Pediatric NM Therapy in an Adult Hospital Setting

William Erwin, MS
Department of Imaging Physics
UT MD Anderson Cancer Center

SAM session - Methods, Mishaps and Musings on Pediatric Theranostics
AAPM 2018 Annual Meeting
July 29-August 2, 2018
Nashville, TN
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)

<table>
<thead>
<tr>
<th>Radiopharmaceutical</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>131I-Nal</strong> (a.k.a, radioiodine or RAI)</td>
<td>thyroid cancer, hyperthyroidism</td>
</tr>
<tr>
<td><strong>89SrCl, 153Sm-EDTMP, 166Ho-DOTMP, 223RaCl₂</strong></td>
<td>skeletal targeted radiotherapy</td>
</tr>
<tr>
<td><strong>90Y-Zevalin (131I-BEXXAR - discontinued)</strong></td>
<td>B-cell non-hodgkin's lymphomas</td>
</tr>
<tr>
<td><strong>90Y microspheres</strong> (SIR-Spheres, TheraSphere)</td>
<td>hepatocellur carcinoma, liver mets</td>
</tr>
<tr>
<td><strong>131I-mIBG</strong></td>
<td>pheochromocyt-, paragangli-oma</td>
</tr>
<tr>
<td><strong>177Lu-DOTATATE</strong></td>
<td>mid-gut neuroendocrine cancers</td>
</tr>
<tr>
<td><strong>225Ac-lintuzumab, 131I-Iomab</strong></td>
<td>leukemia</td>
</tr>
<tr>
<td><strong>90Y-FF21101</strong></td>
<td>p-cadherin+ cancers</td>
</tr>
<tr>
<td><strong>32P-Oncosil</strong></td>
<td>pancreatic tumors (direct infusion)</td>
</tr>
<tr>
<td><strong>177Lu-AvidinOx-Biotin</strong></td>
<td>misc. tumors (AvidinOx direct inf.)</td>
</tr>
<tr>
<td><strong>177Lu-/225Ac-PSMA</strong></td>
<td>prostate cancer</td>
</tr>
</tbody>
</table>
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”

Floor 1/2” Pb
Ceiling 3/8” Pb
MDA Pedi OP NM Therapy Room

(within IP/pedi NM suite)
MDA IP NM Therapy Rooms (1)

Shielding
Doors
- steel
Walls
- med. wt. concrete
- steel
MDA IP NM Therapy Rooms (2)

Shielding
Doors
- 3/4” Pb (4), ½” steel (2)
Walls
- med. wt. concrete (+/- add’l. Pb)
- steel
Proposed Pediatric IP NM Therapy 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 release TEDE calculation (pre-planning)

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

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

110 CFR 35.75, NUREG 1556 Volume 9, Rev 2, Appendix U
2total effective dose equivalent
3to the most-exposed person
§ 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!!!
Radioactive Patient Release

NCRP *Recommendations* (which we follow)

5 mSv (500 mrem) applies to non-pregnant adult family member only

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

<table>
<thead>
<tr>
<th>Group/Activity</th>
<th>Occupancy Factors</th>
<th>Index Distances (m)</th>
<th>Effective Dose Limits (mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Members of patients’ family:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsleeping partner/adult</td>
<td>0.25</td>
<td>1.0</td>
<td>5</td>
</tr>
<tr>
<td>Nonpregnant sleeping partner</td>
<td>0.33</td>
<td>0.3</td>
<td>5</td>
</tr>
<tr>
<td>Pregnant sleeping partner</td>
<td>0.33</td>
<td>0.3</td>
<td>1</td>
</tr>
<tr>
<td>Pregnant women/children</td>
<td>0.25</td>
<td>1.0</td>
<td>1/1</td>
</tr>
<tr>
<td>Child held by patient</td>
<td>0.20</td>
<td>0.3</td>
<td>1</td>
</tr>
<tr>
<td>Public: Co-worker</td>
<td>0.33</td>
<td>1.0</td>
<td>1</td>
</tr>
</tbody>
</table>
Our General (Adult-Centric) Philosophy

**NM Tx Patient Release Calculation Models**

- **RAI Tx**
  - Routine: 3-compartment w/ measured 24-h thyroidal uptake
    - Thyroid Ca: \(^{123}\text{I}\) or \(^{131}\text{I}\) scan, Hyperthyroidism: \(^{123}\text{I}\) probe
  - Thyroid Ca dosimetry study: measured exposure rate & \(T_{\frac{1}{2}\text{eff}}\)

- **All other Tx radiopharmaceuticals**
  - measured exposure rate & \(T_{\frac{1}{2}\text{eff}}\)

Note: For some known combinations of radionuclide other than \(^{131}\text{I}\) (e.g., \(^{90}\text{Y}\), \(^{153}\text{Sm}\), \(^{223}\text{Ra}\)) 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).
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)

### Diagnostic WB 1123 Scan [Uptake Results]

<table>
<thead>
<tr>
<th>Region</th>
<th>Counts</th>
<th>Pixels</th>
<th>Net Counts</th>
<th>% Administered Dose</th>
<th>Thyroid ( \mu \text{Ci}^* )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid</td>
<td>3355</td>
<td>584</td>
<td>3265</td>
<td>1.487</td>
<td>29.030</td>
</tr>
<tr>
<td>Background</td>
<td>77</td>
<td>502</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normalized Background</td>
<td>90</td>
<td>36.5</td>
<td>contrast</td>
<td>Sensitivity</td>
<td></td>
</tr>
<tr>
<td>Neck Standard</td>
<td>13662</td>
<td>425</td>
<td>13652</td>
<td>347.9 counts/( \mu \text{Ci}^* )</td>
<td></td>
</tr>
<tr>
<td>Standard Background</td>
<td>10</td>
<td>408</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole Body</td>
<td>24144</td>
<td>132365</td>
<td>24144</td>
<td>214.6 ( \mu \text{Ci}^* )</td>
<td></td>
</tr>
<tr>
<td>Air Standard</td>
<td>22258</td>
<td>577</td>
<td>22244</td>
<td>580.5 counts/( \mu \text{Ci}^* )</td>
<td></td>
</tr>
<tr>
<td>#Other Uptake</td>
<td>#DIV/0!</td>
<td>#DIV/0!</td>
<td>#DIV/0!</td>
<td>#DIV/0!</td>
<td></td>
</tr>
<tr>
<td>#Other Uptake Background</td>
<td>#OTHER UPTAKE ROIS UPON THE REQUEST OF PHYSICIAN OR PHYSICIST</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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

**Adios Data**

<table>
<thead>
<tr>
<th>Uptake Fraction</th>
<th>Extrathyroidal</th>
<th>Thyroidal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.985</td>
<td>0.015</td>
</tr>
</tbody>
</table>

**Abbreviation Legend**

*\( \mu \text{Ci} \) = microcurie
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 $\leq 100$ mrem to most exposed person
  - no radiation precaution instructions needed
- OP Tx results in $\leq 500$ 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 $T_{1/2}$
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.
Pre-Tx release calculation: date/time post-dosing
- when est. mrem to most-exposed person is $\leq 500$
  (if patient meets criteria and can follow instructions)
- else, when $\leq 100$

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

All other Tx’s
- mR/h, and $T_{1/2\text{eff}}$
  - measured if dosimetry study-based, otherwise modeled

(i.e., same as for adults)
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)
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 care for himself or herself.
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 himself 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.

<table>
<thead>
<tr>
<th>Compartment Uptake</th>
<th>Compartment Effective Occupancy</th>
<th>Start</th>
<th>Stop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circulating</td>
<td>0.8</td>
<td>8.03 days</td>
<td>0.75</td>
</tr>
<tr>
<td>Extrathyroidal</td>
<td>0.903</td>
<td>0.32 days</td>
<td>0.25</td>
</tr>
<tr>
<td>Thyroidal</td>
<td>0.097</td>
<td>7.3 days</td>
<td>0.25</td>
</tr>
</tbody>
</table>

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 3:32 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)
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/h at 1.0 m on Wed, Jan 3, 2018 at 10:45 AM by using instrument
Effective Half-life: 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.
Does not suffer from incontinence.
Sleeps alone.
Is visited by children.
Does not work or attend school outside the home.

Can care for him- or herself.
Lives with others including children.
Must share a bathroom with others.
Can avoid crowded places.
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 half-life, 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
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**


*(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)×48/T_{1/2}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

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

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

\[ AA_{max} = \frac{A^P_{DRC} \cdot F_{48}}{e^{-\lambda_{LU} \cdot 48}} + \frac{A^P_{DRC} \cdot (1 - F_{48})}{e^{-\lambda_{RB} \cdot 48}} \]
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://jnma.snmjournals.org/cgi/data/47/12/1977/DC1/1. The authors regret the errors.

**TABLE 1**

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

was a huge difference!
MDA Pediatric NM Therapy

RAI: “Bloodless” Blood Dosimetry

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

<table>
<thead>
<tr>
<th>Patient group</th>
<th>1 (Metastatic cancer)</th>
<th>2 (Residual thyroid tissue)</th>
<th>3 (Negative scan)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group average f-ratio</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Mean ± 1σ</td>
<td>0.14 ± 0.04</td>
<td>0.14 ± 0.04</td>
<td>0.17 ± 0.05</td>
</tr>
<tr>
<td>(b) Range</td>
<td>0.08 to 0.19</td>
<td>0.03 to 0.21</td>
<td>0.11 to 0.25</td>
</tr>
<tr>
<td>(c) Median</td>
<td>0.16</td>
<td>0.14</td>
<td>0.16</td>
</tr>
</tbody>
</table>

RAI: “Bloodless” Blood Dosimetry

\[ f = 0.14 \]

\[ \frac{D(\text{blood})}{A_0} = \tau_{\text{WB}} [fS_B + (1 - f)S_{\text{REM}}], \]

i.e., \( \tau_{\text{blood}} = \tau_{\text{WB}} \times f \)

\[ \tau_{\text{RB}} = \tau_{\text{WB}} \times (1 - f) \]

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

\[ S(\text{blood} \leftrightarrow \text{blood}) = S_B = [S_{\text{MIRD}}(\text{blood} \leftrightarrow \text{blood})](5200/V_{\text{pl}}) \]

where the factor \( 5200/V_{\text{pl}} \) represents the ratio of the standard man blood volume (5200 mL) to the patient specific blood volume (\( V_{\text{pl}} \)). The whole blood volume for each patient is estimated using Retzlaff’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:

\[ \text{RBCV} = 16.4 \text{ (height, cm)} + 5.7 \text{ (weight, kg)} - 1649 \]

\[ \text{PLV} = 40.5 \text{ (height, cm)} + 8.4 \text{ (weight, kg)} - 4811. \]


PEDI \( S(\text{blood} \leftrightarrow \text{blood}), S(\text{TB} \leftrightarrow \text{TB}) \) & blood ml needed!
MDA Pediatric NM Therapy

RAI: “Bloodless” Blood Dosimetry

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

PEDI blood ml

ICRP Publication 89 Reference Blood Volume (litres)

<table>
<thead>
<tr>
<th>Age</th>
<th>Males</th>
<th>Females</th>
<th>kg (Males)</th>
<th>kg (Females)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>0.27</td>
<td>0.27</td>
<td>3.5</td>
<td>3.5</td>
</tr>
<tr>
<td>1 year</td>
<td>0.5</td>
<td>0.5</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>5 years</td>
<td>1.4</td>
<td>1.4</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>10 years</td>
<td>2.4</td>
<td>2.4</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>15 years</td>
<td>4.5</td>
<td>3.3</td>
<td>56</td>
<td>53</td>
</tr>
<tr>
<td>Adult</td>
<td>5.3</td>
<td>3.9</td>
<td>73</td>
<td>60</td>
</tr>
</tbody>
</table>

Could fit to a polynomial vs.:

- Age
- Mass

OR

Females < 13 y.o.

\[ \text{TBV (L)} = 0.2263 + 0.0326 \times \text{weight (kg)} + 0.0784 \times \text{age (y)} \]

Females 13 - 18 y.o.

\[ \text{TBV (L)} = -2.4854 + 0.0346 \times \text{weight (kg)} + 0.0268 \times \text{height (cm)} \]

Males < 14 y.o.

\[ \text{TBV (L)} = 0.0393 \times \text{weight (kg)} + 0.1299 \times \text{age (y)} \]

Males 14 - 18 y.o.

\[ \text{TBV (L)} = -3.4722 + 0.0298 \times \text{weight (kg)} + 0.0374 \times \text{height (cm)} \]
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(s), 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 $\leq 3.6$ mCi
MDA Pediatric NM Therapy

High-activity $^{153}\text{Sm}$-EDTMP

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

Kidneys ROIs

WB ROIs
MDA Pediatric NM Therapy
High-activity $^{153}\text{Sm}$-EDTMP

\[ 0.35e^{-\ln(2)t/0.99h} + 0.65 \]

assumed skeletal component

Estimated Time of 3.6 mCi Residual Activity

| Time | 340.3 hours |
|      | or          |
|      | 14.2 days   |

Kidneys Biologic Activity vs. Time

| Height | 167.5 cm |
| Weight | 40.4 kg  |
| Therapy Dose | 909.0 mCi |

<table>
<thead>
<tr>
<th>Organ</th>
<th>uCi-h/uCi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Body</td>
<td>44.1648</td>
</tr>
<tr>
<td>Kidneys</td>
<td>0.6497</td>
</tr>
<tr>
<td>Bladder Contents</td>
<td>0.1542</td>
</tr>
<tr>
<td>Total Skeleton</td>
<td>43.2877</td>
</tr>
<tr>
<td>Cortical (0.38 x Total)</td>
<td>16.4493</td>
</tr>
<tr>
<td>Trabecular (0.62 x Total)</td>
<td>26.8384</td>
</tr>
<tr>
<td>Remaider of Body</td>
<td>0.0730</td>
</tr>
</tbody>
</table>

Estimated Absorbed Dose (from OLINDA/EXM 1.0)

<table>
<thead>
<tr>
<th>Organ</th>
<th>Absorbed Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Body</td>
<td>4.5 Gy</td>
</tr>
<tr>
<td>Kidneys</td>
<td>14.2 Gy</td>
</tr>
<tr>
<td>Bladder</td>
<td>2.7 Gy</td>
</tr>
<tr>
<td>Skeleton</td>
<td>207.0 Gy</td>
</tr>
<tr>
<td>Red Marrow</td>
<td>39.2 Gy</td>
</tr>
</tbody>
</table>

15 y.o. model
MDA Pediatric NM Therapy

High-activity $^{153}$Sm-EDTMP

Post-$^{153}$Sm-EDTMP Tx Exposure Rate @ 1m
(813.9 net mCi)

(technically) could be released w/o instructions at this time (< 6 mR/h)

(technically) could be released w/ instructions immediately (< 30 mR/h)

Kept as inpatient up to this point in time

$^{153}$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)

$$ACF = \left[ \frac{C_{\text{blank}}}{C_{\text{trans}}} \right]^{\frac{1}{2}} \equiv e^{(\mu_{\text{Co57}}T/2) \times (\mu_{123}/\mu_{\text{Co57}})} \ ; \ f = 0.914$$

Liver

Lungs

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

FIA_{bio} (123I decay-corr.)
MDA Pediatric NM Therapy

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

- $^{131}$I residence time = $0 \int_{\infty}^{\infty} FIA_{bio}(t) \, e^{-\lambda_{131} t} \, dt$
- 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

<table>
<thead>
<tr>
<th>Organ</th>
<th>cGy/mCi</th>
<th>mCi for 100 cGy</th>
<th>mCi for 200 cGy</th>
<th>mCi for 100 cGy</th>
<th>mCi for 200 cGy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red Marrow</td>
<td>3.85E-01</td>
<td>260</td>
<td>519</td>
<td>8.4</td>
<td>16.8</td>
</tr>
<tr>
<td>Total Body</td>
<td>5.68E-01</td>
<td></td>
<td></td>
<td>5.7</td>
<td>11.4</td>
</tr>
</tbody>
</table>

(Values in mCi/kg)
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 $\div$ Normal Cts/pix
  - 0.65 kg MIRD 15 y.o. $M_{\text{lung}}$ (default = 1 kg adult male)
  - 1.03 g/ml tissue density
  - 0.119 kg $M_{\text{tumor}}$ = 0.119 kg (115 ml VOI)
  - $M_{\text{normal}}$ = 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

\(^{90}\text{Y SIR-Spheres}^{\text{®}}\)

CT Volumes

L, R Lobes

Tumor
MDA Pediatric NM Therapy

**$^{90}$Y SIR-Spheres®**

**Post-Tx $^{90}$Y bremsstrahlung**

**Pre-Tx $^{99m}$Tc MAA**

(T:N = 3.12)

**Prescription:** 2.2 GBq

**Tumor:** 250 Gy

**Normal Liver:** 80 Gy (limiter)

**Lungs:** 13 Gy
Est. net infusion: 1.35 GBq (61%)
Est. tumor Gy: 153.2
Reason for < 2.2 GBq: statis
MDA Pediatric NM Therapy

$^{223}\text{RaCl}_2$ (a.k.a. Alpharadin, Xofigo)

(Alpharadin in 55 kBq/kg monthly $\times$ 6 trial at the time)

- 21 y.o. F w/ chondroblastic osteosarcoma
  - R mandible, L maxilla, R femur, sacrum, spine
  - Prior chemotherapy, surgery, $^{153}\text{Sm}$-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)

- $\sim2\frac{1}{2}$ mos. CIND application process start to 1$^{\text{st}}$ Tx
MDA Pediatric NM Therapy

$^{223}\text{RaCl}_2 (^{99m}\text{Tc-MDP bone scans})$

Baseline

Post-Two Treatment Cycles
MDA Pediatric NM Therapy

\[^{223}\text{RaCl}_2\text{ (a.k.a. Alpharadin, Xofigo)}\]

Could we image for verification (< 100 \(\mu\text{Ci}\))? 

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ra-223 (T(_{1/2}) = 11.43 d)</td>
<td>XR k(\alpha)2</td>
<td>81.069</td>
<td>15.0 %</td>
</tr>
<tr>
<td></td>
<td>XR k(\alpha)1</td>
<td>83.787</td>
<td>24.7 %</td>
</tr>
<tr>
<td></td>
<td>(\gamma)</td>
<td>269.436</td>
<td>13.9 %</td>
</tr>
</tbody>
</table>

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Rn-219 (T(_{1/2}) = 3.96 s)</td>
<td>(\gamma)</td>
<td>271.23</td>
<td>10.8 %</td>
</tr>
<tr>
<td></td>
<td>(\gamma)</td>
<td>401.81</td>
<td>6.6 %</td>
</tr>
</tbody>
</table>

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pb-211 (T(_{1/2}) = 1.781 ms)</td>
<td>(\gamma)</td>
<td>404.853</td>
<td>3.78 %</td>
</tr>
</tbody>
</table>

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bi-211 (T(_{1/2}) = 2.41 m)</td>
<td>(\gamma)</td>
<td>351.06</td>
<td>12.92 %</td>
</tr>
</tbody>
</table>

- 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

$^{223}\text{RaCl}_2$ (a.k.a. Alpharadin, Xofigo)
MDA Pediatric NM Therapy

$^{223}\text{RaCl}_2$ (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., $^{153}\text{Sm-EDTMP}$: 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
    - $^{131}\text{I-mIBG}$ Tx of neuroblastoma
    - $^{131}\text{I-burtomab}$ Tx of CNS neuroblastoma mets (rare, mostly ≤ 5 y.o.’s)
    - (future: $^{177}\text{Lu-DOTATATE}$, others?)