SAM Multidisciplinary Symposium

Dosimetry for Radionuclide Therapies: How do we get there and where can it take us?

Modeling strategies to improve Y-90 radioembolization dosimetry planning

Emilie Roncali\textsuperscript{1,2}

\textsuperscript{1} Department of Biomedical Engineering, \textsuperscript{2} Department of Radiology, University of California Davis
Learning objectives

At the end of this lecture you will be able to:

- Explain why precise and accurate Y-90 dosimetry is important
- Describe the new techniques under development and their promises
- Contrast challenges in Y-90 microsphere therapy with other radionuclide therapies
Outline

• Why do we need “good” dosimetry in Y-90 radioembolization?
  - dose-response relationship
  - Treatment efficacy and safety

• Image-based dosimetry for Y-90 microspheres
  - Pretreatment imaging (dose prediction)
  - Post treatment imaging (dose verification)

• Patient-specific dosimetry based on microsphere transport modeling and Y-90 physics
Dose-response relationship
Dose Matters: Y-90 liver radioembolization

Insights into the Dose–Response Relationship of Radioembolization with Resin $^{90}$Y-Microspheres: A Prospective Cohort Study in Patients with Colorectal Cancer Liver Metastases

Andor F. van den Hoven$^1$, Charlotte E.N.M. Rosenbaum$^1$, Sjoerd G. Elias$^{1,2}$, Hugo W.A.M. de Jong$^1$, Miriam Koopman$^1$, Helena M. Verkooijen$^1$, Abass Alavi$^4$, Maurice A.A.J. van den Bosch$^1$, and Marnix G.E.H. Lam$^1$

$^1$
Improving treatment efficacy and safety through better planning
Clinical Questions

dose prediction: where to inject? how much?

X ray angiogram, pre-treatment

dose verification: how did we do? how much dose?
Dosimetry models for Y-90 radioembolization
Calculate the Absorbed Dose

Dosimetry systems

- Medical Internal Radiation Dose Committee from the Society of Nuclear Medicine (MIRD)
- Body Surface Area (BSA)
  - Image-based dosimetry

Absorbed dose = cumulative dose

- Cumulative activity (activity x time), \( \bar{A} \)
- Energy per radioactive decay, \( E \)
- Absorbed fraction = fraction of energy absorbed within target, \( \phi \)
Y-90 Microsphere Dosimetry Models

**MIRD**

\[ D \ (Gy) = 49.7 \frac{AA \ (Bq) \cdot (1 - LSF)}{mli \ (kg)} \]

**BSA Method**

\[ AA \ (Bq) = (BSA - 0.2) + Tinvolv \]

**Partition Model**

\[ AA \ (Bq) = \frac{D \cdot mli \ (Vtu \cdot TN + Vli)}{0.497 \cdot Vli \cdot TN \ (1 - LSF)} \]

D = dose  
AA = administered activity  
mli = liver mass  
LSF = lung shunt fraction  
BSA = body surface area  
Tinvolv = tumor involvement  
Vli = liver volume  
Vtu = tumor volume  
TN = tumor to normal ratio

*more information in: Bastiaannet, et al., EJNMMI Phys 5:22, 2018*
Discrepancy Between models

- Patient:
  - 160 cm
  - 74 kg
  - Tumor involvement 0.60
  - Lung shunt fraction LFS 0.044
  - Target dose = 120 Gy
  - Liver volume ~1.625 L
  - TN 16.8 estimated from SPECT

<table>
<thead>
<tr>
<th>MIRD</th>
<th>BSA</th>
<th>Partition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity</td>
<td>3.9 GBq</td>
<td>1.7 GBq</td>
</tr>
<tr>
<td>Tumor</td>
<td>120 Gy</td>
<td>40 Gy</td>
</tr>
<tr>
<td>Liver</td>
<td>120 Gy</td>
<td>10.3 Gy</td>
</tr>
<tr>
<td>Lungs</td>
<td>8.5 Gy</td>
<td>3.7 Gy</td>
</tr>
</tbody>
</table>

Large variation in recommended administered activity and subsequent dose to target and organs-at-risk
Cumulative Activity in Y-90 microspheres

\[ \tilde{A} = AA \cdot \tau \]

- Intra-hepatic injection → distribution primarily in the liver, with potential leak to lungs, abdomen
- Permanently implanted → no residence time

\[ \tilde{A} = AA \cdot T_{1/2} / \ln 2 \]
Image-based Dosimetry

Anatomical imaging

Molecular imaging
- Spatial resolution for distribution within target
- Quantification counts → activity (MBq) → dose (Gy)

Dose calculation

Liver segmentation (15 min)
Pretreatment imaging with $^{99m}$Tc-MAA

- Good accuracy in non-tumor tissue*
- Larger inaccuracy in lesions (>100s Gy in 5% patients)*
- Strong effect of catheter placement mismatch**

**Haste et al., J Vasc Interv Radiol, 2017
An Engineering and Translational Perspective: Y-90 microsphere dosimetry with computational fluid dynamics
CFDose Overview

Planning CBCT, Siemens Artis Zeego

Blood fluid properties
Boundary conditions

Flow Rate [m/s]

0 0.5 1

Time [s]

200 ms 800 ms

200 ms

800 ms

Courtesy Amirtaha Taebi
A Multimodal Imaging Approach

Analyze branching with DSA

Identify HA on arterial phase CECT

Segment from CBCT

Localize tumors with equilibrium phase CECT

Doesn’t feed tumor

Feeds tumor

RHA

1st injection

2nd injection

Couinaud segments

61.2 mm

UCDAVIS

Emilie Roncali  eroncali@ucdavis.edu AAPM, July 2020
Flow Simulation: Multiscale Modeling

- Segmented arterial tree combined with RCR Windkessel model for arterioles
  - RCR circuit tuned using whole-body 0D model

Taebi, Vu, Roncali. J. Biomech. (in press)
Optimization of the Boundary Conditions

\[ R_{\text{tot}} = R_p + R_d \]

4 x 10^4 \quad R_{\text{tot}} \text{ [dyne.s/cm}^5\text{]} \quad 8 x 10^4
Blood Flow and Microsphere Distribution

- Lobar injection: segments received 5%-40%
- Selective injection: tumor received 82%
  → Tumor received 49% of microspheres after both injections

Roncali et al. ABMES 2020
CFDose: Estimate Absorbed Dose distribution

- Highly heterogenous dose distribution between segments
- Predicted total dose 125 Gy, consistent with MIRD 137 Gy

Roncali et. al. ABMES (2020), Taebi et. al., J. Biomech. (2020)
What is the energy of the $\beta^-$?
Y-90 PET/CT post treatment

Absorbed dose

Clinical Y-90 PET/CT

axial coronal sagittal

Qualitative agreement between predicted dose and Y-90 PET measured activity

- 6 patients scanned at UC Davis since September 2017
- Quantitative comparison of dose distribution in progress
Conclusions

Success of TRT relies on personalized treatment planning with high accuracy and precision

- Pre-treatment image-based dosimetry still limited by lesion inaccuracies → need for alternative approaches
- We leverage physics principles to predict dose distribution and develop CFDose
- Quantitative Y-90 PET post injection will provide validation at different levels
Acknowledgments

Biomedical Engineering
Amirtaha Taebi, Ph.D.
Gustavo Costa, Ph.D.
Simon Cherry, Ph.D.
MIPET group

Radiation Oncology
Stanley Benedict, Ph.D.

Radiology
Catherine Vu, M.D.
Bahman Roudsari, MD, Ph.D.
Ramsey Badawi, Ph.D.
Denise Caudle, CNMT
Michael Rusnak, CNMT
Benjamin Spencer, Ph.D.

UC Davis Comprehensive Cancer Center
NIH National Cancer Institute

P30 NCI P30CA093373
R21 CA237686

Virtual group meeting, 4-22-20