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Dosimetry Needs and Methods for SRT: Yttrium-90

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Disclosures

- Yuni Dewaraja is a consultant for MIM Software, Inc.

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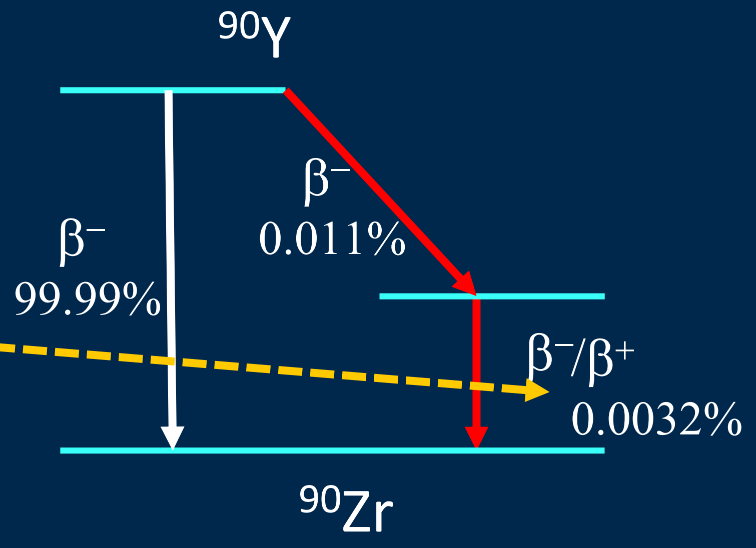
^{90}Y Imaging/Dosimetry

- Almost pure beta emitter
  - E_{ave}= 0.94 MeV; mean tissue penetration=2.5 mm; $T_{1/2}$=64 h
  - Betas can eradicate tumor cells that are not directly targeted
  - ^{90}Y microsphere RE, ^{90}Y ibritumomab, ^{90}Y DOTATOC PRRT
- Imaging: complex
  - SPECT via bremsstrahlung
  - PET via very low probability positron



- Absorbed dose calculation: relatively easy
  - Under certain conditions can assume local energy deposition
    - lack of γ and range of β relative to SPECT/PET resolution

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Bremsstrahlung imaging

- Challenges
  - Inefficient: < 4% of β tissue interactions give photons > 50keV
    - Not suitable for pre-therapy tracer imaging
  - Continuous bremsstrahlung spectrum extending to 2.1 MeV
    - Penetration (downscatter) of high energy photons
  - Tissue dependent bremsstrahlung generation probabilities
    - Yield not same in tissue vs. bone
- Internal bremsstrahlung
    - Photons emitted during the β decay process itself

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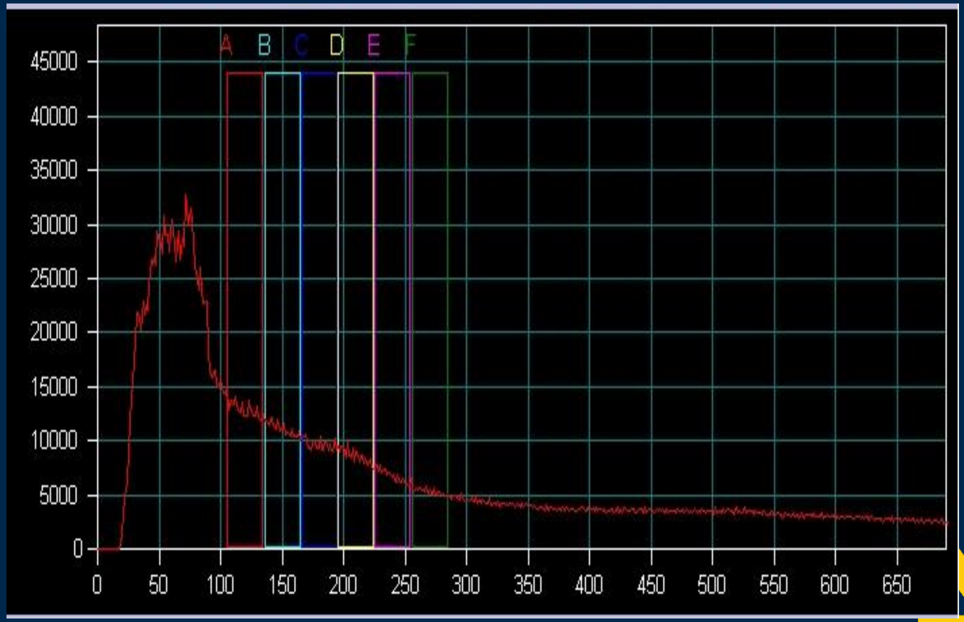
Bremsstrahlung SPECT Imaging: Guidelines

- HE collimator
- Acquisition window
  - Within 100 – 500 keV
    - 100 – 200 keV (avoids x-ray, optimal primary-to-scatter)

- Single (narrow) window vs. multi window reconstruction model

- Model/Monte Carlo based SC
  - Energy window based not suitable with continuous spectrum



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Bremsstrahlung SPECT/CT Reconstruction with Scatter Correction

- **Model based**

  Minarik et al, Phy Med Biol 2008; Rong et al, Med Phys 2012

  – Pre-calculated scatter kernels

- **Fully Monte Carlo**

  Elschot et al, JNM 2013

  – MC reconstruction with 'on the fly' calculation of SC and AC

- **Monte Carlo generated scatter estimate**

  Dewaraja et al, Med Phys 2017

  – Less computationally demanding than fully MC

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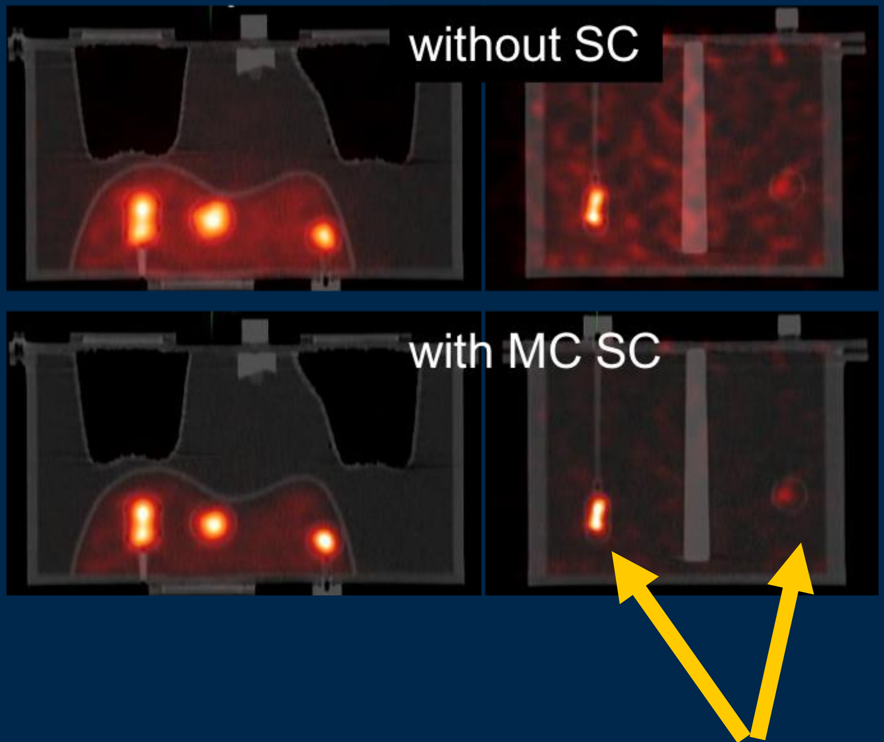
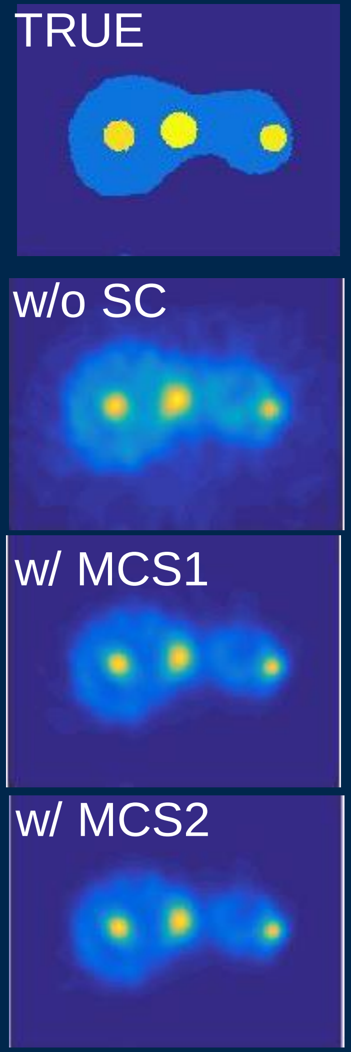
Y-90 SPECT: Impact of scatter correction

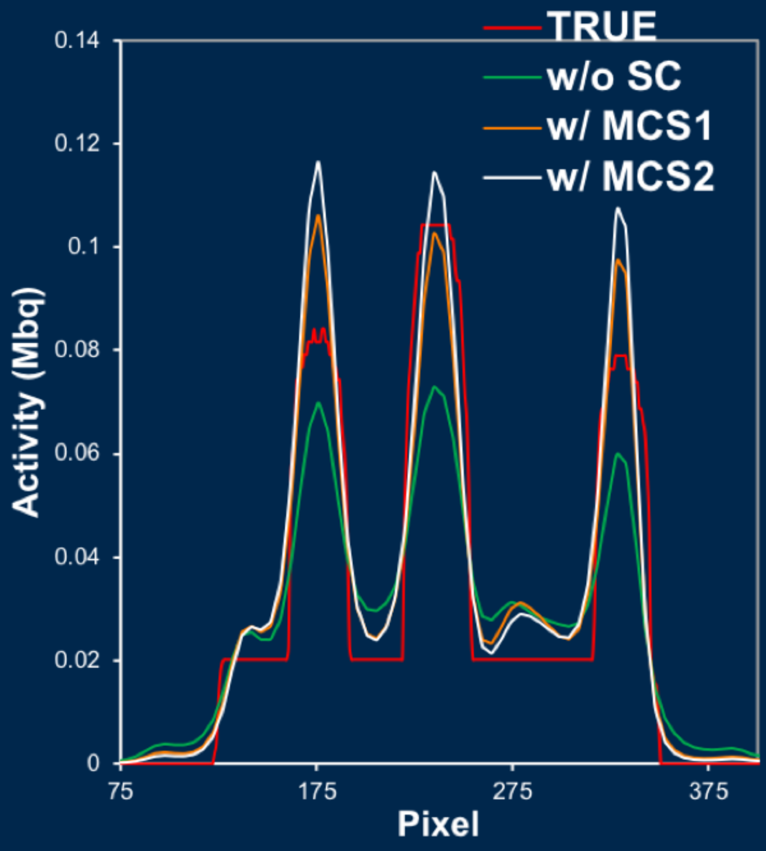
- Improved visibility



Visibility of low uptake objects important for detecting extra hepatic deposition

- Improved contrast/quantification





Dewaraja et al, Med Phys 2017, 6364-76

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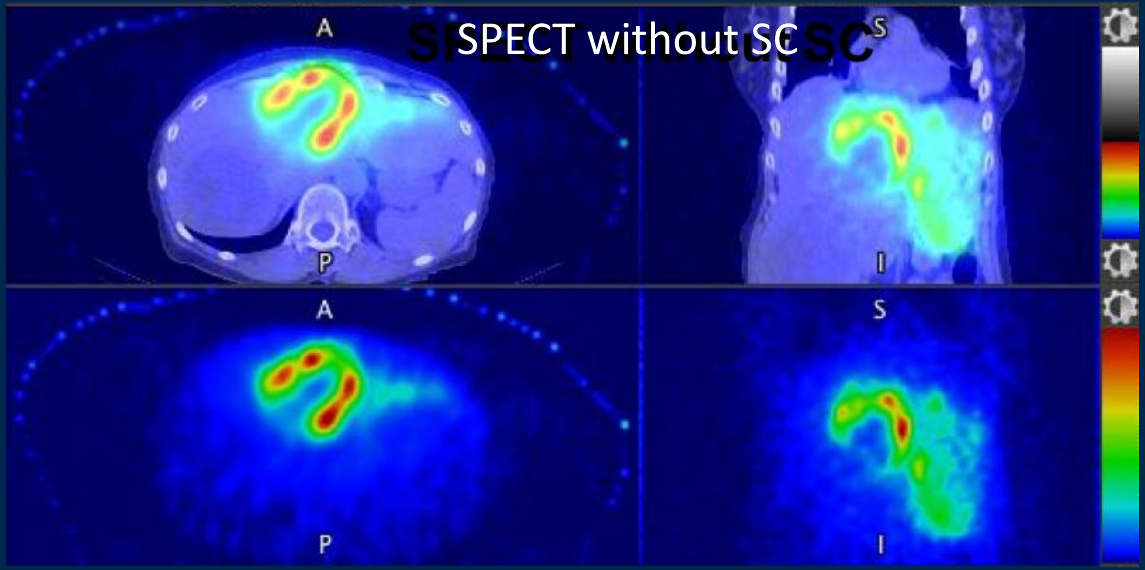
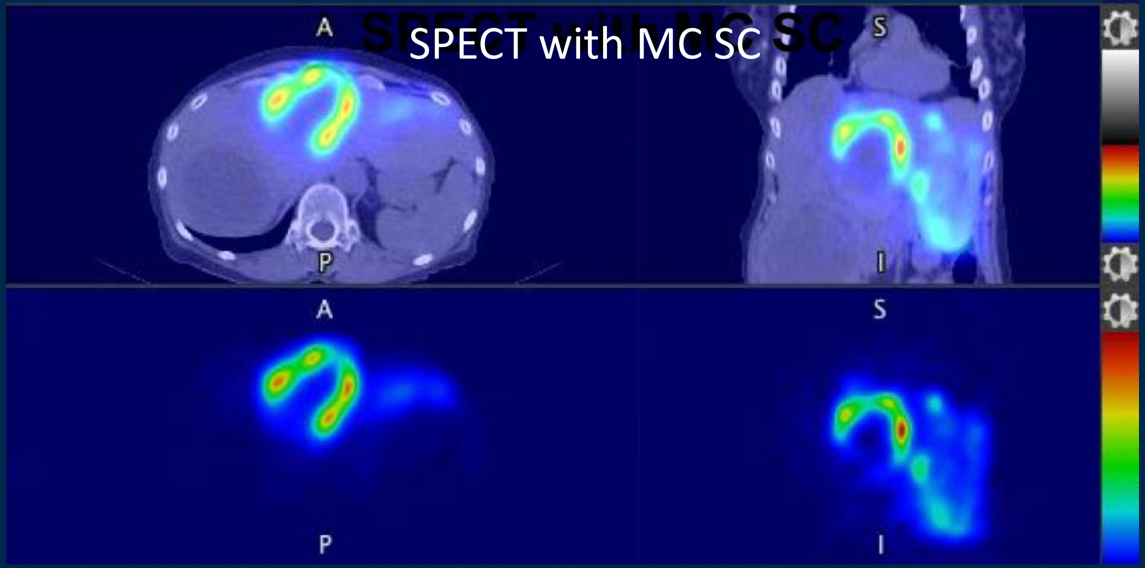
Impact of scatter correction:RE patient example





In 11 lesions (5 patients) without and with MC SC
Mean lesion uptake was 4.9 vs. 7.1 MBq/mL
Mean normal liver uptake was 1.6 vs. 1.5 MBq/mL
Lesion-to-liver uptake ratio was 2.7 vs. 4.3 (P=0.040)

Dewaraja et al, Med Phys 2017, 6364-76

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Tissue dependent bremsstrahlung generation probabilities

- Bremsstrahlung yield $\propto Z^2$
  - Same activity in different tissue will produce different number of photons
  - Impact quantification of heterogeneous tissue

- Can account for this by incorporating probabilities in the reconstruction system matrix and using CT to determine voxel composition

- Yield in bone is 1.5 - 2 times that of tissue

Lim, Fessler, Brooks, Wilderman, Dewaraja . Submitted to PMB and presented at SNMMI Annual Meeting 2017

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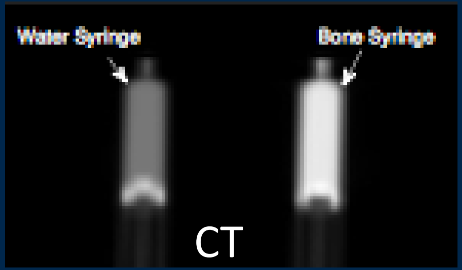
Demonstrating tissue dependent bremsstrahlung yield

Same Y-90 conc in 2 syringes with bone equiv. liquid (potassium salt) & water

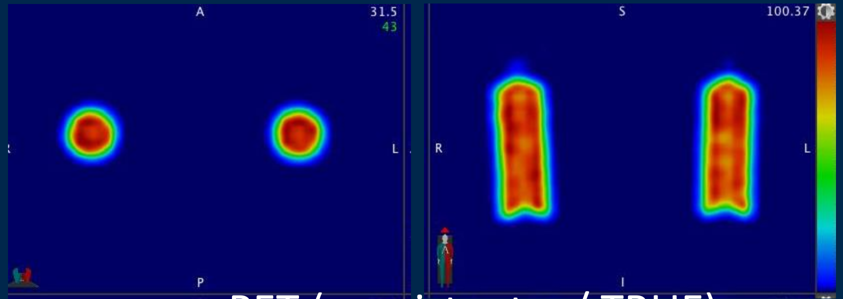
On SPECT/CT camera



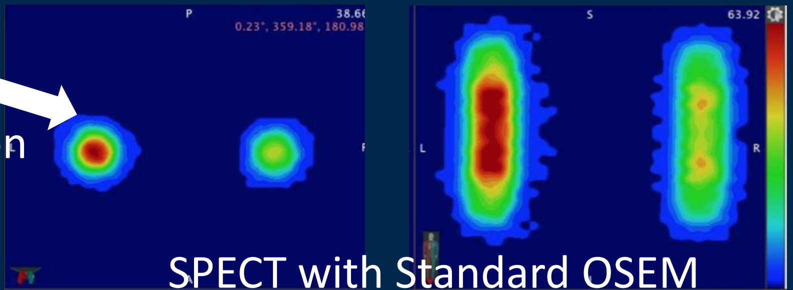
CT

Bone 1.5 times more intense although same Y-90 concentration

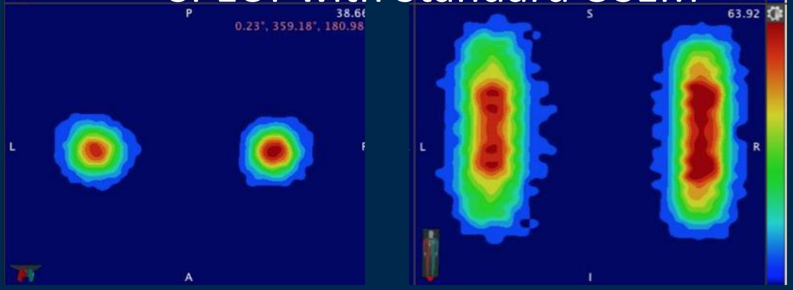
Bone Water Bone Water



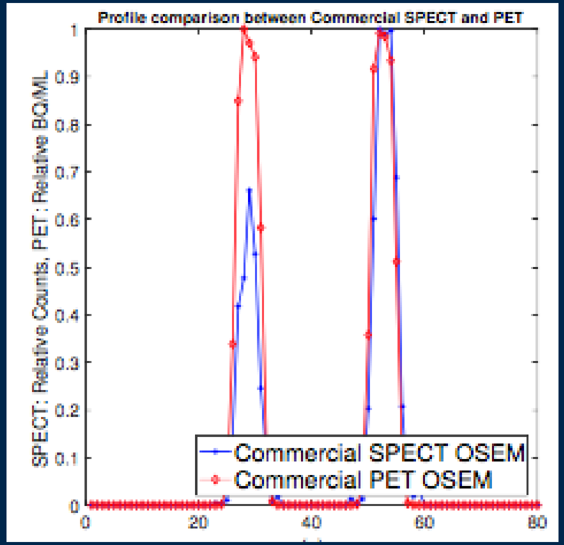
PET (consistent w/ TRUE)

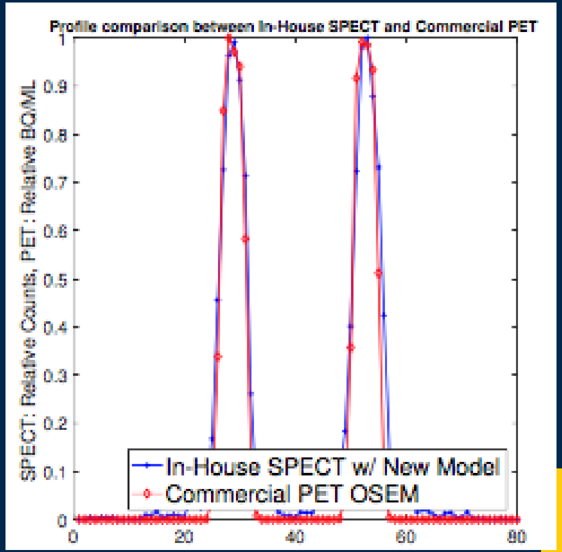


SPECT with Standard OSEM



SPECT with new system matrix (consistent w/ TRUE)





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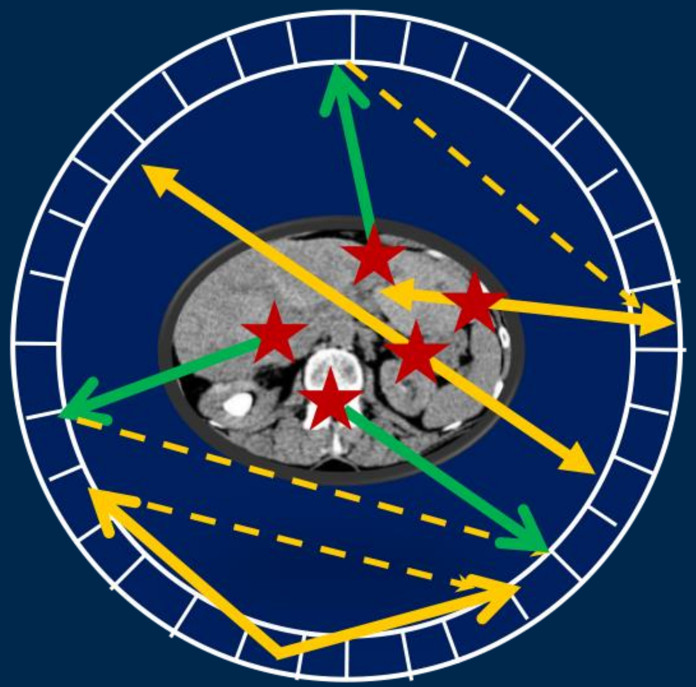
Lim, Fessler, Brooks, Wilderman, Dewaraja . Phys Med Biol 2018 and presented at SNMMI Annual Meeting 2017

Y-90 PET

- Very low probability positron (low true coincidences) in the presence of bremsstrahlung (high random coincidences)

- Poor image quality
  - Improved with time-of-flight



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Y-90 SPECT vs PET

- SPECT: higher visibility lower resol.
- PET: higher resolution, high noise

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Patient specific dosimetry in Y-90 radioembolization

- Need only a single imaging point to get time-integrated activity

- Voxel level dosimetry can be based on local energy deposition

- Pre-therapy 99mTc-MAA SPECT/CT study for better planning ?
  - Currently mostly used to assess extra-hepatic deposition
    - Differences between MAA and microsphere distribution

- Post therapy Y-90 PET and SPECT can be used for
  - Safety, dose verification (immediate prediction of response)
  - Establishing lesion dose – response, normal liver dose-toxicity

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Y-90 RE: Initial results from ongoing study at U Michigan

- Methods to improve Y-90 post therapy imaging
  - Dewaraja et al. Improved quantitative 90Y bremsstrahlung SPECT/CT reconstruction with Monte Carlo scatter modeling. *Med Phys. 2017;44:6364-6376.*
  - Lim H, Dewaraja Y, Fessler J. A PET reconstruction formulation that enforces non-negativity in projection space for bias reduction in Y-90 imaging. *Phys Med Biol 2018*

- Dosimetry based on Tc-MAA SPECT/CT, Y-90 SPECT/CT & PET/CT
  - Patients with HCC or liver mets treated with glass microspheres
  - Radiologist defined lesions, 3D dosimetry using DPM MC code

- Follow up for dose – outcome
  - RECIST, mRECIST, liver function tests

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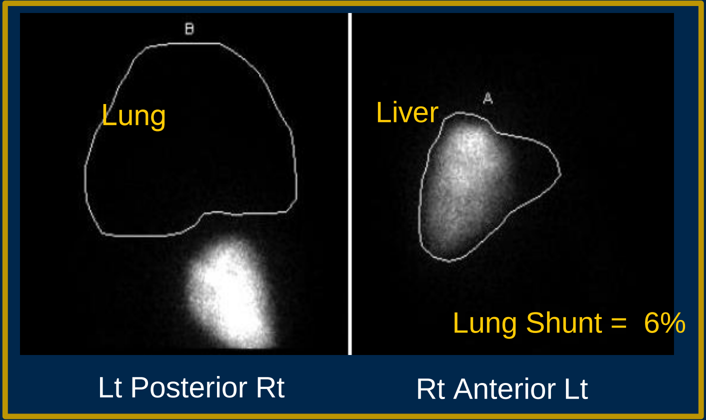
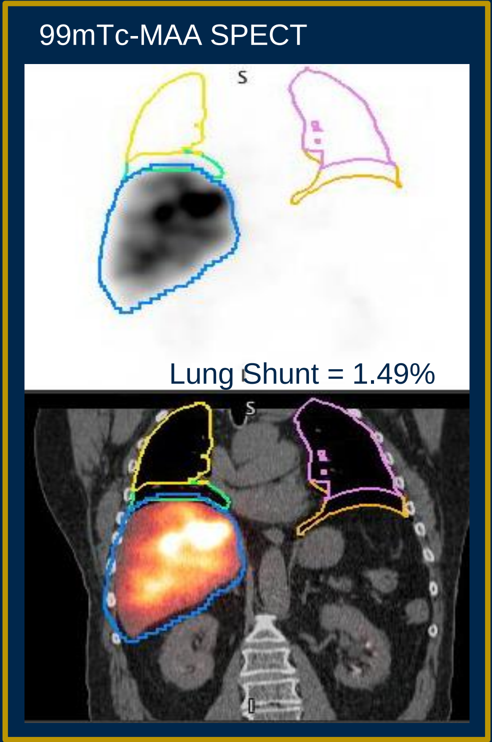
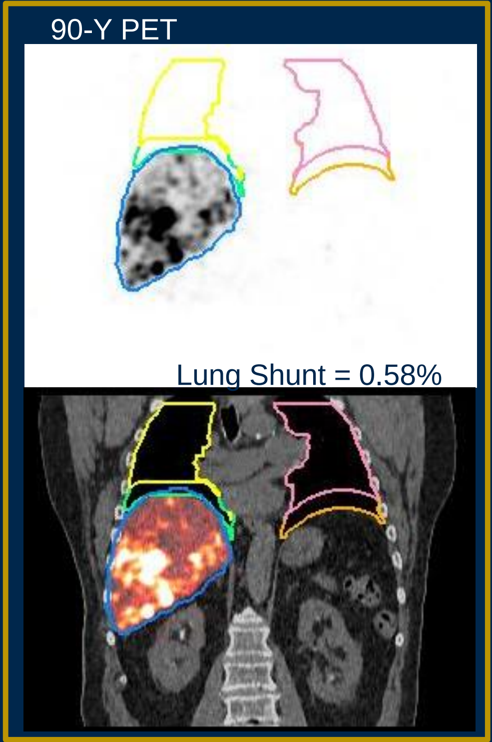
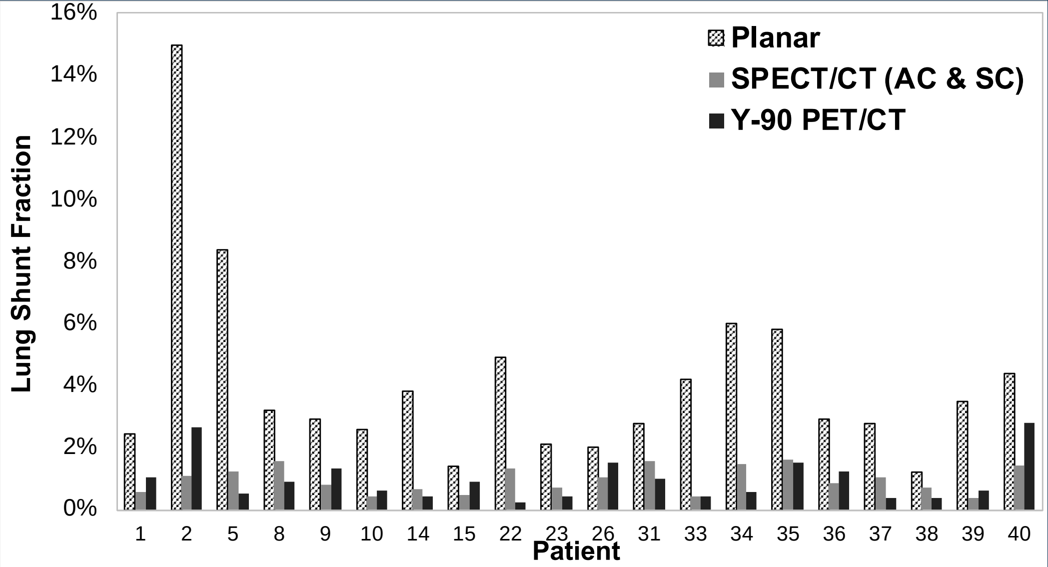
Value of Tc-MAA SPECT/CT for Lung Shunt Estimation

- Planar calculation, used in clinic, overestimates LS
- SPECT/CT based
  - Higher accuracy
  - Auto liver/lung contouring
  - Less variability









Allred et al, Submitted to EJNMMI Research 2018

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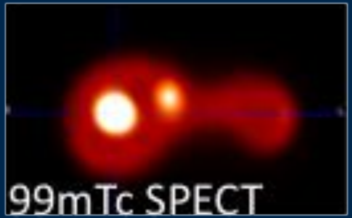
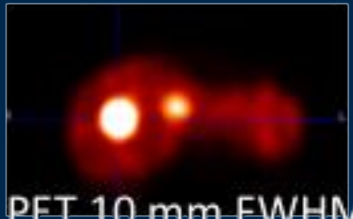
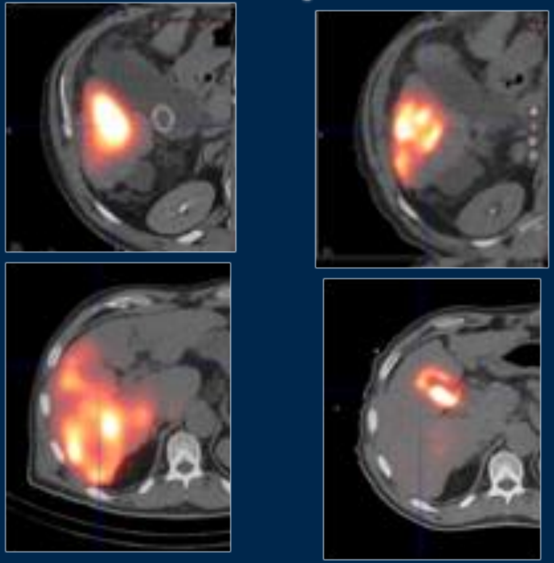
Tc-99m MAA SPECT vs Y-90 PET spatial concordance

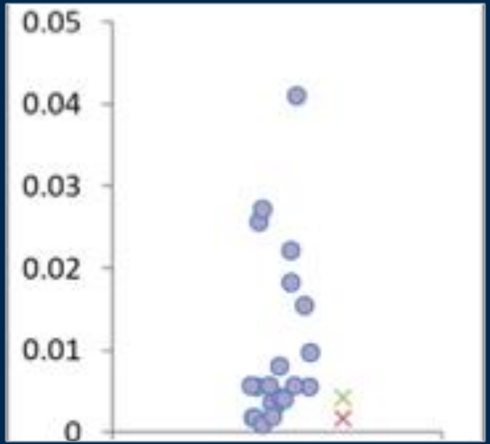
- Phantom: good spatial concordance





- Patients: poor concordance





Mikell et al, presented at EANM Annual Meeting, 2017

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Tc-MAA predicted vs. Y-90 delivered mean absorbed dose

Mikell et al, EANM Annual Meeting 2017

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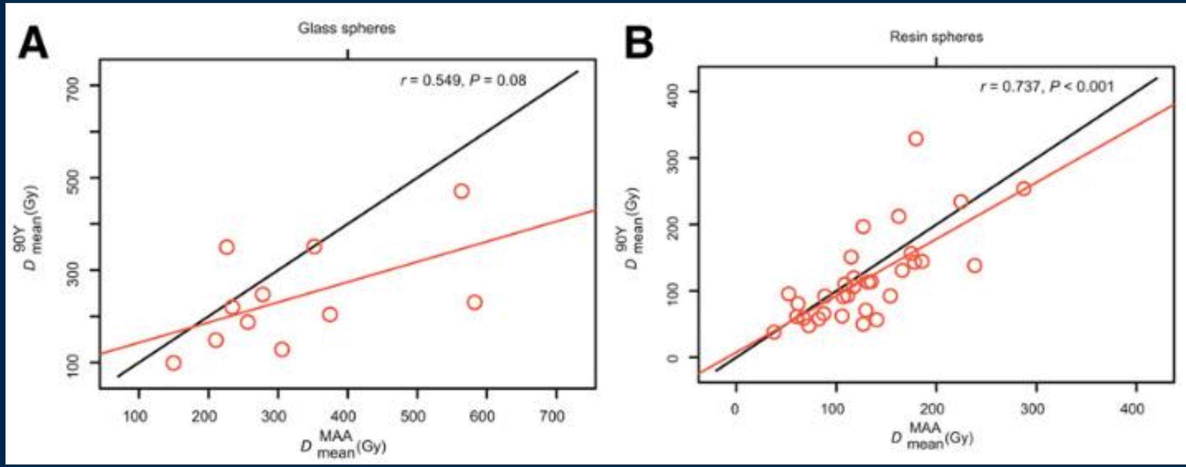
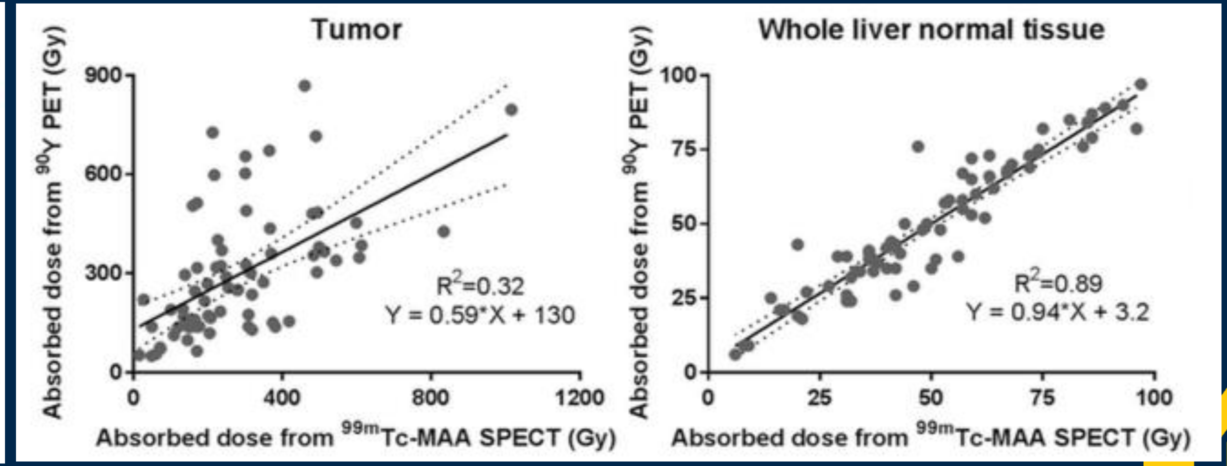
Past studies looking at Tc MAA – Y90 concordance

- Mixed conclusions

	Spatial granularity	registration	device	Analysis	90Y	Cath tip info?	
Wondergem et al JNM 2013	segment	?	resin	BlandAlt	SPECT	Y	Poor correlation
Gnesin et al JNM 2016	tumor	?	mix	ccc of dose ratio mean, D70	PET	N	moderate
Kneusarek et al TCRT 2010	Voxel-level	CT-CT	resin	Correlation coefficient, L2 norm	SPECT	N	Poor to highly correlated



Gnesin et al, JNM 2016



Haste et al, J Vasc Interv Radiol 2017

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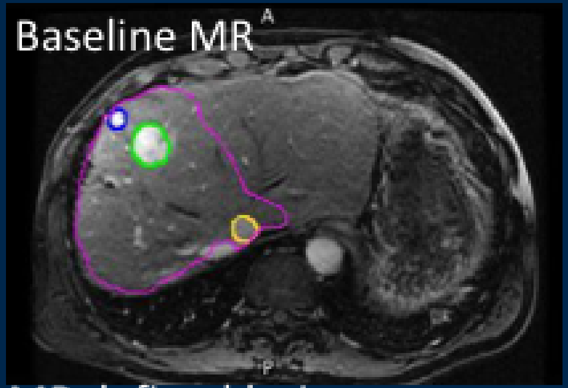
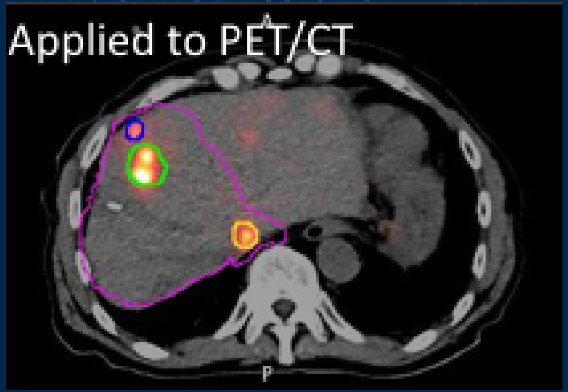
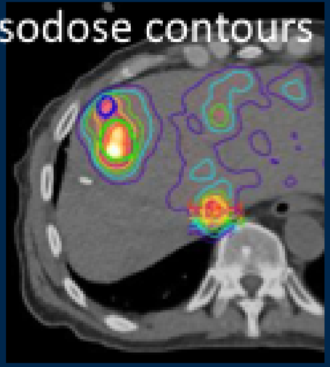
Patient example: Y-90 PET/CT based dosimetry

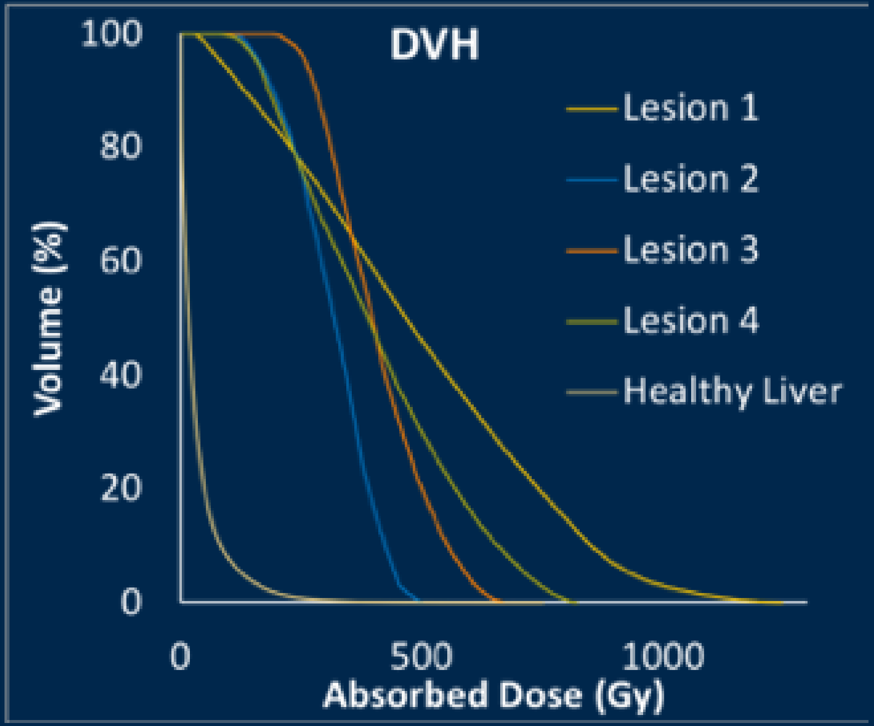


MR defined lesions
Applied to PET/CT



Isodose contours





Name	Volume cc	Max Dose (Gy)	Min Dose (Gy)	Mean Dose (Gy)	SD
Lesion 1	11	1256	23	488	268
Lesion 2	1	504	99	313	85
Lesion 3	2	674	177	407	102
Lesion 4	5	825	69	404	175
Healthy Liver	1140	780	0	33	49

RECIST
Criteria:SD

Follow up

mRECIST
Criteria: PR

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Lesion Dose-Response

Absorbed dose significantly ($p < 0.05$) associated with shrinkage. Median absorbed dose among responding and non-responding tumors was 209 and 130 Gy ($p=0.024$) with RECIST and 271 and 97 Gy ($p=0.004$)with mRECIST criteria.

Dewaraja et al, to be presented at SNMMI 2018

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^{90}Y RE with glass microspheres: past dose-response studies

- Threshold lesion dose predictive of response around 100-500 Gy

- Mostly based on predicted doses from Tc-MAA SPECT/CT
  - Garin, JNM 2012 (predictive of survival in HCC); Chiesa, EJNM 2015 (predictive of response in HCC); Kokabi,J Vasc Interv Radiol, 2014 (predictive of survival in HCC)

- Post therapy imaging based
  - Y-90 Bremsstrahlung SPECT/CT based
    - Strigari et al, JNM 2010 (predictive of response in HCC)
  - Y-90 PET/CT based
    - Fowler et al, Cardiovasc Interv Radiol, 2016(dose-response for CRC only); Srinivas et al, Front in Oncol, 2014 (HCC no dose- response)

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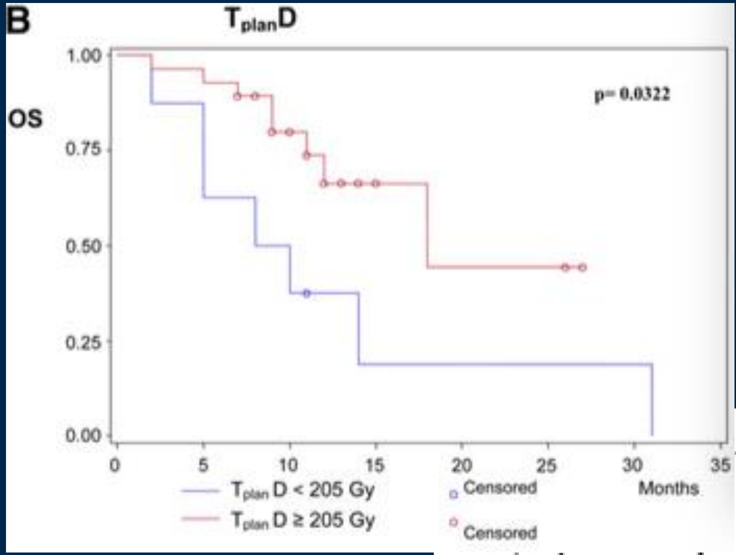
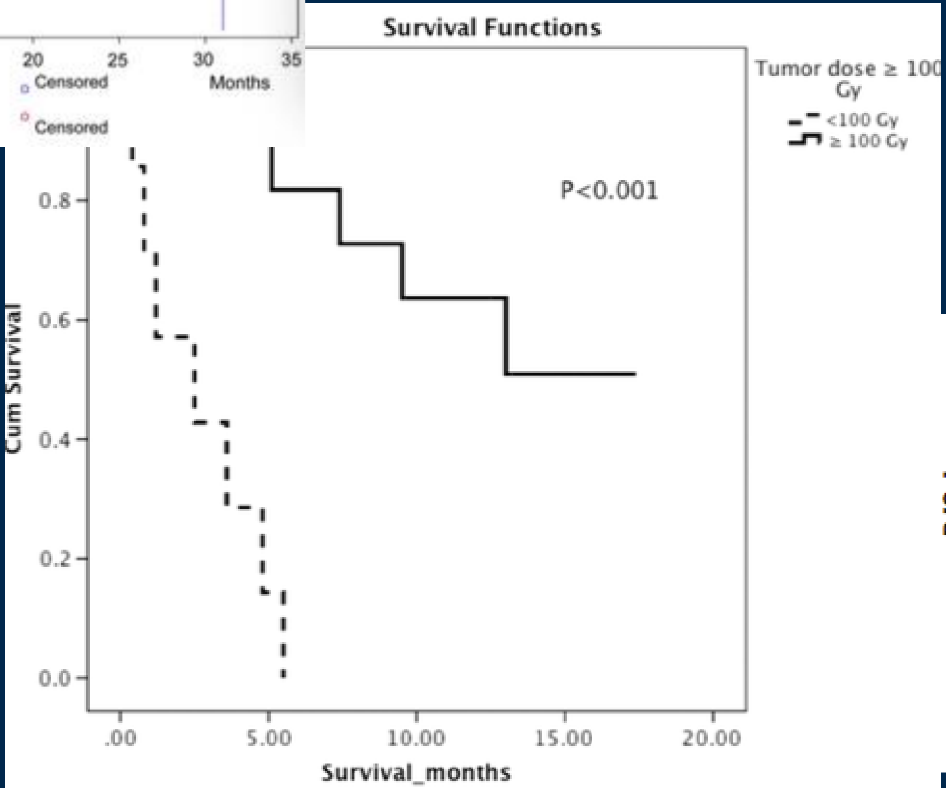
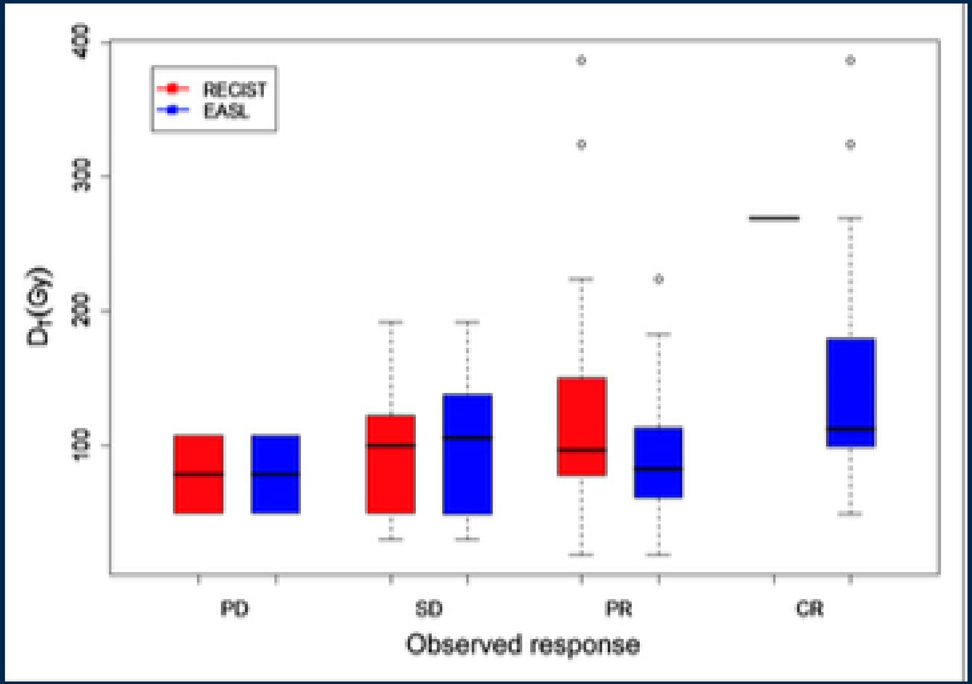
Y-RE: Past dose – response studies



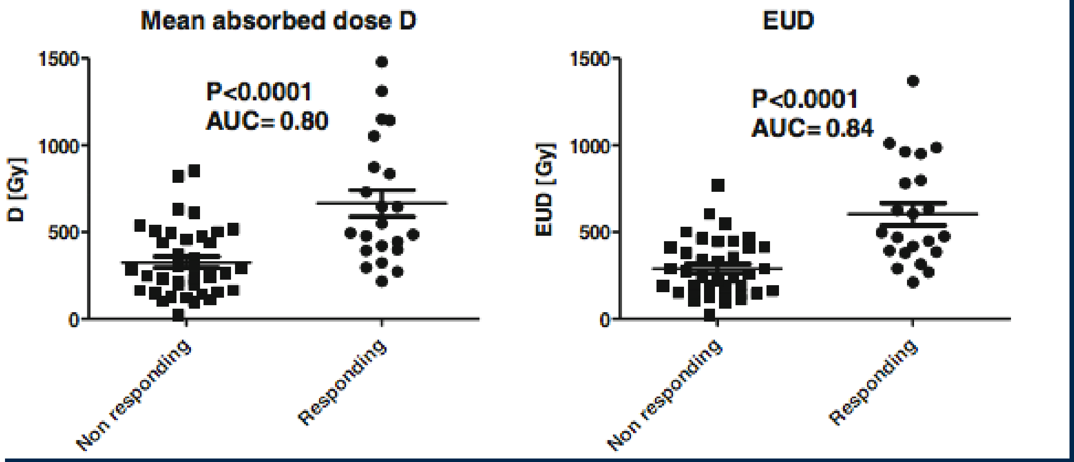
Garin et al



Kokabi et al



Strigari et al



Chiesa et al

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