Dosimetry of therapeutic beta emitters using GATE Monte Carlo simulation and its experimental validation

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Background

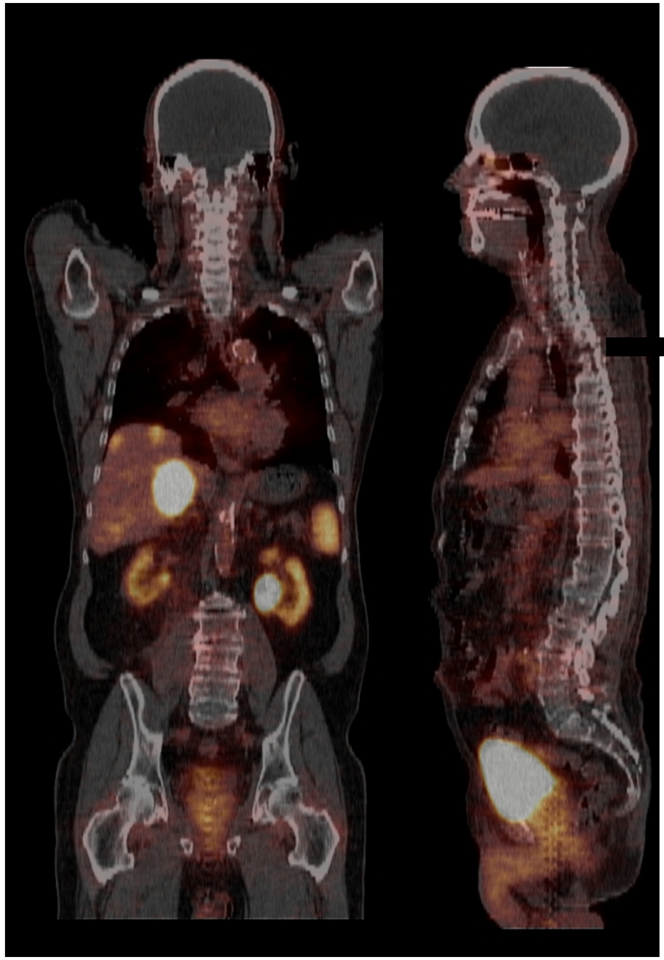
- Current radiopharmaceutical therapy: one-size-fits-all approach but absorbed dose is patient-specific
- We must calculate the patient-specific required activity
- Absolutely necessary because we do not want to kill surrounding healthy tissues
- Dose calculation:

1. Organ-based (MIRD) dosimetry (old method)
2. 3D voxel-wise dosimetry (new method)

Dose point kernels - voxel level

- Dose Point Kernels (DPKs)
  - radial distribution of mean absorbed dose around isotropic point source in infinite homogeneous medium
  - method to compute the absorbed dose from the non-uniform activity or high gradient activity distributions
  - radionuclide-specific and tissue-specific
- Usefulness of kernels?
  - dose distributions using the convolution of 3D-dose kernel matrix with cumulated activity map furnished by quantitative SPECT/CT or PET/CT images
- Ultimate goal: patient-specific dosimetry

Goal: Patient-specific dosimetry



Activity map of patient

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I-131 dose point kernels

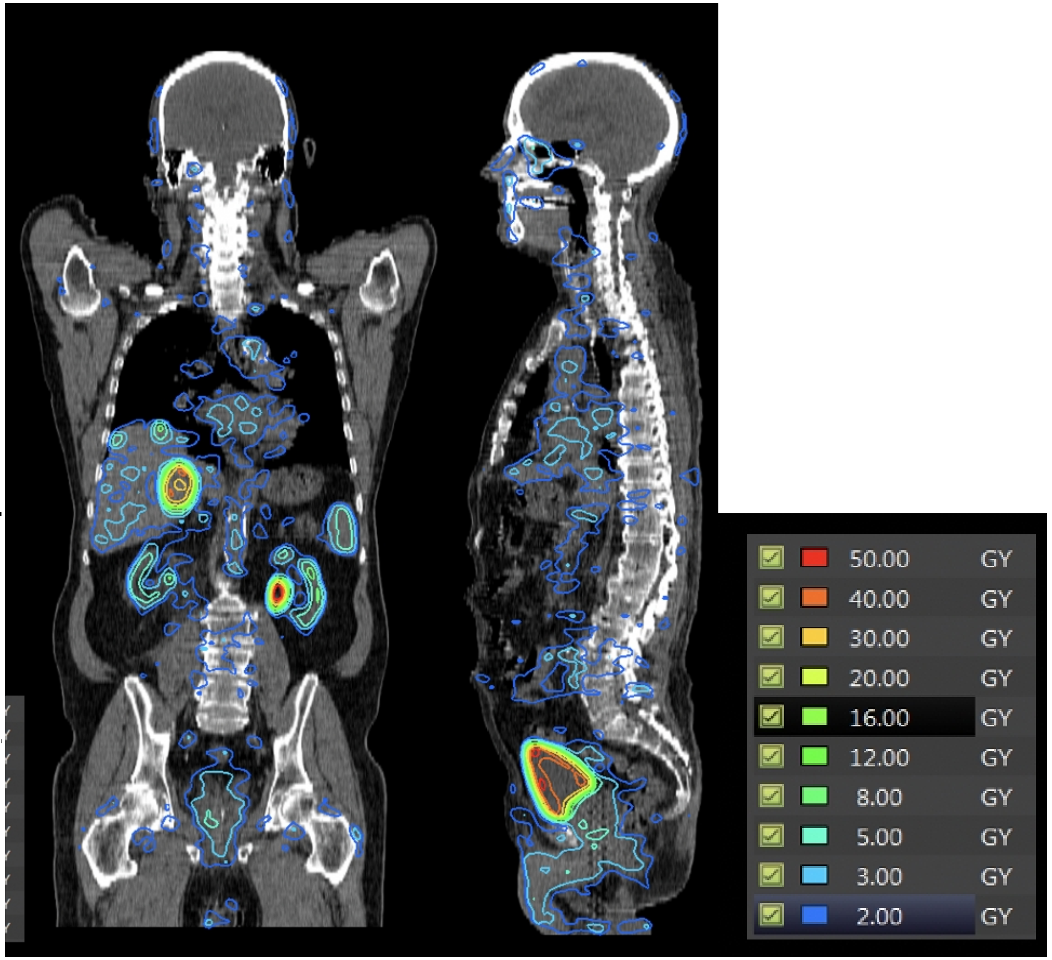
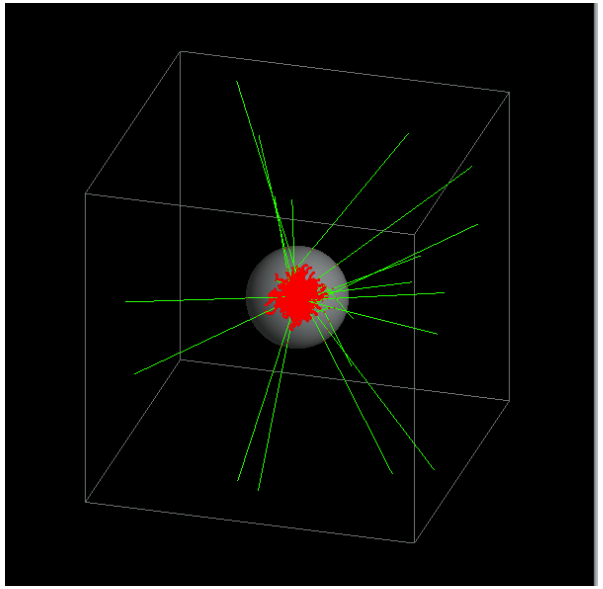


Fig: PET/CT scan of patient and resulting dose calculations from convolution with the full-sized kernel.

First part: Simulation of dose point kernels

- Human body is composed of different tissues: soft tissue, bone, blood, lung, adipose, red marrow …

Materials	bone	blood	lung	water	red marrow	adipose
Z_{eff}	11.87	7.78	7.74	7.42	7.21	6.47
ρ (g/cm^3)	1.85	1.06	0.26	1.00	1.03	0.92



- First, we want to check whether the DPKs depends on tissue types by simulating beta dose point kernels in various tissue types.

Simulation setup

Monoenergetic electron DPKs:

$$J(r/R_{CSDA}) = 4\pi r^2 D(r,E)\frac{R_{CSDA}}{E_0}$$

Beta spectrum DPKs:

$$J(r/X_{90}) = 4\pi r^2 D(r,E)\frac{X_{90}}{E}$$

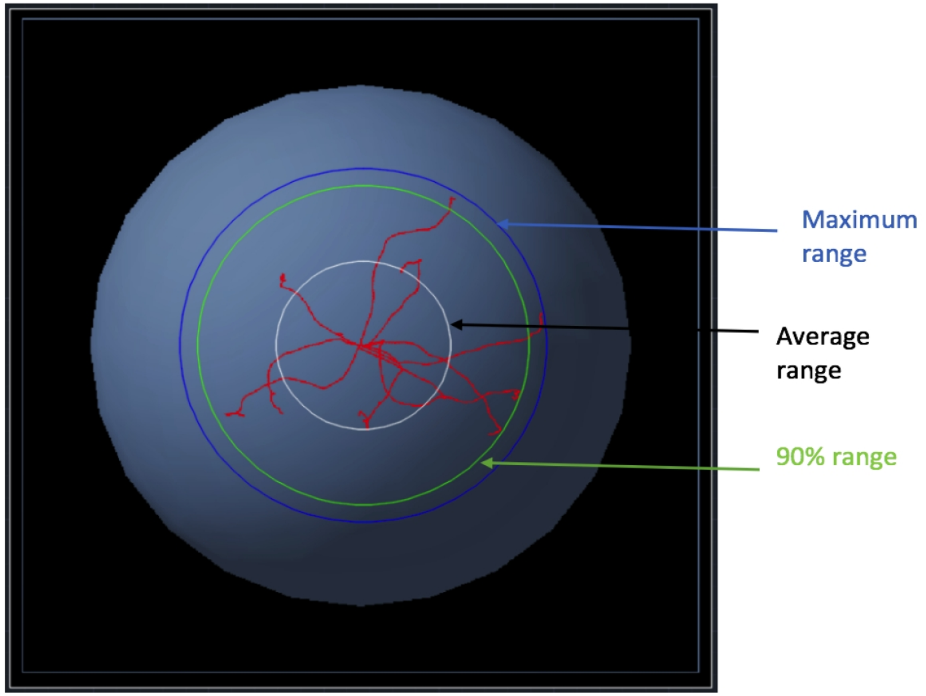


Fig: Spherical phantom geometry

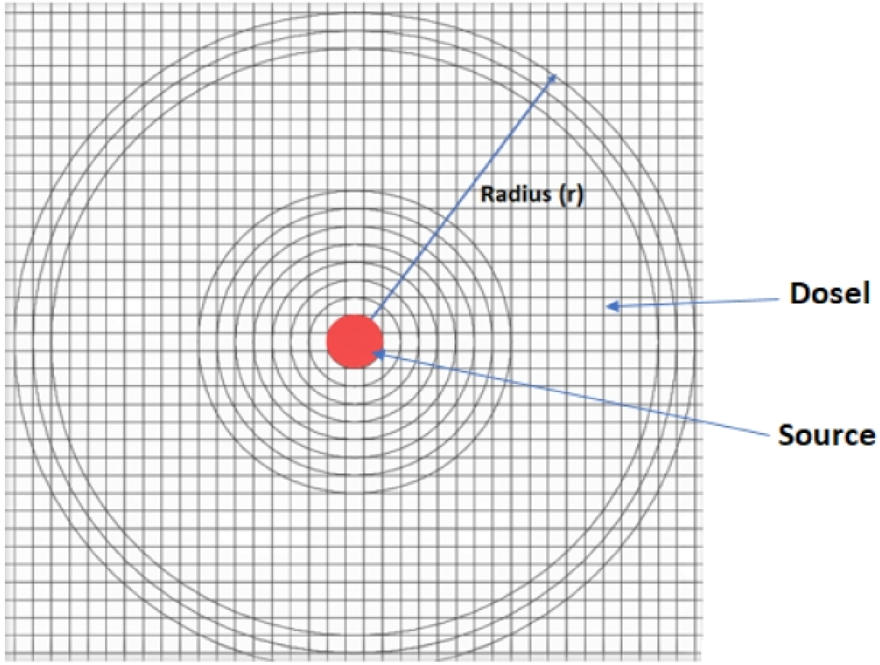
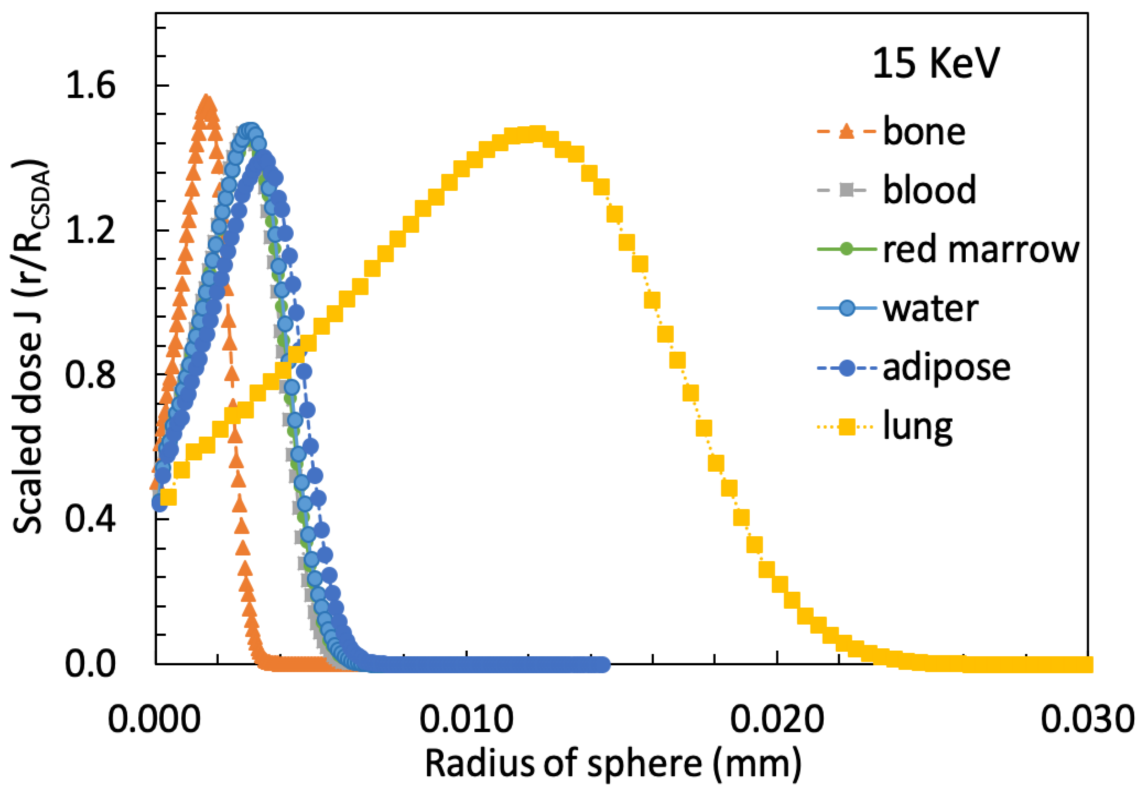
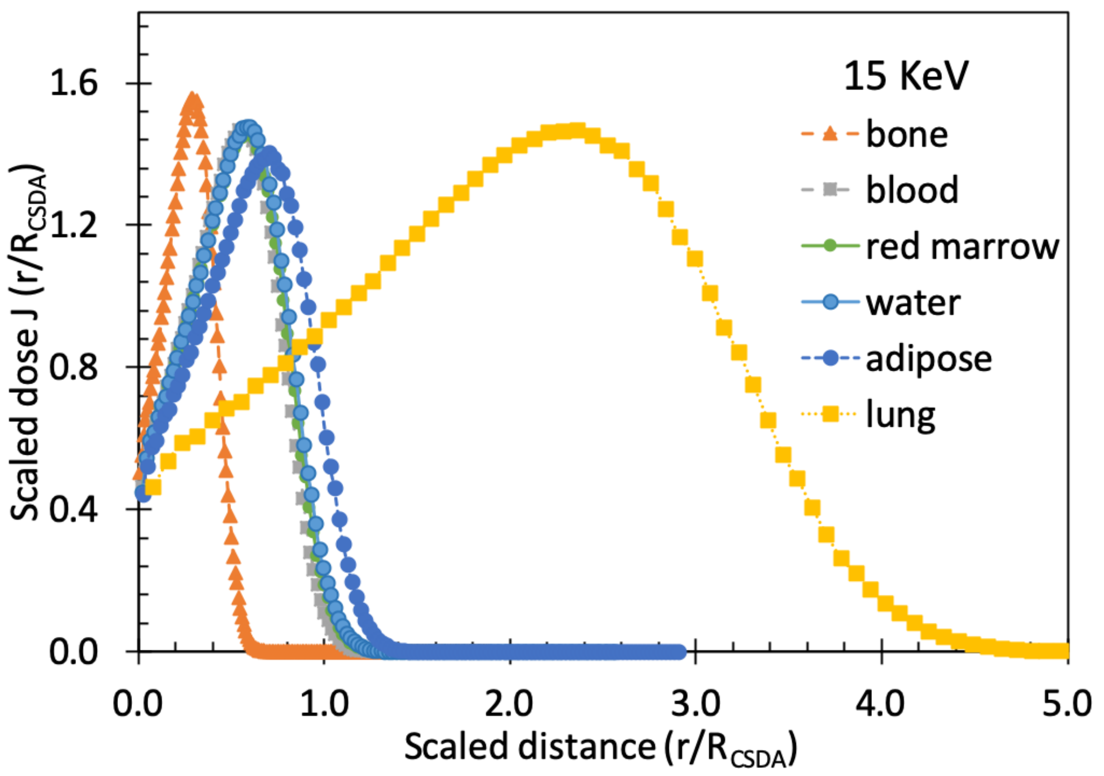


Fig: grids (voxels) of the phantom

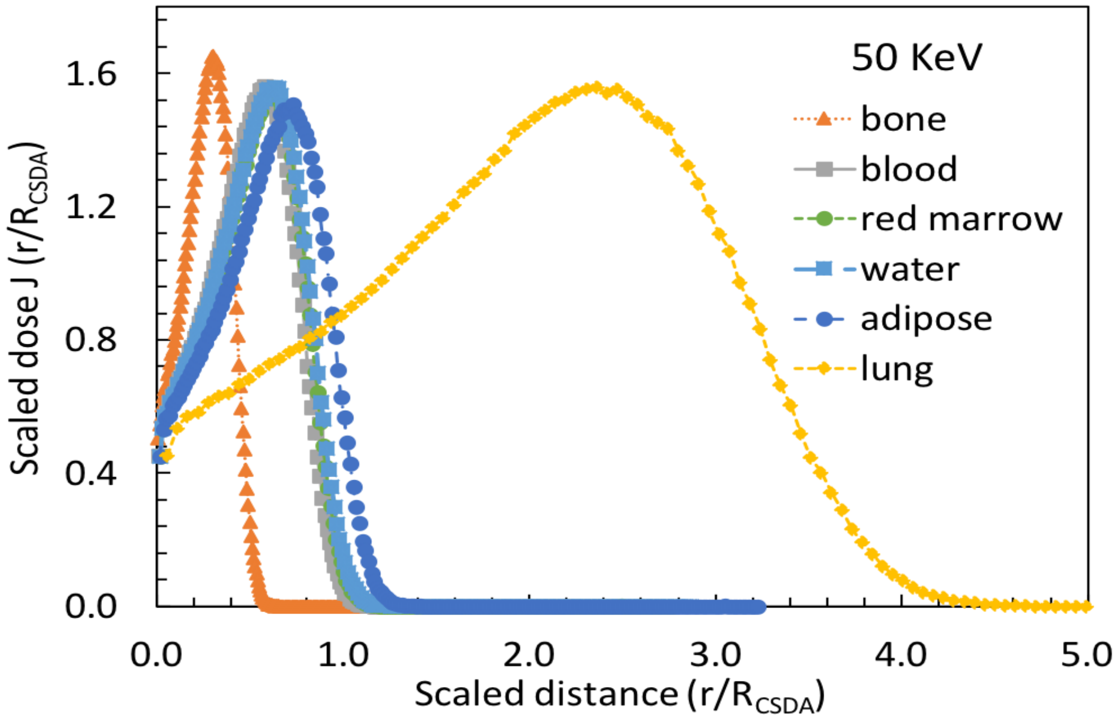
Results: Monoenergetic electrons dose point kernels (15 keV – 10 MeV)

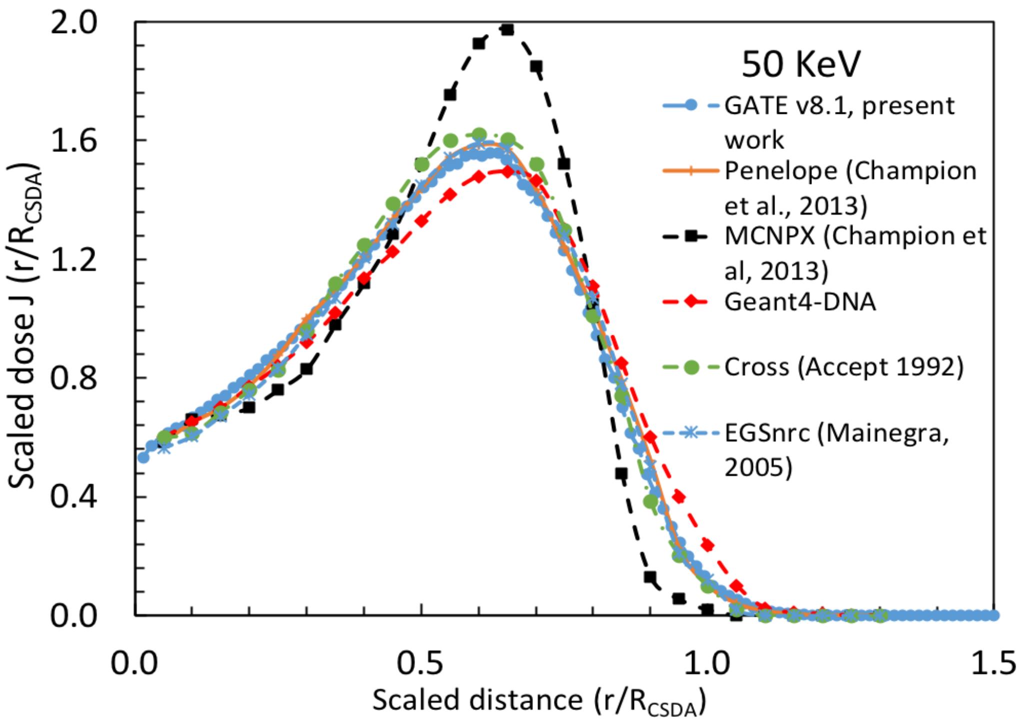




- Minimal differences in height of the kernels – stopping power (Z/A)
- Horizontal spacing – difference in densities

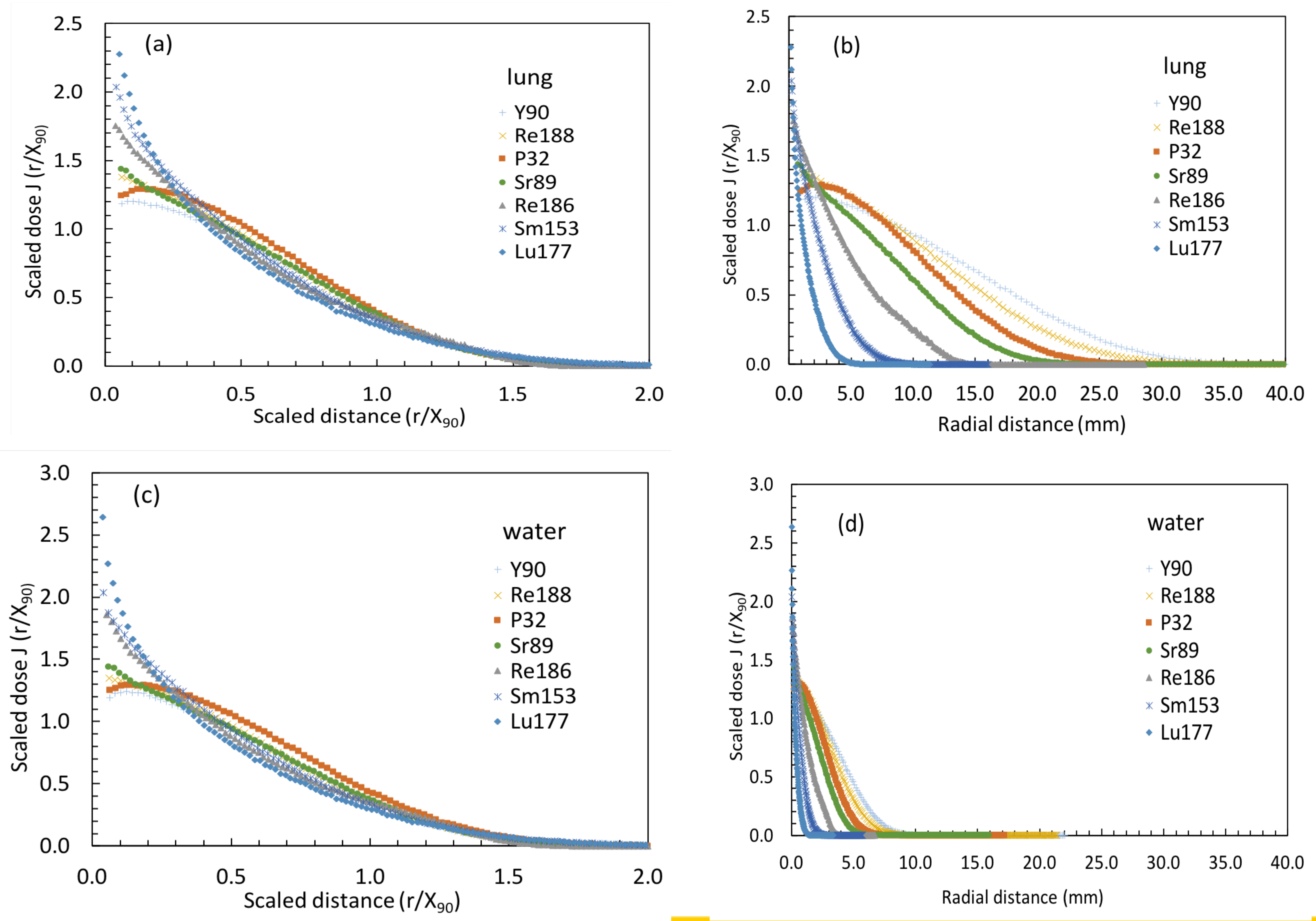
Comparison against literature kernels





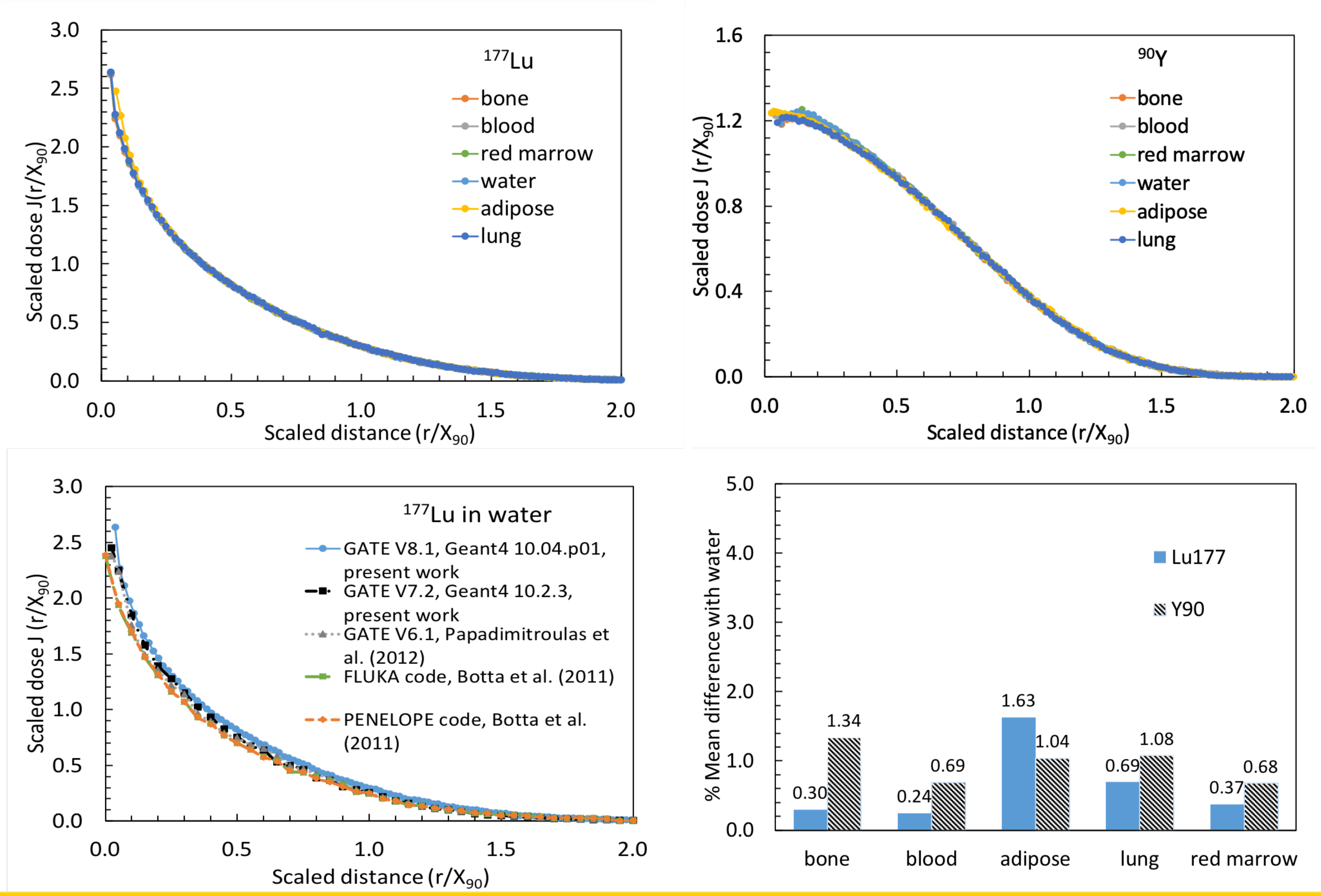
- Summary of this work is available at: *"Measurements of dose point kernels using GATE Monte Carlo toolkit for personalized convolution dosimetry", Ashok Tiwari, Stephen A. Graves, and John Sunderland, SNMMI Annual Meeting, USA, 2019.*
- Kernels are available in: *"The Impact of Tissue Type and Density on Dose Point Kernels for Patient-Specific Voxel-Wise Dosimetry: A Monte Carlo Investigation" Ashok Tiwari, Stephen A. Graves and John Sunderland, Radiat Res (2020) 193 (6): 531–542.*

Results: (ii) beta radionuclides dose point kernels



- Dose point kernels are found to be similar in shape regardless of tissue types (a & c)
- Dose point kernels spacing are due to the difference in tissue densities (b)

Impact of tissue type on dose point kernels?



- Use of single kernel generated in water may be sufficient for 3D dose calculations if densities are taken into account.

Conclusions from dose point kernels simulations

- Dose point kernels of 7 therapeutic beta emitting radionuclides using 6 different tissue types has been generated
- Minimal discrepancies are observed between water and other tissues kernels when scaled with X_{90} for all simulated isotopes
- Impact of tissue type has been found to be minimal for purposes of dosimetry

➢ Now, we we want to check whether simulated dose point kernels are correct by the experimental validation of beta absorbed doses.

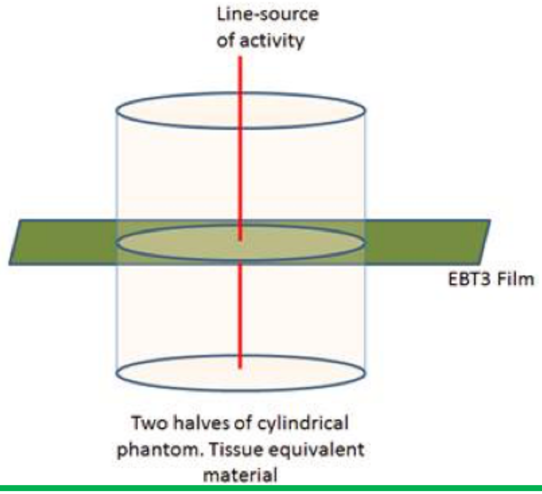
Second part: Validation of <u>beta</u> dose point kernels?

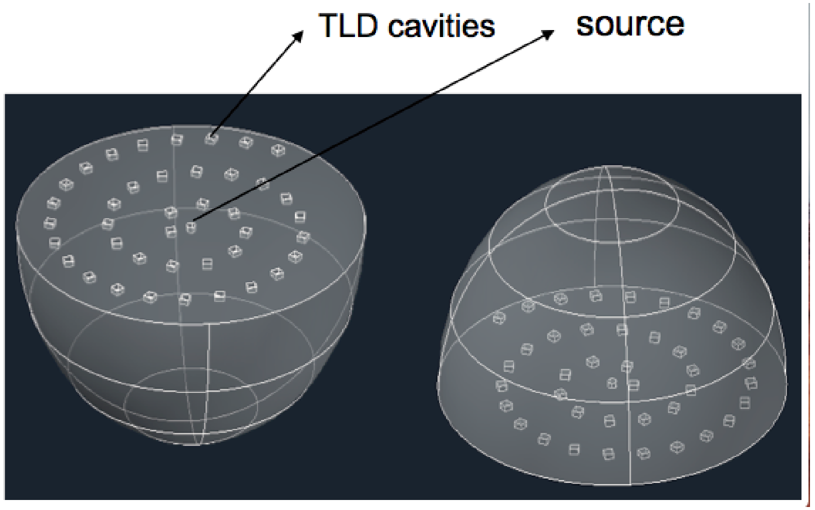
- Absorbed dose delivered by betas are ~(100-1000) times more compared to photons dose
- Since ranges of beta particles are small, can we create a suitable geometry for experiment?
- Only a couple of photons kernels validation work have been published (Giap et al. 1995, Gardin et al. 2003 & Wilderman et al. 2007)
- To the best of our knowledge, nobody has performed the experimental validation of beta dose point kernels
- EBT3 films and tissue eq. materials were utilized for absorbed dose measurements

Validation work continued:

We initially thought two types of experimental methods:

1. phantom with line source and Gafchromic film (EBT3)
2. phantom with point source and Thermoluminiscent dosimeters (TLDs)





Method 1: Phantom with EBT3 film using a line source

Method 2: Phantom with TLD cavities using a point source

Monte Carlo simulation and experiment setup

Sources: ^{90}Y and ^{177}Lu
Phantoms: Polyethylene (0.95 g/cm³), bone (1.90 g/cm³), lung (0.30 g/cm³)

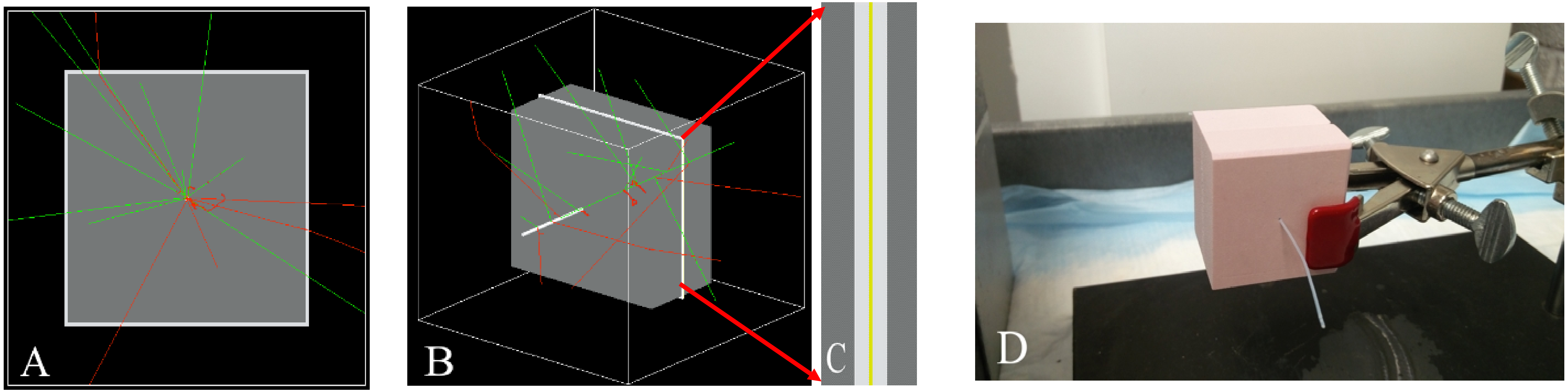


Fig: (A-C) GATE Monte Carlo simulation set-up with the line source and EBT3 film and (D) experimental setup.

Film calibration and calibration curve

- **<u>Calibration</u>**: 6MV photons using Siemens Oncor
- **<u>Scan protocol</u>**: Epson 12000XL, scan one at a time, 508 dpi, RGB format, 48-bit, TIFF image, reflective mode, no color corrections

Calibration function:

$$X(D) = \frac{b + D}{a + D c}$$

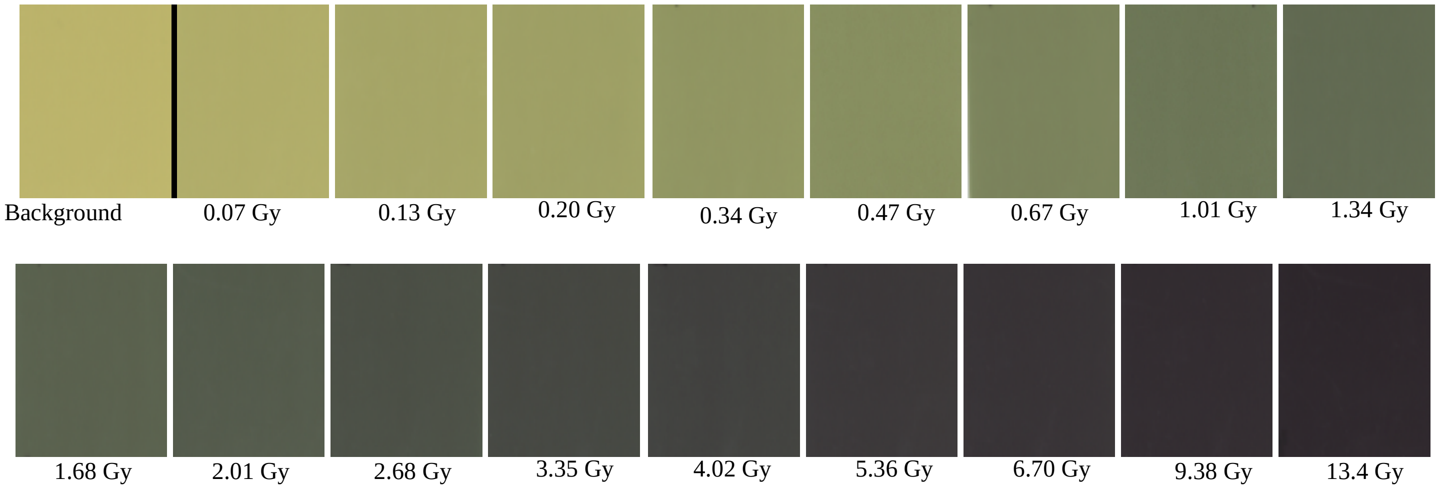
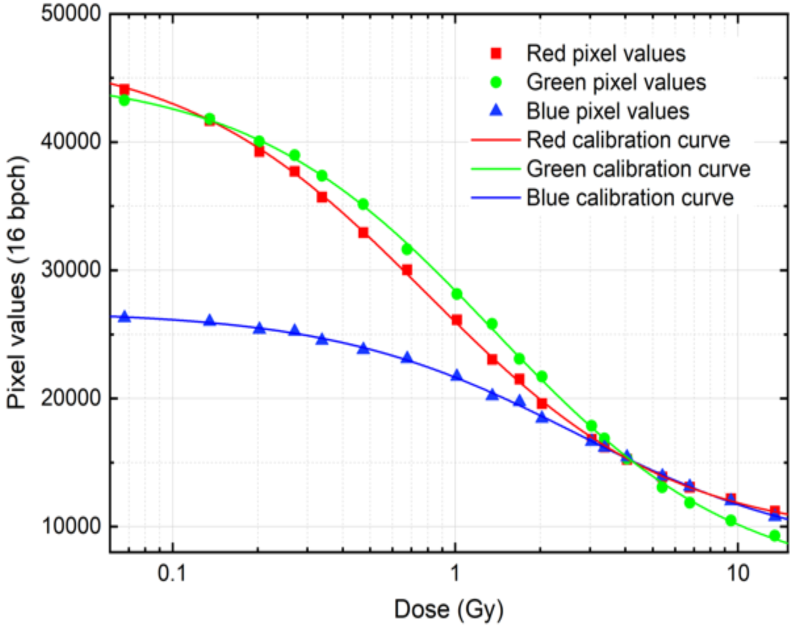


Fig: Scanned images of calibration films



Experimental film exposures

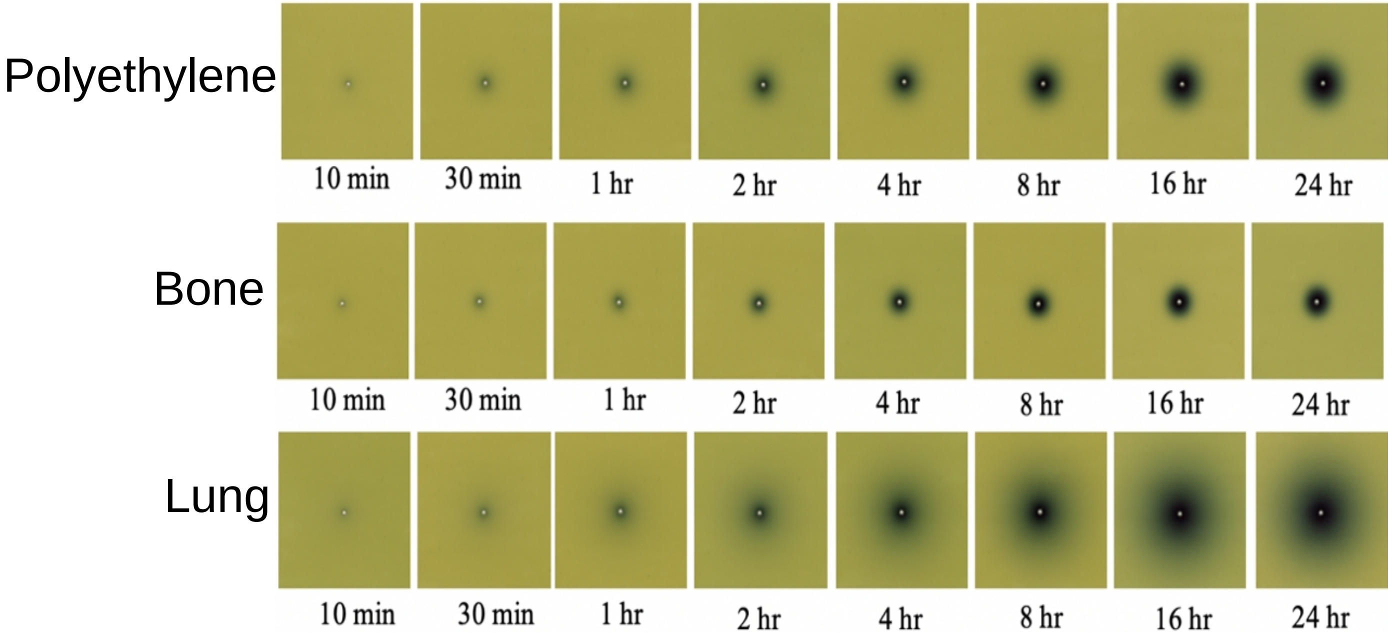


Fig 1: Scanned images of ^{90}Y **exposed** films in different tissue eq. materials.

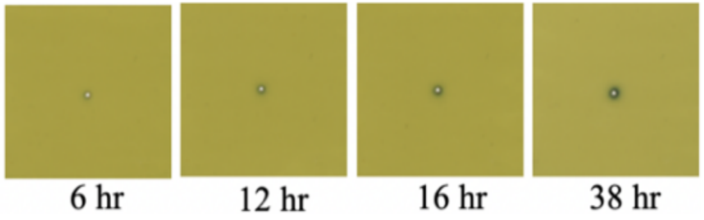
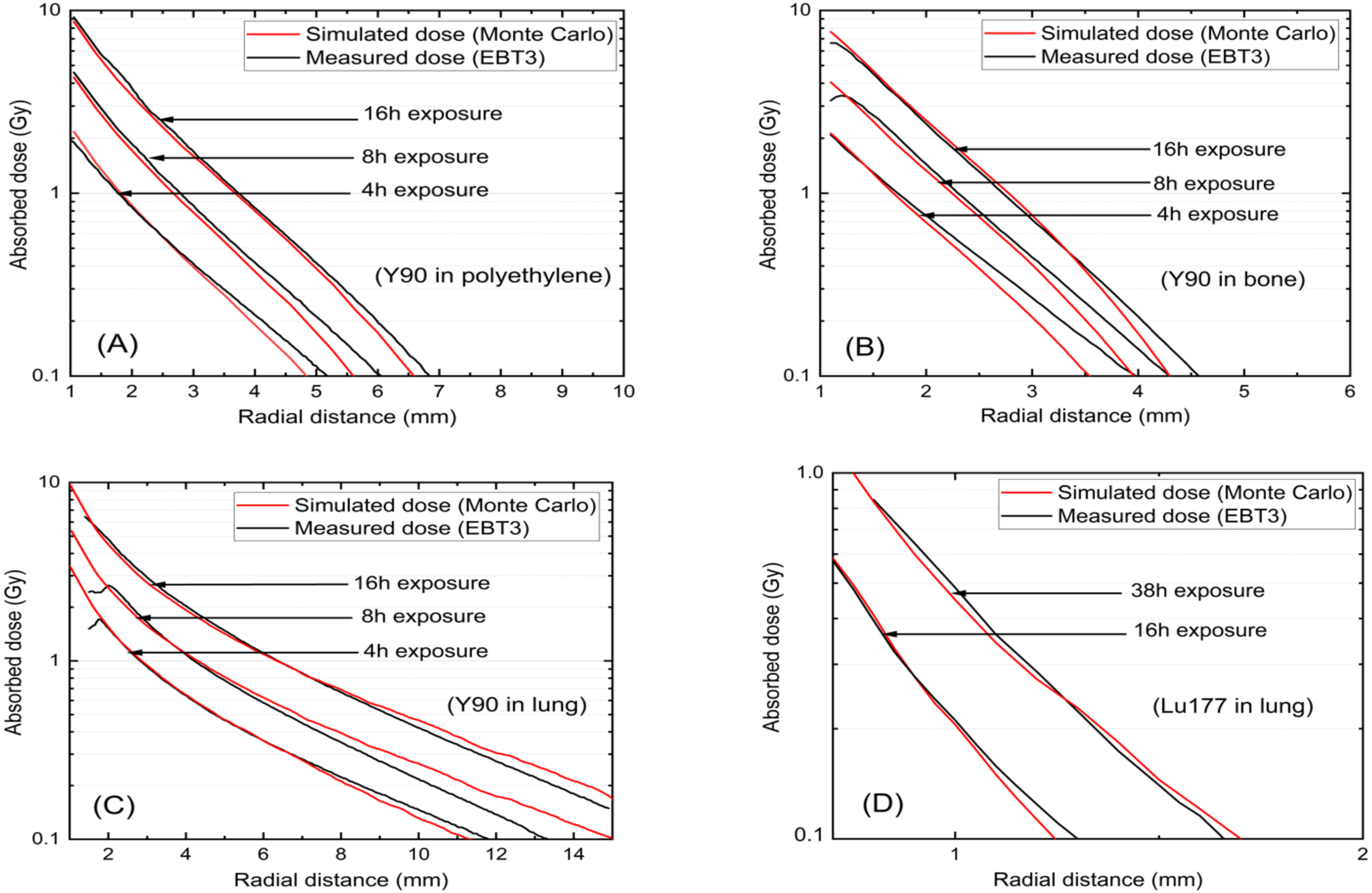


Fig 2: Scanned images of ^{177}Lu **exposed** films in lung eq. material.

Results: Experimental vs GATE Monte Carlo simulation



Error estimations

❖ Experiment

Uncertainties source	Calculated uncertainties
Optical density measurements	0.78% (red), 0.80% (green) and 1.12% (blue)
Exposure time: (4-38) hours	< 1.00%
Activity measurements	5.82%
Curve fitting	2.20% (red), 3.61% (green) and 4.22% (combined)
Measurement of absorbed dose	4.56%
Overall uncertainty	8.64% (combined)

❖ Monte Carlo simulation

- Uncertainties were calculated in each voxel with the doseActor *Uncertainty Edep.*
- Average statistical uncertainties in all simulations were < 4.5% for the absorbed dose range of (0.1–10) Gy.

Details in: *"Absorbed dose distributions from beta-decaying radionuclides: experimental validation of Monte Carlo tools for radiopharmaceutical dosimetry",* Tiwari et al., Med Phys, 2020 (in press).

Conclusion from validation experiment

- Good agreement was observed between the experimental beta absorbed doses compared with the GATE Monte Carlo simulations.
- Beta high-resolution dosimetry is possible using EBT3 films.
- Monte Carlo generated beta dose point kernels can be used confidently in 3D voxel-wise dosimetry.
- These physics-based conclusions help moving forward one step closer to the clinical dosimetry.

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Thank you OpenGATE collaboration for this platform.

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