

# Y90 Dosimetry Course: Pre-CIO 2025

*Sponsored by an educational grant from Sirtex*

**CIO**

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UC San Diego
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Senior Member, Interventional Radiology  
Moffitt Cancer Center and Research Institute
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Miami Cancer Institute  
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Director of Interventional Oncology
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Associate Professor of Radiology  
Director of Interventional Oncology  
Director of Interventional Research  
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Assistant Professor of Radiology  
University of North Carolina – Chapel Hill

# Faculty Disclosures

- **Osman Ahmed, MD-** Advisory Board: Argon Medical, Boston Scientific, Trisalus; Consultant: Bard/BD, Medtronic, Canon, Okami, Asahi, Philips; Speaker: Penumbra; Chief Medical Officer, Flow Medical
- **Zach Berman, MD-** Consultant: AstraZeneca, Boston Scientific, Sirtex, Trisalus Life Sciences; Speakers Bureau: Trisalus Life Sciences. Guerbet, Varian
- **Ghassan El-Haddad, MD-** Consultant: Bayer HealthCare, BD, ITM Radiopharma, Johnson & Johnson, Curium pharma, Lantheus
- **Ripal T. Gandhi, MD-** Advisory Board- Trisalus Life Sciences; Consultant- ABK Biomedical, Argon, BD Life Sciences, Cook, Medtronic, Quantum surgical, Renovorx, Sirtex, Teilx; Speaker's Bureau- Genentech, Quantum surgical, Sirtex, Trisalus Life Sciences
- **Nima Kokabi, MD-** Consultant: Boston Scientific, Sirtex Medical Ltd, Terumo Medical, Okami Medical, Trisalus Life Sciences
- **Venkatesh Krishnasamy, MD-** Advisory Board: Cook, Boston Scientific, Delcath; Consultant: Varian, Merit, Guerbet; Research funding: Guerbet, Boston Scientific, Siemens, Philips
- **Alex Villalobos, MD-** Consultant: Guerbet, LLD, Sirtex Medical, LTD

# Disclosures

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the U.S. Food and Drug Administration).
  - Applicable CME staff have no relationships to disclose relating to the subject matter of this activity
  - This activity has been independently reviewed for balance
  - This continuing medical education activity may include device or medicine brand names for participant clarity purposes only; no product promotions or recommendations should be inferred

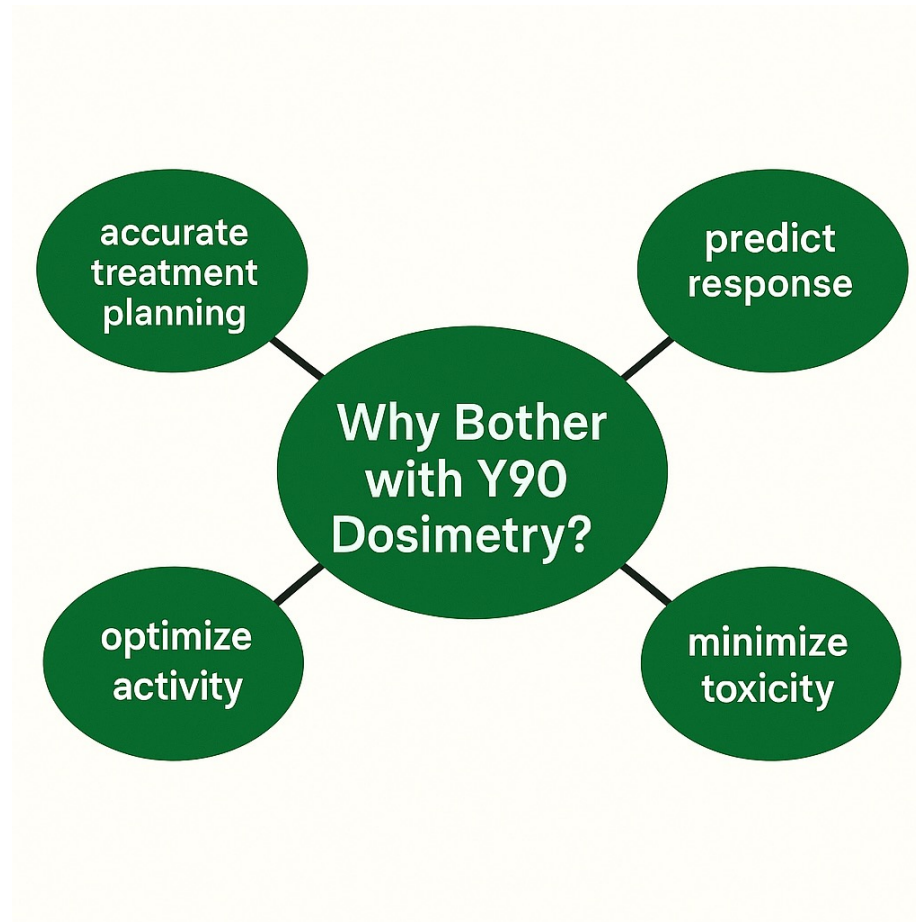
# Learning Objectives

- To become familiar with clinically relevant dosimetry models for treatment planning in patients undergoing Y90 radioembolization.
- To become familiar with most clinically relevant and contemporary clinical data on correlation between dosimetry, oncologic outcomes and treatment related toxicity
- To become familiar with commercially available dosimetry software's used in the United States for Y90 treatment planning with emphasis on MIM Y90 Dosimetry Software and Cancer Y90 App
- To gain hands-on skills of using dosimetry software's and simulate treatment planning for multiple therapeutic intent cases using MIM and Cancer Y90

# Why Bother with Y90 Dosimetry?

Nima Kokabi, MD & Ripal Gandhi, MD

October 16, 2026



# Agenda

- 8 AM-9:45 AM: **Didactics**
  - Deep Dive in Dosimetry and Dose Distribution
  - Y90 Treatment Logistics
- 9:45 AM-10 AM: **Break**
- 10 AM-12 PM: **Parallel Sessions**
  - **Group 1:** Hands-on Dosimetry Planning & Confirmation
  - **Group 2:** Implementing a Y90 Program
- 12 PM-1 PM: **Lunch**
- 1 PM-3 PM: **Parallel Sessions**
  - **Group 2:** Hands-on Dosimetry Planning & Confirmation
  - **Group 1:** Implementing a Y90 Program
- 3 PM-3:15 PM: **Post Fellowship Logistics**
- 3:15 PM-3:30 PM: **Q&A**

# Clinically Relevant Dosimetry Models



**Alex Villalobos, MD**

University of North Carolina – Chapel Hill

Background: Fig 1 and Fig 2 from Villalobos et. Al. "Yttrium-90 Radioembolization Dosimetry: Dose Considerations, Optimization, and Tips"

# Yttrium-90 Dosimetry Can Be A Complex Topic...

Seminars in  
Interventional  
Radiology



[Semin Intervent Radiol.](#) 2020 Dec; 37(5): 543–554.

PMCID: PMC7732571

Published online 2020 Dec 11. doi: [10.1055/s-0040-1720954](https://doi.org/10.1055/s-0040-1720954)

PMID: [33328711](https://pubmed.ncbi.nlm.nih.gov/33328711/)

*Seminars in IR Liver Oncology*

Guest Editor, Siddharth A. Padia, MD

## Yttrium-90 Radioembolization Dosimetry: What Trainees Need to Know

[Alexander Villalobos](#), MD,<sup>1</sup> [Mohamed M. Soliman](#), MD,<sup>2</sup> [Bill S. Majdalany](#), MD,<sup>1</sup> [David M. Schuster](#), MD,<sup>3</sup> [James Galt](#), PhD,<sup>3</sup> [Zachary L. Bercu](#), MD,<sup>1</sup> and [Nima Kokabi](#), MD<sup>1</sup>

# Compartments/Dosimetry Are Estimated...

nm/mird PAMPHLET NO. 5, REVISED

JANUARY 1978

ESTIMATES OF SPECIFIC ABSORBED FRACTIONS FOR PHOTON  
SOURCES UNIFORMLY DISTRIBUTED IN VARIOUS ORGANS  
OF A HETEROGENEOUS PHANTOM

Walter S. Snyder, Mary R. Ford, and Gordon G. Warner

Health Physics Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee 378:

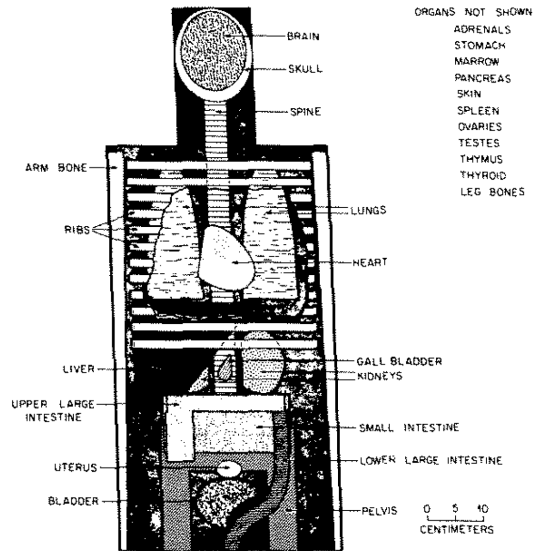


FIG. B-2. Anterior view of the principal organs in the head and trunk of the phantom.

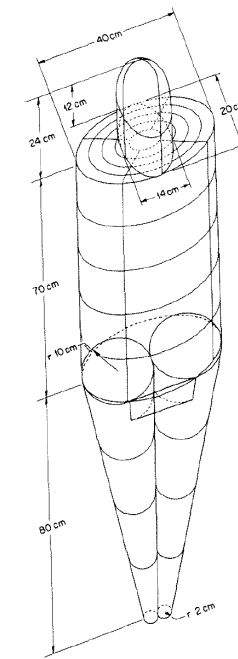
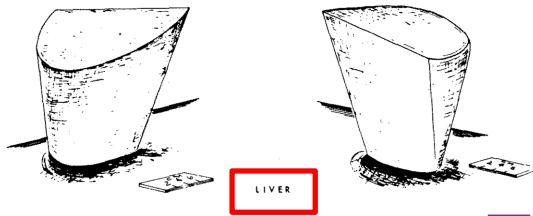


FIG. B-1. Exterior of the adult phantom.



...This is Reflected in the Equations

# Compartments/Dosimetry Assumptions

- Densitovolumetry relationships don't change
  - What about changes in tissue density? (e.g., cirrhosis, emphysema)
- Radioisotope distribution is *perfectly* uniform
  - What about in large heterogenous tumors?
- Radioisotope distribution does not change (i.e. permanent)
  - What about Tc-99m MAA particle fragmentation?
- 100% of the isotope decay occurs within the tissues
  - What about Y90 excretion in urine?

# Important Dosimetry Definitions

- **Activity** = Decays per second = Becquerel (Bq)
  - USA uses Curie (Ci) which equals 37 GBq
- **Volume** = Tissue mass (kg) where activity will be deposited
  - Mass can be estimated from volume by densitovolumetry techniques
- **Absorbed Dose** = Amount of energy (J) deposited within the volume (kg) = Gray (Gy)
- **Compartment** = Number of areas radioisotope deposition



# Manufacturer Recommendations for Dosimetry Model Utilization

- **Resin** Y90-RE
  - Body Surface Area (BSA)
    - Not really a dosimetry model
  - Partition Dosimetry
- **Glass** Y90-RE
  - MIRD Dosimetry
  - Partition Dosimetry

In Reality:

You can use **MIRD** or **Partition Model** Dosimetry for either particle!

# Clinically Relevant Dosimetry Models

## ~~Body Surface Area (BSA)~~

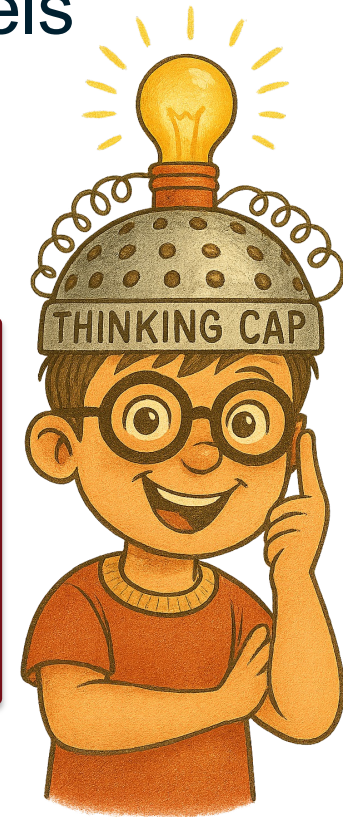
- Not really a dosimetry model

– MIRD Dosimetry

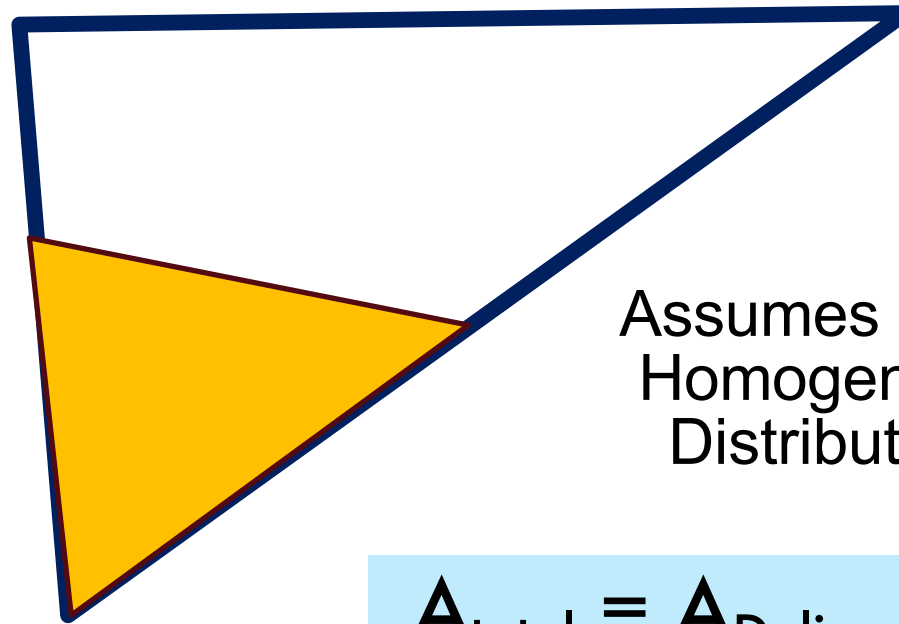
– Partition Dosimetry

Personalized  
Dosimetry

Let's Explore What These Are  
(Conceptually and Mathematically)



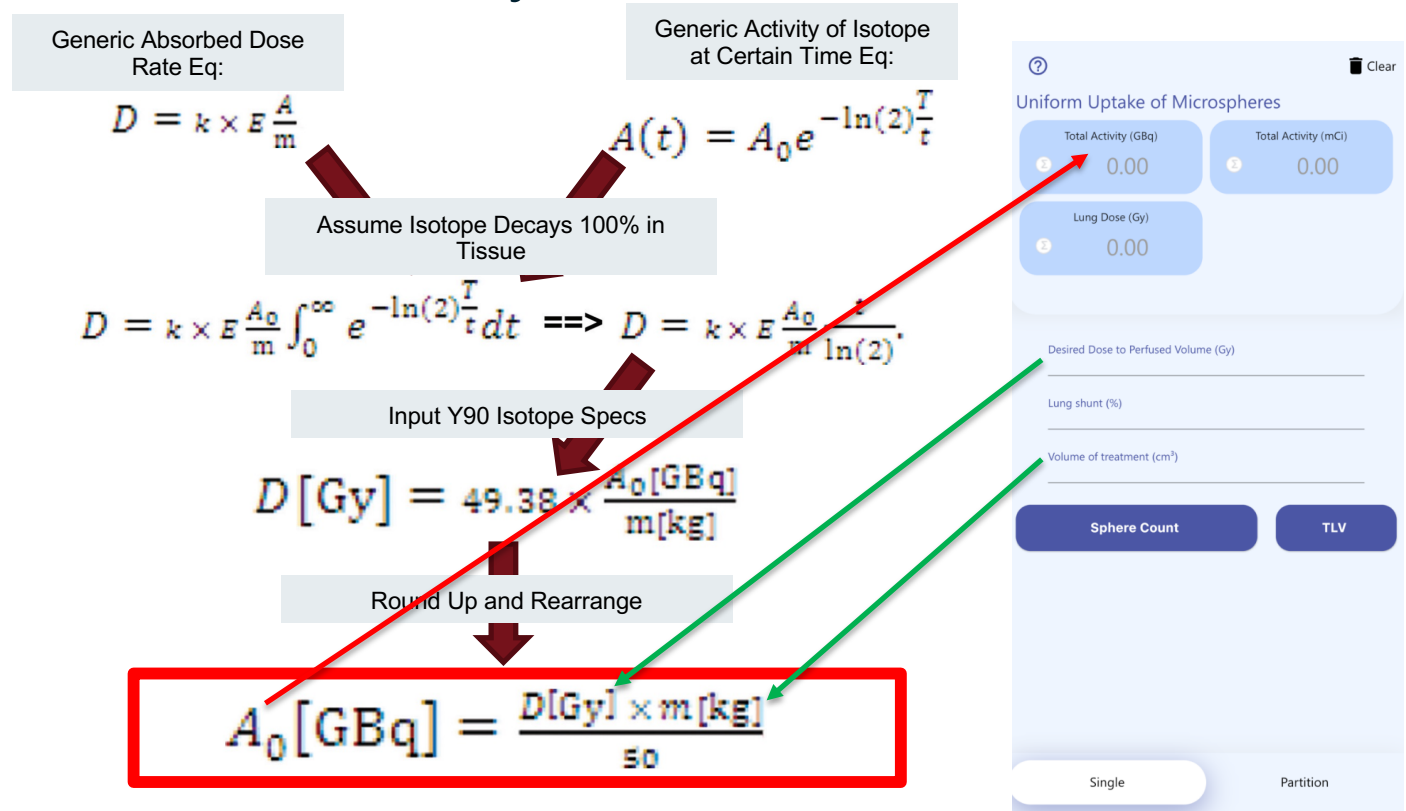
# MIRD Model Conceptually



Assumes **ONE**  
Homogenous  
Distribution

$$A_{\text{total}} = A_{\text{Delivered}}$$

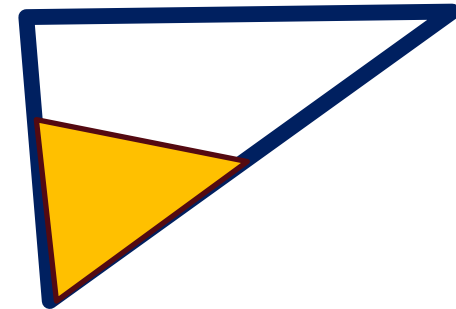
# Medical Internal Radiation Dose (MIRD) Dosimetry Model



# MIRD Model Summary

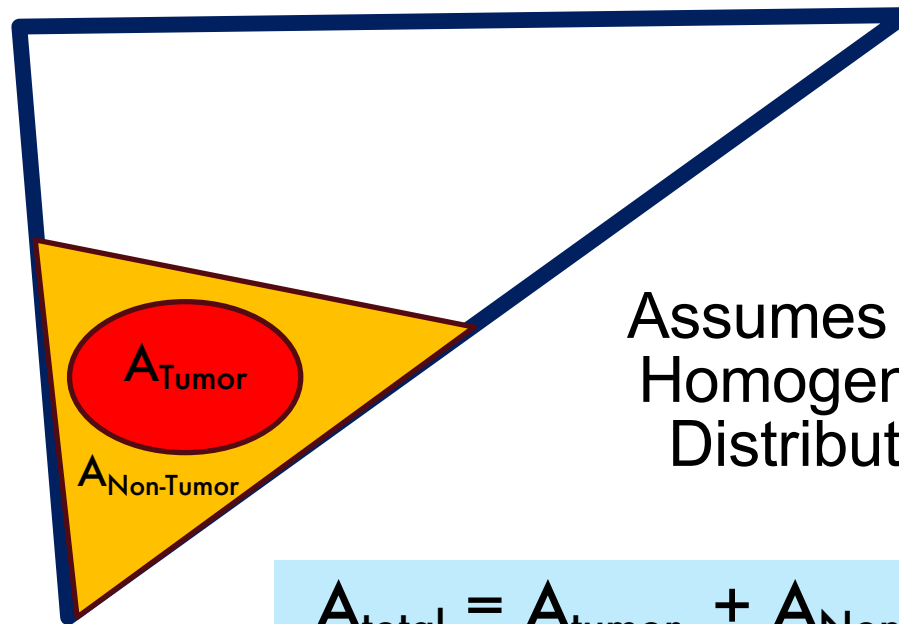
$$A_0[\text{GBq}] = \frac{D[\text{Gy}] \times m[\text{kg}]}{S_0}$$

- Single-Compartment Model (Simplest Form)
  - Assumes *uniform* activity distribution within the targeted tissue
- Input:
  - Desired dose for angiosome
  - Mass/volume of angiosome
- Output:
  - Activity to give



Not So Bad... Right?

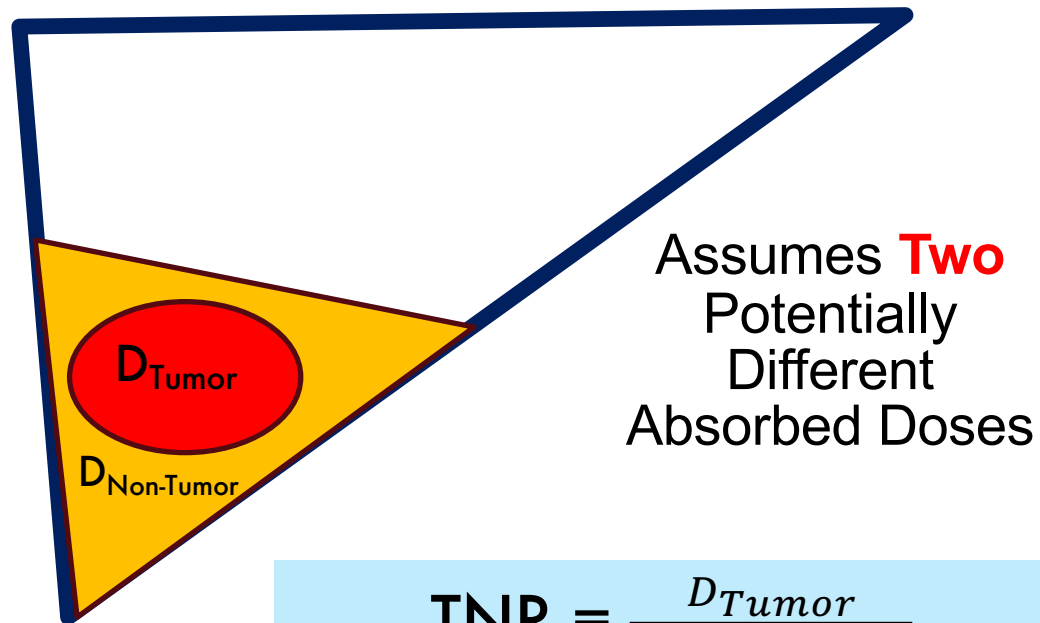
# Partition Model Conceptually - Pt.1



Assumes **Two**  
Homogenous  
Distribution

$$A_{total} = A_{tumor} + A_{Non-Tumor}$$

## Partition Model Conceptually - Pt.2



$$TNR = \frac{D_{Tumor}}{D_{Non-Tumor}}$$

# Partition Dosimetry Model

$$\frac{R_T}{N} = \frac{D_T[\text{Gy}]}{D_N[\text{Gy}]} = \frac{49.38 \times \frac{A_T[\text{GBq}]}{m_T[\text{kg}]}}{49.38 \times \frac{A_N[\text{GBq}]}{m_N[\text{kg}]}} \implies R_T = \frac{A_T/m_T}{A_N/m_N} \implies R_T = \frac{A_T \times m_N}{A_N \times m_T} \implies A_T = \frac{R_T \times A_N \times m_T}{m_N}$$

Activity within Non-Tumor Tissue

$$A_0[\text{GBq}] = \frac{D[\text{Gy}] \times m[\text{kg}]}{50}$$

$$A_T = \frac{R_T \times D_N \times m_T}{50}$$

Line it up

$$A_{\text{total}} = A_{\text{tumor}} + A_{\text{Non-Tumor}}$$

$$A_{\text{Total}} = \frac{R_T \times D_N \times m_T}{50} + \frac{D_N \times m_N}{50}$$

Rearrange

$$A_{\text{Total}} = \frac{D_N \times \left\{ \left( \frac{R_T \times m_T}{N} \right) + m_N \right\}}{50}$$

Partition Dosimetry Clear

Activity for (GBq)	
Tumor Treatment	Normal liver
0.00	0.00
Lung Dose (Gy)	Normal Liver Dose (Gy)
0.00	0.00
Mean Dose for Treated Volume (Gy)	<b>Total Activity</b>
0.00	GBq    mCi
	0.00    0.00

Desired dose to tumor (Gy)   

Volume of normal liver (cm<sup>3</sup>)

Volume of tumor (cm<sup>3</sup>)

T:N ratio    ⊞

Lung shunt (%)

Sphere Count
TLV

Single
Partition

# Partition Dosimetry Model (Adapted for Clinical Practice)

How to adapt the formula for  
Desired Tumor Dose ( $D_T$ )

$$R_T = \frac{A_T}{m_T}$$

$$R_T = \frac{D_T}{D_N}$$

Rearrange

$$D_N = \frac{D_T}{R_T}$$

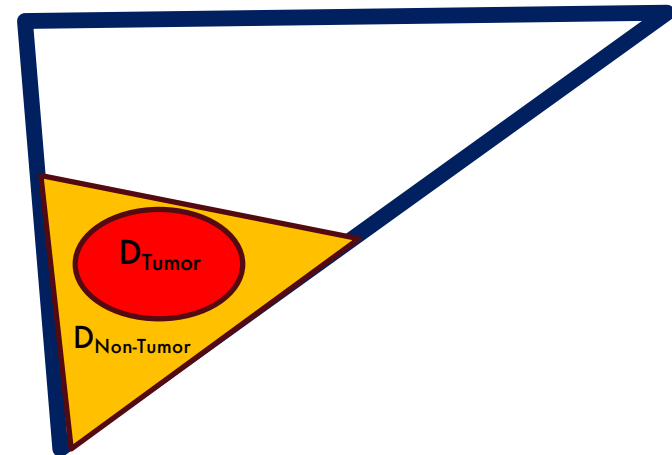
Incorporate to Eq.

$$A_{Total} = \frac{\frac{D_T}{R_T} \times \left( \left( \frac{R_T}{N} \times m_T \right) + m_N \right)}{50}$$

## Partition Dosimetry Model Summary

$$A_{Total} = \frac{\frac{D_T}{R_T} \times \left\{ \left( \frac{R_T}{\bar{N}} \times m_T \right) + m_N \right\}}{50}$$

- Two-Compartment Model (Simplest Form)
  - Assumes uniform activity distribution within the tumor and non-tumor tissue within the targeted angiosome
- Input:
  - Desired Tumor Dose
  - Mass/volume of Tumor
  - Mass/volume of Non-Tumor
  - TNR
- Output:
  - Activity to give



# Ok... Let's Summarize



# Dosimetry: Don't Just Memorize... Understand It!

## Compartments/Dosimetry are Estimated...

nm/mird PAMPHLET NO. 5, REVISED

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ESTIMATES OF SPECIFIC ABSORBED FRACTIONS FOR PHOTON SOURCES UNIFORMLY DISTRIBUTED IN VARIOUS ORGANS OF A HETEROGENEOUS PHANTOM

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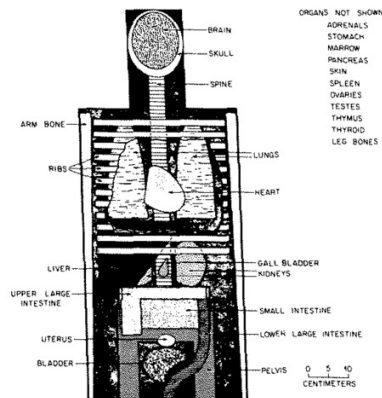
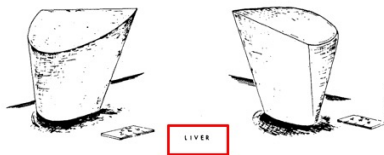


FIG. B-2. Anterior view of the principal organs in the head and trunk of the phantom.

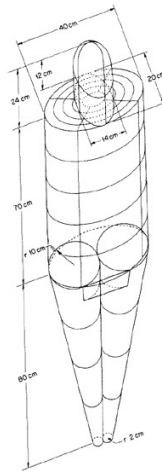


FIG. B-1. Exterior of the adult phantom.

## Understanding the Nuances of Dosimetry Via Deriving the Equations



*Semin Intervent Radiol.* 2020 Dec; 37(5): 543–554.

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*Seminars in IR Liver Oncology*

Guest Editor, Siddharth A. Padia, MD

PMCID: PMC7732571

PMID: [33328711](https://pubmed.ncbi.nlm.nih.gov/33328711/)

### Yttrium-90 Radioembolization Dosimetry: What Trainees Need to Know

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Review paper

A guide to <sup>90</sup>Y radioembolization and its dosimetry

S. Peter Kim<sup>a,\*</sup>, Claire Cohalan<sup>b</sup>, Neil Kopek<sup>c</sup>, Shirin A. Enger<sup>a,d,e</sup>

<sup>a</sup> Medical Physics Unit, McGill University, Montreal, Quebec H4A 3J1, Canada

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# Clinically Relevant Dosimetry Models

## ~~Body Surface Area (BSA)~~

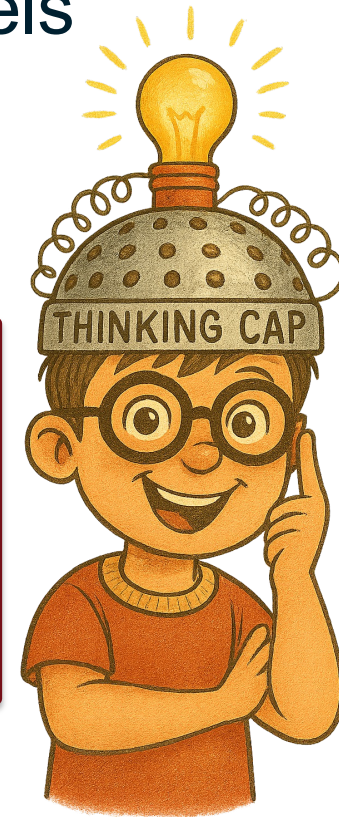
- Not really a dosimetry model

– MIRD Dosimetry

– Partition Dosimetry

Personalized  
Dosimetry

Tip: Always Aim to  
Utilize Personalized Dosimetry!



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THE UNIVERSITY  
*of* NORTH CAROLINA  
*at* CHAPEL HILL

**cio**

SYMPOSIUM  
ON CLINICAL  
INTERVENTIONAL  
ONCOLOGY

# Important Contemporary Glass and Resin Dosimetry Studies

Zach Berman, MD

Associate Professor at Clinical Radiology  
UC San Diego

The goal of this talk is to look at ways we can improve TARE dosimetry to do this we will discuss:

- What dosing “physically means”
- Current dose targets based on treatment intent for HCC
- Future of dosimetry for metastatic disease

# How we think about treatments in 2025



More is  
better

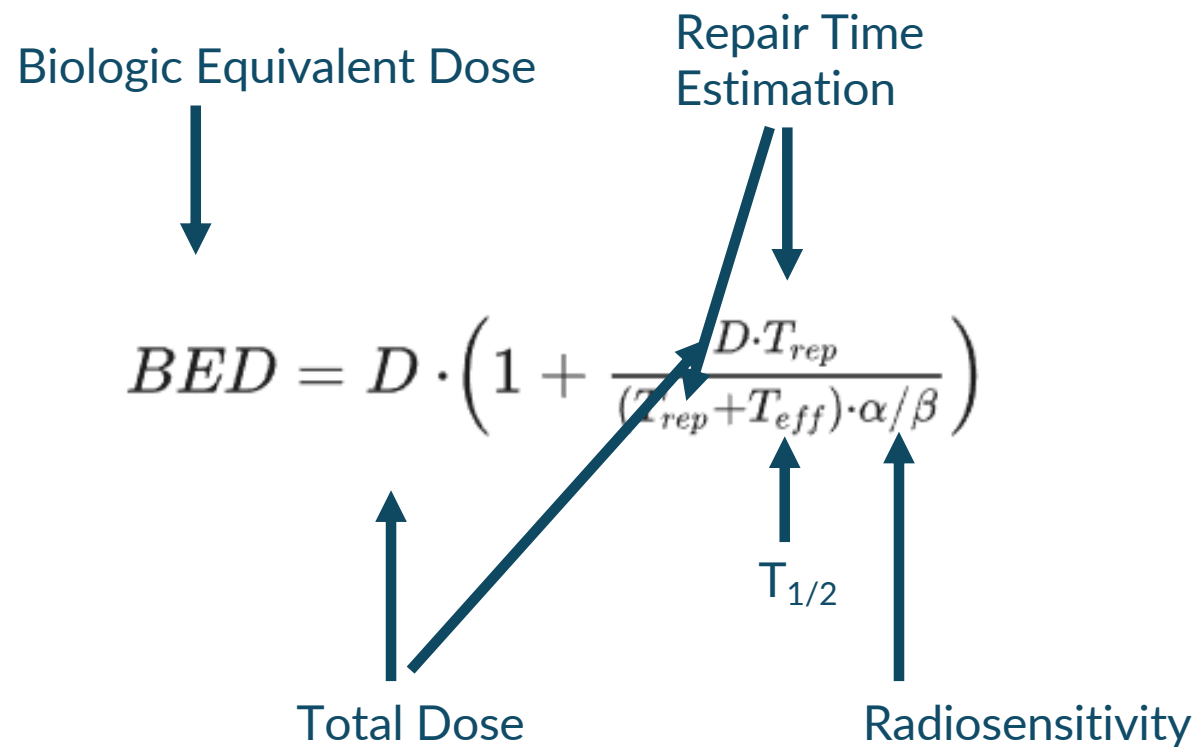
# How we think about treatments in 2025



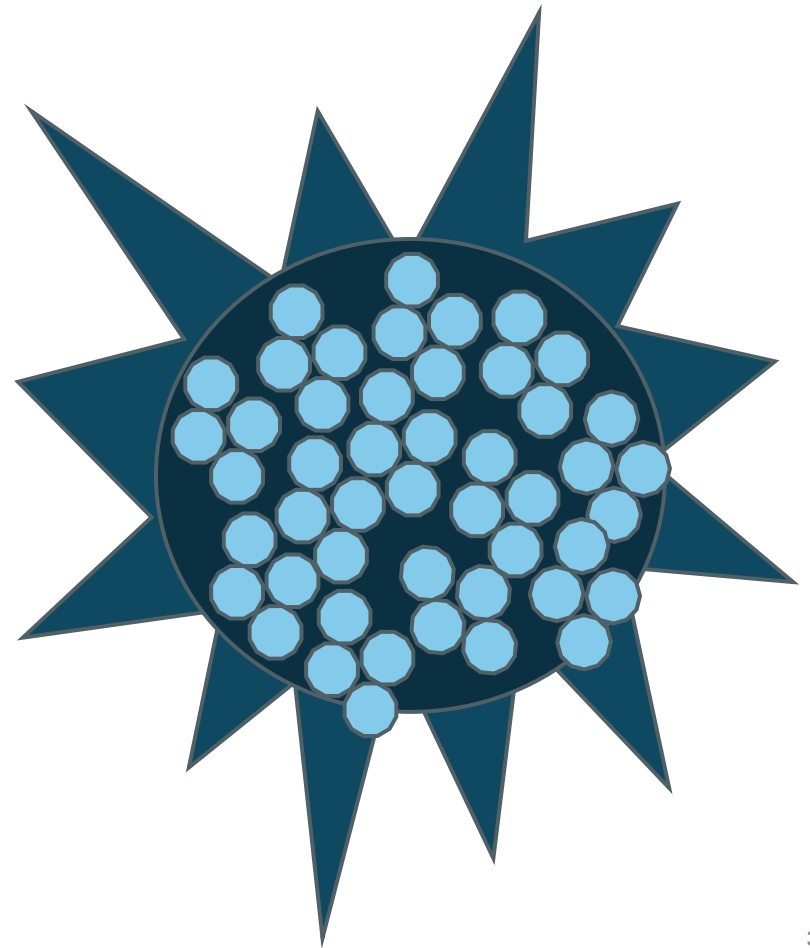
## Dose

- Commonly used in units of Gray (Gy)
    - Energy absorbed by tissue from radiation exposure...
    - 1 joule of energy deposited in 1 kilogram of tissue
- What it isn't: A description of the biological effects of different types of radiation.

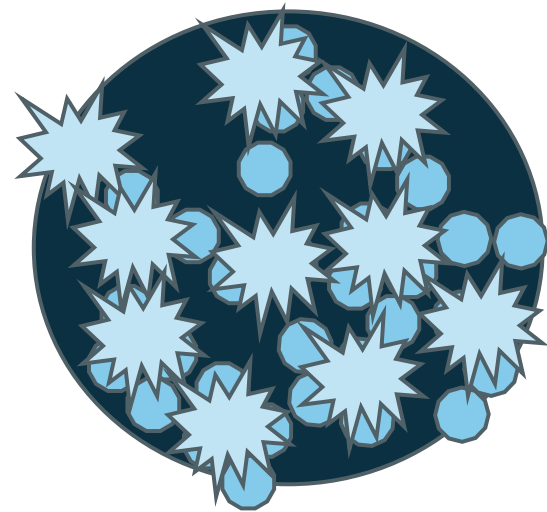
# Biologic Equivalent Dose – The Known Unknowns



With our dosing models we assume symmetry



Reality is that is not always the case



Why our 2025 understanding is suboptimal



## Why our 2025 understanding is suboptimal



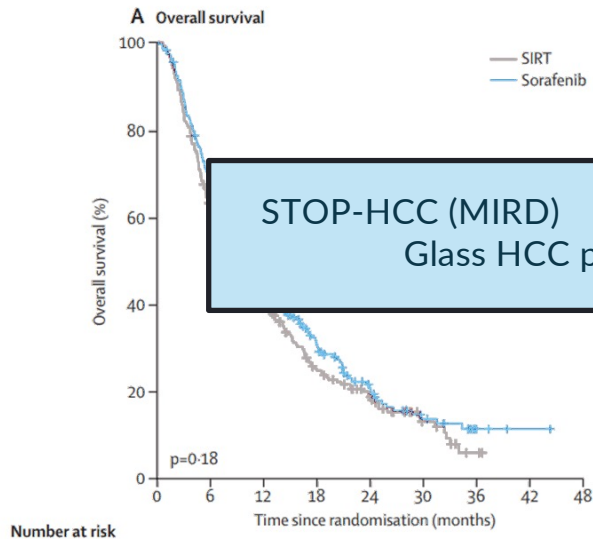


MA is the reason why doses are different between products  
as MA converges between both – so will dose

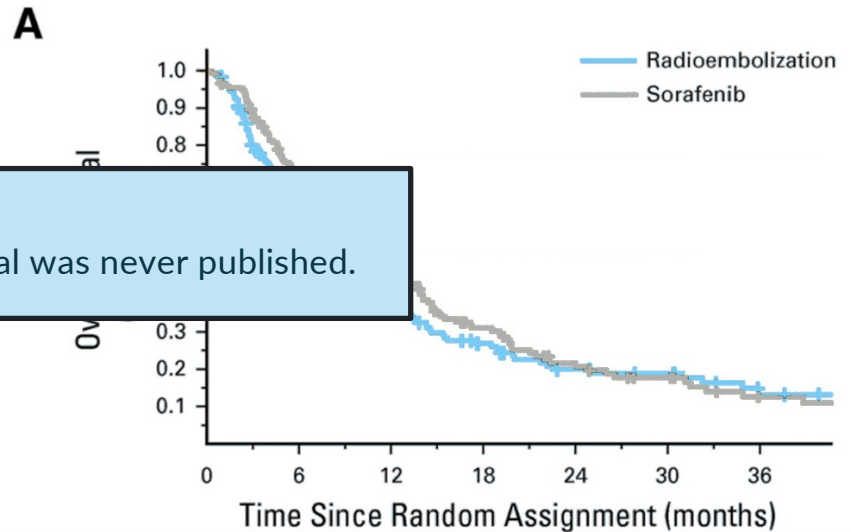


At least three phase 3 trials with empiric dosing have been negative in HCC

SARAH Trial (BSA)  
Resin Y90 vs Sorafenib (median OS ~9 mo)



SIRveNIB Trial (BSA)  
Resin Y90 vs Sorafenib (median OS ~9 mo)



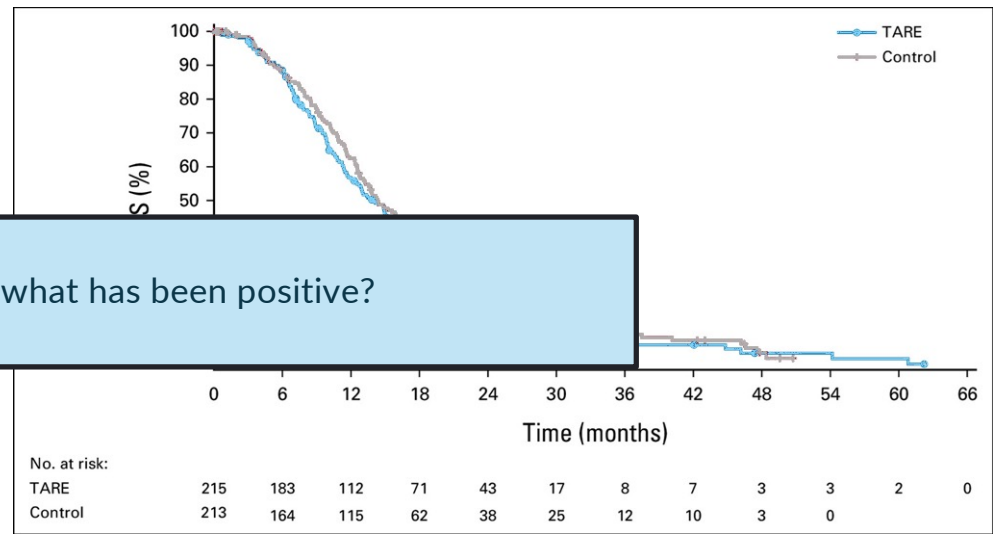
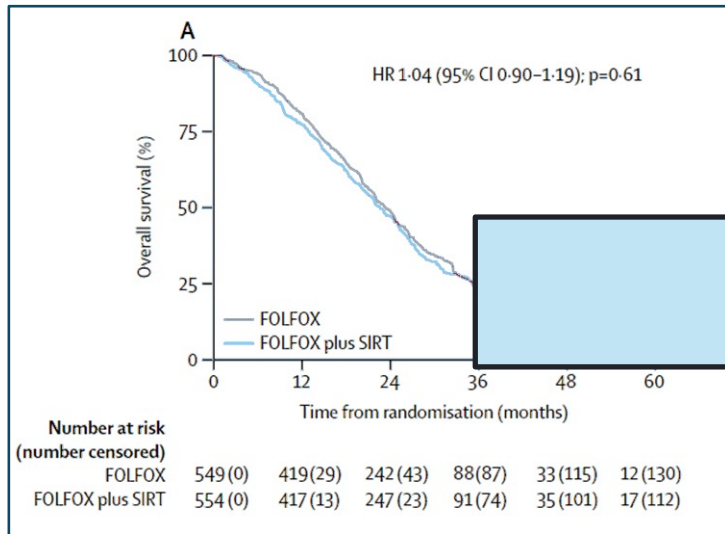
STOP-HCC (MIRD)  
Glass HCC phase 3 trial was never published.

Vilgrain V, et al. "Efficacy and safety of selective internal radiotherapy with yttrium-90 resin microspheres compared with sorafenib in locally advanced and inoperable hepatocellular carcinoma (SARAH): an open-label randomised controlled phase 3 trial." *The Lancet. Oncology*. 2017;18:12. Chow, Pierce KH, et al. "SIRveNIB: Selective Internal Radiation Therapy Versus Sorafenib in Asia-Pacific Patients With Hepatocellular Carcinoma." *JCO*. 2018;36(19):1913-1921.

# Negative empiric dosing trials (CRC)

SIRFLOX, FOXFIRE, FOXFIRE Global (Resin)

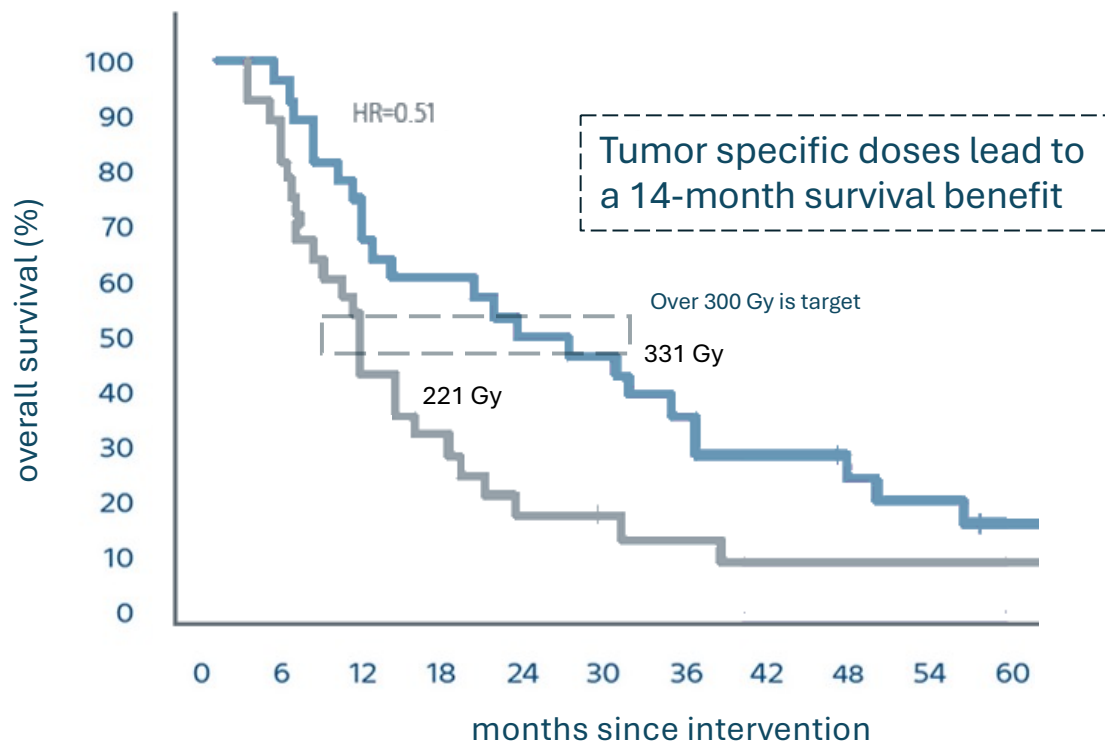
EPOCH (Glass)



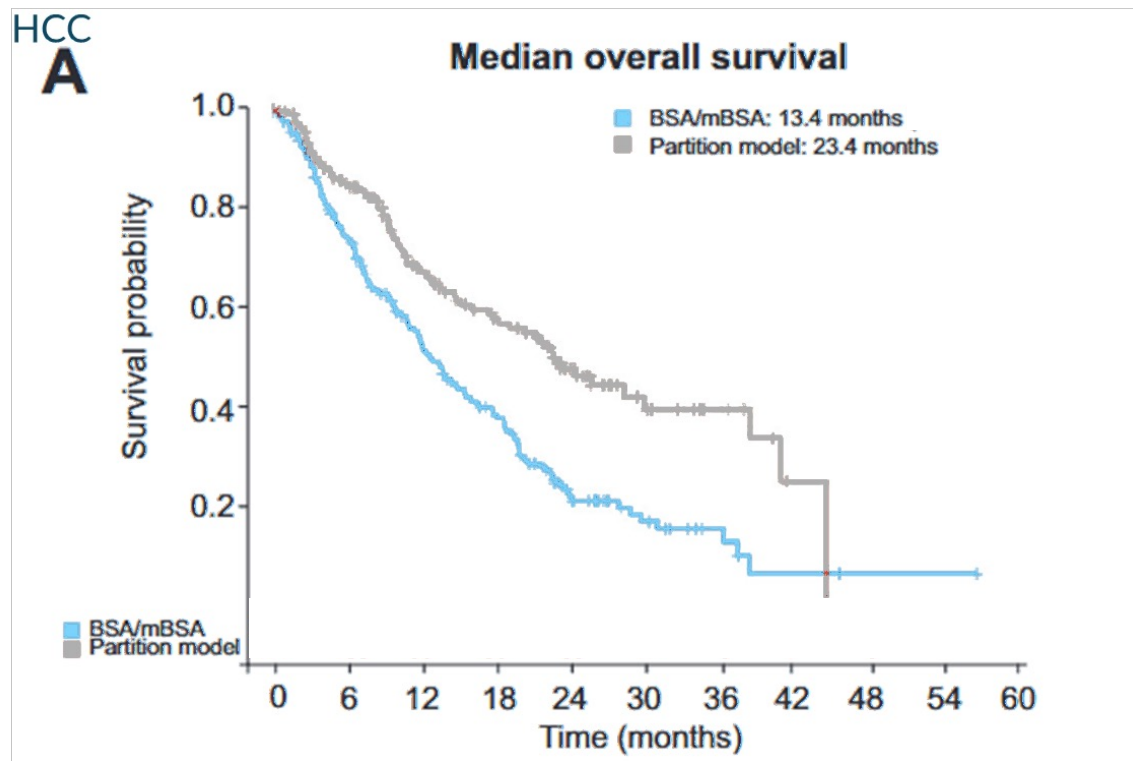
\*Technically positive with PFS/hPFS as primary endpoints; but hasn't moved the needle without OS

Wasan, Harpreet S et al. "First-line selective internal radiotherapy plus chemotherapy versus chemotherapy alone in patients with liver metastases from colorectal cancer (FOXFIRE, SIRFLOX, and FOXFIRE-Global): a combined analysis of three multicentre, randomised, phase 3 trials." *The Lancet. Oncology* vol. 18,9 (2017). Mulcahy, Mary F et al. "Radioembolization With Chemotherapy for Colorectal Liver Metastases: A Randomized, Open-Label, International, Multicenter, Phase III Trial." *JCO* vol. 39,35 (2021): 3897-3907.

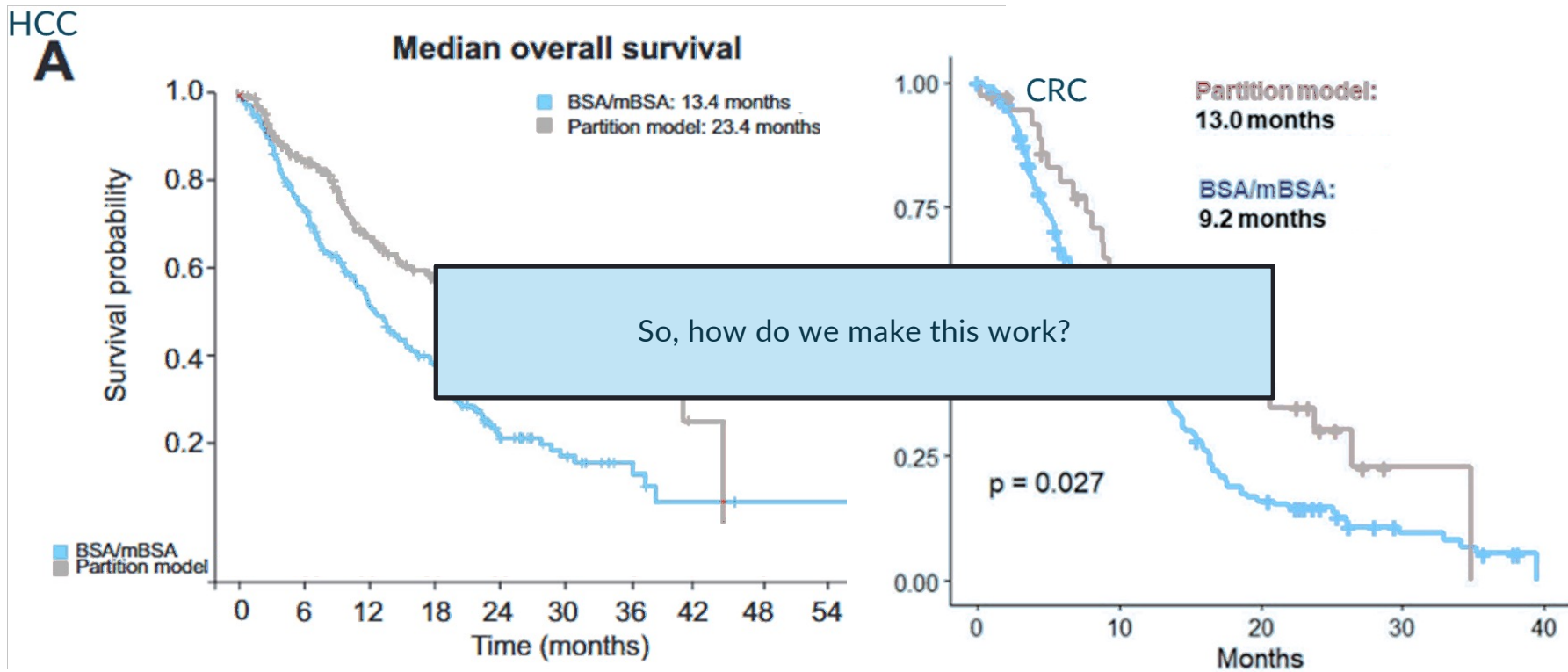
Increased tumor dose is correlated with OS; best at doses >300 Gy for tumors ~10cm in size with TIV



Personalized dosimetry has also shown survival benefit in large continent-wide registries, as well

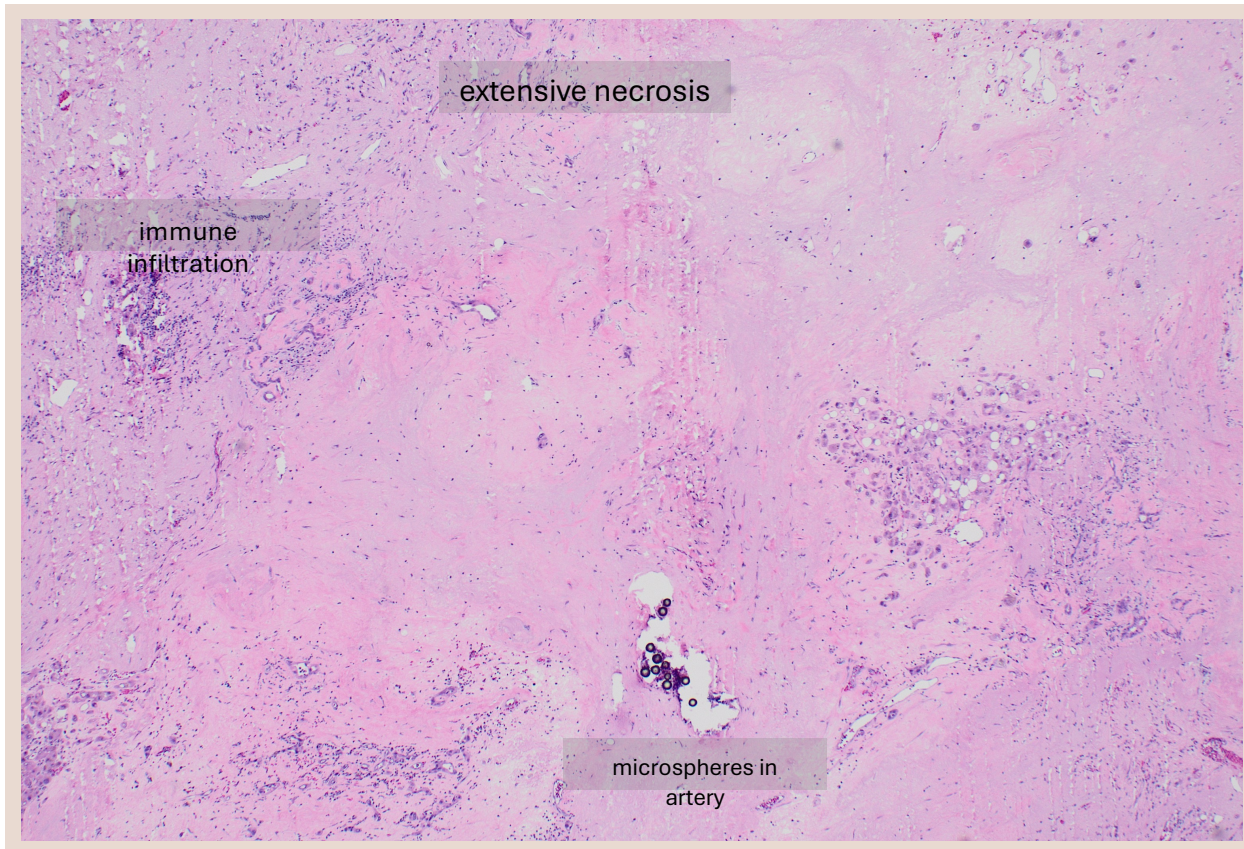


Personalized dosimetry has also shown survival benefit in large continent-wide registries, as well



Necrosis at the cellular level is the ultimate objective of any curative therapy

this is the table stakes for the rest of this talk



# A short interlude thought experiment



If we want to optimize ablative radioembolization dosimetry we will have to optimize each controllable variable

*Dose = Microsphere Activity x Microsphere Density x C*

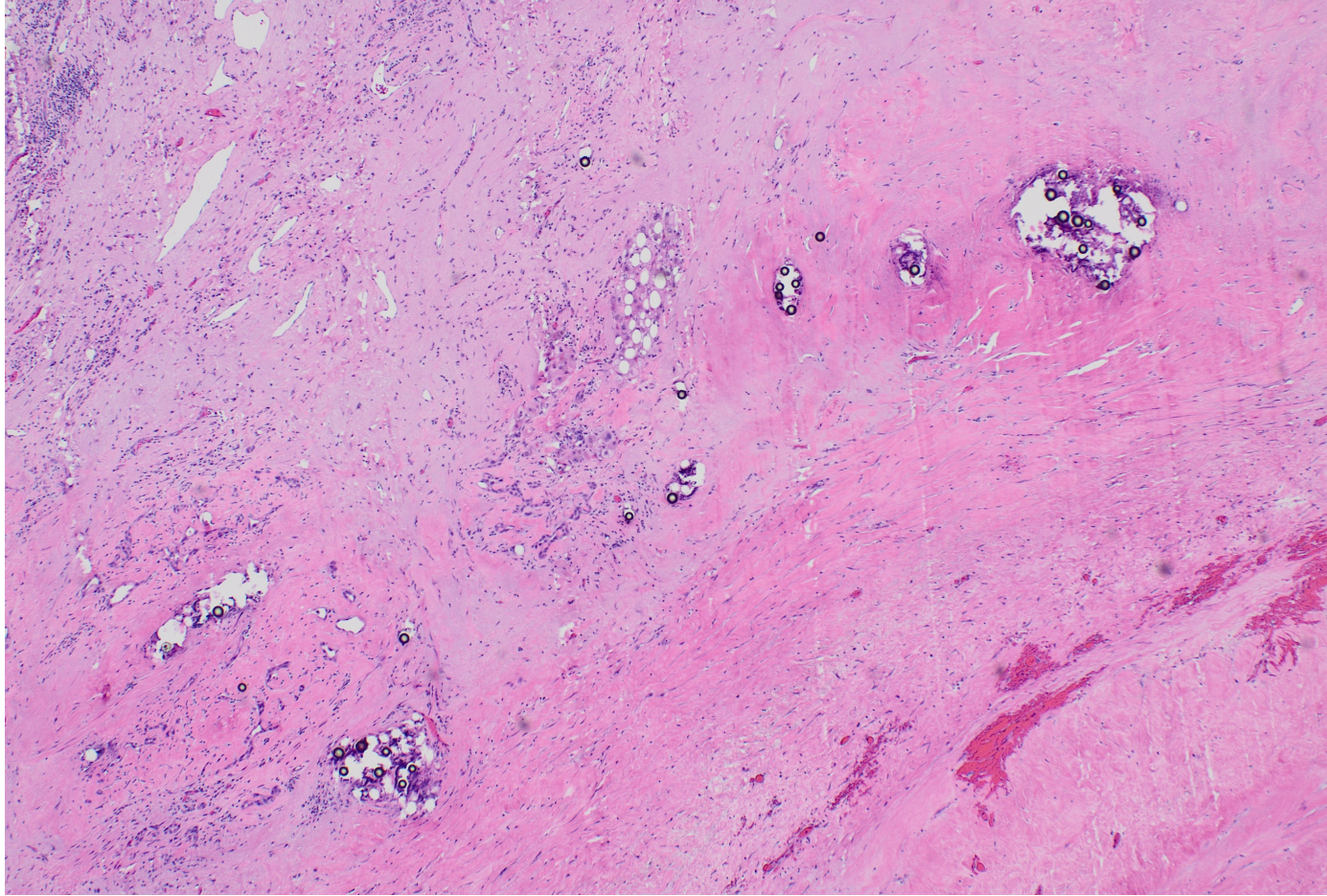
$\frac{\text{Bq}}{\text{kG}}$

~~$\frac{\text{Bq}}{\text{sphere}}$~~

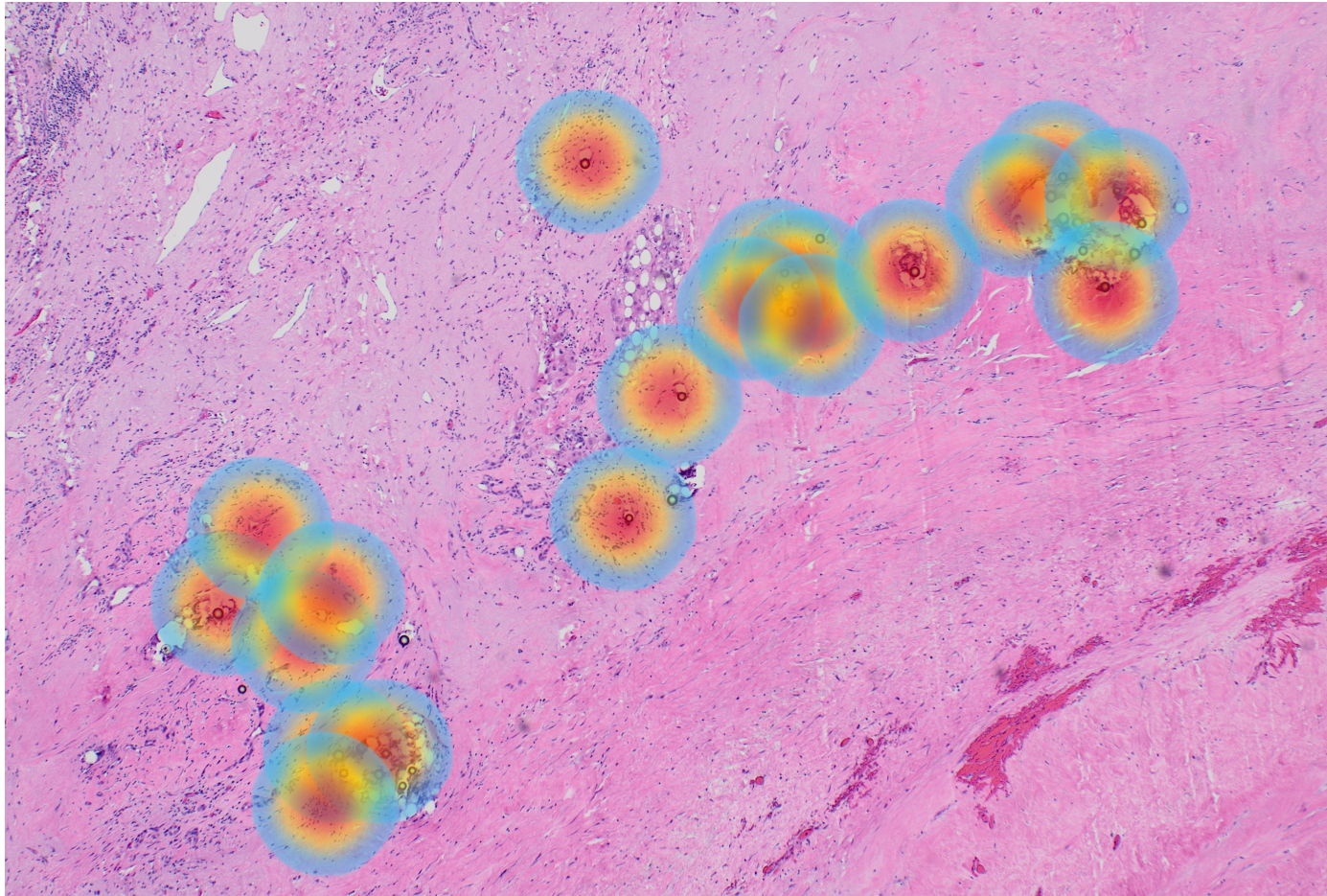
~~$\frac{\text{Bq}}{\text{kg}}$~~

~~$\frac{\text{sphere}}{\text{mL}}$~~

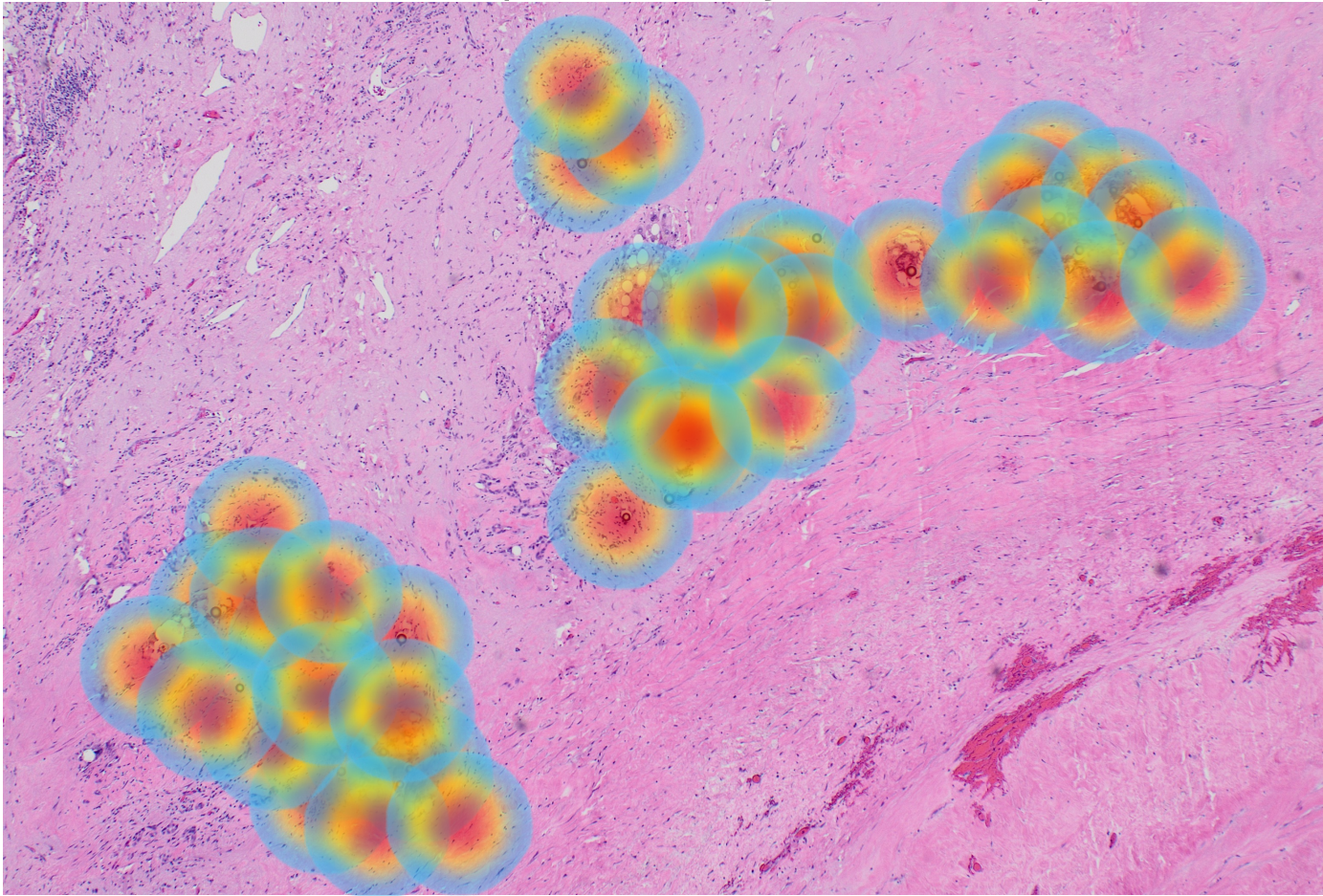
~~$\frac{\text{mL}}{\text{kG}}$~~



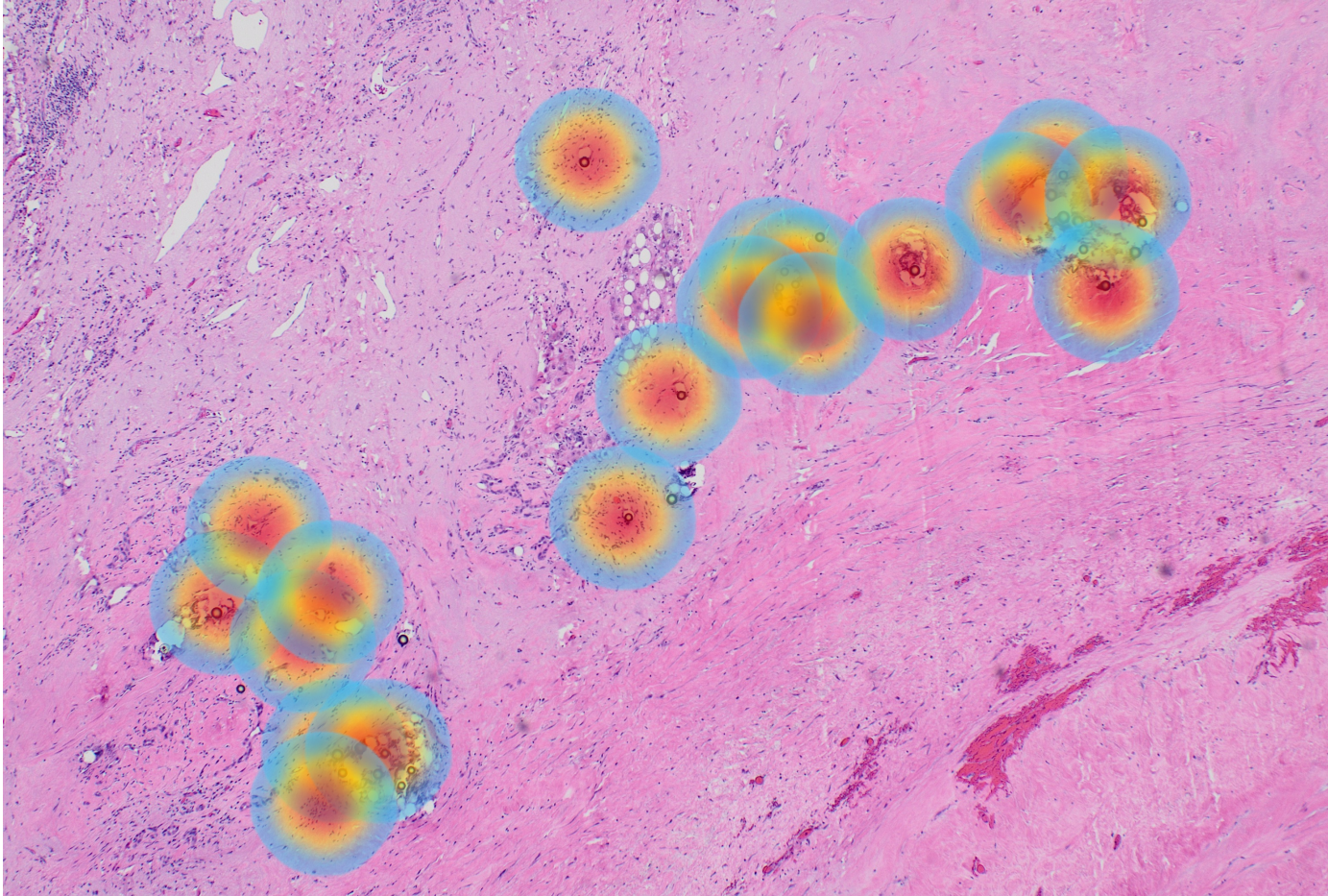
Baseline



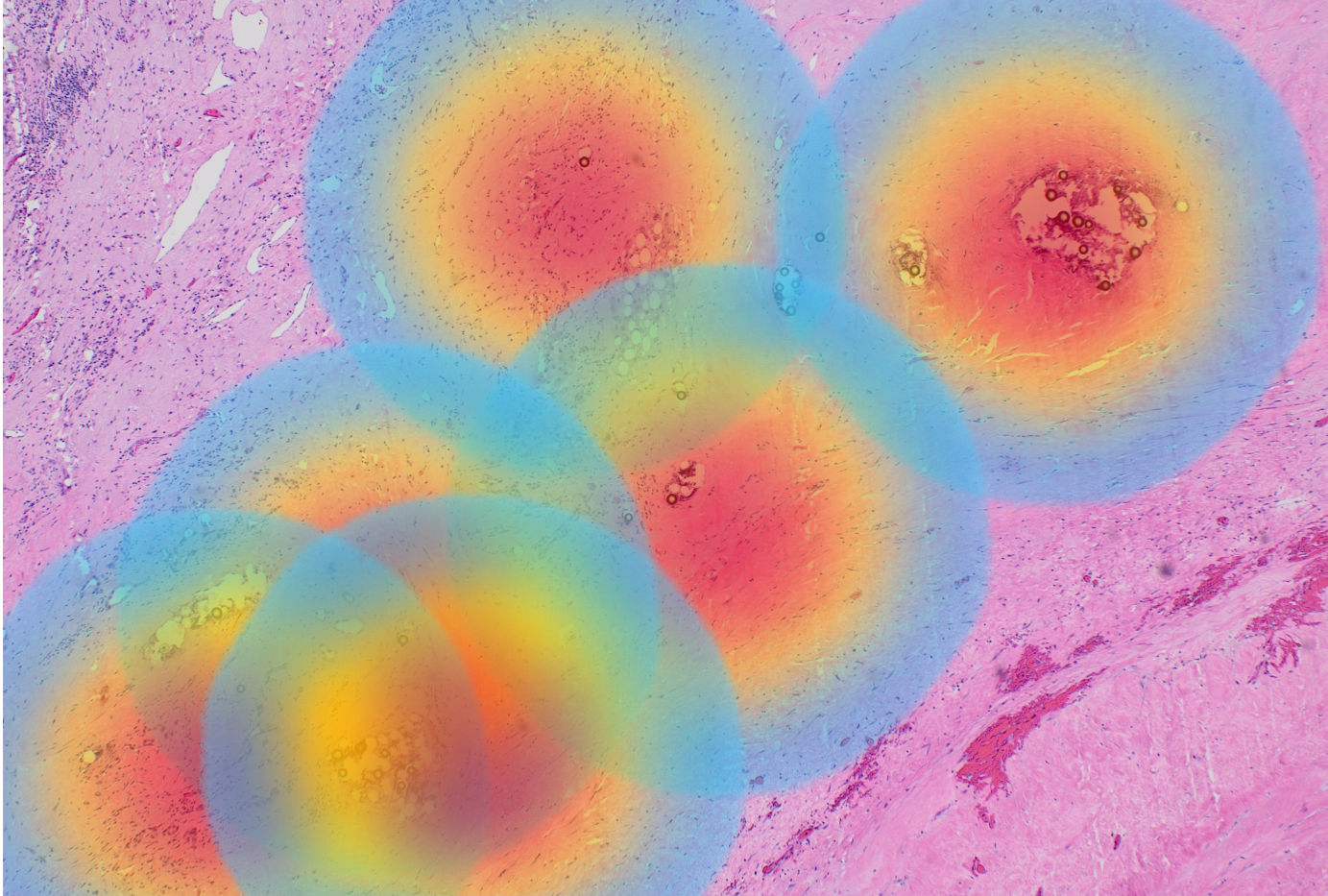
More spheres with same microsphere activity does not equal more necrosis



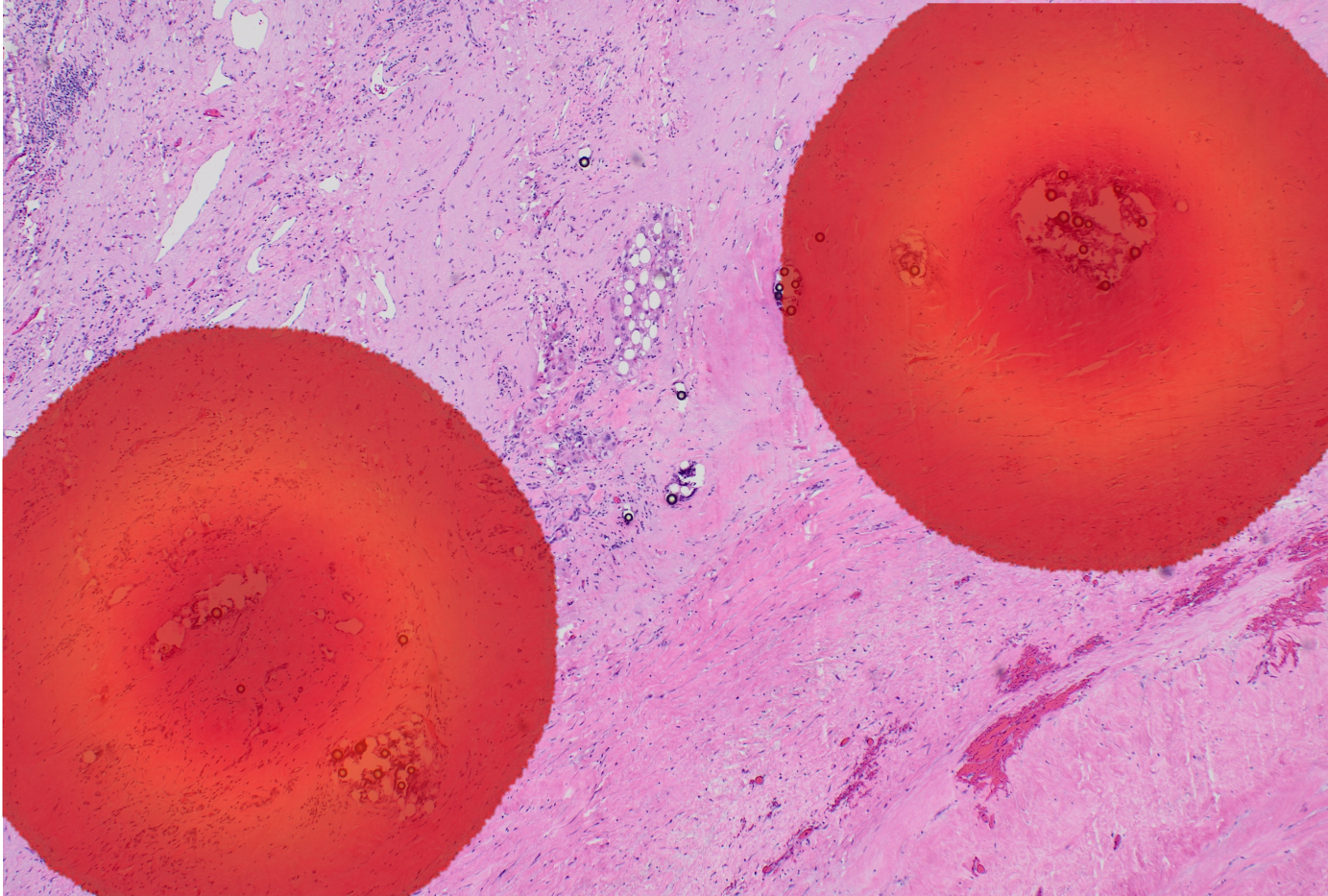
Let's go back to our baseline model



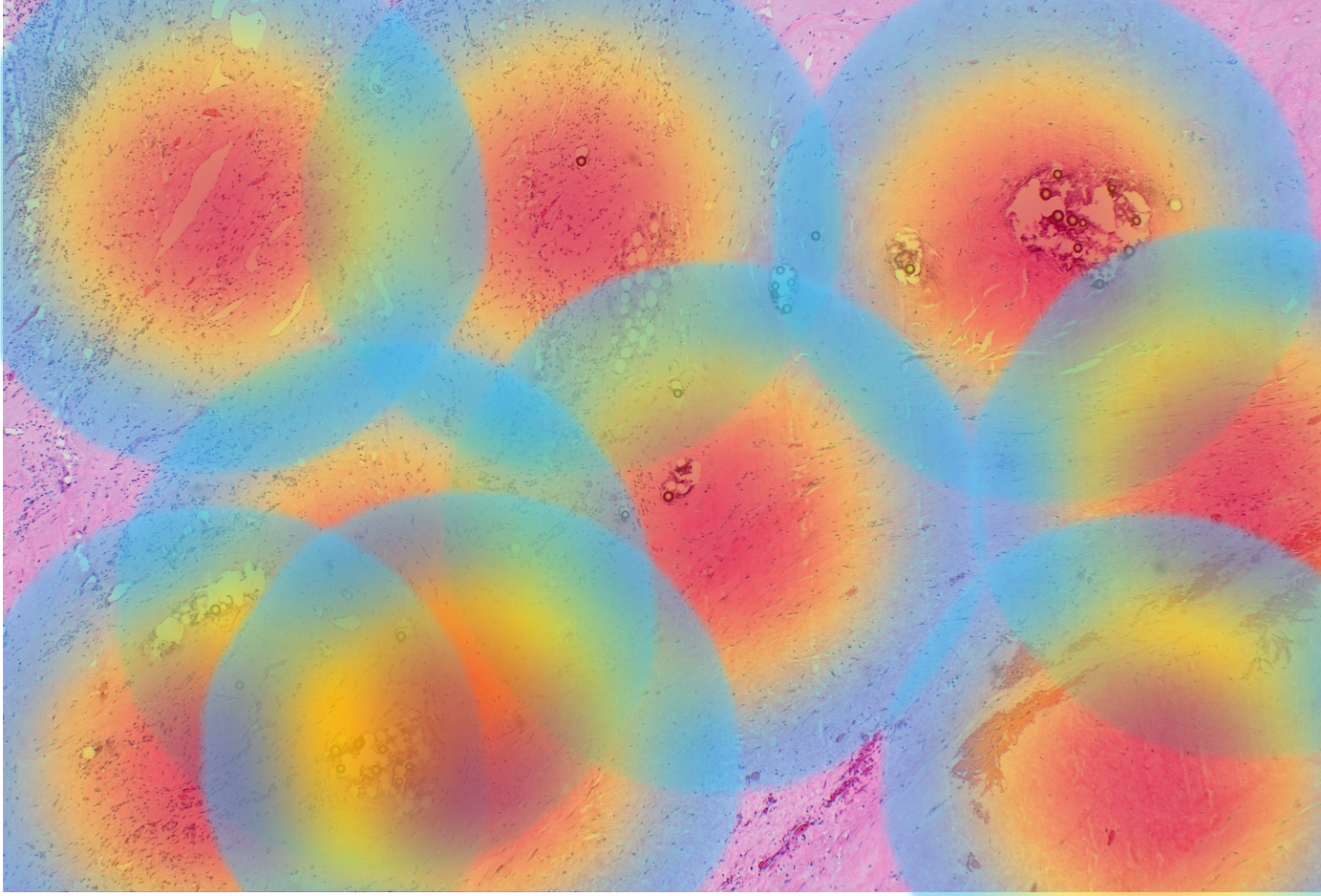
Fewer spheres with higher microsphere activity **CAN** equal more necrosis



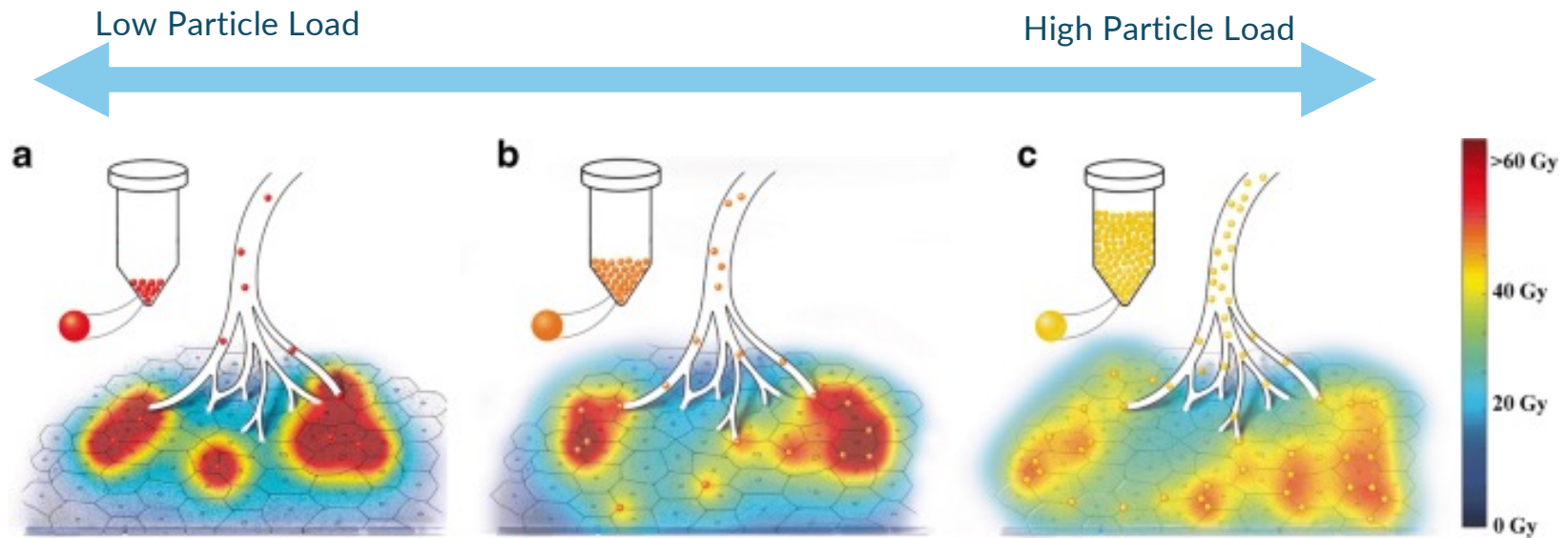
but you can have too few spheres even if infinitely hot...



The correct microsphere activity and density leads to necrosis

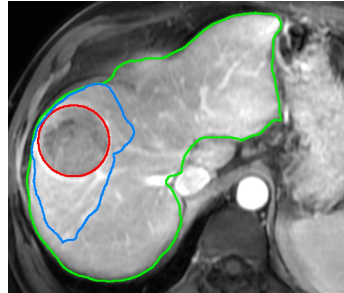


# Tailoring Correct Sphere Density for the Occasion

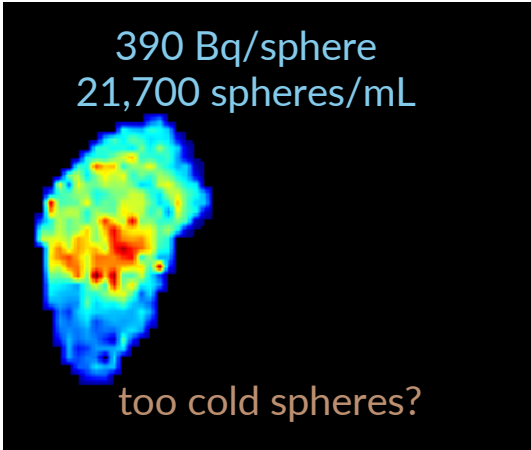
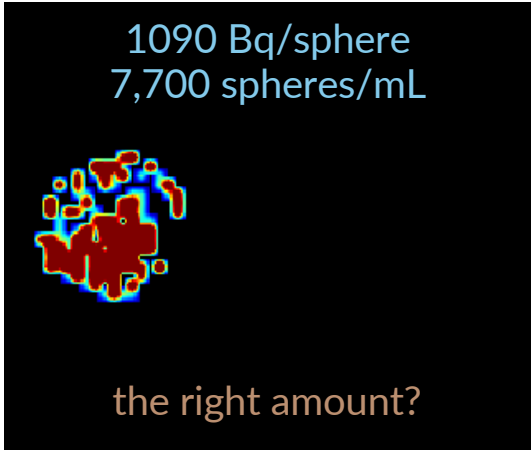
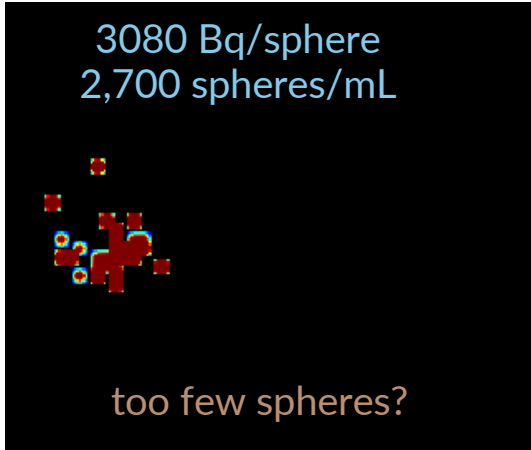


# The correct microsphere activity and density lead to necrosis

It is a spectrum –  
dose does **not** tell  
entire story!



MIRD Dose: 400 Gy

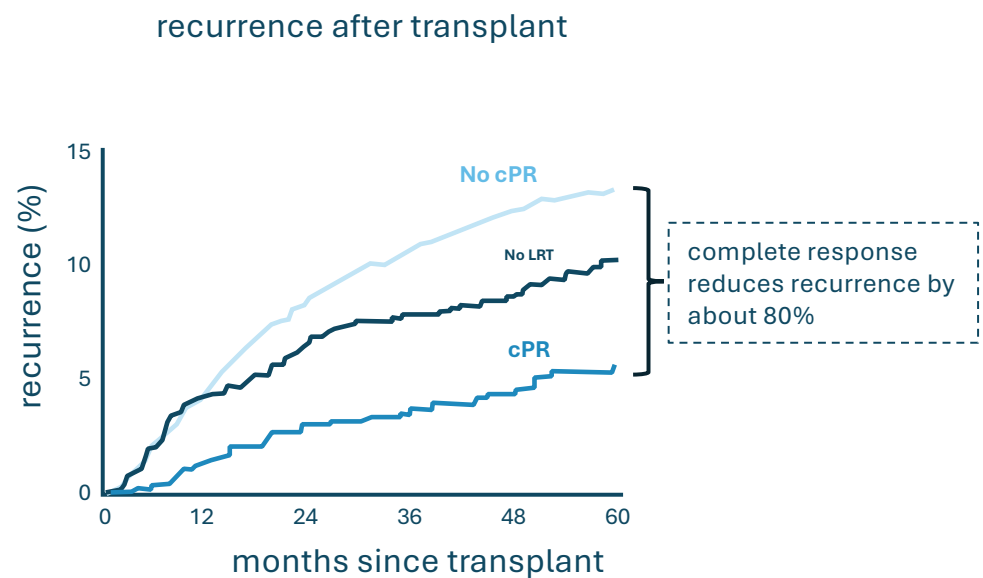


# Complete pathologic response predicts improved recurrence-free and survival rates after transplantation

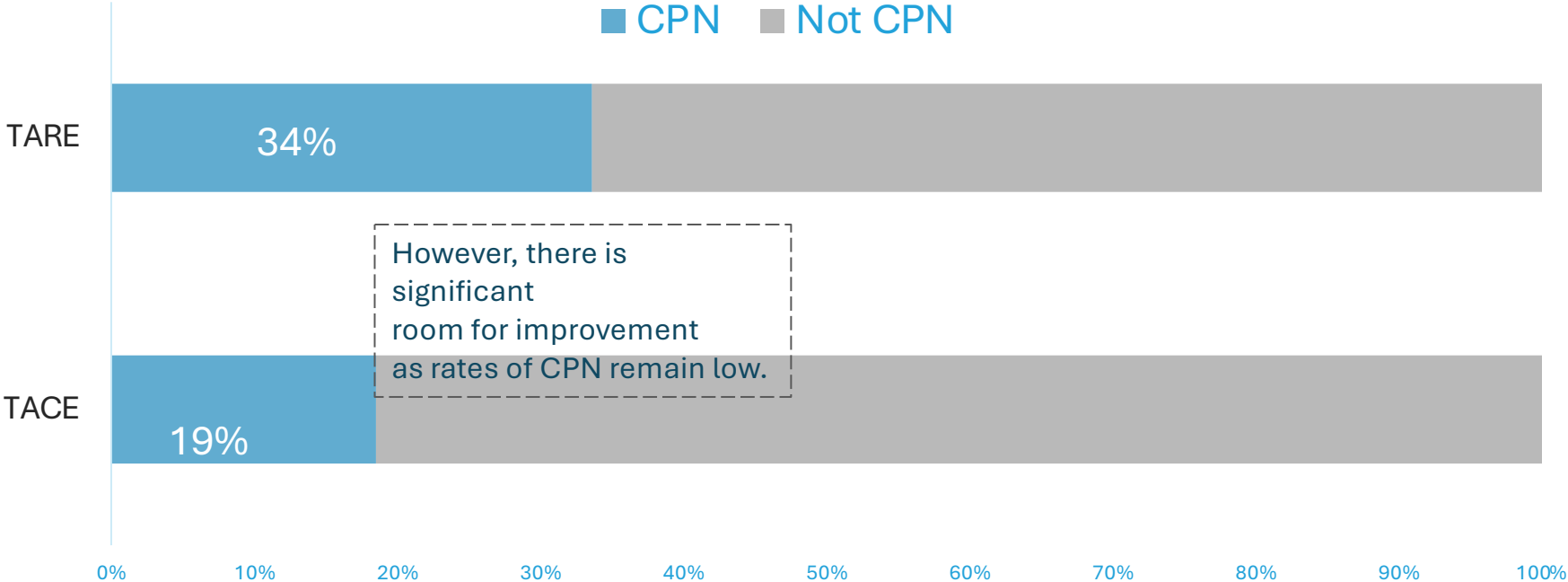
and partial response is worse than no therapy



N= 3,601



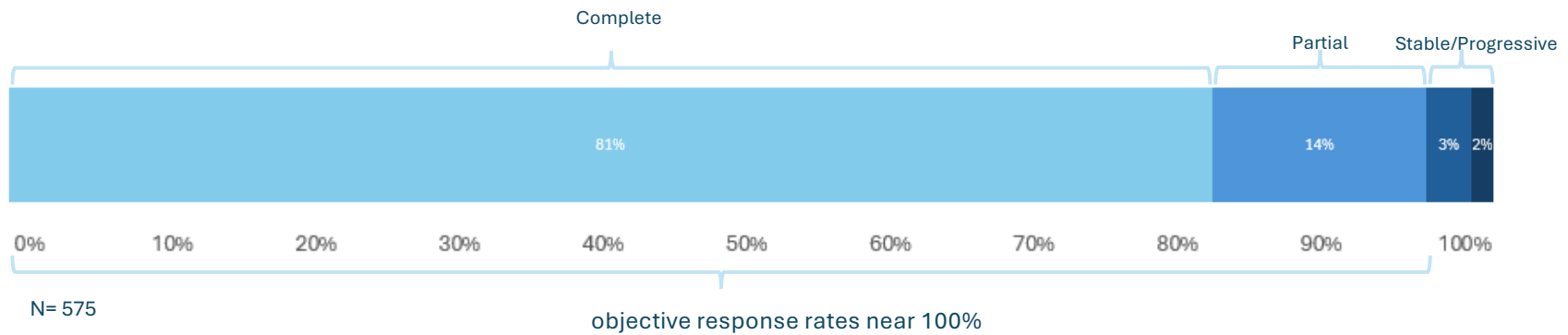
# In the US national database (UNOS), TARE was more likely to lead to CPN than TACE



N= 6,265

# Ablative RE leads to mostly complete imaging response with nearly all patients having a response

## mRECIST Response to Rad Seg Across Multiple Studies



complete pathologic response with contemporary dosing thresholds between 76-100%

This holds true for **smaller tumors**, as well – though we don't often consider tumor dose and opt for **single compartment dosing**

Ochsner

Tumor absorbed dose (Gy), median (range)	923 (252–2,629)
--	-----------------

UCSD

MIRD Dose	D95	D70	D50
> 466	> 719	> 1021	> 1229

Tumor specific doses leads to complete necrosis

Mayo Clinic

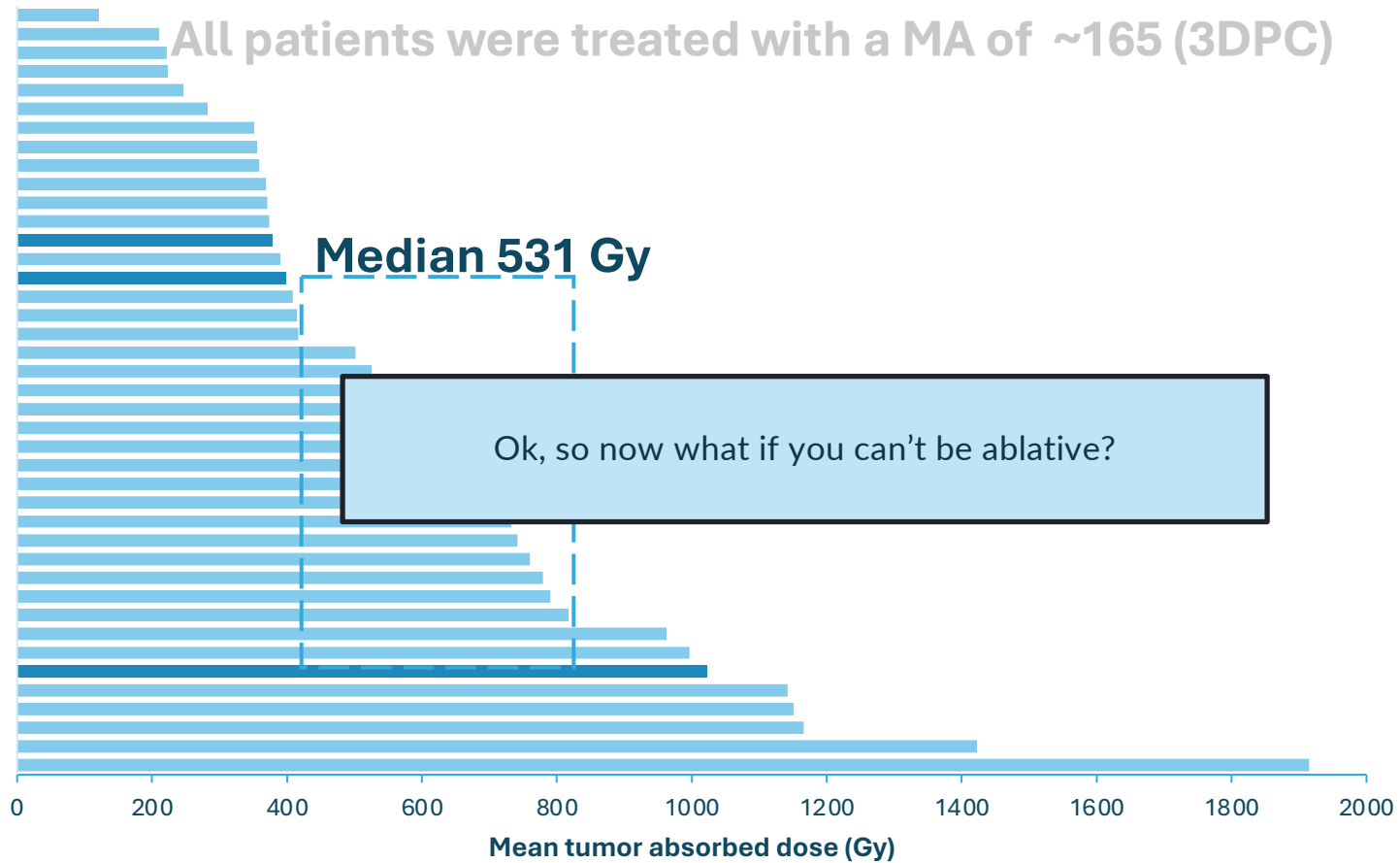
Tumor dose (Gy)	1086 (848–1632)
-----------------	-----------------

BID (resin)

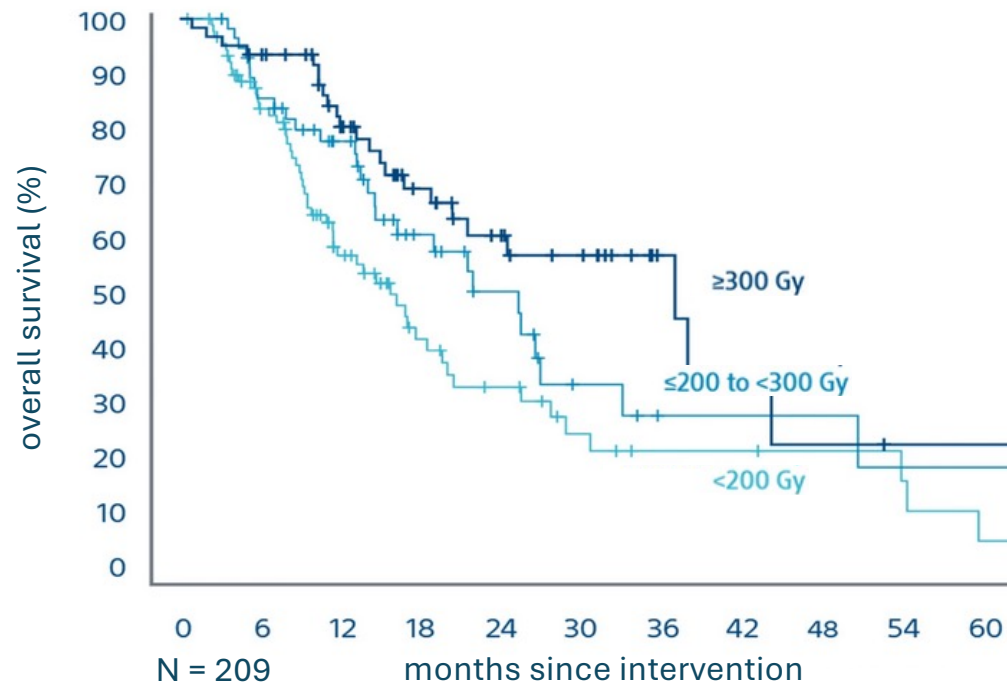
D50 (Gy)            531 (291–833)

D95 (Gy)            263 (137–371)

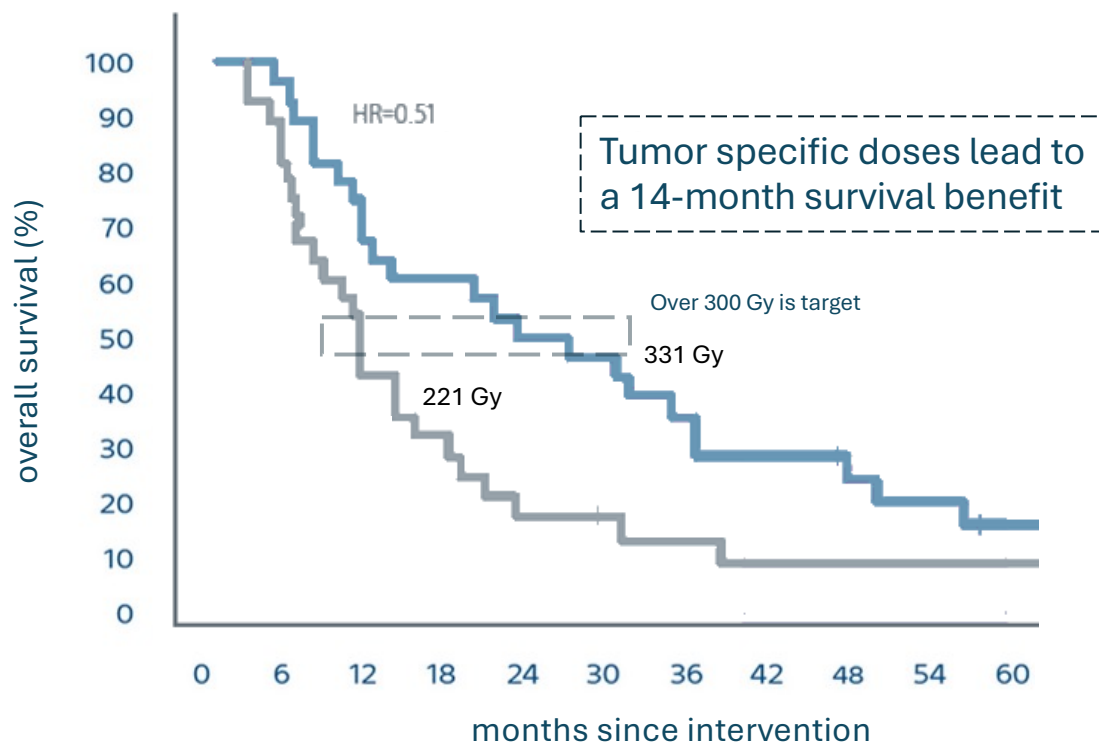
Data is less concrete but developing with resin microspheres



Median tumor dose is correlated with survival odds for tumors ~7 cm in size with optimal outcomes seen at doses that are greater than 300 Gy



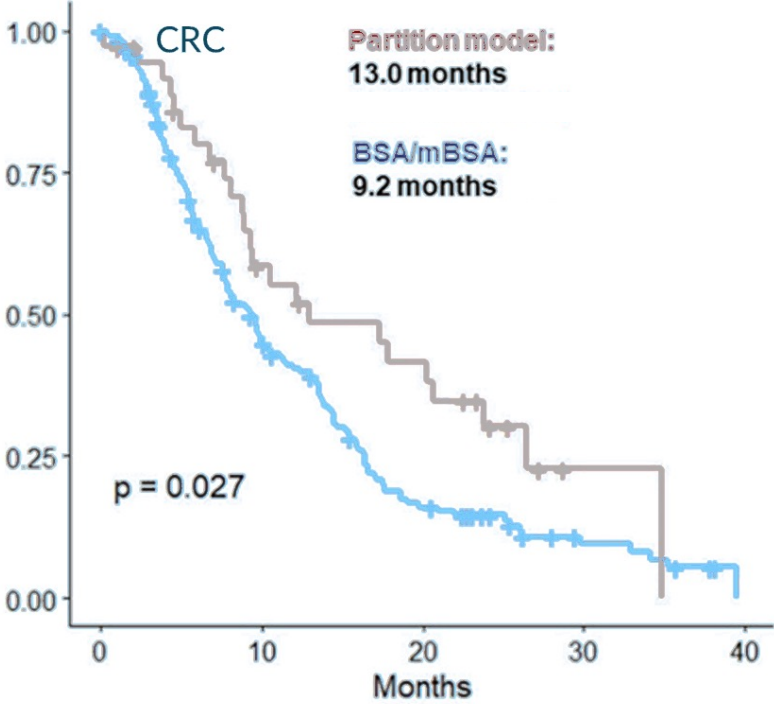
Increased tumor dose is correlated with OS; best at doses >300 Gy for tumors ~10cm in size with TIV



Metastatic disease can be a large part of your practice, and appropriate personalized dosimetry is even more crucial.

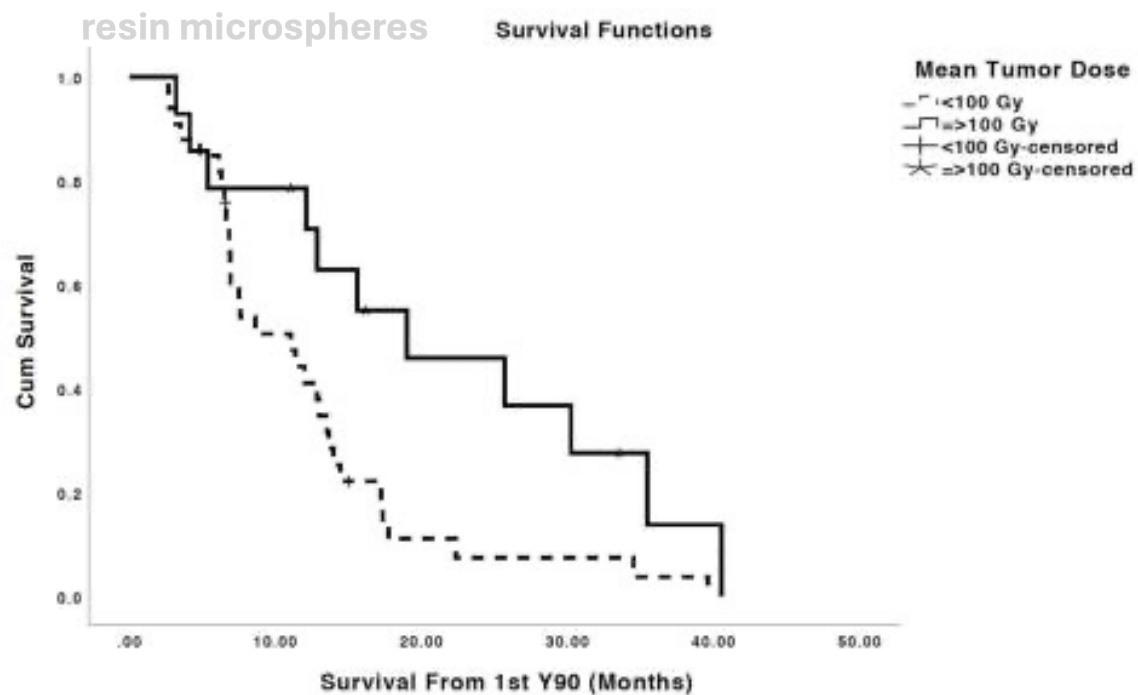


Regardless of what “dose” was used, the act of thinking about dose is beneficial for CRC



Schaefer N. Prognostic Factors for Effectiveness Outcomes After Transarterial Radioembolization in Metastatic Colorectal Cancer: Results From the Multicentre Observational Study CIRT. Clin Colorectal Cancer. 2022

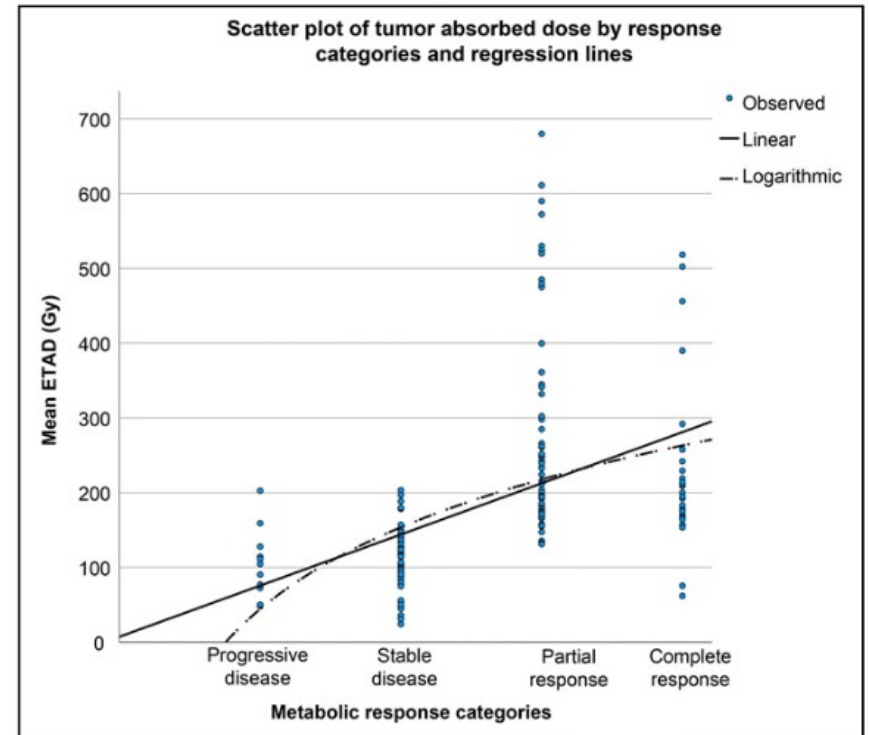
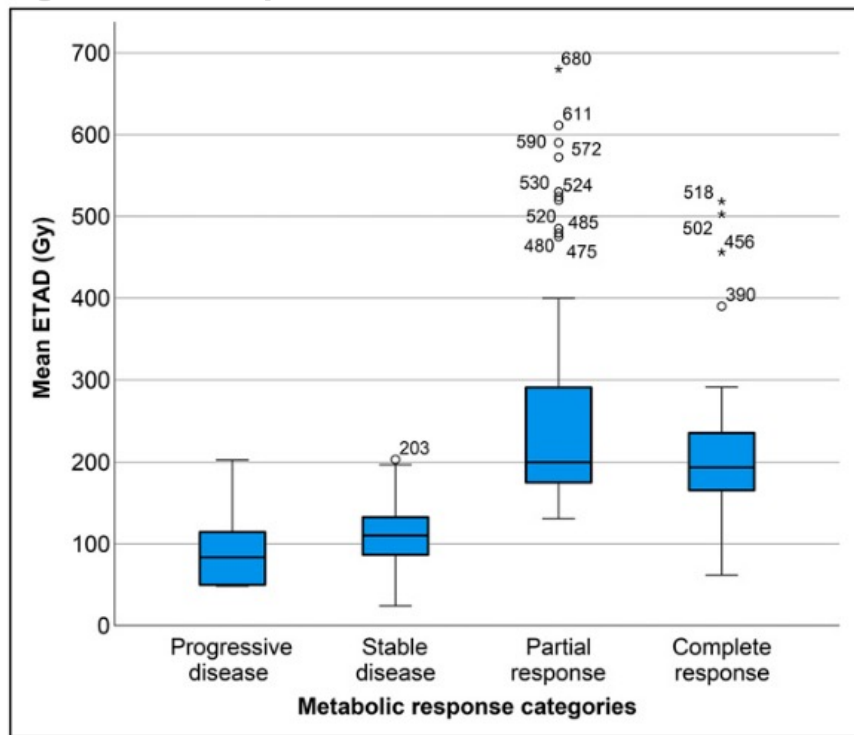
Regardless of what “dose” was used, the act of thinking about dose is beneficial for CRC



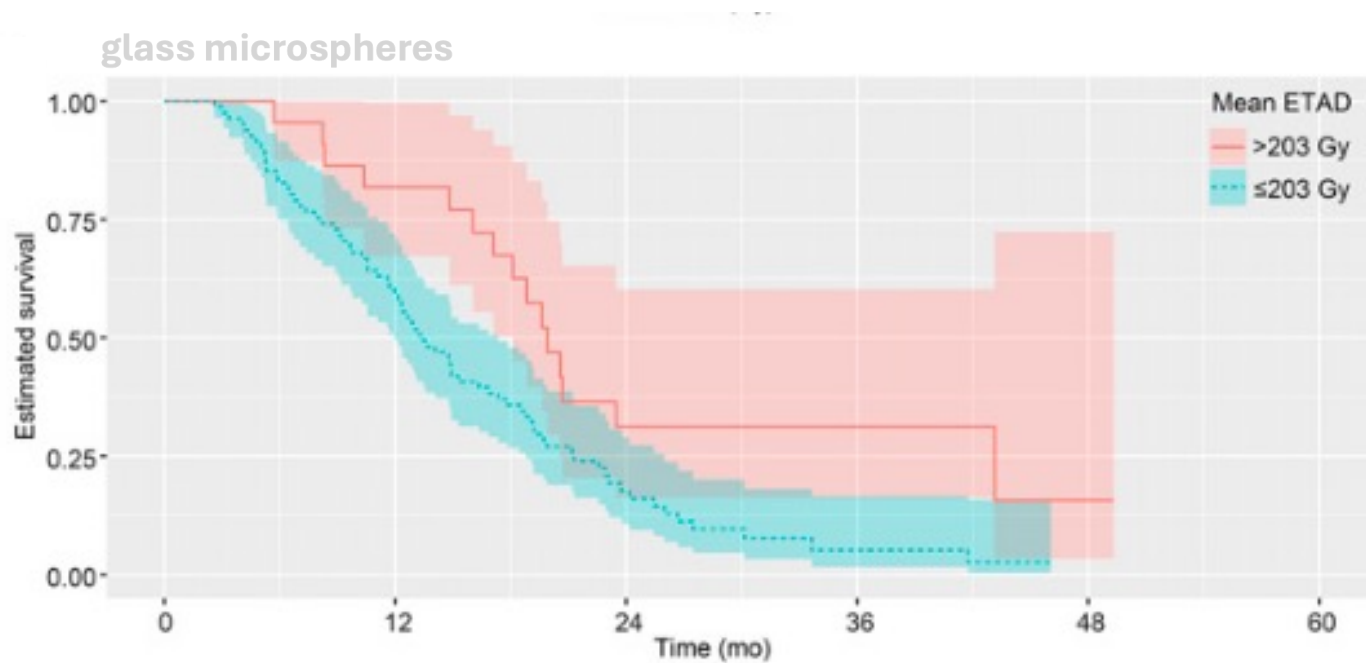
Sankhla T, Cheng B, Nezami N, Xing M, Sethi I, Bercu Z, Brandon D, Majdalany B, Schuster DM, Kokabi N. Role of Resin Microsphere Y90 Dosimetry in Predicting Objective Tumor Response, Survival and Treatment Related Toxicity in Surgically Unresectable Colorectal Liver Metastasis: A Retrospective Single Institution Study. Cancers (Basel).

Regardless of what “dose” was used, the act of thinking about dose is beneficial for CRC

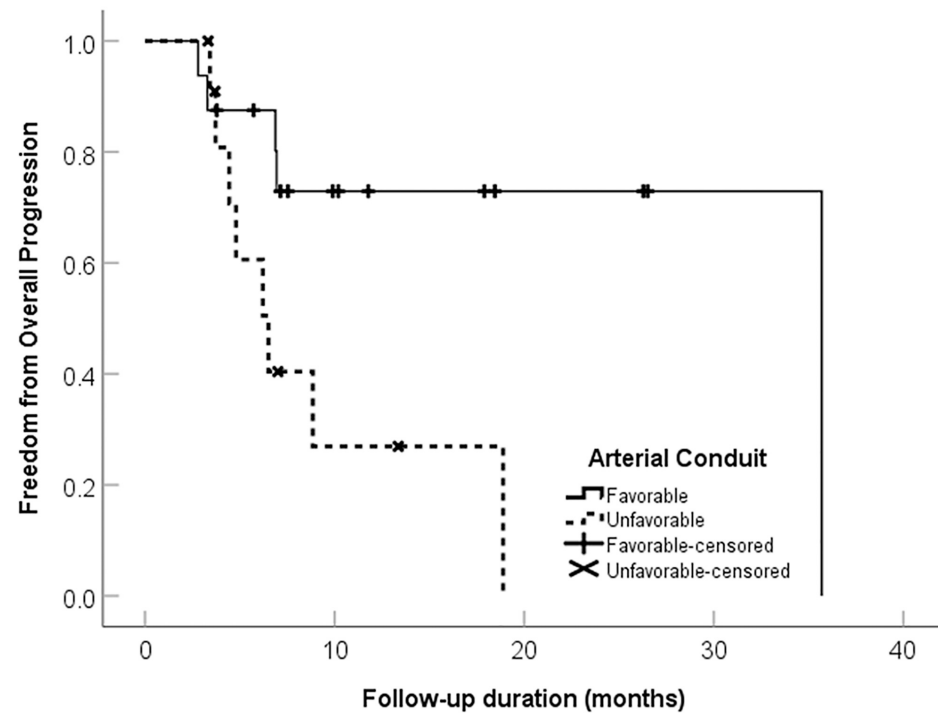
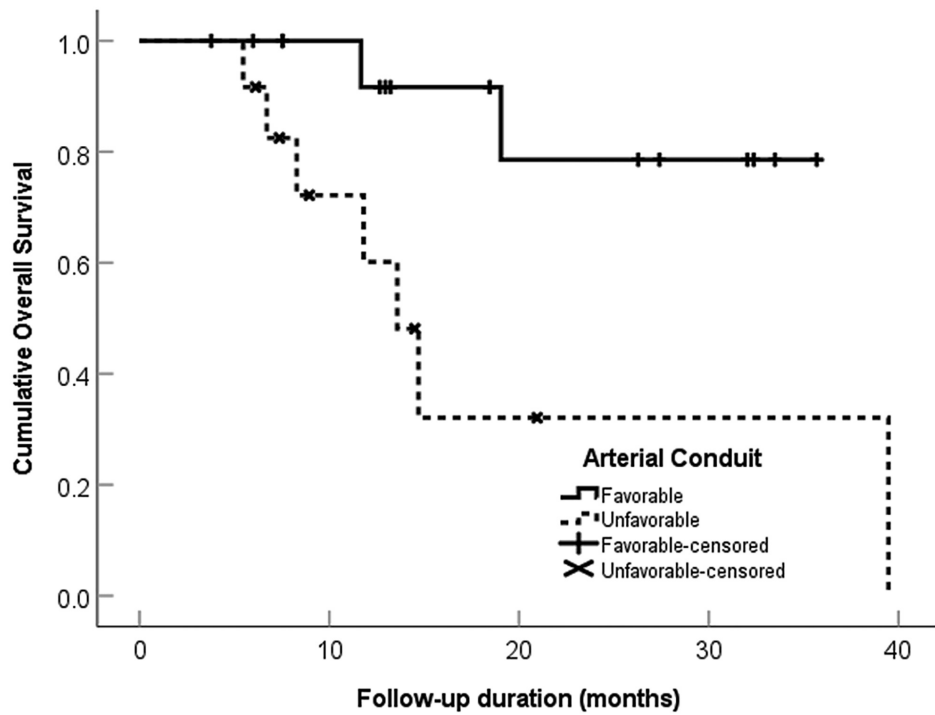
glass microspheres



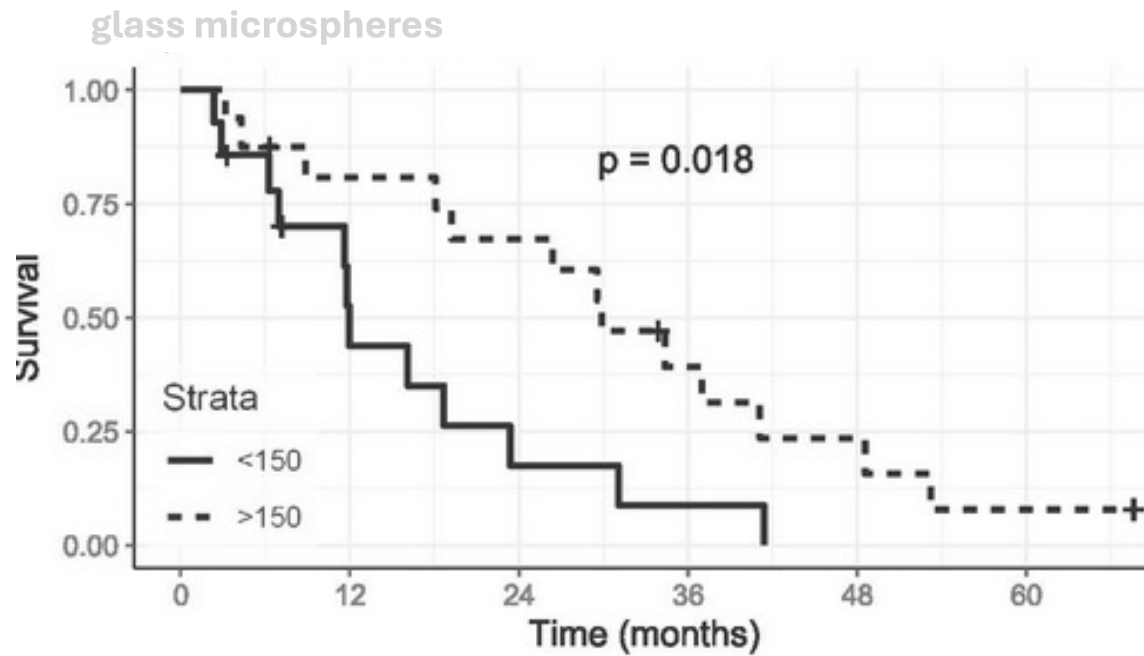
Regardless of what “dose” was used, the act of thinking about dose is beneficial for CRC



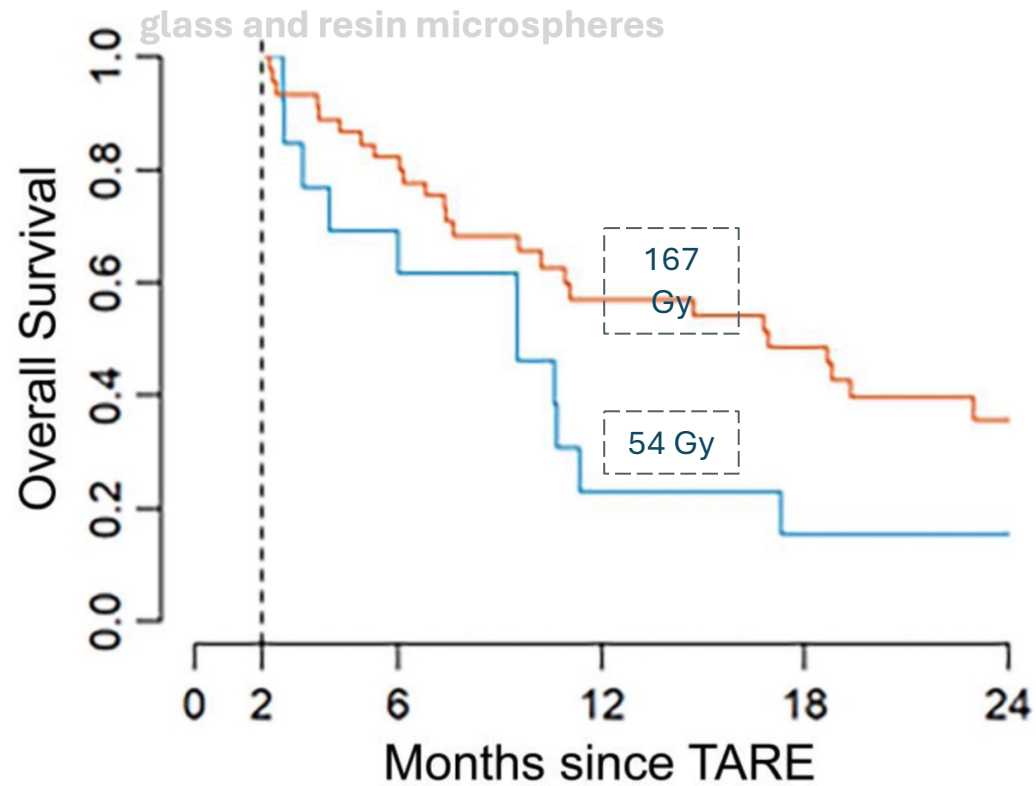
This benefit may be in part to better patient selection  
 arterial conduit suitability is critical for effective and safe dosimetry



The same dose-responses are seen with other malignancies, as well  
in this case, neuroendocrine tumors



The same dose-responses are seen with other malignancies, as well  
in this case, breast tumors



So where am I at today with **metastatic** disease?

**Glass**

Tumor Dose: 150-200  
Normal Liver Dose: 80

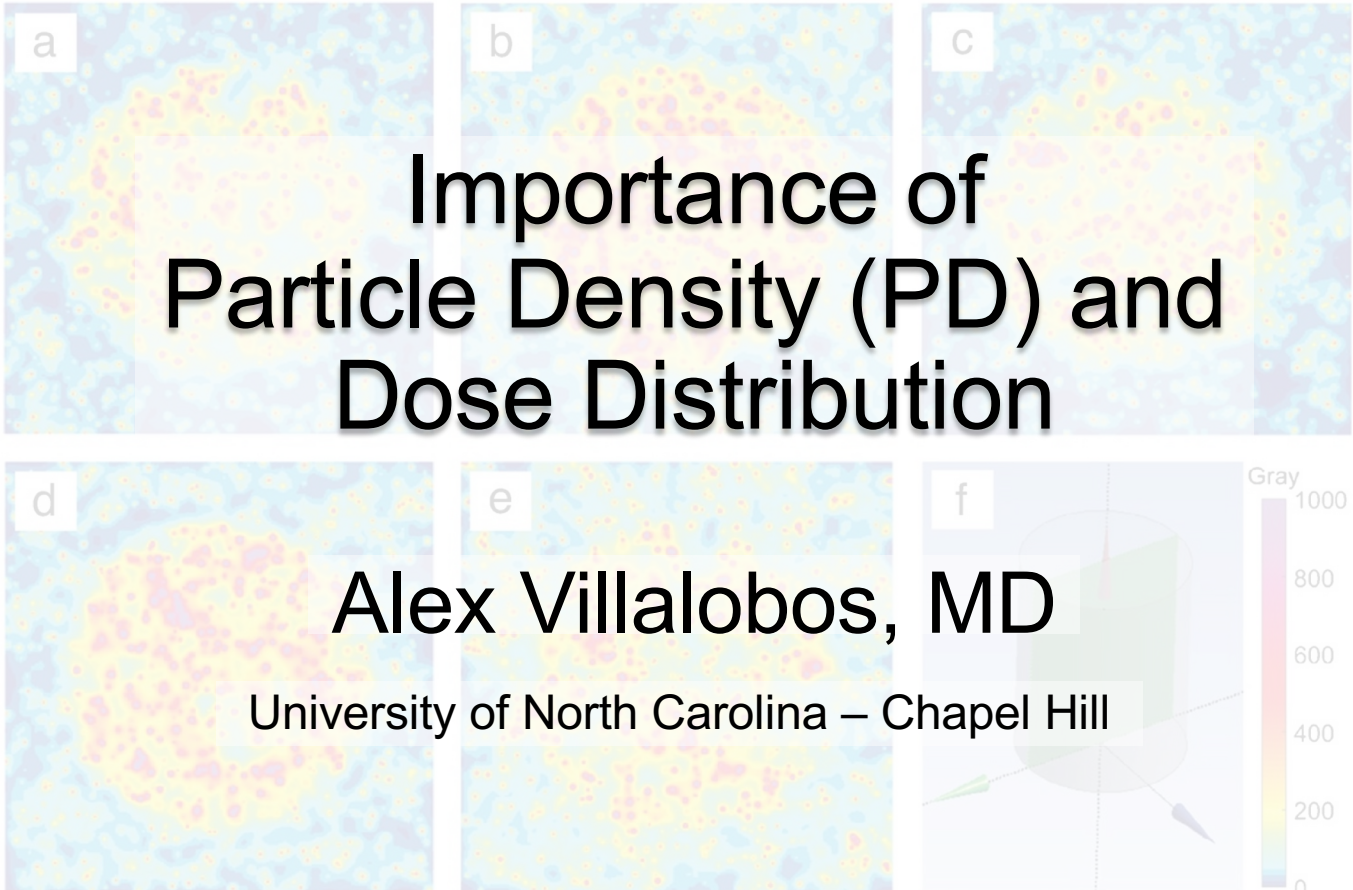
**Resin**

Tumor Dose: 130+  
Normal Liver Dose: 40

resin is going to become more pre-calibrated  
further pushing the convergence of the products

The goal of this talk was to look at ways we can improve  
TARE dosimetry :

- What dosing “physically means”
- Current dose targets based on treatment intent for HCC
- Future of dosimetry for metastatic disease



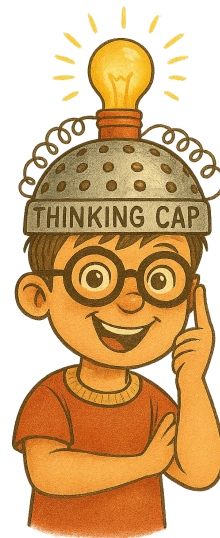
# Importance of Particle Density (PD) and Dose Distribution

Alex Villalobos, MD

University of North Carolina – Chapel Hill

Background: Fig 1 from Lam et. Al. "The relationship between yttrium-90 glass microspheres specific activity, particle density and treatment outcomes in HCC and mCRC"

# Definitions & Theory



# Definitions

- Particle Density: # of Particles per Unit Volume (Microspheres/mL)

- What Impacts Tumor Particle Density?

- Number of Particles

$Total\ Number\ Of\ Delivered\ Y90\ [Microspheres] \times (1 - LSF)$

- Volumes Treated

$Tumor\ Volume\ [mL] + \left( \frac{NonTumor\ Volume\ [mL]}{TNR} \right)$

- Tumor Vascularity (e.g. TNR)

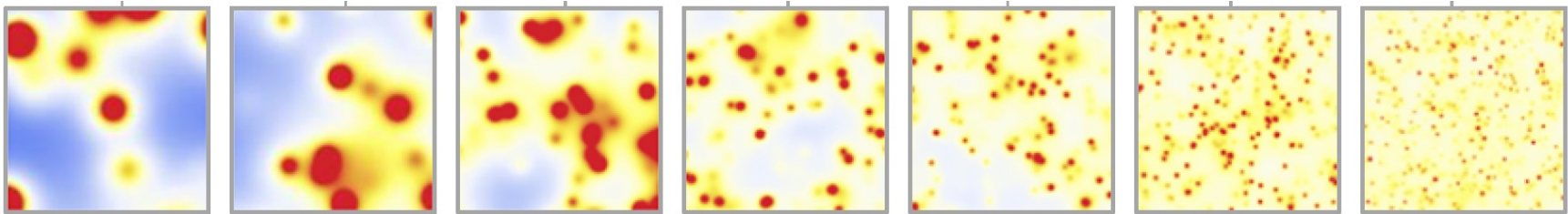
$=\ Tumor\ Particle\ Density\ [Microspheres/mL]$

- Lung Shunt Fraction

# Theory: Why is PD Important?

(At Same Target Doses)

Low Particle Density = More Coverage Gaps



More Coverage Gaps = Need Higher Specific Activity Particles  
to Compensate

Fig 5 from Maxwell et. Al. "Optimizing Y90 Particle Density Improves Outcomes After Radioembolization"

# Theory: How Does PD Impact Clinically?

Editorial > [Eur J Nucl Med Mol Imaging](#). 2014 Apr;41(4):634-8. doi: 10.1007/s00259-013-2674-6.

## The dosimetric importance of the number of $^{90}\text{Y}$ microspheres in liver transarterial radioembolization (TARE)

[Carlo Spreafico](#)<sup>1</sup>, [Marco Maccauro](#), [Vincenzo Mazzaferro](#), [Carlo Chiesa](#)

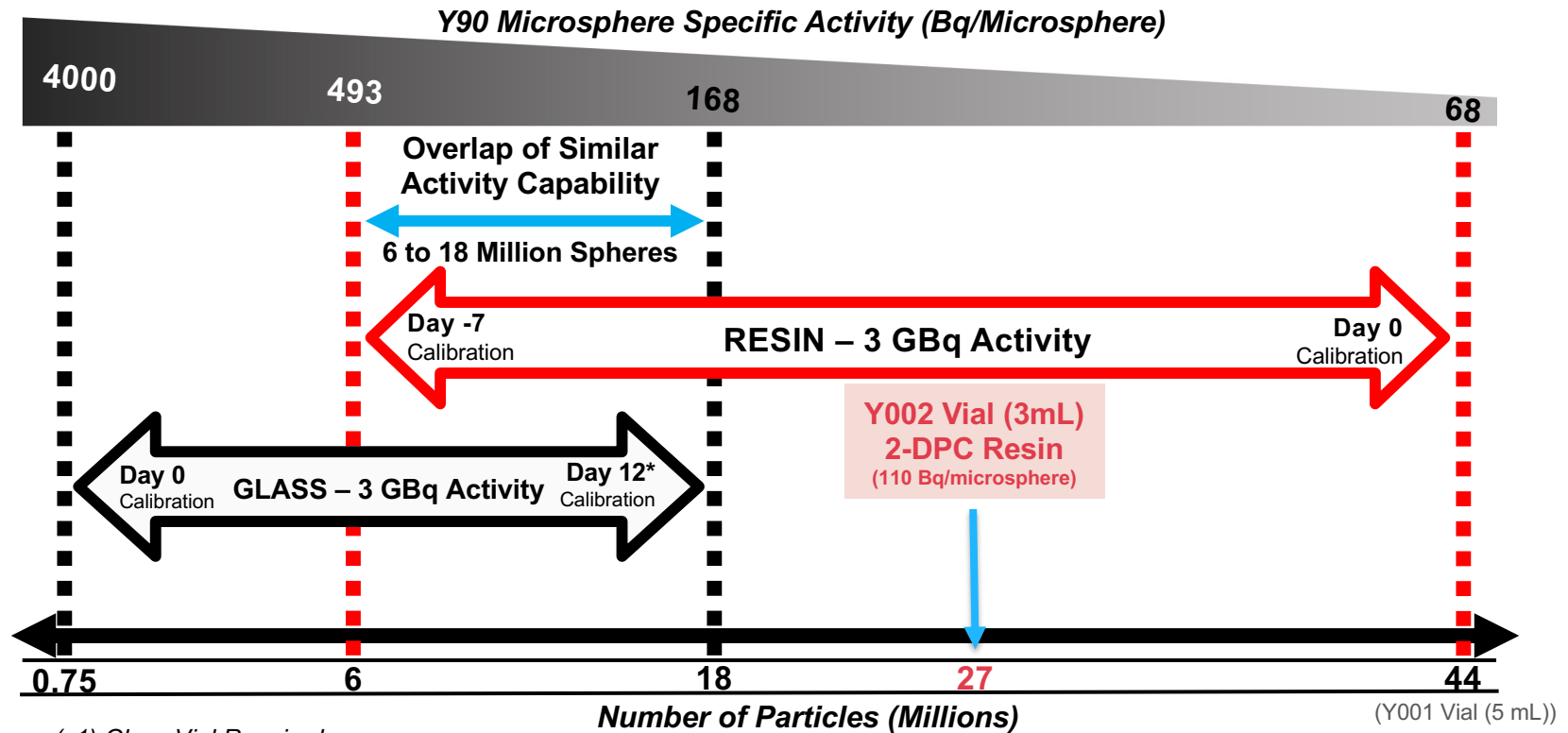
Affiliations + expand

PMID: 24477451 DOI: [10.1007/s00259-013-2674-6](#)

“For a fixed mean absorbed dose, the higher is the number of particles per giga becquerel [i.e. higher number of lower specific activity particles], the higher is the biological effect.”

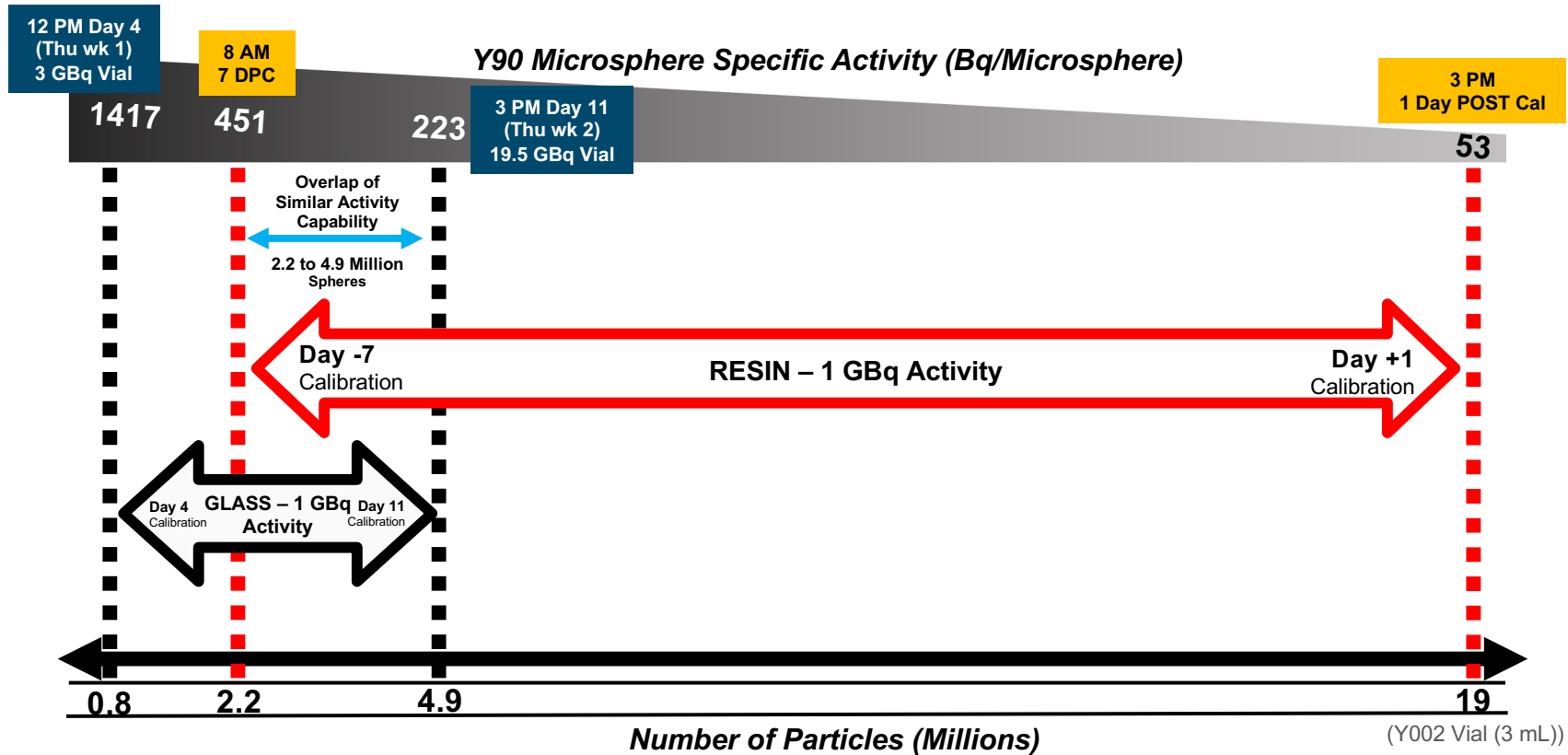
i.e.: The same biological effect can be achieved with lower specific activity particles at lower doses than with higher specific activity particles at higher doses (Both **OR** and **Toxicity**)

# Theoretical Max Particles per Device (To Achieve 3 GBq (81 mCi))

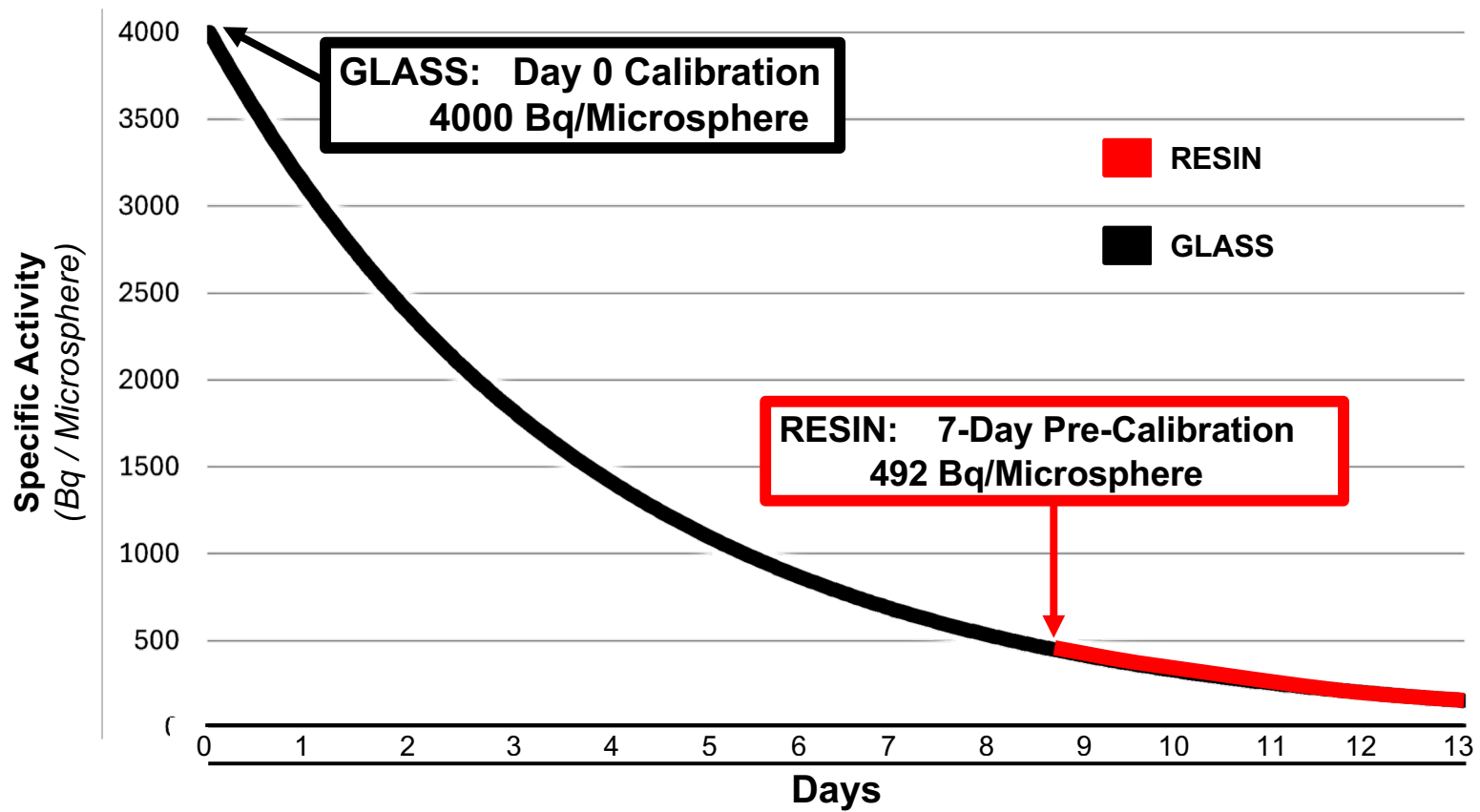


\*More than one (x1) Glass Vial Required

# Practical Max Particles per Device (To Achieve 1 GBq (27 mCi) with a Single (x1) Vial)



## Rate of Activity Loss Decreases Over Time



## Y90 Devices Are Built Differently

	Glass	Resin
Radioisotope attachment	Incorporated into glass matrix	Attached to resin surface
Mean diameters ( $\mu\text{m}$ )	25	$32 \pm 10$
Diameter range ( $\mu\text{m}$ )	20–30	20–60
Microspheres per vial	3 GBq: 0.75 million 20 GBq: 5 million	44 $\pm$ 2.6 Million (5 mL Vial) 27.3 Million (3 mL Vial)
Available standard doses (GBq) at calibration	3, 5, 7, 10, 15, and 20	1.8 GBq $\pm$ 10% (3 mL vial)
Specific activity (Bq per microsphere) at calibration	4,000	68
Specific gravity (g/mL)	3.6	1.125–1.6
Preservation medium	0.6 mL sterile water	5 mL sterile water
Delivery medium	Normal saline	Dextrose 5% water

Ok, But...

How Many Particles Do I Need?

# A Microdosimetric Analysis of Absorbed Dose to Tumor as a Function of Number of Microspheres per Unit Volume in $^{90}\text{Y}$ Radioembolization

J Nucl Med 2016; 57:1020–1026  
DOI: 10.2967/jnumed.115.163444

Alexander S. Pasciak<sup>1,2</sup>, Austin C. Bourgeois<sup>1,3</sup>, and Yong C. Bradley<sup>1</sup>

European Journal of Nuclear Medicine and Molecular Imaging (2020) 47:816–827  
<https://doi.org/10.1007/s00259-019-04588-x>

ORIGINAL ARTICLE



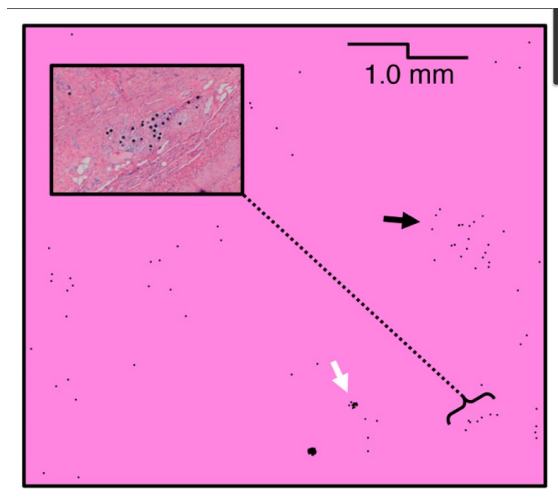
## The number of microspheres in Y90 radioembolization directly affects normal tissue radiation exposure

Alexander S. Pasciak<sup>1</sup> · Godwin Abiola<sup>1</sup> · Robert P. Liddell<sup>2</sup> · Nathan Crookston<sup>3</sup> · Sepideh Besharati<sup>4</sup> · Danielle Donahue<sup>5</sup> · Richard E. Thompson<sup>6</sup> · Eric Frey<sup>7</sup> · Robert A. Anders<sup>4</sup> · Matthew R. Dreher<sup>8</sup> · Clifford R. Weiss<sup>2</sup>

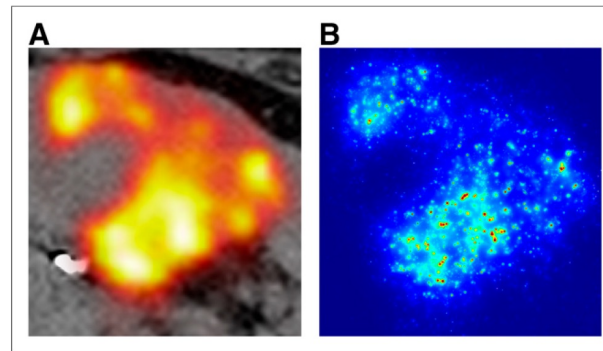
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Alexander S. Pasciak<sup>1,2</sup>, Austin C. Bourgeois<sup>1,3</sup>, and Yong C. Bradley<sup>1</sup>

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**FIGURE 2.** Microscopic deposition of spheres at number density of 50,000 spheres/mL. Small clusters (white arrow) and large clusters (black arrow) are apparent. Monte Carlo process allows for realistic microscopic distribution consistent with experimental findings, including oblique clusters. For comparison, expanded section shows microscopic view of oblique cluster of resin microspheres surrounding arteriole in animal tissue.

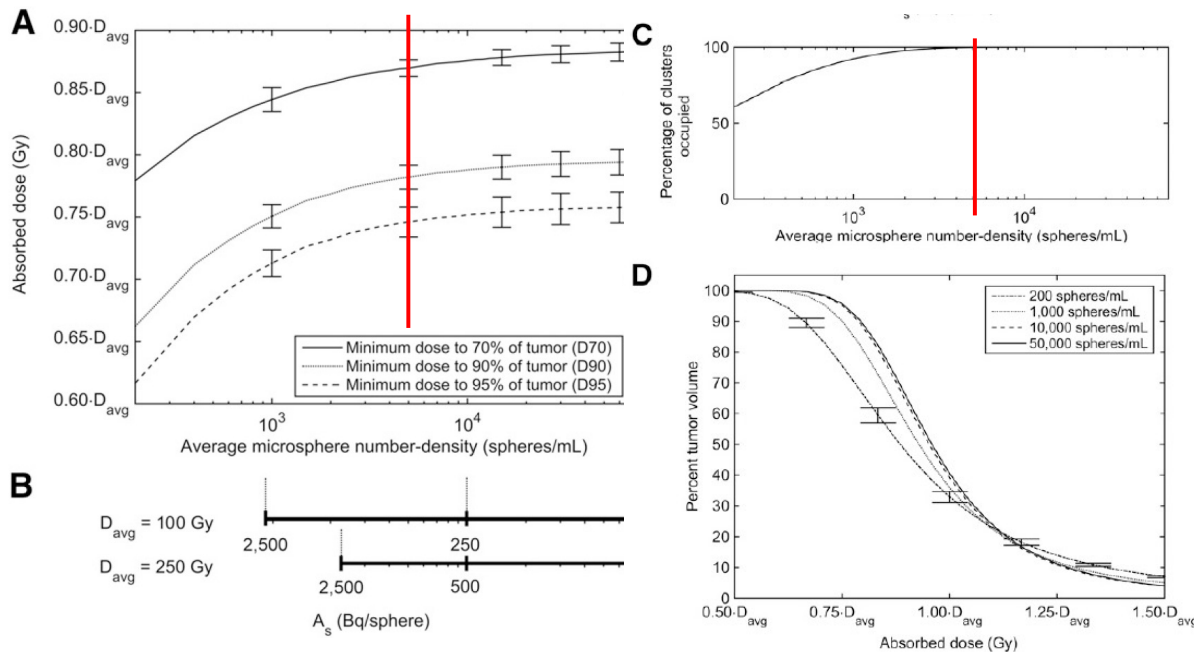


**FIGURE 4.** (A)  $^{90}\text{Y}$  PET/CT of left-lobe tumor reveals peripheral deposition of microspheres. (B) Corresponding microdosimetric absorbed-dose heat map of 100- $\mu\text{m}$  slice after population of tumor volume with average number density of 10,000 spheres/mL.

- Microspheres deposit non-uniformly
- Form cluster-like formations\*

\*Cluster assumption based on explanted animal samples and PET/CT Data\*

# Importance of Particle Density on Minimum Absorbed Dose



- At >5,000 particles/mL, increasing particle density does not meaningfully impact minimum absorbed dose to the tumor nor % of clusters occupied
- In other words:
  - Study recommends **>5,000 particles/mL** to achieve coverage

## A Microdosimetric Analysis of Absorbed Dose to Tumor as a Function of Number of Microspheres per Unit Volume in <sup>90</sup>Y Radioembolization

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@Villalobos\_MD



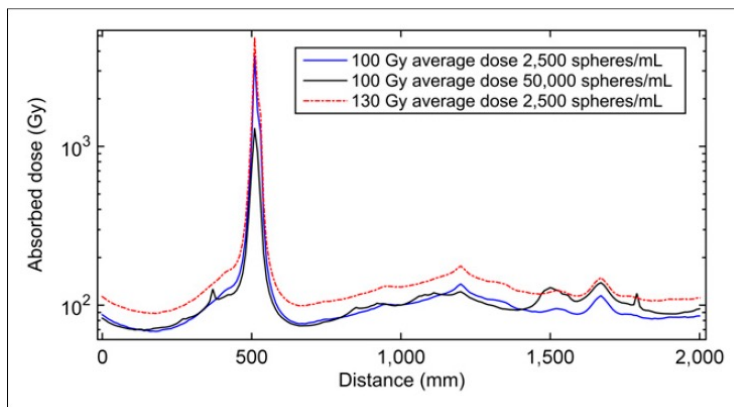
THE UNIVERSITY  
of NORTH CAROLINA  
at CHAPEL HILL

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**FIGURE 7.** Line profile showing absorbed dose across section of tumor with uniform macroscopic deposition. Data for 100-Gy average dose are presented at microsphere-number densities of 50,000 and 2,500 spheres/mL. Characteristic higher peaks and lower troughs at lower microsphere-number densities are apparent. Data are also presented at 2,500 spheres/mL at 130-Gy average absorbed-dose endpoint, consistent with lower limit of recommended treatment activity for radioembolization using glass microspheres. This increase in average tumor-absorbed dose easily overcomes differences due to microsphere-number density.

- Same minimum absorbed dose can be achieved by
  - Increasing Particle Density of lower specific activity particles at lower absorbed dose
- OR
- Keep decreased Particle Density, but use higher specific activity particles with higher absorbed dose

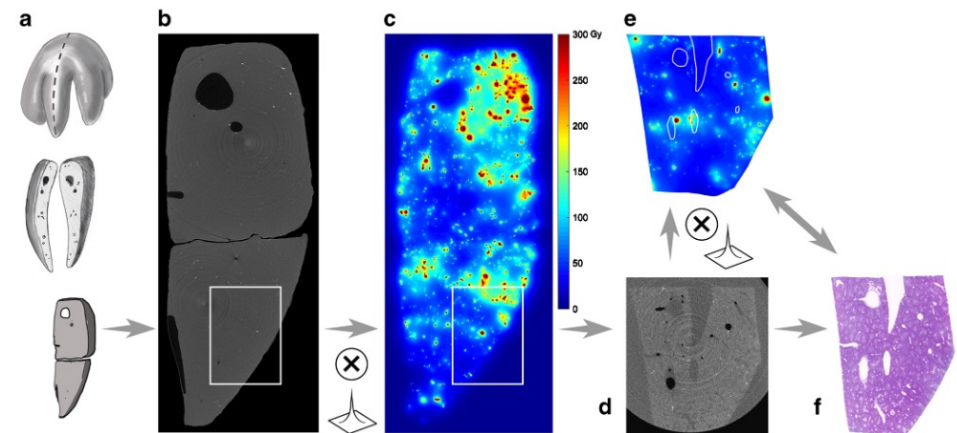
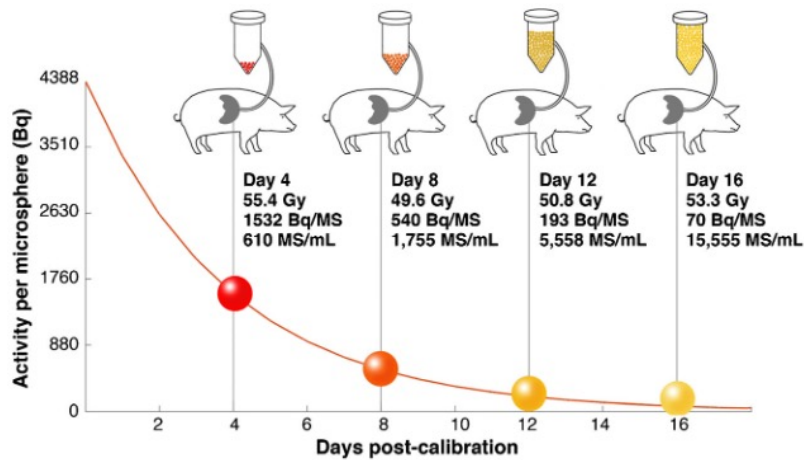
← Applicable to Resin!

← Applicable to Glass!

Glass

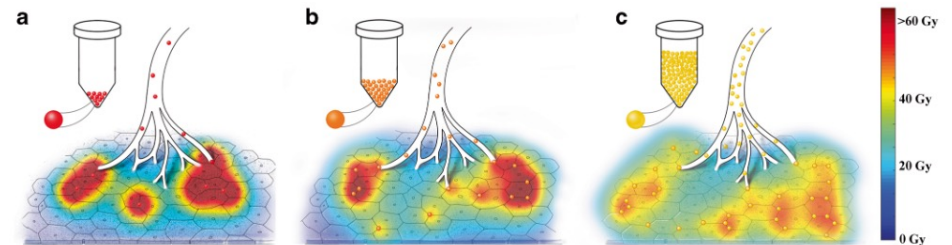
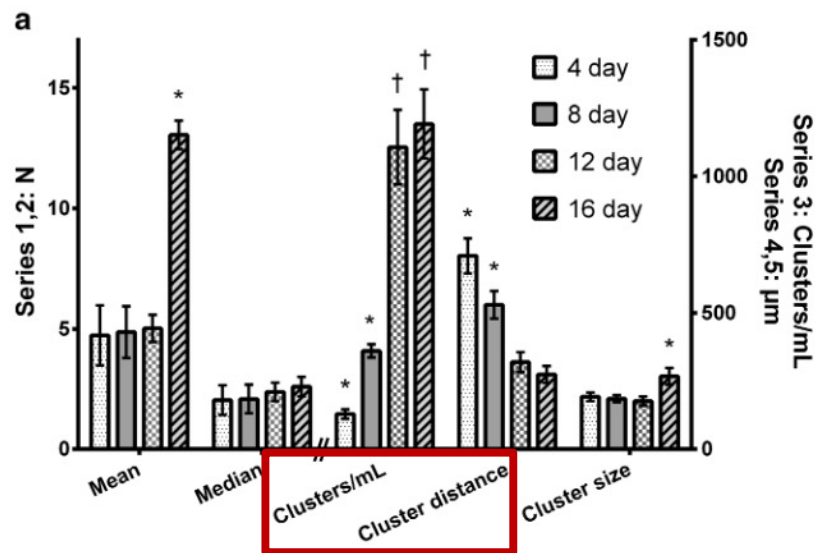
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**Fig. 2** Methodology flowchart. **a** Explanted, fixed livers ( $N = 4$ ) with treated lobe ( $N = 1$  per animal) grossly sectioned to conform to Micro CT field-of-view limitations ( $N = 2-3$  gross sections per animal). **b** Micro CT with re-approximation of sectioned pieces and automated sphere identification. **c** Convolution with DPK to yield 3D microscopic absorbed-dose map. **d** Tissue specimens further sectioned for histopathology and embedded in paraffin ( $N = 10-14$  per treated lobe). Micro CT was performed of paraffin-embedded blocks with automated sphere identification. **e** Convolution with DPK to yield 3D microscopic absorbed-dose map of paraffin-embedded blocks. **f** Correlation of microscopic absorbed dose with histopathology

# Lower Specific Activity = Improved Absorbed-Dose Homogeneity



Glass Cluster/mL & Cluster Distance plateaus around ~5,500(?) microspheres/mL

Table 2 Glass microsphere cluster data. *N* is the number of glass microspheres per cluster

	4 day	8 day	12 day	16 day
Avg MS/mL	610.2	1755.1	5558.1	15555.6
Mean ( <i>N</i> )	4.73 (3.50–5.98)	4.87 (3.80–5.95)	5.02 (4.47–5.59)	13.05 (12.40–13.51)*
Median ( <i>N</i> )	2.04 (1.44–2.62)	2.09 (1.50–2.68)	2.38 (1.98–2.77)	2.60 (2.20–2.98)
Max ( <i>N</i> )	650	709	807	6272
Clusters per mL	129.0 (111.9–146.1)*	360.4 (336.1–383.9)*	1107.2 (972.1–1241.8)†	1192.0 (1067.7–1316.3)†
Distance ( $\mu\text{m}$ )	708.3 (644.8–771.8)*	529 (479.5–579.5)*	319.1 (282.4–355.7)†	274.1 (243.5–304.7)†
Size ( $\mu\text{m}$ )	192.0 (176.2–207.2)	186.4 (171.9–198.0)	176.2 (159.5–192.4)	267.8 (236.6–297.5)*
Percentage <i>N</i> > 10	7.3%	9.25%	8.19%	17.1%*
Percentage <i>N</i> > 50	1.1%	0.96%	0.95%	4.6%*



## A Microdosimetric Analysis of Absorbed Dose to Tumor as a Function of Number of Microspheres per Unit Volume in <sup>90</sup>Y Radioembolization

Alexander S. Pasciak<sup>1,2</sup>, Austin C. Bourgeois<sup>1,3</sup>, and Yong C. Bradley<sup>1</sup>  
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ORIGINAL ARTICLE



The number of microspheres in Y90 radioembolization directly affects normal tissue radiation exposure

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- There is a **MINIMUM** particle density required to get the absorbed dose coverage you need
  - Maybe >5,000 microspheres/mL?
- Higher particle density improves absorbed-dose homogeneity
  - Increases minimum absorbed dose in all the angiosome tissue
  - Theoretically increases toxicity risk in normal tissue
    - Not an issue in Segmentectomy, but maybe in lobar?

All this explains why Glass has higher dose thresholds than Resin!

So...  
How much PD do I need?

Min: >5,000 particles/mL

Ideal vs Max: ??? Data is Evolving...

# Real World Clinical Data

> Eur J Nucl Med Mol Imaging. 2025 May 22. doi: 10.1007/s00259-025-07334-8. Online ahead of print.

## The relationship between yttrium-90 glass microspheres specific activity, particle density and treatment outcomes in HCC and mCRC

Marnix G E H Lam <sup>1</sup>, Etienne Garin <sup>2</sup>, Kirk D Fowers <sup>3</sup>, Armeen Mahvash <sup>4</sup>, Siddharth A Padia <sup>5</sup>, Riad Salem <sup>6</sup>

**Results:** No efficacy relationship was found relative to treatment week for TARGET or EPOCH. mRECIST ORR in TARGET for weeks 1 and 2 were 74/125 (59.2%) and 55/84 (65.5%), and by RECIST 1.1 in EPOCH were 54/142 (38.0%) and 15/43 (34.9%), respectively ( $p > 0.05$ ). Median OS for TARGET weeks 1 and 2 were 21.4 and 20.3 months ( $p = 0.07$ ), and in EPOCH were 14.9 and 16.4 months, respectively ( $p = 0.37$ ). No difference in the TARGET primary endpoint of hyperbilirubinemia was noted for weeks 1 and 2, odds ratio 0.64,  $p = 0.59$ . TARGET  $\geq$  grade 3 device-related adverse events (AEs) for weeks 1 (16.8%) and 2 (26.2%) were not significantly different ( $p = 0.11$ ). EPOCH rates of  $\geq$  grade 3 asthenia for weeks 1 (9.2%) and 2 (23.3%) were statistically different ( $p = 0.01$ ).

Higher Glass PD associated with more tiredness?

But No PD is Reported? ☹️

Table 9 EPOCH device-related Adverse Events of interest for week 1 and 2

AEs (n, %)	week 1 (N= 142)	week 2 (N= 43)	p-value <sup>a</sup>
All Grade 3 or 4 AEs <sup>b</sup>	96 (67.6)	31 (72.1)	0.578
Granulocytopenia	36 (25.4)	13 (30.2)	0.525
Abdominal discomfort	12 (8.5)	2 (4.7)	0.527
Anemia	9 (6.3)	4 (9.3)	0.504
Asthenia	13 (9.2)	10 (23.3)	0.014
Gastrointestinal hemorrhage	0	3 (7.0)	0.012
Lymphocyte count decreased	5 (3.5)	3 (7.0)	0.391

<sup>a</sup> By Fisher's exact test

<sup>b</sup> All  $\geq$  grade 3 AEs occurring in  $\geq 5\%$  of patients (either week 1 or week 2)

> Eur J Nucl Med Mol Imaging. 2025 Aug 5. doi: 10.1007/s00259-025-07471-0. Online ahead of print.

## Histopathologic outcomes of hepatocellular carcinoma treated with transarterial radioembolization with yttrium-90 resin microspheres

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$< 0.001$ ) than tumors with incomplete pathologic necrosis. Additionally, more resin microspheres were delivered per cc of tumor tissue in tumors with CPN compared to tumors with incomplete pathologic necrosis (median 78,306 sphere/cc (IQR, 55,288 - 125,009 sphere/cc) vs. median 45,224 sphere/cc (IQR, 23,700 - 52,594 sphere/cc);  $P = 0.006$ ). A statistically significant difference in tumor volume was found between tumors

**Conclusion:** Among HCC patients who underwent 90Y-TARE with resin microspheres, 73% achieved complete pathologic necrosis. All tumors with a mean tumor absorbed dose  $\geq 433$  Gy achieved CPN.

Higher Resin PD associated with more CPN

But focus of study is on achieving the Dose Thresholds!



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# Real World Clinical Data

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## Achieving Complete Pathologic Necrosis in Hepatocellular Carcinoma Treated with Radiation Segmentectomy before Liver Transplantation: A Comprehensive Glass Microsphere Analysis

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**Conclusion:** CPN was predicted by a SA of  $\geq 570$  Bq, total angiosome dose of  $\geq 439$  Gy, tumor dose of  $\geq 844$  Gy, and angiosome hepatic parenchymal dose  $\geq 420$  Gy. A total angiosome PD of  $\geq 11.4 \times 10^3$ /ml was associated with CPN in tumors treated with SA  $< 570$  Bq. Both single-compartment and multi-compartment dosimetry had similar performance when optimized per the identified thresholds.

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## Optimizing <sup>90</sup>Y particle density improves outcomes after radioembolization

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**Results:** As more particles were delivered, doses on <sup>90</sup>Y SPECT/CT became more uniform throughout the treatment volume: tumor and liver doses became more similar ( $p=0.04$ ), and microscopic cold spots between particles disappeared. For hypervascular tumors (tumor-to-normal ratio  $> 2.6$  on MAA scan), delivering fewer particles ( $< 6000$  particles/cm<sup>3</sup> treatment volume) was associated with better LPFS ( $p=0.03$ ). For less vascular tumors (tumor-to-normal ratio  $< 2.6$ ), delivering more particles ( $> 6000$  particles/cm<sup>3</sup>) was associated with better LPFS ( $p=0.02$ ). In matched pairs of patients, using the optimal particle density resulted in improved overall survival (11.5 vs 6.8 months,  $p=0.047$ ), compared to using suboptimal particle density. Microdosimetry resulted in better predictions of LPFS ( $p=0.03$ ), and overall survival ( $p=0.02$ ), compared to conventional dosimetry.

TLDR:

Particle Density Matters!

...but it is nuanced...

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## Summary

# Particle Density Goals:

Minimum: >5,000 particles/mL

Ideal vs Max: ?Unknown? (focus on Dose Threshold)

## Don't Forget PD Theory Fundamentals!

Y90 Devices are **Different**

Higher PD + Lower SA = Better Theoretical Coverage, requires **Lower** Dose Thresholds

Lower PD + Higher SA = Worse Theoretical Coverage, requires **Higher** Dose Thresholds

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