Personalized Kidney Dosimetry for Y-90 DOTATOC Radionuclide Therapy

M. T. Madsen[1], Y. Menda[1], J. J. Sunderland[1],
D. Bushnell[1], M. K. Schultz[1], G. L. Watkins[1],
M. E. Martin[2], T. M. O'Dorisio[3], M. S. O'Dorisio[2]

[1]Radiology, University of Iowa, Iowa City, IA,
[2]Pediatrics, University of Iowa, Iowa City, IA,
[3]Internal Medicine, University of Iowa, Iowa City, IA

Disclosures & Acknowledgements

- No Financial Disclosures
- ^{68}Ga DOTATOC & ^{90}Y DOTATOC are investigational agents. Studies presented here are performed under a physician sponsored investigational new drug (IND) approval.
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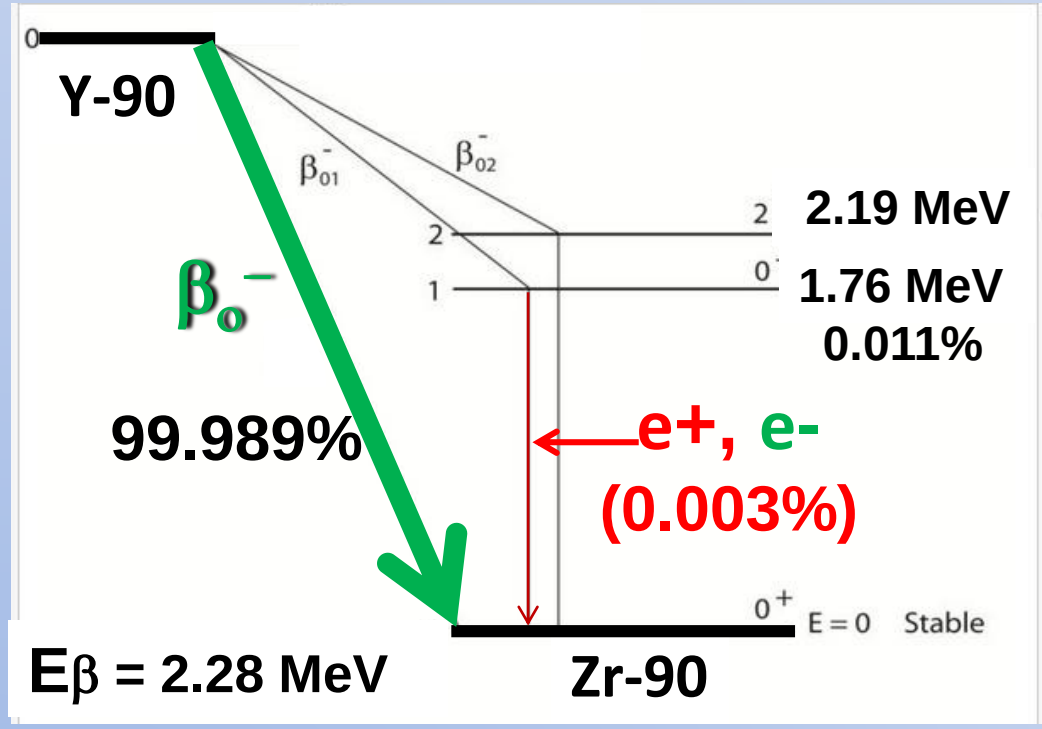
Introduction

- At the University of Iowa, the **Image Guided Diagnosis and Therapy of Neuroendocrine Tumors** project uses ^{68}Ga DOTATOC to determine the eligibility of subjects to receive 3 therapeutic cycles of ^{90}Y DOTATOC.
- The kidneys are the critical organ and limit the amount of ^{90}Y DOTATOC that can be safely administered.
- Sequential bremsstrahlung SPECT/CT at 5, 24, 48 & 72 hours determines kinetics while PET/CT imaging at 5 hours determines absolute kidney activity.

Y-90 Decay: β^- & pair production

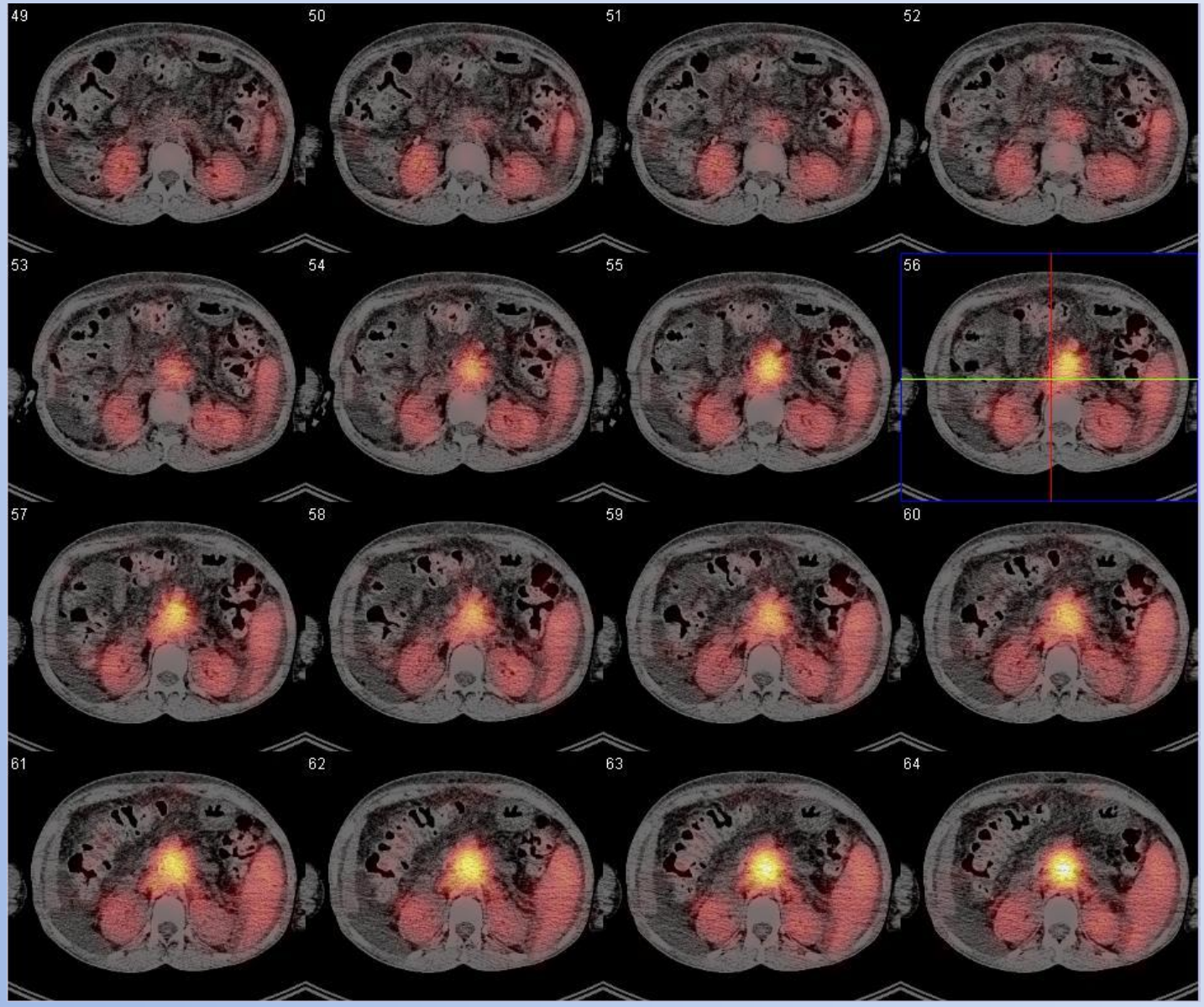


- 64 hour life
- Emits 2.28 MeV beta minus (mean energy: 0.934 MeV)
- Bremsstrahlung interactions with tissue produce sufficient x-rays for SPECT imaging.

- Also has a pair production branch that results in a positron ~ 30/1,000,000 decays.

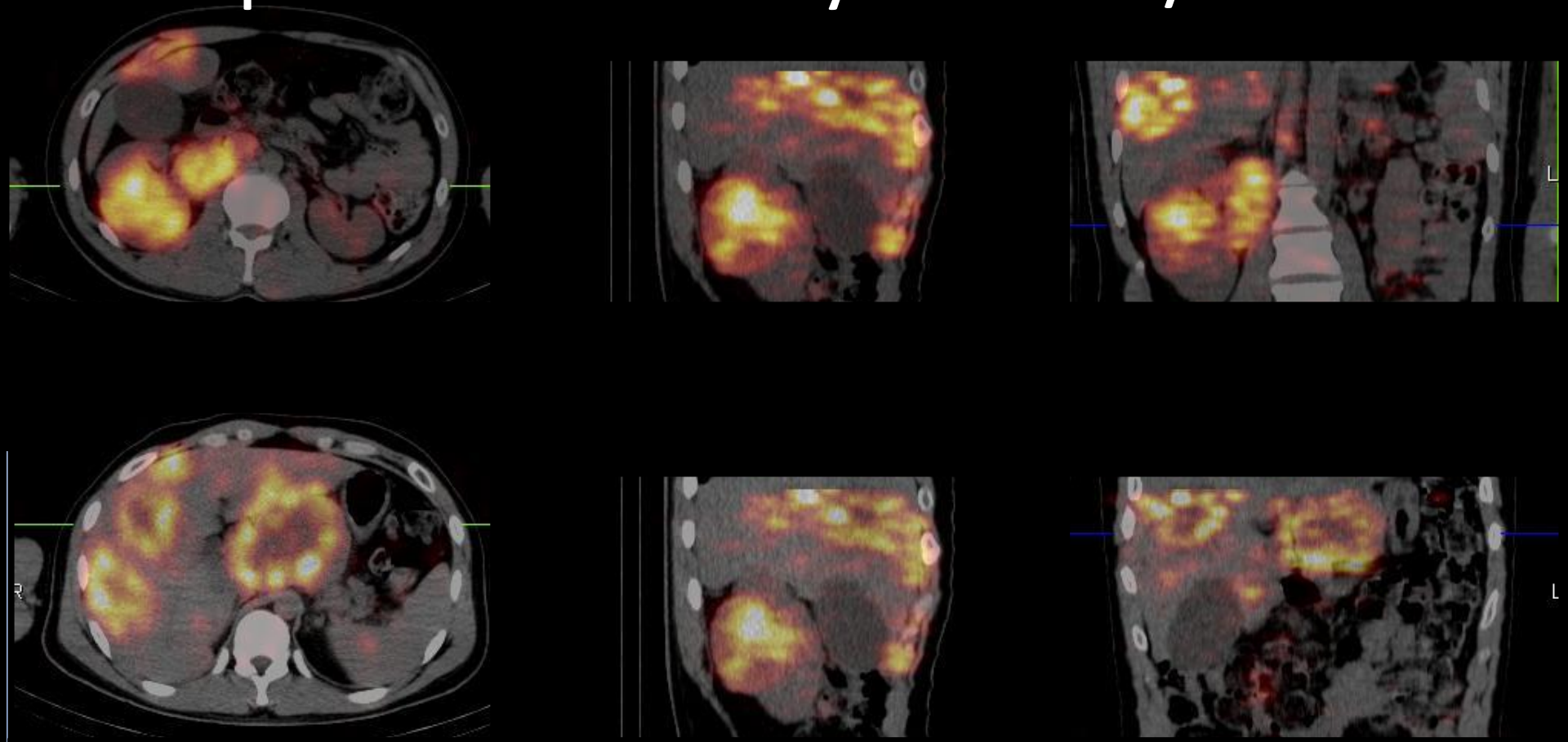
Assaying and PET Imaging of Ytrrium-90: 1>>34ppm>0
RJ Nickles, et al. IEEE MIC, 2004

Y-90 DOTATOC PET/CT Kidney Imaging

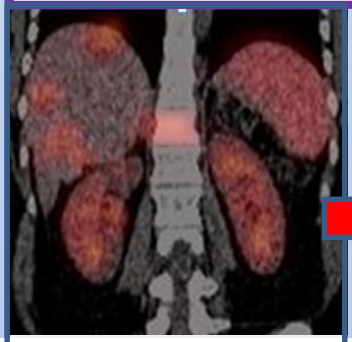


Y-90 DOTATOC PET/CT Tumor Imaging

Y-90 uptake in tumors is easily seen on PET/CT

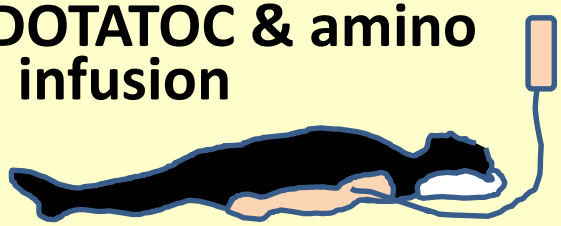


METHODS



^{68}Ga DOTATOC eligibility scan

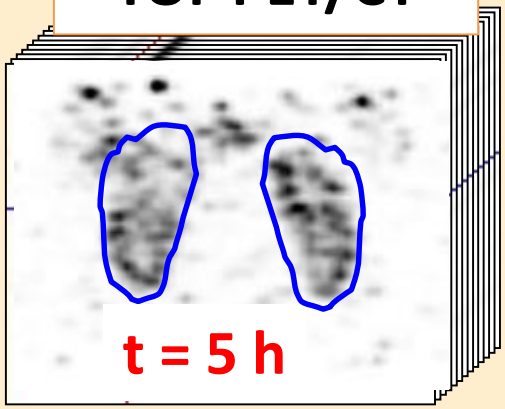
^{90}Y DOTATOC & amino acid infusion



Cycle 1: 4.4 GBq
Cycle 2: <5.6 GBq* (6 weeks)
Cycle 3: <5.6 GBq* (12 weeks)

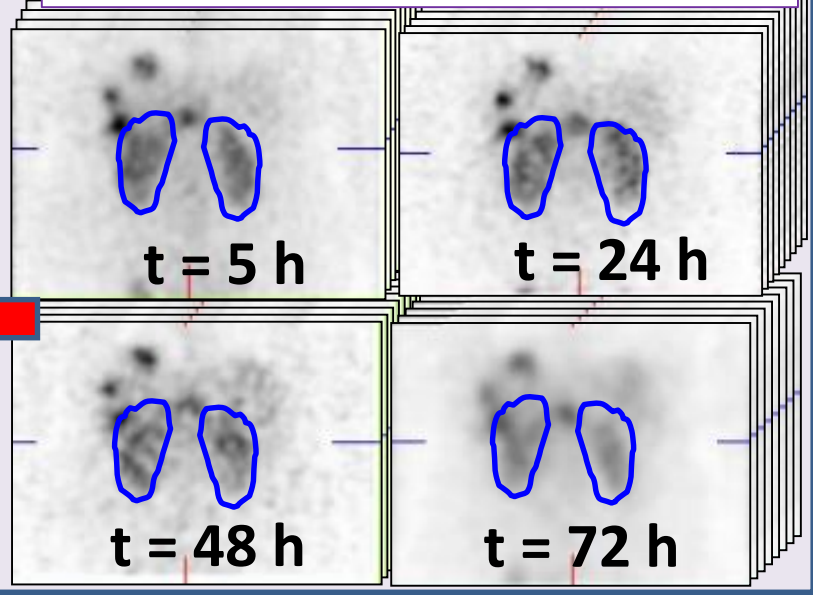
*Activity modified by kidney dose determined from previous treatments to keep below 23 Gy

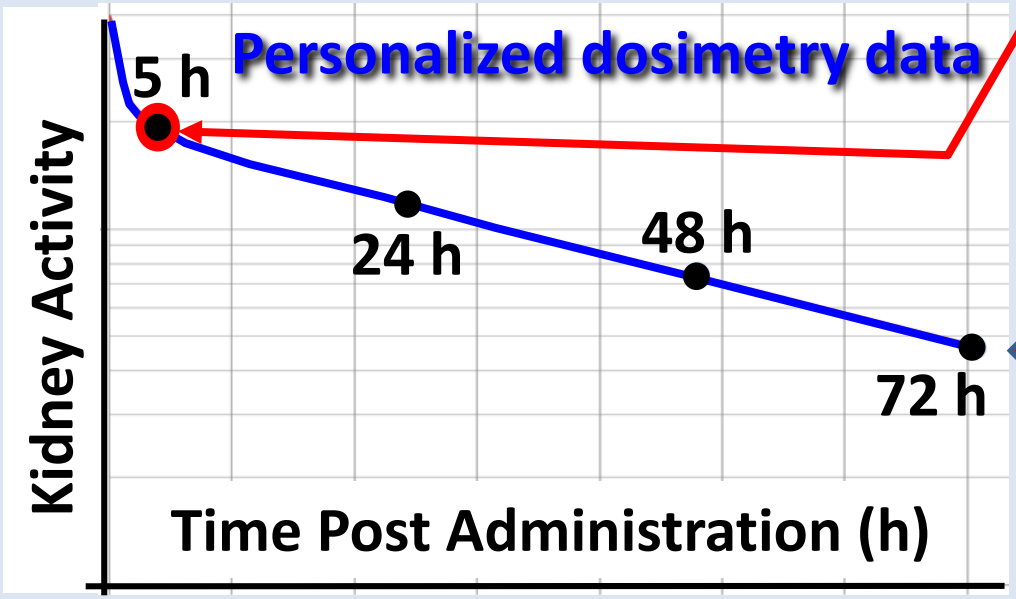
TOF PET/CT



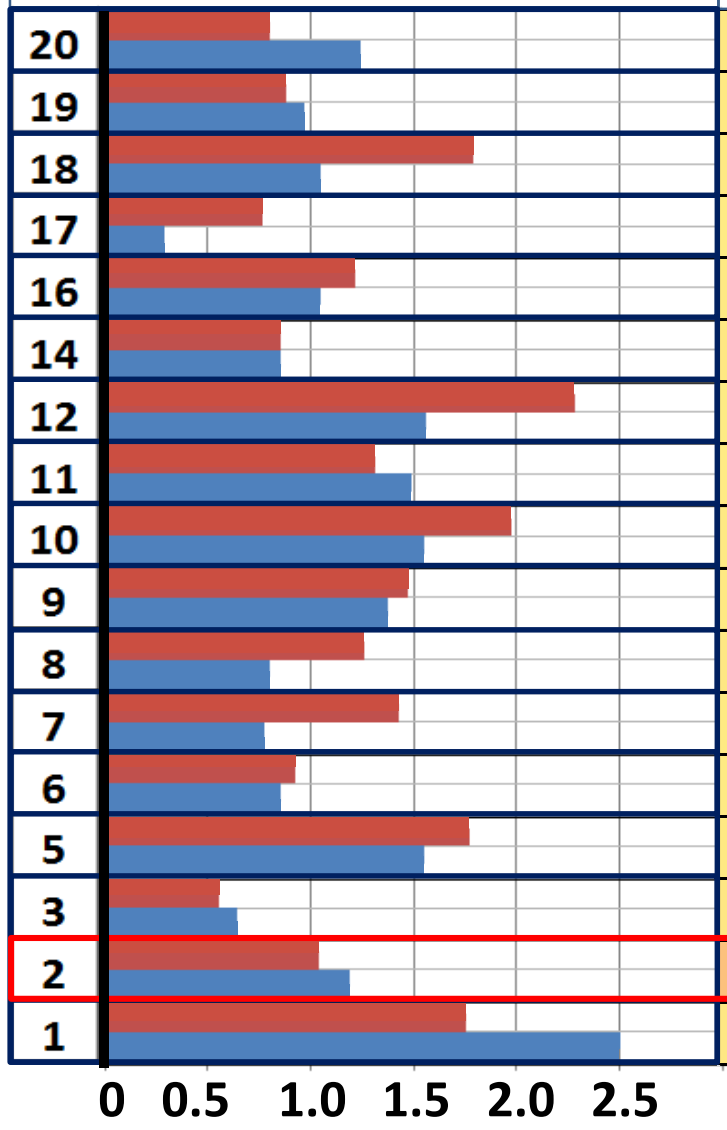
30 minute TOF PET scan;
PET kidney activity calibrates SPECT clearance data.

Bremsstrahlung SPECT/CT





Results: Kidney Dose/Activity & Treatment Modifications



Subject	Administered Activity (GBq) Cycle 1	Cycle 2	Cycle 3	Baseline Creatinine	Follow up Creatinine	Time Post Treatment (Months)
20	4.4	5.6				
19	4.4	5.5	5.2			
18	4.4	5.5				
17	4.5	4.7	5.6			
16	4.4	5.6	5.5			
14	4.4	5.5	5.5			
12	4.5	4.0	2.3	0.7	0.8	3
11	4.5	4.9	5.5	0.8	0.9	6
10	4.4	4.7	2.6	0.8	0.9	6
9	4.4	5.5	4.5	1.3	1.5	6
8	4.4	5.5	5.5	0.9	0.9	7
7	4.5	5.5	5.4	1.1	0.9	6
6	4.5	5.6	4.5	1.2	0.9	6
5	4.4	4.5	3.6	1.2	1.1	9
3	4.4	5.6	5.6	1.3	1.4	9
2	3.8	3.9	3.9	0.9	0.7	10
1	4.4	2.7	3.6	1.0	1.0	11

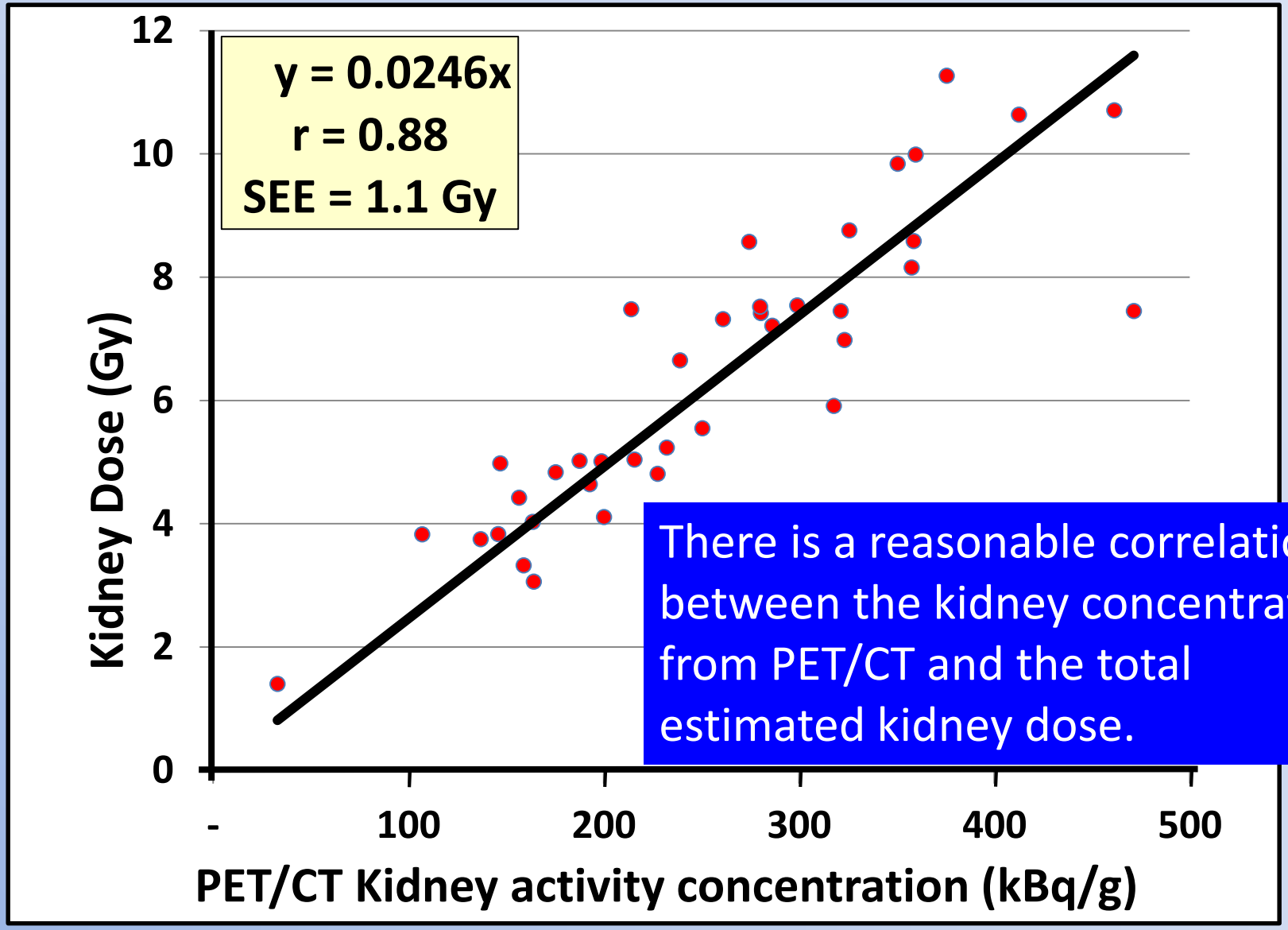
Cycle 2

Cycle 1

Simplified Dose Estimate?

- SPECT/CT imaging sessions over 72 hours puts a burden on both patients and nuclear medicine clinic.
- We observed that the slow component clearance (~ 35 hour half time) was fairly consistent among subjects.
- Could a single measurement be sufficiently predictive for estimating tumor dose?

Kidney Dose Estimated From PET/CT Renal Activity Concentration



There is a reasonable correlation between the kidney concentration from PET/CT and the total estimated kidney dose.

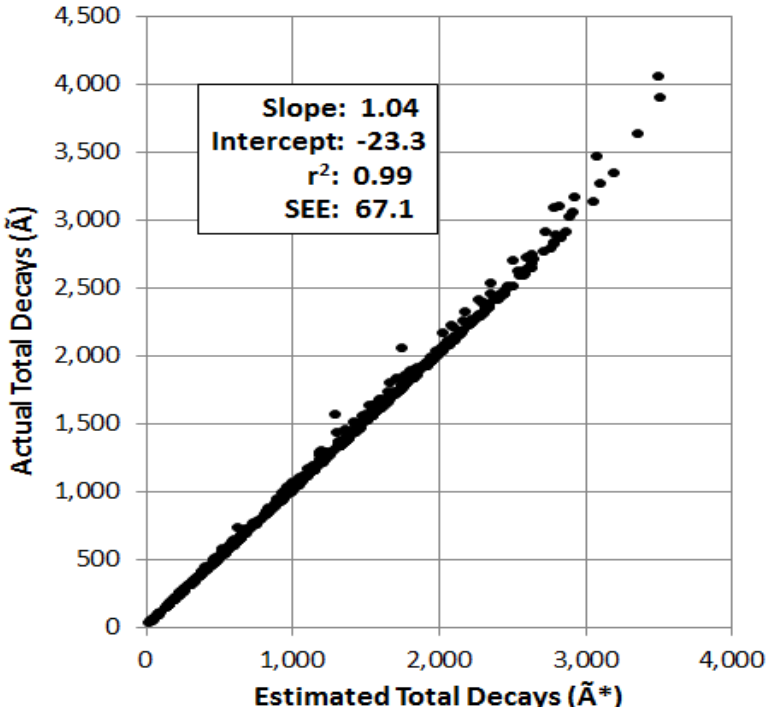
Single Time Point Dose Estimate

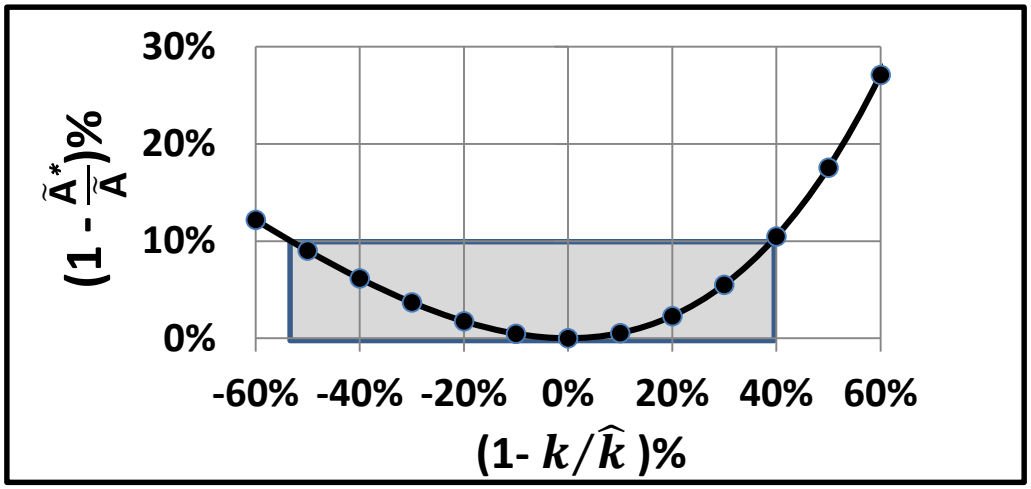
- Exponential clearance (mono- or biexponential clearance).
- Mean clearance rate is known and the sd is on the order of 25%.
- Optimal sampling time is at τ_{eff} (effective mean life).
- Variations in the actual rate constants of up to 50% result in dose estimates with 10% accuracy.

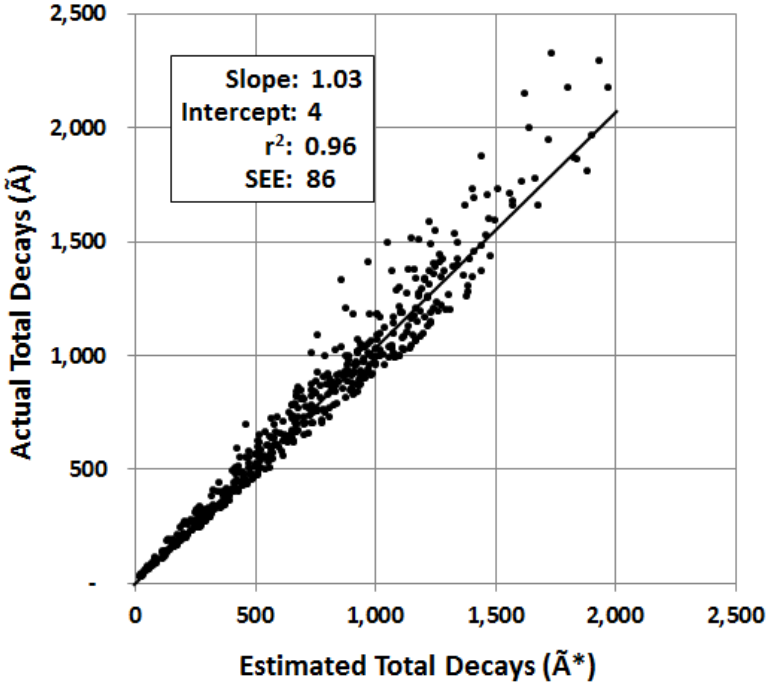
Single Time Point Derivation

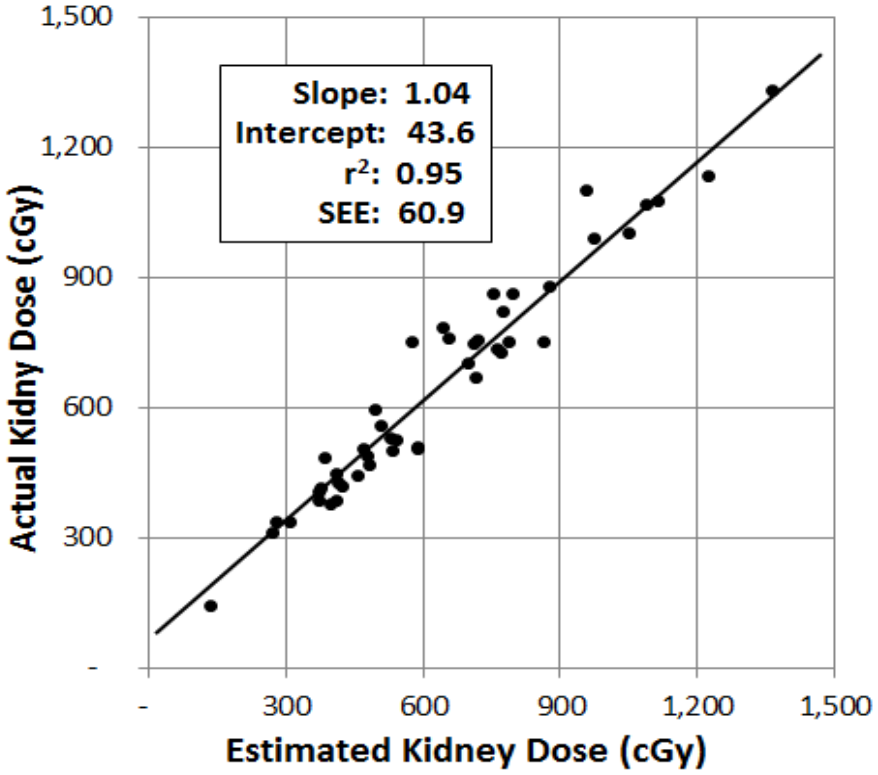
Estimated Parameters For Y-90 DOTATOC

- $\hat{k}_2$: 0.02/h
- $\hat{c}$: 1.1 (ratio of A_1 and A_2)
- $\hat{a}$: 12.1 (ratio of k_1 and k_2)


Slope: 1.04
Intercept: -23.3
r²: 0.99
SEE: 67.1
Actual Total Decays (Ã)
Estimated Total Decays (Ã*)
4,500
4,000
3,500
3,000
2,500
2,000
1,500
1,000
500
0
0
1,000
2,000
3,000
4,000


30%
20%
10%
0%
(1 - Ã*/Ã)%
-60% -40% -20% 0% 20% 40% 60%
(1- k/k̂)%


Slope: 1.03
Intercept: 4
r²: 0.96
SEE: 86
Actual Total Decays (Ã)
Estimated Total Decays (Ã*)
2,500
2,000
1,500
1,000
500
-
0
500
1,000
1,500
2,000
2,500


Slope: 1.04
Intercept: 43.6
r²: 0.95
SEE: 60.9
Actual Kidny Dose (cGy)
Estimated Kidney Dose (cGy)
1,500
1,200
900
600
300
-
-
300
600
900
1,200
1,500

Summary & Conclusions

- There is sufficient ^{90}Y signal to quantify kidney uptake with PET/CT and this can be used to calibrate clearance curves for the calculation of kidney absorbed dose for multi-cycle treatment protocols.
- Kidney dose assessment is likely required for each cycle since treatment related changes to the distribution of activity may occur.
- A single ^{90}Y DOTATOC PET study may be sufficient to estimate kidney dose with enough accuracy to determine treatment administrations.
- The method for estimating kidney dose can be applied to estimate the dose to tumor or other tissues in the PET field of view.

Another Rejection

Thursday, 31-MAR-2016

Dear Dr. Mark Madsen:

On behalf of the SNMMI, we thank you for submitting your abstract, as referenced below, for presentation to the SNMMI 2016 Annual Meeting in San Diego, CA, June 11-15.

Abstract Control #582
Abstract Title: Personalized kidney dosimetry for Y-90 DOTATOC radionuclide therapy

However, we regret to inform you that this abstract was not accepted for presentation this year. We wish to encourage you to continue submitting abstracts to the SNMMI Scientific Program for consideration in future years. We also hope you can still join us in San Diego! Registration info can be found here: http://www.snmmi.org/AM/Registration/Content.aspx?ItemNumber=12340&navItemNumber=12341&navItemNumber=12198

For question or comments, please contact the SNMMI Senior Program Manager, Delicia Hurdle at dhurdle@snmmi.org.

Sincerely,

Satoshi Minoshima, MD, PhD
Chair, SNMMI Scientific Program Committee

Results

	Cycle 1	Cycle 2	Cycle 3
Subjects	21	17	15

Results Averaged Over All Subjects & Cycles

	Mean	sd
Administered Activity (GBq)	4.7	0.63
Kidney Activity (MBq)	105.8	42
%Kidney Activity	2.3%	0.88%
Kidney Mass (g)	415.3	82
Kidney Dose (Gy) per Cycle	6.4	2.39
Kidney Dose/Activity (mGy/MBq)	1.4	0.54

Results: Kidney Dose May Change with Treatment

Treatment effects can alter the distribution enough to change the dose delivered to the kidneys and other tissues.

Cycle 1
Kidney Dose:
1.13 mGy/MBq

Cycle 2
Kidney Dose:
1.93 mGy/MBq