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

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 ...

<table>
<thead>
<tr>
<th>Materials</th>
<th>bone</th>
<th>blood</th>
<th>lung</th>
<th>water</th>
<th>red marrow</th>
<th>adipose</th>
</tr>
</thead>
<tbody>
<tr>
<td>$Z_{\text{eff}}$</td>
<td>11.87</td>
<td>7.78</td>
<td>7.74</td>
<td>7.42</td>
<td>7.21</td>
<td>6.47</td>
</tr>
<tr>
<td>$\rho$ (g/cm$^3$)</td>
<td>1.85</td>
<td>1.06</td>
<td>0.26</td>
<td>1.00</td>
<td>1.03</td>
<td>0.92</td>
</tr>
</tbody>
</table>

- 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.
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 want to check whether simulated dose point kernels are correct by the experimental validation of beta absorbed doses.
Second part: Validation of beta 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/cm$^3$), bone (1.90 g/cm$^3$), lung (0.30 g/cm$^3$)

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

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

Calibration function:

\[ X(D) = \frac{b + cD}{a + D} \]

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

(A) Absorbed dose (Gy) vs Radial distance (mm) for Y90 in polyethylene.

(B) Absorbed dose (Gy) vs Radial distance (mm) for Y90 in bone.

(C) Absorbed dose (Gy) vs Radial distance (mm) for Y90 in lung.

(D) Absorbed dose (Gy) vs Radial distance (mm) for Lu177 in lung.
Error estimations

❖ **Experiment**

<table>
<thead>
<tr>
<th>Uncertainties source</th>
<th>Calculated uncertainties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optical density measurements</td>
<td>0.78% (red), 0.80% (green) and 1.12% (blue)</td>
</tr>
<tr>
<td>Exposure time: (4-38) hours</td>
<td>&lt; 1.00%</td>
</tr>
<tr>
<td>Activity measurements</td>
<td>5.82%</td>
</tr>
<tr>
<td>Curve fitting</td>
<td>2.20% (red), 3.61% (green) and 4.22% (combined)</td>
</tr>
<tr>
<td>Measurement of absorbed dose</td>
<td>4.56%</td>
</tr>
<tr>
<td>Overall uncertainty</td>
<td>8.64% (combined)</td>
</tr>
</tbody>
</table>

❖ **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.

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.
Thank you OpenGATE collaboration for this platform.

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