14E-10 | 2.11E-10 | 1.30E-10 | 2.38E-10 | 2.08E-10 |
| | | | | | | | | | | | | | | | |
| Phantom 4 | 0 | 1.67E-10 | 1.99E-10 | 7.51E-10 | 2.32E-10 | 2.32E-10 | 1.61E-09 | 3.59E-10 | 2.09E-10 | 1.67E-10 | 1.53E-10 | 3.06E-10 | 1.25E-10 | 5.18E-10 | 4.46E-10 |
| Phantom 4 | 1.42 | 1.74E-10 | 2.79E-10 | 5.66E-10 | 2.05E-10 | 2.12E-10 | 1.11E-09 | 2.71E-10 | 2.21E-10 | 1.84E-10 | 1.94E-10 | 2.35E-10 | 1.01E-10 | 3.74E-10 | 3.34E-10 |
| Phantom 4 | 4.11 | 1.83E-10 | 3.83E-10 | 3.43E-10 | 1.84E-10 | 1.96E-10 | 4.72E-10 | 1.85E-10 | 2.26E-10 | 2.01E-10 | 2.22E-10 | 1.74E-10 | 7.46E-11 | 2.22E-10 | 2.10E-10 |
| Phantom 4 | 20.2 | 1.90E-10 | 2.36E-10 | 2.33E-10 | 1.80E-10 | 1.93E-10 | 1.96E-10 | 1.55E-10 | 2.31E-10 | 2.11E-10 | 2.34E-10 | 1.44E-10 | 6.21E-11 | 1.64E-10 | 1.62E-10 |
| | | | | | | | | | | | | | | | |
| Phantom 5 | 0 | 1.88E-10 | 1.96E-10 | 1.66E-10 | 2.16E-10 | 2.50E-10 | 1.56E-09 | 3.57E-10 | 2.05E-10 | 1.98E-10 | 1.94E-10 | 2.92E-10 | 1.82E-10 | 4.42E-10 | 4.08E-10 |
| Phantom 5 | 1.42 | 2.01E-10 | 3.21E-10 | 1.54E-10 | 1.85E-10 | 2.25E-10 | 1.09E-09 | 2.68E-10 | 2.16E-10 | 2.38E-10 | 2.72E-10 | 2.64E-10 | 1.66E-10 | 3.58E-10 | 2.98E-10 |
| Phantom 5 | 4.11 | 2.16E-10 | 4.94E-10 | 1.76E-10 | 1.69E-10 | 2.05E-10 | 4.99E-10 | 1.86E-10 | 2.22E-10 | 2.68E-10 | 3.21E-10 | 2.36E-10 | 1.46E-10 | 2.65E-10 | 1.85E-10 |
| Phantom 5 | 20.2 | 2.25E-10 | 2.18E-10 | 1.32E-10 | 1.71E-10 | 1.99E-10 | 2.37E-10 | 1.59E-10 | 2.29E-10 | 2.82E-10 | 3.37E-10 | 2.00E-10 | 1.30E-10 | 2.27E-10 | 1.44E-10 |

# Final SW product

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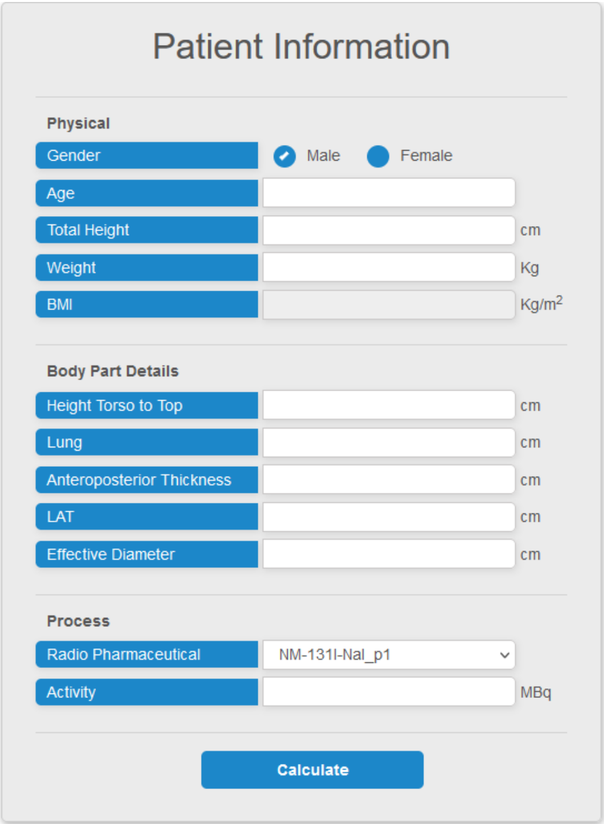
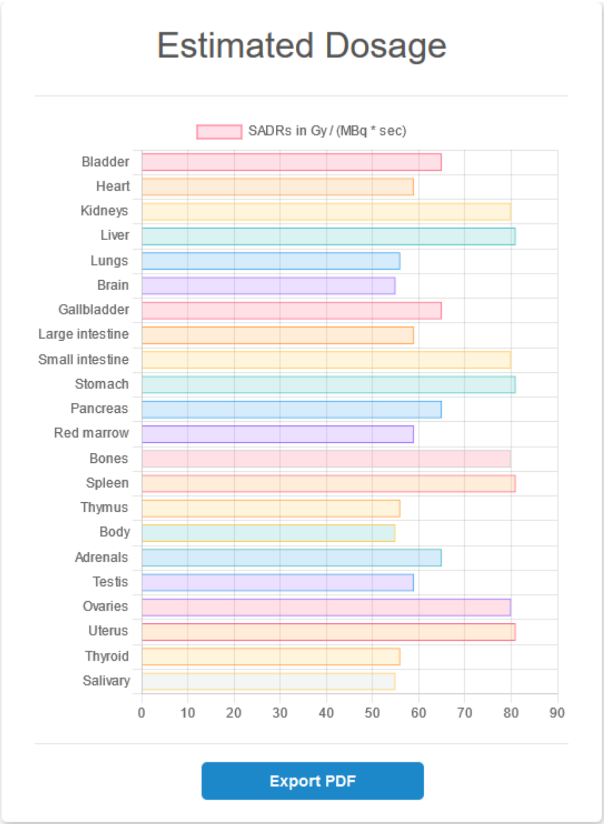
## “Dosimetry SW and AI model for dosimetry prediction”

- ✓ mysql database build in a Spring Boot (Java).
- ✓ ML prediction will is based on XGBoost (<8% average differences).
- ✓ A draft version of the SW has been developed.

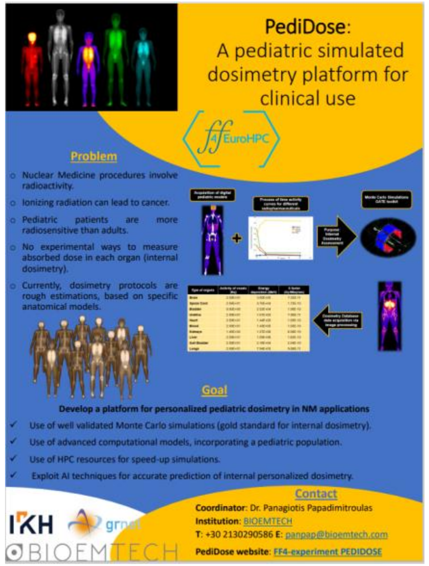


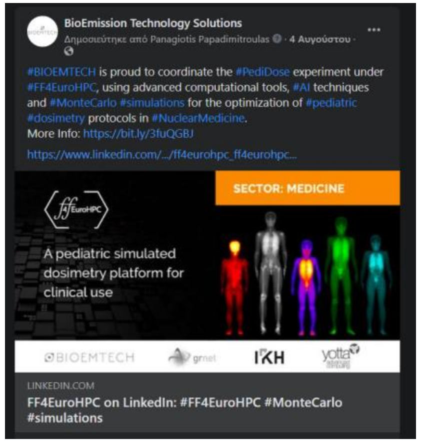



# Dissemination / Exploitation

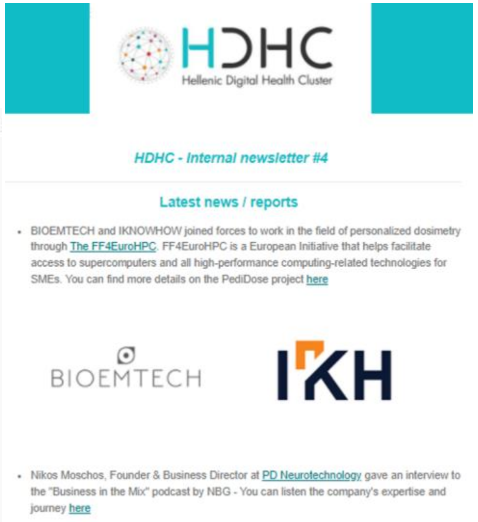
**Create awareness!!!**

- ✓5 general presentations of the experiment
- ✓1 video presentation in YouTube
- ✓2 abstract conferences MCMA & ECMP 2022
- ✓Social media presence (LinkedIn – Facebook)
- ✓HDHC cluster's Newsletter announcement
- ✓Lean canvas – KER table completed







# PediDose: Conference Abstracts

BIOEMTECH



## Exploitation of HPC for realistic pediatric dosimetry simulations using GATE

Georgios Savvidis[1], Konstantinos Chatzipapas[1] and Panagiotis Papadimitroulas[1,*]

[1]*BIOEMTECH, Mesogeion Av. 387, 15343, Athens, Greece*

**Introduction**

The objective of this research concerns the development of … estimation of absorbed dose rate at different … radiopharmaceuticals with clinically … Medicine (NM) procedures … (HPC) resources …

**Acknowledgements**

This project has received funding from the European High-Performance Computing Joint Undertaking Joint Undertaking (JU) under grant agreement No 951745. The JU receives support from the European Union's Horizon 2020 research and innovation programme and Germany, Italy, Slovenia, France, Spain. (Experiment 001 – PediDose).e

**Presented in MCMA 2022**

… Monte Carlo toolkit [2]. For … IT'IS [4]), with different anatomical … were simulated using $5x10^8$ primary events. Four … MDP, 123I-mIBG, … and 153Sm-EDTMP) were … specified activity distribution [5]. The radiation activity of each organ … data, at different time points (eg. 4 time points for Tc-99m was assumed: T=0h, … T=4.11h, T=20.2h), and used for the calculation of dose rate at the respective time points. Simulations were executed on YOTTA HPC centre, to accelerate their execution, having 112 parallel jobs running. YOTTA HPC consist of compute nodes that each one includes 28-Core Intel Broadwell CPUs and 512GB of memory. The "Dose actor" concept was utilized to measure the deposited energy per voxel, producing 112 dose maps for each case. They were then merged to a single file for minimizing uncertainty, during the calculation of the absorbed dose rate per organ (Figure 1a).

**Results**

## A Machine Learning approach for personalized dosimetry prediction in pediatric Nuclear Medicine applications

**Accepted in ECMP 2022**

Purpose

Personalized dosimetry in pediatric patients is of great interest, due to the higher radiosensitivity that children experience in comparison to adults. Artificial Intelligence developments in medical applications can serve towards the personalization of dosimetry protocols. The objective of this study is the design, development and evaluation of a machine learning model that predicts the dose rate per organ of interest in pediatric patients.

Material and Methods

A previously developed realistic dosimetry database was utilized. The database includes simulated absorbed dose rates of 27 different organs in a pediatric population of computational phantoms. The GATE MC toolkit (v9.1) was used for the dosimetry simulations of several commonly used radiopharmaceuticals. For this specific application 99mTc-MDP was considered, together with its specified activity distribution in 28 voxelized pediatric models (virtual patients), with different anatomical characteristics and varying age, gender, mass, height and organs' sizes. The radiation activity of each organ derived from clinical data, at different time points (4 time points for Tc-99m were assumed: T=0h, T=1.42h, T=4.11h, T=20.2h), and was used for the dosimetry assessment.
For the development of a dosimetry predictive model, the effectiveness of several machine learning regression algorithms (Random Forest Regressor, XGBoost Regressor, Gradient Boosting Regressor, Decision Tree Regressor, Support Vector Regressor, Ridge Regression & Linear Regression) has been investigated. The ML models were trained using 9 anthropometric features as input: Age, Gender, Weight, Height, BMI, Anteroposterior thickness, Lateral width, Lung size and Effective diameter. Single and multiple organ input-output models, based on each ML algorithm, were trained, and validated using the Leave One Out cross validation method.

# Challenges

## Challenges of the experiment

- <u>ML prediction models:</u>
  Larger simulated datasets (more pediatric computational models) are expected to provide more accurate results.

- <u>Development of the SW dosimetry tool:</u>
  Incorporate the developments in the current commercial software tool ®evorad (by IKH).

- <u>IPs definition between SMEs.</u>

- <u>Clinical evaluation of the SW:</u>
  Beta version of the SW is expected to be clinically evaluated.

# Next Steps

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- Integrate the ML model in the SW (GUI).
- Optimize the SW, incorporating visualisation features.
- Develop a beta version of the SW to be tested in clinical environment
- Definition of the IPs and a common Marketing Strategy plan.

# Benefits of FF4EuroHPC

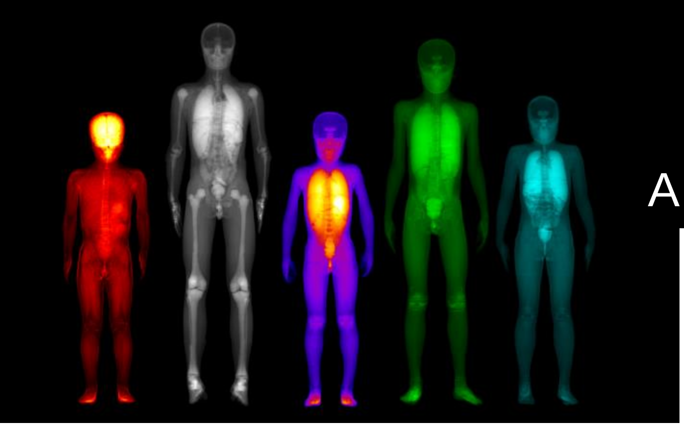
BIOEMTECH

- ✓New collaboration between 2 SMEs with a common goal to release a new product.
- ✓Complementary expertise of the partners to achieve the main objective.
  **BIOEMTECH**: Exploits its expertise in the field adopting HPC methodologies within the company and enters in the medical SW market.
  **GRNET**: HPC expert supports the execution of the simulations
  **IKH**: Enhances its customers, extending to the market of dosimetry SW.
- ✓HPC is expected to be a daily procedure for BIOEMTECH's activities including other applications.
- ✓Staff was trained on HPC procedures.
- ✓FF4EuroHPC provided the opportunity for new collaborations.
  Other proposals have been submitted by the partners.

# General Thoughts - Discussion

BIOEMTECH

- Years of thoughts for an in-house cluster
- HPC could be considered a daily tool for business
  - ✓ Developers’ daily use (like cloud services – Share files etc.)
  - ✓ Many tasks could benefit from HPC (clinical data processing, patients’ management, personalized medicine, simulations, AI)
- Industrial access on HPC???
  - Funds? National support – resources?
  - Training – internal/external expert?
- HPC providers’ awareness
  - Attract interest of SMEs / Start-ups
  - Enhance quality of results and daily workflow
  - Training & Dissemination activities (create awareness)
  - Industry should identify its needs!
  - Different sectors of applications

**The role of HPC technologies today**

PediDose

A pediatric simulated dosimetry platform for clinical use

# Thank you

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