Y90 Radioembolization for Hepatocellular Carcinoma

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YTTRIUM-90

Almost a Pure beta emitter

Half life - 64.1 hours

Energy max - 2.27 MeV, mean 0.93 MeV

<table>
<thead>
<tr>
<th>RANGE</th>
<th>Air</th>
<th>Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max</td>
<td>9.6 m</td>
<td>11 mm</td>
</tr>
<tr>
<td>Mean</td>
<td>3.7 m</td>
<td>2.5 mm</td>
</tr>
</tbody>
</table>

Enough energy to easily damage DNA/kill tissue

Regular X-rays ~100 KeV
Y90 Radioembolization
(selective internal radiation therapy – SIRT)

• Takes advantage of differential hepatic arterial supply to liver tumors (rather than portal venous supply)
• Enables high local tumor doses (>200Gy) and low prencychmal doses (<30Gy)
**THERASPHERES**

- Canada, Nordion
- First available
- Focus on HCC
- 20-30 micron glass bead
- Dose from volume
- Y90 embedded (high dose/bead)

**SIRSPHERES**

- Australia, SirTex
- First FDA approved
- Focus on Liver Mets
- 20-60 micron plastic bead
- Dose from body size
- Y90 coated (50x < dose/bead)
Y90: OHSU PATIENT SELECTION

- Tbili < 2 (ideally < 1.5)
  - Lobar treatments
  - May have more flexibility for selective delivery
- ECOG 0-2 (ideally 0-1)
- May include more advanced disease
  - Large tumor burden
  - Vascular invasion
  - Main portal vein involvement
  - Infiltrative disease
STEPS FOR A Y90 PATIENT

Planning Angiogram: Arterial supply to liver tumor
Pulmonary Shunt Calculation

Dose Calculation: Volume Calculations
Average liver size for height and weight

Dose Preparation: Deliver at the correct time
Deliver the correct amount

Dose Delivery: Microcatheters
Y90 Workup

Detailed angiographic evaluation of hepatic and enteric arterial supply

- Cystic artery
- Gastroduodenal artery
- Left gastric/right gastric arterial arcade
- Hepatic falciform ligament artery
- Pancreaticoduodenal branches

Determination of pulmonary shunt fraction

- Intraarterial Tc-99m MAA
- Planar/SPECT imaging
CYSTIC ARTERY
CYSTIC ARTERY

? Necessary to embolize
GASTRODUODENAL ARTERY

Protect small bowel/pancreas
GASTRODUODENAL ARTERY
(No longer as common)
RIGHT GASTRIC ARTERY

Protect stomach
RIGHT GASTRIC ARTERY
RIGHT GASTRIC ARTERY
RIGHT GASTRIC ARTERY
HEPATIC FALCIFORM LIGAMENT ARTERY
(supplies soft tissues near umbilicus)
Variant Anatomy
Y90 Workup

$^{99m}$Technetium – Macroaggregated albumin

Lyophilized powder of human albumin “aggregate”

Mixed with $^{99m}$Tc at room temperature – 15 minutes

90% must be between 10-90 microns
no particles to exceed 150 microns

Typical dose: 3-4 mCi (100,000-250,000 particles)

Small particles trapped in liver / spleen (macrophage)
Room Set up for Radioembolic Delivery

Protective Measures

Sheath

Water proof barriers

Floor mat

“Double Booties”
DELIVER Tc-99M MAA
DELIVER Tc-99M MAA
SAFELY DISPOSE OF WASTE SCREEN FOR SPILLS
Pulmonary Shunt Fraction

Anterior View

<table>
<thead>
<tr>
<th></th>
<th>Ant. counts</th>
<th>Post. counts</th>
<th>Geometric Mean</th>
<th>% Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Left Lung</td>
<td>21079</td>
<td>26977</td>
<td>23846.3</td>
<td>6.2</td>
</tr>
<tr>
<td>2 Right Lung</td>
<td>25984</td>
<td>21826</td>
<td>23814.4</td>
<td>6.2</td>
</tr>
<tr>
<td>3 Stomach</td>
<td>25</td>
<td>300</td>
<td>86.6</td>
<td>0.0</td>
</tr>
<tr>
<td>4 Liver</td>
<td>369953</td>
<td>303765</td>
<td>335229.4</td>
<td>87.6</td>
</tr>
</tbody>
</table>

Posterior View
CALCULATE DOSE

Liver Volume: 2636.0 cc
Average CT#: 53.5 H.U.
CALCULATE DOSE

Finding Name: 7-Finding 1
Volume: 526.3 cc
Avg CT#: 58.5 H.U.
SD: 27.2 H.U.

Liver Volume: 2636.0 cc
Average CT#: 53.5 H.U.
ORDER AND DELIVER THE DOSE
Y90 Dose Calculations
SIRSPHERES AND THERASPHHERES USE DIFFERENT METHODS

SIRSPHERES: (Activity – GBq or mCi)
Disintegrations per second

THERASPHHERES: (Dose – gray or rads)
Radiation energy absorbed per Kg tissue
SIRSPHERE DOSING METHODS:

Empiric: no longer used

Body Surface Area:

Standardized liver size based upon body habitus

Newer “volume based”:

Similar to TheraSphere calculations
### SIRSPHERES

Empiric: (no longer used)

<table>
<thead>
<tr>
<th>Tumor Involvement in the Liver (%)</th>
<th>Recommended Activity (GBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;50</td>
<td>3.0</td>
</tr>
<tr>
<td>25–50</td>
<td>2.5</td>
</tr>
<tr>
<td>&lt;25</td>
<td>2.0</td>
</tr>
</tbody>
</table>
SIRSPHERES

Body Surface Area:

\[
\text{SIR-Spheres: } A \ (\text{GBq}) = \text{body surface area (m}^2) - 0.2 + (\% \text{ tumor involvement/100})
\]

Body surface area = 0.20247 \times \text{height}^{0.725} \times \text{weight}^{0.425} (\text{kg})

<table>
<thead>
<tr>
<th>Height</th>
<th>Weight</th>
<th>BSA</th>
<th>% tumor</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>5’2”</td>
<td>105 lb</td>
<td>1.45 (m^{2})</td>
<td>50%</td>
<td>1.75 GBq</td>
</tr>
<tr>
<td>5’11”</td>
<td>170 lb</td>
<td>1.97 (m^{2})</td>
<td>50%</td>
<td>2.27 GBq</td>
</tr>
<tr>
<td>5’11”</td>
<td>230 lb</td>
<td>2.24 (m^{2})</td>
<td>50%</td>
<td>2.54 GBq</td>
</tr>
</tbody>
</table>
**Body Surface Area:**

Fine tuning of % tumor based upon fraction of treated liver

<table>
<thead>
<tr>
<th>Height</th>
<th>Weight (lb)</th>
<th>BSA (m²)</th>
<th>Part of Liver</th>
<th>% tumor</th>
<th>Dose (GBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5’2”</td>
<td>105</td>
<td>1.45</td>
<td></td>
<td>50</td>
<td>1.75</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>60% (right)</td>
<td></td>
<td>1.05</td>
</tr>
<tr>
<td>5’11”</td>
<td>170</td>
<td>1.97</td>
<td></td>
<td>50</td>
<td>2.27</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>60% (right)</td>
<td></td>
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<tr>
<td>5’11”</td>
<td>230</td>
<td>1.45</td>
<td></td>
<td>50</td>
<td>2.54</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>40% (left)</td>
<td>30</td>
<td>0.94</td>
</tr>
</tbody>
</table>
THERASPERES

Dose based (per kilogram)

Authorized User chooses target dose.

Min = 80 Gy, Max = 150 Gy
OHSU averages 120-130 Gy

Calculate activity of $^{90}$Y required.

\[
\text{TheraSphere: } A (\text{GBq}) = \left[ D (\text{Gy}) \times \frac{M (\text{kg})}{50} \right] / 50, \text{ or }
\]
\[
\text{Activity required (GBq)} = \left[ \text{desired dose (Gy)} \right] \times \left[ \text{target liver mass (kg)} \right] / 50
\]
## THERASPERHES

<table>
<thead>
<tr>
<th>Target Dose (Gy)</th>
<th>Volume (mL)</th>
<th>Mass (Kg)</th>
<th>Activity (GBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>1250</td>
<td>1.288</td>
<td>2.58</td>
</tr>
<tr>
<td>125</td>
<td>1250</td>
<td>1.288</td>
<td>3.22</td>
</tr>
<tr>
<td>125</td>
<td>750</td>
<td>0.773</td>
<td>1.93</td>
</tr>
</tbody>
</table>

TheraSphere: \( A \, (\text{GBq}) = \left[ D \, (\text{Gy}) \times M \, (\text{kg}) \right] / 50 \), or

Activity required (GBq) =

\[ [\text{desired dose (Gy)}] \times [\text{target liver mass (kg)}] / 50 \]
Y90 ADVERSE EFFECTS

• Fatigue (predominant sequelum)
• Non-target embolization
  – Cholecystitis
  – GI ulceration
• Hepatic fibrosis
• Radiation induced liver disease
• Radiation induced lung disease
Caution with Y90 for HCC: Arteriovenous Shunting
Lung Scan after Transarterial Injection of Tc99m

<table>
<thead>
<tr>
<th>Location</th>
<th>Ant Rt Lung</th>
<th>Ant Lt Lung</th>
<th>Post Rt Lung</th>
<th>Post Lt Lung</th>
<th>Lung Geo Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ant Lung</td>
<td>280810.50</td>
<td>306772.00</td>
<td>191453.00</td>
<td>130413.75</td>
<td>434883.06 Cts</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Location</th>
<th>Ant Liver</th>
<th>Post Liver</th>
<th>Ant Gastric</th>
<th>Post Gastric</th>
<th>Liver Geo Mean</th>
<th>Gastric Geo Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>31694.00</td>
<td>14306.25</td>
<td>4604.50</td>
<td>2597.25</td>
<td>21293.71</td>
<td>3458.18</td>
</tr>
</tbody>
</table>

Total Geometric Mean Counts = 459634.97
Lung/Total ratio = 95 %
TOTAL ABD GEO MEAN=736.455
LIVER GEO MEAN=505.364
LIVER/ABD RATIO=88.6%
Sesatimibi Myocardial Nucs Study the Day Prior!!
Y90 OUTCOMES

• Salem et al. Gastroenterology 2010;138:52–64
  – N = 291, single center prospective cohort study
  – TTP 7.9 mo; OS CTP A: 17.2 mo, CTP B: 7.7 mo
Y90 OUTCOMES

• Sangro et al. Hepatology 2011;54:868–878
  – N = 325, multicenter retrospective
  – OS BCLC A: 24.4 mo, B: 16.9 mo, C: 10.0 mo
Y90 OUTCOMES

- Salem et al. Gastroenterology 2011;140:497–507
  - Y90 (n = 123) vs TACE (n = 122), retrospective
  - OS Y90: 20.5 mo, TACE 17.4mo (p = 0.232)
  - OS BCLC B Y90 17.2mo vs TACE 17.5mo (p = 0.42)
  - TTP Y90 13.3mo, TACE 8.4mo (p = 0.046)
  - Some benefit to those waiting for transplant
Y90: EMERGING TECHNIQUES
Y90: Radiation Segmentectomy

- “Ablative” approach for solitary tumor
- Dosimetry to entire lobe delivered to 1-2 segments (typical dose >190-200Gy)
- Treated segment(s) usually atrophy
Y90: Radiation Segmentectomy

• Vouche et al., Hepatology 2014, epub
  – 102 patients
  – 86% with complete or partial response
  – Median Time to Progression: 33.1 months
  – Median Overall Survival: 53.4 months
    • Similar to ablation
Y90: Radiation Segmentectomy
Y90: Radiation Segmentectomy
Y90: Radiation Segmentectomy
Radiation Segmentectomy
Radiation Segmentectomy
(~250-300Gy calculated tumor dose)
7+cm HCC for Segmentectomy
Complex blood supply
Consolidation of Y90
8 month follow up headed for resection
Infiltrative HCC
9 month follow up
Associated Left Lobe Hypertrophy
Atrophy-Hypertrophy Effect
Y90 Radioembolization takes advantage of tumor arterial blood supply to deliver very high local doses to the liver.

OHSU protocol
- Preserved liver function
- Advanced stage disease
- Portal vein invasion

Newer approaches include targeted ‘ablative’ techniques (radiation segmentectomy), and preoperative techniques (radiation lobectomy).