Yttrium-90 Microsphere Therapy Planning and Dose Calculations

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Educational Objectives

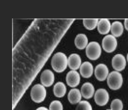
- To understand the imaging sequence for Yttrium-90 microsphere therapy
- To understand calculation of lung shunt fraction and estimation of absorbed dose for lung and liver
- To become familiar with radiation safety and regulations surrounding Yttrium-90 microsphere therapy

Outline

- Overview of ^{90}Y-microsphere therapy
- Patient imaging prior to ^{90}Y-microsphere therapy
- Calculation of the lung shunt fraction
- ^{90}Y-microsphere therapy dose calculations
- Patient imaging post ^{90}Y-microsphere therapy
- Three-compartment partition model
- Measurement of ^{90}Y activity and admin. activity
- Radiation Safety
- Challenges and Summary

^{90}Y-microsphere Therapy

- Trans-arterial delivery of radioactive ^{90}Y-labeled microspheres via a catheter directly at disease sites (targeted infusion)
- Microspheres (20-30 μm) trapped in tumor capillary vessels due to their embolic size and targeted delivery



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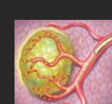

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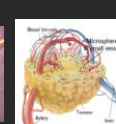


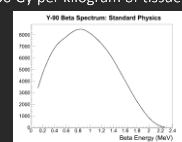
- β emissions from trapped ^{90}Y-microspheres are capable of delivering lethal radiation doses to (proximal) neoplastic tissue while sparing (more distal) surrounding normal tissue

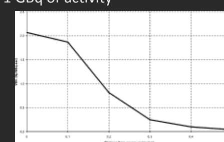
^{90}Y-microsphere Therapy

- ^{90}Y-microsphere therapy usually target the liver
- ^{90}Y-microsphere therapy takes advantage of the unique circulatory system in the liver
  - Portal vein (normal liver) & hepatic artery (tumor)
- Liver directed EB-RT are limited in scope
  - Radiation tolerance of normal hepatocytes < neoplastic tissue
  - Max. tolerated doses 30–40 Gy (Emami et al, IJROBP 21, 1991; McGinn et al, J Clin Onc 16, 1998)
- With ^{90}Y-microspheres, total liver radiation doses up to 80 Gy were well tolerated with no hepatic radiation damage (Gray et al, Annals Oncology 12, 2001; Burton et al, Radiology 175, 1990)
- ^{90}Y-microsphere therapy is approved by the FDA for the treatment of unresectable HCC and metastatic colorectal cancer

Properties of Yttrium-90

- Production: Y-89 (n,γ) Y-90
- Decay: Y-90 (β^-, 64.1 hr) Zr-90; a pure β^- emitter
  - Y-90 also emits β^+ at low yields (~32 ppm) via internal pair-production
- β energy: 0.937 MeV (mean) and 2.28 MeV (max)
- Tissue penetration depth: 2.5 mm (mean) and 11 mm (max)
- ^{90}Y deposits >90% of its energy in the first 5 mm of tissue
- ^{90}Y deposits >90% of its energy in the first 11 days
- Permanently implanted ^{90}Y can deliver radiation absorbed doses of ~50 Gy per kilogram of tissue for 1 GBq of activity (Berger, JNM 12, 1971)





(Sarfaraz et al., Med Phys 31, 2004)

Commercial ^{90}Y-microsphere Products

SIR-Spheres®

- Sirtex Medical, Sydney, Australia
- Insoluble, biocompatible resin matrix
- 30–35 μm glass spheres
- 3 GBq (81 mCi) activity = 30–60 x 10^6 spheres
- Maximum activity available: 3 GBq (81 mCi)
- Indicated for the treatment of unresectable metastatic liver tumors from primary colorectal cancer with adjuvant chemotherapy (FUDR)

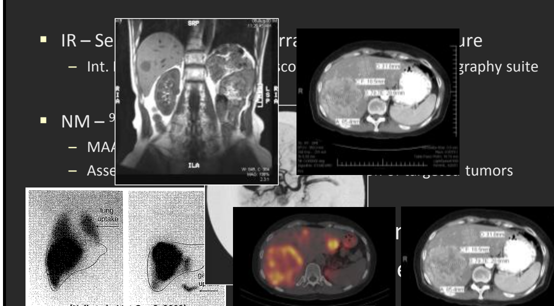
TheraSphere®

- MDS Nordion, Ottawa, Canada
- Insoluble, biocompatible glass matrix
- 20–30 μm glass spheres
- 3 GBq (81 mCi) activity = ~1.2 x 10^6 spheres
- Maximum activity available: 20 GBq (540 mCi)
- Indicated for radiation treatment or as a neoadjuvant for surgery or transplantation in patients with unresectable HCC

Liver is common site of metastases from a variety of neoplasms
→ Clinical trials on management of metastatic liver disease

Patient Imaging Prior to 90Y-TAR

- CT or MRI – Estimate target tumor mass
- IR – Se ... rra ... ure
  - Int. ... co ... graphy suite
- NM – 9 ...
  - MA ...
  - Asse ... tumors



(Hall et al., J Int Onc 2, 2009)

Lung Dose Consideration

- Prevention of radiation pneumonitis
  - Arterio-venous shunting in neoplastic vasculature
  - Tc-99m MAA scans used to assess lung shunt fraction and lung dose
  - Exclude patients with lung shunting that could result in lung radiation dose >25-30 Gy per treatment or >50 Gy cumulative

(Ho et al, EJNM 24, 1997)

SIR-Spheres	
Lung Shunting	Reduction Factor
<10 %	No Reduction
10 % - 15 %	20 % reduction
15 % - 20 %	40 % reduction
> 20 %	No Treatment
Lung dose per treatment < 25 Gy	

TheraSphere	
Lung Dose Limit	Gy
Per Treatment	30
Cumulative	50

Lung Shunt (LS) Fraction

- 2-4 mCi of ^{99m}Tc-MAA delivered trans-arterially in IR suite
- Planar scintigraphy of Thorax and Abdomen (AP and PA)
- Calculate Lung Shunt (LS) using the following formula

$$\text{Lung Shunt (\%)} = \frac{\text{Lung Counts}}{\text{Lung Counts} + \text{Liver Counts}} \times 100$$

- SIR-Spheres: geometric-mean images
- TheraSphere: Image type not explicitly described

Example Lung Shunt Calculation

LS (%) = Lung GM-counts / (Lung GM-counts + Liver GM-counts) x 100
= 77278 / (77278 + 973962) x 100 = 7.35%

- SIR-Spheres:
  LS < 20% (no modification)
  → 81 mCi ^{90}Y activity limit
- TheraSphere:
  30 Gy lung dose limit
  → 222 mCi ^{90}Y activity limit

	Left	Right
Lung ANT	38787	44174
Lung POST	34282	37703
Liver ANT	1641103	
Liver POST	578027	
GM Lung Total		77278
GM Liver Total		973962
% Lung Shunt		7.35%

^{90}Y-Therapy Planning: SIR-Spheres

- SIR-Spheres therapy doses are based on activity (not target radiation dose) – maximum activity of 81 mCi
- Empirical dosimetry models
  - Basic: Activity based on maximum activity & tumor fraction
  - BSA: Activity based on BSA & tumor involvement in liver
  - Lung Shunt modification: No treatment for LS > 20%
- Average liver dose < 80 Gy and lung dose < 25 Gy

Tumor Fraction Modification	
Tumor fraction in liver	Recommended ^{90}Y-activity
> 50 %	3.0 GBq (81 mCi)
25 - 50 %	2.5 GBq (67.5 mCi)
< 25 %	2.0 GBq (54 mCi)

Lung-Shunt Fraction Modification	
Lung Shunting	Reduction Factor
<10 %	No Reduction
10 % - 15 %	20 % reduction
15 % - 20 %	40 % reduction
> 20 %	No Treatment
Lung dose per treatment < 25 Gy	

^{90}Y-Therapy Planning: TheraSphere

- TheraSphere therapy doses are based on desired radiation dose to target mass; typically 120 to 150 Gy

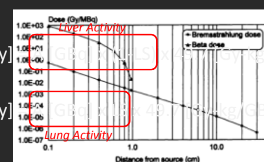
$$\text{Activity Required [GBq]} = \frac{\text{Desired Dose [Gy] x Target Mass [kg]}}{\text{50 [Gy-kg/GBq]}}$$

- Target mass = whole liver or liver lobe or liver segment
  - Patient-specific vasculature and catheter approach (common or left or right hepatic artery) to target mass defines target mass
- Therapy must maintain lung dose lower than 30 Gy
  - Maximum activity depends on the Lung Shunt fraction

Radiation Absorbed Dose

- $Dose_{tissue}$ [Gy] = A_{tissue} [GBq] x 49.7 [Gy-kg/GBq] / M_{tissue} [kg]
  - Self dose from β emission: >90% energy deposit in <5mm
  - 49.7 [Gy-kg/GBq] = equilibrium accumulated dose constant
  - Bremsstrahlung dose << β dose

(Berger, JNM 12, 1971; Stabin et al, JNM 35, 1994; Gulec et al, JNM 47, 2006)



Liver Dose [Gy] = A [GBq] x (1-LS) x 49.7 [Gy-kg/GBq] / M_{liver} [kg]

Lung Dose [Gy] = A [GBq] x LS x 49.7 [Gy-kg/GBq] / M_{lung} [kg]

- Error in liver mass propagates into liver dose calculation
- Model estimates average dose to target volume assuming uniform microsphere uptake within volume

Dose Calculations: TheraSphere

Max Activity [mCi] = 30 [Gy] x M_{lung} [kg] / (LS x 0.037 [GBq/mCi] x 49.7 [Gy-kg/GBq])

Activity [mCi] = D_{liver} [Gy] x M_{liver} [kg] / ((1-LS) x 0.037 [GBq/mCi] x 49.7 [Gy-kg/GBq])

- Lung Shunt = 0.0735
- Maximum Activity = 222 mCi, for lung dose = 30 Gy
- Liver dose [Gy] = 378 [Gy-kg] / M_{liver} [kg]
  = 198 Gy for M_{liver} = 1.91 kg (MIRD Std. Man)
  = 154 Gy for M_{liver} = 2.46 kg (Weight-based)
  = 137 Gy for M_{liver} = 2.76 kg (CT-based)

- Target liver dose = 120 Gy
  → 134.6 mCi of ^{90}Y → Lung dose delivered = 18.2 Gy

Dose Calculations: SIR-Spheres

M, 53 kg, 174.5 cm → BSA = 1.60 m^2		
Tumor involvement (TI)	45%	Dose modification YES
Lung Shunt (LS)	7.35%	Dose modification NO

Basic model: 2.5 GBq (67.5 mCi)

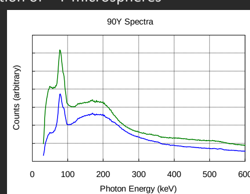
BSA model: (BSA[m^2] – 0.2) + TI[%]/100 = 1.85 GBq (50.1 mCi)

Liver Dose [Gy] = A [GBq] x (1-LS) x 49.7 [Gy-kg/GBq] / M_{liver} [kg]
= 44.7 Gy (< 80 Gy)

Lung Dose [Gy] = A [GBq] x LS x 49.7 [Gy-kg/GBq] / M_{lung} [kg]
= 6.8 Gy (<25 Gy)

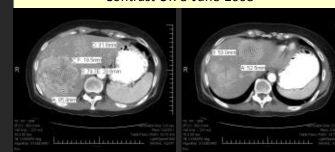
Patient imaging day of ^{90}Y-Therapy

- Interventional Radiologist - Angiography suite
  - verify catheter placement, assess flow
  - deliver ^{90}Y-microspheres
- NM Planar & SPECT ^{90}Y-bremsstrahlung imaging
  - 79keV/26% window, MELP collimation, 128x128 matrix, 4.8 mm^2 pixels, 128 views/360°, 28 s/view, non-circular step-shoot
  - Assess delivery and distribution of ^{90}Y-microspheres
- Follow-up evaluations at 2-3 months – CT or MRI

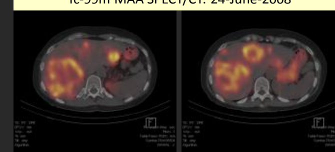


Prior to ^{90}Y-microsphere Therapy

Contrast CT: 3-June-2008



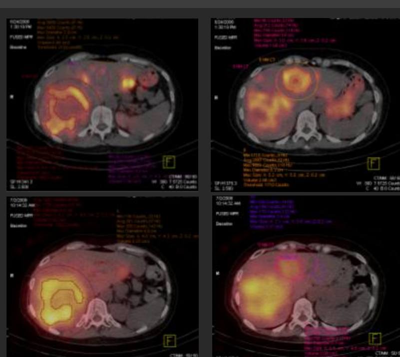
Tc-99m MAA SPECT/CT: 24-June-2008



SPECT Concordance: ^{99m}Tc-MAA & ^{90}Y

Tc-99m MAA SPECT/CT 24-June-2008

Y-90 SPECT/CT 2-July-2008

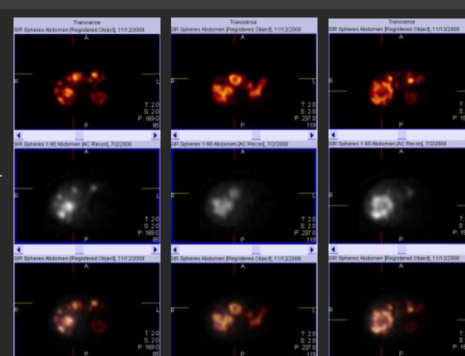


SPECT Concordance: ^{99m}Tc-MAA & ^{90}Y

Tc-99m MAA SPECT/CT 24-June-2008

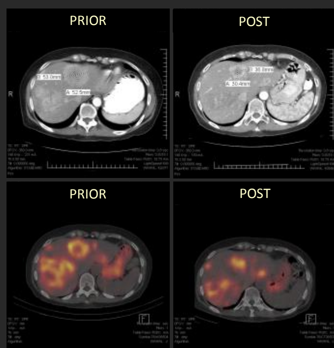
Y-90 SPECT/CT 2-July-2008

Fused SPECT: Tc-99m MAA and Y-90



Pre and Post ^{90}Y-microsphere Therapy

CT
3-June-2008



CT
5-Sept-2008

Tc-99m MAA
SPECT/CT
24-June-2008

Tc-99m MAA
SPECT/CT
2-Sept-2008

SAM Question 1

The physical properties of Yttrium-90 that makes it well suited for internal radionuclide therapy are that ^{90}Y is a pure β^- emitter with a max. energy of 2.28 MeV corresponding to a:

0% A. maximum tissue penetration depth of ~0.1 mm
12% B. maximum tissue penetration depth of ~1 mm
88% C. maximum tissue penetration depth of ~10 mm
0% D. maximum tissue penetration depth of ~100 mm

SAM Question 1: Answer

- The physical properties of Yttrium-90 that makes it well suited for internal radionuclide therapy are that ^{90}Y is a pure β^- emitter with a maximum energy of 2.28 MeV corresponding to a:
  A. maximum tissue penetration depth of ~0.1 mm
  B. maximum tissue penetration depth of ~1 mm
  C. maximum tissue penetration depth of ~10 mm
  D. maximum tissue penetration depth of ~100 mm

- *Reference: Sarfaraz M, Kennedy AS, Lodge MA, Li XA, Wu X, Yu CX, "Radiation absorbed dose distribution in a patient treated with yttrium-90 microspheres for hepatocellular carcinoma," Medical Physics 31(9):2449-53, 2004*

SAM Question 2

The most common route of ^{90}Y-microsphere administration for liver–directed therapy is:

0% A. Peri-tumoral injection
0% B. Implantation of 90Y-brachytherapy seeds
3% C. Systematic administration via intravenous injection
97% D. Trans-hepatic arterial administration via catheter

SAM Question 2: Answer

- The most common route of ^{90}Y-microsphere administration for liver–directed therapy is:
  A. Peri-tumoral injection
  B. Implantation of 90Y-brachytherapy seeds
  C. Systematic administration via intravenous injection
  D. Trans-hepatic arterial administration via catheter

- *Reference: Murthy R, Nunez R, Szklaruk J, et al., "Yttrium-90 microsphere therapy for hepatic malignancy: devices, indications, technical considerations, and potential complications," Radiographics 25(Supplement 1):S41-55, 2005*

SAM Question 3

The lung shunt fraction (LSF) based on ^{99m}Tc-MAA Planar images, used to estimate lung absorbed doses from ^{90}Y-microsphere therapy, is calculated as:

6% A. $\text{Lung Shunt Fraction (\%)} = \frac{\text{Lung Counts}}{\text{Liver Counts}} \times 100$

0% B. $\text{Lung Shunt Fraction (\%)} = \frac{\text{Liver Counts}}{\text{Lung Counts}} \times 100$

94% C. $\text{Lung Shunt Fraction (\%)} = \frac{\text{Lung Counts}}{\text{Lung Counts} + \text{Liver Counts}} \times 100$

0% D. $\text{Lung Shunt Fraction (\%)} = \frac{\text{Lung Counts} + \text{Liver Counts}}{\text{Lung Counts}} \times 100$

SAM Question 3: Answer

- The lung shunt fraction (LSF) based on ^{99m}Tc-MAA Planar images, used to estimate lung absorbed doses from ^{90}Y-microsphere therapy, is calculated as:
  A. $\text{Lung Shunt Fraction (\%)} = \frac{\text{Lung Counts}}{\text{Liver Counts}} \times 100$
  B. $\text{Lung Shunt Fraction (\%)} = \frac{\text{Liver Counts}}{\text{Lung Counts}} \times 100$
  C. $\text{Lung Shunt Fraction (\%)} = \frac{\text{Lung Counts}}{\text{Lung Counts} + \text{Liver Counts}} \times 100$
  D. $\text{Lung Shunt Fraction (\%)} = \frac{\text{Lung Counts} + \text{Liver Counts}}{\text{Lung Counts}} \times 100$

- *Reference: Gulec S, Mesoloras G, Stabin M, "Dosimetric techniques in 90Y-microsphere therapy of liver cancer: The MIRD equations for dose calculations," J Nuclear Medicine 47:1209–11, 2006*

SAM Question 4

The typical range of planned absorbed doses to target liver tissue in ^{90}Y-microsphere internal radionuclide therapies is around:

0% A. 40 – 60 cGy
24% B. 40 – 60 Gy
6% C. 80 – 120 cGy
70% D. 80 – 120 Gy

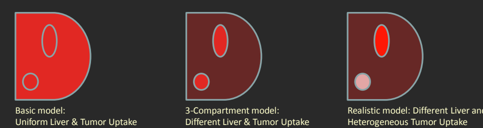
SAM Question 4: Answer

- The typical range of planned absorbed doses to target liver tissue in ^{90}Y-microsphere internal radionuclide therapies is around:
  - A. 40 – 60 cGy
  - B. 40 – 60 Gy
  - C. 80 – 120 cGy
  - D. 80 – 120 Gy

- *Reference: Salem R, Thurston KG, "Radioembolization with 90Yttrium microspheres: a state-of-the-art brachytherapy treatment for primary and secondary liver malignancies—Part 1: Technical and methodologic considerations," J Vasc Interv Radiology 17:1251–1278, 2006*

Limitations of ^{90}Y-microsphere Dosimetry

- Not intended to calculate dose to individual tumors
- Uses conservative assumptions to ensure safety
- Assumes uniform uptake of microspheres in tumor and normal liver compartments



- Three-compartment model: lung, liver, and tumor
  - Accounts for differential uptake of microspheres in liver versus tumor
  - All tumors, independent of their sizes or locations, grouped into the tumor compartment with a single uptake value (Ho et al., EJNM 23, 947-52, 1996)

Three-compartment Partition model

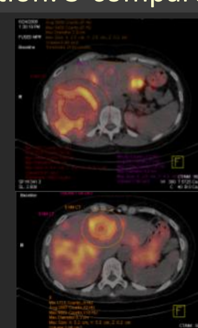
- Additional information needed (Ho et al., EJNM 23, 947-52, 1996)
  - Tumor burden (M_{tumor}) and Tumor uptake ratio (R)
- Estimation of fractional Tumor Involvement (TI)
  - $M_{total} = M_{liver} + M_{tumor}$
  - $M_{tumor} = TI \times M_{total}$ and $M_{liver} = (1\text{-}TI) \times M_{total}$
- Estimation of Tumor Uptake Ratio (R)

$$R = \frac{\text{Tumor MAA uptake [counts/pixel]}}{\text{Liver MAA uptake [counts/pixel]}}$$

- A_{liver} [mCi] = A [mCi] x (1-LS) x M_{liver} / (M_{liver} + R x M_{tumor})
- A_{tumor} [mCi] = A [mCi] x (1-LS) x R x M_{tumor} / (M_{liver} + R x M_{tumor})
- $Dose_{organ}$ [Gy] = A_{organ} [GBq] x 49.7 [Gy-kg/GBq] / M_{organ} [kg]

Example Dose Calculation: 3-compartment

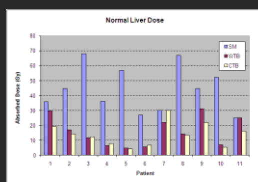
- LS = 7.35%
- Total Activity = 222 mCi
- Total liver = 2.76 kg
- TI = 45%
- T/N: R = 632.9/32.8 = 19.3
- Normal Liver
  - Mass = 1.52 kg
  - Activity = 12.3 mCi
  - Dose = 14.7 Gy
- Tumor
  - Mass = 1.24 kg
  - Activity = 193.4 mCi
  - Dose = 284.5 Gy



- Prior estimate of liver dose = 137 Gy with T/N=1

Three Compartment Model: Normal Liver Dose

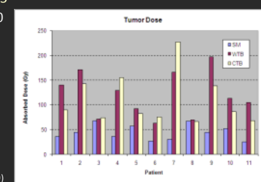
- Quantify differences of 3 dosimetry models
  - Empirical model (STD)
  - Weight-based 3-compartment model (WTB)
  - CT-based 3-compartment model (CTB)
  - Differences in lung mass, liver mass, T/N Ratio, TI
- Median ± 1σ difference, t-test p-values
  - WTB < STD: -27.7 ± 20.5 Gy; p<0.001
  - CTB < STD: -28.2 ± 19.3 Gy; p<0.001
  - CTB ~ WTB: -0.7 ± 5.5 Gy; p>0.10
- Linear correlation, r
  - WTB & STD: r = -0.26; p>0.10
  - CTB & STD: r = -0.37; p>0.10
  - CTB & WTB: r = 0.92; p=0.004



(Kappadath et al., JNM 50, 2009)

Three Compartment Model: Tumor Dose

- Quantify differences of 3 dosimetry models
  - Empirical model (STD)
  - Weight-based 3-compartment model (WTB)
  - CT-based 3-compartment model (CTB)
  - Differences in lung mass, liver mass, T/N Ratio, TI
- Median ± 1σ difference, t-test p-values
  - WTB > STD: 80.1 ± 52.1 Gy; p<0.0002
  - CTB > STD: 48.5 ± 58.0 Gy; p<0.0015
  - CTB ~ WTB: -10.2 ± 37.1 Gy; p>0.10
- Linear correlation, r
  - WTB & STD: r = -0.19; p>0.10
  - CTB & STD: r = -0.26; p>0.10
  - CTB & WTB: r = 0.80; p=0.011



(Kappadath et al., JNM 50, 2009)

Assay of ^{90}Y Activity

- Dose calibration setting determined on-site with calibrated ^{90}Y activity

Dose Calibrator S/N	Calibration Number
15722	47 x 10
15724	47 x 10
15725	47 x 10
15728	47 x 10
15729	47 x 10
151034	45 x 10
510034	46 x 10

- SIR-Spheres
  - Activity delivered as 81 mCi microspheres in water, 5 ml total volume
  - Draw microsphere solution by volume to desired activity

D. Divide activity by the number of ml in vial to calculate mCi per ml
Original activity in vial = 80 mCi ÷ 5 ml = 16 mCi/ml Concentration

2. Calculate volume required for the prescribed dose:
(Divide the prescribed dose by the mCi per ml calculated above)
Prescribed dose 48 mCi ÷ 16 mCi/ml Concentration = 3 ml required

4. Measure residual to estimate activity drawn:

Residual activity = 34 mCi
Original 80 mCi – Residual 34 mCi in dose vial = 46 mCi in syringe

Assay of ^{90}Y Activity

- TheraSphere
  - Modification of the delivered activity is not allowed
  - Ordered activity would account for day/time of therapy

Target Volume (cc):	929.0	Target Liver Mass (kg): 0.957
Desired Dose (Gy):	120	
Time Zone Variance (h):	1	Variance from Eastern Standard Time (EST)
Lung Shunt Fraction (% LSF):	5.59%	Imported automatically from Lung Shunt Calculation worksheet
Anticipated Residual Waste (%):	2.00%	Optional estimated value
Previous Dose to the Lungs (Gy):	0.0	
Required Activity at Administration (GBq):	2.48	This value is corrected for LSF and Residual Waste if values are entered above.

Activity Size Selected (GBq):	7
Date & Time for Administration:	Thursday

Dose Delivered (Gy) for: 5 GBq Activity

Time	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
8:00 AM	Calibration Day @ 12:00 EST	193	149	115	88	68
12:00 PM		184	142	110	85	65
4:00 PM		177	136	105	81	63
8:00 PM		169	131	101	78	60

Dose Delivered (Gy) for: 7 GBq Activity

Time	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
8:00 AM	Calibration Day @ 12:00 EST	270	208	160	124	96
12:00 PM		258	199	154	119	91
4:00 PM		247	191	147	114	88
8:00 PM		237	183	141	109	84

Dose Delivered (Gy) for: 10 GBq Activity

Time	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
8:00 AM	Calibration Day @ 12:00 EST	385	297	229	177	136
12:00 PM		369	285	220	169	131
4:00 PM		353	273	210	162	125
8:00 PM		338	261	201	155	120

^{90}Y-microsphere Therapy Preparation

Calculation of Administered Activity

- Percentage of activity delivered to the patient can be based on ion-chamber exposure rate measurements
  - Before administration: dose-vial in acrylic shield
  - After administration: the 2L Nalgene jar with beta shield containing waste and residual activity

- The percentage of activity delivered to the patient

$$\text{Activity Delivered [\%]} = 100 \times \left(1 - \frac{\text{Waste measurement after therapy}}{\text{Dose vial measurement before therapy}}\right)$$

- Activity delivered to patient

$$\text{Activity Delivered [mCi]} = \text{Dose Vial Activity [mCi]} \times \text{Activity Delivered [\%]} / 100$$

Radiation Safety

- Transport
  - Acrylic shield will stop all beta emission and keep exposure rate low
  - <2 mR/hr at 1 m for up to 300 mCi of activity in acrylic shield
- During administration
  - Highest potential for exposure is to administering staff in IR suite when spheres are located in catheter between v-vial and the patient
  - Stand behind shield and maintain distance
- Survey personnel leaving the room with GM survey meter
- Store radioactive material until the container surface radioactivity cannot be distinguished from background
- Long-lived contaminants ^{91}Yand ^{88}Y may be present with reactor production of ^{90}Y
  - Long-lived radioactive by-products may not be a problem using carrier free ^{90}Y from a ^{90}Sr generator

Some Challenges for ^{90}Y-Therapy

- ROIs on 2D Planar images introduce uncertainties
  - Estimate lung shunt fraction and lung dose
  - Split dose calculation – lobar separation of liver not visualized
- MAA is a sub-optimal surrogate for microspheres
  - Biologic degradation time 1–3 hours → free 99mTc-pertechnatate
  - Free 99mTc biodistribution differs from MAA; thyroid & stomach uptakes free 99mTc ← introduce error in LSF
  - Non-spherical shape; Size range 10-to-100 µm
- Additional objective measures of response
  - Tumor volume reduction is the mainstay (Gray et al, Aus & NZ J Surgery 62, 1992; Van Hazel et al, J Sur Onc 88, 2004; Lau et al, IJROBP 40, 1998; Sangro et al, IJROBP 66, 2006)
  - Metabolic response: observed in higher proportion than an CT-based anatomical response for mCRC ($p<0.0002$) (Wong et al, EJNMMI 29, 2002)
  - Functional response: >50% change in TLG at 6 weeks for mCRC lesions with tumor doses >46 Gy (Flamen et al, PMB 53, 2008)

Summary

- ^{90}Y-microsphere therapy is a promising and an increasingly popular treatment option for palliative care of patients with metastatic liver disease and unresectable HCC
- Decreased tumor volumes and increased time to tumor progression have been reported
- New objective measures of response are under investigation
- Improved imaging and dosimetry are beginning to yield more accurate dose estimates