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Internal dosimetry in diagnostic and therapeutic nuclear medicine using GATE and GAMOS Monte Carlo simulations

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Outline

- Nuclear medicine
- Internal dosimetry
- Monte Carlo simulations with GATE and GAMOS
- Diagnostic dosimetric studies:

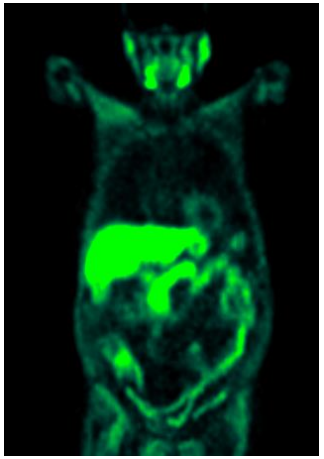
  ^{18}F-choline PET/CT
- Therapy planning dosimetric studies:

  ^{90}Y-microspheres TARE via ^{99m}Tc-MAA SPECT/CT

Nuclear medicine

Employs radioactive nuclei (administered as radiopharmaceuticals) for diagnostic and therapeutic purposes

Diagnostics: Functional imaging



$$A = \frac{dN_{decays}}{dt} \text{ (Bq)}$$

Therapy: Molecular RadioTherapy (MRT)

Internal dosimetry

Asses radiation absorbed doses to tissues and organs imparted by radiopharmaceuticals:

- Therapy planning and monitoring
- Benefit/risk healthy tissues
- Radiation protection
- Diagnositc protocols

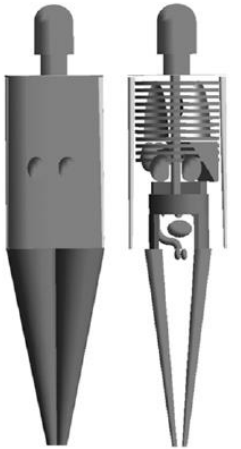
$$\mathrm{D} = \frac{d\mathrm{E}_{\mathrm{abs}}}{d\mathrm{m}} \left(\mathrm{Gy} = \frac{\mathrm{J}}{\mathrm{kg}} \right)$$

3D antropomorphic phantoms:

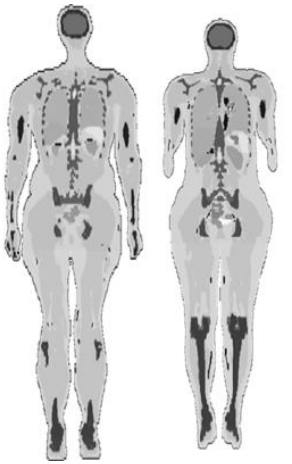
- mathematical models
- voxel level
  - average human models
  - patient-specific

Calculation approaches:

- Local energy deposition
- Dose point kernels
- S-factors
- Direct Monte Carlo simulation



MIRD5 mathematical phantom

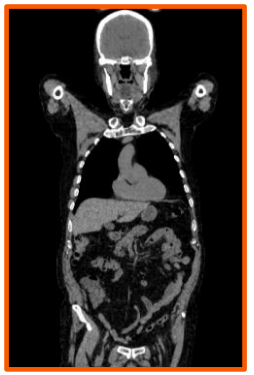


ICRP reference voxelized phantoms

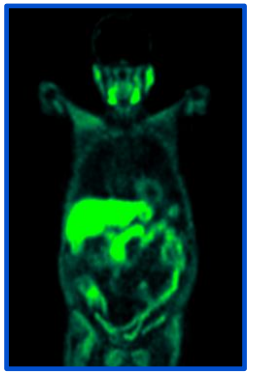
Monte Carlo simulations

Voxel level patient-specific direct MC

- Morphologic data: CT scans → voxelized phantom



- Functional data: SPECT or PET scans → voxelized radionuclide spatial distribution



Direct MC in internal dosimetry: simulation of radionuclide decay and interaction of its daughters with living matter

MC algorithms + e.m. and hadronic physics → particles/radiation – matter interaction simulation

- tracking "history" of simulated particles → retrieving statistical quantities in defined geometries (e.g. deposited energy, angular distributions...)

Pro: most accurate and patient-specific method

Cons: long computational time

Dewaraja, Y. K. et al. "MIRD pamphlet No. 23: quantitative SPECT for patient-specific 3-dimensional dosimetry in internal radionuclide therapy". *The Journal of Nuclear Medicine* 53(8), 1310–1325 (2012) DOI: 10.2967/jnumed.111.100123.

GATE and GAMOS MC simulations

Import 3d images (e.g. dicom, mhd)

- CT → voxelized phantom volume → materials and densities
- PET/SPECT → voxelized source spatial distribution → nuclide decay spatial probability

Setting:

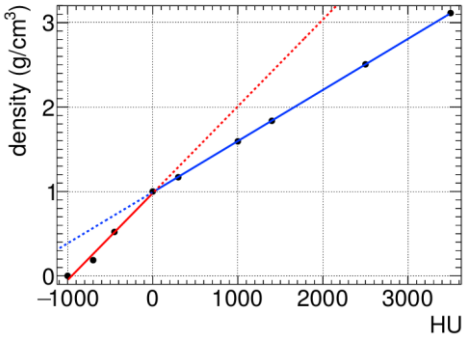
- physics models and databases
- processes
- primary particles
- N. of evt, scoring and storing quantities of interest

GATE

- Assign material (diff. chemical composition) from HU intervals
- Define submaterials (same chem. comp.) from HU subintervals
- assign density to submaterials from HU-density relation

GAMOS

- Assign density directly converting through HU-density relation
- Assign material (chemical composition) from density intervals

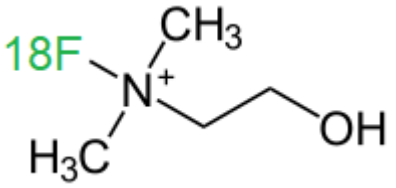


Diagnostic case: ^{18}F-choline PET

D. Pistone et al. MONTE CARLO BASED DOSE-RATE ASSESSMENT IN ^{18}F-CHOLINE PET EXAMINATION: A COMPARISON BETWEEN GATE AND GAMOS CODES *Atti della Accademia Peloritana dei Pericolanti Classe di Scienze Fisiche, Matematiche e Naturali* Vol. 98, No. 1, A5 (2020) DOI: https://doi.org/10.1478/AAPP.981A5

- ^{18}F: β^+ (97%)
  - $\langle E_{\beta+} \rangle = 633.5$ keV
  - $t_{1/2} = 109.8$ m
- Choline:
  - synthesized by liver
  - enhanced uptake in tumors

$\longrightarrow$ ^{18}F-choline: evaluate slow-growing neoplasms (e.g. prostate cancer)



Simulations

- data: co-registered ^{18}F-choline PET/CT
- phantom: materials in Tab
- physics: G4EmStandardPhysics_option3
- primaries: ^{18}F (10^8 evts)

Material	HU intervals	ρ (g/cm^3)
G4_AIR	HU $\leq$ -855.75	$\rho \leq 0.10$
G4_LUNG_ICRP	-855.75 $<$ HU $\leq$ -126.50	$0.10 < \rho \leq 0.85$
G4_ADIPOSE_TISSUE_ICRP	-126.50 $<$ HU $\leq$ -38.98	$0.85 < \rho \leq 0.94$
G4_TISSUE_SOFT_ICRP	-38.98 $<$ HU $\leq$ 343.61	$0.94 < \rho \leq 1.2$
G4_BONE_CORTICAL_ICRP	HU $>$ 343.61	$\rho > 1.2$

Diagnostic case: ^{18}F-choline PET

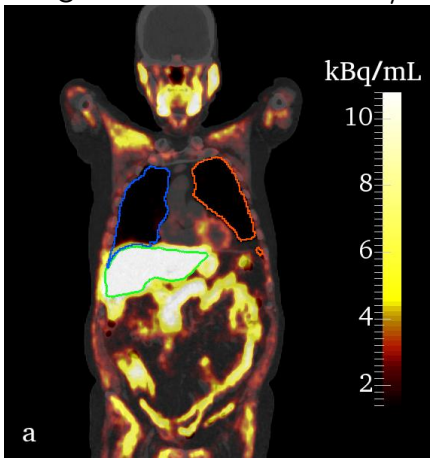
- Dose rate calculation

$$\dot{D}_{ijk}(t_s) = \frac{D_{ijk}}{N_{evts}} \cdot A(t_s)$$

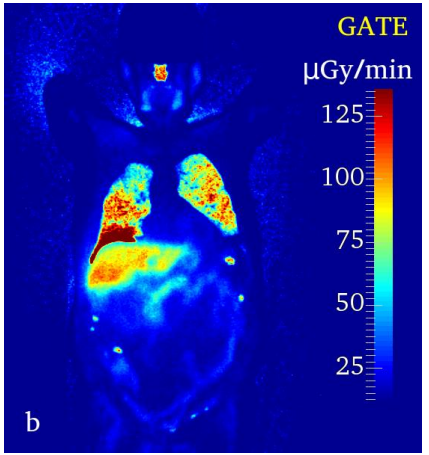
- mean values into VOIs: liver, lungs

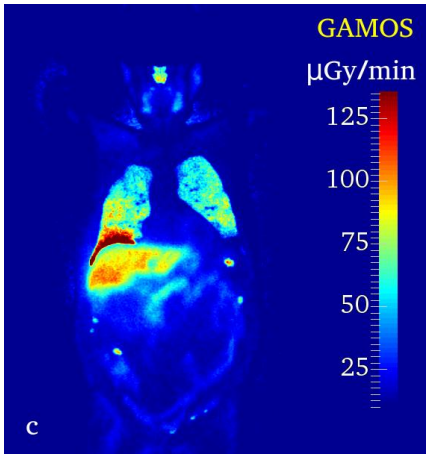
VOI	Liver	Right Lung	Left Lung
Volume (cc)	1074	2091	1797
$\langle \dot{D} \rangle_{GATE}$ (μGy/min)	83.3	71.4	59.8
δ_{GATE} (%)	± 5.5	± 14.5	± 15.6
$\langle \dot{D} \rangle_{GAMOS}$ (μGy/min)	84.3	62.7	50.7
δ_{GAMOS} (%)	± 5.5	± 13.2	± 14.3
ε (%)	-1.1	+ 13.8	+ 18.0

co-registered ^{18}F-choline PET/CT



dose rate maps





δ = relative statistical uncertainty

$$\varepsilon = \frac{\langle \dot{D}_{ijk}^{GATE} \rangle - \langle \dot{D}_{ijk}^{GAMOS} \rangle}{\langle \dot{D}_{ijk}^{GAMOS} \rangle} \cdot 100$$

Diagnostic case: ^{18}F-choline PET

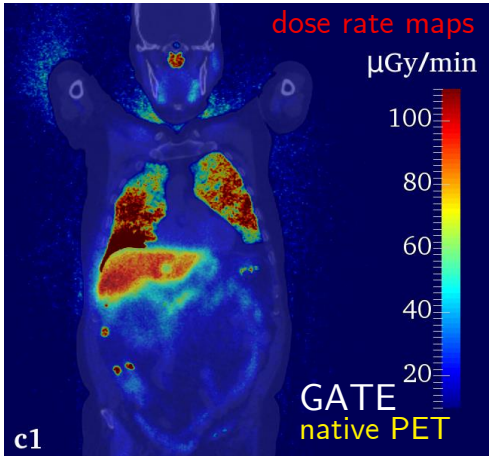
Background and artifacts treatment

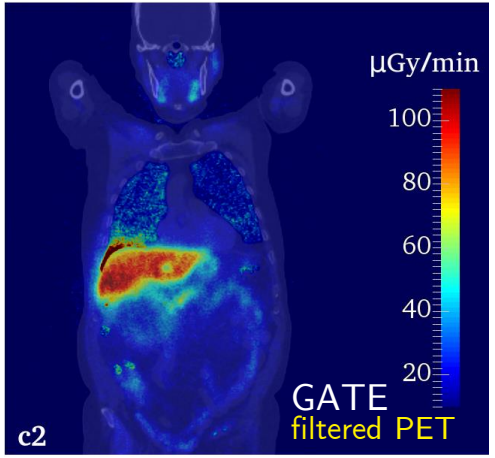
PET filtering technique

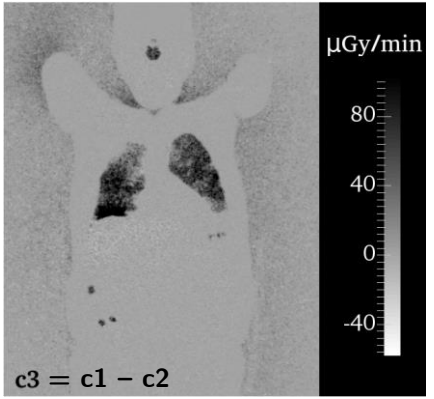
- $c_{A\ PET} = 0$ if $HU_{CT} < -855$ (setting zero decay probab. in air)
- $c_{A\ PET} > 100$ Bq/ml (removing background noise)

filtered PET simulations

VOI	Liver	Right Lung	Left Lung
Volume (cc)	1074	2091	1797
$\langle \dot{D} \rangle_{GATE\ fil}$ (μGy/min)	86.3	38.4	28.5
$\delta_{GATE\ fil}$ (%)	± 5.6	± 19.8	± 22.2
$\langle \dot{D} \rangle_{GAMOS\ fil}$ (μGy/min)	86.8	37.4	26.9
$\delta_{GAMOS\ fil}$ (%)	± 5.6	± 17.7	± 20.2
ε_{fil} (%)	- 0.64	+ 2.6	+ 5.9
κ_{GATE} (%)	+ 3.5	- 46.3	- 52.3
κ_{GAMOS} (%)	+ 3.0	- 40.4	- 46.8







δ = relative statistical uncertainty

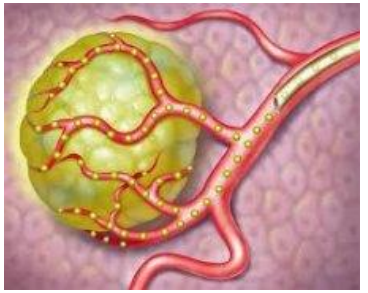
$$\varepsilon = \frac{\langle \dot{D}_{ijk}^{GATE} \rangle - \langle \dot{D}_{ijk}^{GAMOS} \rangle}{\langle \dot{D}_{ijk}^{GAMOS} \rangle} \cdot 100$$

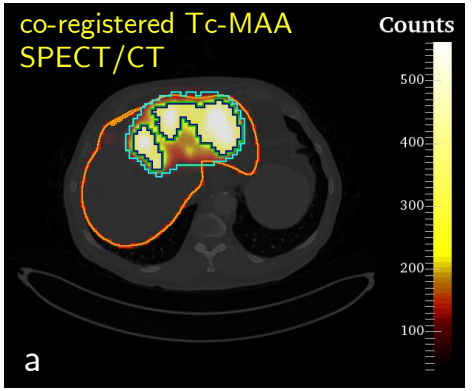
$$\kappa = \frac{\langle \dot{D}^{fil} \rangle - \langle \dot{D}^{unfil} \rangle}{\langle \dot{D}^{unfil} \rangle} \cdot 100$$

Therapy case: ^{90}Y-microspheres TARE

Trans-Arterial Radio-Embolization (TARE) of HepatoCellular Carcinoma (HCC)

- radioembolization via ^{90}Y glass microspheres
- pre-therapy ^{99m}Tc macroaggregated albumin (Tc-MAA) scintigraphy





Simulations

- data: 3 patients, co-registered Tc-MAA SPECT/CTs (Fig. a)
- phantom: materials in Tab
- physics: GATE G4EmStandard_opt3, GAMOS GmEMExtendedPhysics
- primaries: ^{90}Y (10^8 evts)
- source: Tc-MMA SPECT to simulate ^{90}Y distribution

GAMOS: Auditore, L. et al "Internal dosimetry for TARE therapies by means of GAMOS Monte Carlo simulations". *Physica Medica: European Journal of Medical Physics* 64, 245–251 (2019) DOI: 10.1016/j.ejmp.2019.07.024.

GATE: preliminary results

Material	HU intervals	ρ (g/cm^3)
G4_AIR	HU ≤ -855.75	ρ ≤ 0.10
G4_LUNG_ICRP	-855.75 < HU ≤ -126.50	0.10 < ρ ≤ 0.85
G4_ADIPOSE_TISSUE_ICRP	-126.50 < HU ≤ -38.98	0.85 < ρ ≤ 0.94
G4_TISSUE_SOFT_ICRP	-38.98 < HU ≤ 343.61	0.94 < ρ ≤ 1.2
G4_BONE_CORTICAL_ICRP	HU > 343.61	ρ > 1.2

Therapy case: ^{90}Y-microspheres TARE

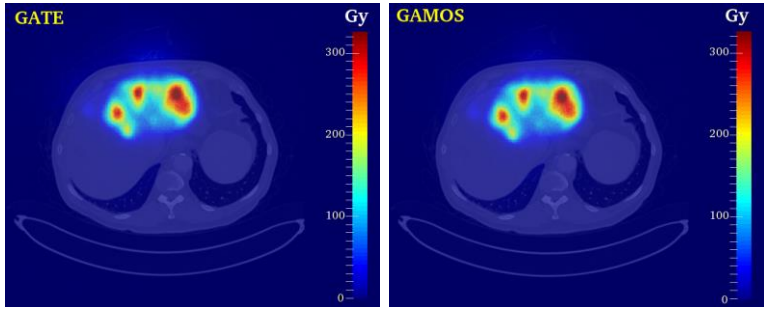
- Dose calculation
  - $D_{corr} = \frac{D_{output}}{N_{evts}} \cdot \tilde{A} \cdot b$
  - no biological clearance → effective decay time = physical nuclide decay time
  - assuming instantaneous uptake

$$\tilde{A} = \int_0^\infty A(t)\,dt = A(0)\int_0^\infty e^{-\mu_{90Y}t}\,dt = A(0)\cdot \tau_{90Y}$$

  - $b = \frac{A_{whole\ SPECT}}{A_{liver\ VOI}}$ for background correction

$$\varepsilon = \frac{\langle \dot{D}_{ijk}^{GATE} \rangle - \langle \dot{D}_{ijk}^{GAMOS} \rangle}{\langle \dot{D}_{ijk}^{GAMOS} \rangle} \cdot 100$$

dose maps patient 2



- mean values into VOIs:

liver, lesion (segmented on CT)
liver perfused (segmented on SPECT)
healthy liver (= liver - lesion)
healthy liver perfused (= liver perfused - lesion)

patient 1	A(0) (MBq)	739			
VOI	Liver	Liv. Per.	Lesion	H. Liv.	H. L. P.
$\langle D \rangle_{GATE}$ (Gy)	29.4	137.2	152.5	7.9	80.6
$\langle D \rangle_{GAMOS}$ (Gy)	29.4	136.0	150.4	8.1	83.0
ε (%)	0.03	0.90	1.38	-2.99	-2.86
patient 2	A(0) (MBq)	2490			
VOI	Liver	Liv. Per.	Lesion	H. Liv.	H. L. P.
$\langle D \rangle_{GATE}$ (Gy)	44.5	145.4	235.0	15.9	84.9
$\langle D \rangle_{GAMOS}$ (Gy)	44.6	140.1	222.4	17.4	83.2
ε (%)	-0.16	3.78	5.66	-8.35	2.07
patient 3	A(0) (MBq)	2720			
VOI	Liver	Liv. Per.	Lesion	H. Liv.	H. L. P.
$\langle D \rangle_{GATE}$ (Gy)	56.0	107.5	237.4	44.1	83.2
$\langle D \rangle_{GAMOS}$ (Gy)	56.3	105.3	229.2	44.3	81.4
ε (%)	-0.54	2.08	3.59	-0.45	2.26

Conclusions

- Direct MC simulation + voxel imaging for internal dosimetry
  - most accurate and patient-specific technique
  - dealing with sub-organ density inhomogeneities and activity non-uniformities
  - functional scan filtering (thresholds + logical operations) could lead to more realistic simulations
- GATE and GAMOS simulations
  - good agreement for perfused VOIs and soft tissue densities
  - scan filtering → better agreement also for low density non-source VOIs
- Prospects:

Diagnostics

- ^{18}F-choline PET:
- extend to larger statistical sample
- focus on lung voxel dosimetry →
- further optimize PET filtering technique (e.g. redistribution of removed counts in perfused regions), try different approaches (e.g. lungs average density simulations)
- ideally: multiple time point scans → cumulated activity → Dose

Therapy planning

- ^{90}Y TARE via Tc-MAA SPECT:
- apply SPECT filtering for lungs dose evaluation (whole body scans needed)
- eventual optimization of dose estimation in lungs → improve protocols (optimize administered activity value)

Thank you for your attention

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