Y90 Personalized Dosimetry

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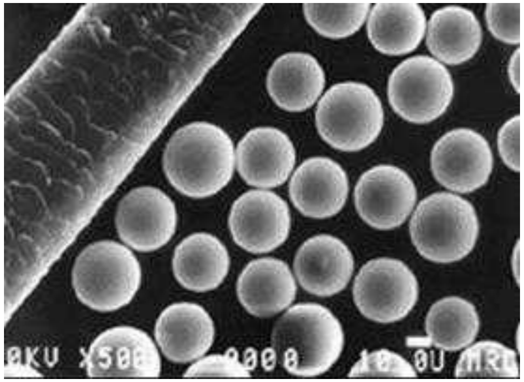
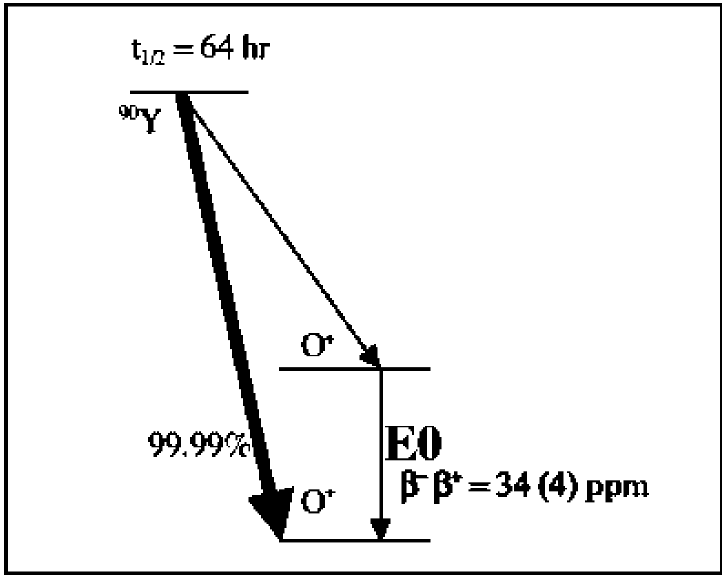
Yttrium Y-90

- Pure β emitter
  - Production: Y-89 (n,γ)Y-90
  - T1/2: 62 hrs (2.7 days)
  - Maximum energy: 2.28 MeV
  - Mean energy: 0.93 MeV
  - Travelling range
    - Max: 11 mm, Mean: 2.5 mm in water/tissue

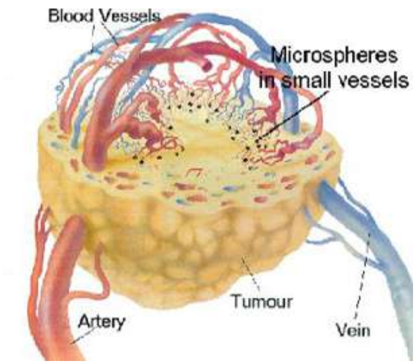


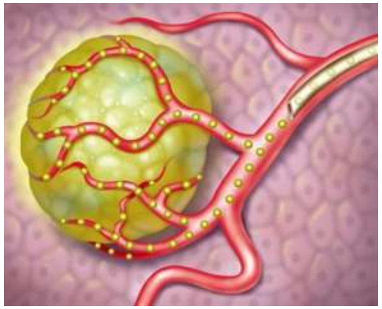
- Decay: Y-90 → Zr90 (Ziconium)(99.98%)
- 0.01% photon emission, internal pair production



Y-90 Microspheres Therapy

- 35 microns resin microspheres
- Microspheres lodge in the micro-vascular network of the tumor
- The radiation from Y-90 is largely confined to a tissue depth of 5mm
- Liver directed EB-RT, max tolerated dose 30-40 Gy to normal hepatocytes (Emami et al, IJROBP 21, 1991; McGinn et al, J Clin Onc 16, 1998)
- With Y90 microspheres, total liver radiation dose up to 80Gy (Gray et al, Annals Oncology 12, 2001; Burton et al, Radiology 175, 1990)





Prior to SIR-Spheres Implant

- Perform a preliminary radiological work-up including:
  - hepatic angiogram
  - PET/CT
  - Embolization of the gastro-duodenal or other artery that might result in inadvertent delivery of SIR-Spheres microspheres, and
  - Triple-phase Computed tomography
  - MAA nuclear medicine SPECT scan.

Triple-phase Computed Tomography

FIG. 1. Representative three phase image set. (A) Noncontrast initial image, (B) arterial phase, and (C) venous phase. Window=level is 380=10 for the three images.
Dezarn et al Medical Physics, Vol. 38, No. 8, August 2011

PET/ CT

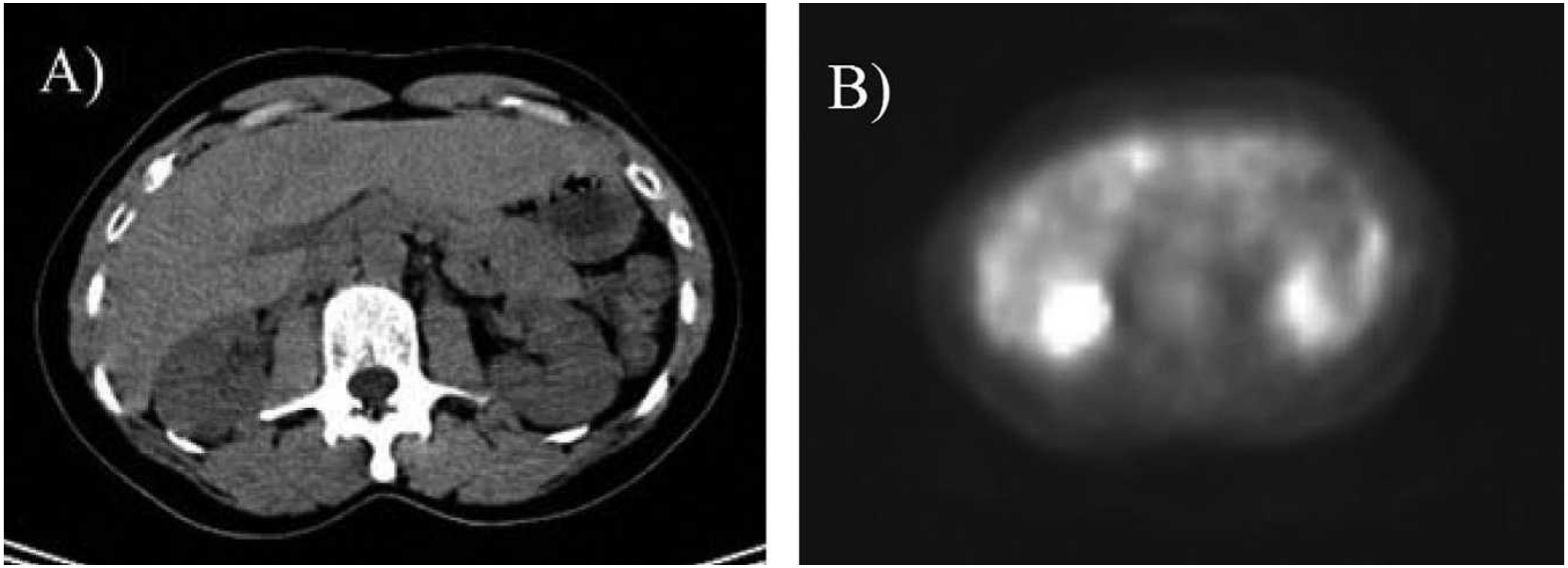


FIG. 2. Representative PET=CT image. (A) CT and (B) 18F-FDG PET image sets.

NM Planar and SPECT liver

- MAA injected via the catheter
- Low Energy High Resolution collimator
- Tc-99m 140keV window,
- Planar views: (1) anterior and posterior lungs, (2) anterior and posterior liver.
  - 300 sec per frame, 256 matrix, zoom 1, Word mode
- SPECT liver:
  - 25 sec per frame, 6 degrees per step, 360 degrees arc, 128 matrix, zoom 1

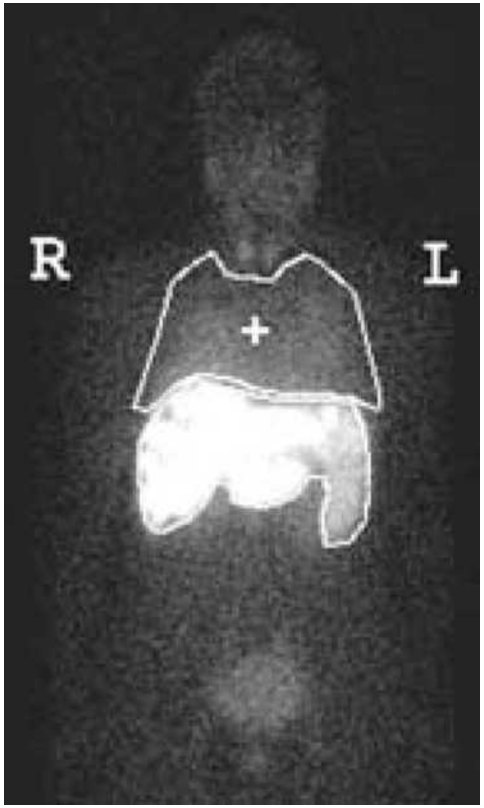


FIG. 4. Planar gamma camera image with ROI drawn.

Role of Tc-99m MAA

- Estimate the lung shunting in planar image
- Simulate the Y90 particles distribution in tumor, normal liver parenchyma, bowel and gall bladder

Limitation of MAA

- (in both partition model and BSA model)
  - Suboptimal surrogate for microsphere
  - Inject a small numbers of particles (~500K) when compared with number of Y90 particles (40-80 millions)
  - Non-spherical shape; size range 10-100 μm
  - Clumping of MAA
  - Homogeneity of MAA during injection (suspended in 1 ml solution)

Lung shunting

$$\text{Lung shunting \%} = \frac{\text{Lung Count}}{\text{Lung Counts + Liver Counts}} \times 100\%$$

For Empirical and BSA model,

Percent Lung Shunting	***Activity of SIR-Spheres microspheres***
<10%	Deliver full amount of SIR-Spheres
10% to 15%	Reduce amount of SIR-Spheres by 20%
15% to 20%	Reduce amount of SIR-Spheres by 40%
>20%	Do not give SIR-Spheres microspheres

Radiation dosimetry

- 90% of the emitted energy is absorbed within a sphere of 5mm

- Total dose is found by summing together the contribution of all the individual point source in the vicinity

- MIRD theory is used to estimate the dose

MIRD – Medical internal radiation

- Dose rate in a generic tissue mass

$$\dot{D} = k \frac{A}{m} \langle E \rangle ,$$

- Assumption
  - No bremsstrahlung
  - All decay energy absorbed within the mass
  - Effective half-life is radioactive half-life
  - Cumulated activity = A_ox T1/2

- Dose rate over the time

$$D = \frac{k \langle E \rangle A_0}{m} \int_0^{\infty} e^{-\ln(2)t/T_{1/2}} dt = k \frac{A_0}{m} \langle E \rangle \frac{T_{1/2}}{\ln(2)} .$$

$$k\langle E\rangle \frac{T_{1/2}}{\ln(2)} = \left(\frac{0.9267\ \text{MeV}}{\text{dis}}\right)\left(\frac{1.6022\text{x}10^{-13}\text{J}}{\text{MeV}}\right) \times \left(\frac{\text{Gykg}}{\text{J}}\right)\left(\frac{10^{9}\ \text{dis}}{\text{sGBq}}\right)\left(\frac{86400\ \text{s}}{\text{day}}\right) \times \left(\frac{2.6684\ \text{day}}{\ln(2)}\right) = 49.38 \pm 0.05\frac{\text{Gykg}}{\text{GBq}}$$

- Absorb dose to the tissue

$$D[\text{Gy}] = 49.38\frac{A_0[\text{GBq}]}{m[\text{kg}]}.$$

1 GBq of ^{90}Y per kilogram of tissue results in a delivered dose of 49.67 Gy to that tissue.

Y90 prescription models

- Empirical model
- BSA (Body Surface Area) model
- Partition model

Empirical

- Based on clinical experience
- Amount of Y-90 should be reduced if lung shunting is greater than 10%

Activity Recommendations

Estimated Degree of Tumour Involvement of the Liver	Recommended Yttrium-90 Amount for Treatment
>50%	3GBq
25-50%	2.5GBq
<25%	2GBq

BSA

- This model
  - Variant of empiric method
  - Is suitable for diffuse tumor
- Depends on
  - the size of tumor within the liver and the size of the patient
- Adjusted by
  - Lung shunting
  - Previous chemotherapy, systemic or loco-regional treatment
- A range of 1.3-2.5 GBq Y-90 is injected to the patient

SIR-Spheres Microspheres – Dose Calculation using SMAC (Sirtex Medical Activity Calculator)

The BSA Method – The Formula

$$A_{Yttrium\text{-}90}\ [GBq] = (BSA-0.2) + \frac{V_{Tumour}}{V_{Total\ Liver}}$$

With:

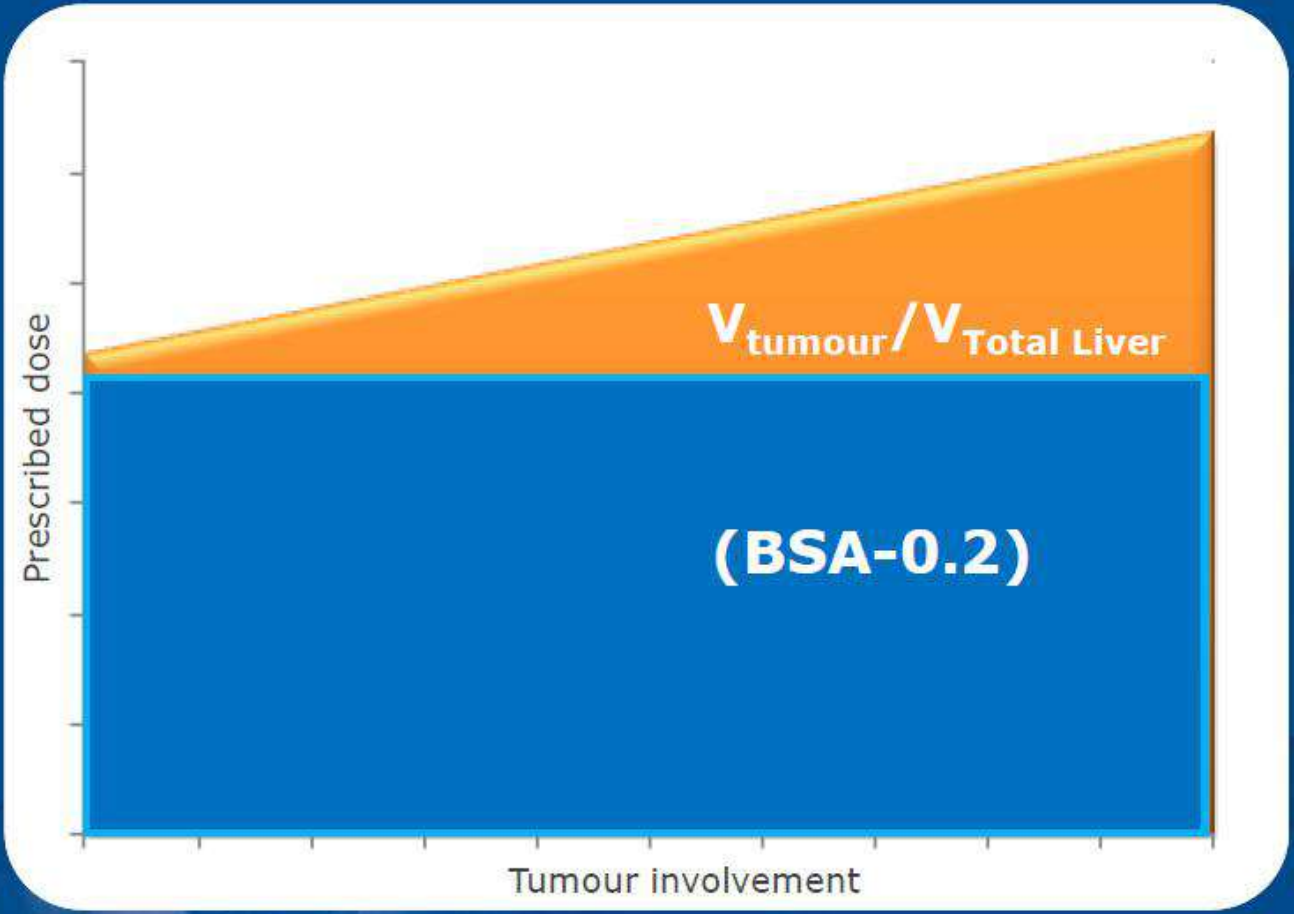
V_{Tumour} = Volume of the total tumour mass in the liver

$V_{Total\ Liver}$ = Volume of the total liver (inclusive tumour).

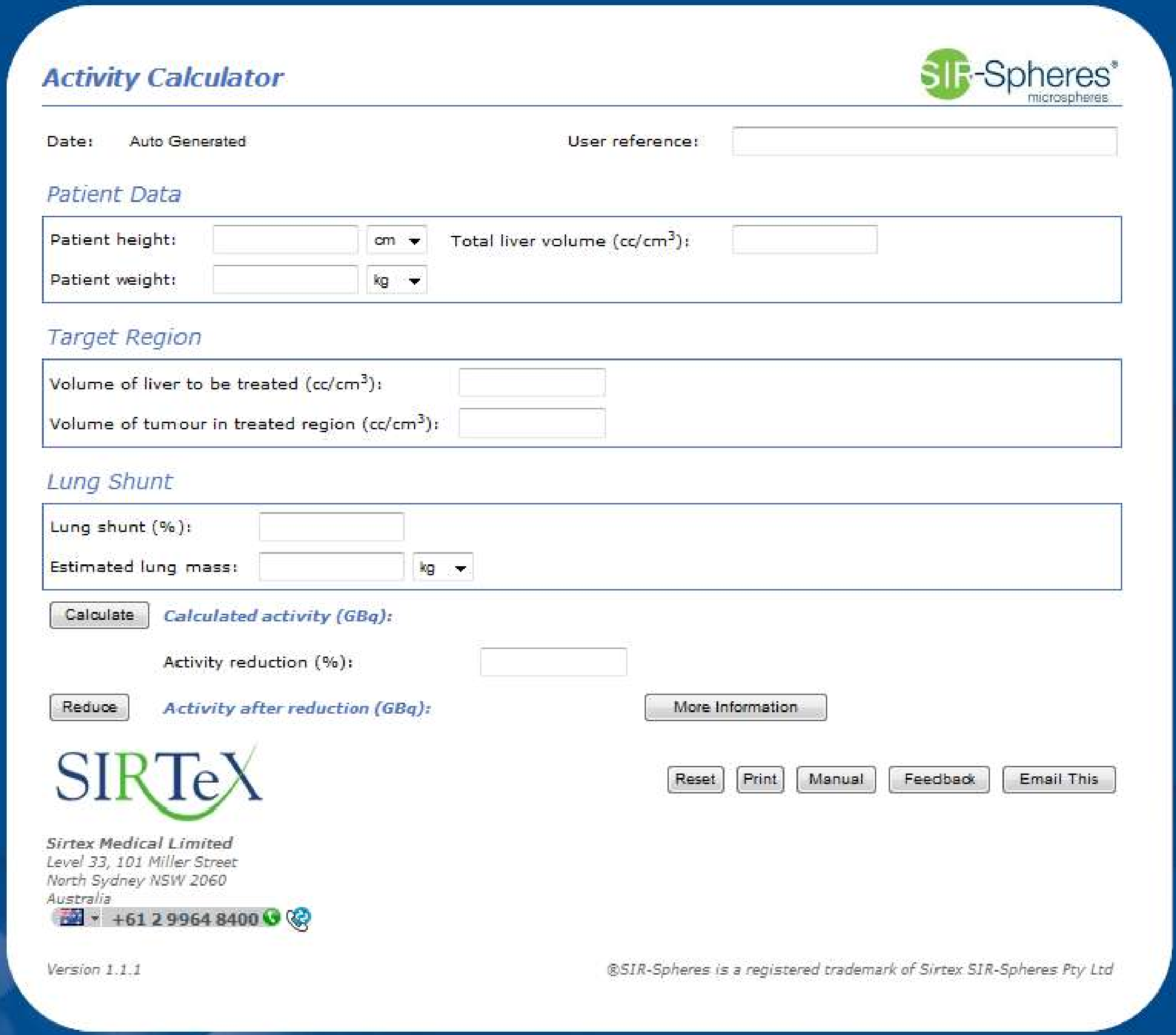
BSA [m^2] = 0.20247 x height[m]$^{0.725}$ x weight [kg]$^{0.425}$

* If the height is measured in centimetres use 0.007184 instead of 0.20247

The BSA Method - Components



SIR-Spheres Microspheres – Dose Calculation using SMAC (Sirtex Medical Activity Calculator)



SIRTeX

SIR-Spheres Microspheres – Dose Calculation using SMAC (Sirtex Medical Activity Calculator)

The BSA Method – Whole Liver Treatment

$$A_{Yttrium\text{-}90}\ [GBq] = (BSA - 0.2) + \frac{V_{Tumour}}{V_{Total\ Liver}}$$

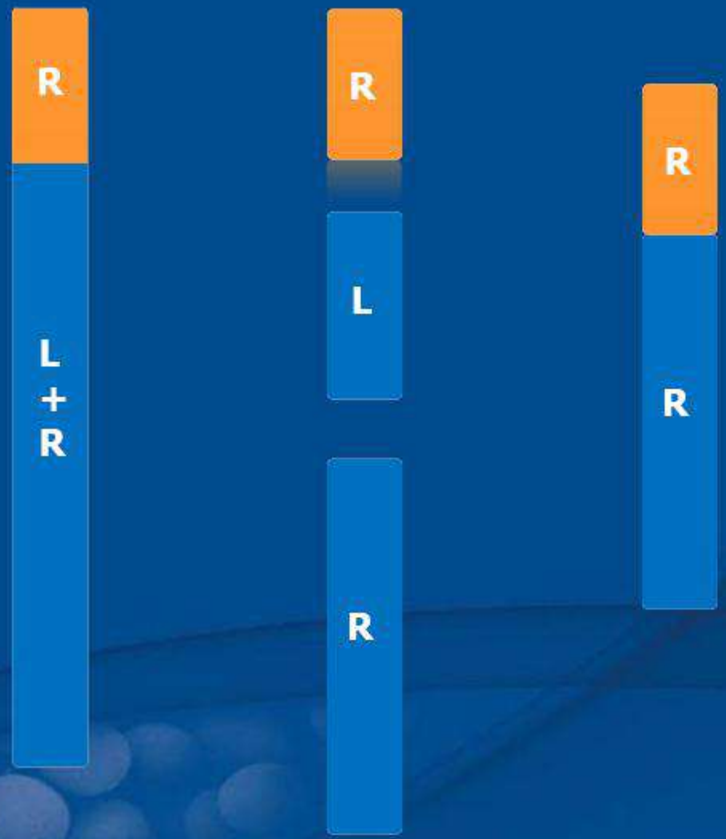
SIRTeX

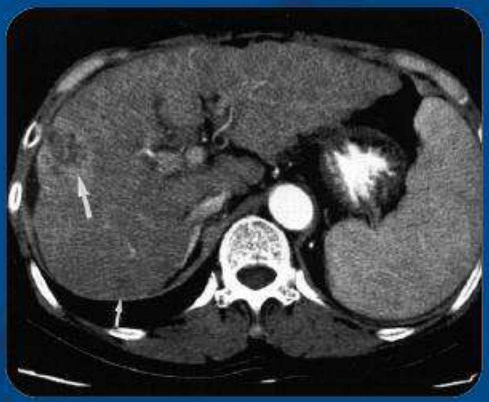
SIR-Spheres Microspheres – Dose Calculation using SMAC (Sirtex Medical Activity Calculator)

The BSA Method – Lobar/Segmental Treatment

$$\frac{V_{tumour}}{V_{Total\ Liver}}$$

(BSA-0.2)





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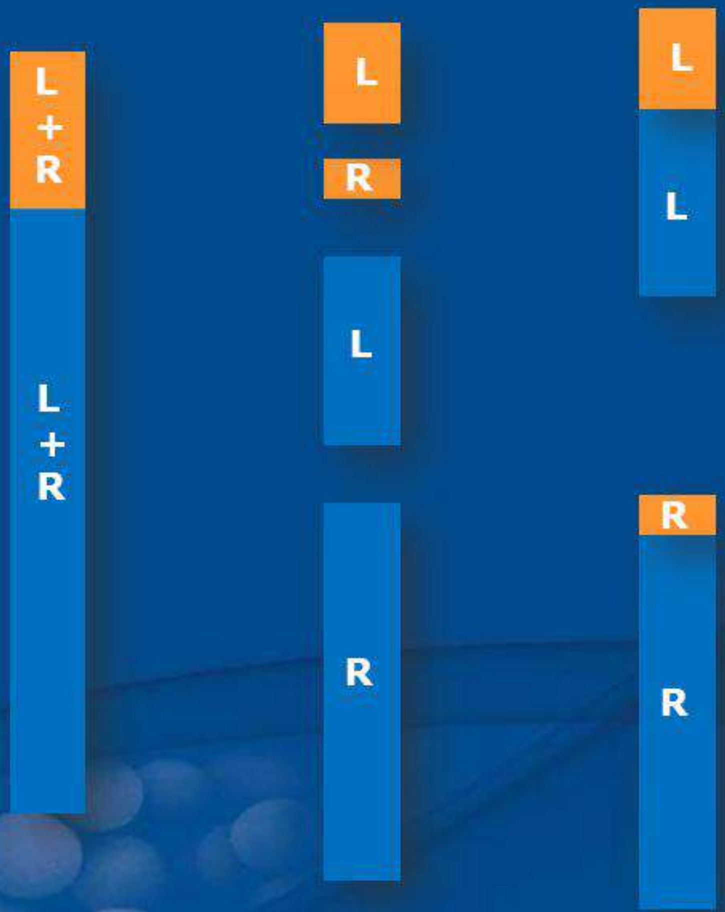
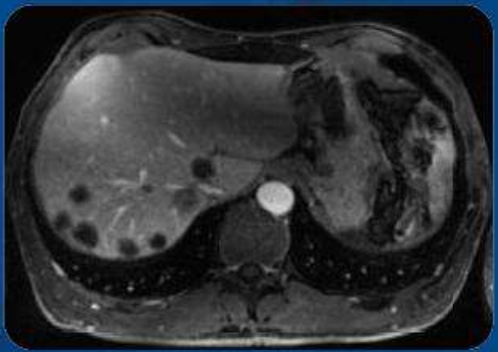
SIR-Spheres Microspheres – Dose Calculation using SMAC (Sirtex Medical Activity Calculator)

The BSA Method – Bi-lobar lobar

$$\frac{V_{tumour}}{V_{Total\ Liver}}$$

(BSA-0.2)

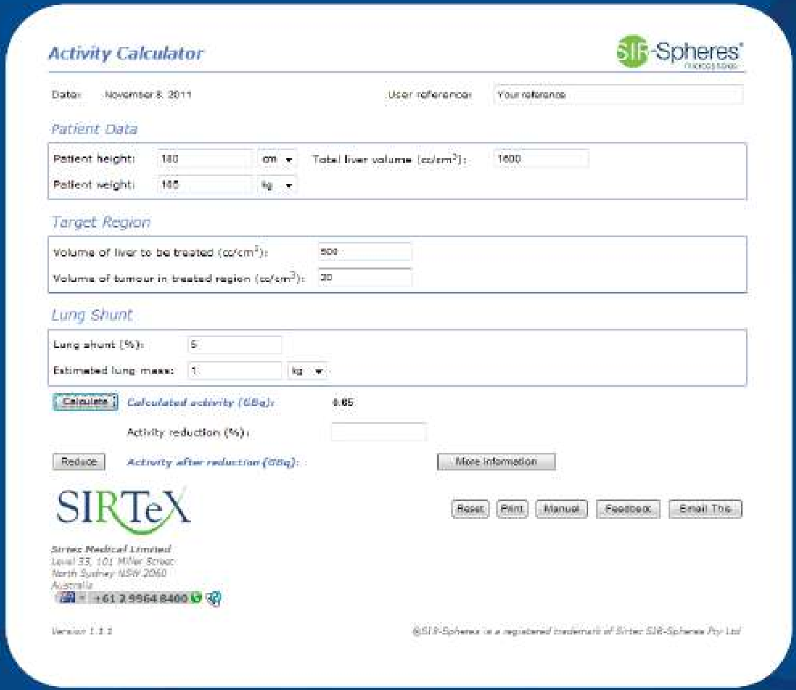




SIRTeX

SIR-Spheres Microspheres – Dose Calculation using SMAC (Sirtex Medical Activity Calculator)

Lung- Shunting – Bi-lobar lobar treatment



$$(Dose_{left} + Dose_{right}) * \frac{\text{lung-shunting}}{100} \leq 0.5 \text{ GBq}$$

SIRTeX

Table 1 Advantages and disadvantages of the BSA method

Advantages	Disadvantages
Simple and user friendly	Less personalized than partition modeling
Strong historical data of clinical use	Low scientific basis. Not a true 'dosimetric' method
Recommended for use in subcentimeter tumors or tumors with ill-defined margins, by *visual estimation* of the overall tumor burden	The desired Y-90 activity in cases of high liver-to-lung shunting is adjusted empirically using standard reference tables provided by the manufacturer
	Artificially limits the injected Y-90 activity between 1.0 and 3.0 GBq
	Tumor radiation dose (Gy) is unknown unless the estimated T/N ratio is also calculated

GBq Gigabecquerel, *Gy* gray, *T/N ratio* tumor-to-normal liver ratio

Kao Y.H., et al. Ann Nucl Med (2011) 25:455–461

Partition Model

- Basic assumption:
  - Uniform distribution of MAA and Y90 particles to the tumor and normal liver
- HCC with one predominant nodule +/- a few nodules
- Involves implantation the highest possible activity to the tumour without exceed the tolerance of lung and normal liver

Partition Model

- MIRD principle

1 GBq of ^{90}Y per kilogram of tissue results in a delivered dose of 49.67 Gy to that tissue.

- Tumorcidal dose: 120Gy
- Normal liver dose tolerance: 70Gy
- Liver with previous chemotherapy: 50Gy
- Lung : 25Gy

Lau WY, Kennedy AS, Kim YH, et al. Patient selection and activity planning guide for selective internal radiotherapy with yttrium-90 resin microspheres. Int J Radiat Oncol Biol Phys 2012;82:401-7.

- In Partition model, T/N ratio:
- *Tumor to liver ratio:*

$$T/N = (A_{\text{Tumor}}/m_{\text{Tumor}})/(A_{\text{NormalLiver}}/m_{\text{NormalLiver}}).$$

- Dose to the lung, normal liver and tumor

$$D_{\text{Lung}} = 49.38\,\frac{A_{\text{Total}}}{m_{\text{Lung}}}\,L.$$

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

$$D_{\text{NormalLiver}} = \frac{49.38 A_{\text{Total}}(1-L)}{m_{\text{NormalLiver}} + T/N\; m_{\text{Tumor}}}.$$

- Not practical for
  - Diffuse tumours with ill defined border
  - Multicentric HCC
  - Multiple liver metastases

- Difficulty in
  - Tumors with poor CT enhancement in arterial phase and portovenous phases
  - Portal vein invasion with thrombus in the more distal branches
    - Is it tumor thrombus or just blood clot?

Table 2 Advantages and disadvantages of the partition model

Advantages	Disadvantages
Personalized dosimetry	More complex and resource intensive
More scientifically sound than the BSA method	Less historical clinical data as compared to the BSA method
The desired Y-90 activity in cases of high liver-to-lung shunting is adjusted on the basis of predicted lung radiation dose (Gy)	Unsuitable for subcentimeter tumors or tumors with ill-defined margins
No theoretical limit to the Y-90 activity to be injected	
Greater physician control over radiation doses (Gy) to lung, liver and tumor compartments	

Gy gray

Kao Y.H., et al. Ann Nucl Med (2011) 25:455–461

Personalized Dosimetry

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

Yung Hsiang Kao[1], Andrew Eik Hock Tan[1], Mark Christiaan Burgmans[2], Farah Gillian Irani[2], Li Ser Khoo[2], Richard Hoau Gong Lo[2], Kiang Hiong Tay[2], Bien Soo Tan[2], Pierce Kah l
and Anthony Soon Whatt Goh[1]

J Nucl Med 2012; 53:559–566

Conclusion:

Compliance with radiobiologic principles of radionuclide internal dosimetry is fundamental to 90Y radioembolization success. Image-guided personalized predictive dosimetry by artery-specific SPECT/CT partition modeling achieves high clinical success rates for safe and effective 90Y radioembolization.

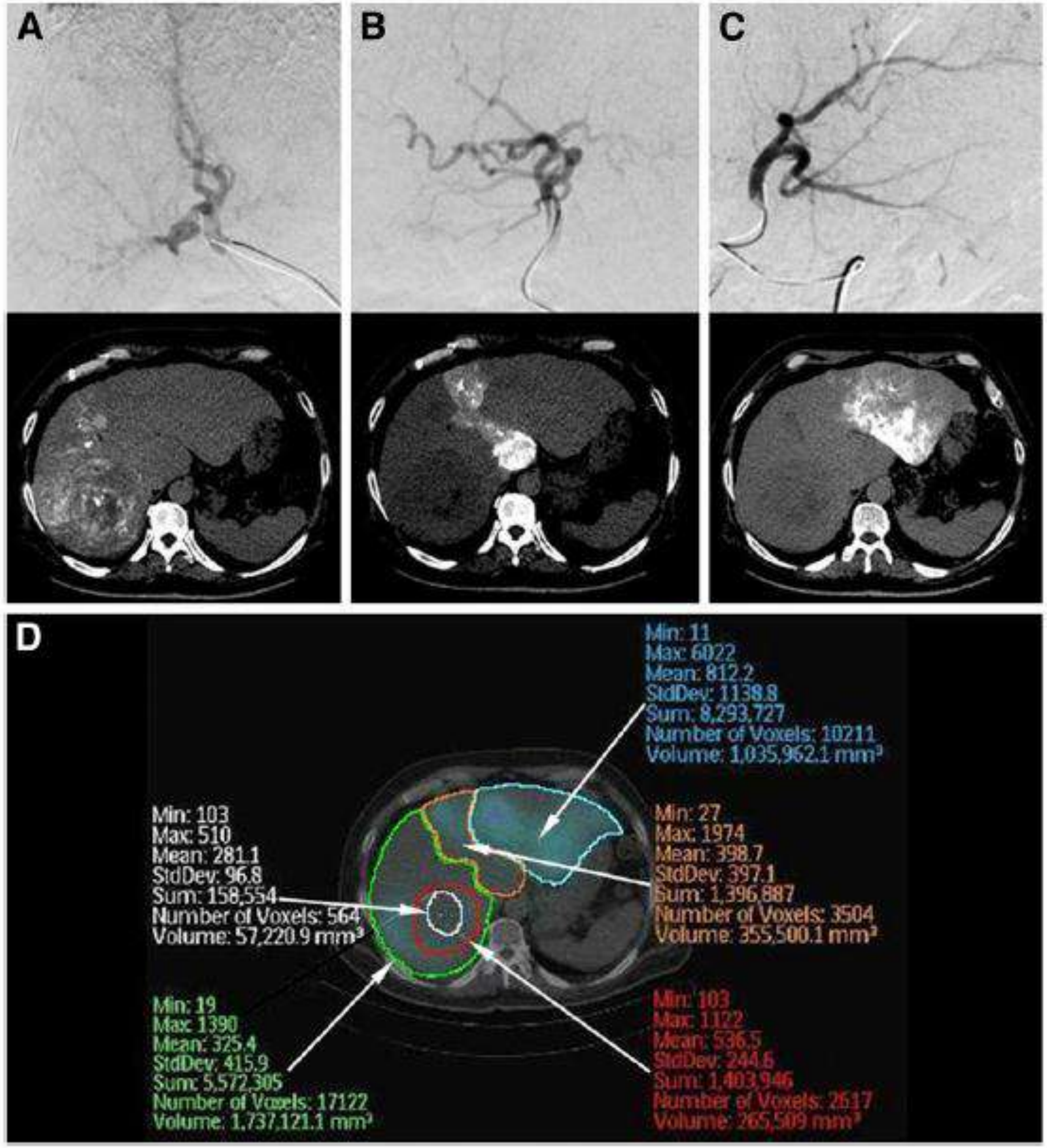


FIGURE 1. Example of artery-specific SPECT/CT partition modeling of 3 arterial territories. (A–C) Liver with multifocal HCC supplied by right (A), middle (B), and left (C) hepatic arteries is depicted in digital subtraction angiography (top) and catheter-directed CTHA (bottom). (D) Regions of interest (ROI) are drawn on ^{99m}Tc-MAA SPECT/CT transaxial slices representing left (blue ROI), middle (orange ROI), and right (green ROI) hepatic artery planning target volumes, implanted tumor (red ROI), and necrotic tumor (white ROI).

Intraprocedural CT-PET

Intraprocedural Yttrium-90 Positron Emission Tomography/CT for Treatment Optimization of Yttrium-90 Radioembolization

Austin C. Bourgeois, MD, Ted T. Chang, MD, Yong C. Bradley, MD, Shelley N. Acuff, CNMT, and Alexander S. Pasciak, PhD

ABSTRACT

Radioembolization with yttrium-90 (^{90}Y) microspheres relies on delivery of appropriate treatment activity to ensure patient safety and optimize treatment efficacy. We report a case in which ^{90}Y positron emission tomography (PET)/computed tomography (CT) was performed to optimize treatment planning during a same-day, three-part treatment session. This treatment consisted of (*i*) an initial ^{90}Y infusion with a dosage determined using an empiric treatment planning model, (*ii*) quantitative ^{90}Y PET/CT imaging, and (*iii*) a secondary infusion with treatment planning based on quantitative imaging data with the goal of delivering a specific total tumor absorbed dose.

J Vasc Interv Radiol 2014; 25:271–275

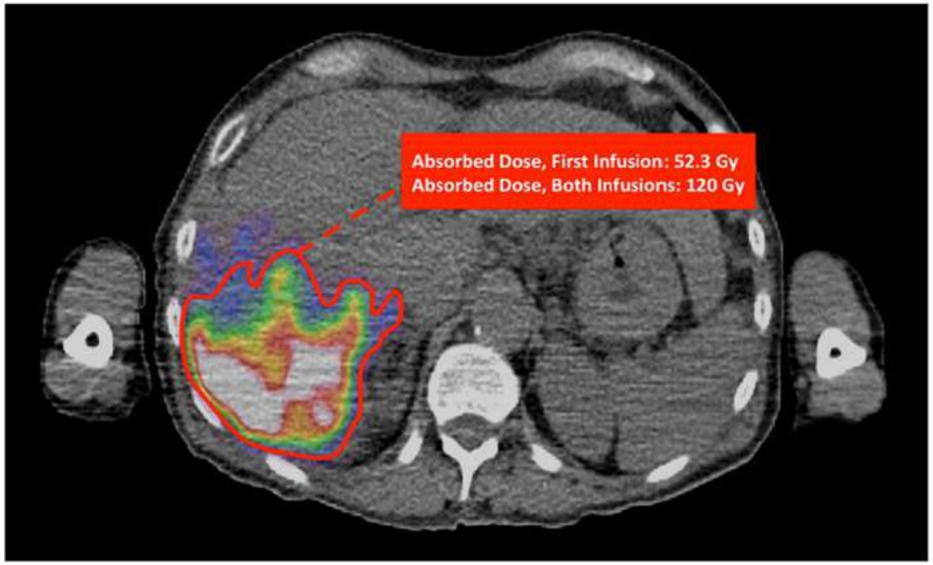


Figure 3. Absorbed dose map generated from quantitative ^{90}Y PET/CT after initial infusion of ^{90}Y microspheres. Total absorbed doses for the region of interest are shown after the initial infusion and after both infusions.

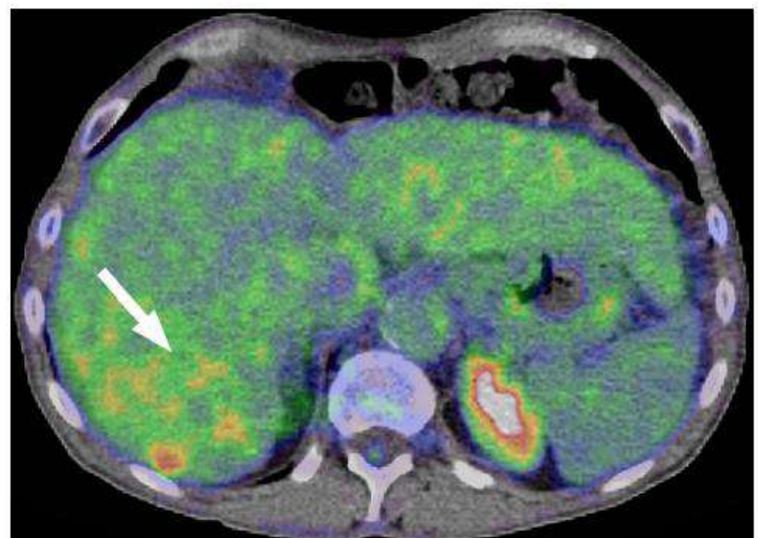
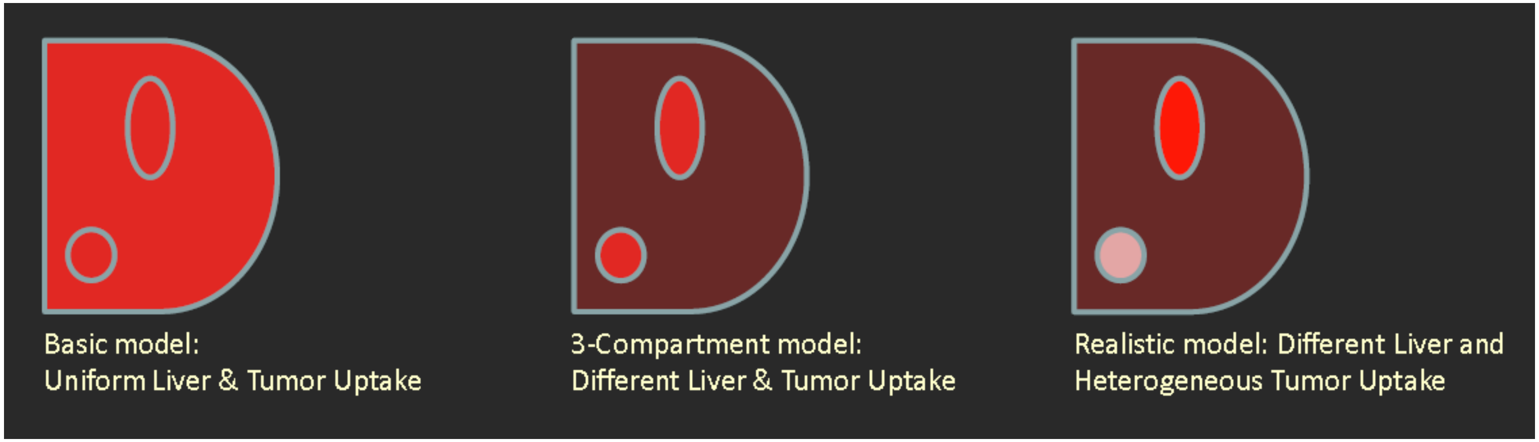


Figure 4. Axial ^{18}FDG-PET/CT performed 12 weeks after ^{90}Y radioembolization showed partial metabolic response to therapy (arrow).

Limitation of Y90 microsphere dosimetry

- Not intended to calculate dose to individual tumors
- Uses conservative assumptions to ensure safety
- It is NOT uniform uptake of microspheres in tumor and normal liver compartments (Fox RA et al. IJROBP 1991; 21: 463-7)



Future dosimetry

- Computer-assisted radiation dose modeling
- Positron-emitting microparticles for pre-therapy assessment
- Delineation of target atrial territory
- Microsphere trajectory selection
- Post-radioembolization Y-90 PET/CT

Thank you!