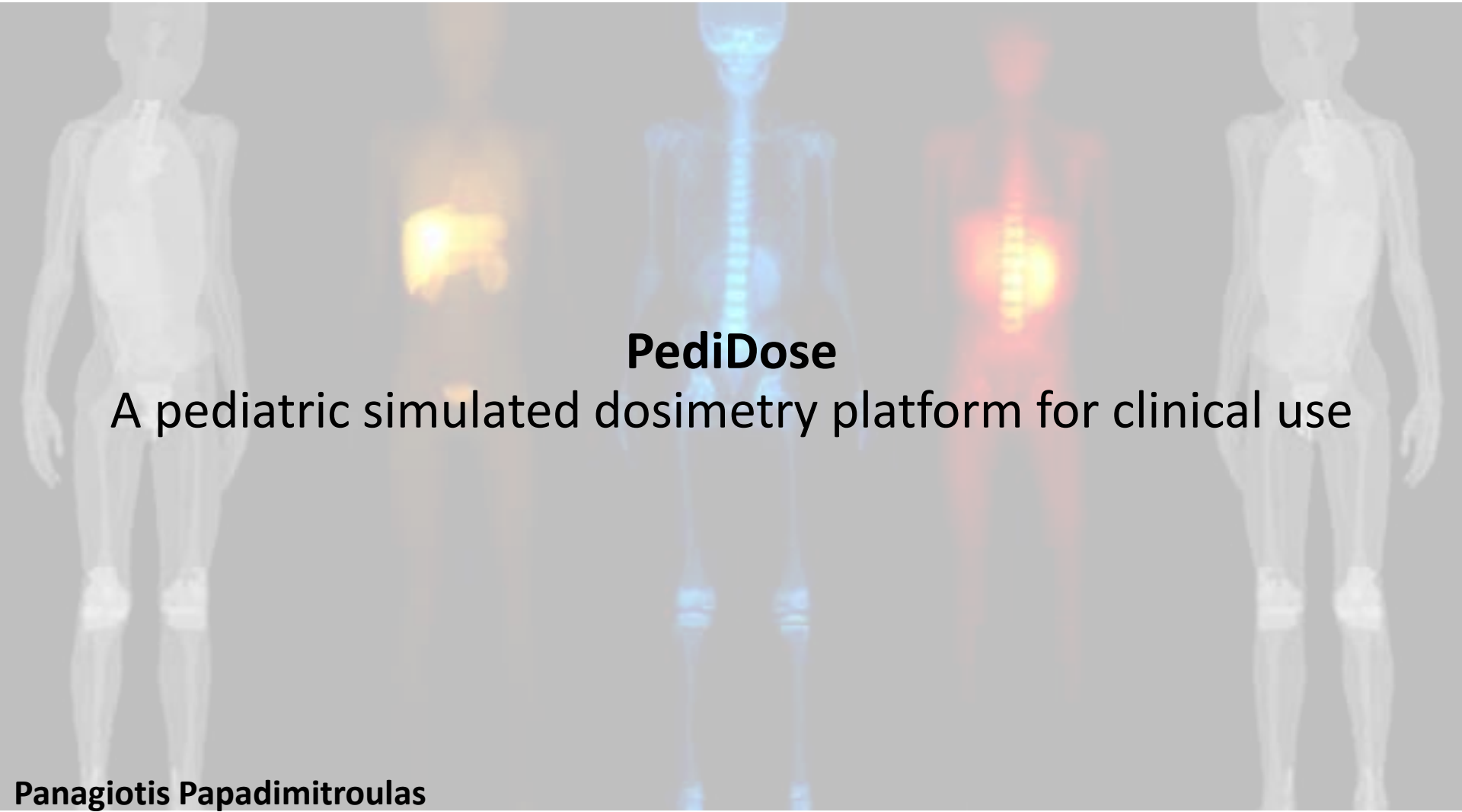




PediDose

A pediatric simulated dosimetry platform for clinical use

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PhD Medical Physics

Project Director @ BIOEMTECH

Athens, 17.06.2021

Background (a bit of history...)

- 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)

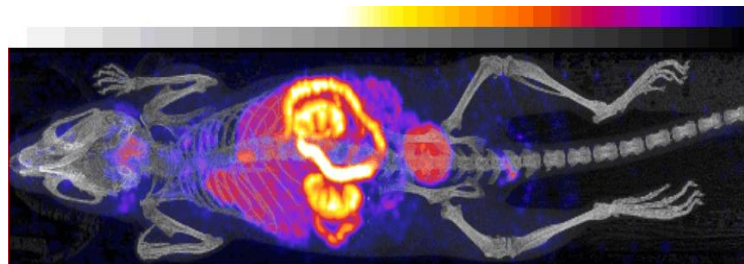
*Evaluation of Diagnostic, Therapeutic and Dosimetric Protocols in Nuclear Medicine,
with the Development of Computational Models and the Use of Monte Carlo Simulations*



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



Intensive Monte Carlo simulations for medical purposes using anthropomorphic computational models with the GATE toolkit



- ✓ 2011 – Access in MareNostrum HPC
(1 month visit)



- ✓ 2017 – Access in ARIS HPC
(Application for projects involving industry - Pilot Call)

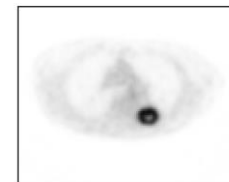


Figure 1: Clinical PET image

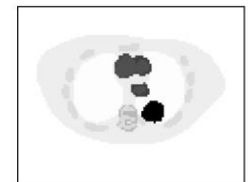


Figure 2: NCAT phantom, adapted to the clinical data with homogeneous tumor

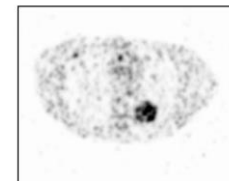


Figure 3: Simulated reconstructed image from the NCAT phantom in HPC (MareNostrum).

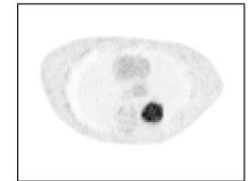


Figure 4: Simulated reconstructed image from the NCAT phantom in GateLab.

CANCEL-MC (1st Pilot Call)

MC: CANCEL (4th Production Call)

NuPeDose (5th Production Call)

- T. Kostou, P. Papadimitroulas, P. Papaconstadopoulos, D. Slobodan, J. Seuntjens, G.C. Kagadis
"Body Size-Specific Dose Estimates for pediatric chest, abdomen/pelvis and head CT scans"
 Physica Medica, 65:181-190, 2019, DOI: <https://doi.org/10.1016/j.ejmp.2019.08.020>
(Journal publication)
- P. Papadimitroulas, W.D. Erwin, V. Iliadou, T. Kostou, G. Loudos, G.C. Kagadis
"A personalized, Monte Carlo-based method for internal dosimetric evaluation of radiopharmaceuticals in children"
 Medical Physics, 45(8):3939-3949, 2018, DOI: <https://doi.org/10.1002/mp.13055>
(Journal publication)
- K. Chatzipapas, P. Papadimitroulas, M. Obeidat, K. McConnell, N. Kirby, G. Loudos, N. Papanikolaou, G.C. Kagadis
"Quantification of DNA double-strand breaks using Geant4-DNA"
 Medical Physics, 46(1):405-413, 2019, DOI: <https://doi.org/10.1002/mp.13290>
(Journal publication)
- T. Kostou, P. Papadimitroulas, G.C. Kagadis
"Moving forward to personalized pediatric dosimetry on computed tomography applications"
 Physica Medica, 52(Suppl 1), 2018, DOI: <https://doi.org/10.1016/j.ejmp.2018.06.372>
(Conference Proceedings - Poster)
- T. Kostou, P. Papadimitroulas, D. Mihailidis, G. Loudos, G.C. Kagadis,
"Pediatric chest, abdomen/pelvis and head computed tomography exams for personalized dosimetry using GATE Monte Carlo simulations"
 60th Annual Meeting & Exhibition of AAPM, 2018, <https://w3.aapm.org/meetings/2018AM/index.php>
(Conference Proceedings - Poster)
- T. Kostou, P. Papadimitroulas, D. Mihailidis, I. Kopsinis, G. Loudos, G.C. Kagadis,
"Optimizing pediatric CT dosimetry using Monte Carlo and Machine Learning techniques"
 60th Annual Meeting & Exhibition of AAPM, 2018, <https://w3.aapm.org/meetings/2018AM/index.php>
(Conference Proceedings - Oral)
- K. Chatzipapas, P. Papadimitroulas, N. Papanikolaou, N. Kirby, G.C. Kagadis
"Quantification of DNA Damage After an Ionizing Irradiation Session"
 Medical Physics, 46(6): E444-E444, 2019,
(Conference Proceedings - Poster)
- K. Χατζηπαπάς, Π. Παπαδημητρώλας, Γ. Λούντος, Ν. Παπανικολάου, Γ. Καγκάδης
"Ποσοτικοποίηση της βιολογικής βλάβης στο DNA από ιοντίζουσα ακτινοβολία, με χρήση ειδικής δοσιμετρικής τεχνικής και προσεγγίσεων Monte Carlo"
 24ο Διαπανεπιστημιακό συνέδριο ακτινολογίας, Πάτρα, 14-16 Νοεμβρίου 2019
(Conference Proceedings - Poster)

A pediatric simulated dosimetry platform for clinical use

New project / experiment

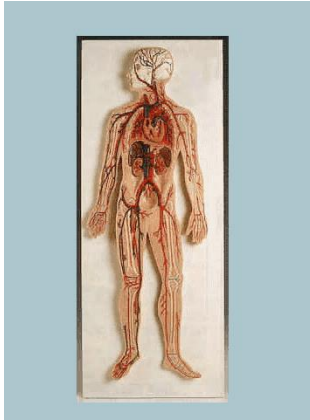
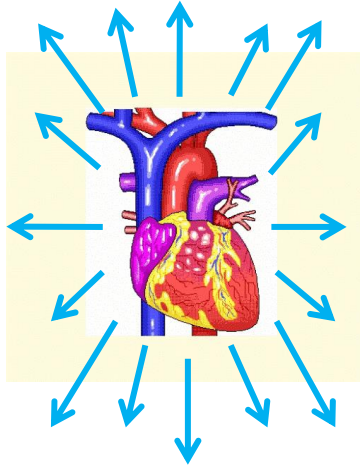
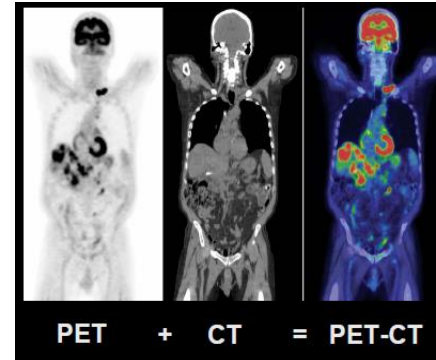
- Call: FF4EuroHPC Call-1
- Consortium: 2 SMEs & 1 HPC expert
BIOEMTECH – IKNOWHOW – GRNET
- Duration: 15 months (*just started*)



“Targets highest quality experiments involving innovative, agile SMEs and with work plans built around innovation targets arising from the use of advanced HPC services.”

“The key concept behind FF4EuroHPC is to demonstrate to SMEs how they can strongly benefit from the use of advanced HPC services and thereby take advantage of these innovative ICT solutions for business benefit.”

The problem...

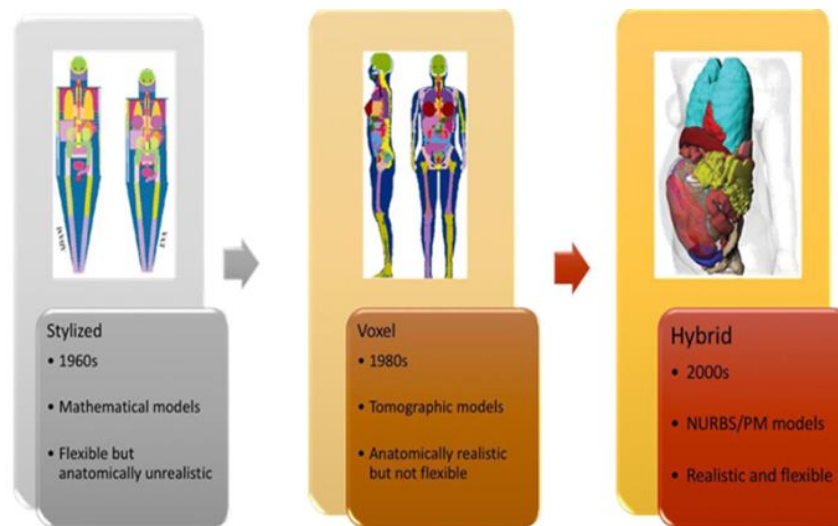


- Nuclear Medicine procedures involve radioactivity
- No way to measure the absorbed dose in each organ (internal dosimetry)
- Ionizing radiation can lead to cancer
- Estimations based on the images
- Pre-calculations with MC simulations based on standard models
- Pediatric patients are higher radiosensitive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



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

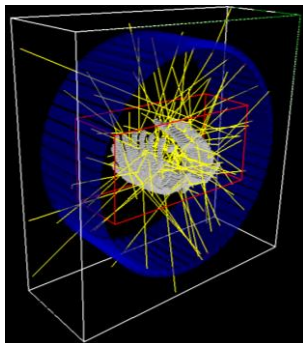
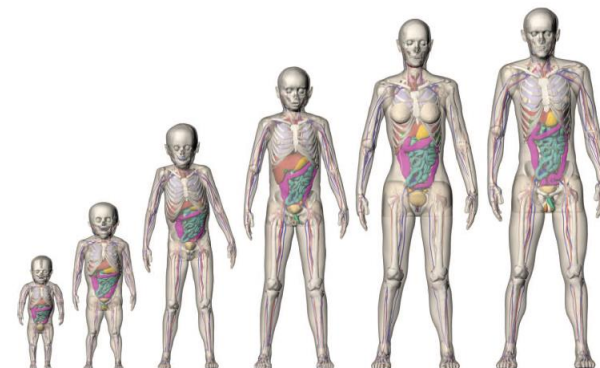
- MC techniques took their name from the Monte Carlo Casino.
- >40 years MC techniques are applied in Medical Physics.
- MC simulations serve as ground truth for dosimetry.
- Calculations of doses per/organ from a specific adult phantom (rescaling for pediatrics)



- Non IT experts
- Develop a new product – clinical software tool – assist clinicians
- Personalized pediatric dosimetry prediction
- Based on a methodology previously developed
(H2020-MSCA-RISE ERROR project (<https://error.upatras.gr/>))

All the appropriate tools and technology exist

- MC tools well validated (high accuracy)
- Advanced computational anthropomorphic models
- HPC resources (highly demanding in computational time)

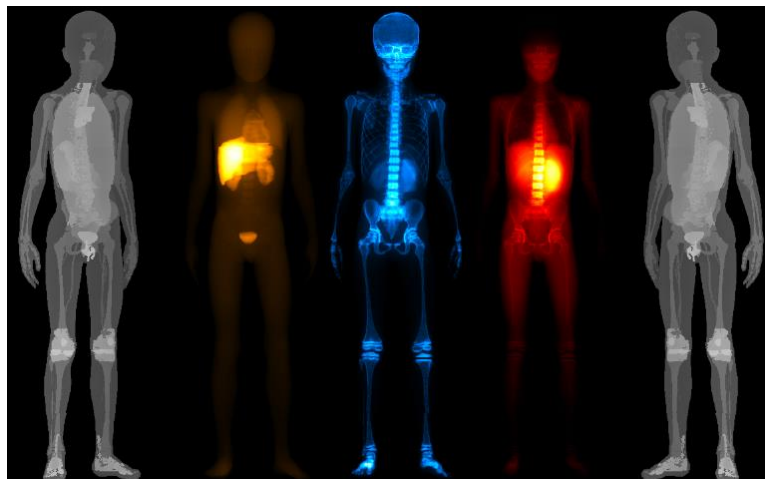
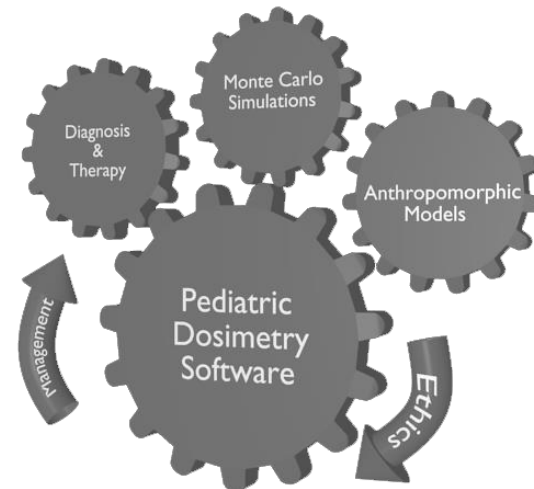


The goal...

Development of a platform for personalized pediatric dosimetry

Creation of a product: support tool for clinicians

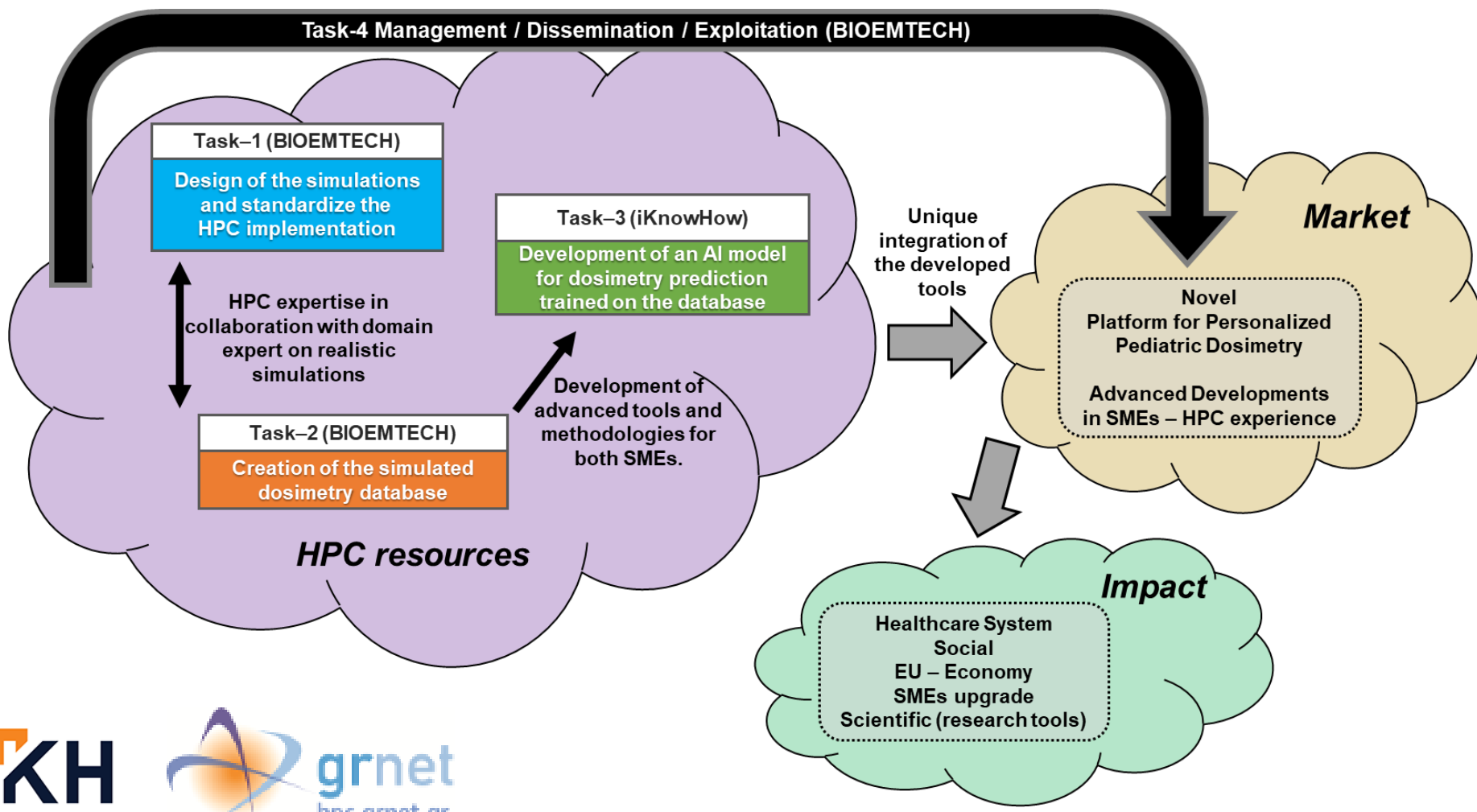
- Develop a platform with a Graphical User Interface (GUI), using computational tools and MC simulations, for the calculation of the absorbed dose / organ before the acquisition of NM examinations.
- Exploit Artificial Intelligence: ML/DL techniques
- The clinician will have a good estimation and could reconsidered the applied protocol.



MC simulations

Use clinical data to create dosimetry databases for all organs of interest on a population of pediatric phantoms with different anatomies.

150-16e patients																								
5 boy 50.76 Kg	TIME	Bladder	Heart	Kidneys	Liver	Lungs	Brain	Gallbladder	Large intestine	Small intestine	Stomach	Pancreas	Red marrow	Bones	Spleen	Thymus	Body	Adrenals	Testis	Thyroid	Salivary			
	0	22.6	41.1	31.7	34.9	32.4	16.6	27.4	37.9	42.3	229.5	83.6	19.1	19.5	71.9	25.4	18.5	49.5	15.9	21.7	18.1			
	4	30.6	33.7	30.9	31.0	26.7	19.1	27.4	35.7	38.9	131.7	99.8	20.0	20.0	49.4	24.2	16.7	38.9	17.1	21.0	25.7			
	23	15.1	29.6	29.3	28.8	25.2	20.4	27.8	35.5	38.2	67.4	44.0	20.6	20.3	34.0	24.3	18.9	31.8	18.7	23.7	25.5			
	47	40.8	32.3	30.7	30.3	29.3	18.8	29.0	40.7	44.9	87.0	51.3	20.4	20.1	39.1	25.7	18.9	34.4	18.2	21.4	22.9			
70	0	34.4	31.7	31.0	30.3	32.3	18.5	31.1	46.1	52.3	49.7	45.9	20.6	20.2	31.3	27.3	19.0	31.3	17.9	23.6	20.1			
	TIME	Bladder	Heart	Kidneys	Liver	Lungs	Brain	Gallbladder	Large intestine	Small intestine	Stomach	Pancreas	Red marrow	Bones	Spleen	Thymus	Body	Adrenals	Testis	Thyroid	Salivary			
	0	18.1	32.7	29.7	27.2	28.0	11.0	22.9	32.1	31.3	297.3	73.2	9.9	14.3	55.6	18.6	12.7							
	4	27.1	25.6	25.1	23.2	20.5	12.7	21.8	27.2	27.2	113.5	49.1	11.4	14.6	37.6	17.2	13.1							
	23	11.9	21.5	22.1	20.6	18.6	11.8	21.2	24.8	25.7	55.9	31.0	12.2	14.8	25.7	17.1	13.3							
17.7 Kg	0	39.1	23.9	23.6	21.8	22.0	12.6	22.2	29.3	31.1	73.5	39.3	11.6	14.7	30.2	18.1	11.2							
	47	30.2	23.0	22.9	21.1	24.0	12.4	22.9	32.5	35.9	41.5	32.0	11.5	14.8	24.6	19.1	13.3							
	TIME	Bladder	Heart	Kidneys	Liver	Lungs	Brain	Gallbladder	Large intestine	Small intestine	Stomach	Pancreas	Red marrow	Bones	Spleen	Thymus	Body	Adrenals	Testis	Thyroid	Salivary			
	0	12.8	18.1	19.4	19.6	19.3	8.0	17.0	16.9	39.6	205.7	32.6	7.6	10.0	34.9	12.7	8.8							
	4	18.8	15.5	17.1	16.7	13.4	9.2	16.0	16.4	28.5	61.9	24.8	8.0	10.4	24.5	12.0	9.1							
25.6 Kg	23	23.0	22.2	14.3	15.6	14.8	12.7	9.9	15.4	16.7	21.6	31.6	19.7	9.2	10.6	17.4	12.2	9.3						
	47	27.3	15.4	16.4	15.6	14.9	9.1	16.2	19.9	26.4	40.9	22.5	8.7	10.6	19.8	13.0	9.2							
	0	22.5	15.5	16.1	14.9	16.6	9.0	16.7	23.4	25.9	24.2	21.4	8.8	10.6	16.2	14.1	9.3							
	TIME	Bladder	Heart	Kidneys	Liver	Lungs	Brain	Gallbladder	Large intestine	Small intestine	Stomach	Pancreas	Red marrow	Bones	Spleen	Thymus	Body	Adrenals	Testis	Thyroid	Salivary			
	0	10.8	20.7	24.1	21.4	16.6	6.9	17.2	17.9	20.4	117.4	32.0	6.4	9.2	39.1	12.4	8.6	43.7	12.8	11.6				
25.64 Kg	4	14.2	16.5	19.1	17.2	11.4	8.0	16.1	17.4	18.9	68.1	34.6	7.3	9.4	26.4	11.7	8.9							
	23	16.2	14.2	16.2	14.9	12.6	8.5	15.7	18.0	18.9	33.9	22.6	7.8	9.6	17.7	11.8	9.0	20.3	18.5	16.3				
	47	18.7	15.6	17.7	15.8	15.1	7.9	17.0	21.3	22.7	43.9	26.7	7.4	9.6	26.7	12.5	9.0	23.2	18.0	18.3				
	0	16.2	15.2	16.8	14.9	17.1	7.8	18.4	25.3	27.3	24.6	20.8	7.3	9.8	18.5	13.5	9.0	18.3	20.4	18.7				
	TIME	Bladder	Heart	Kidneys	Liver	Lungs	Brain	Gallbladder	Large intestine	Small intestine	Stomach	Pancreas	Red marrow	Bones	Spleen	Thymus	Body	Adrenals	Testis	Thyroid	Salivary			
14 boy 50.38 Kg	0	7.8	12.4	17.9	18.1	14.3	4.3	11.2	12.7	14.8	99.8	41.7	5.4	8.5	28.5	7.3	4.6	27.5	5.1					
	4	10.7	10.3	13.8	11.5	8.6	5.0	11.7	12.5	14.4	53.9	27.0	6.1	6.6	10.9	7.1	4.7	19.1	6.0					
	23	12.4	9.3	11.0	9.8	8.5	5.4	10.8	13.0	14.3	28.2	16.9	6.6	6.7	12.5	7.3	4.8	13.1	6.4					
	47	14.8	10.0	12.0	10.4	10.2	5.0	11.6	15.6	17.6	34.2	20.4	6.5	6.8	14.5	7.7	4.8	14.8	6.1					
	0	13.1	10.0	10.8	9.8	11.9	4.9	11.9	18.9	21.1	18.5	15.3	6.6	7.0	11.1	8.3	4.8	11.4	6.1					
14y Girl 4.0E+01	TIME	Bladder	Heart	Kidneys	Liver	Lungs	Brain	Gallbladder	Large intestine	Small intestine	Stomach	Pancreas	Red marrow	Bones	Spleen	Thymus	Body	Adrenals	Testis	Thyroid	Salivary			
	0	10.6	24.9	18.6	21.6	15.9	5.2	20.1	20.8	25.2	136.7	50.8	7.8	8.4	34.1	12.2	7.6	32.1	10.7	10.9	7.6	6.5		
	4	14.5	18.1	15.9	16.8	12.8	4.0	17.0	18.7	23.8	90.4	34.2	8.1	8.4	23.5	11.0	7.8	23.1	12.9	13.6	8.2	10.7		
	TIME	Bladder	Heart	Kidneys	Liver	Lungs	Brain	Gallbladder	Large intestine	Small intestine	Stomach	Pancreas	Red marrow	Bones	Spleen	Thymus	Body	Adrenals	Testis	Thyroid	Salivary			
	0	10.6	24.9	18.6	21.6	15.9	5.2	20.1	20.8	25.2	136.7	50.8	7.8	8.4	34.1	12.2	7.6	32.1	10.7	10.9	7.6	6.5		
131I-NaI_p1	4	14.5	18.1	15.9	16.8	12.8	4.0	17.0	18.7	23.8	90.4	34.2	8.1	8.4	23.5	11.0	7.8	23.1	12.9	13.6	8.2	10.7		
	TIME	Bladder	Heart	Kidneys	Liver	Lungs	Brain	Gallbladder	Large intestine	Small intestine	Stomach	Pancreas	Red marrow	Bones	Spleen	Thymus	Body	Adrenals	Testis	Thyroid	Salivary			
	0	10.6	24.9	18.6	21.6	15.9	5.2	20.1	20.8	25.2	136.7	50.8	7.8	8.4	34.1	12.2	7.6	32.1	10.7	10.9	7.6	6.5		
	4	14.5	18.1	15.9	16.8	12.8	4.0	17.0	18.7	23.8	90.4	34.2	8.1	8.4	23.5	11.0	7.8	23.1	12.9	13.6	8.2	10.7		
	23	15.1	29.6	29.3	28.8	25.2	20.4	27.8	35.5	38.2	67.4	44.0	20.6	20.3	34.0	24.3	18.9	31.8	18.7	23.7	25.5			
131I-NaI_p2	0	30.6	33.7	30.9	31.0	26.7	19.1	27.4	35.7	38.9	131.7	99.8	20.0	20.0	49.4	24.2	16.7	38.9	17.1	21.0	25.7			
	TIME	Bladder	Heart	Kidneys	Liver	Lungs	Brain	Gallbladder	Large intestine	Small intestine	Stomach	Pancreas	Red marrow	Bones	Spleen	Thymus	Body	Adrenals	Testis	Thyroid	Salivary			
	0	18.1	32.7	29.7	27.2	28.0	11.0	22.9	32.1	31.3	297.3	73.2	9.9	14.3	55.6	18.6	12.7							
	4	27.1	25.6	25.1	23.2	20.5	12.7	21.8	27.2	27.2	113.5	49.1	11.4	14.6	37.6	17.2	13.1							
	23	11.9	21.5	22.1	20.6	18.6	11.8	21.2	24.8	25.7	55.9	31.0	12.2	14.8	25.7	17.1	13.3							
131I-NaI_p3	0	39.1	23.9	23.6	21.8	22.0	12.6	22.2	29.3	31.1	73.5	39.3	11.6	14.7	30.2	18.1	11.2							
	47	30.2	23.0	22.9	21.1	24.0	12.4	22.9	32.5	35.9	41.5	32.0	11.5	14.8	24.6	19.1	13.3							
	TIME	Bladder	Heart	Kidneys	Liver	Lungs	Brain	Gallbladder	Large intestine	Small intestine	Stomach	Pancreas	Red marrow	Bones	Spleen	Thymus	Body	Adrenals	Testis	Thyroid	Salivary			
	0	12.8	18.1	19.4	19.6	19.3	8.0	17.0	16.9	39.6	205.7	32.6	7.6	10.0	34.9	12.7	8.8							
	4	18.8	15.5	17.1	16.7	13.4	9.2	16.0	16.4	28.5	61.9	24.8	8.0	10.4	24.5	12.0	9.1							
131I-NaI_p4	23	23.0	22.2	14.3	15.6	14.8	12.7	9.9	15.4	16.7	21.6	31.6	19.7	9.2	10.6	17.4	12.2	9.3						
	47	27.3	15.4	16.4	15.6	14.9	9.1	16.2	19.9	26.4	40.9	22.5	8.7	10.6	19.8	13.0	9.2							
	0	22.5	15.5	16.1	14.9	16.6	9.0	16.7	23.4	25.9	24.2	21.4	8.8	10.6	16.2	14.1	9.3							
	TIME	Bladder	Heart	Kidneys	Liver	Lungs	Brain	Gallbladder	Large intestine	Small intestine	Stomach	Pancreas	Red marrow	Bones	Spleen	Thymus	Body	Adrenals	Testis	Thyroid	Salivary			
	0	10.8	20.7	24.1	21.4	16.6	6.9	17.2	17.9	20.4	117.4	32.0	6.4	9.2	39.1	12.4	8.6	43.7	12.8	11.6				
131I-NaI_p5	4	14.2	16.5	19.1	17.2	11.4	8.0	16.1	17.4	18.9	68.1	34.6	7.3	9.4	26.4	11.7	8.9							
	23	16.2	14.2	16.2	14.9	12.6	8.5	15.7	18.0	19.9	33.9	22.6	7.8	9.6	17.7	11.8	9.0	20.3	18.5	16.3				
	47	18.7	15.6	17.7	15.8	15.1	7.9	17.0	21.3	22.7	43.9	26.7	7.4	9.6	26.7	12.5	9.0	23.2	18.0	18.3				
	0	16.2	15.2	16.8	14.9	17.1	7.8	18.4	25.3	27.3	24.6	20.8	7.3	9.8	18.5	13.5	9.0	18.3	20.4	18.7				
	TIME	Bladder	Heart	Kidneys	Liver	Lungs	Brain	Gallbladder	Large intestine	Small intestine	Stomach	Pancreas	Red marrow	Bones	Spleen	Thymus	Body	Adrenals	Testis	Thyroid	Salivary			
131I-NaI_p6	0	7.8	12.4	17.9	18.1	14.3	4.3	11.2	12.7	14.8	99.8	41.7	5.4	8.5	28.5	7.3	4.6	27.5	5.1					
	4	10.7	10.3	13.8	11.5	8.6	5.0	11.7	12.5	14.4	53.9	27.0	6.1	6.6	10.9	7.1	4.7	19.1	6.0					
	23	12.4	9.3	11.0	9.8	8.5	5.4	10.8	13.0	14.3	28.2	16.9	6.6	6.7	12.5	7.3	4.8	13.1	6.4					
	47	14.8	10.0	12.0	10.4	10.2	5.0	11.6	15.6	17.6	34.2	20.4	6.5	6.8	14.5	7.7	4.8	14.8	6.1					
	0	13.1	10.0	10.8	9.8	11.9	4.9	11.9	18.9	21.1	18.5	15.3	6.6	7.0	11.1	8.3	4.8	11.4	6.1					
131I-NaI_p7	TIME	Bladder	Heart	Kidneys	Liver	Lungs	Brain	Gallbladder	Large intestine	Small intestine	Stomach	Pancreas	Red marrow	Bones	Spleen	Thymus	Body	Adrenals	Testis	Thyroid	Salivary			
	0	10.6	24.9	18.6	21.6	15.9	5.2	20.1	20.8	25.2	136.7	50.8	7.8	8.4	34.1	12.2	7.6	32.1	10.7	10.9	7.6	6.5		
	4	14.5	18.1	15.9	16.8	12.8	4.0	17.0	18.7															



➤ Large number & Intensive simulations:

- There is ~20 pediatric models (2-15 years old)
- Test at least 5 radiopharmaceuticals (most common)
- To have an accurate dosimetry assessment, 4 time points will be used.

Total: ~400 different simulations.

- Rough estimation **320.000 core hours.**
- Need of memory RAM (**> 50 GB**).
- Enough space in the hard drive, that probably slows down the simulation.



➤ Machine Learning training models:

- 1st attempt in HPC
- Previous experience shows slow procedure (Training models could take ~1 week in CPU)
- In house speed up – (high end GPU unit)



Activity Map



Attenuation Map



Dose Map

HPC: Experience so far

1. To access ARIS we use specific IP with SSH key.
2. GATE macro simulation files are split manually, using in-house scripts. Splitting is done in ARIS.
3. Indicative procedure (our common practice):
 - 1 simulation is split in 120 files
 - Utilize 3 full nodes (fat nodes)
 - Use 10 GB of ram
 - Set a time limit of 30 clock hours.
4. Output file size can reach 100 Gb (specific cases).
 - Typical dosimetry don't exceed ~15 Gb.
5. Output is merged after transferring all the files to our PC using in-house scripts (avoid corrupted files).
6. Transfer of files is done using scp & the ssh key.

```
#!/usr/bin/env python

import sys, os
from math import *
from random import *
import time

n_threads = int(sys.argv[1]) #number of threads per angles
template_macro = str(sys.argv[2])
timeDuration = 20.0

for i in range(n_threads):

    j = 0 + i * timeDuration
    k = 0 + (i * timeDuration) + timeDuration
    file = open(template_macro).readlines()
    trg = open('automac_%02i.mac' % (i+0), 'w')
    for line in file:
        line = line.replace('$i', '%02i' % (i+0))
        #line = line.replace('$rnd', '%i' % randint(0,999999999))
        line = line.replace('$rnd', '%i' % 123456789)
        line = line.replace('$j', '%f' % j)
        line = line.replace('$k', '%f' % k)
        trg.write(line)
    trg.close()
```

NM-Dosimetry

1a

Choose the anatomical parameters of the patient

Gender	
Age	
Height	
Weight	
BMI	

2

Choose the radiopharmaceutical

99mTc-MIBI	
18F-FDG	
99mTc-MDP	
etc	

3

Choose the administered activity

1b

Load the DICOM CT file of the patient

Submit

Viewer

- 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 (image processing, simulations, AI) I



- Industrial access on HPC???

- Funds? National support – resources?
- Training – internal/external expert?



- Next steps – enhance quality of results and daily workflow

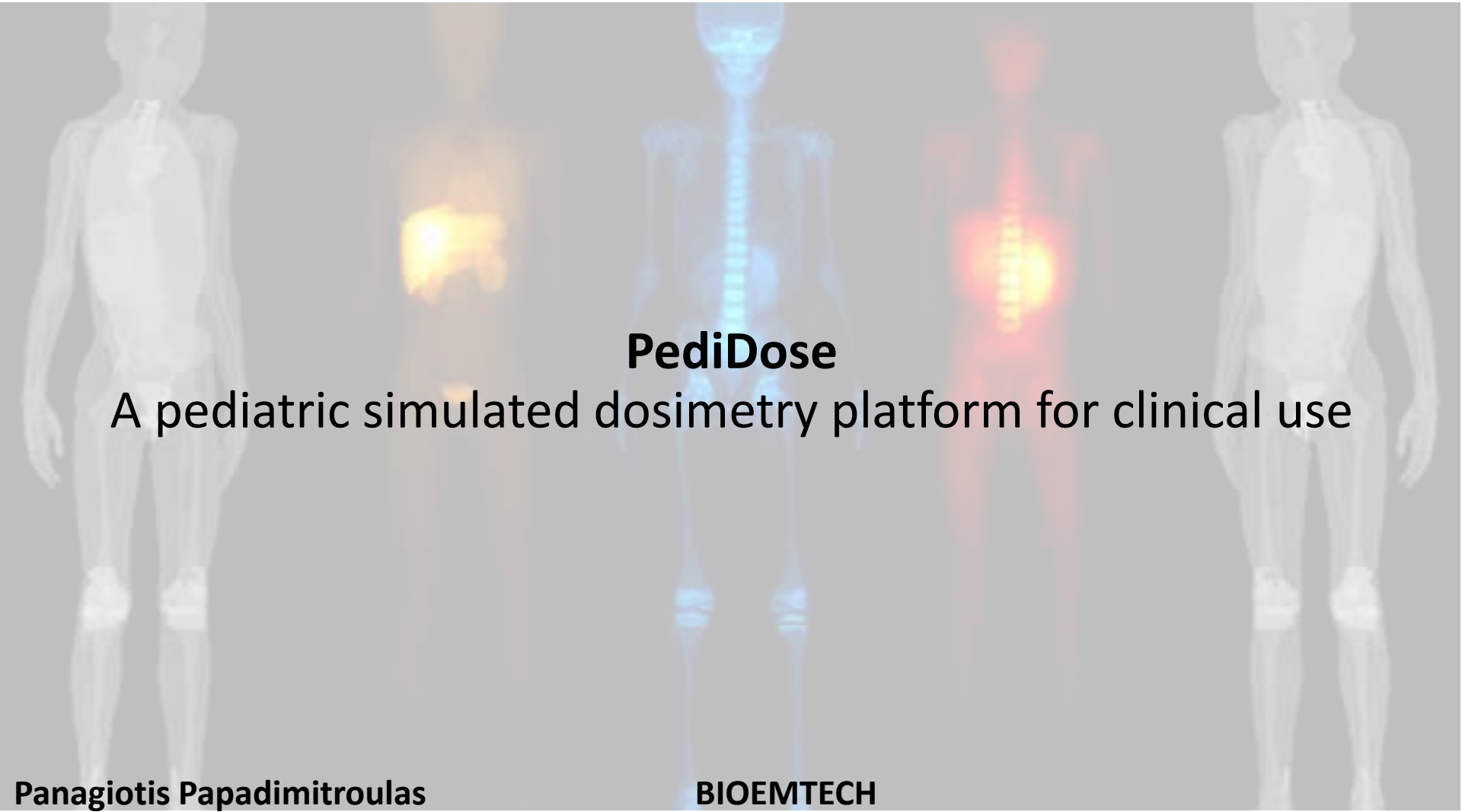
- Attract interest of SMEs / Start-ups
- Training & Dissemination activities (create awareness)
- Industry should identify their needs!



Thank you !!!

BIOEMTECH



The background of the slide features four semi-transparent human figures. Each figure displays a different simulated radiation dose distribution: the first is mostly white, the second has a bright yellow/orange spot on the chest, the third has a blue spine and joints, and the fourth has a red/yellow area on the lower back.

PediDose

A pediatric simulated dosimetry platform for clinical use

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