Simulation of liver cancer treatment using $^{90}$Y microspheres based on anatomical image segmentation technique and Geant4 toolkit

**Speaker:** Ha Nguyen Hong

*QuyNhon, August 2019*
The 10 Most Common Causes of Cancer Death, World, 2012 Estimates

Worldwide cancer statistics – Cancer Research UK
- Surgery

- Chemotherapy

- **Radioembolization (with $^{90}$Y microspheres)**

  - $^{90}$Y: Pure-beta emitter;
    - $E_{\beta_{\text{max}}} = 2.28$ MeV;
    - beta-penetration depth in tissue: 11.4 mm
Radioembolization with $^{90}$Y

**STEPS TO IMPLEMENT**

1. Clinical examination

2. Pre-treatment
   - CT and SPECT scan
   - Using $^{99m}$Tc-MAA (Macroaggregated albumin) through microcatheter
   - Calculate lungs shunt fraction (LSF)

3. Activity planning of $^{90}$Y
   - BSA; Partition model; MIRD methods.

4. Treatment
1. Empiric Method Calculation:

Tumor $\leq 25\%$ of the liver mass $\rightarrow$ 2 GBq for whole liver

Tumor $>25\%$ but $<50\%$ of the liver mass $\rightarrow$ 2.5 GBq for whole liver

Tumor $>50\%$ of liver mass $\rightarrow$ 3 GBq for whole liver
2. Body Surface Area (BSA) Method Calculation:

\[ \text{BSA} [\text{m}^2] = 0.20247 \times (\text{height [m]})^{0.725} \times (\text{weight [kg]})^{0.425} \]  

(1)

\[ A [\text{GBq}] = (\text{BSA} - 0.2) + \frac{\text{vol of tumor}}{\text{vol of tumor} + \text{vol of liver}} \]  

(2)
3.2 Limitations of current dosimetry models

Recent work has noted that there is no known association correlating a patient’s BSA with liver volume, tumour volume or radiation sensitivity [53]. Inherent in the BSA method is the assumption of a fixed mean TN liver ratio of 1 for all patients, sacrificing accuracy for simplicity, although patients typically present with a more favourable ratio [19].
Limitations of Body Surface Area–Based Activity Calculation for Radioembolization of Hepatic Metastases in Colorectal Cancer

Marnix G.E.H. Lam, MD, PhD, John D. Louie, MD, Mohamed H.K. Abdelmaksoud, MD, MS, George A. Fisher, MD, PhD, Cheryl D. Cho-Phan, MD, and Daniel Y. Sze, MD, PhD


**Results:** The standard BSA-based administered activity (range, 0.85–2.58 GBq) did not correlate with $D_{WL}$ (mean, 50.4 Gy; range, 29.8–74.7 Gy; $r = -0.037$; $P = .809$) because liver weight was highly variable (mean, 1.89 kg; range, 0.94–3.42 kg) and strongly correlated with $D_{WL}$ ($r = -0.724$; $P < .001$) but was not accounted for in the BSA method. Patients with larger livers were relatively underdosed, and patients with smaller livers were relatively overdosed. Patients who received $D_{WL} > 50$ Gy experienced more toxicity and adverse events (> grade 2 liver toxicity, 46% vs 17%; $P < .05$) but also responded better to the treatment than patients who received $D_{WL} < 50$ Gy (disease control, 88% vs 24%; $P < .01$).
3. Partition Model Calculation

\( A_{\text{total - lung}} = \frac{D_{\text{lung}} \times M_{\text{lung}} \times \text{LSF}}{49670} \)  \hspace{1cm} (3)

\( A_{\text{total - normal liver}} = \frac{D_{\text{normal liver}} \times (M_{\text{normal liver}} + T:N \times M_{\text{tumor}})}{49670 \times (1 - \text{LSF})} \)  \hspace{1cm} (4)

\[ T:N = \left( \frac{A_{\text{tumor}}}{M_{\text{tumor}}} \right) / \left( \frac{A_{\text{normal liver}}}{M_{\text{normal liver}}} \right) \]  \hspace{1cm} (5)

\( D_{\text{lung}} \): Limiting lung dose – 25Gy

\( D_{\text{normal liver}} \): Limiting normal liver dose – 80 Gy

(70 Gy for patients with cirrhosis)

\( \text{LSF} \): Lungs shunt fraction (%)
A recent study compared activity planning and dosimetry in 26 patients with RMS using 3 models (BSA, empirical and PM) showing that maximum differences in injected activities between BSA and PM methods vary from 123%-417% [55].
MIRD Method:

MIRD Pamphlet 5 mathematical phantom


Not visible:
Brain (inside the skull)
Research objective

STEPS TO IMPLEMENT

1. Clinical examination

2. Pre-treatment
   - CT and SPECT scan
   - Using $^{99m}$Tc-MAA (Macroaggregated albumin) through microcatheter
   - Calculate lungs shunt fraction (LSF)

3. Activity planning of $^{90}$Y
   - BSA; Partition model; MIRD methods.

4. Treatment

Image-based simulation method
• Based on MCNPX

• Simulated on human voxel model and ORNL mathematical model
VIDA toolkit

- Based on Geant4

### Table 3. Dose Factors for Source and Target Organs in the Radiation Dose Assessment Resource Adult Male Phantom

<table>
<thead>
<tr>
<th>Source</th>
<th>Target</th>
<th>$^{131}I$</th>
<th>$^{90}Y$</th>
</tr>
</thead>
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<tr>
<td>Liver</td>
<td>Lungs</td>
<td>8.05E-07</td>
<td>8.09E-07</td>
</tr>
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<td>Liver</td>
<td>2.27E-05</td>
<td>2.28E-05</td>
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<td>Kidneys</td>
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<td>1.14E-06</td>
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<td>Spleen</td>
<td>3.05E-07</td>
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<td>Pancreas</td>
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<td>1.11E-06</td>
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<td>Lungs</td>
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<td>2.40E-06</td>
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<tr>
<td>Pancreas</td>
<td>Pancreas</td>
<td>2.44E-04</td>
<td>2.49E-04</td>
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</tbody>
</table>

FIG. 3. Anterior views of the RADAR adult male NURBS phantom. NURBS, Non-Uniform Rational B-Spline; RADAR, Radiation Dose Assessment Resource.

VIDA: A Voxel-Based Dosimetry Method for Targeted Radionuclide Therapy Using Geant4
3D-RD toolkit

- Based on EGSnrc, extension of prior dosimetry package 3D-ID
- Images input: SPECT, PET, CT

**Figure 4.** DVH comparison between FLUKA, 3D-RD and MCID DMC simulation in water for a VOI including a hot sphere in the PET_1 phantom. Error bars represent 1 sigma uncertainty; when not visible, they are fully included in the lines.

MCID - MC Integration Internal Dosimetric (based on MCNP5)

**Figure 3.** Profile comparison between FLUKA, 3D-RD and MCID DMC simulation in water (PET_1 phantom). Error bars are not visible because they are fully included in the lines, except for the region outside the phantom (at the profile edges) exhibiting low statistic.

Use of the FLUKA Monte Carlo code for 3D patient-specific dosimetry on PET-CT and SPECT-CT images
Monte Carlo simulation

Geometry

Physics process

Decay model

Transport model
Materials and methods

Geometry

Geometry construct

Material

$^{90}$Y distribution
Materials and methods

Geometry

Geometry construct

Material

$^{90}$Y distribution
Materials and methods

Geometry construct

**Individual 3D imaging (e.g., CT)**

- Segmentation
- Edge detection
- 3D reconstruction

How to validate?
Materials and methods

Geometry

- Geometry construct
- Material
- $^{90}$Y distribution
Materials and methods

Material

CT numbers

Electron Density Phantom model M062M

HU Fidelity of the AquilionLB:
Materials and methods

Material

CT number-density

How to validate?
Materials and methods

- Geometry
- Material
- $^{90}$Y distribution
Materials and methods

\[ ^{90}Y \text{ distribution} \]

Using SPECT image

\[ ^{99m}\text{Tc-MAA SPECT imaging} \]

Using SPECT-CT image

Planning MAA-SPECT/CT
Monte Carlo simulation

Geometry

Physics process

Decay model

Transport model
Materials and methods

Geant4, an most advance OOP toolkit for the simulation of the passage of particles through matter. Its areas of application include high energy, nuclear and accelerator physics, as well as studies in medical physics.
Geant 4 Medical applications

PET, SPECT

Radiotherapy with external beams, IMRT

Hadrontherapy

Radiation Protection

Brachytherapy
Decay model

Week interaction: \[ n \rightarrow p + e^- + \nu_e \]

In Geant4: \textit{G4RadioactiveDecay()} provides:

- nuclear half-lives,
- nuclear level structure for the parent or daughter nuclide
- decay branching ratios
- the energy of the decay process.

These data taken from the \textbf{Evaluated Nuclear Structure Data File (ENSDF) - National Nuclear Data Center - Brookhaven National Laboratory}
The shape of the energy spectrum of the emitted electron:

\[
\frac{d^2n}{dEdp_e} = (E_0 - E_e)^2 E_e p_e F(Z, E_e) S(Z, E_0, E_e)
\]

Where:

- \( E_0 \): Endpoint energy of decay, taken from ENSDF data
- \( E_e, p_e \): Emitted electron energy and momentum
- \( Z \): Atomic number
- \( F \): Fermi function
- \( S \): Shape factor

\[
F(Z, E_e) = 2(1 + \gamma) (2p_e R)^{2\gamma - 2} e^{\pm \pi \alpha Z E_e / p_e} \frac{|\Gamma(\gamma + i\alpha Z E_e / p_e)|^2}{\Gamma(2\gamma + 1)^2}
\]

- \( R \): Nuclear radius
- \( \gamma = \sqrt{1 - (\alpha Z)^2} \)
- \( \alpha \): Fine structure constant
- \( |\Gamma(\gamma + i\alpha Z E_e / p_e)|^2 \) computed using Wilkinson approximation
Transport model

Materials and methods

Electron

- Ionisation
- Bremsstrahlung (photon)
- Photo electric
- Compton scattering
- Pair production

δ electron
**Materials and methods**

**Transport model**

**G4LivermoreIonisation**

- Shell structure
- Semi-empirical model, data from EEDL

\[
\frac{dE}{dx} = \sum_s \left( \sigma_s(T) \frac{\int_{T_{c}}^{T_{\text{max}}} t \frac{d\sigma}{dt} dt}{\int_{0.1eV}^{T_{\text{max}}} \frac{d\sigma}{dt} dt} \right)
\]

- T: incident energy.
- \(T_c\): secondary electron production threshold
- \(T_{\text{max}} = 0.5T\) : maximum energy transferred to a secondary electron.
- \(\sigma_s(T)\): total cross-section for the shell s at incident kinetic energy T

**G4PenelopeIonisation**

- Shell structure
- Based on Generalized Oscillation Strength (GOS) model

\[
\sigma^{-}(E) = \sigma_{\text{dis},l} + \sigma_{\text{dis},t} + \sigma_{\text{clo}}
\]

\[
\sigma_{\text{dis},l} = \frac{2 \pi \alpha^4}{m_e v^2} \sum_{\text{shells}} f_k \frac{1}{W_k} \ln \left( \frac{W_k Q_k^{\text{min}}}{W_k + 2 m_e c^2} \right) \Theta(E - W_k)
\]

- \(m_e\): mass of the electron;
- \(v\): velocity of the electron;
- \(\beta\): velocity of the electron in units of c;
- \(f_k\): number of electrons in the \(k\)-th atomic shell;
- \(\Theta\): Heaviside step function;
- \(W_k\): resonance energy of the \(k\)-th atomic shell oscillator;
- \(Q_k^{\text{min}}\): minimum kinematically allowed recoil energy for energy transfer \(W_k\);
- \(\delta_F\): Fermi density effect correction.
Materials and methods

Transport model

Most recommended: G4EmStandardPhysics_option4

Benchmark:
- Livermore
- Penelope
- EmStand_opt4
- Experimental
Materials and methods

Transport model

Ionisation cross section for water with cut 10 eV

Source: V. Ivanchenko, CERN & Geant4 Associates International
Materials and methods

Ionisation cross section for water with cut 10 eV

Transport model
Transport model

Materials and methods

Develope new semi-empirical model based on Livermore

FIG. 2. Total scattering cross section, \(Q_T\), of H\(_2\)O. A comparison is made of the experimental cross sections obtained by Szmytkowski (Ref. 21), Sueoka et al. (Ref. 26), Zecca et al. (Ref. 22), Nishimura and Yano (Ref. 23), and Saglam and Aktekin (Refs. 24 and 25). The theoretical elastic cross section obtained by Tennyson et al. (Ref. 28) is also shown for comparison.

<table>
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<th>Cross section ((10^{-16}) cm(^2))</th>
<th>Energy (eV)</th>
<th>Cross section ((10^{-16}) cm(^2))</th>
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Cross Sections for Electron Collisions with Water Molecules
Materials and methods

How to validate?

- Dose
- Cross section
- Mean free path
- ...

Compare with experimental result published.
Applications and Perspectives

- Calculate for several treatment cases
- Developing a platform
Comparision

This research

Simulation

Dose distribution

Compare

108 Military Hospital

post-treatment PET/CT scan

Dose distribution

b.
Preliminary result
Geometry constructed from DICOM CT of a patient treated in Hospital 108 (Vietnam)
Generate MAA distribution based on SPECT.

- Using ITK toolkit: `itkImageSeriesReader` class
- A new class implemented into G4 for generating MAA distribution
Preliminary result

Exported to **gdd** format for being displayed by gMocren
THANK YOU FOR YOUR ATTENTION