Radiation Dose: External Beam Radiation Therapy Conventions and the Evolving Field of Radiopharmaceutical Therapy

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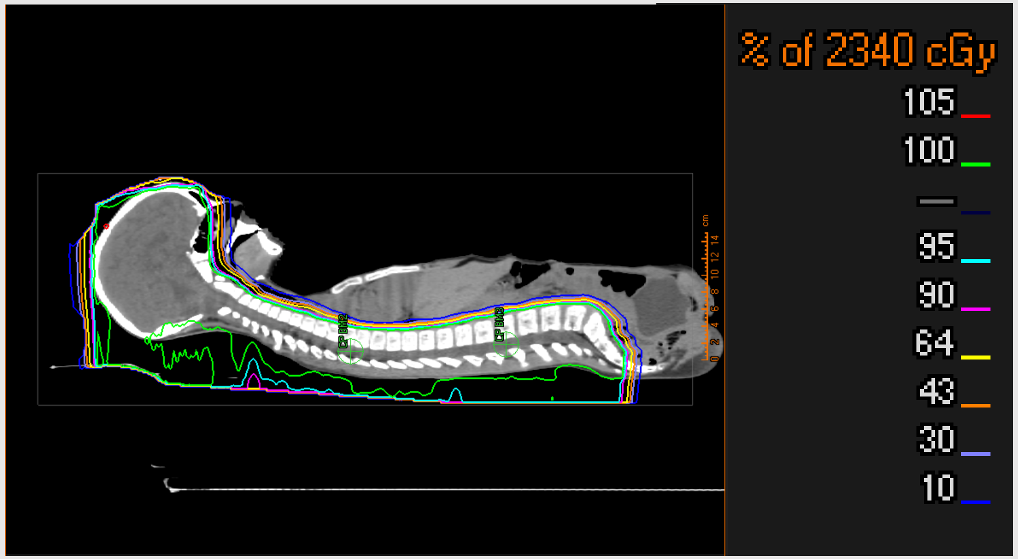
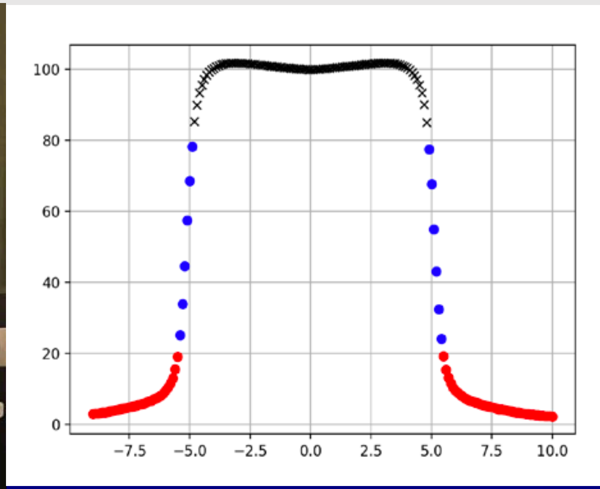
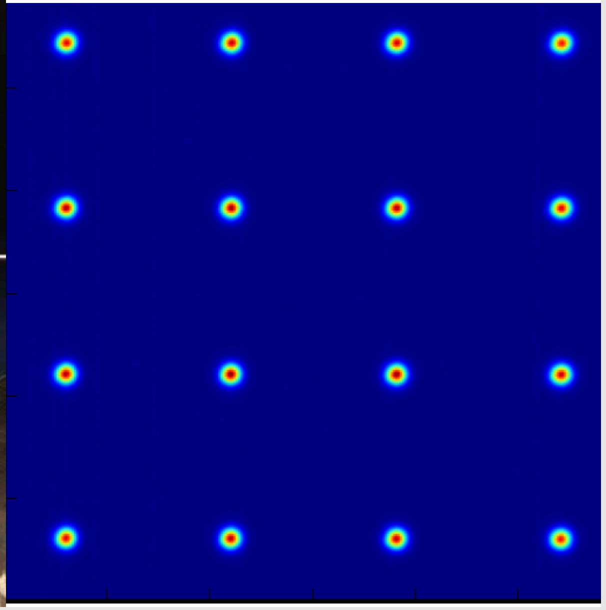
Disclosures

- No financial disclosures
- I work in therapeutic medical physics





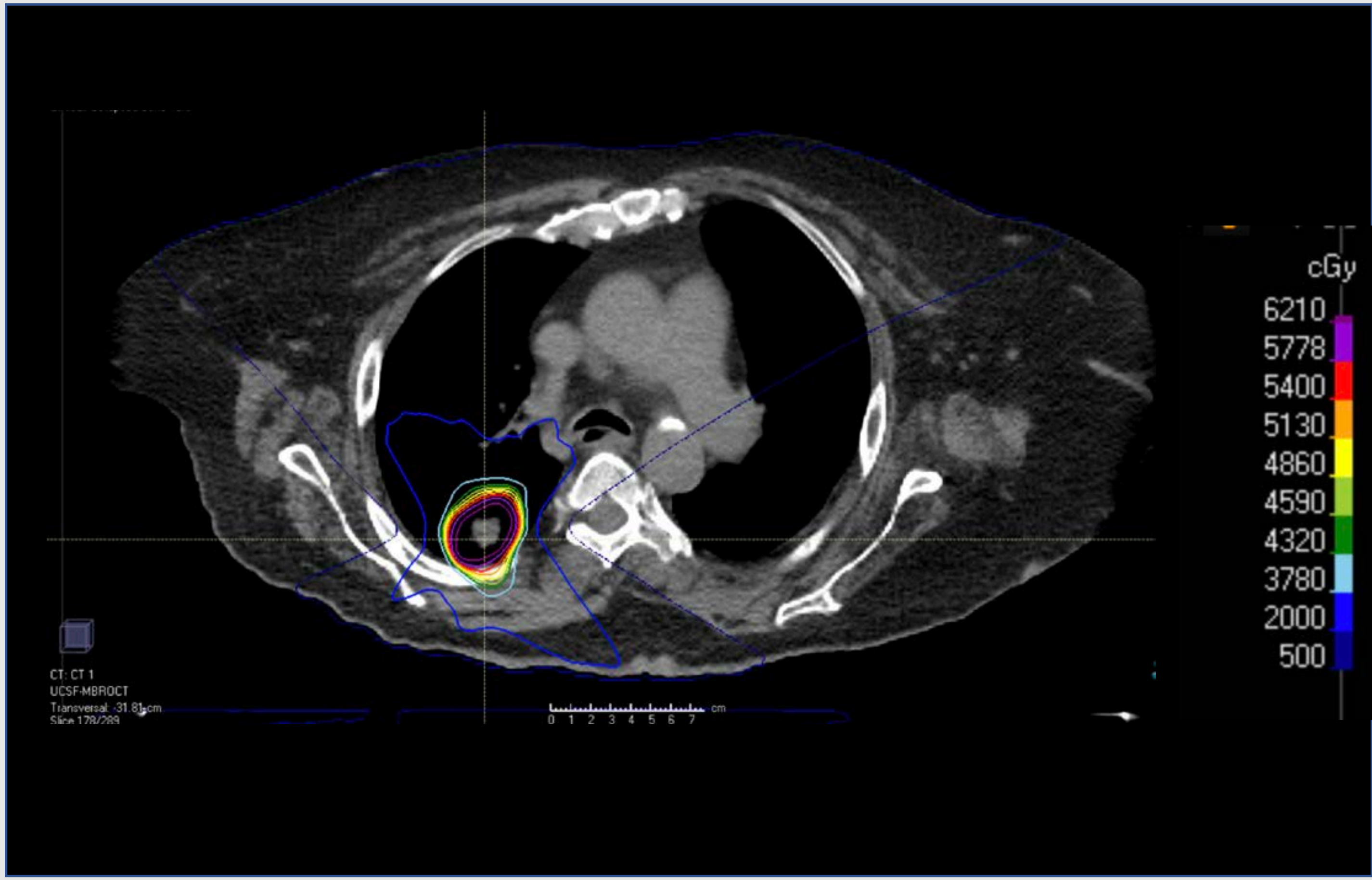


External Beam Radiation Therapy

- In external beam therapy, patients receive a conformal radiation dose to targets, while healthy structures receive minimal radiation dose.

- Every treatment plan is designed for the individual patient. Most patients treatment plans are based upon CT and/or MR images.

- Patient setup is highly reproducible; most patients are setup with daily x-ray images and/or CBCT images.

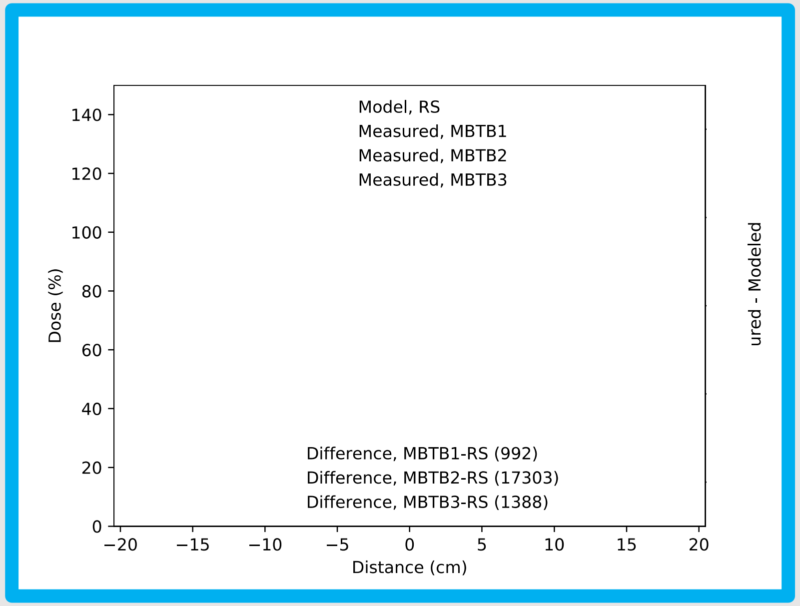


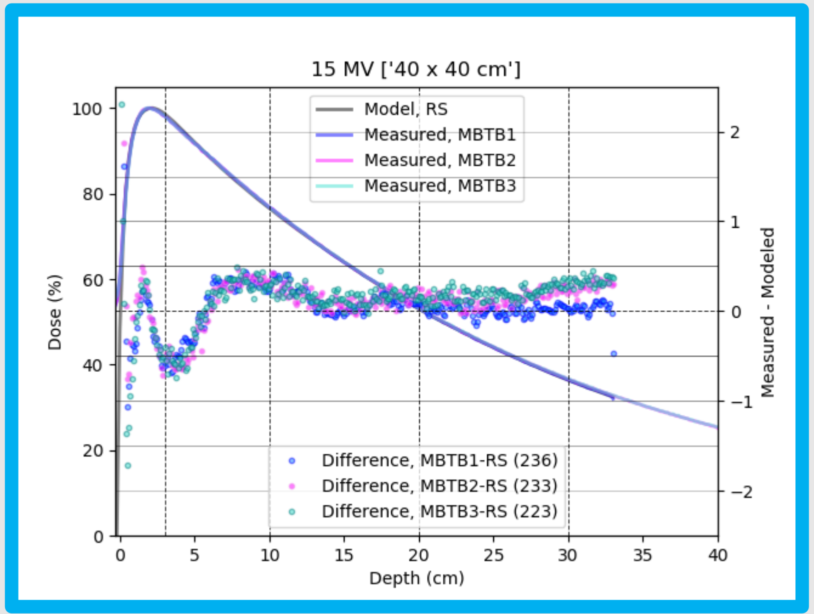
An example of a patient treatment plan

Image from geology.com

Commissioning of Linear Accelerators

- Before a linear accelerator is used for clinical treatments it is fully characterized.
- A complex beam model is created in the treatment planning system (TPS)
- The beam model is validated by creating many treatment plans that test the system, and measuring the dose (point or 3D measurements)





Output Calibrations: TG-51

After characterizing the radiation produced by the linac, physicists will calibrate the output so that a known number of monitor units produce a known amount of radiation:

e.g. 100 MU = 100 cGy for a 10 cm X 10 cm field at 100 cm SSD at a depth of dmax.

AAPM's TG-51 protocol for clinical reference dosimetry of high-energy photon and electron beams

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D. W. O. Rogers[a)]
Ionizing Radiation Standards, National Research Council of Canada, Ottawa K1A OR6, Canada

(Received 17 September 1998; accepted for publication 4 June 1999)

TG–51 Worksheet A: Photon Beams

1. Site data
   - Institution: ______
   - Physicist: ______
   - Date: ______
   - Accel or ^{60}Co Mfr: ______
   - Model &serial number: ______
   - Nominal photon energy/beam identifier: ______ MV
2. Instrumentation
   - a. Chamber model: ______
     - Serial number: ______
     - cavity inner radius (r_{cav}, Table III): ______ cm
     - Waterproof: yes ◯ no ◉
     - If no, is waterproofing $\leq$ 1 mm PMMA or thin latex?: yes ◉ no ◯
   - b. Electrometer model: ______
     - Serial number: ______
     - i. P_{elec}, electrom. corr factor(Sec.VII.B): ______ C/C or C/rdg.
   - c. Calibration Factor $N_{D,w}^{60Co}$ (Sec.V): ______ Gy/C (or Gy/rdg)
     - Date of report (not to exceed 2 years): ______
3. Measurement Conditions (10×10cm^2, point of measurement at 10 cm depth (water equivalent))
   - a. Distance (SSD or SAD): ______ cm SAD ◯ or SSD ◯
   - b. Field size: ______ cm^2
     - on surface(SSD setup): ☐
     - at detector(SAD setup): ☐
   - c. Number of monitor units: ______ MU (min for ^{60}Co)
4. Beam Quality (Sec.VIII.B –not needed for ^{60}Co)
   - If energy < 10 MV, use no lead foil.
     - Measure $\%dd(10)$ [% depth-dose at 10 cm depth for curve shifted upstream by 0.6 r_{cav}]
     - Field size 10×10cm^2 on surface,SSD=100 cm: yes ◯ no ◯
     - a. $\%dd(10)_x = \%dd(10)$ ______
   - If energy $\geq$ 10 MV
     - Distance of 1 mm lead foil from phantom surface 50±5cm ◯ 30±1cm ◯
     - Measure $\%dd(10)_{Pb}$ [% depth-dose at 10 cm depth for curve shifted upstream by 0.6 r_{cav}]
     - Field size 10×10cm^2 on surface,SSD=100 cm: yes ◯ no ◯
     - $\%dd(10)_{Pb}$ (includes e$^-$ contamination): ______

50 cm: $\%dd(10)_x = [0.8905 + 0.00150\%dd(10)_{Pb}]\,\%dd(10)_{Pb}$ $[\%dd(10)_{Pb} \geq 73\%]$ Eq.(13)

30 cm: $\%dd(10)_x = [0.8116 + 0.00264\%dd(10)_{Pb}]\,\%dd(10)_{Pb}$ $[\%dd(10)_{Pb} \geq 71\%]$ Eq.(14)

If $\%dd(10)_{Pb} < 71\%$ (30cm) or 73%(50cm): $\%dd(10)_x = \%dd(10)_{Pb}$

- b. $\%dd(10)_x$ (for open beam): ______

Has lead foil been removed? yes ◯ no ◯

External Validation : IROC OSLDs

Institutions can verify the calibration by irradiating small phantoms with TLDs or OSLDs inserted in them

A known radiation dose is delivered and the phantoms are returned to IROC.

The received radiation dose is externally verified by IROC

Listed below are the results for the TLD irradiated June 26, 2014 on the Mobetron s/n 49:

Electron Energy	TLD Ratio – MDACC/INST (difference in mm between TLD depth and Inst depth)
6 MeV	1.00 (-1 mm)
9 MeV	1.00 (0 mm)
12 MeV	1.00 (0 mm)

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PHOTON BEAM OSL IRRADIATION FORM

Please Note the Form Change

Correct? (see change form)

Institution: ____ ☐ Yes ☐ No
Person to receive report: ____ ☐ Yes ☐ No
Email address of Person to receive report: ____

Person Irradiating OSL, if different from above: Name ____ Phone: (____
For questions regarding OSL irradiation, if different from above:
Name ____ Phone: (____) ____

MACHINE:		IRRADIATION SET-UP FOR BLOCK:	
In-House Designation:	____	Date Irradiated (mm/dd/yyyy):	/ /
Serial #:	____	MU (time) set at console:	mu (min)
Energy:	____	Net Beam on:	____ mu (min)
Beam Quality: TMR 20	____ or % dd(10)x	Distance to top of RPC's folding plastic platform: (NOT to top of OSL block)	cm

DESCRIBE YOUR CALIBRATION PROCEDURE

Distance from source to your output specification point = ____ cm (see instructions)

Output at this point in a 10 x 10 cm field at time of OSL irradiation = ____ cGy/mu (cGy/min.)

Output stated above is (check one):
Nominal output
Daily check reading (day of OSL irradiation)
Ion chamber calibration (day of OSL irradiation)
Dose is specified to: (check one)
Muscle (RPC standard for dose prescription
Water is absorbed dose to muscle)

Output is specified at (check one):
SSD = ____ cm, Or
SAD = cm
At depth of (check one):
dmax = ____ cm, Or
Other depth ____ cm
If other depth, provide TPR (or TMR) at dmax = ____
AND TPR (or TMR) at other depth =

Calibration Protocol (check one) TG-51 TG-21 Other ____

DOSE DELIVERED

Dose to output specification point for MU (time) setting given above = ____ cGy
For Co-60 only, date dose is exact (mm/dd/yyyy): / /

FOR RPC USE ONLY

BATCH	CODE/MACH#	DATE SENT	DATE RECEIVED

NATIONAL CANCER INSTITUTE The RPC is an NCI-funded resource to cooperative group clinical trials.

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History®

American Association of Physicists in Medicine

From : http://rpc.mdanderson.org/RPC/home.htm

In addition …

- To participate in clinical trials, end-to-end testing is also required.
- Phantoms with TLDs are shipped to the institution where they are imaged and a treatment plan is created and delivered.
- The phantoms are then shipped back to IROC, where the radiation dose delivered to the TLDs is determined.
- The credentialing process ensures that participating sites are capable of delivering complex radiation treatment plans as intended

Report of Lung
Phantom Irradiation

Date of Report:	January 6, 2017
Institution:	University of California - San Francisco
Physicist:	Joey Cheung
Radiation Machine:	Varian, TrueBeam (1737) – 6 MV
Collimator:	MLC
Technique:	IMRT - VMAT
Treatment Planning System:	Philips, Pinnacle (3D/IMRT) – Collapsed Cone Convolution
Date of Irradiation:	November 18, 2016

Description of procedure:

An anthropomorphic lung phantom incorporating a cylindrical dosimetry insert that simulated the left lung was placed in the supine position in a CT scanner and imaged. The insert contained a spherical centered target. TLD capsules located near the center of the target provided point dose information and three sheets of GAFChromic™ Dosimetry Media provided dose distributions in the axial, coronal and sagittal planes. The phantom included heart and spinal cord structures, each one containing one TLD capsule. The right lung was also included. The phantom with the insert was irradiated to approximately 6 Gy using a IMRT technique. The analyses of the results were based on dose calculation applying correction for tissue heterogeneity.

The dosimetric precision of the TLD is 3%, and the spatial precision of the film and densitometer system is 1 mm.

Summary of TLD and film results:

Location	IROC-H vs. Inst.	Criteria	Acceptable
PTV_TLD_sup	0.97	0.92 – 1.05	Yes
PTV_TLD_inf	0.98	0.92 – 1.05	Yes

Film Plane	Gamma Index*	Criteria	Acceptable
Axial	96%	≥ 80%	Yes
Coronal	95%	≥ 80%	Yes
Sagittal	92%	≥ 80%	Yes
Average over 3 planes	94%	≥ 85%	Yes

*Percentage of points meeting gamma-index criteria of 7% and 5 mm

The phantom irradiation results listed in the table above **do meet** the criteria established by the IROC Houston in collaboration with the cooperative study groups. Therefore, your institution **has satisfied** the phantom irradiation component of the credentialing process to enter patients onto clinical trials.

TLD and Film Analysis by: Paige Taylor, M.S. and Hunter Mehrens

Report Checked by:

David S. Followill, Ph.D.
Director, IROC Houston QA Center

Daily, Monthly and Annual QA

- In addition to the calibration described, routine QA is performed on linacs to ensure dose constancy.
- This includes daily QA, monthly QA and performing TG-51 annually
- IROC OSLDs are irradiated annually.
- For complex treatments (e.g. IMRT), patient specific QA is also performed before the patient receives treatment

TABLE I. Daily.

	Machine-type tolerance		
Procedure	Non-IMRT	IMRT	SRS/SBRT
Dosimetry			
X-ray output constancy (all energies)			
Electron output constancy (weekly, except for machines with unique e-monitoring requiring daily)		3%	

Task Group 142 report: Quality assurance of medical accelerators[a)]

Eric E. Klein[b)]
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Hackensack University Medical Center, Hackensack, New Jersey

John Bayouth
University of Iowa, Iowa City, Iowa

Fang-Fang Yin
Duke University, Durham, North Carolina

William Simon
Sun Nuclear Corp., Melbourne, Florida

Sean Dresser
Northside Hospital, Atlanta, Georgia

Christopher Serago
Mayo Clinic, Jacksonville, Florida

Francisco Aguirre
M. D. Anderson Cancer Center, Houston, Texas

Lijun Ma
University of California, San Francisco, San Francisco, California

Bijan Arjomandy
M. D. Anderson Cancer Center, Houston, Texas

Chihray Liu
University of Florida, Gainesville, Florida

Consultants:

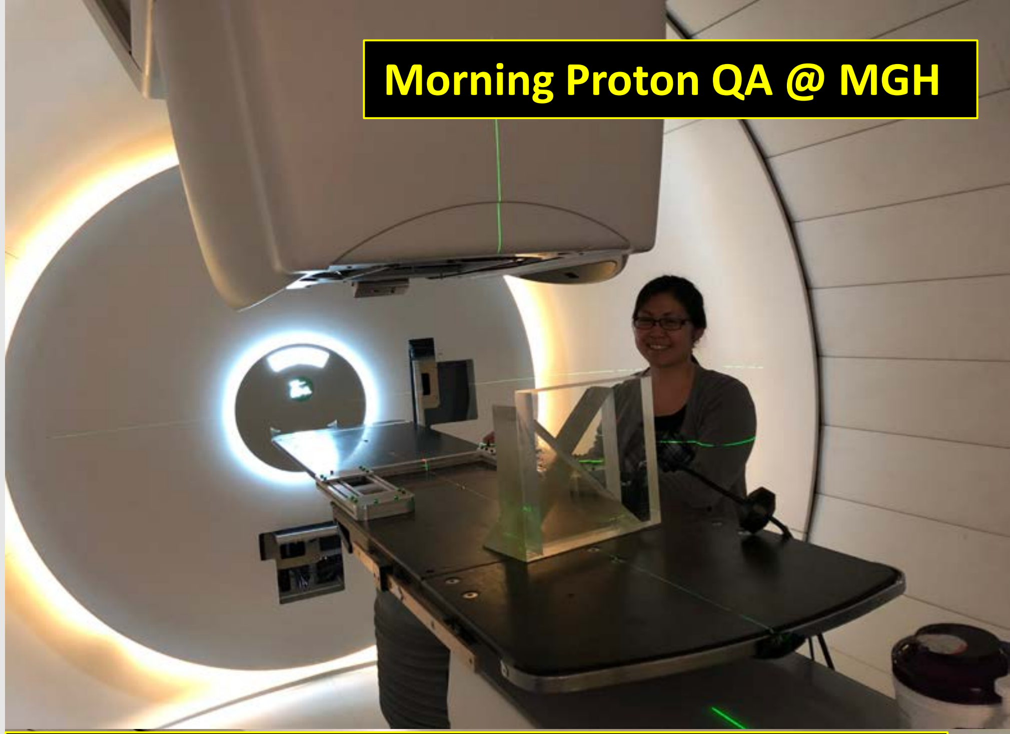
Carlos Sandin
Elekta Oncology, Crawley, United Kingdom

Todd Holmes
Varian Medical Systems, Palo Alto, California

Training physicists in external beam RT

- Board certification by the ABR in therapeutic radiation physics requires a CAMPEP accredited residency

- Residents have many opportunities to learn how accelerators are calibrated and how routine QA is performed



Morning Proton QA @ MGH

Linac commissioning and acceptance @ UCSF

Part 2: Radionuclide Therapy

^{177}Lu-DOTATATE

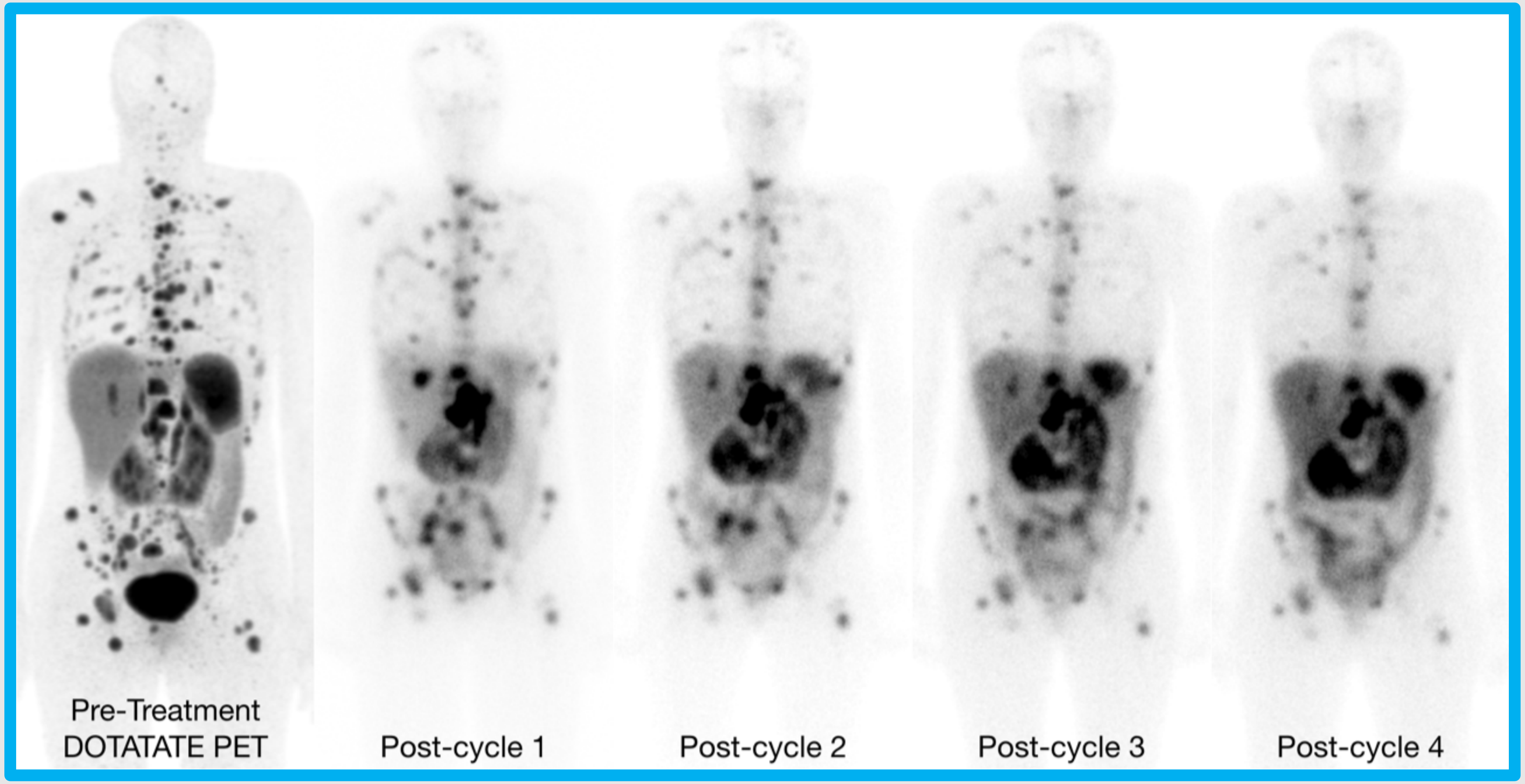
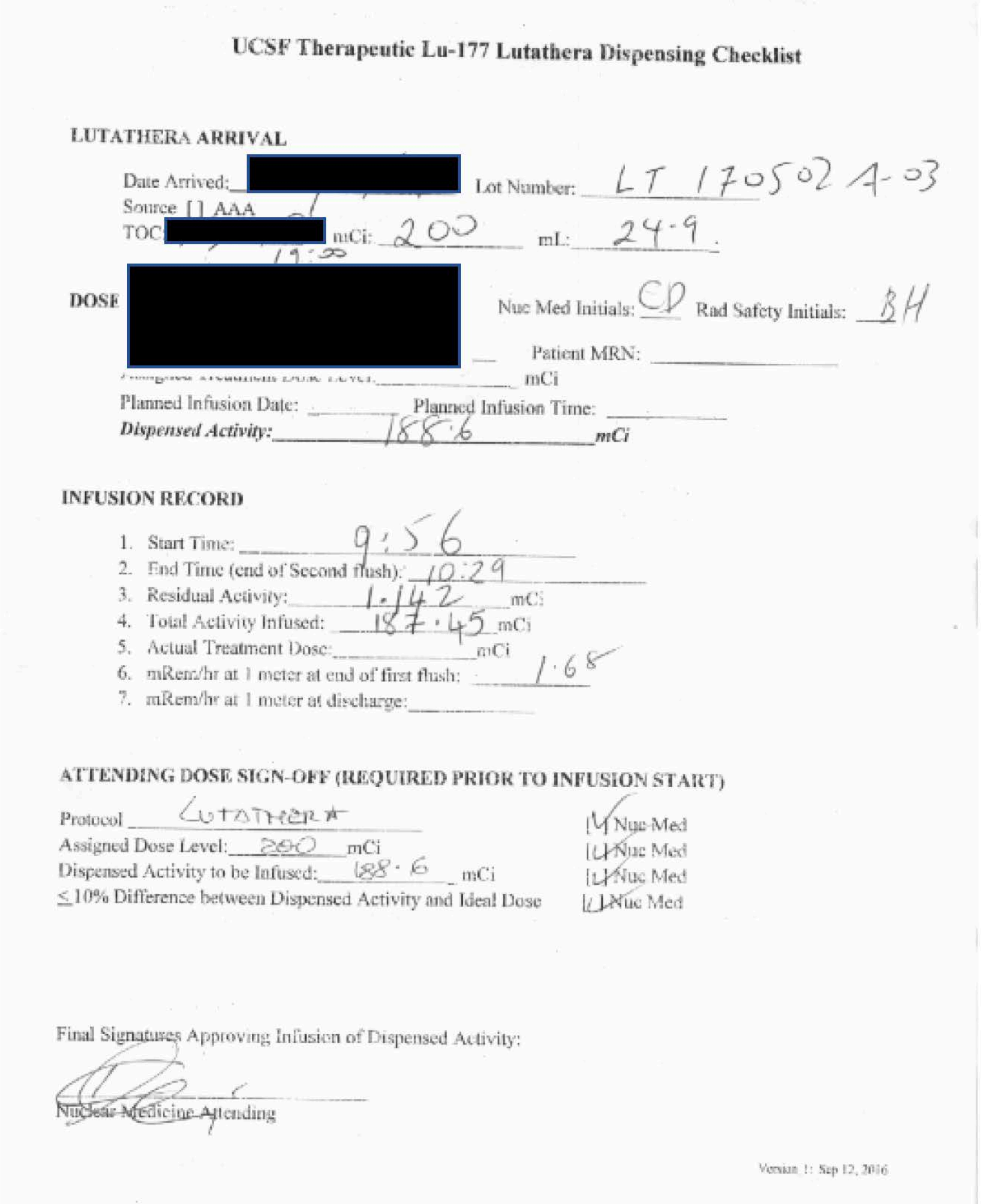


Image courtesy of Dr. Thomas Hope, UCSF Department of Radiology



UCSF Therapeutic Lu-177 Lutathera Dispensing Checklist

LUTATHERA ARRIVAL

Date Arrived: [redacted] Lot Number: LT 170502 A-03

Source [] AAA

TOC [redacted] mCi: 200 mL: 24.9

DOSE [redacted] Nuc Med Initials: CD Rad Safety Initials: BH

Patient MRN: ______

[redacted] mCi

Planned Infusion Date: ______ Planned Infusion Time: ______

Dispensed Activity: 188.6 ***mCi***

INFUSION RECORD

1. Start Time: 9:56
2. End Time (end of Second flush): 10:29
3. Residual Activity: 1.142 mCi
4. Total Activity Infused: 187.45 mCi
5. Actual Treatment Dose: ______ mCi
6. mRem/hr at 1 meter at end of first flush: 1.68
7. mRem/hr at 1 meter at discharge: ______

ATTENDING DOSE SIGN-OFF (REQUIRED PRIOR TO INFUSION START)

Protocol Lutathera [✓] Nuc Med

Assigned Dose Level: 200 mCi [✓] Nuc Med

Dispensed Activity to be Infused: 188.6 mCi [✓] Nuc Med

≤10% Difference between Dispensed Activity and Ideal Dose [✓] Nuc Med

Final Signatures Approving Infusion of Dispensed Activity:

Nuclear Medicine Attending

Version 1: Sep 12, 2016

What would we get if we asked for the radiation dose record for a patient treated with TRT?

^{177}LU-DOTATATE PHASE 3 TRIAL IN MIDGUT NEUROENDOCRINE TUMORS

SUPPLEMENTARY APPENDIX

TABLE OF CONTENTS

Supplementary Table S2. ^{177}Lu-DOTATATE Exposure.*

Patients who completed treatment phase (N=103†)	no. (%)
Number of administrations	
4	79 (77)
3	6 (6)
2	12 (12)
1	5 (5)
0	1 (1)
All treated patients (N=111)	
No DMT	103 (93)
DMT	8 (7)

* DMT denotes dose-modifying toxicity.

† Excluding patients still under treatment (n=8) or no treatment (n = 5).

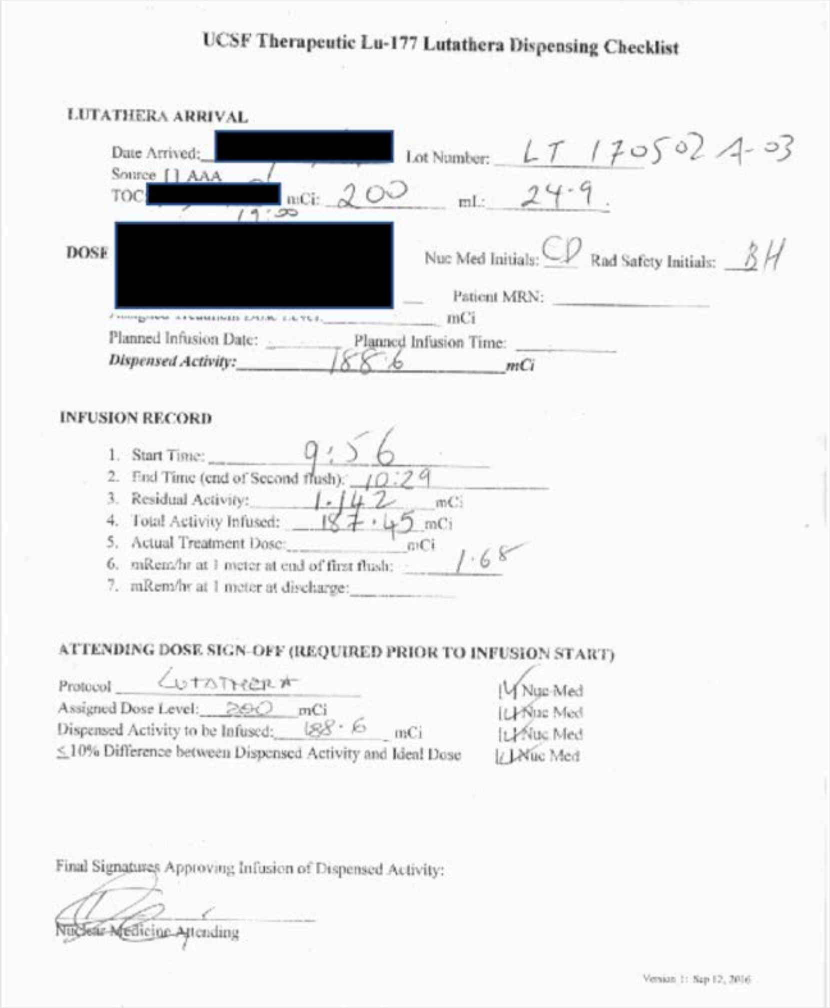
Phase 3 Trial of ^{177}Lu-Dotatate for Midgut Neuroendocrine Tumors

J. Strosberg, G. El-Haddad, E. Wolin, A. Hendifar, J. Yao, B. Chasen, E. Mittra, P.L. Kunz, M.H. Kulke, H. Jacene, D. Bushnell, T.M. O'Dorisio, R.P. Baum, H.R. Kulkarni, M. Caplin, R. Lebtahi, T. Hobday, E. Delpassand, E. Van Cutsem, A. Benson, R. Srirajaskanthan, M. Pavel, J. Mora, J. Berlin, E. Grande, N. Reed, E. Seregni, K. Öberg, M. Lopera Sierra, P. Santoro, T. Thevenet, J.L. Erion, P. Ruszniewski, D. Kwekkeboom, and E. Krenning, for the NETTER-1 Trial Investigators*

24 hour post-administration SPECT/CT

All patients treated with Lu-177 DOTATATE at UCSF have a 24 hour post-administration SPECT/CT scan

These scans are used qualitatively



UCSF Therapeutic Lu-177 Lutathera Dispensing Checklist

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mCi
Planned Infusion Date: ______ Planned Infusion Time: ______
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Protocol LUTATHERA [✓] Nuc Med
Assigned Dose Level: 200 mCi [✓] Nuc Med
Dispensed Activity to be Infused: 188.6 mCi [✓] Nuc Med
≤10% Difference between Dispensed Activity and Ideal Dose [✓] Nuc Med

Final Signatures Approving Infusion of Dispensed Activity:

Nuclear Medicine Attending

Version 1: Sep 12, 2016

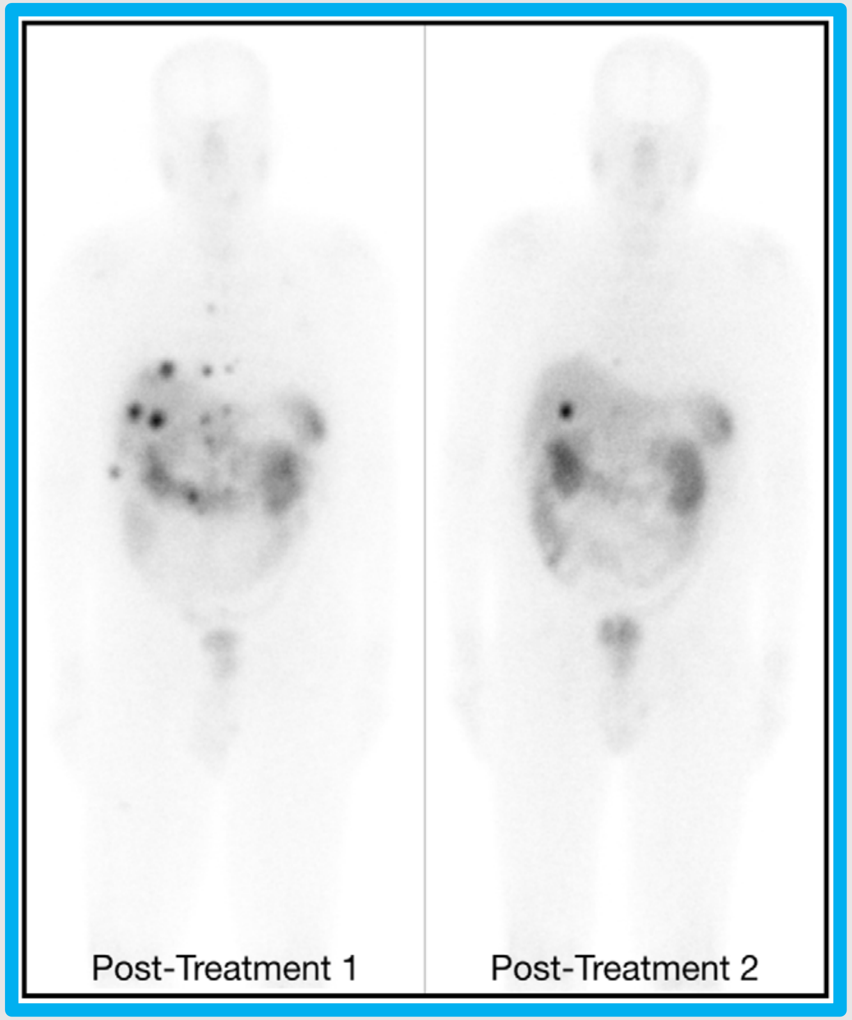


Image courtesy of Dr. Thomas Hope, UCSF Department of Radiology

Beyond Administered Activity...

- To report patient dose in Gy requires several additional steps
  - **Calibrated** SPECT/CT or PET/CT scanner
  - **Validated** dose calculation algorithm
  - Recording the dose in a standardized format (e.g. RTDose)

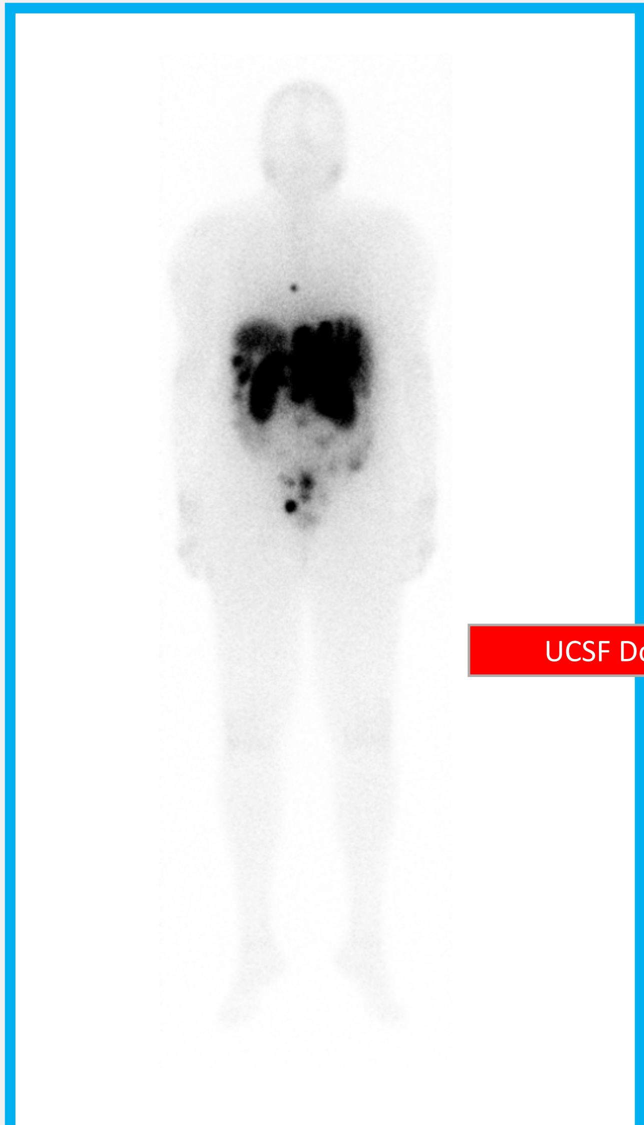
SPECIAL CONTRIBUTIONS

MIRD Pamphlet No. 26: Joint EANM/MIRD Guidelines for Quantitative ^{177}Lu SPECT Applied for Dosimetry of Radiopharmaceutical Therapy

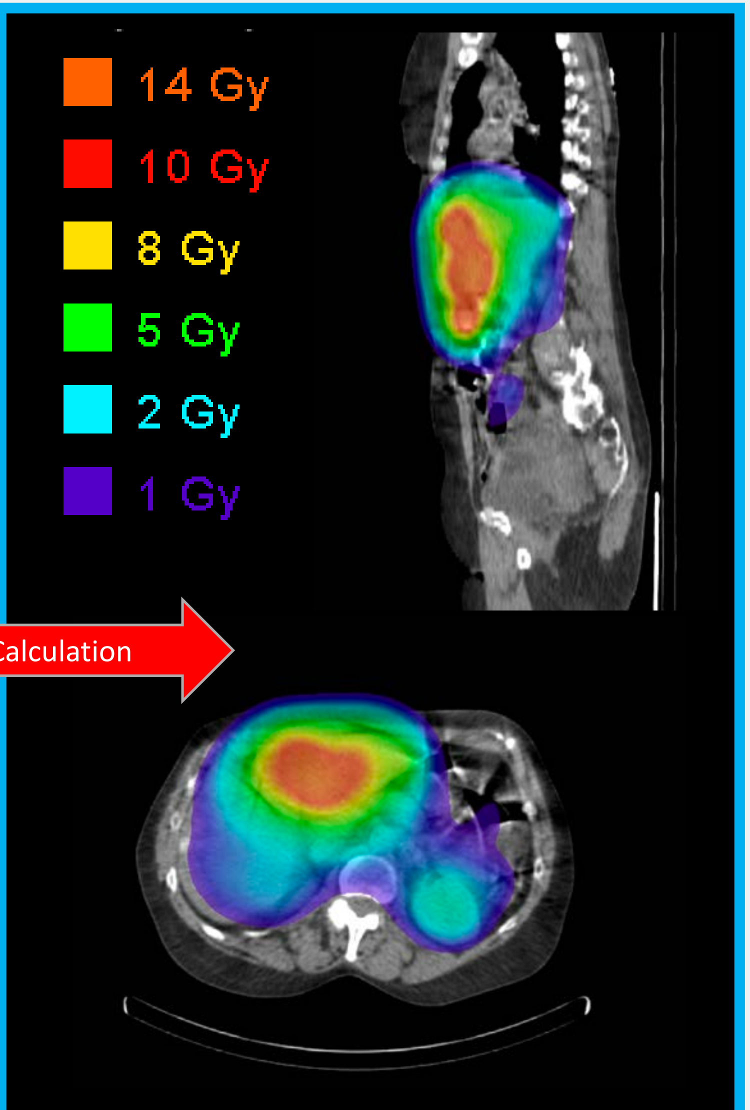
Michael Ljungberg[1], Anna Celler[2], Mark W. Konijnenberg[3], Keith F. Eckerman[4], Yuni K. Dewaraja[5], and Katarina Sjögreen-Gleisner[1]

In collaboration with the SNMMI MIRD Committee: Wesley E. Bolch, A. Bertrand Brill, Frederic Fahey, Darrell R. Fisher, Robert Hobbs, Roger W. Howell, Ruby F. Meredith, George Sgouros, and Pat Zanzonico, and the EANM Dosimetry Committee: Klaus Bacher, Carlo Chiesa, Glenn Flux, Michael Lassmann, Lidia Strigari, and Stephan Walrand.

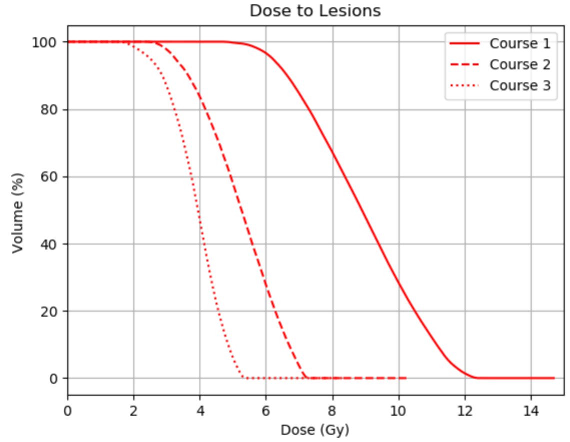
Kinetics of the agent must also be considered



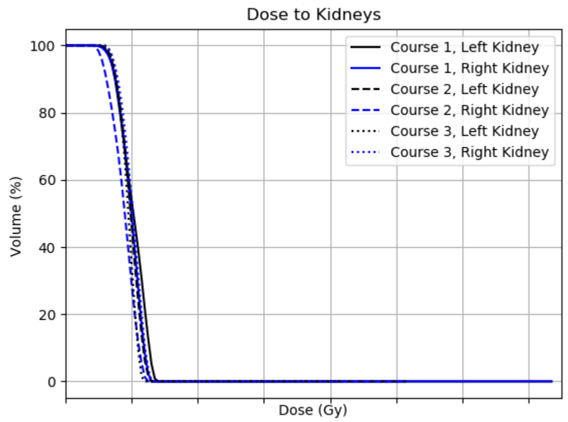
^{177}Lu-DOTATATE SPECT/CT



Received Radiation Dose (Gy)



Dose to Targets



Dose to Organs at Risk

Work done in collaboration with Dr. Thomas Hope, UCSF Department of Radiology

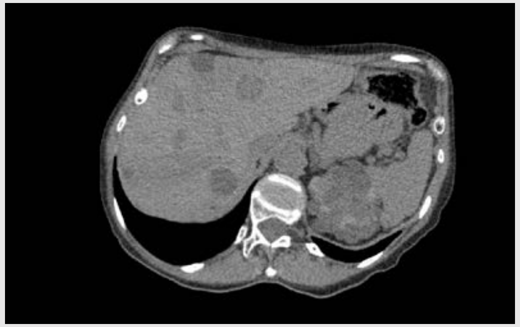
External Beam RT

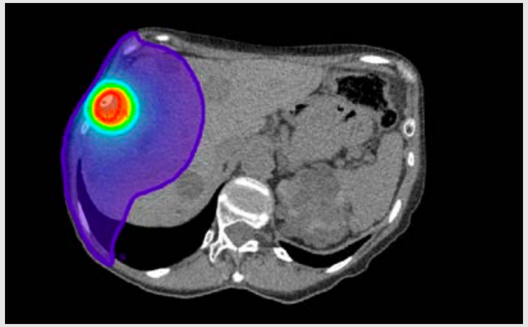
Standardized Calibration Procedures

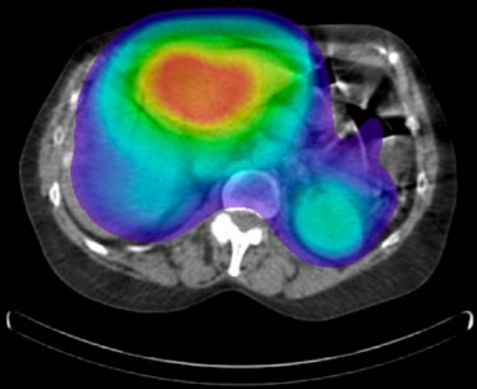
External Dose Validation Methods (phantoms)

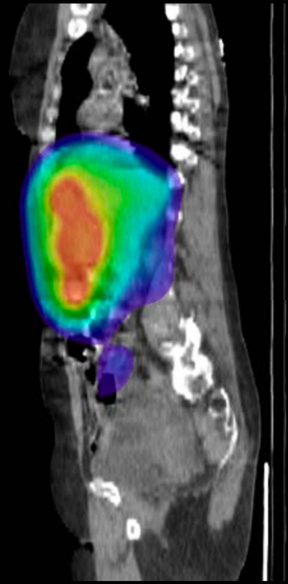
Training for physicists who perform calibrations

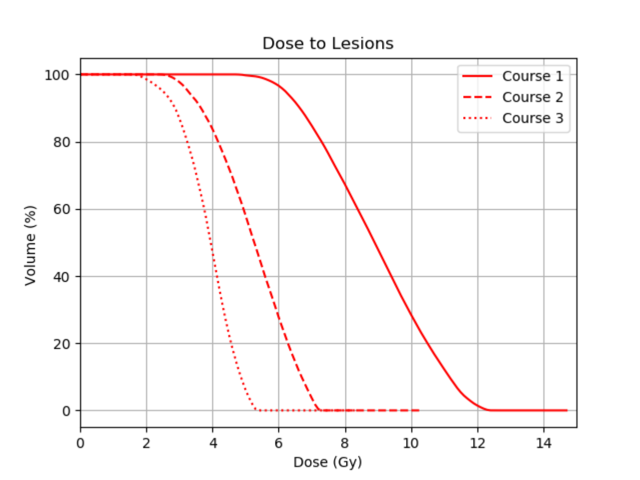
Routine QA & tolerances

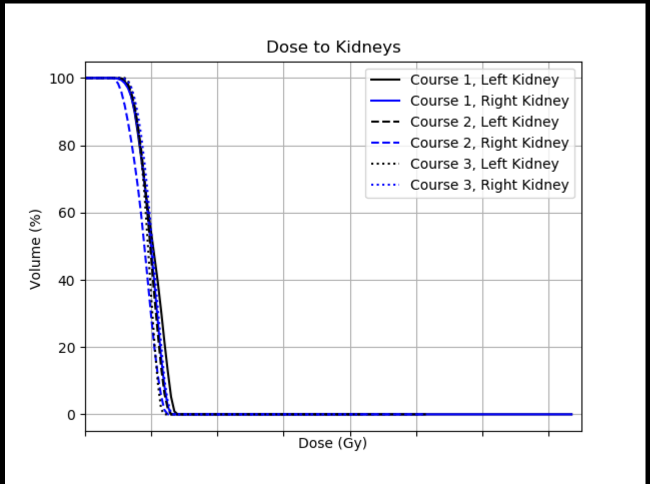












Targeted Radionuclide Therapy