Practical SIRT (Selective Internal Radiation Therapy) for $^{90}$Y Liver Radio-embolic Therapy

Dose Calculation and Post-Therapy Imaging

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Emory University Department of Radiology
Atlanta, GA

Special thanks to David Liu MD
No COI
Talk can be found at radiology.emory.edu
Emory Imaging Center Opens

A new Emory Imaging Center, in Buford, Georgia, will open its doors later this month to serve the Buford and surrounding communities. On opening day, the center will provide high-quality diagnostic imaging services in MRI, X-ray and Ultrasound, in a convenient outpatient setting at 3425 Buford Drive in Buford, one block north of the Mall of Georgia.

Center is situated on the ground floor of the building occupied by an urgent care center, Physicians Immediate Medicine, Ear, Nose and Throat specialty group and a Physical Therapy group.

Read more in the May Rad Report.
The faculty of the Emory Division of Nuclear Medicine & Molecular Imaging offers the highest quality patient care, incorporating the latest knowledge, innovation and equipment. Nuclear Medicine not only uses the most advanced methods, but also helps set the bar for the field. All of our physicians are board certified in nuclear medicine, and some are double-boarded in other fields, particularly Radiology; many have national and international reputations in their fields.

Equipment includes PET/CT and SPECT/CT scanners at Emory University Hospital (Clifton campus) and Emory University Hospital Midtown. We offer a wide variety of specialized nuclear medicine therapies including that for thyroid cancer, bone cancer pain palliation, lymphoma, neuroendocrine tumors and Y-90 liver therapy in cooperation with Interventional Radiology. Research devices at our disposal include a high-resolution brain PET scanner, micro-PET/CT for animal research, and a research cyclotron. A full range of nuclear medicine and PET/CT services are also provided at Grady Memorial Hospital and the Atlanta VA Medical Center. The Division is integrally involved in research as well as close collaboration with colleagues in Radiology, Cardiology and the Emory Winship Cancer Institute. Our faculty are principal investigators and co-investigators on many research grants including those sponsored by the NIH.

- David M. Schuster, MD
  Director, Division of Nuclear Medicine
  and Molecular Imaging

Recent Conferences
Emory Symposium on Image-guided Cancer Therapies
March 17, 2012.
Let’s Start with a Case

55 year old male with central-right lobar hepatoma.

Treated with $^{90}$Y TheraSphere.

How did we do?
$^{99m}$Tc MAA Planning study

Bremsstrahlung post-study matches very well
Fusion of MR with MAA (left) and Bremsstrahlung (right): only a small area of tumor is left untreated.

Acceptable and patient will be followed.
One example:
Proper imaging
Team planning

Appropriate dose delivered to the correct area.

Confirmed again with imaging.

In turn, useful for followup.
How do we do it?

- Start with IR Consult often after referral from surgical or medical oncology
- **Weekly IR-NM \(^{90}\)Y Conference**
  - Images reviewed with IR
    - Ideally before MAA study
  - Therapy plan
  - Usually one lobe or less at a time
    - Hepatic reserve
  - Also review and critique prior cases
Weekly NM-IR $^{90}$Y Conference
How Do We Do It?

• Patient undergoes $^{99}$Tc MAA shunt study
  – Vascular anatomy mapped
  – Pulmonary shunt or extrahepatic activity?
    • Planar and SPECT-CT
• Calculate therapy dose
  – Volumes of liver and tumor
  – Which lobe or segment and if split dose
  – Lung shunt
  – Labs (LFTs)
  – Dictate NM planning note
    • email information to attendings of that day
  – Script signed by AU
**Ceramic Microspheres (TheraSphere)**

- **Partition Model**
- Based on Liver Mass
- High Specific Activity Particles

**Resin Microspheres (SIR-Spheres)**

- **BSA Model**
- Based on body surface area, and tumor infiltration
- Lower Specific Activity Particles
Other methods

Image-Guided Personalized Predictive Dosimetry by Artery-Specific SPECT/CT Partition Modeling for Safe and Effective $^{90}$Y Radioembolization

Yung Hsiang Kao¹, Andrew Eik Hock Tan¹, Mark Christian Burgmans², Farah Gillian Irani², Li Ser Khoo³, Richard Hoau Gong Lo³, Kiang Hiong Tay³, Bien Soo Tan³, Fierce Kah Hoe Chow³, David Chee Eng Ng¹, and Anthony Soon Wai Tatt Goh¹

¹Department of Nuclear Medicine and PET, Singapore General Hospital, Singapore; ²Department of Diagnostic Radiology, Singapore General Hospital, Singapore; ³Department of General Surgery, Singapore General Hospital, Singapore; and ⁴Office of Clinical Sciences, Duke-NUS Graduate Medical School, Singapore

Nuclear Medicine & Radiation Therapy

Special Issue Article

Patient Specific 3D Image-Based Radiation Dose Estimates for 90Y Microsphere Hepatic Radioembolization in Metastatic Tumors

Andrew Kennedy*, William Dezarn* and Alec Weiss*

*Co-Medical Director, Wake Radiology Oncology, 300 Asheville Ave., Suite 110, Cary, NC, 27518 USA
Adjunct Associate Professor, Department of Biomedical Engineering, Department of Mechanical and Aerospace Engineering, North Carolina State University, Raleigh, NC, USA
Department of Biologic Systems Engineering, Campus Box 7910, Broughton Hall 4160, North Carolina State University, Raleigh, NC 27695-7910 USA

More on these later…
Let’s start with SIR-Spheres at most basic level:
Empiric “eyeball” method

\[ A \text{ [GBq]} = \text{Liver Involvement Activity} \times \text{LSM} \times \text{LPM} \]

<table>
<thead>
<tr>
<th>Estimated degree of liver involvement</th>
<th>Standard dosage of Y-90 [GBq]</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;50%</td>
<td>3</td>
</tr>
<tr>
<td>25%–50%</td>
<td>2.5</td>
</tr>
<tr>
<td>&lt;25%</td>
<td>2</td>
</tr>
<tr>
<td>Lung shunting</td>
<td></td>
</tr>
<tr>
<td>&lt;10%</td>
<td>1.0</td>
</tr>
<tr>
<td>10%–15%</td>
<td>0.8</td>
</tr>
<tr>
<td>15%–20%</td>
<td>0.6</td>
</tr>
<tr>
<td>&gt;20%</td>
<td>Do not proceed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Part of liver</th>
<th>Liver part modifier (LPM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole liver</td>
<td>1.0</td>
</tr>
<tr>
<td>Right lobe only</td>
<td>0.7</td>
</tr>
<tr>
<td>Left lobe only</td>
<td>0.3</td>
</tr>
</tbody>
</table>

But we prefer using more “objective” approach. Let’s deconstruct to understand what we need.

**SIR-Spheres calculation:**

\[
\text{Dose in GBq} = (\text{BSA} - 0.2) + \left(\frac{\% \text{ tumor involvement of liver}}{100}\right)
\]

In this method, BSA is a proxy for liver volume.

If lobar therapy is used would just then multiply by that lobar fraction of entire liver (e.g. right lobe, 60%). Then reduce per standard reduction factors.
Actually employ a more advanced variant which requires right and left lobe tumor and liver volumes to be known

Lobar dose in GBq =

\[(BSA - 0.2) + (\% \text{ tumor involvement of lobe to be treated}/100)\] X [percent of total liver that treated lobe comprises]

Then apply various correction factors.
Liver and Tumor Volumes from OctreoScan SPECT-CT on an Advanced Workstation

Calculated in 3-dimensions
Another Example Using a PET-CT

Try to use molecular imaging when possible but same concepts apply to using anatomic imaging
This Method Has Higher Kappa than “Eyeballing”

- In a small study at Emory, objective approach yields better precision compared to subjective estimation.
- Factors that contributed to observed deviance:
  - necrosis
  - difficulty in defining margins of infiltrative tumors
  - discrepancy between the PET and CT derived volumes
Modified Partition Model to Solve for Lung and Normal Liver Dose Limits Using Ratios of Tumor Uptake to Normal Liver on MAA

\[ \frac{T}{N} = \frac{A_{\text{tumor}}/m_{\text{tumor}}}{A_{\text{tumor}}/m_{\text{tumor}}} \]

\[ D_{\text{NormalLiver}} = \frac{49.38 A_{\text{Total}} (1-L)}{m_{\text{NormalLiver}} + \frac{T}{N} m_{\text{Tumor}}} \]

\[ D_{\text{Lung}} = 49.38 \frac{A_{\text{Total}}}{m_{\text{Lung}}} L \]

T/N values may vary considerably over a tumor and tumors in a region.
Ingredients for Equation

- BSA
- Volumes
- Lung shunt
- Recent bili, albumin
- Other factors such as recent and heavy chemotherapy

Lung counts:
- Lung counts ANT = 227.02k
- Lung counts POST = 214.95k
- Lung average counts = 220.90k

Both lung and liver counts:
- Both lung and liver counts ANT = 1628.09k
- Both lung and liver counts POST = 1174.44k
- Both lung and liver average counts = 1382.78k

Lung ratio = 15.98%
Common Reduction Factors

• Shunt per Sirtex online calculator
  – http://apps01.sirtex.com/smac/
  – 30 Gy to lungs per session; 50 Gy cumulative
• Recent multiple or long-term chemotherapy (20%)
  – Recommend wait 2 weeks after Avastin
• Abnormal LFTs  Bili>2.0, Albumin <3.0 (30%)
• Small tumor load <5% (20%)
• Previous Radiotherapy except Cyberknife (20%)
• For HCC diffuse tumor: reduce by 25%
  – (abnormal LFTs, as above, contraindicated)
• Selective therapy protects liver; may use higher doses
We plug into equation using either on-line system and/or internal spreadsheet.
### Emory University Hospital

**SIRTEX Dose Calculation Sheet**

<table>
<thead>
<tr>
<th>Calculation: (BSA - 0.2 + % involvement) x 27 x (1- redux factor) x (% liv lobe treated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date: (mm/dd/yyyy)</td>
</tr>
<tr>
<td>Patient Last name:</td>
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<tr>
<td>Patient First name:</td>
</tr>
<tr>
<td>MRN:</td>
</tr>
<tr>
<td>DOB/(Age):</td>
</tr>
<tr>
<td>Sex:</td>
</tr>
<tr>
<td>Reduction Factors:</td>
</tr>
<tr>
<td>Diagnosis/Tumor Type:</td>
</tr>
<tr>
<td>Shunt:</td>
</tr>
<tr>
<td>HT (cm):</td>
</tr>
<tr>
<td>WT (kg):</td>
</tr>
<tr>
<td>BSA</td>
</tr>
<tr>
<td>% Lung Shunt (3 months):</td>
</tr>
<tr>
<td>Volume (cc)</td>
</tr>
<tr>
<td>Total Liver Organ Volume</td>
</tr>
<tr>
<td>Abnormal LFT's (Bilirubin &gt;2, Albumin &lt;3) Reduce by 20-30%</td>
</tr>
<tr>
<td>Increased Alkaline Phosphatase OK</td>
</tr>
<tr>
<td>If Rising Bilirubin - Therapy not-advised</td>
</tr>
<tr>
<td>RT Liver Organ Volume</td>
</tr>
<tr>
<td>62.95%</td>
</tr>
<tr>
<td>LT Liver Organ Volume</td>
</tr>
<tr>
<td>37.05%</td>
</tr>
<tr>
<td>RT Liver Tumor Load Estimate</td>
</tr>
<tr>
<td>26.27%</td>
</tr>
<tr>
<td>LT Liver Tumor Load Estimate</td>
</tr>
<tr>
<td>56.19%</td>
</tr>
<tr>
<td>Lobe to be treated (RT / LT)</td>
</tr>
<tr>
<td>Reduction Factor</td>
</tr>
<tr>
<td>Calculations: (Automatic)</td>
</tr>
<tr>
<td>Calculated RT Lobe Dose</td>
</tr>
<tr>
<td>Calculated LT Lobe Dose</td>
</tr>
<tr>
<td>Estimated Lung Dose</td>
</tr>
<tr>
<td>ACTUAL THERAPY:</td>
</tr>
<tr>
<td>Date: (mm/dd/yyyy) / Time</td>
</tr>
<tr>
<td>Y90 SirTex Dose Administered:</td>
</tr>
<tr>
<td>Lung Dose Administered:</td>
</tr>
<tr>
<td>A (GBq) x F x 50 x [1-R], Assume lung mass 1kg, upper limit = 30 Gy</td>
</tr>
<tr>
<td>Total accumulated Lung dose = 50 Gy</td>
</tr>
<tr>
<td>THERAPY HISTORY:</td>
</tr>
<tr>
<td>Previous Y-90 SIR Dose (s)</td>
</tr>
<tr>
<td>Total Y-90 SIR to Date</td>
</tr>
<tr>
<td>Cumulative Lung Dose</td>
</tr>
<tr>
<td>NM Staff Signature:</td>
</tr>
</tbody>
</table>

We carry spreadsheet through after therapy and keep running tally for future
Special Situations

- **Hepatomegaly**
  - BSA will underestimate volume of liver (and dose).
  - Probably best to use empiric. Treat each lobe as its own liver and wait 2 months between therapies.
  - Each lobe gets about 2-3 GBq.

- **Prior Hepatectomy**
  - BSA method will overestimate remaining liver if you are treating whole liver.
  - So may:
    - Measure out pre-resection volume if available.
    - Take current volume and increase by 25-33% to get theoretical “whole” liver volume (or reduce dose similarly).
Then Dictate Planning Note

**Nuclear Medicine Planning for Patients Receiving Y-90 Labeled Microspheres**

**Consult Date:** 4/19/2012 for Therapy on: 5/1/12

- **Height (cm):** 176.6 cm
- **Weight (kg):** 70.4 kg
- **BMI (kg/m²):** 1.8

**Diagnostic Imaging:**

- Most recent FDG PET CT on 4/17/2012 demonstrated extensive hepatic metastasis, right greater than left, with liver dominant disease.
- Most recent CT abdomen on 4/17/2012 demonstrated same.

The available imaging studies were reviewed with the interventional radiologist. Hepatomegaly is present. The hepatic volume is 5450 cc, with 4263 cc right lobe and 1187 cc left lobe. Tumor burden is 3199 cc in the right lobe and 24 cc in the left lobe. The anatomic size differential is 78% from the right lobe and 22% from the left lobe, with 75% tumor involvement of the right lobe and 25% tumor involvement of the left lobe.

- Tc-99m-HA hepatic perfusion shunt study from 4/16/2012 showed a pulmonary percent shunt calculation of 18%. No significant extrahepatic or gastric uptake was identified. Based on the value of the pulmonary shunt calculation, the dose was not reduced.

**Laboratory Data:**

- **Albunin:** 2.4 g/dL (3.5-4.8)
- **Total Bilirubin:** 2.5 mg/dL (0.3-1.2)

Based on the laboratory values, the calculated dose was reduced. The dose is reduced by 25% secondary to abnormal LFTs, though modified by hepatomegaly and most of tumor burden on the right which will be treated, protecting the left lobe.

**Other Pertinent History:**

- Previous liver radiation: None
- Chemotherapy within the past 2 weeks (especially Avastin): No

**Criteria for Y-90 SIR-Spheres dose reduction:**

a. Shunt per Sirtex online calculator (http://apps01.sirtex.com/smac/)

b. Recent multiple or long-term chemotherapy (20%)

c. Abnormal LFTs: Bilirubin >2.0, Albumin <3.0 (10%)

d. Small tumor load <5% (10%)

e. Previous Radiodensity except Cyberknife (20%)

**Treatment Plan:**

- Hepatic lobe to be treated: Right. Left lobe may be treated in the future.

The patient has not been treated with Y-90 SIR-Spheres in the past. The total Y-90 SIR-Spheres dose delivered thus far is 0 mcI. The total estimated Y-90 SIR-Spheres lung dose received thus far is 0 Gy. Y-90 SIR-Spheres lung dose limit per treatment is 30 Gy, lifetime cumulative lung dose is 50 Gy.

**Recommendations:**

Based on the above data, the amount of Y-90 SIR-Spheres to be administered was calculated in mcI. The calculated dose was reduced by 25% as above. Reduction was modified by hepatomegaly and the fact that most of tumor burden is on the right which will be treated, protecting the left lobe. The dosimetry falls within the accepted guidelines of the Y90 SIR-Spheres manufacturer and government regulatory agencies.

The calculated dose to the right lobe of Y90-SIR-Spheres is 37.2 mcI, with an estimated lung dose of 10.1 Gy.

Please refer to the dose calculation form on file in nuclear medicine. Script signed. Single dose confirmed.

Additional pending labs to be reviewed: None

I. David M. Schuster, MD, personally planned this therapy and reviewed all imaging.

**Signature Line**

***Final***

Electronically Signed By: SCHUSTER, DAVID M on 04/24/2012 15:12
Dictated by: SCHUSTER, DAVID M
Billing for Planning

- CPT 77261: Therapeutic Radiology Treatment Planning; Simple
- CPT 77331: Special Dosimetry
- Please consult with your coding/billing department for appropriate codes in your particular situation
So How About TheraSphere?
Y-90 Microspheres Compared:
For SIR-Spheres, draw desired dose from vial and stop at completion/stasis. For TheraSphere, give entire vial, so must order correct activity vial.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Glass TheraSphere</th>
<th>Resin SIR-Spheres</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>20 - 30 µm</td>
<td>20 - 60 µm</td>
</tr>
<tr>
<td>Isotope</td>
<td>Y90 in glass matrix</td>
<td>Y90 on resin surface</td>
</tr>
<tr>
<td>Dose activity</td>
<td>Partition Model</td>
<td>Body Surface Model</td>
</tr>
<tr>
<td>Manufacture</td>
<td>Reactor (neutron flux)</td>
<td>Generator (Sr-90)</td>
</tr>
<tr>
<td>Specific Gravity</td>
<td>3.6g/dL</td>
<td>1.6g/dL</td>
</tr>
<tr>
<td>Activity/Sphere</td>
<td>150-2200 Bq *</td>
<td>65-140 Bq</td>
</tr>
<tr>
<td>Right Liver Dose</td>
<td>4.75 GBq</td>
<td>1.5GBq</td>
</tr>
<tr>
<td>Status</td>
<td>HDE</td>
<td>PMA</td>
</tr>
<tr>
<td>Endpoint</td>
<td>Target Dose</td>
<td>Target Dose or Stasis</td>
</tr>
<tr>
<td># of Spheres/Dose</td>
<td>2.5 - 30 Million</td>
<td>15 - 19 Million</td>
</tr>
</tbody>
</table>
Volume Analysis: Dose Based On Volume Infused, Not Tumor. Calculate for 120 Gy to Target Volume
Let’s Look at Calculation for TheraSphere

Activity Required (GBq) =

\[
\text{Desired Dose (Gy)} \times \text{mass of liver (kg)} \times \frac{50 \times [1 - \text{LSF}] \times [1 - \text{R}]}{80 - 150 \text{ Gy, typically 120 Gy}}
\]

Dose is more in 2-5 GBq range
Similar Concepts but Key Differences

- Need recent LFTs and Lung Shunt from MAA
- Volume of area critical but do not need volume of tumor per se
- Other LFTs on Package Insert

A retrospective study of 121 patients from 5 clinical trials has shown that the following 5 Pre-treatment High Risk Factors have been associated with at least 48% of all serious adverse events that were possibly related to use of the device and with 11 of the 12 deaths that were possibly related to use of the device:

- infiltrative tumor type
- “Bulk disease” (tumor volume > 70% of the target liver volume, or tumor nodules too numerous to count)
- AST or ALT > 5 times ULN
- bilirubin > 2 mg/dL
- tumor volume > 50% combined with an albumin < 3 g/dL

The physician should always take the above-noted Pre-treatment High Risk Factors into consideration for each patient when making decisions regarding the use of TheraSphere for treatment.
Calculate Volume of Therapy

Use anatomic or functional image. In this case we knew area to be treated exactly from MAA distribution. So derived volume based on MAA.
### Dose Selection (GBq):

**Use the following tables to select a dose size where the Desired Dose (above) is at a suitable treatment time.**

<table>
<thead>
<tr>
<th>Dose Delivered (Gy) for</th>
<th>3</th>
<th>5</th>
<th>7</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>4.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBq dose size</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Week 1 treatment</strong></td>
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<tr>
<td>8:00 AM</td>
<td>110</td>
<td>106</td>
<td>107</td>
<td>97</td>
<td>169</td>
<td>162</td>
<td>224</td>
</tr>
<tr>
<td>12:00 PM Day Eastern</td>
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<td>169</td>
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<td>224</td>
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<td>4:00 PM Day Eastern</td>
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<tr>
<td><strong>Week 2 treatment</strong></td>
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<td><strong>Week 3 treatment</strong></td>
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<td>115</td>
<td>131</td>
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<td>177</td>
</tr>
</tbody>
</table>

### Cumulative Dose to Lungs (Gy): 6.51

**Calculated Dose to Lungs (Gy):** 30

**Cumulative Dose to Lungs (Gy):** 6.51

**Desired Dose (Gy):** 120

### Use the following tables to select a dose size where the Desired Dose (above) is at a suitable treatment time.

<table>
<thead>
<tr>
<th>Dose Delivered (Gy) for</th>
<th>3</th>
<th>5</th>
<th>7</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>4.5</th>
</tr>
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<tbody>
<tr>
<td>GBq dose size</td>
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<td></td>
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<tr>
<td><strong>Week 1 treatment</strong></td>
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<td>97</td>
<td>169</td>
<td>162</td>
<td>224</td>
</tr>
<tr>
<td><strong>Week 2 treatment</strong></td>
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<tr>
<td>8:00 AM</td>
<td>127</td>
<td>122</td>
<td>122</td>
<td>115</td>
<td>131</td>
<td>124</td>
<td>177</td>
</tr>
<tr>
<td>12:00 PM Day Eastern</td>
<td>127</td>
<td>122</td>
<td>122</td>
<td>115</td>
<td>131</td>
<td>124</td>
<td>177</td>
</tr>
<tr>
<td>4:00 PM Day Eastern</td>
<td>142</td>
<td>122</td>
<td>122</td>
<td>115</td>
<td>131</td>
<td>124</td>
<td>177</td>
</tr>
<tr>
<td>8:00 PM Day Eastern</td>
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<td>122</td>
<td>115</td>
<td>131</td>
<td>124</td>
<td>177</td>
</tr>
<tr>
<td><strong>Week 3 treatment</strong></td>
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<td>8:00 AM</td>
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<td>115</td>
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<td>124</td>
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<td>4:00 PM Day Eastern</td>
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<td>131</td>
<td>124</td>
<td>177</td>
</tr>
</tbody>
</table>

### Dose Delivered (Gy) for a Custom Dose size:

<table>
<thead>
<tr>
<th>GBq dose size</th>
<th>4.5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Week 1 treatment</strong></td>
<td></td>
</tr>
<tr>
<td>8:00 AM Monday</td>
<td>266</td>
</tr>
<tr>
<td>12:00 PM Day Eastern</td>
<td>184</td>
</tr>
<tr>
<td>4:00 PM Day Eastern</td>
<td>142</td>
</tr>
<tr>
<td>8:00 PM Day Eastern</td>
<td>115</td>
</tr>
<tr>
<td><strong>Week 2 treatment</strong></td>
<td></td>
</tr>
<tr>
<td>8:00 AM Monday</td>
<td>266</td>
</tr>
<tr>
<td>12:00 PM Day Eastern</td>
<td>184</td>
</tr>
<tr>
<td>4:00 PM Day Eastern</td>
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<td>8:00 PM Day Eastern</td>
<td>115</td>
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<tr>
<td><strong>Week 3 treatment</strong></td>
<td></td>
</tr>
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</tr>
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<td>142</td>
</tr>
<tr>
<td>8:00 PM Day Eastern</td>
<td>115</td>
</tr>
</tbody>
</table>

### All dose will have Sunday calibration at 12:00 Eastern Time.

**Standard dose vial sizes (3, 5, 7, 10, 15, 20 GBq) are available from inventory for next-day shipping. Order as required. Custom dose vial sizes should be ordered by end of business Tuesday prior to Sunday calibration to ensure availability.**

---

**Spreadsheet to calculate dose and to time therapy.**

**Need volume, lung shunt, and desired dose to area (typically 120 Gy).**

**Can now do a custom vial size (in increments of 0.5 GBq between 3 and 20 GBq)** to best tailor time of administration.
Manufacturing Cycle – Tuesday Order Cut-off for Custom Dose but Standard Dose Vials May be Ordered Any Time

<table>
<thead>
<tr>
<th>Sunday</th>
<th>Monday</th>
<th>Tuesday</th>
<th>Wednesday</th>
<th>Thursday</th>
<th>Friday</th>
<th>Saturday</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><strong>TheraSphere Order Cut-off 12:00 hrs ET</strong></td>
<td>TheraSphere Manufacturing Day</td>
<td>Ship TheraSphere</td>
<td>Ship TheraSphere</td>
<td></td>
</tr>
<tr>
<td>COMPLETE PATIENT EVALUATION</td>
<td>TREATMENT WINDOW ILLUSTRATOR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TheraSphere Calibration 12:00 hrs ET</td>
<td>TheraSphere</td>
<td>Ship / Use TheraSphere</td>
<td>Ship / Use TheraSphere</td>
<td>Ship / Use TheraSphere</td>
<td>Ship / Use TheraSphere</td>
<td></td>
</tr>
<tr>
<td><strong>TREATMENT WEEK ONE</strong></td>
<td><strong>TREATMENT WEEK TWO</strong></td>
<td>Ship / Use TheraSphere</td>
<td>Ship / Use TheraSphere</td>
<td>Ship / Use TheraSphere</td>
<td>Use TheraSphere</td>
<td></td>
</tr>
<tr>
<td>TheraSphere Expiration @ 24:00 Friday ET</td>
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</tr>
</tbody>
</table>
Dose Calculation

• If you want to use more beads, order a larger dose and let it decay longer.
On Day of $^{90}\text{Y}$ Therapy

- Procedure team effort IR, NM, RSO oversight
- Running checklist completed.
  - NM Tech and Faculty visit patient in holding area to review radiation safety precautions and “put a face to a name.”
  - NM Faculty in room when dose actually pushed by IR, but NM tech prepares all beforehand.
    - Other technical checklists and forms filled out by NM tech.
Some Team Members

Mary “Lee” Nichols, IR NP

Jason Roberts and Jim Fitz (Chief Tech)
NM $^{90}$Y Team
Checklist and Rad Safety Forms

SIRTEX ORDER OF PROCEDURE

Patient: ____________________________ Date: ____________________________

NUC. MED ATTENDING: PIC CELL

READING ROOM 2-7434

BACKUP NM ATTENDING: PIC CELL

(CALL TO ORDER):

This checklist should be reviewed prior to the agent being brought to the IR suite by the AU and Physician or designee, as below, and verbally called out in the IR suite before the procedure is begun. On the evening before the therapy a copy of the Therapy Plan will be presented, along with the dose calculation sheet and Call to Order Sheet, to the NM resident or if not available, the NM Physician who will be attending the therapy. (Jim Fitz)

Before the door is drawn up, Dr. Kim will notify the NM Physician in is due to be split. Preferably, this will be known in advance when the door is initially calculated. If possible, NM Physician should introduce himself/herself to the patient at which time patient ID will be reconfirmed.

PRIOR TO PROCEDURE- Reviewed by NM Physician:

- Confirm patient’s non-pregnant status if applicable. (Female Patients ≤50 yo with child-bearing potential- semen pregnancy test)
- Confirm that any last minute lab values have been ordered
- Confirm dose calculation and written directive match. (Attending/Resident)
- Confirm dose is correct based on given volumes
- Confirm which liver lobe(s) will be treated
- Confirm total dose to that lobe matches the physician directive
- Confirm how many injection doses were requested and prepared and the vascular location for each injection

IN PROCEDURE ROOM - Reviewed by Physicist:

- Confirm Door Name, Isotope and Patient Name match
- Septum is pierced until AU is available and Call to Order Sheet reviewed.
- Confirm that the flooring around the injection area has been appropriately covered
- Confirm that all pre-therapy radiation measurements have been made and recorded

I, R. Call to order confirmed

Authorized User Signature: ____________________________ Physicist/Res/Designee Signature: ____________________________

Emory University Hospital - Division of Nuclear Medicine

RADIATION SAFETY INSTRUCTIONS FOR PATIENTS RECEIVING Y-90 MICROSPHERES

What Precautions are Necessary after Receiving Yttrium-90 Microspheres?

You have received a treatment involving radioactive materials. The radioactive material that has been administered is in the form of microspheres, which become trapped in the small blood vessels in the liver and remain there permanently. While the microspheres remain in your liver tissue, the radioactivity decays away, so that after 14 days, only 2.3% of the original amount remains and after one month virtually no radioactivity remains in your body.

Radiation from yttrium-90 microspheres does not penetrate outside the body, but a small amount of the radioactive material may become unattached from the microspheres and be present (for about a week following treatment) in body fluids, such as blood and urine. Certain precautions are suggested for one week after treatment to limit any potential radiation exposure to others. You should wash your hands thoroughly after urination and not use a condom during sexual intercourse.

You can usually return to work and your usual activities following treatment. The following are recommended instructions after treatment with yttrium-90 microspheres:

**Recommended Instructions**

**After Treatment with Yttrium-90 Microspheres:**

<table>
<thead>
<tr>
<th>Interval After Treatment</th>
<th>Recommended Instruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Days</td>
<td>Clean up spilled urine. Wash hands thoroughly after using toilet. No preschool children. Sleep alone. Keep a distance of 1’ from others. Do not allow children to pass on your lap.</td>
</tr>
<tr>
<td>1 Week</td>
<td>Use condoms for sexual relations</td>
</tr>
<tr>
<td>27 Days</td>
<td>In the event of a medical emergency or death, a family member or guardian should notify the attending medical staff or freight director of the date and type of radioactive material treatment.</td>
</tr>
</tbody>
</table>

Please direct any questions you have to the: Nuclear Medicine Department at 404-712-3017.

I have read these instructions and agree to follow them.

Signature: ____________________________ Date: ____________________________
After the Therapy

- Bremsstrahlung scan post-procedure
  - Planar and SPECT-CT at 1-24 hours.
  - Look for adequacy of coverage and rare extrahepatic deposition.
- Compared with MAA and tumor imaging
  - Especially useful to plan next therapy since now know exact distribution of one lobe, can derive what is left.
Importance of SPECT-CT

- SPECT/CT
  - 3D quantification for therapy dose with more accuracy than planar imaging
  - Useful in pre and post therapy imaging
    - To demonstrate $^{90}\text{Y}$ microsphere uptake by region/tumor and extrahepatic uptake
  - May aid in the future for more precise personalized dosimetry
Importance of SPECT-CT

- *Hamami ME et. al.*  
  *J Nucl Med*  
  2009;50:688

  - SPECT/CT increases sensitivity and specificity of $^{99m}$Tc SPECT for detecting extrahepatic arterial shunting

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Planar</td>
<td>25%</td>
<td>87%</td>
<td>72%</td>
</tr>
<tr>
<td>SPECT</td>
<td>56%</td>
<td>87%</td>
<td>79%</td>
</tr>
<tr>
<td>SPECT/CT</td>
<td>100%</td>
<td>94%</td>
<td>96%</td>
</tr>
</tbody>
</table>
Bremsstrahlung

- Braking Radiation
- $^{90}$Y also decays with few positrons which can be imaged with newer generation PET scanners
**$^{99m}$Tc Spectrum Made with a Scintillation Camera**

- **$^{99m}$Tc (Technetium 99m)**
  - Internal Transition
  - 6 hour half-life
  - 140 keV gamma ray

- **$^{90}$Y (Yttrium 90)**
  - Beta- Decay
  - 64 hour half-life
  - Only Bremsstrahlung Radiation

---

**$^{99m}$Tc**

- Photopeak
- Characteristic x-ray from Lead Collimator
- Compton Scatter

**$^{90}$Y**

- Characteristic x-ray from Lead Collimator
- Bremsstrahlung mixed with Compton Scatter
Fusion helps post-therapy

Fused FDG and Bremsstrahlung confirms $^{90}$Y coverage of tumor
Bremsstrahlung imaging to prove entire liver treated and no extrahepatic deposition

Right lobe therapy  Left lobe therapy  Fusion to complete the puzzle
Another case where Bremsstrahlung demonstrated how much tumor was treated and that additional therapy needed.

Detail from OctreoScan

Post-left lobe Bremsstrahlung

Fusion shows portion of tumor (white) untreated in this session (black). (Unavoidable 2° vascular anatomy)

Residual can be quantified
Unexpected Extrahepatic Uptake

Patient with Breast Carcinoma Metastatic to Liver. MAA 10% shunt.

FDG PET-CT

Right lobe treated 36 mCi with $^{90}$Y without complication

Bremsstrahlung SPECT-CT
Unexpected Extrahepatic Uptake

But when we treated left lobe with 14.5 mCi

Also activity tracking along umbilical vessels to umbilicus
Unexpected Extrahepatic Uptake

In retrospect, visible on MAA only if very highly windowed
Unexpected Extrahepatic Uptake

Patient developed radiation burn which later granulated and resolved.

Falciform artery may only be visible on extended contrast injection and prolonged imaging.
Unexpected uptake with $^{90}$Y Therapy post right hepatectomy. No uptake seen on MAA and GDA had been coiled. We calculated 1.7% of dose. Patient placed on Carafate and Pepcid proactively and did well with transient abdominal pain.
But with Careful Planning

- Such complications are very uncommon
- Post-therapy imaging is critical in picking up these cases
Cutting Edge

  
  – Utilizes CT Hepatic Angiography, MAA SPECT-CT and partition modeling for dosimetric planning
    – 10 HCC patients
  – Certainly more elegant and scientifically valid
    – BSA method is highly empiric
  – More labor intensive
  – Which tumors should this be specifically applied to besides HCC?
  – Are all components such as CTHA needed?
Cutting Edge: We are also working with colleagues in Radiation Oncology to calculate Absorbed Dose and correlate with response.

Adapted courtesy of Bree Eaton, MD
• Eaton et al. Image-Based Dosimetry for $^{90}$Y Selective Internal Radiation Therapy (SIRT) of Hepatic Metastatic Melanoma: Dose-Volume Analysis Predict FGD-PET Response. ASTRO abstract submission.

  – Minimum tumor dose/BED ($p = 0.02$) and percent volume of tumor receiving $\geq 10$ Gy ($p = < 0.01$) significantly associated with SUV response.
  – Maximum tumor dose/BED ($p = 0.01$) and percent volume of tumor receiving $\geq 40$ Gy ($p < 0.01$) significantly correlated with absolute reduction in TLG.

• Tumor volume absorbed dose and BED calculations showed a statistically significant association with metabolic tumor response.

• The significant dose-response relationship points to the clinical utility of patient-specific absorbed dose calculations for radionuclide therapy.
Other Cutting Edge Questions:
How do we modify dose for differences in anatomic tumor versus functional tumor?
Young male with metastases to liver from colorectal primary.

Received first line chemotherapy.

Post $^{90}$Y radioembolization to (presumed right hepatic territory).

Images show localization of $^{90}$Y microspheres in the left hepatic region (segment 4A not segment 8).

*Courtesy Dr. Abdul Ismail, Kuwait.*
Yttrium-90 Emission Tomography?

- SPECT/CT of Y-90 Bremsstrahlung
  - Limited potential for quantitation and improved resolution
- PET/CT has more promise
  - Better resolution
  - Better quantitation

  - But
    - PET/CT is more expensive
    - How long will clinical PET/CT scans take?
      - Need to cover full liver and lower lungs (3 bed positions)
    - SPECT/CT may be adequate

- Can we use $^{90}$Y TOF PET to further optimize Y-90 SPECT?
- PET with $\beta^+$ spheres could also help in dosimetry
Phantom Studies with $^{90}$Y Microspheres

- **Findings**
  - Spiral of IV line provided a row of dots at 1 cm intervals
  - Individual dots could not be resolved clearly by SPECT or PET
  - But, PET seemed to be on verge…
  - For SPECT and Planar Scintigraphy, higher energy windows (over 200 keV) appeared to have significantly more background counts.
In Conclusion

• $^{90}$Y microsphere therapy holds great promise as part of the clinical armamentarium in the therapy of metastatic and primary hepatic carcinoma.

• Dose calculations may be performed with different methods, but ultimately a practical dosimetry based approach will be important for clinical and research applications.

• Currently available SPECT-CT techniques are valuable for pre and post-therapy planning and evaluation.