Dosimetry and dosimetric challenges in paediatric radiology and radiotherapy

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Conflict of Interest

n/a

Outline of the presentation

- Aim of the presentation
- Benefits of Medical Imaging – Therapy
- Paediatric diagnostic and therapy approaches
- Why paediatric dosimetry matters?
- Challenges
- The future

Aim of the presentation

Provide an update on dosimetry and dosimetric challenges in paediatric radiology and radiotherapy procedures, discuss on research being conducted in the area, and end with future prospects

Paediatric diagnostic / therapy approaches I

- Children patients are often prescribed diagnostic examinations involving radiation
- Benefits of these exams:
  - Earlier establishment of disease diagnosis
  - Earlier treatment
  - Improved patient outcomes
  - Quick and less invasive diagnosis

Treves ST, SNM 2014

Paediatric diagnostic / therapy approaches II

- Those procedures guide patient management and therapy decisions
- Additionally, a tool for follow up
- Not often, radiotherapy procedures may be deemed necessary

Issues related to these procedures

- False positives -> follow up exams
- Incidental findings -> consequent exams to rule out disease
- Contrast reactions
- Costs
- Exposure to Radiation

Radiation protection rules and RD metrics

- Key Principles of Radiological Protection:
  - Principle of **Justification**; any decision that alters radiation exposure should do more good than harm
  - Principle of Optimization of Protection (**ALARA**); all exposures should be kept **A**s **L**ow **A**s **R**easonably **A**chievable, taking into account economic/societal factors
  - Principle of **Application of Dose Limits**; total dose to any individual in planned exposure situations should not exceed appropriate limits
- Effective Dose: It estimates whole body patient dose representing the stochastic health risk to the patient due to radiation exposure

ICRP Publication 103

Why radiation dose to children matter?

- Importance of dosimetry for this patient group is more challenging:
  - Radiation sensitivity higher compared to adults
  - Higher Risk to develop cancer (relative radiosensitivity of various body tissues, sex, age) compared to adults receiving the same EqD
  - Longer life expectancy, and thus longer period for radiation-induced complications, or as future parents for passing radiation-induced genetic effects
- For these reasons, diagnostic procedures and therapy schemes should be reconsidered reflecting individual characteristics of children

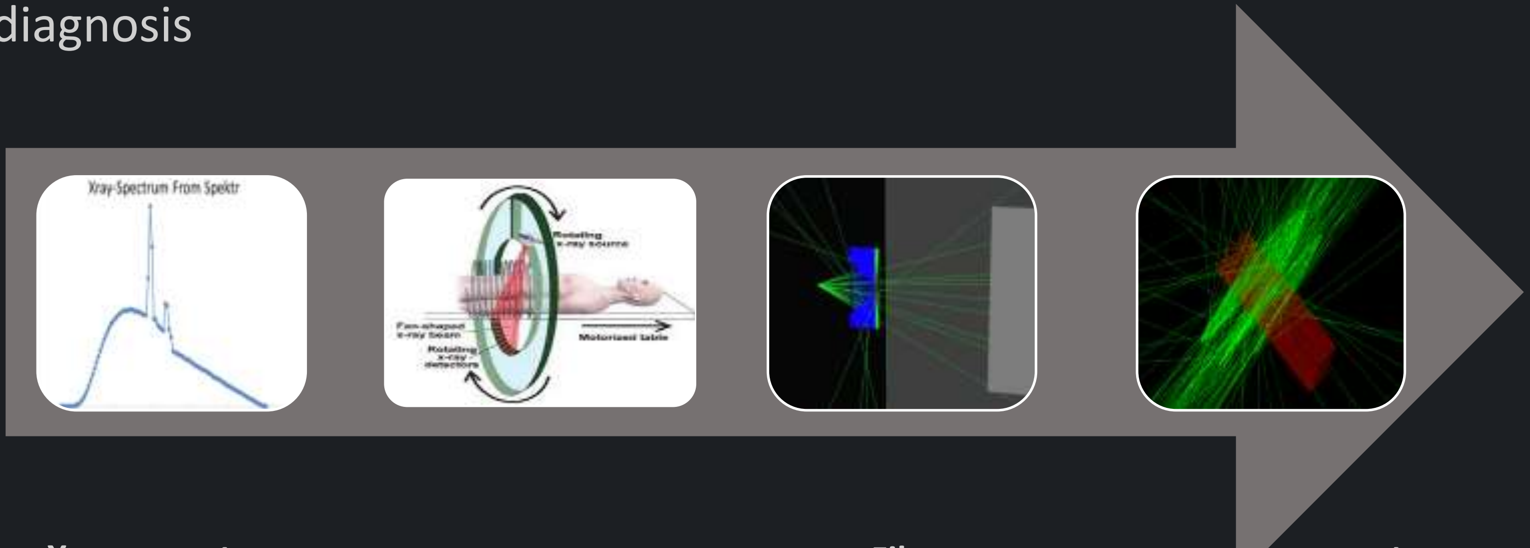
Papadimitroulas P, IEEE TRPMS 2019

Ultimate goal – Challenges

- Maintain high diagnostic image quality
- Deliver therapeutic radiation dose accurately when needed, while sparing normal tissue
- Minimizing Radation Dose

Radiology procedures

- Radiology X-rays:
    - Attenuation of X-rays within the body of the patient
    - Used for diagnosis

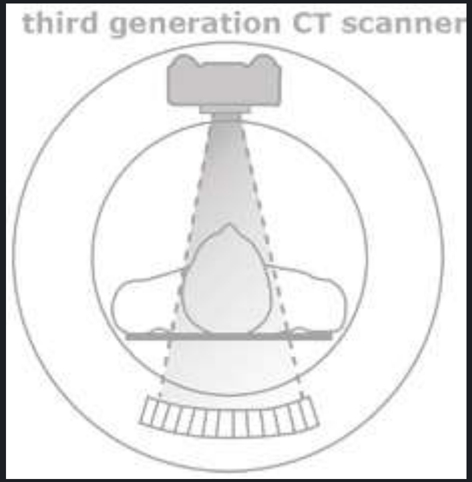


X-rays spectrum | Geometry | Filters | Source path

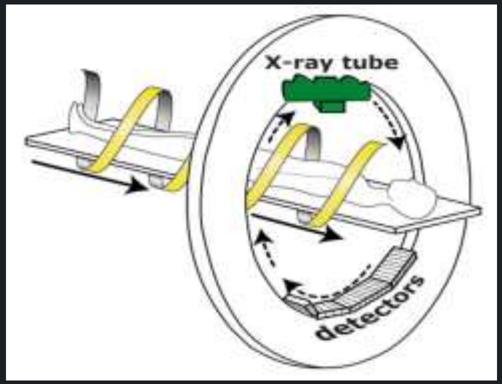
Radiology procedures

- The main application that increases radiation dose is considered CT
- Rapid developments and advances in CT technology
  - Faster scanning times and improved resolution, have increased accuracy and usefulness
  - Dramatic increase in number and variety of applications

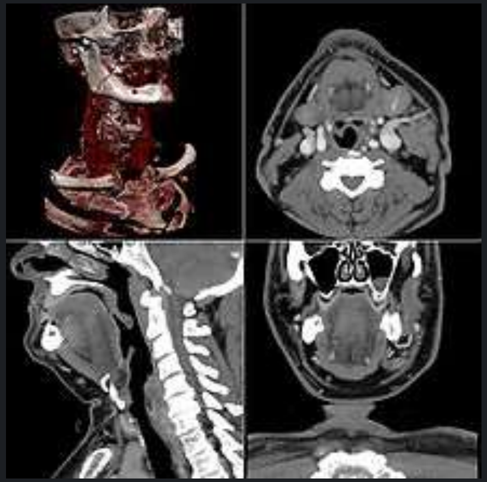
Third-generation CT scanner



Helical CT technique

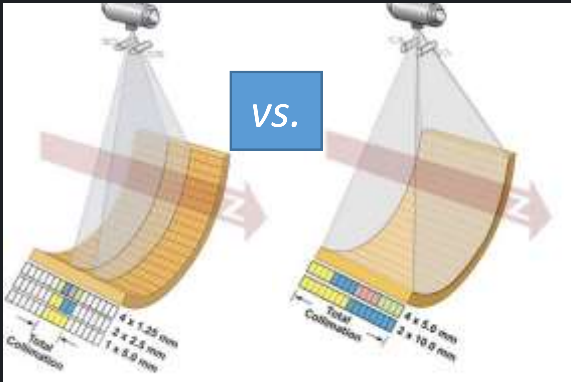


3D visualization in CT



Radiology procedures

- Methods to reduce dose
  - Radiation-free alternative imaging methods
  - X-Ray exposure should be undertaken only when a clear medical benefit is expected
  - Safest imaging protocols and techniques matched to the size (not age) of the individual patient <- one size doesn’t fit all!
  - Need for accurate methods towards CT Dose Estimation




Patient-Size AEC

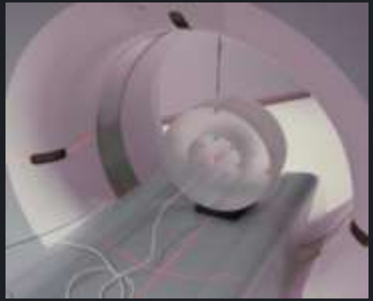

Z-axis AEC

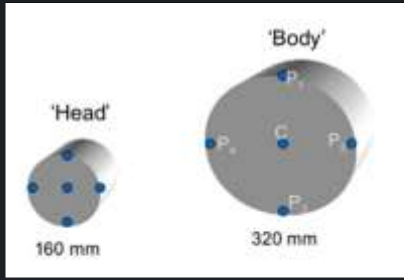

Rotational or Angular AEC

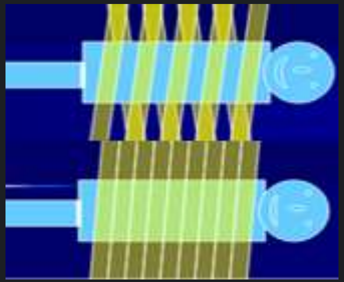

Combination of all

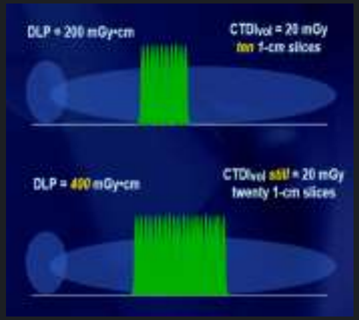
Singh, Radiology 2009

Radiology procedures









$CTDI_{100}$

Weighted
$CTDI_{w}$

CTDI Volume
$CTDI_{vol}$

Dose-Length Product
DLP

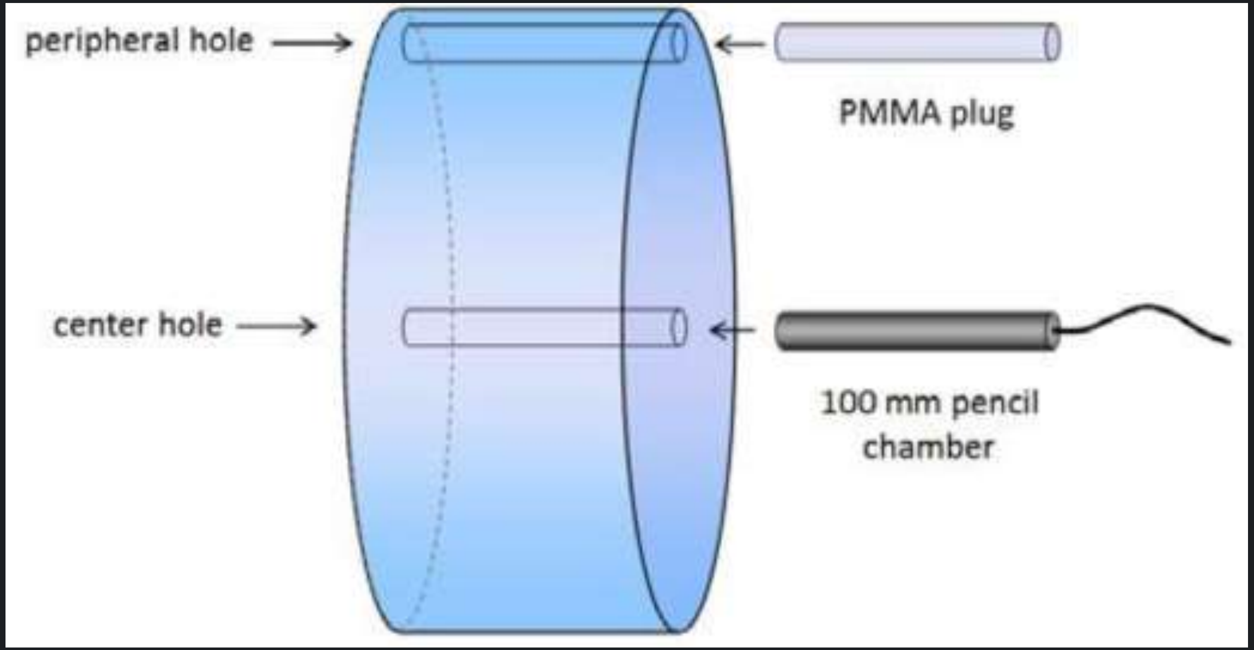
EFFECTIVE DOSE

Radiology procedures

Effective dose (ED): **Commonly estimated from pre-calculated factors in clinical practice**

$$ED\ (mSv) = k\ (mSv\ mGy^{-1}\ cm^{-1}) * DLP_{clinical}(mGy * cm)$$

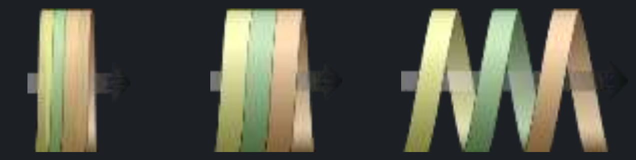
We measure the dose profile in one 'slice': $DLP\ (Dose - Length\ product) = CTDI_{vol} * Scan\ Length$



$$CTDI_{100} = \frac{1}{nT}\int_{-50\ mm}^{+50\ mm} D(z)\ dz$$

$$CTDI_w = \frac{1}{3}CTDI_{100}^{center} + \frac{2}{3}CTDI_{100}^{periphery}$$

$$CTDI_{vol} = \frac{CTDI_w}{pitch}$$

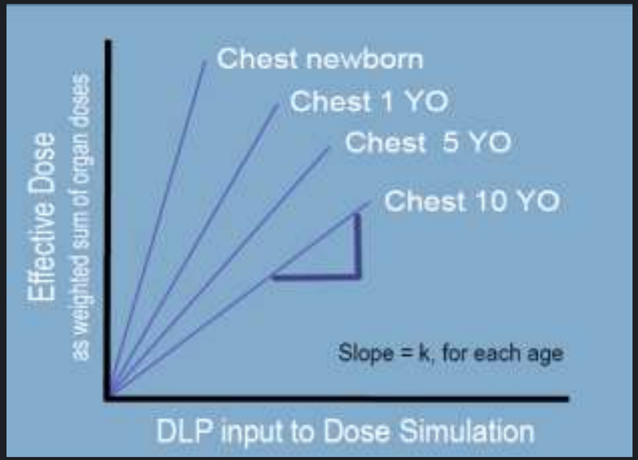


Radiology procedures

- **Determination of k-factors**

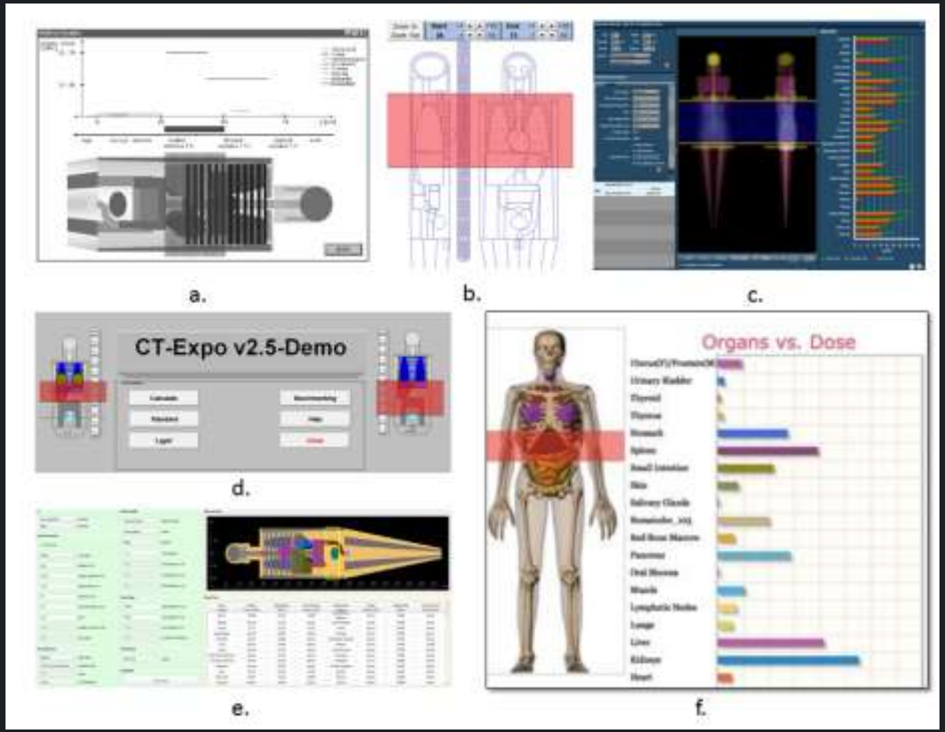
- Estimated with Monte Carlo (MC) simulations and reference or size specific computational phantoms representing different ages and body sizes
- For different simulated protocols and DLPs

- $k\ (mSv\ mGy^{-1}\ cm^{-1}) = \dfrac{ED_{simulated}(mSv)}{DLP_{simulated}(mGy*cm)}$



Radiology procedures; challenges

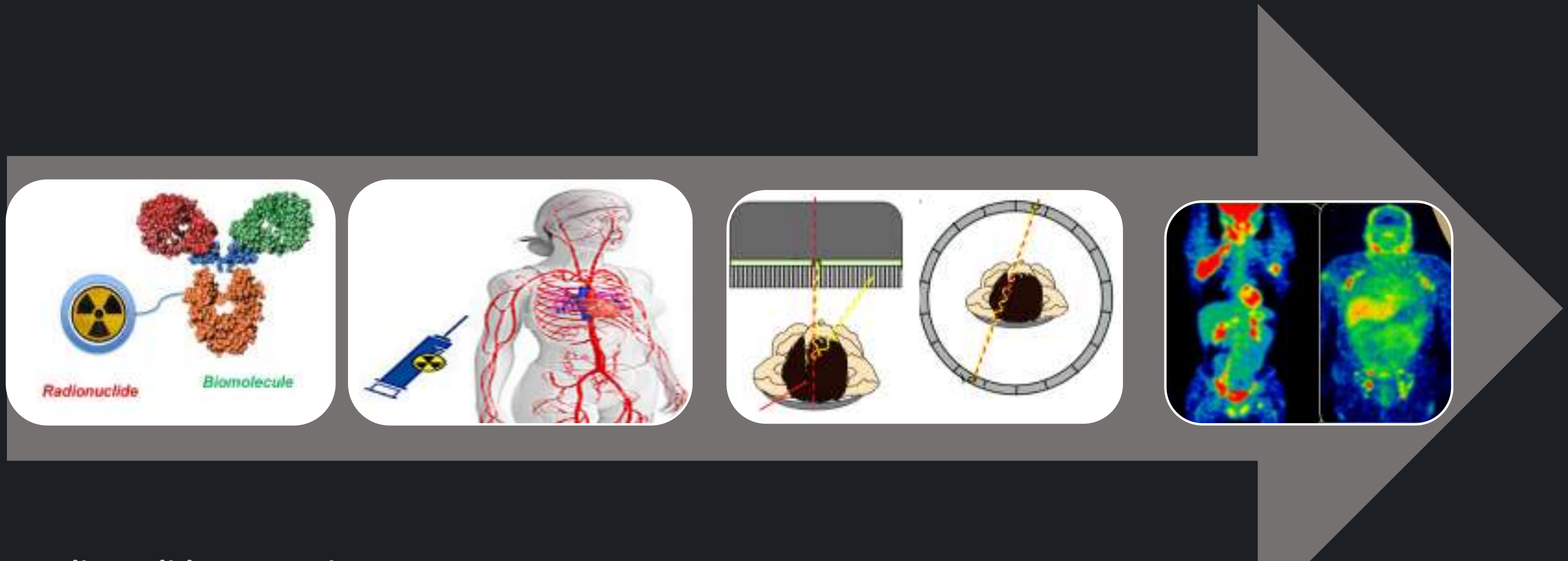
- These simulated and pre-calculated k-factors have been integrated in few software applications (sw) for automatic dose calculation in clinical practice
- But:
  - One size doesn't fit. They don't incorporate patients' variability
  - Are expensive
  - Are mainly based on low-resolution phantoms
- Therefore, there's need for an extended paediatric CT dosimetric DB where phantoms are of high resolutions, cover both sexes, have various sizes, …



a. WinDose, b. CTDosimetry, c. eXposure, d. CT-Expo, e. ImpactDose, f. VirtualDose

Nuclear Medicine procedures

- Nuclear Medicine (NM):
  - Involves use of radiopharmaceuticals for diagnosis and therapy
  - Spatial distribution of a radiopharmaceutical inside the body



Radionuclide generation Radiochemistry | **Injection** | **SPECT / PET Detection** | **SPECT / PET Image**

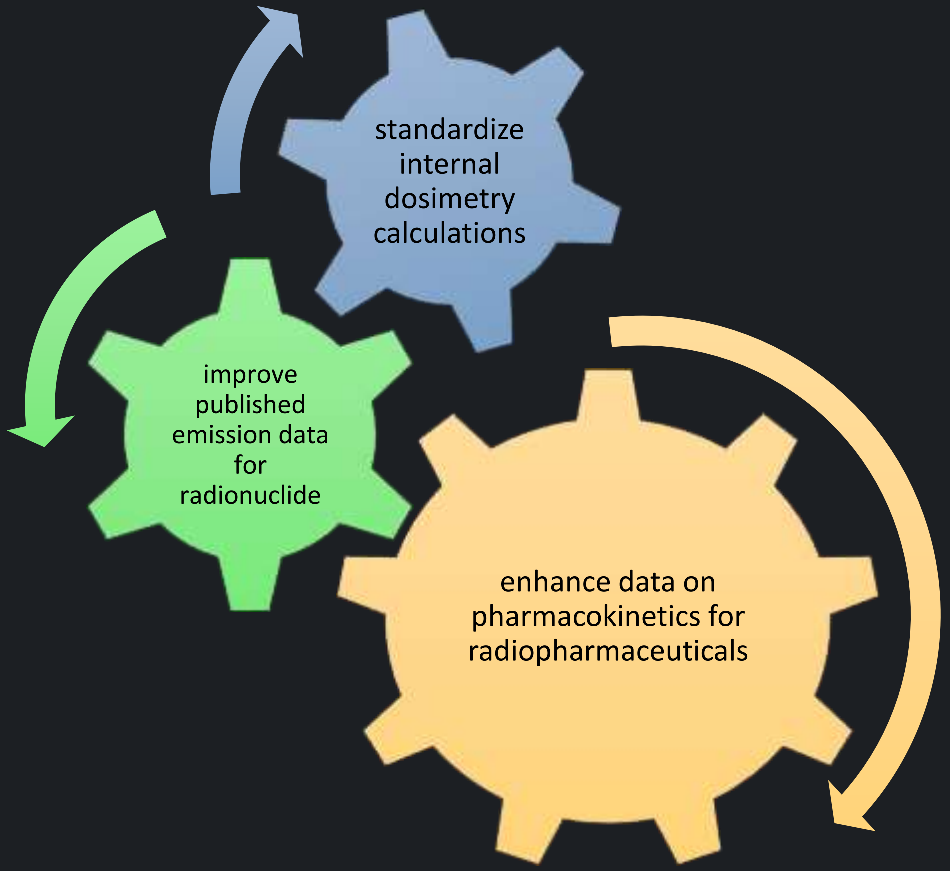
Nuclear Medicine procedures

- Administered activity needs be optimized and personalized BUT time, effort, and cost of carrying out individual dosimetry plans are limited.
- For clinical applications, administered activity of a radiopharmaceutical is often given as:
  - Fixed activity amounts
  - Functions of body weight or body surface area
  - Calculations are mainly based on few measurements with a well-type detector

Nuclear Medicine procedures

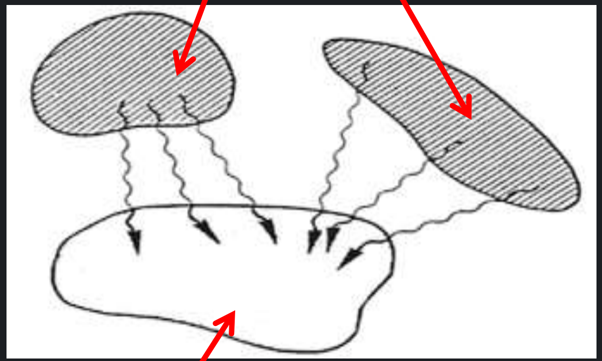
- Methods to reduce dose:
  - Appropriate use of the protocol
  - Image Processing to avoid over exposure
  - Develop advanced systems that may lead to advanced quality for less dose
  - Adjust Protocol
  - Update dose guidelines

Nuclear Medicine: the MIRD formalism



Symbol	**Parameter**
R	Type of radiation
r_S	Source region
r_T	Target region
T_D	Integration period

Source – organs



Target organ

Nuclear Medicine: the MIRD formalism

- Absorbed Dose D to a target region due to activity in a source region is calculated as the product of time-integrated activity $\widetilde{\mathrm{A}}$ and the S value

$$D = \tilde{A} * S$$

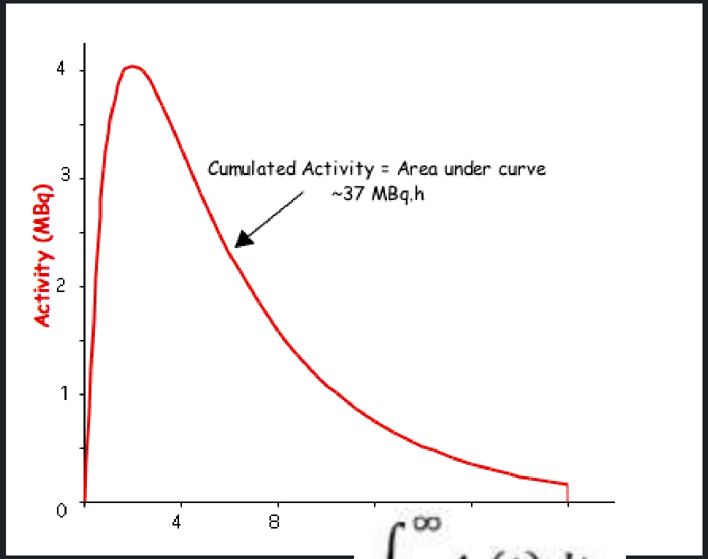
absorbed dose
Gray (Gy)
(1 J/kg = 1 Gy)

Cumulative activity:
Becquerel · s
decays that take place in a certain source region

absorbed dose rate per unit activity
$\mathrm{Gy \cdot (Bq \cdot s)^{-1}}$
often $\mathrm{mGy \cdot (MBq \cdot s)^{-1}}$

Nuclear Medicine: the MIRD formalism

- $\widetilde{A}$ is calculated as the area under the curve (AUC) that describes A as a function of time
- It’s most commonly determined by:
  - Indirect quantitave imaging sessions
  - Direct A measurements on tissue or blood samples
  - Compartmental modeling (theoretical approach)



$$\int_0^\infty A_s(t)\,dt$$

Nuclear Medicine: the MIRD formalism

S-values

- are estimated with MC simulations employing reference or size specific computational phantoms

$$S(r_T \leftarrow r_S) = \frac{E \, * \, Y \, * \, \varphi_i(r_T \leftarrow r_S)}{m_{r_T}}$$

***E * Y* : Δ**
mean energy emitted per decay

mass of target region

Absorbed fraction = $E_{deposited}$ / $E_{emitted}$

Depends on:

- **shape, size and mass**
- **distance** and **type** of material
- **type of radiation**

- Can be clinically found on:
  - MIRD Pamphlet No. 11
  - OLINDA/EXM sw
  - RADAR web site (www.doseinfo-radar.com)

Most paediatric S-values are calculated by rescaling adult pre-defined values. <u>Need S-values calculation optimization in paediatric applications with advanced phantoms that represent children anatomies.</u> No data available taking into account the biodistribution

Radiation Therapy procedures

- RT procedures span from radionuclide therapies, like ^{90}Y, ^{177}Lu, etc., brachy, to external RT ones
- Need to simulate the procedure before application to the patient
  - Model and validate the RT unit that is going to be used
  - Ad hoc MC simulation for the individual patient before therapy
- Goal; simulate the RT plan for the individual patient before the RT procedure itself

Cravo, S, EJMP, 2020
Matsumoto, S, Med Phys 2019
Chatzipapas, K, Med Phys, 2016

How can we evolve to this direction?

- Use Monte Carlo simulations for the calculation of various parameters
- Develop more computational models that match the patient's chars
- Use state-of-the-art Artificial Intelligence algorithms that can optimize procedures

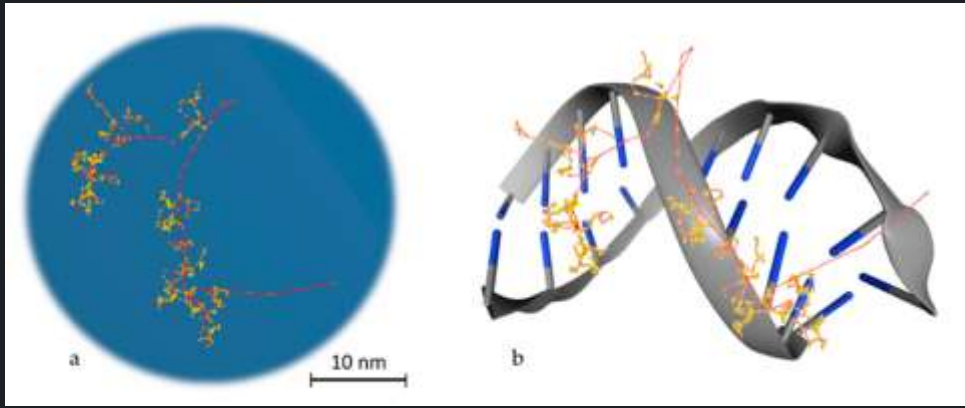
Monte Carlo simulations

- Direct measurement of energy deposition in various tissues/organs
- Experimental measurements using dosimeters embedded within physical phantoms
- MC simulations, are deemed to be the gold standard technique for dosimetry calculations

Akhavanallaf A, PMB 2020

Monte Carlo simulations

- The MC Simulation Method
  - Applies mathematical methods for the analysis of complex, real-world problems
  - Calculations based on random numbers (MC Core)
    - practically, the randomness is necessary to simulate the randomness in the nature of the problem to be solved
  - Firstly developed to demonstrate the stability of the first man-made nuclear reactor



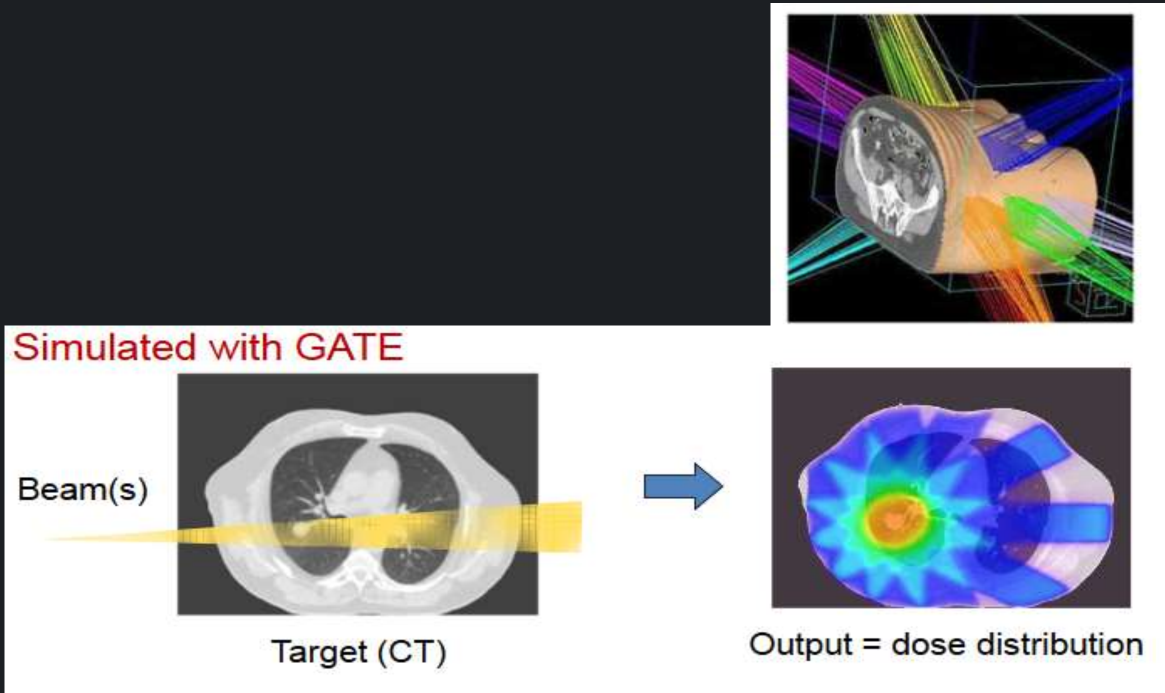
- Assumes:
  - the system is described by probability density functions (PDFs)
  - a large number of random tests for proper sampling

Monte Carlo simulations

- Why is it used in the Medical Physics clinical routine?
  - Random nature of radiation matter interactions
  - A PDF describes each interaction mechanism
  - The path of every particle can be modeled as a random walk as collisions with atoms occur with well-defined probability

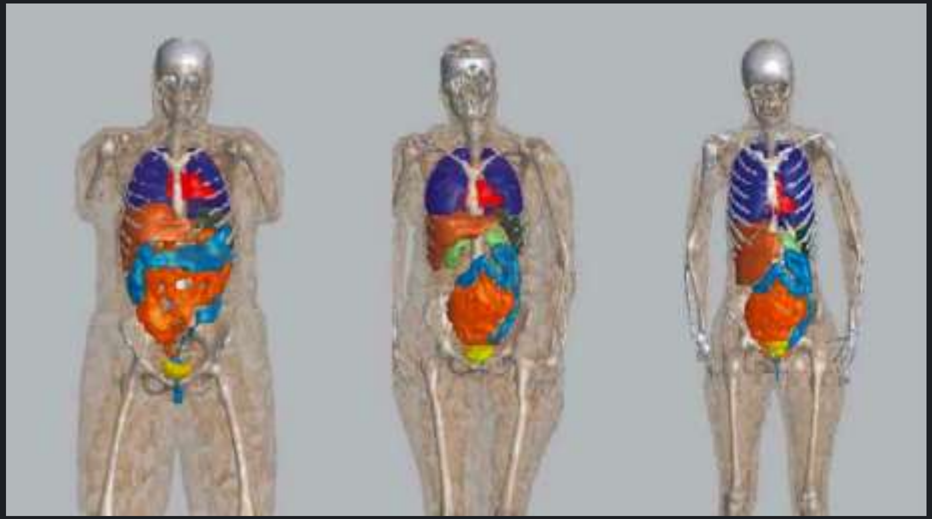
GATE MC code

- Generic and dedicated codes for a plethora of applications exist (i.e. Minerva, Celldose, RADAR, just few to mention)
- Geant4 Application for Emission Tomography (GATE)
  - Open-source MC toolkit validated and dedicated to SPECT, PET, CT, and RT sims
  - First release on May 2004, latest release v9.0 on March 2020
- GATE can be used for:
  - Dose distribution related problems (RT, X-ray imaging, brachy, DNA dosimetry, etc.)
  - Evaluation of new systems and new image processing algorithms
  - Handling computational models



Computational phantoms

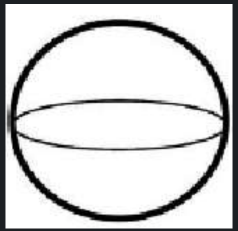
- Computer-based computational models give the
  - flexibility to model unlimited set of anatomies differing on age, sex, size
  - potential to estimate patient-specific organ and effective dose
- Therefore, we can develop a large DB of children phantoms that represent various anatomies and ages for accurate dose estimation



DeMarco, PMB, 2007

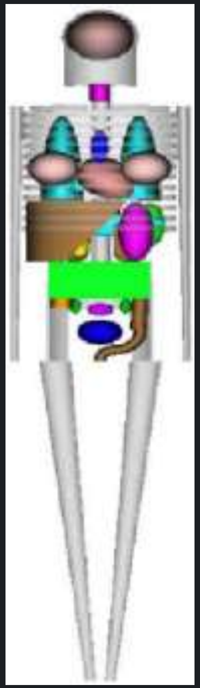
Computational phantoms: the evolution

1960s



ICRU sphere

1980s



MIRD anthropomorphic models

1990 - 2000s

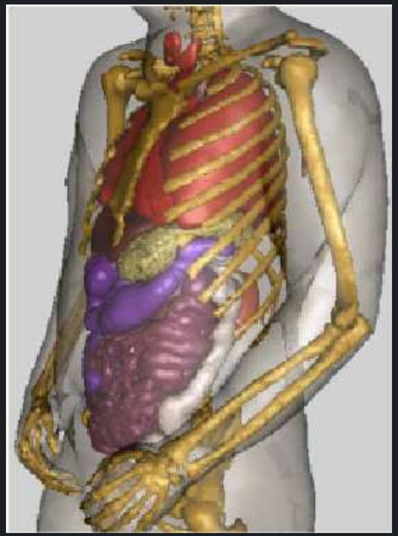
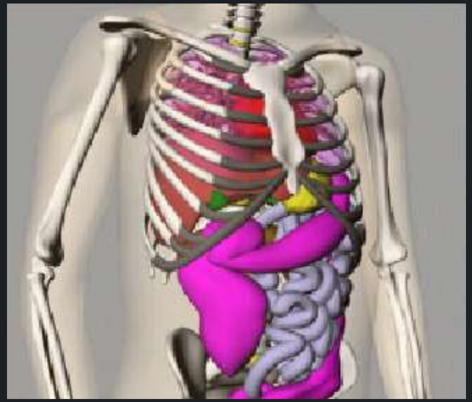


Image-based grid 3D models

2001 - 2015



Deformable and moving (dynamic) 4D models

Mathematical or Stylized Phantoms

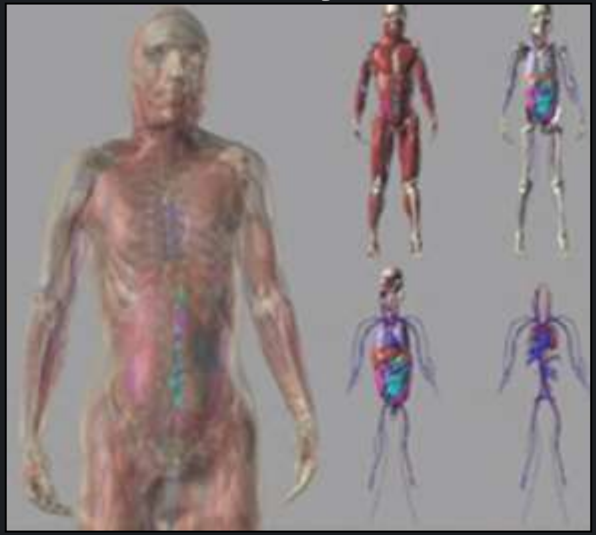
Patient-Based / Voxelized Phantoms

Boundary Representation (BREP) / Hybrid Phantoms

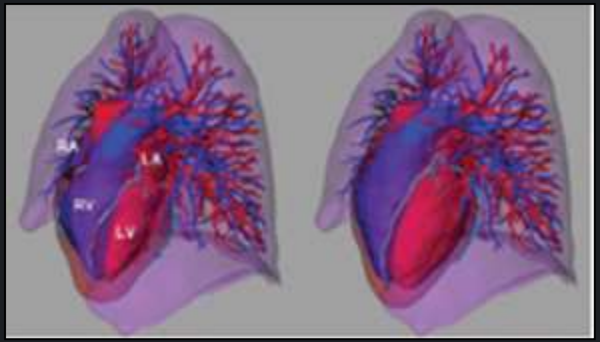
Computational phantoms: Hybrid

4D XCAT Phantom Anatomy

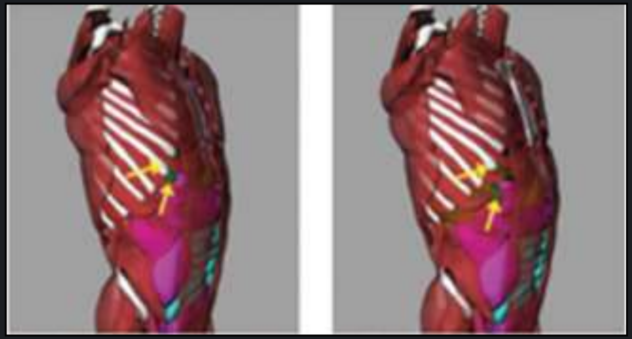
XCAT Male Adult



XCAT Female Adult



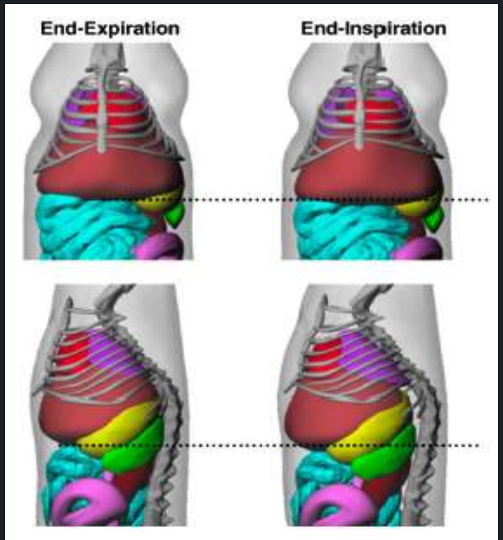
End-diastole End-systole
4D Beating Heart



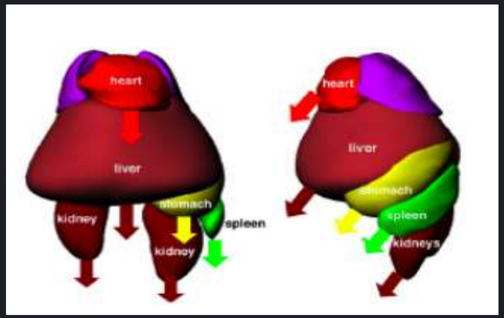
End-expiration End-inspiration
4D Respiration

MOBY

MOBY mouse phantom



Diaphragm’s motion



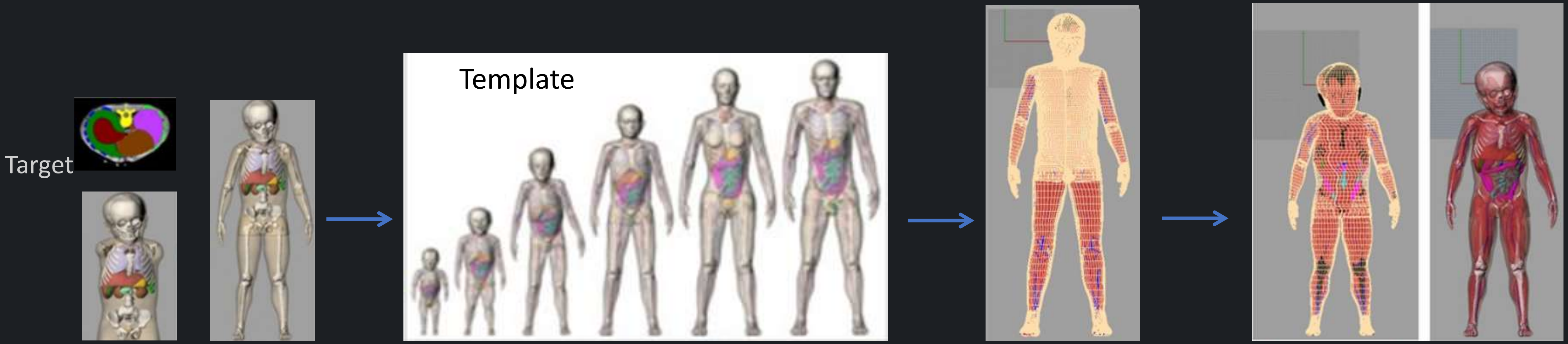
Inspiratory and expiratory motions of the liver

Computational phantoms: anatomical variations

- Modeling patient’s individual characteristics is essential
- Need populations of realistic phantoms to represent the population under study
- Manual segmentation is an extremely daunting procedure

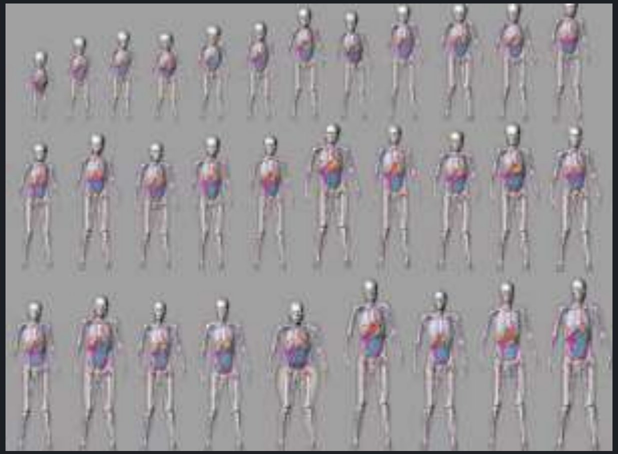
Computational phantoms: anatomical variations

- Therefore, to develop a phantom for an individual patient:
  - Select a reference phantom that closely matches the target based on age/gender/size
  - Utilize mapping algorithms to morph the phantom to the target population

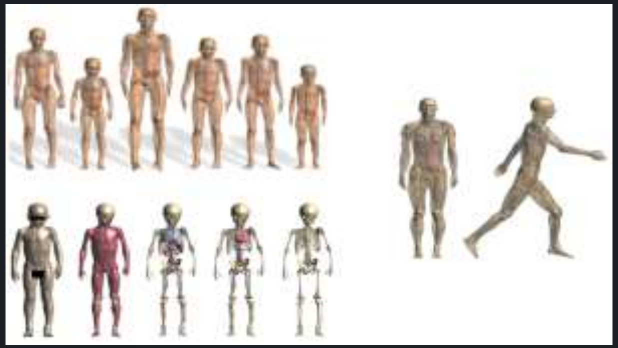


New XCAT Phantom Based on Patient Data

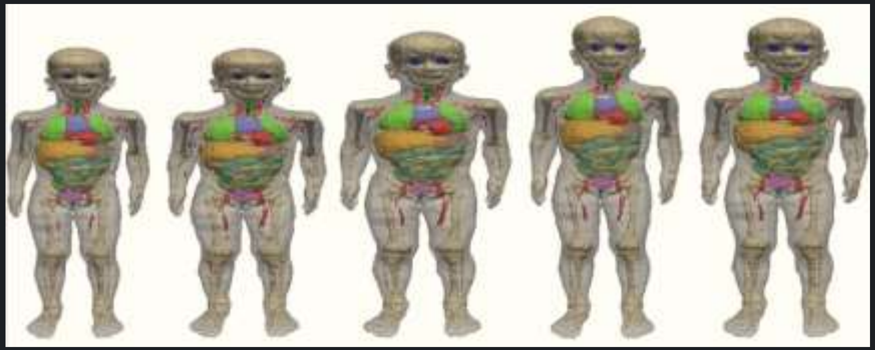
Computational phantoms: population

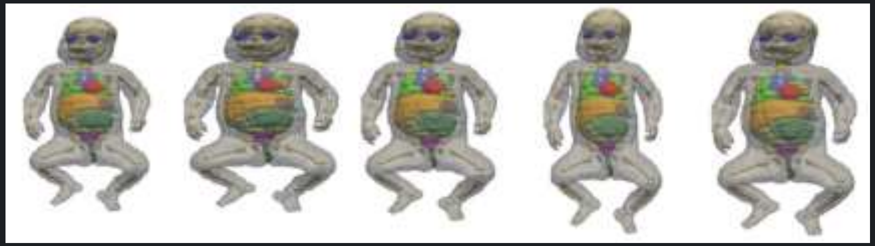


XCAT, 2014 - 2015



***ITIS* foundation,** 2009-2011





Lee et al., The largest library available today
including 1.100 female and male pediatric phantoms, 2017

Use state-of-the-art Artificial Intelligence algorithms

- AI: Intelligence demostrated by machines, unlike natural intelligence demonstrated by humans and animals
- Dramatic evolution in hw, i.e. NVIDIA GPU card
- Evolution in GUIs gives the potential to use this technology by non-CS experts
- Cloud computing for ML, i.e. Google, Azure, PRACE
- Access to very big DBs -> Big Data

Chartrand G, Radiographics, 2017

Use state-of-the-art Artificial Intelligence algorithms

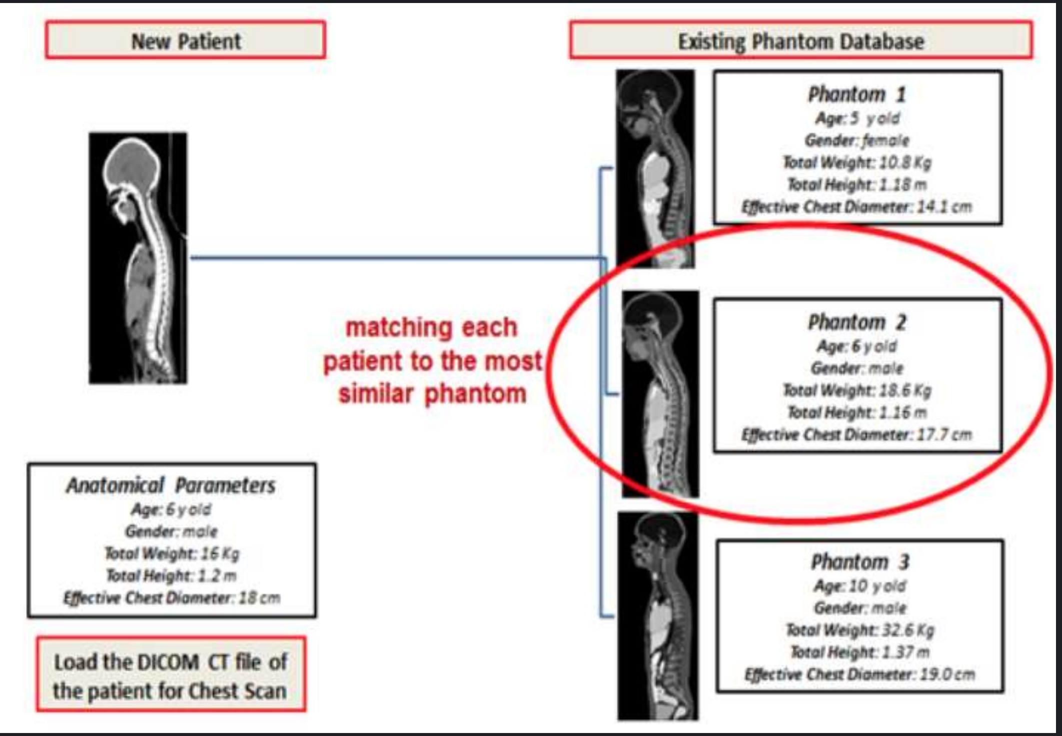
- AI: potential to develop the virtual model – phantom of a patient *ad hoc,* in real time
- Therefore, individual characterists will be passed on to the model created
- Run MC simulations in real time
- Consequently, the dosimetric characteristics for the individual patient and specific procedure will be calculated before the procedure
- Optimization

Research being conducted

- Several studies are being conducted in EU, USA, etc. towards these goals
- The end product should help the clinician optimize procedures based on individual patient characteristics in real time, and before the procedure

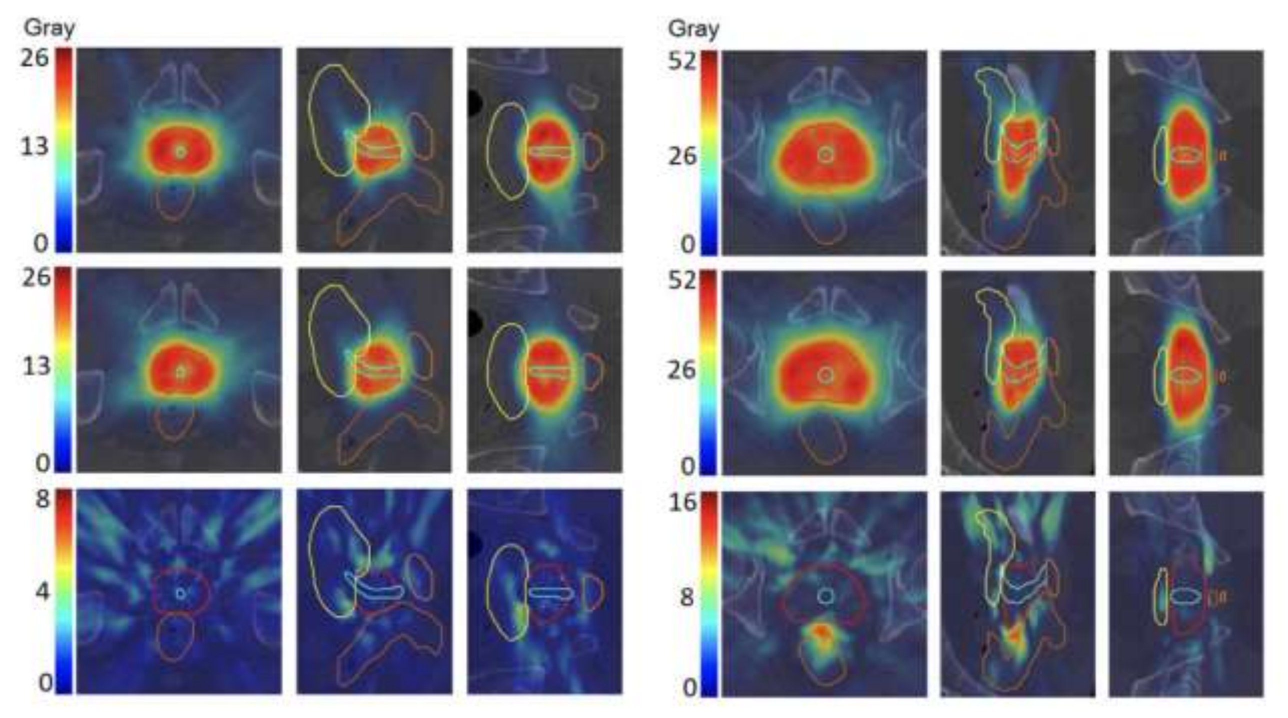
Research being conducted – examples

- ERROR: European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement No 691203 (https//:error.upatras.gr).



Research being conducted - examples

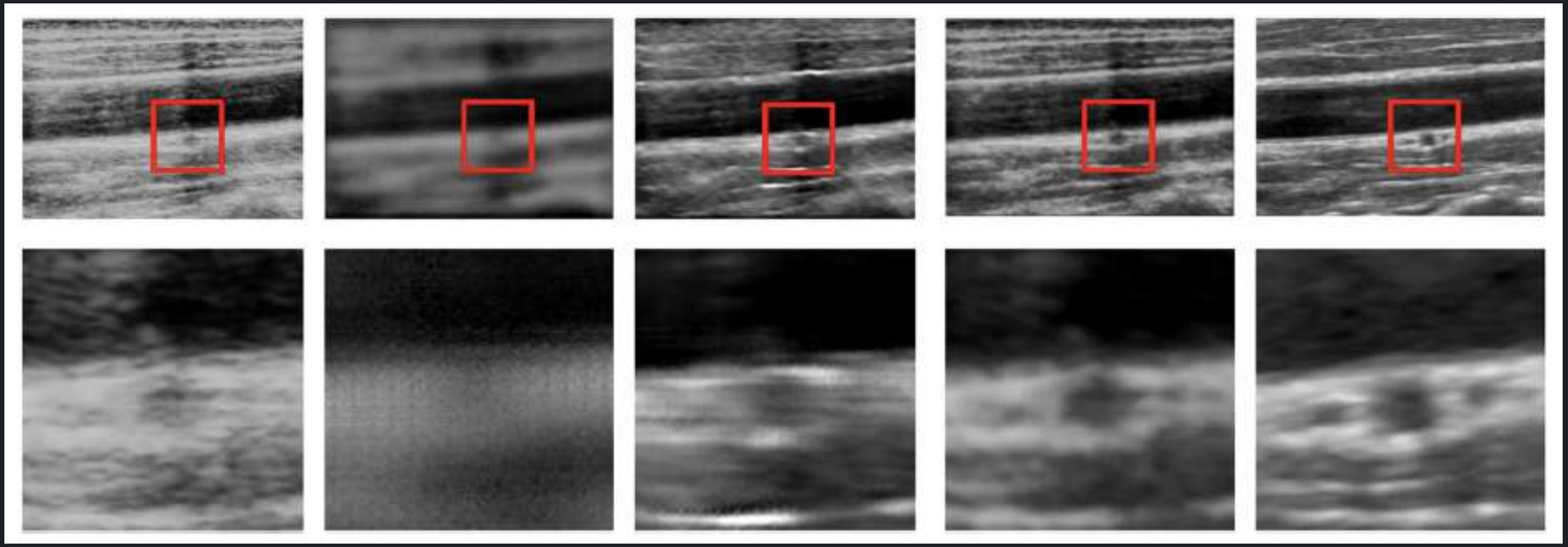
- DL algorithms have been developed to utilize patient anatomy and raw imaging information to predict radiation dose and consequently increase TP efficiency and improve RT plan quality



Kearney, V, Scientific Reports, 2020

Research being conducted - examples

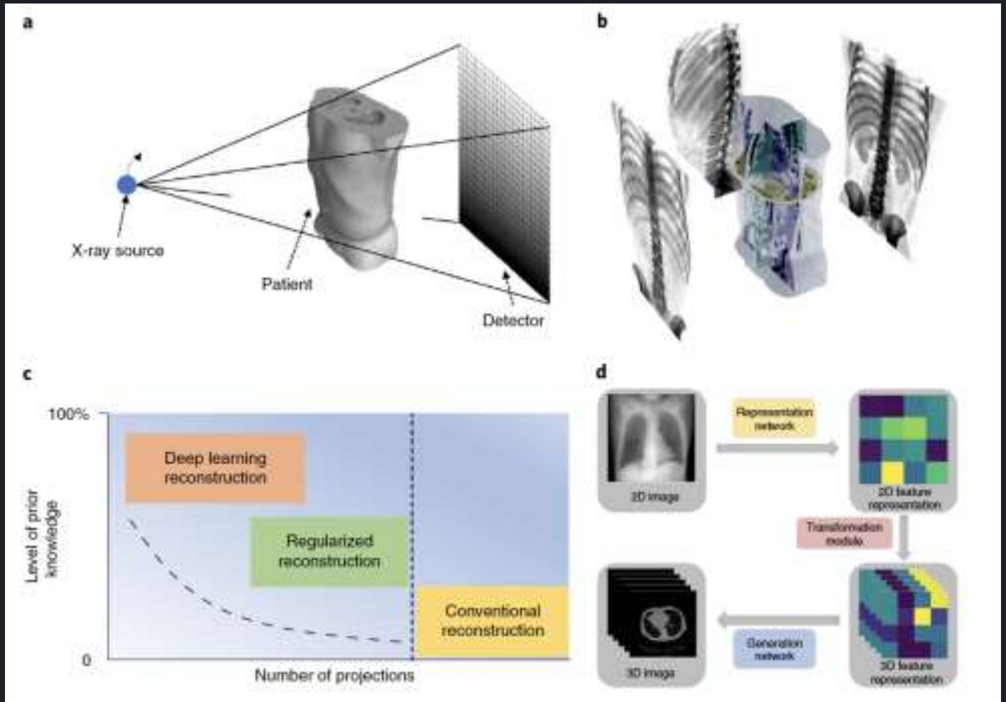
- Generative Model (SSC U-Net) has been developed to improve image quality of portable US images.



Wang, R, Journal on Advances on SP, 2019

Research being conducted – examples

- DL algorithms to develop the 3D reconstruction image of a patient from 2D projections



Shen, L, Nature Biomed Engin, 2019

Research being conducted - examples

- Deep convolutional neural networks have been used to estimate dose rate maps……

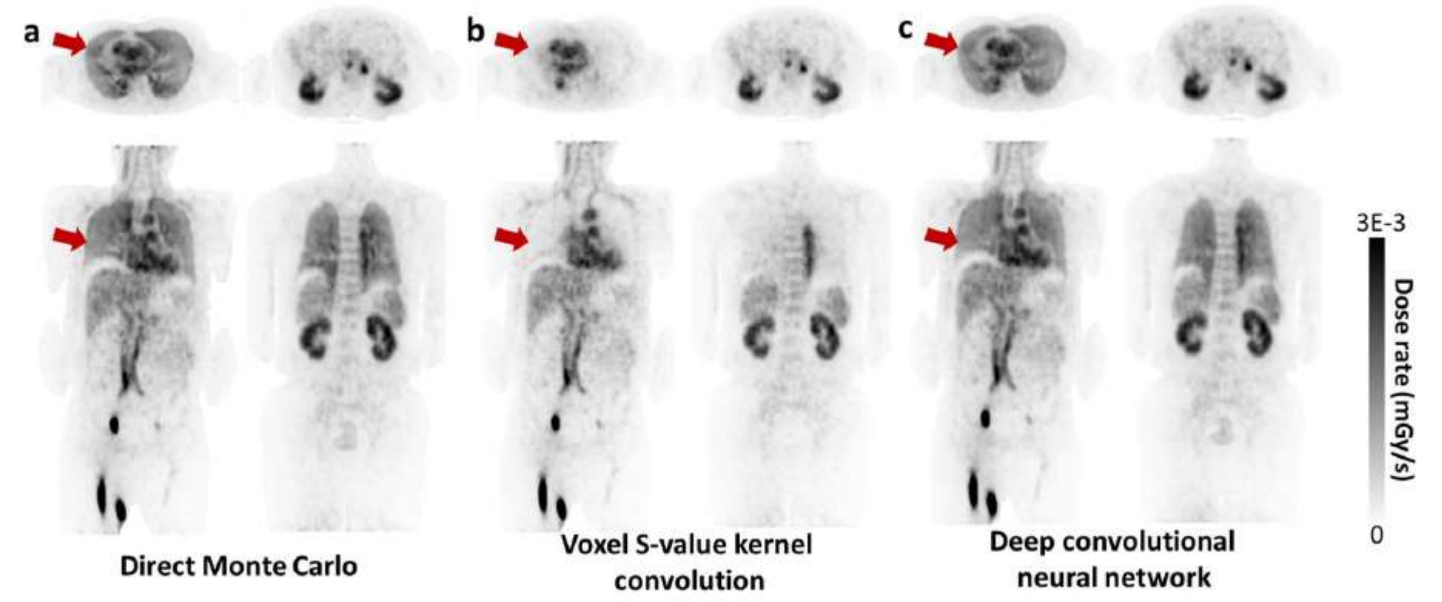


Figure 2. Dose rate maps estimated by (**a**) direct Monte Carlo, (**b**) VSV kernel convolution, and (**c**) deep convolutional neural network.

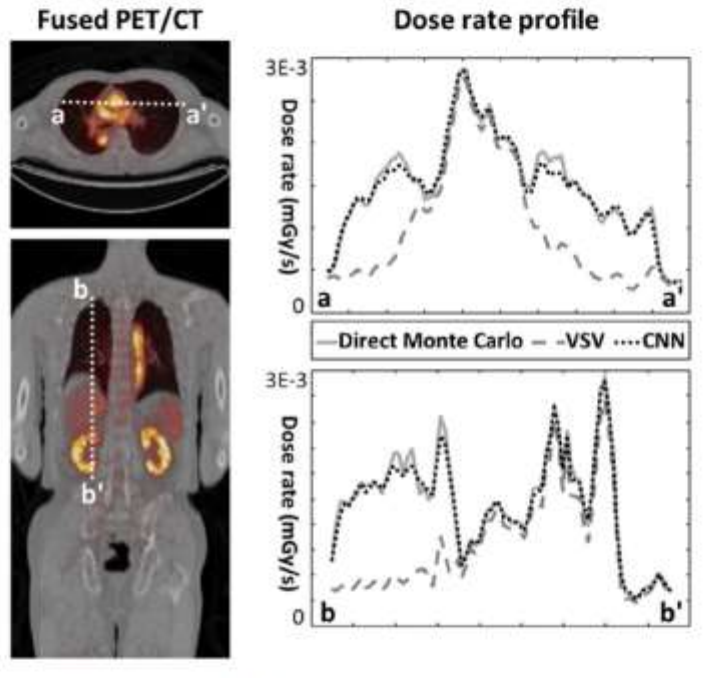
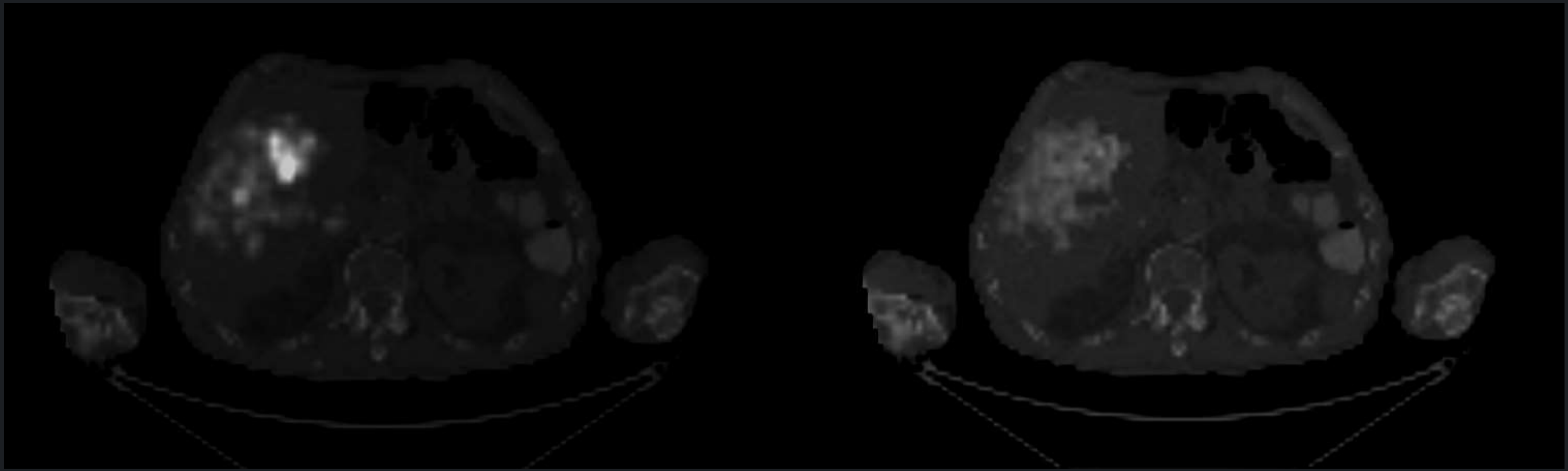


Figure 3. Two dose rate profiles drawn on the axial and coronal slices.

Lee, M.S., Sci Rep, 2019

Research being conducted - examples

- DL algorithms are being utilized to predict post therapy ^{90}Y biodistribution from pre therapy SPECT ^{99m}Tc MAA (*in progress*)

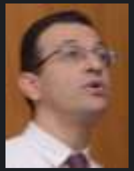
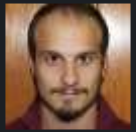


Plachouris, D, in progress, 2020

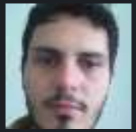
Future – Conclusion

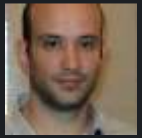
- We now are in the future
- Use technology evolution so that:
  - Develop bigger phantom DBs taking into account individual patient characteristics
  - Make MC simulations faster
  - Optimize procedures to minimize radiation burden to normal tissue
  - Foretell a therapy result from the diagnostic procedure
  - Minimize error
- Do this in real time…..

Acknowledgments

Name	Position	expertise
George Kagadis	Prof. Med Physics – Med Informatics	Dosimetry, MC sims, ML
Dimitris Karnabatidis	Prof Radiology	Radiology
Nikos Papathanasiou	Prof Nuclear Medicine	Nuc Medicine
Dimitris Plachouris	PhD student	MC sims, ML, phantoms
Konstantinos Chatzipapas	PhD student	MC sims, dosimetry, image recons
Thomas Nanos	PhD student	MC sims and ML
Fotis Papathanasopoulos	PhD	Technical – admin support
Christos Alexakos	PhD	Data Protection specialist, web developer, cloud specialist
Stavros Tsantis	PhD	ML and DL algorithms
Ilias Gatos	PhD	ML and DL algorithms



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THANK YOU!