Microbrachytherapy: Example - Microspheres

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Preliminaries

1. The presenter has no known conflicts of interest, doggonit!

2. The objective of this presentation is that we all understand some of the safety aspects of treatments using radioactive microspheres.
Safety Issues Discussed

- Procedure
- Safety
- Dosimetry
Purpose

- To treat cancer metastatic to the liver.
- The 20-40μm, ⁹⁰Y-labeled microspheres are injected intra-arterially through the hepatic artery.
- They then get caught in the mouth of the capillary bed and irradiate the tumor.
Liver tumors are selectively fed by the hepatic artery.

Normal liver is mostly fed through the portal vein.
Availability

Vendors:

- SIRTex, maker of SIR-Spheres, polymer spheres approved for colorectal cancer.
- Nordion, maker of TheraSpheres, glass spheres approved for hepatocellular cancer.
Caveat

My experience has only been with SIR-Spheres
Procedure
TheraSpheres Delivery

(components not to scale)

1. Catheter inserted into hepatic artery
2. Catheter enters femoral artery
3. Delivery line
4. TheraSphere dose vial
5. 3-way stopcock
6. 3-way stopcock evacuation line
7. Empty vial in lead pot
TheraSpheres Delivery System
Delivery Box
Delivery Box from the Side
The solution with the microspheres is a slurry (or a sludge).

The injection uses pulses of water going into the vial to mix up the microspheres, taking them off the top.
Catheter Connection
Delivery (Continued)

- The first pulses must be short to prevent clogging (about 1/3 of the tube to the catheter).
- As the solution clears, the infusions can be larger.
- At the end, the outgoing needle is pushed to the bottom and the vial filled with air.
Safety
Dressing Up
During the delivery

Watching for

- Bubbles on the outside of the vial’s diaphragm.
- Watching for clogging in the lines
- Watching to make sure the catheter hasn’t moved or the capillary bed filled.
Surveying the Room
Surveying Participants
Surveying Feet
Measuring the Exposure from the Patient

- Measurement at 1 m.
- Maximum allowed reading is 5 mR/h
- Typical readings 0.3 – 3 mR/h
Dosimetry
Part of delivering a consistent dose requires that the user be able to verify the manufacturer’s assay in each case.

- That requires an independent calibration of the user’s dose calibrator.
- That also requires that the radiopharmaceutical be assayable.
Independent Calibration of the Users Dose Calibrator

This could be:

- Sources with an NIST traceable calibration independent of the therapeutic source manufacturer, but with identical geometry, or
- Sources from the manufacturer calibrated at NIST, or
- ADCL calibration of dose calibrations (using, assumedly sources as above).
UW Experience with Assay

- The shipping vials are each individual.
- The calibration factor = setting to read manufacturer’s assay.
- Dose calibrator is RadCal so factor is arithmetic not rheostat.
- Range covers ±11%.

<table>
<thead>
<tr>
<th>Date</th>
<th>Calibration Factor</th>
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<td>13-Feb-03</td>
<td>37.9</td>
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<td>28-May-03</td>
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<td>09-Jun-03</td>
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<td>04-Sep-03</td>
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<tr>
<td>09-Sep-03</td>
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</tr>
<tr>
<td>01-Oct-03</td>
<td>37.1</td>
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<tr>
<td>01-Oct-03</td>
<td>37.1</td>
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<tr>
<td><strong>Average</strong></td>
<td><strong>37.7</strong></td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td><strong>33.5 - 41.7</strong></td>
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Shipping Vials
Shipping Vials Closer
An Accurate Method of Relating the Assay to Dose

Here we have a problem.

- Dose is related to the radionuclide concentration.
- We assess the concentration using SPECT or (shudder) planar imaging using the bremsstrahlung.
  - Neither modality gives concentration
  - The conversion from counts is based on experiment and applies only to that geometry.
Dose Calculation

\[
D_{\text{Liver}} = \frac{50 \text{ Gy} \cdot \text{kg}}{\text{GBq}} \frac{A_{\text{instilled}} (1 - F_{\text{shunt}})}{(T : N) M_{\text{tumor}} + M_{\text{liver}}}
\]

where \(D_{\text{Liver}}\) = nominal dose to the liver;

\(F_{\text{shunt}}\) is the fraction of counts shunted to the lungs on the 99mTc labeled MAA study;

\(M_{\text{liver}}\) = total mass of liver estimated by computed tomography;

\(M_{\text{tumor}}\) = total mass of metastases estimated by computed tomography;

\(T:N = (A_{\text{tumor}} / M_{\text{tumor}}) / (A_{\text{liver}} / M_{\text{liver}})\) from MAA scan

where \(A_{\text{tumor}} / M_{\text{tumor}}\) = activity per mass in tumor, and \(A_{\text{liver}} / M_{\text{liver}}\) = activity per mass in liver (excluding tumor).
Y-90

- Equilibrium dose constant = 0.54 kg•Gy•GBq⁻¹•h⁻¹
- Mean life = 1.44•half-life = 1.44•64.2 h = 92.4 h
- Multiplying gives 49.8 Gy•kg/GBq
Dose to Tumor

\[ D_{\text{tumor}} = \frac{50 \text{Gy} \cdot \text{kg}}{\text{GBq}} \frac{A_{\text{instilled}}}{M_{\text{tumor}}} \left(1 - F_{\text{shunt}}\right) + \frac{M_{\text{liver}}}{(T : N)} \]
# Actual Method for Prescribed Activity

<table>
<thead>
<tr>
<th>Extent of Disease</th>
<th>Fraction of liver involvement</th>
<th>Base Activity in GBq</th>
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<tbody>
<tr>
<td></td>
<td>&gt;50%</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>25% - 50%</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>&lt; 25%</td>
<td>2</td>
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<table>
<thead>
<tr>
<th>Lung Shunting</th>
<th>Fraction of counts in the lung</th>
<th>Dosage Modifier</th>
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</thead>
<tbody>
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<td>&lt; 10%</td>
<td>1.0</td>
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<tr>
<td></td>
<td>10% - 15%</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>15% - 20%</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>&gt; 20%</td>
<td>0.0 (DO NOT PROCEED)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Target</th>
<th>Part of Liver</th>
<th>Dosage Modifier</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Whole Liver</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Right Lobe Only</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>Left Lobe Only</td>
<td>0.3</td>
</tr>
</tbody>
</table>
Calculation of the Prescribed Activity

The prescribed activity
= Base Activity x Lung-shunt Modifier x Fraction-of-liver Modifier.
Dose to Neighboring Structures

- Due to shunting
  - Lung shunting is measured
  - GI shunting can come from overfilling the hepatic capillaries (retrograde flow)

- Due to proximity
- Due to leaching
The desired dose remains elusive.

- Treatments have been delivered in terms of activity injected, assuming we know that.
- Since the concentration depends on many variables, the doses patients have received have varied widely while remaining unknown.