Pediatric NM Therapy in an Adult Hospital Setting

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SAM session - Methods, Mishaps and Musings on Pediatric Theranostics

AAPM 2018 Annual Meeting

July 29-August 2, 2018

Nashville, TN

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

Learning Objective

To learn what are important aspects of adapting a historically adult-only NM therapy clinical practice to pediatrics

MDA Adult NM Therapies
Past, Present and Future

(Since I started in ’01 – not exhaustive, i.e., I may have missed some)

Radiopharmaceutical	**Indication**
^{131}I-NaI (a.k.a, radioiodine or RAI)	thyroid cancer, hyperthyroidism
^{89}SrCl, ^{153}Sm-EDTMP, ^{166}Ho-DOTMP, **$^{223}RaCl_2$**	skeletal targeted radiotherapy
^{90}Y-Zevalin (^{131}I-BEXXAR - discontinued)	B-cell non-hodgkin's lymphomas
^{90}Y microspheres (SIR-Spheres, TheraSphere)	hepatocellur carcinoma, liver mets
^{131}I-mIBG	pheochromocyt-, paragangli-oma
^{177}Lu-DOTATATE	mid-gut neuroendocrine cancers
^{225}Ac-lintuzumab, ^{131}I-Iomab	leukemia
^{90}Y-FF21101	p-cadherin+ cancers
^{32}P-Oncosil	pancreatic tumors (direct infusion)
^{177}Lu-AvidinOx-Biotin	misc. tumors (AvidinOx direct inf.)
^{177}Lu-/^{225}Ac-PSMA	prostate cancer

MDA NM Therapies
Applied to Pediatric* Patients

(Since I started in ’01- that I am aware of)

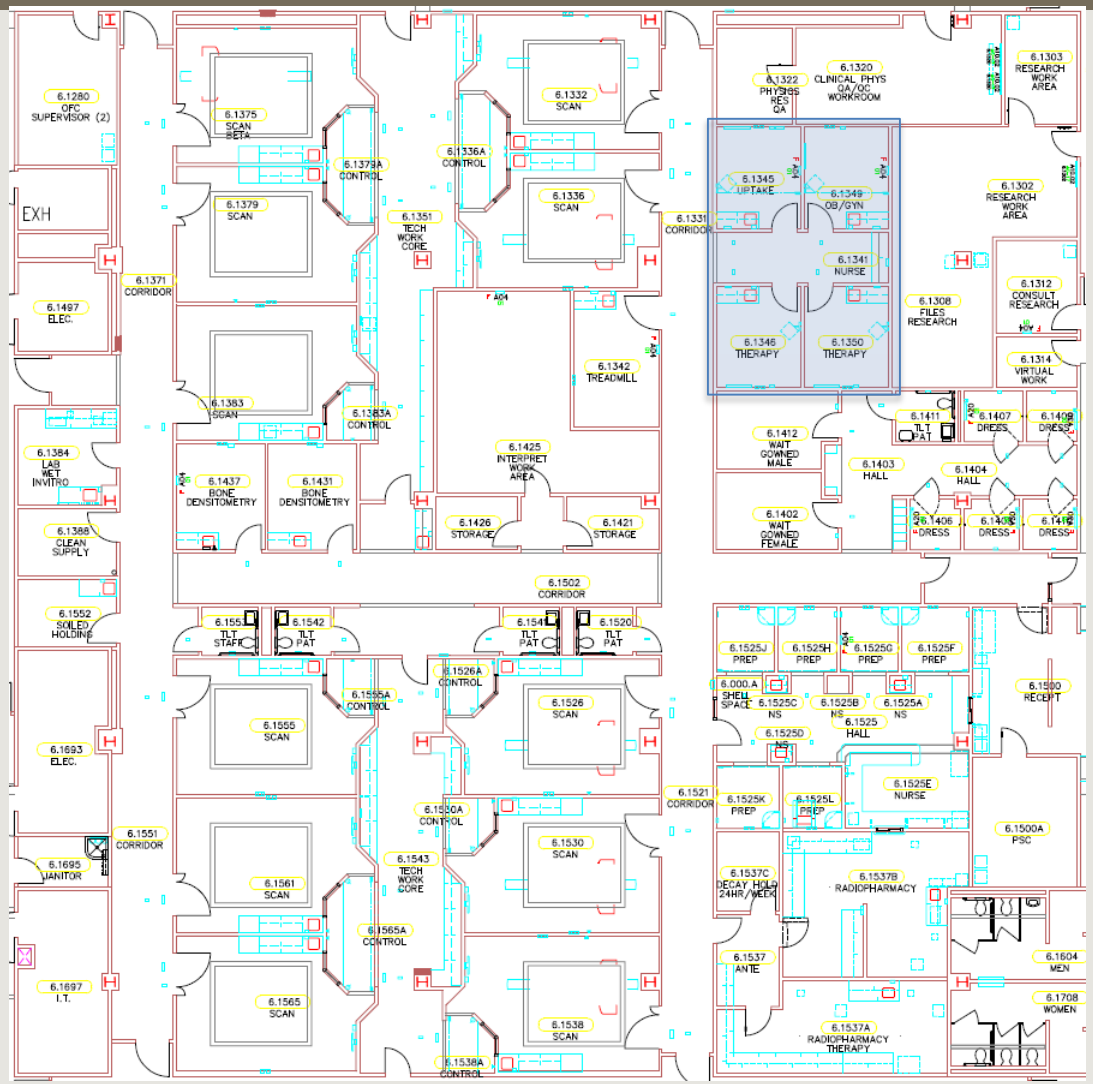
- RAI — 9/year (averaged over the last 5 y) (~6% of all radioiodine therapies)
- ^{131}I-mIBG — 1 (+ 2 dosimetries w/ intent to treat)
- ^{153}Sm-EDTMP — 3
- SIR-Spheres — 2
- $^{223}RaCl_2$ — 1

*”pediatric” at MDA includes up to 21 y.o. young adults

MDA NM Therapy Rooms

- Adult Outpatient (OP) The “Quad”
  - embedded in adult-only outpatient clinic NM suite
- Pediatric OP A single room
  - embedded in inpatient (i.e., hospital) NM suite
- Inpatient (IP) 14 rooms
  - ~1/4 of the 10th floor of the hospital
  - dual-purpose (as opposed to dedicated) rooms
    - Available for regular inpatients when not in use for NM Tx
  - All NM therapy patients (no segregated pediatric area)

The “Quad”


6.1280 OFC SUPERVISOR (2)
6.1375 SCAN BETA
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6.1320 CLINICAL PHYS QA/QC WORKROOM
6.1322 PHYSICS RES QA
6.1303 RESEARCH WORK AREA
EXH
6.1379 SCAN
6.1351 TECH WORK CORE
6.1336 SCAN
6.1345 UPTAKE
6.1349 OB/GYN
6.1331 CORRIDOR
6.1302 RESEARCH WORK AREA
6.1371 CORRIDOR
6.1341 NURSE
6.1308 FILES RESEARCH
6.1312 CONSULT RESEARCH
6.1497 ELEC.
6.1346 THERAPY
6.1350 THERAPY
6.1342 TREADMILL
6.1314 VIRTUAL WORK
6.1383 SCAN
6.1383A CONTROL
6.1411 TLT PAT
6.1407 DRESS
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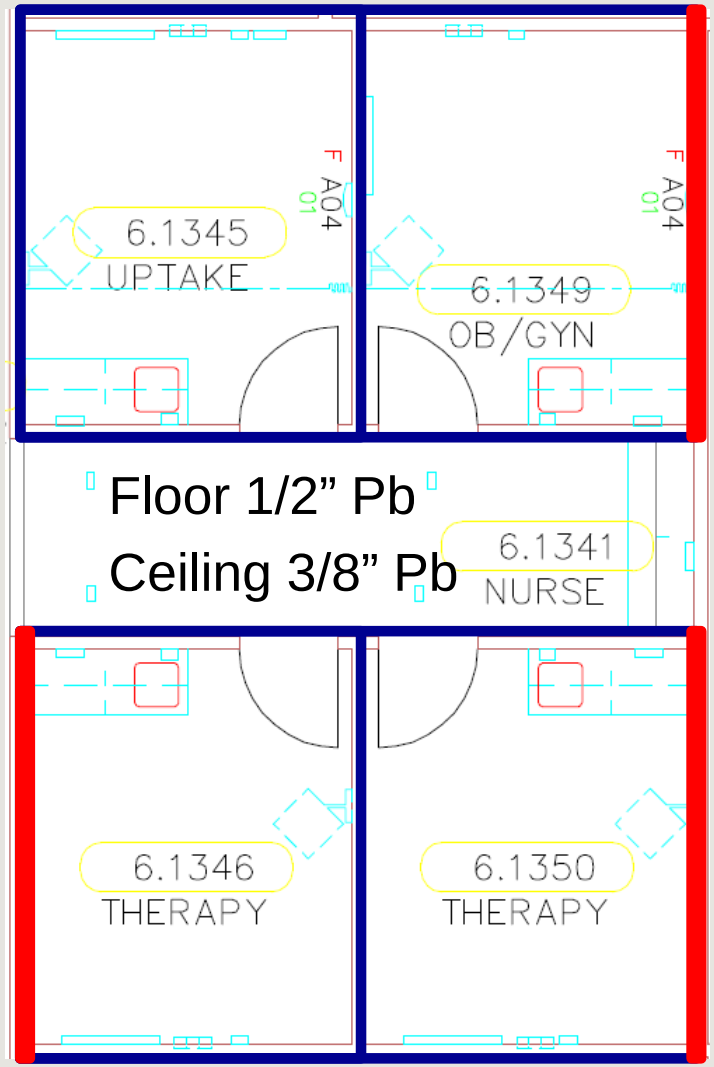
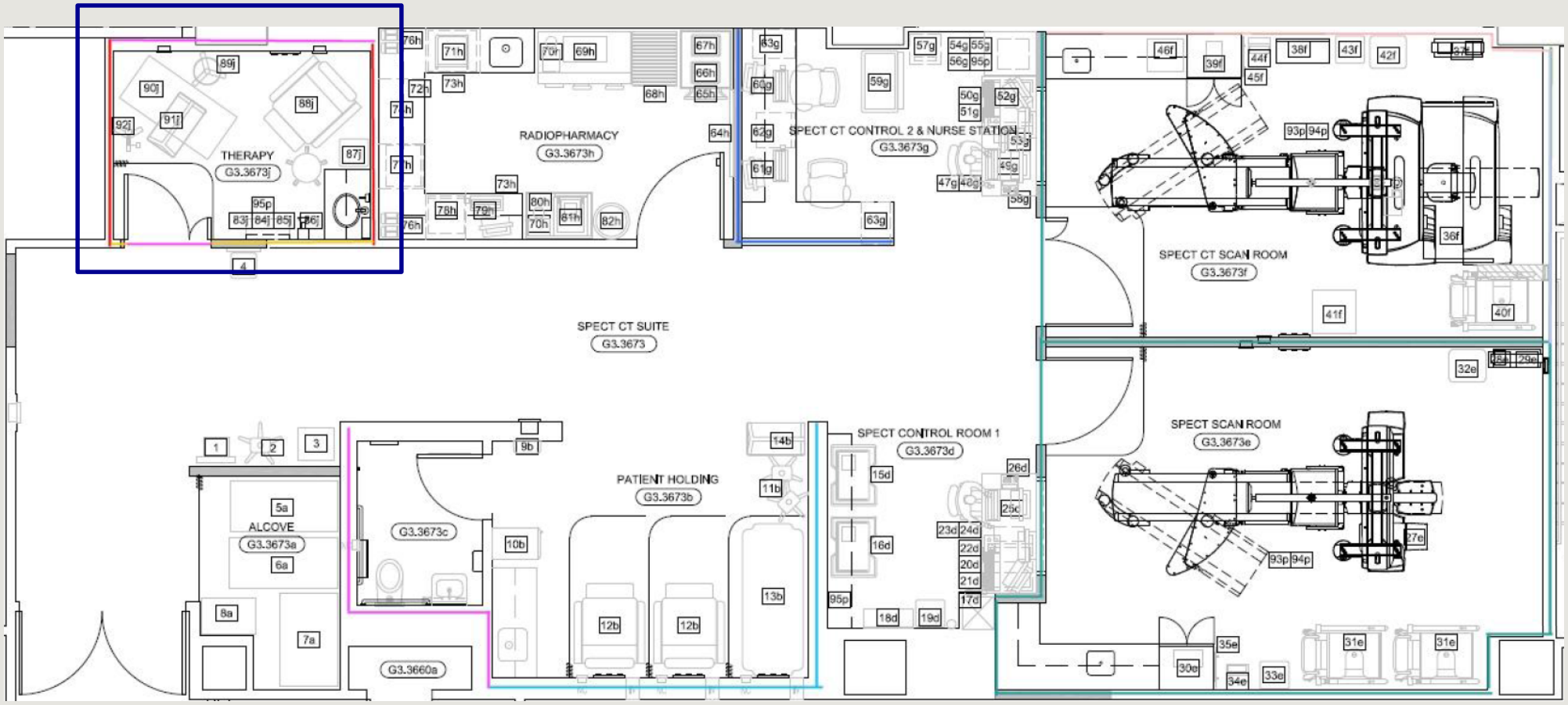
6.1384 LAB WET INVITRO
6.1425 INTERPRET WORK AREA
6.1412 WAIT GOWNED MALE
6.1403 HALL
6.1404 HALL
6.1437 BONE DENSITOMETRY
6.1431 BONE DENSITOMETRY
6.1426 STORAGE
6.1421 STORAGE
6.1402 WAIT GOWNED FEMALE
6.1406 DRESS
6.1409 DRESS
6.1410 DRESS
6.1388 CLEAN SUPPLY
6.1502 CORRIDOR
6.1552 SOILED HOLDING
6.1555 TLT STAFF
6.1542 TLT PAT
6.1541 TLT PAT
6.1520 TLT PAT
6.1525J PREP
6.1525H PREP
6.1525G PREP
6.1525F PREP
6.1526A CONTROL
6.000.A SHELL SPACE
6.1525C NS
6.1525B NS
6.1525A NS
6.1500 RECEPT
6.1555A CONTROL
6.1526 SCAN
6.1525 HALL
6.1693 ELEC.
6.1555 SCAN
6.15250 NS
6.1521 CORRIDOR
6.1525K PREP
6.1525L PREP
6.1525E NURSE
6.1530A CONTROL
6.1500A PSC
6.1551 CORRIDOR
6.1530 SCAN
6.1543 TECH WORK CORE
6.1537C DECAY HOLD 24HR/WEEK
6.1537B RADIOPHARMACY
6.1695 JANITOR
6.1561 SCAN
6.1565A CONTROL
6.1537 ANTE
6.1604 MEN
6.1697 I.T.
6.1565 SCAN
6.1708 WOMEN
6.1538 SCAN
6.1537A RADIOPHARMACY THERAPY
6.1538A CONTROL


6.1345 UPTAKE
6.1349 OB/GYN
F A04 01
F A04 01
Floor 1/2” Pb
Ceiling 3/8” Pb
6.1341 NURSE
6.1346 THERAPY
6.1350 THERAPY
Pb
5/8”
1”

MDA Pedi OP NM Therapy Room

Pb 1/2" 3/8" 1/4"

(within IP/pedi NM suite)



MDA IP NM Therapy Rooms (1)

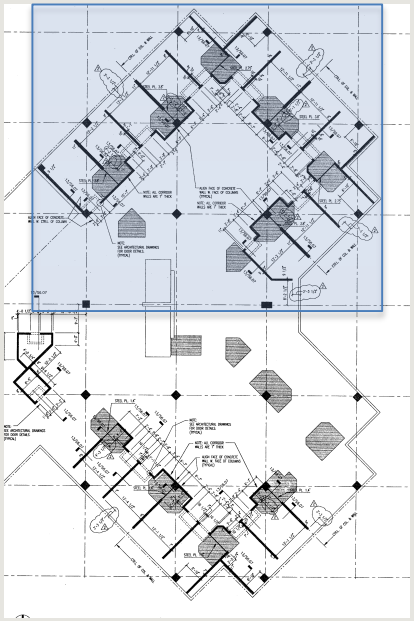
<u>Shielding</u>

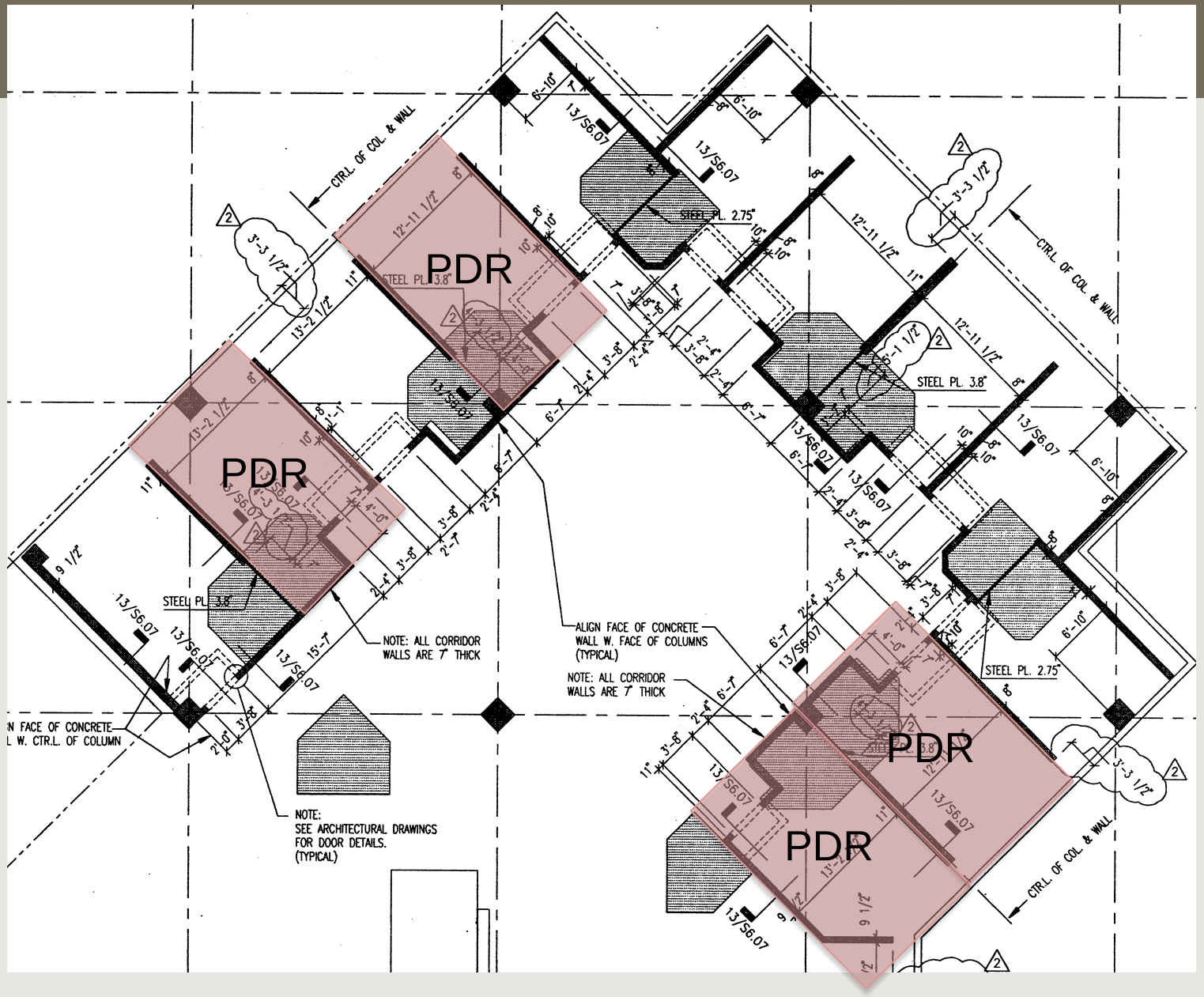
Doors

- steel

Walls

- med. wt. concrete
- steel





MDA IP NM Therapy Rooms (2)

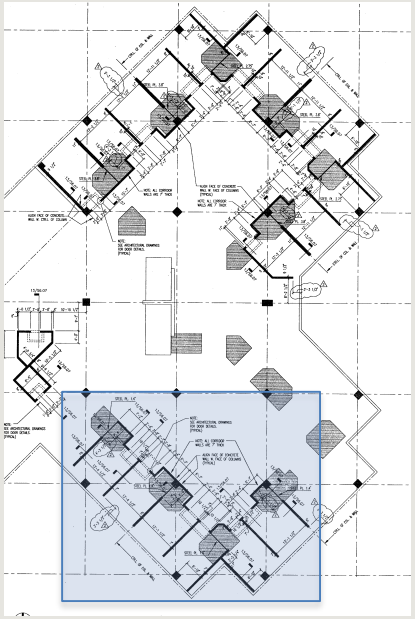
Shielding

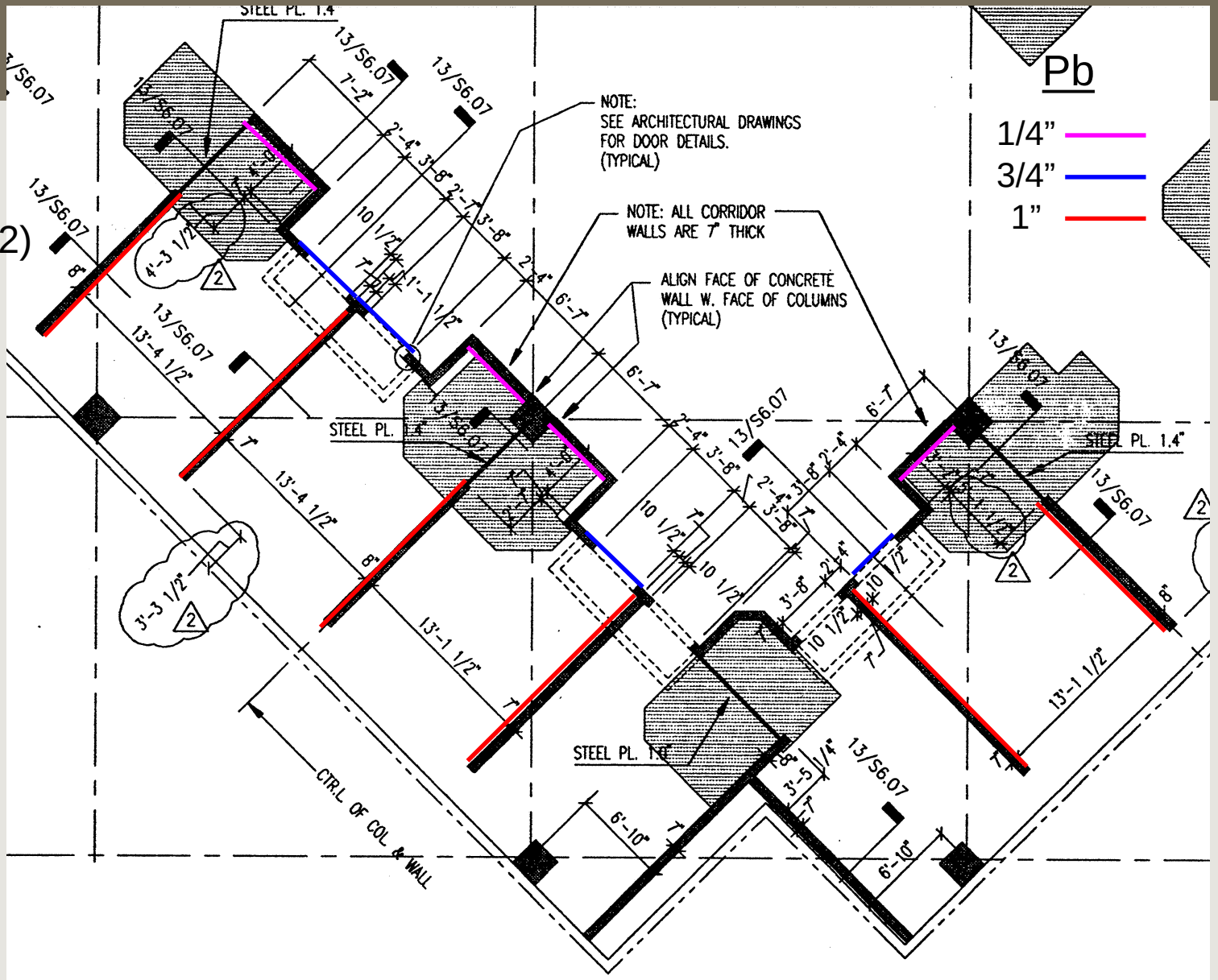
Doors

- ¾” Pb (4), ½” steel (2)

Walls

- med. wt. concrete (+/- add’l. Pb)
- steel



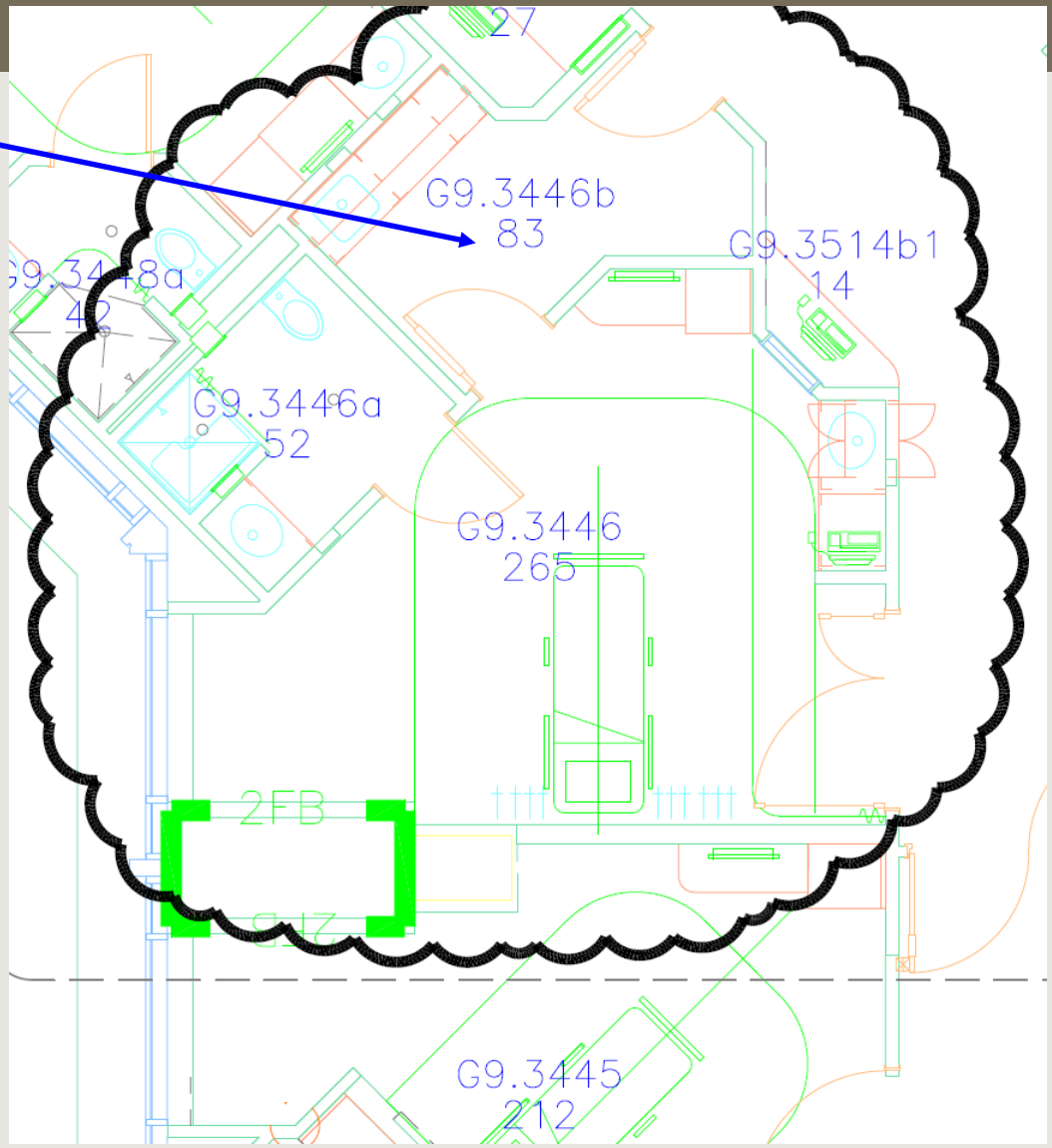


Proposed Pediatric IP NM Therapy Room

future parent “ante room”

Pediatric Oncology wants:

- “in on” Draximage ^{131}I-mIBG pediatric protocol
  - (+ other new pedi NM Tx’s)
- A dual-purpose shielded room on pediatric inpatient floor
  - Rather than a room on 10th floor using adult nursing staff
  - Pediatric nursing staff better suited to caring for such patients



Our General (Adult-Centric) Philosophy

IP vs. OP NM Tx

- No dedicated IP NM Tx rooms
  - used for non-radioactive IPs when not in use for NM Tx
  - IP occupancy always near 100%
  - difficult to reserve a NM Tx room ahead of time
- IP vs. OP pre-screening, taking into account
  - patient status, lifestyle and ability to comply w/ instructions
  - radiopharmaceutical and amount of radioactivity
  - NRC-compliant[1] release TEDE[2] calculation[3] (pre-planning)

Result: > 90% of all our NM Tx's are OP

Some (e.g., TheraSphere/SIR-Spheres, Xofigo, LutaThera) are OP by default

[1]10 CFR 35.75, NUREG 1556 Volume 9, Rev 2, Appendix U

[2]total effective dose equivalent [3]to the most-exposed person

Radioactive Patient Release

U.S. NRC ***Regulations*** (10 CFR 35.75)

§ 35.75 Release of individuals containing unsealed byproduct material or implants containing byproduct material.

(a) A licensee may authorize the release from its control of any individual who has been administered unsealed byproduct material or implants containing byproduct material if the total effective dose equivalent to any other individual from exposure to the released individual is not likely to exceed 5 mSv (0.5 rem).[1]

(b) A licensee shall provide the released individual, or the individual's parent or guardian, with instructions, including written instructions, on actions recommended to maintain doses to other individuals as low as is reasonably achievable if the total effective dose equivalent to any other individual is likely to exceed 1 mSv (0.1 rem). If the total effective dose equivalent to a nursing infant or child could exceed 1 mSv (0.1 rem) assuming there were no interruption of breast-feeding, the instructions must also include—

(1) Guidance on the interruption or discontinuation of breast-feeding; and

(2) Information on the potential consequences, if any, of failure to follow the guidance.

(c) A licensee shall maintain a record of the basis for authorizing the release of an individual in accordance with § 35.2075(a).

(d) The licensee shall maintain a record of instructions provided to a breast-feeding female in accordance with § 35.2075(b).

Note: NO distinction between adults, children or pregnant females related to exposure limit in NRC regulations!!!

https://www.nrc.gov/reading-rm/doc-collections/cfr/part035/part035-0075.html

Radioactive Patient Release

NCRP ***Recommendations**** (which we follow)

5 mSv (500 mrem)

applies to non-pregnant adult family member only

TABLE A.1—*Occupancy factors, index distances, and effective dose limits.*

Group/Activity	Occupancy Factors	Index Distances (m)	Effective Dose Limits (mSv)
Members of patients' family:			
Nonsleeping partner/adult	0.25	1.0	5
Nonpregnant sleeping partner	0.33	0.3	5
Pregnant sleeping partner	0.33	0.3	1
Pregnant women/children	0.25	1.0	1/1
Child held by patient	0.20	0.3	1
Public: Co-worker	0.33	1.0	1

*NCRP Report No. 155: Management of radionuclide therapy patients.

Our General (Adult-Centric) Philosophy
NM Tx Patient Release Calculation Models

- RAI Tx
  - Routine: 3-compartment w/ measured 24-h thyroidal uptake
    - Thyroid Ca: ^{123}I or ^{131}I scan, Hyperthyroidism: ^{123}I probe
  - Thyroid Ca dosimetry study: measured exposure rate & $T_{½eff}$
- All other Tx radiopharmaceuticals
  - measured exposure rate & $T_{½eff}$

Note: For some known combinations of radionuclide other than ^{131}I (e.g., ^{90}Y, ^{153}Sm, ^{223}Ra) and (relatively low) administered activity, we “treat and street” (legally) without instructions, based on administered activity and physical half life (i.e., no measurements needed).

RAI Tx 3-Compartment Model

NUREG 1556 Vol. 9, Rev. 2, App. U*

Equation B-5:

$$D(\infty) = \frac{34.6\,\Gamma\,Q_0}{(100\,cm)^2}\left\{E_1\,T_p\,(0.8)(1-e^{-0.693(0.33)/T_p}) + e^{-0.693(0.33)/T_p}E_2\,F_1\,T_{1eff} + e^{-0.693(0.33)/T_p}\,E_2\,F_2\,T_{2eff}\right\}$$

where:
F_1 = Extrathyroidal uptake fraction;
F_2 = Thyroidal uptake fraction;
E_1 = Occupancy factor for the first 8 hours; and
E_2 = Occupancy factor from 8 hours to total decay.

NUREG - 1556, Vol. 9, Rev 2 U-20

Table U.6 Uptake Fractions and Effective Half-Lives for Iodine-131 Treatments

	Extrathyroidal Component		Thyroidal Component	
Medical Condition	Uptake Fraction F_1	Effective Half-Life T_{1eff} (day)	Uptake Fraction F_2	Effective Half-Life T_{2eff} (day)
Hyperthyroidism	0.20[1]	0.32[2]	0.80[1]	5.2[1]
Post-Thyroidectomy for Thyroid Cancer	0.95[3]	0.32[2]	0.05[3]	7.3[2]

Note: We use “24-h thyroid uptake” measurement for F_2 ($F_1 = 1 – F_2$)

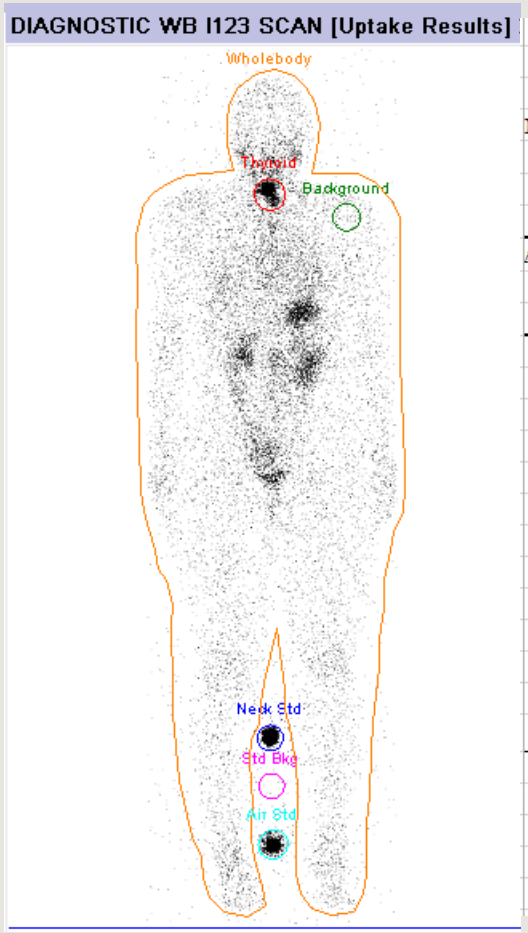
*https://www.nrc.gov/reading-rm/doc-collections/nuregs/staff/sr1556/v9/r2/

RAI Tx 3-Compartment Model

"Thyroidal" Compartment Uptake

Thyroid Cancer (post-thyroidectomy)

1.5% (neck)



		Assay Date/Time	Decay Corrected	
Activity Dispensed (uCi*):	2010.0	2/27/18 2:02 PM	1952.8	uCi* @ Administered Date/Time
Residual Activity (uCi*):			0.0	uCi*@ Administered Date/Time
Neck Standard Activity (uCi*):	163.0	2/27/18 8:58 AM	39.2	uCi* @ Image Date/Time
Air Standard Activity (uCi*):	159.0	2/27/18 8:59 AM	38.3	uCi* @ Image Date/Time

		Dispensed - Residual
Activity Administered. Date/Time:	2/27/18 2:35 PM	1952.8
Image Acquisition. Date/Time:	2/28/18 12:05 PM	
Decayed Activity (uCi*):	631.5	

Region	Counts	Pixels	Net Counts	% Administered Dose	Thyroid uCi*
Thyroid	3355	584	3265	1.487	29.030
Background 1	77	502			
Normalized Background	90	36.5	contrast	Sensitivity	
Neck Standard	13662	425	13652	347.9	counts/uCi*
Standard Background	10	408			
Whole Body	24144	132365	24144	214.6	uCi*
Air Standard	22258	577	22244	580.5	counts/uCi*
#Other Uptake			#DIV/0!	#DIV/0!	#DIV/0! uCi*
#Other Uptake Background			#OTHER UPTAKE ROIS UPON THE REQUEST OF PHYSICIAN OR PHYSICIST		

Thyroid uptake at 21:30:00 **hours is** **1.5** **% of the ingested I-123**

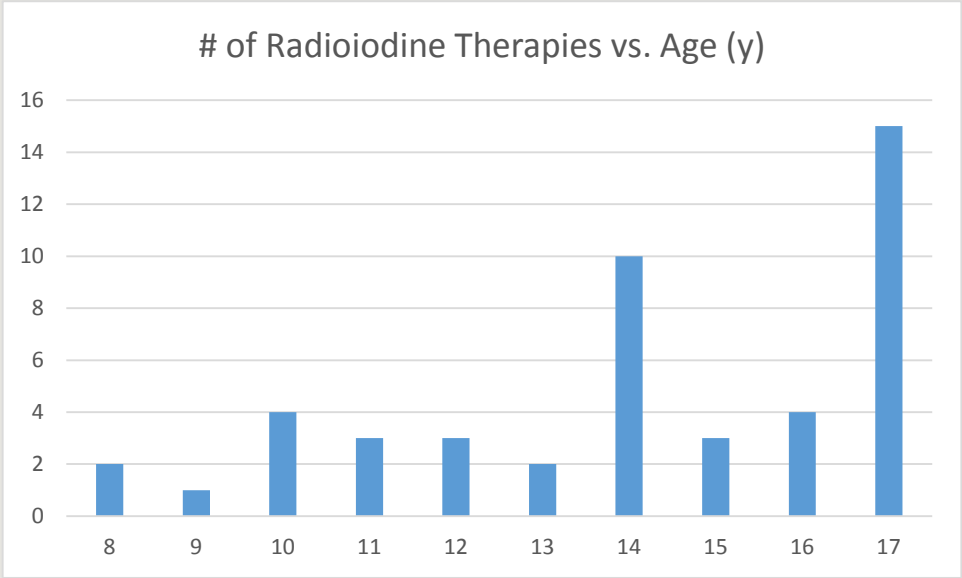
Actual time difference between administration and imaging is: 21:30:00

Abbreviation Legend
*uCi= microcurie

Adios Data	
Uptake Fraction	
Extrathyroidal	0.985
Thyroidal	0.015

MDA Pediatric RAI NM Therapy
The Last Five Years (N=47)

Age (y): mean, median: 14 (range: 8 – 17)



Activity (mCi): 94 ± 40 (range: 12 – 157)

IP: 75%

IP stays: 1 d (32), 2 d (2), 3 d (1)

MDA Pediatric NM Therapy

IP vs. OP – When?

(information provided by our RSO)

IP Tx assumed UNLESS pre-Tx release planning calculations indicate:

- OP Tx results in ≤ 100 mrem to most exposed person
  - no radiation precaution instructions needed
- OP Tx results in ≤ 500 mrem AND
  - we are confident patient can and will follow instructions (typically reserved for “older”, i.e., teenage patients)

MDA Pediatric NM Therapy

Handling of IPs (1)

(information provided by our RSO)

- adult hospital with a pedi “sub”hospital inside
- competency training for handling radioactive pedi IPs
  - a subset of adult IP NM Tx floor nursing staff
  - “borrow” and radiation safety train pediatric IP floor staff
- pediatric IP radiation safety
  - If possible, train the patient the same as an adult
  - Paper the room in the same fashion as for an adult
  - Extended stays under special circumstances only

    very sick pt, high activity, high tumoral uptake, long $T_{1/2eff}$

MDA Pediatric NM Therapy
Handling of IPs (2)

(information provided by our RSO)

- 30 min per day per patient visitor
  - except for small children needing more contact
- IP ^{131}I-mIBG Tx
  - tends to be extended stay (higher activity than that for RAI)
  - more parental responsibility typically required
    (some nursing activities, e.g., monitoring temperature, vitals)
  - parents trained as radiation workers and badged
  - portable shields used if parents insist on being present 24/7
    (as we currently have no pedi NM Tx rooms with ante rooms)

MDA Pediatric NM Therapy

Handling of IPs (3)

(information provided by our RSO)

Parent Radiation Safety Training

- the treatment itself
- the various types of radiation hazards
- activity level
- shielding
- gowning/de-gowning, double gloving
- room papering
- entertainment for the child (we have Xboxes)
- handling radioactive urine, etc.

MDA Pediatric NM Therapy
IP and OP Release Conditions

Pre-Tx release calculation: date/time post-dosing

- when est. mrem to most-exposed person is ≤ 500
  (if patient meets criteria and can follow instructions)
- else, when ≤ 100

Criteria for release at > 100 mrem

- Can follow instructions
- Can care for himself/herself
- Does not suffer from incontinence

MDA Pediatric NM Therapy

Lifestyle Questions for Release

(If to be released at < 500 mrem but > 100 mrem)

- Living w/ **any siblings < 18 yo** or pregnant women?
- Sleep > 6 ft from anyone else **(sibling for pedi)**?
- Sole, exclusive use of a bathroom?
- **Visited by children** or pregnant women?
- Can avoid crowd places?
  (buses, restaurants, stores, religious gatherings, club meetings)
- Work or **attend school**?
- w/in 6 ft of co-workers, **classmates**, “one-time” others?
- Traveling with others? If yes, distance from & duration?

MDA Pediatric NM Therapy "take-home" Instructions Template

Radionuclide: I-131 **Half-life:** 8.0 days **Dosage:** 200.5 mCi
Date and Time of Administration: Wed, Jun 27, 2018 at 4:36 PM
Measured Exposure Rate: 24 mR/hr at 1.0 m on Wed, Jun 27, 2018 at 4:38 PM
Date and Time of Planned Release from Radiation Safety Restrictions: Thu, Jun 28, 2018 at 10:00 AM

These are your personal instructions. They are different from those given to other patients. They use the information that you have given us. Please follow them to protect the safety of others.

- Do not start your travel before Thu, Jun 28, 2018 at 10:00 AM.
- Sleep alone (farther than six feet from anyone else) until Thu, Jul 19, 2018 at 6:10 AM.
- Completely stay away from children and pregnant women until Fri, Jun 29, 2018 at 1:00 PM.
- Then limit time closer than six feet to children and pregnant women until Thu, Jul 12, 2018 at 4:48 PM.
- Stay farther than six feet from others until Tue, Jul 3, 2018 at 3:07 AM.
- Do not go back to work or school before Tue, Jul 3, 2018 at 3:07 AM.

Upon Discharge: After you have been discharged, please leave the premises immediately and return to your accommodations. Please do not stop into the clinics, pick up prescriptions, eat at a restaurant or go shopping after your discharge.

For the next week, please

- Rinse the bathroom sink well after use.
- Flush the toilet three times after each use.
- Sit to urinate (both ladies and gentlemen). This will minimize splashing.

You should carry with you a copy of your specific release instructions for the next few days. The information about your therapy might be helpful in an emergency situation.

Contact Information: If, in the next day or two, you have questions about your instructions, please contact the Nuclear Medicine Department

MDA Pediatric NM Therapy Release Calculation/Planning Models

RAI

- three-compartment model (if 24-h uptake study-based)
  thyroidal tissue compartment = 24-h fractional uptake
- mR/h, and estimated $T_{1/2eff}$ (if dosimetry study-based)

All other Tx's

- mR/h, and $T_{1/2eff}$
  measured if dosimetry study-based, otherwise modeled

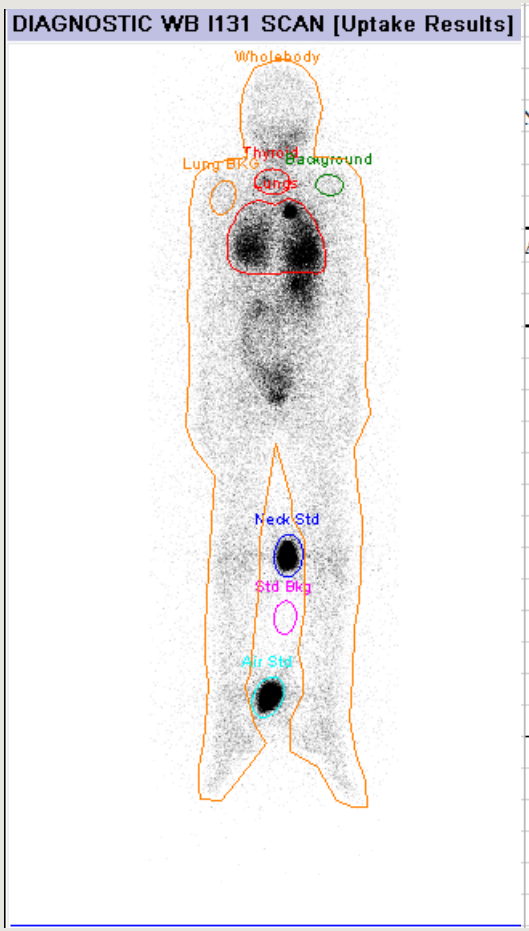
(i.e., same as for adults)

MDA Pediatric NM Therapy

RAI: Three-Compartment Model

RAI (24-h uptake study, three-compartment model)

ALL thyroidal tissue uptake (e.g., 9.7% = 0.254% neck + 9.5% lung mets in this case)



		Assay Date/Time:	Decay Corrected	
Activity Dispensed (uCi*):	1100.0	8/2/17 1:35 PM	1099.7	uCi*@ Administered Date/Time
Residual Activity (uCi*):	6.0	8/2/17 1:43 PM	6.0	uCi* @ Administered Date/Time
Neck Standard Activity (uCi*):	69.0	8/2/17 8:30 AM	63.0	uCi* @ Image Date/Time
Air Standard Activity (uCi*):	50.0	8/2/17 8:40 AM	45.7	uCi*@ Image Date/Time

		Dispensed - Residual
Activity Administered Date/Time:	8/2/17 1:40 PM	1093.7
Image Acquisition Date/Time:	8/3/17 9:40 AM	
Decayed Activity (uCi*):	1017.9	

Region	Counts	Pixels	Net Counts	% Administered Dose	Thyroid uCi*	
Thyroid	1112	576	527	0.254	2.782	
Background 1	380	374				
Normalized Background	585	0.9	contrast	Sensitivity		
Neck Standard	12969	807	12824	203.4	counts/uCi*	
Standard Background	85	474				
Whole Body	87959	76272	87959	464.6	uCi*	
Air Standard	17096	844	16945	370.7	counts/uCi*	
#Other Uptake	24128	4963	19579	9.5	103.4	uCi*
#Other Uptake Background	472	515	#OTHER UPTAKE ROIS UPON THE REQUEST OF PHYSICIAN OR PHYSICIST			

Thyroid uptake at 24^ hours is **0.3** **% of the ingested I-131**

^Actual time difference between administration and imaging is: 20:00:00

Abbreviation Legend
*uCi= microcurie

for patient release

Adios Data	
Uptake Fraction	
Extrathyroidal	0.903
Thyroidal^	0.097
^Includes Lung Uptake	

MDA Pediatric NM Therapy

RAI: Three-Compartment Model

Radionuclide: I-131 **Half-life:** 8.0 days **Dosage:** 103 mCi
Date and Time of Administration: Thu, Aug 3, 2017 at 6:30 PM
Measured Exposure Rate: 21 mR/hr at 1.0 m on Thu, Aug 3, 2017 at 6:35 PM
Date and Time of Actual Release: Fri, Aug 4, 2017 at 12:00 PM

Interviewed by: Bony Cherian, CNMT **Interview Summary:** This patient

- Can follow instructions.
- Does not suffer from incontinence.
- Sleeps close to another person.
- Is visited by children.
- Does not work or attend school outside the home.
- Can care for him- or herself.
- Lives with others including children.
- Has sole, exclusive use of a bathroom.
- Can avoid crowded places.
- Will travel with others at a distance of 4 feet for 0.5 hours.

Determination of Release from Radiation Safety Restrictions: Based upon the three compartment model parameters below, this patient may be released after Thu, Aug 3, 2017 at 6:30 PM. Under the conditions of this release, the most exposed person is unlikely to receive a total dose of more than 500 mrem.

Compartment	Uptake	T-effective	Occupancy	Start	Stop
Circulating	0.8	8.03 days	0.75	0.0 days	0.33 days
Extrathyroidal	0.903	0.32 days	0.25	0.33 days	100.0 yrs
Thyroidal	0.097	7.3 days	0.25	0.33 days	100.0 yrs

Instructions for the Patient: This patient has been given the following instructions orally and in writing.

These are your personal instructions. They are different from those given to other patients. They use the information that you have given us. Please follow them to protect the safety of others.

- Do not start your travel before Fri, Aug 4, 2017 at 12:00 PM.
- Sleep alone (farther than six feet from anyone else) until Sun, Aug 20, 2017 at 12:41 AM.
- Completely stay away from children and pregnant women until Thu, Aug 10, 2017 at 12:00 PM.
- Then limit time closer than six feet to children and pregnant women until Mon, Aug 14, 2017 at 5:32 AM.
- Stay farther than six feet from others until Mon, Aug 7, 2017 at 6:14 AM.
- Do not go back to work or school before Fri, Aug 4, 2017 at 12:00 PM.

Estimated Doses to Exposed Persons:

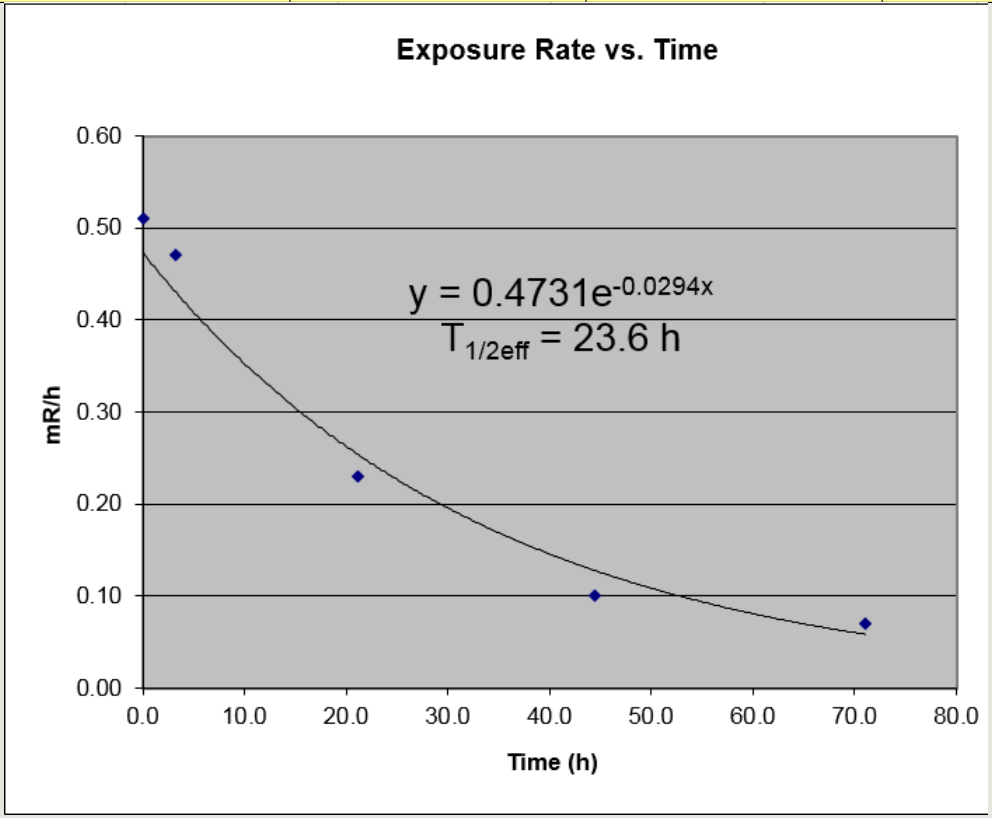
Most Exposed Person: 208 mrem | Fellow Traveler: 3 mrem | Children and Pregnant Woman: 100 mrem

MDA Pediatric NM Therapy

RAI: Measured mR/h and $T_{1/2eff}$

(from pre-Tx dosimetry study)

Hours post-admin	0.0	3.2	21.2	44.5	71.0
Exposure rate (mR/hr @ 1m)	0.51	0.47	0.23	0.10	0.07



MDA Pediatric NM Therapy

RAI: Measured mR/h and $T_{1/2eff}$

Release of a Patient from Radiation Safety Restrictions

Patient:
Radionuclide: I-131 **Half-life:** 8.0 days **Dosage:** 154.2 mCi
Date and Time of Administration: Tue, Jan 2, 2018 at 6:22 PM
Measured Exposure Rate: 5.7 mR/hr at 1.0 m on Wed, Jan 3, 2018 at 10:45 AM by using instrument
Effective Halflife: 23.6 hours
Date and Time of Planned Release: Wed, Jan 3, 2018 at 12:00 PM

Interviewed by: **Interview Summary:** This patient

Can follow instructions.	Can care for him- or herself.
Does not suffer from incontinence.	Lives with others including children.
Sleeps alone.	Must share a bathroom with others.
Is visited by children.	Can avoid crowded places.
Does not work or attend school outside the home.	Will travel with others at a distance of 2 feet for 3.5 hours.

Determination of Release from Radiation Safety Restrictions: Based upon measured exposure rate and effective halflife, this patient may be released after Wed, Jan 3, 2018 at 10:45 AM. Under the conditions of this release, the most exposed person is unlikely to receive a total dose of more than 500 mrem.

Instructions for the Patient: This patient has been given the following instructions orally and in writing.

These are your personal instructions. They are different from those given to other patients. They use the information that you have given us. Please follow them to protect the safety of others.

- Do not start your travel before Wed, Jan 3, 2018 at 12:00 PM.
- Sleep alone (farther than six feet from anyone else) until Wed, Jan 3, 2018 at 10:26 PM.
- Limit time closer than six feet to children and pregnant women until Wed, Jan 3, 2018 at 12:00 PM.
- Stay farther than six feet from others until Thu, Jan 4, 2018 at 9:20 AM.
- Do not go back to work or school before Wed, Jan 3, 2018 at 12:00 PM.

Estimated Doses to Exposed Persons:

Most Exposed Person: 269 mrem | Fellow Traveler: 49 mrem | Children and Pregnant Woman: 86 mrem

MDA Pediatric NM Therapy

RAI: Dosimetry-Based Tx Planning

Treatment of distant metastases: **200 mCi or greater**

- estimate marrow or blood-as-surrogate dose, < 2 Gy recommended

Total body retention at 48 h:

- 120 mCi (to reduce myelosuppression risk)
- 80 mCi (w/ diffuse lung mets, to reduce radiation pneumonitis risk)

SNMMI Procedure Guideline for Therapy of Thyroid Disease with Iodine-131 (Sodium Iodide) 3.0, 2012, based on Benua et al. AJR 1962

Sgouros et al. J Nucl Med 2006; 47(12):1977-84

(Major error in original hardcopy! Use corrected, on-line version!)

- adaptation of “80 mCi @ 48 h” rule
- corrects for differences in patient size, e.g., children vs. adults

MDA Pediatric NM Therapy

RAI: “80 mCi @ 48 h” Rule (for lung mets)

Original Benua et al. AJR 1962 “80 mCi at 48 h” constraint

- based on measurements/outcomes of 15 adult females
- Activity to Administer (AA) = 80 mCi × $e^{\ln(2)\times 48/T_{½}eff}$
- can it be adapted to pediatric patients?

A *simplistic* approach: Scale AA by

- Pediatric Total Body Mass / Adult Female Total Body Mass, or
- Pediatric Lung Mass / Adult Female Lung Mass

OR

A more complicated approach:

Implement Sgouros et al Lung Dose Rate Constraint for pedi pts

MDA Pediatric NM Therapy

RAI: Sgouros et al Lung DRC

$$DR^P(T) = A_T \cdot F_T \cdot S^P_{LU \leftarrow LU} + A_T \cdot (1 - F_T) \cdot S^P_{LU \leftarrow RB}$$

$DR^P(T)$ = lung dose rate (dD/dt) at time T for MIRD phantom P

A_T = whole body activity remaining at time T

F_T = fraction of A_T in the lungs at time T

$1 - F_T$ = fraction of A_T in the "remainder of the body" at time T

$S^P_{LU \leftarrow LU}$ = lung self dose factor (mGy/MBq-s)

$S^P_{LU \leftarrow RB}$ = "remainder of the body"-to-lung dose factor

$DR^P(48\text{ h}) = \text{DRC}$, we get

$$A^P_{DRC} = \frac{DRC}{F_{48} \cdot S^P_{LU \leftarrow LU} + (1 - F_{48}) \cdot S^P_{LU \leftarrow RB}}$$

$$AA_{\max} = \frac{A^P_{DRC} \cdot F_{48}}{e^{-\lambda_{LU} \cdot 48}} + \frac{A^P_{DRC} \cdot (1 - F_{48})}{e^{-\lambda_{RB} \cdot 48}}$$

MDA Pediatric NM Therapy

RAI: Sgouros et al Lung DRC

The article "Lung Toxicity in Radioiodine Therapy of Thyroid Carcinoma: Development of a Dose-Rate Method and Dosimetric Implications of the 80-mCi Rule," by Sgouros et al. (*J Nucl Med.* 2006;47:1977–1984), contained substantive errors in the reported data. A corrected PDF version is available online at http://jnm.snmjournals.org/cgi/data/47/12/1977/DC1/1. The authors regret the errors.

TABLE 1
Values for Parameters in Reference Phantoms

Reference phantom	M_{TB} (kg)	M_{LU} (kg)	$S_{LU \leftarrow LU}$ (mGy/MBq-s)	$S_{LU \leftarrow TB}$ (mGy/MBq-s)	$S_{LU \leftarrow RB}$ (mGy/MBq-s)	$SP_{LU \leftarrow LU}$ (mGy/MBq-s)
Male adult	73.7	1.00	3.40×10^{-5}	7.22×10^{-7}	2.64×10^{-7}	3.60×10^{-6}
Female adult	56.9	0.80	4.28×10^{-5}	9.34×10^{-7}	3.37×10^{-7}	4.80×10^{-6}
15-y-old	56.8	0.65	5.16×10^{-5}	9.33×10^{-7}	3.46×10^{-7}	4.90×10^{-6}
10-y-old	33.2	0.45	7.34×10^{-5}	1.48×10^{-6}	4.85×10^{-7}	6.29×10^{-6}

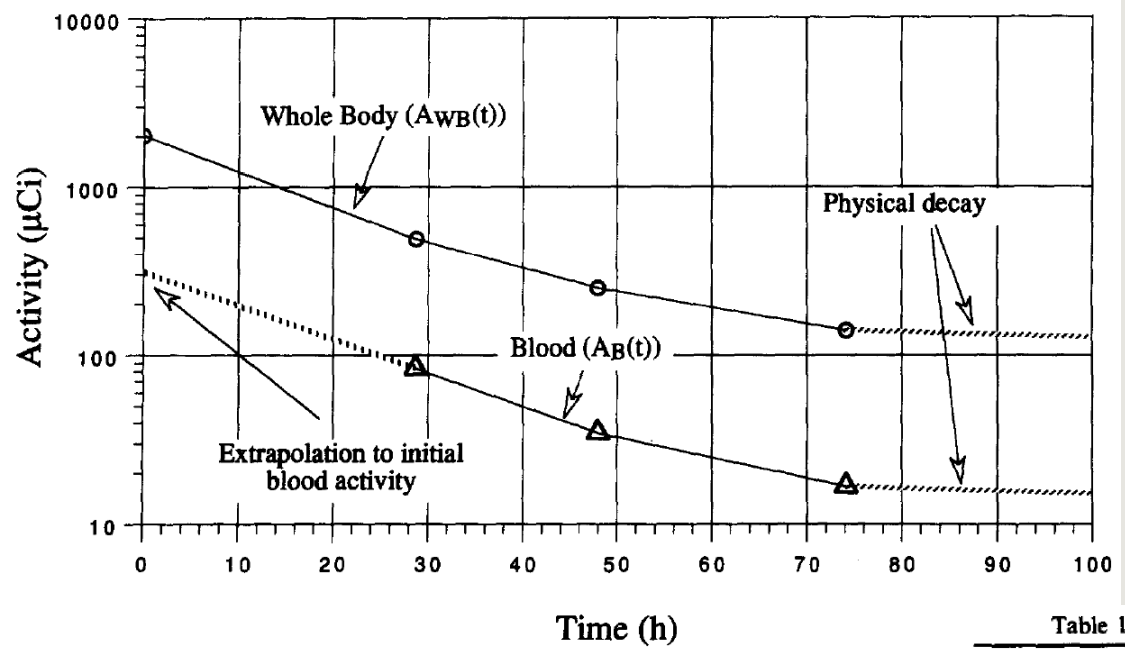
was

$S_{LU \leftarrow RB}$ (mGy/MBq-s)
1.92×10^{-5}
2.36×10^{-5}
2.98×10^{-5}
3.51×10^{-5}

a huge difference!

MDA Pediatric NM Therapy

RAI: “Bloodless” Blood Dosimetry



f

Table 1. f-ratio (f = activity in blood divided by activity in whole body: A_B/A_{WB})

	Patient group		
	1 Metastatic cancer ($n = 8$)	2 Residual thyroid tissue ($n = 19$)	3 Negative scan ($n = 22$)
Group average f-ratio			
(a) Mean $\pm 1\sigma$	0.14 ± 0.04	0.14 ± 0.04	0.17 ± 0.05
(b) Range	0.08 to 0.19	0.03 to 0.21	0.11 to 0.25
(c) Median	0.16	0.14	0.16

Thomas et al. Nucl Med Biol 1993; 20:157-62

MDA Pediatric NM Therapy

RAI: "Bloodless" Blood Dosimetry

ADULT

$$f = 0.14$$

$$\bar{D}(\text{blood})/A_0 = \tau_{WB}[f S_B + (1-f) S_{REM}],$$

$$i.e., \tau_{blood} = \tau_{WB} \times f$$

$$\tau_{RB} = \tau_{WB} \times (1-f)$$

$$S_{REM} = S(\text{blood} \leftarrow \text{REM}) = S(\text{TB} \leftarrow \text{TB})$$

$$S(\text{blood} \leftarrow \text{blood}) = S_B$$
$$= [S_{MIRD}(\text{blood} \leftarrow \text{blood})](5200/V_{pt})$$

where the factor $5200/V_{pt}$ represents the ratio of the standard man blood volume (5200 mL) to the patient specific blood volume (V_{pt}). The whole blood volume for each patient is estimated using Retzloff's formula as the sum of the red blood cell volume (RBCV) and the plasma volume (PLV) where:

(a) for males:

$$\text{RBCV} = 8.2\,(\text{height, cm}) + 17.3\,(\text{weight, kg}) - 693$$
$$\text{PLV} = 23.7\,(\text{height, cm}) + 9\,(\text{weight, kg}) - 1709$$

(b) for females:

$$\text{RBCV} = 16.4\,(\text{height, cm}) + 5.7\,(\text{weight, kg}) - 1649$$
$$\text{PLV} = 40.5\,(\text{height, cm}) + 8.4\,(\text{weight, kg}) - 4811.$$

Thomas et al. Nucl Med Biol 1993; 20:157-62

PEDI S(blood←blood), S(TB←TB) & blood ml needed!

MDA Pediatric NM Therapy

RAI: “Bloodless” Blood Dosimetry

PEDI blood ml

ICRP Publication 89 Reference Blood Volume (litres)				
Age	Males	Females	kg (Males)	kg (Females)
Newborn	0.27	0.27	3.5	3.5
1 year	0.5	0.5	10	10
5 years	1.4	1.4	19	19
10 years	2.4	2.4	32	32
15 years	4.5	3.3	56	53
Adult	5.3	3.9	73	60

Could fit to a polynomial vs.:

- Age

or

- Mass

OR

ORNL/TM-12814 (From a little web surfing)

Reference Values for Total Blood Volume and Cardiac Output in Humans

Females < 13 y.o.

$$TBV\ (L) = 0.2263 + 0.0326 \times weight\ (kg) + 0.0784 \times age\ (y)$$

Females 13 - 18 y.o.

$$TBV\ (L) = -2.4854 + 0.0346 \times weight\ (kg) + 0.0268 \times height\ (cm).$$

Males < 14 y.o.

$$TBV\ (L) = 0.0393 \times weight\ (kg) + 0.1299 \times age\ (y)$$

Males 14 - 18 y.o.

$$TBV\ (L) = -3.4722 + 0.0298 \times weight\ (kg) + 0.0374 \times height\ (cm).$$

MDA Pediatric NM Therapy

Expanded Access (Compassionate Use)

CIND: Application for use of an investigational drug, biologic or medical device outside clinical trial setting for treatment purposes. Qualifiers:

- Disease or condition: serious or immediately life threatening
- No comparable or satisfactory alternative therapy
- Enrollment in a clinical trial is not possible
- Potential patient benefit justifies potential risks of treatment
- Providing investigational product will not interfere with trials supporting development or market approval for Tx indication
- Approvals needed: FDA, IRB, manufacturer(, insurance?)

https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm

MDA Pediatric NM Therapy
High-activity ^{153}Sm-EDTMP

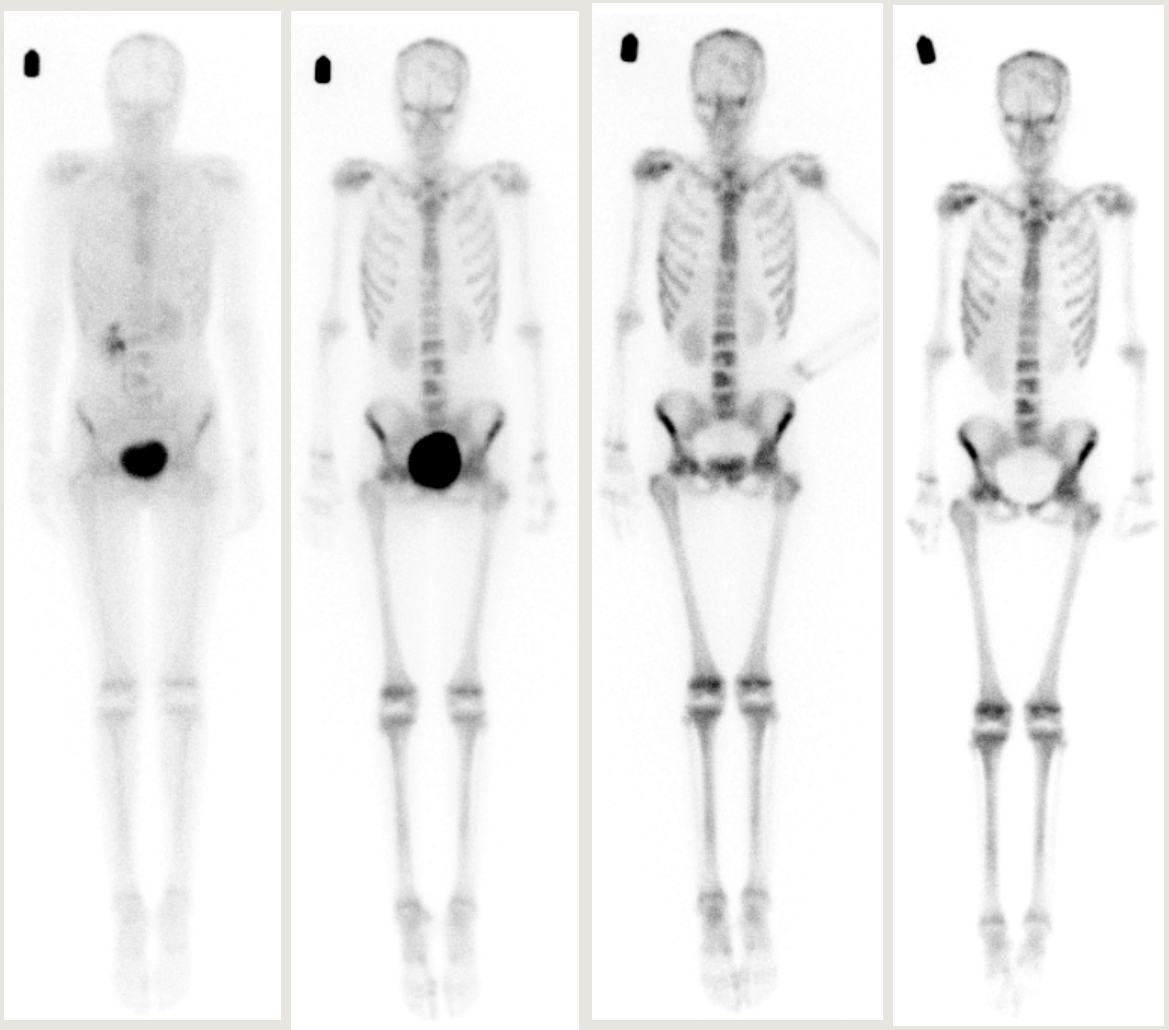
16 y.o. F, Ewing sarcoma, extensive bone mets

- Referred for pre-BMT, “high-dose” (22.5 mCi/kg) Tx (CIND)
- Pre-Tx 30 mCi dosimetry study (0-,2-,4- and 24-h WB scans)
- Geometric mean planar quantification (“0-h” WB = atten. std.)
- Source organs:
  - kidneys, bone, bladder (and rem. of body = WB – others)
- Target organs of concern:
  - kidneys, bladder (20 Gy max.)
  - NOT marrow (BMT subsequent to NM Tx)
- BMT after remaining (i.e., skeletal) ^{153}Sm activity ≤ 3.6 mCi

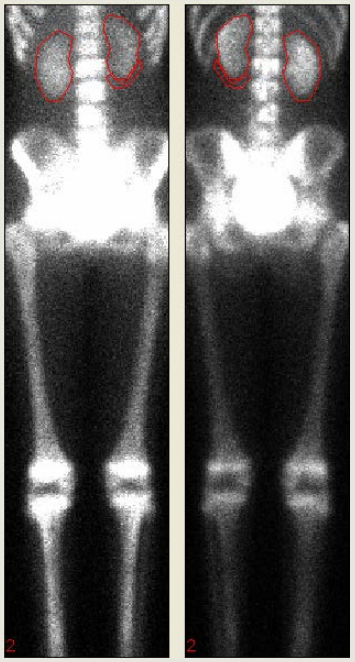
MDA Pediatric NM Therapy

High-activity ^{153}Sm-EDTMP

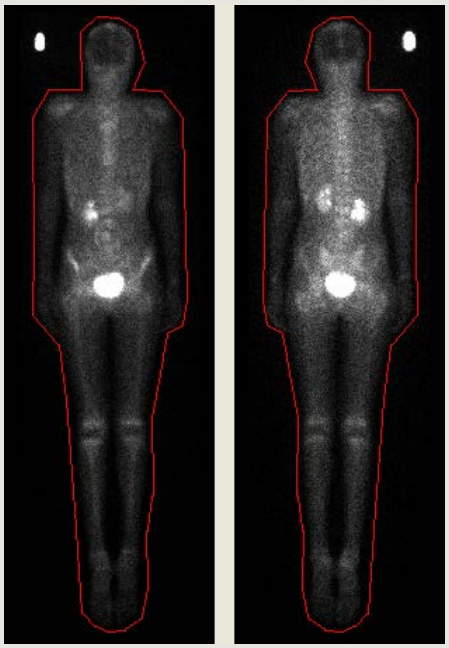
0-h 2-h 4-h 24-h



Kidneys ROIs

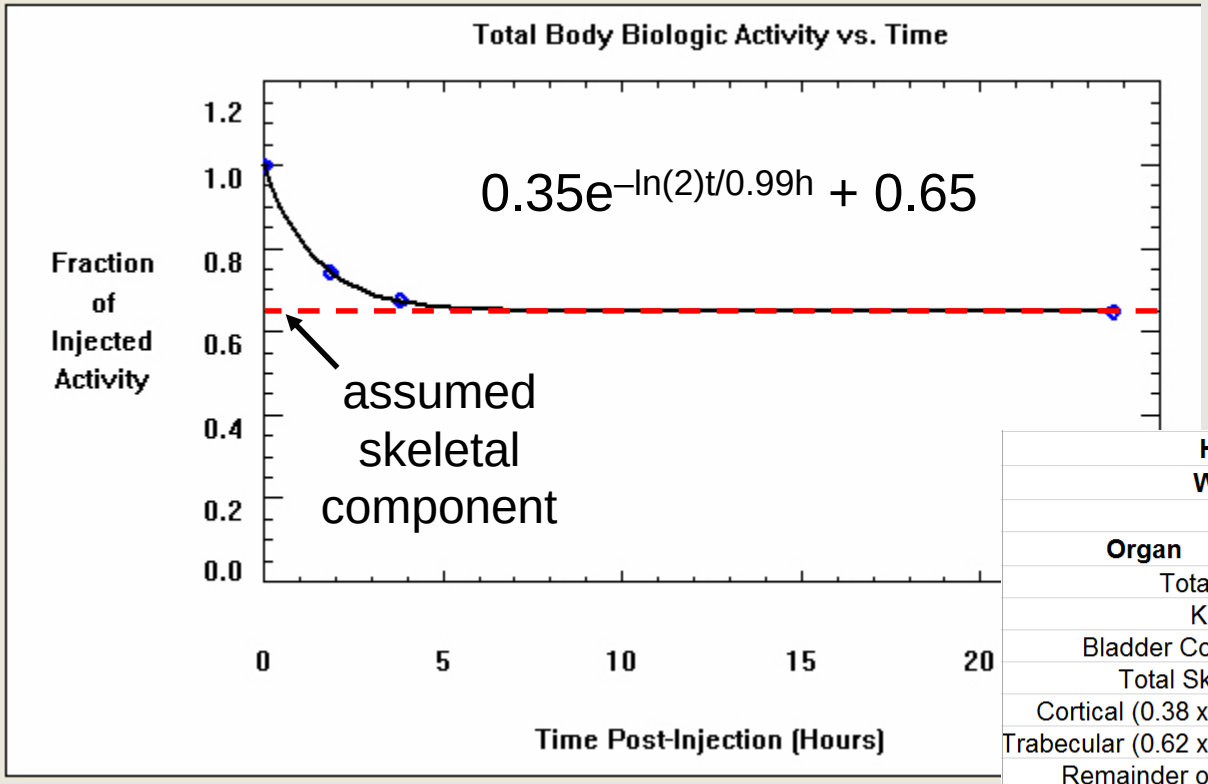


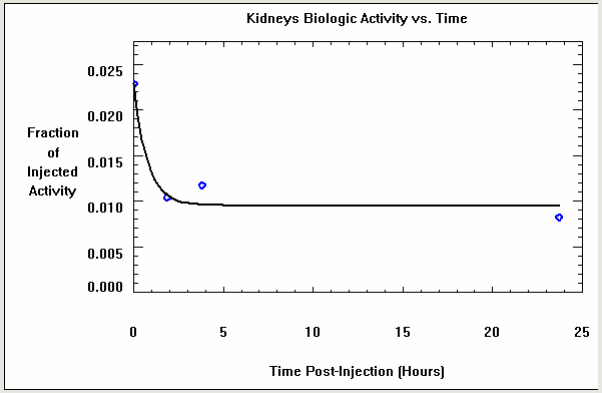
WB ROIs



MDA Pediatric NM Therapy

High-activity ^{153}Sm-EDTMP





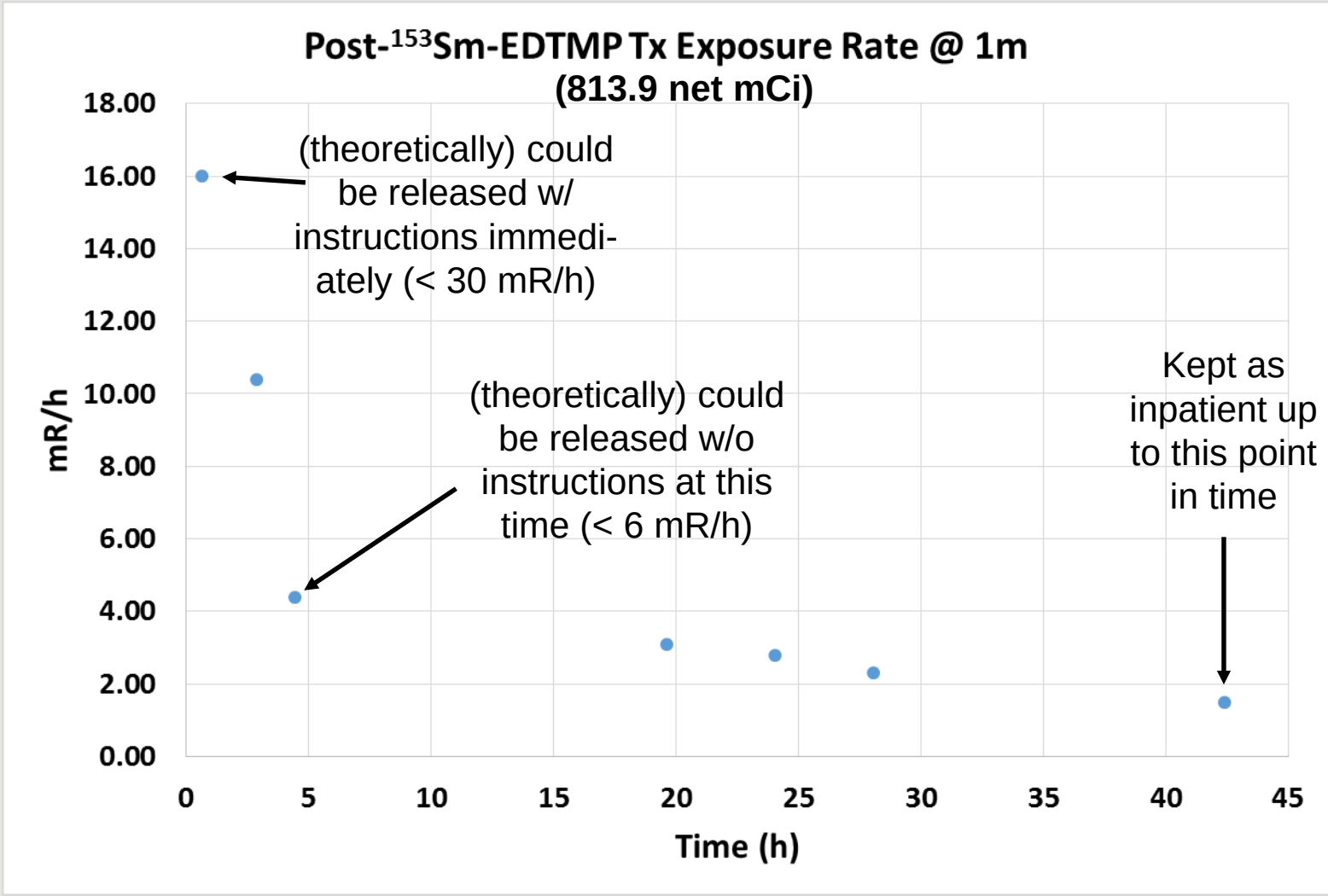
Height	167.5	**cm**	Therapy Dose		
Weight	40.4	**kg**	909.0	**mCi**	
Organ	**uCi-h/uCi**				
Total Body	44.1646				
Kidneys	0.6497	Skeleton F x e-(ln(2)*t/T/12bio)			
Bladder Contents	0.1542	F	T1/2bio (h)	T1/2eff (h)	
Total Skeleton	43.2877	0.648	100000.0	46.3	
Cortical (0.38 x Total)	16.4493				
Trabecular (0.62 x Total)	26.8384				
Remainder of Body	0.0730				
	Estimated Absorbed Dose	**(from OLINDA/EXM 1.0)**			
Total Body	**4.5**	**Gy**			
Kidneys	**14.2**	**Gy**			
Bladder	**2.7**	**Gy**			
Skeleton	**207.0**	**Gy**			
Red Marrow	**39.2**	**Gy**			

15 y.o. model

Estimated Time of 3.6 mCi Residual Activity	**340.3**	**hours**
or	**14.2**	**days**

MDA Pediatric NM Therapy

High-activity ^{153}Sm-EDTMP

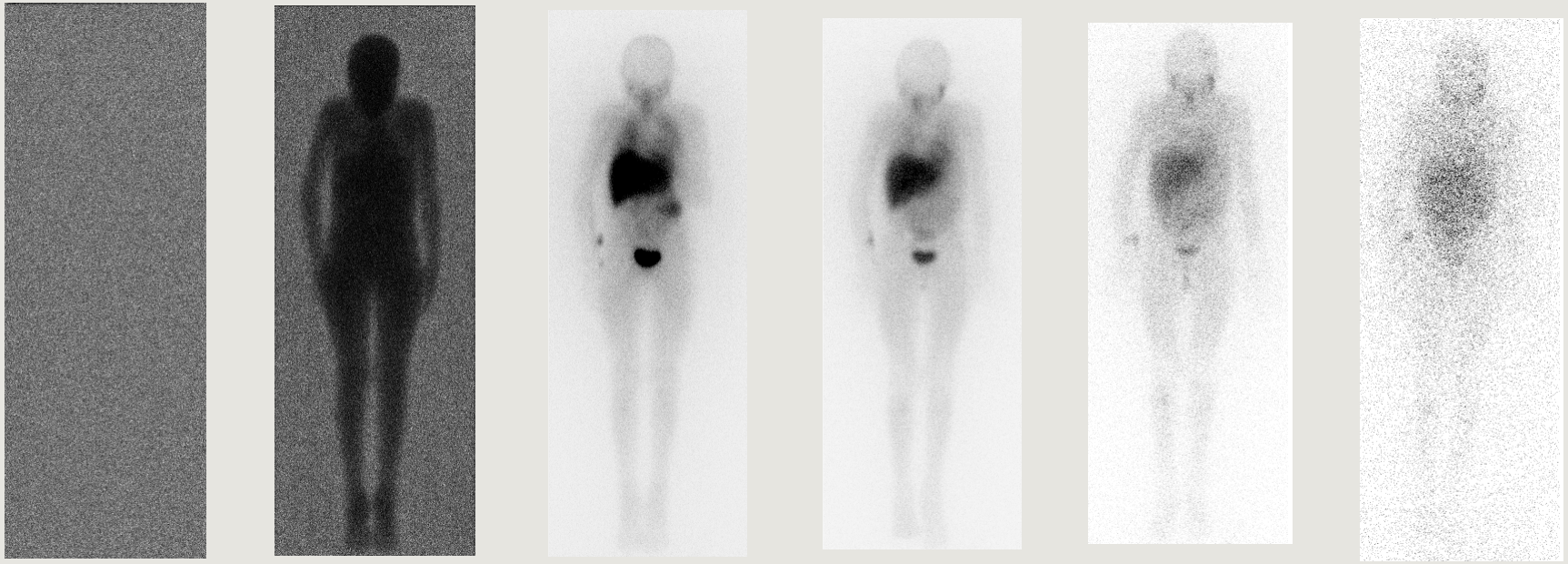


MDA Pediatric NM Therapy

^{131}I-mIBG (intent to treat)

6 y 11 mos. old, 31 kg F, neuroblastoma

- ^{123}I-mIBG (5.3 mCi) dosimetry for possible high-activity ^{131}I Tx
- WB ^{57}Co sheet source blank & trans scans (for GM counts AC)
- 0-,2-,24- and 48-h A+P WB scans (“beanie bag” immobilization)

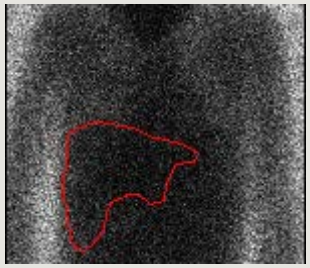


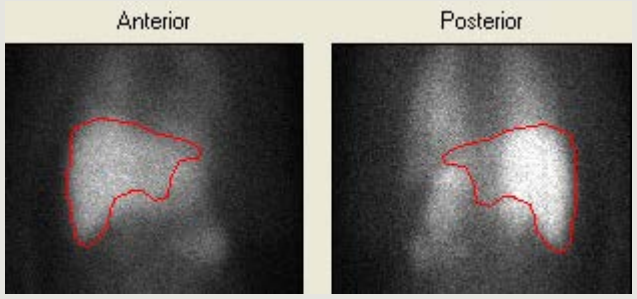
MDA Pediatric NM Therapy

^{131}I-mIBG (intent to treat)

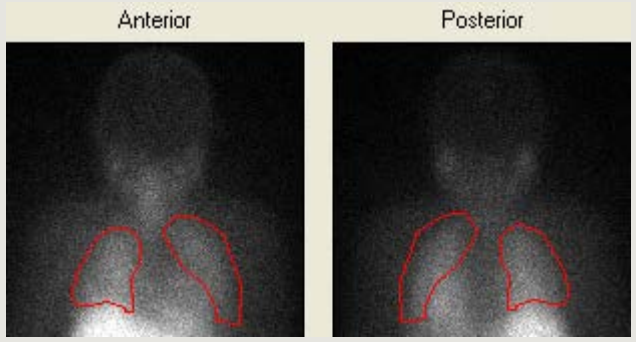
$$ACF = [\ (C_{blank} / C_{trans})^{½}\ ]^{f} \equiv e^{(\mu_{Co57} T/2) \times (\mu_{I123}/\mu_{Co57})}\ ;\ f = 0.914$$

Liver



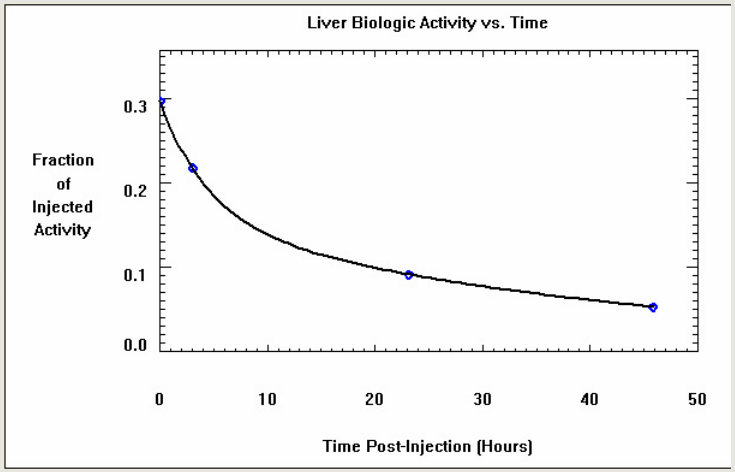


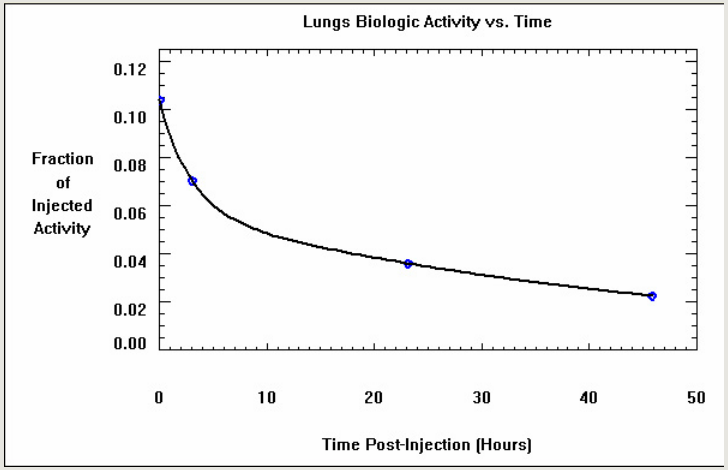
calib. std
(+pre-t=0 void)



Lungs

FIA_{bio} (^{123}I decay-corr.)





MDA Pediatric NM Therapy

^{131}I-mIBG (intent to treat)

- ^{131}I residence time = $\int_0^\infty FIA_{bio}(t)\, e^{-\lambda_{I131} t}\, dt$
- Sources: lungs, heart wall, liver, kidneys, bladder, rem.
- Organ doses of interest: marrow, total body
- OLINDA/EXM (dose estimates)
  - 5 y.o. (19 kg) or 10 y.o. (32 kg) phantom?
  - 6 y 11 mos. closer to 5, but 31 kg very close to 32 kg

		mCi for	mCi for
	cGy/mCi	100 cGy	200 cGy
Red Marrow	**3.85E-01**	**260**	**519**
		(mCi/kg)	(mCi/kg)
		8.4	16.8

		mCi for	mCi for
	cGy/mCi	100 cGy	200 cGy
Total Body	**5.68E-01**	**176**	**352**
		(mCi/kg)	(mCi/kg)
		5.7	11.4

MDA Pediatric NM Therapy

^{90}Y SIR-Spheres®

17 y.o. F, met desmoplastic small round cell ca

- Referred for radioembolization with SIR-Spheres (CIND)
- R Lobe Tx (partition model-based prescription*)
  - T:N = ^{99m}Tc MAA SPECT Tumor Cts/pixel ÷ Normal Cts/pix
  - 0.65 kg MIRD 15 y.o. M_{lung} (default = 1 kg adult male)
  - 1.03 g/ml tissue density
  - 0.119 kg M_{tumor} = 0.119 kg (115 ml VOI)
  - M_{normal} = 0.912 kg (R Lobe 1000 ml VOI – tumor VOI)
  - 7.48% lung shunt (^{99m}Tc MAA planar)

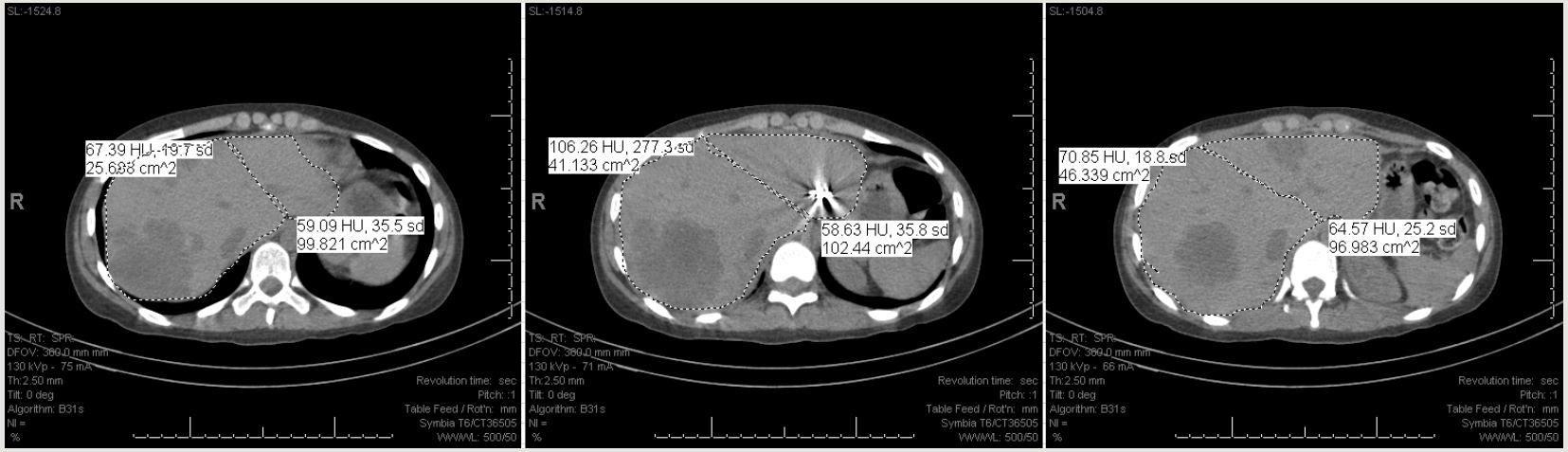
**Dezarn WA et al. AAPM TG 144. Med Phys 2011;38(8):4824-45*

MDA Pediatric NM Therapy

^{90}Y SIR-Spheres®

CT Volumes

L, R Lobes



Tumor

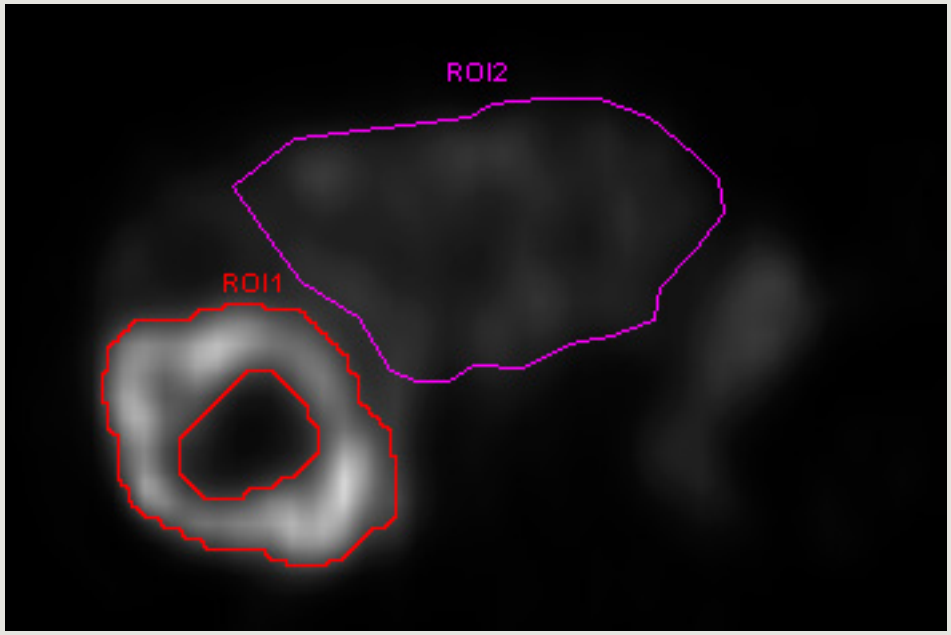
MDA Pediatric NM Therapy

^{90}Y SIR-Spheres®

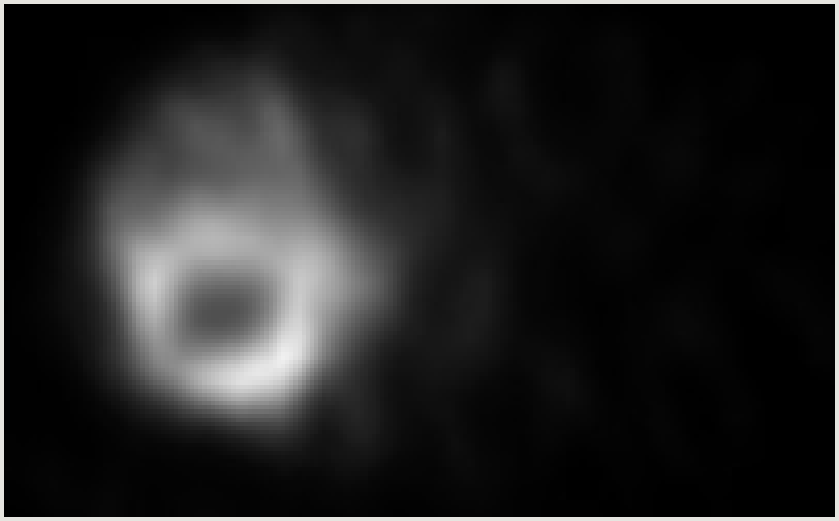
Prescription: 2.2 GBq

Tumor:	250 Gy
Normal Liver:	80 Gy (limiter)
Lungs:	13 Gy

Pre-Tx ^{99m}Tc MAA
(T:N = 3.12)



Post-Tx ^{90}Y bremsstrahlung

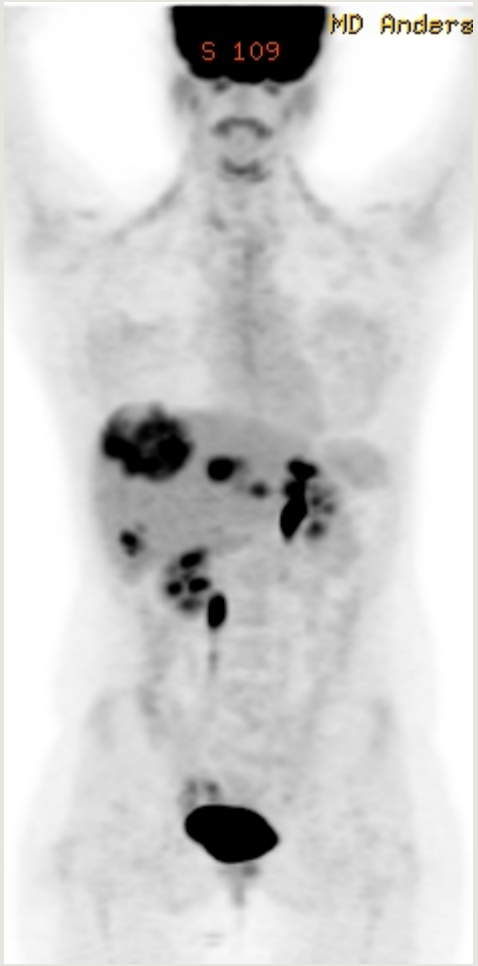


MDA Pediatric NM Therapy

^{90}Y SIR-Spheres®

Est. net infusion:
1.35 GBq (61%)
Est. tumor Gy:
153.2
Reason for < 2.2 GBq:
statis

Pre-Tx FDG



5 wk post-Tx

MDA Pediatric NM Therapy

$^{223}RaCl_2$ (a.k.a. Alpharadin, Xofigo)

(Alpharadin in 55 kBq/kg monthly × 6 trial at the time)

- 21 y.o. F w/ chrondoblastic osteosarcoma
  - R mandible, L maxilla, R femur, sacrum, spine
  - Prior chemotherapy, surgery, ^{153}Sm-EDTMP

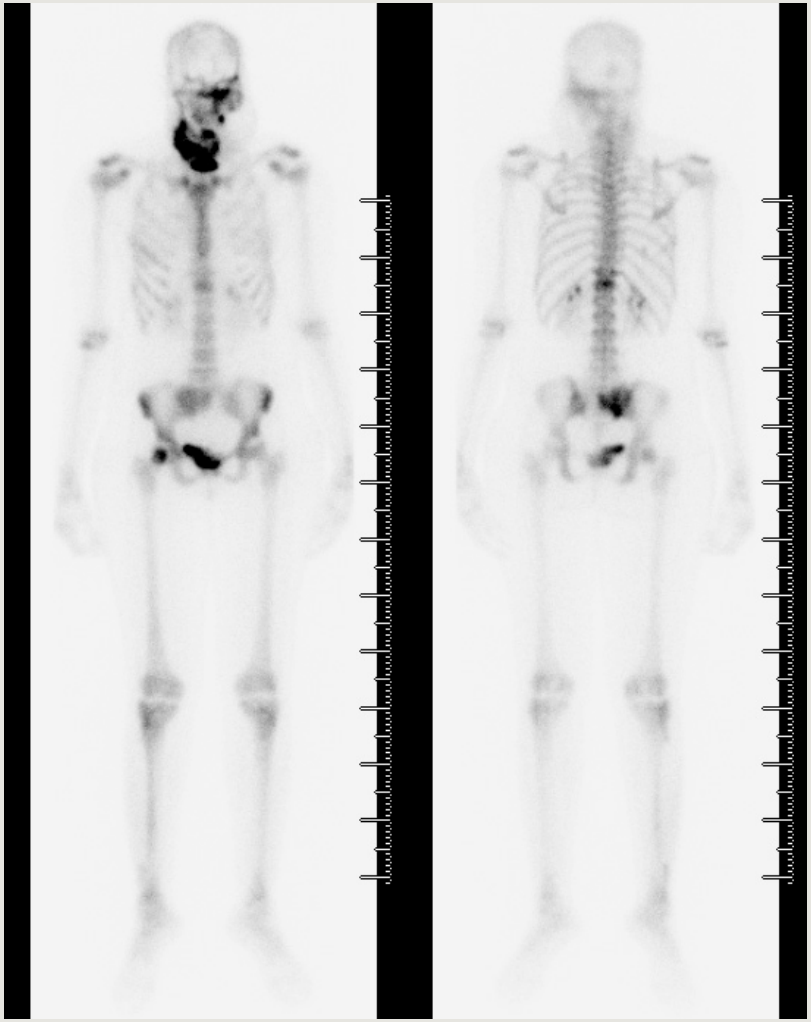
- Needed (ASAP, in short order, tout de suite, yesterday)
  - Expedited CIND (FDA, IRB, European mfr.)
  - State of Texas (Expedited RAM license amendment for ^{223}Ra)
  - Dose calibrator setting for ^{223}Ra (on-site dose dispensing)

- ~2½ mos. CIND application process start to 1st Tx

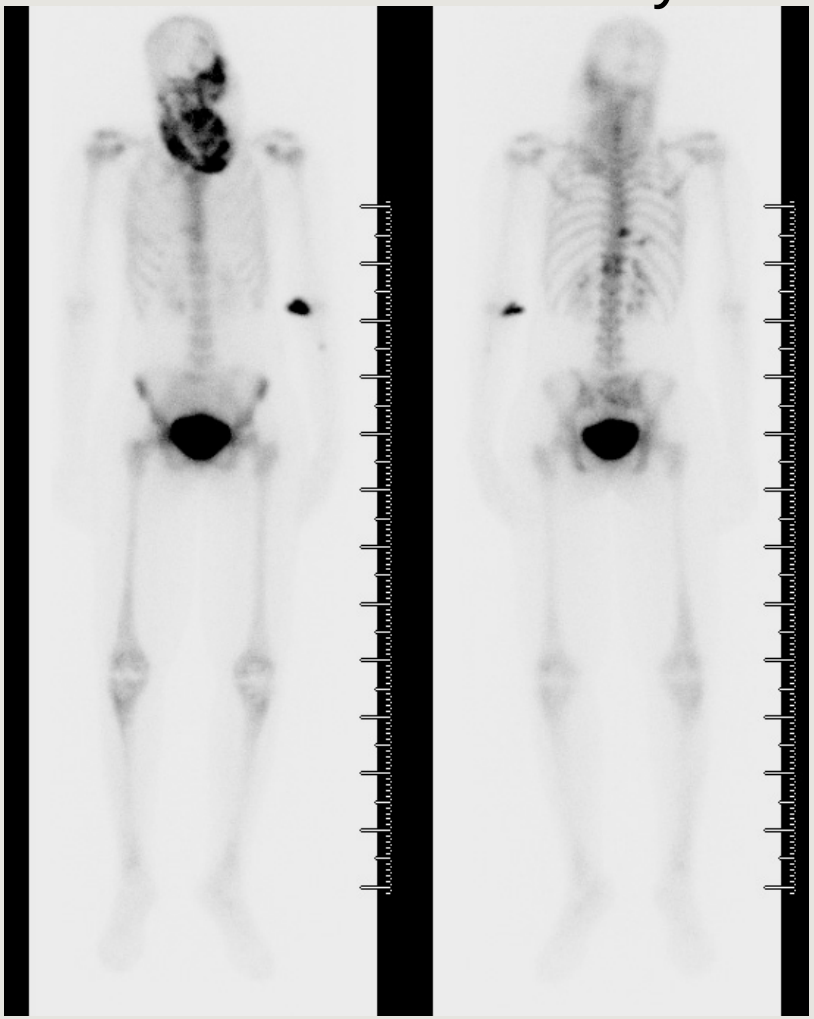
MDA Pediatric NM Therapy

$^{223}RaCl_2$ (^{99m}Tc-MDP bone scans)

Baseline



Post-Two Treatment Cycles



MDA Pediatric NM Therapy

$^{223}RaCl_2$ (a.k.a. Alpharadin, Xofigo)

Could we image for verification (< 100 μCi)?

Ra-223 ($T_{1/2}$ = 11.43 d)

XR kα2	81.069	15.0 %
XR kα1	83.787	24.7 %
γ	269.436	13.9 %

Rn-219 ($T_{1/2}$ = 3.96 s)

γ	271.23	10.8 %
γ	401.81	6.6 %

Pb-211 ($T_{1/2}$ = 1.781 ms)

γ	404.853	3.78 %

Bi-211 ($T_{1/2}$ = 2.41 m)

γ	351.06	12.92 %

81.0 & 83.8
= 39.7% yield

269.4 & 271.2
= 24.7% yield

401.8 & 404.9
= 10.4% yield

MDA Pediatric NM Therapy

$^{223}RaCl_2$ (a.k.a. Alpharadin, Xofigo)

Window Number	Center (keV)	Width (%)	Shift (%)	Type	Parent
A1	83	30	0	Photopeak	
B2	270	15	0	Photopeak	
C3		30		Lower Scatter	A1
D4		30		Upper Scatter	A1
E5		15		Lower Scatter	B2
F6		10		Upper Scatter	B2

Window Center (keV):

Window Width (%): 10

Window Shift (%):

Group A

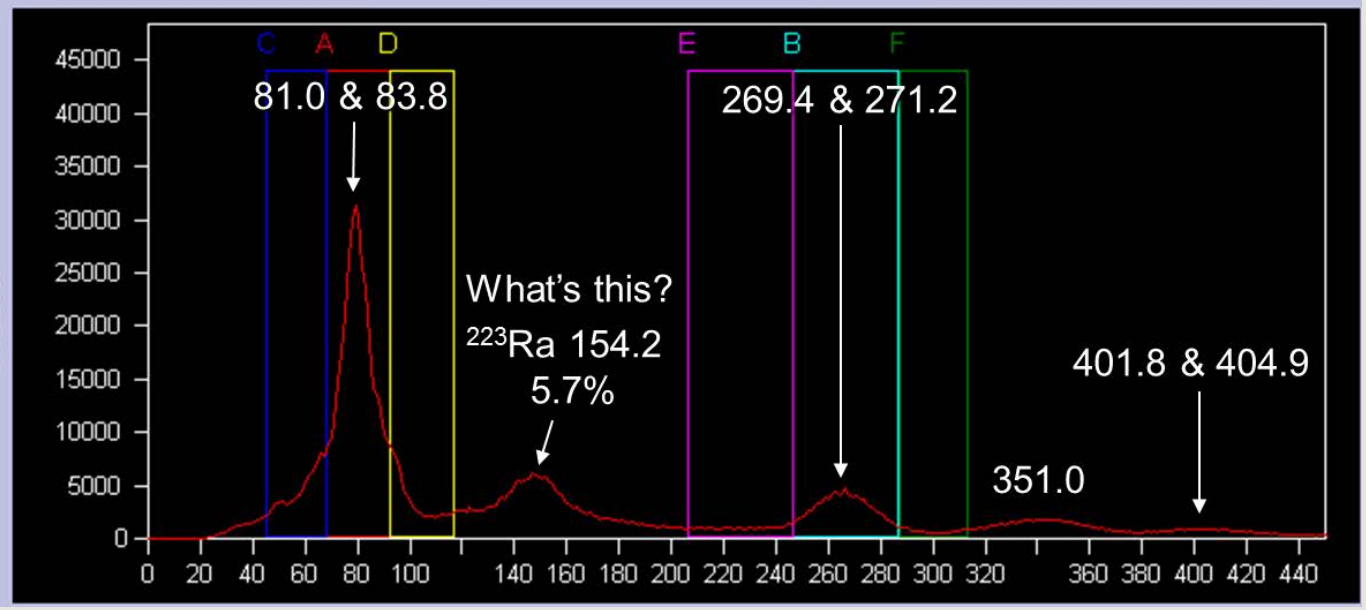
Group B

Group C

Group D

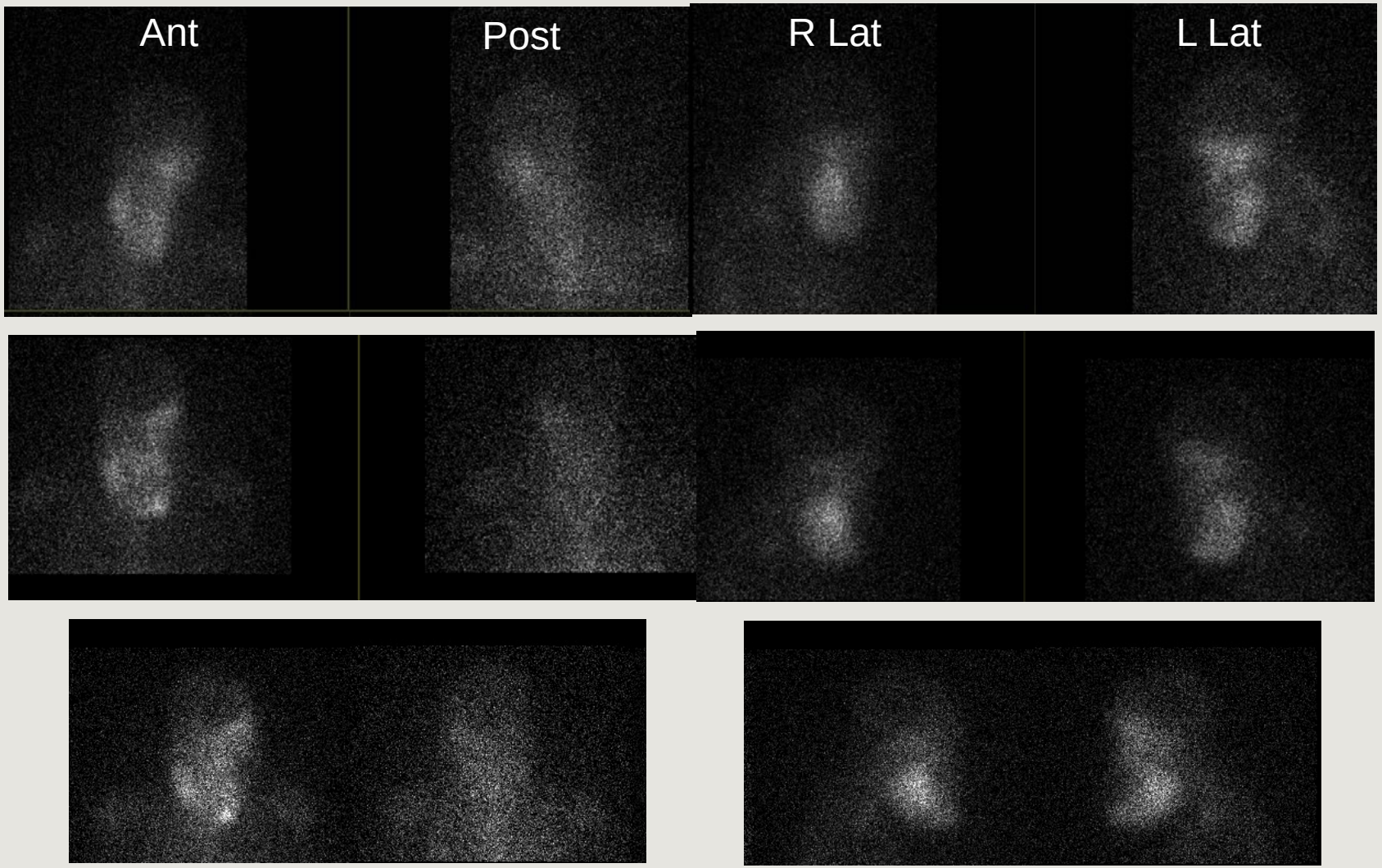
Group E

Group F



MDA Pediatric NM Therapy

$^{223}RaCl_2$ (a.k.a. Alpharadin, Xofigo)



MDA Pediatric NM Therapy in our Adult Hospital Setting

- Our experience to date
  - predominantly RAI (with which we are quite comfortable now)
  - otherwise, “special” “one-offs” (each a unique scenario)

    e.g., ^{153}Sm-EDTMP: 13 y.o. (mandibular ossifying fibroma and one kidney)
  - skewed toward “older” children
- Our “hopes for the future” (driven by referring pedi MDs)
  - shielded room on our dedicated pediatric inpatient floor
  - participation in pediatric NM therapy clinical trials

    ^{131}I-mIBG Tx of neuroblastoma

    ^{131}I-burtomab Tx of CNS neuroblastoma mets (rare, mostly ≤ 5 y.o.’s)

    (future: ^{177}Lu-DOTATATE, others?)