I-131: Rethinking Public Exposure

Kiernan McCullough, MS, DABR
Colorado Associates in Medical Physics
Penrose Cancer Center

Spring RMAAPM Meeting
June 9, 2018
Today’s Objectives

• Iodine 131 – Then and Now
• Consensus ‘Attitude’
  – NRC Guidelines
• Patient Specific Factors
• Assessment of Risk
• Considerations and Challenges
• Solutions?
Get to Know: Iodine

- Purple metallic solid
- Sublimes to form a purple gas
- Heaviest and least abundant halogen
- Heaviest essential mineral
- Predominantly mined in Chile and Japan.

Table: estimated iodine reserves per region
Sources: 2016 USGS Mineral Commodity Summary.

<table>
<thead>
<tr>
<th>Origin</th>
<th>Region</th>
<th>Reserves $x1000$ ton</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underground brines</td>
<td>Japan</td>
<td>5000</td>
</tr>
<tr>
<td>USA</td>
<td></td>
<td>250</td>
</tr>
<tr>
<td>Indonesia</td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Turkmenistan, Azerbaijan, Russia</td>
<td></td>
<td>360</td>
</tr>
<tr>
<td>Caliche Ore</td>
<td>Chile</td>
<td>1800</td>
</tr>
<tr>
<td>Seaweed</td>
<td>China</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total estimated reserves</strong></td>
<td><strong>Total estimated reserves</strong></td>
<td><strong>7514</strong></td>
</tr>
</tbody>
</table>
Get to Know: Iodine

- Essential in production of triiodothyronine (T3) and thyroxine (T4), both produced by the thyroid.
  - Iodine composes 59% of T3 and 65% of T4
- Important for temperature, metabolism, and heart rate regulation.
Get to Know: Iodine 131

- Fission product of U-235
- Te-130 (n,γ) Te-131m → I-131

\[
\begin{align*}
131^{I} & \rightarrow \beta + \bar{\nu}_{e} + 131^{Xe*} + 606 \text{ keV} \\
131^{Xe*} & \rightarrow 131^{Xe} + \gamma + 364 \text{ keV}
\end{align*}
\]
## Historic Use of Radiolodine

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1934</td>
<td>Enrico Fermi creates I-128</td>
</tr>
<tr>
<td>1938</td>
<td>Glenn Seaborg creates I-131 at Berkeley</td>
</tr>
<tr>
<td>1941</td>
<td>I-131 used to treat thyrotoxicosis</td>
</tr>
<tr>
<td>1943</td>
<td>Medical use of I-131 extended to cancer</td>
</tr>
<tr>
<td>1946</td>
<td>I-131 widely available due to war-driven fission testing</td>
</tr>
<tr>
<td>1960</td>
<td>IAEA standardizes method of measuring thyroid uptake</td>
</tr>
</tbody>
</table>
Thyroid Terms

• Euthyroid: healthy thyroid
• Thyrotoxicosis: toxicity caused by thyroid activity
  – Hyperthyroidism
• Myxedematous - hypothyroidism
• Goiter: enlargement of the thyroid
• Thyroiditis: inflammation of the thyroid

• Grave’s Disease: autoimmune disorder that results in an overactive thyroid
  – Commonly associated with bulging eyes and retracted eyelids
Radiolodine in Medicine

• Most frequently prescribed treatment for hyperthyroidism

• Treatment of residual tissue post-thyroidectomy

• I-131 tagged to monoclonal antibodies
Radioiodine in Medicine

**Hyperthyroidism**
- Thyroid intact
- Patient retains most of dose
- I-131 retention: 30-80%
- Prescription: 5 – 30 mCi

**Cancer Ablation**
- Thyroid removed surgically
- Most of dose excreted through bodily fluids
- I-131 retention: 2-5%
- Prescription: 50 – 200 mCi
Public Exposure

- NRC restrictions: 10 CFR 20 and 10 CFR 35
  - Patient may be released if dose to members of the public is < 5 mSv (500 mrem)
  - Written instruction required if exposure to any individual is to exceed 1 mSv (100 mrem)

- Attempt to keep doses to children < 100 mrem
Public Exposure Calculated

- NRC Regulatory Guide 8.39 has all the answers

Table 2. Activities and Dose Rates Above Which Instructions Should be Given When Authorizing Patient Release

<table>
<thead>
<tr>
<th>RADIONUCLIDE</th>
<th>COLUMN 1 ACTIVITY ABOVE WHICH INSTRUCTIONS ARE REQUIRED</th>
<th>COLUMN 2 DOSE RATE AT 1 METER ABOVE WHICH INSTRUCTIONS ARE REQUIRED</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(GBq)</td>
<td>(mCi)</td>
</tr>
<tr>
<td>Ag-111</td>
<td>3.8</td>
<td>100</td>
</tr>
<tr>
<td>Au-198</td>
<td>0.69</td>
<td>19</td>
</tr>
<tr>
<td>Cr-51</td>
<td>0.96</td>
<td>26</td>
</tr>
<tr>
<td>Cu-64</td>
<td>1.7</td>
<td>45</td>
</tr>
<tr>
<td>Cu-67</td>
<td>2.9</td>
<td>77</td>
</tr>
<tr>
<td>Ga-67</td>
<td>1.7</td>
<td>47</td>
</tr>
<tr>
<td>I-123</td>
<td>1.2</td>
<td>33</td>
</tr>
<tr>
<td>I-125</td>
<td>0.05</td>
<td>1</td>
</tr>
<tr>
<td>I-125 implant</td>
<td>0.074</td>
<td>2</td>
</tr>
<tr>
<td>I-131</td>
<td>0.24</td>
<td>7</td>
</tr>
</tbody>
</table>
8.39 Guidelines

E = 0.75 when a physical half-life, an effective half-life, or a specific time period under consideration (e.g., bladder holding time) is less than or equal to 1 day.

E = 0.25 when an effective half-life is greater than 1 day if the patient has been given instructions, such as,

- Maintain a prudent distance from others for at least the first 2 days,
- Sleep alone in a room for at least the first night, Do not travel by airplane or mass transportation for at least the first day,
- Do not travel on a prolonged automobile trip with others for at least the first 2 days,
- Have sole use of a bathroom for at least the first 2 days,
- Drink plenty of fluids for at least the first 2 days.

E = 0.125 when an effective half-life is greater than 1 day if the patient has been given instructions, such as,

- Follow the instructions for E = 0.25 above,
- Live alone for at least the first 2 days,
- Have few visits by family or friends for at least the first 2 days.
Consensus Guidelines

• Most sources give similar instructions that are in keeping with assumptions of NRC 8.39.
  – Radiologyinfo.org
  – American Association of Endocrine Surgeons
  – Society of Nuclear Medicine and Molecular Imaging
  – Cardinal Health
  – Restrictions for several days, some up to a week.
  – Vague instructions
Consensus Guidelines?

Sultanate of Oman: Ministry of Health
Patients receiving over 400 MBq (~10 mCi) must be hospitalized

American Thyroid Association
NIH
Ohio State University

Restrictions are very specific and stringent
- E.g. No working for 7 days

Purposely vague instructions with wide ranges
- 6-23 days of restrictions!

Patients should be hospitalized 24 hrs for Rx > 8mCi
Why the Disparity?

• It’s complicated!
• Not all I-131 administrations are equal.
• Public safety concerns are very different depending on disease type, dosage, and patient specific factors.
Radioiodine in Medicine

Hyperthyroidism
• Thyroid intact
• Patient retains most of dose
• $^{131}$I retention: 30–80%
• Prescription: 5–30 mCi

Cancer Ablation
• Thyroid removed surgically
• Most of dose excreted through bodily fluids
• $^{131}$I retention: 2–5%
• Prescription: 50–200 mCi
Cancer Ablation

- Patient retains very little of prescription
  - 2% retention of 200 mCi, means 180 mCi of I-131 will be eliminated over 48 hours!
- Contamination is the largest risk factor.
- Healthy thyroid – average 66% expelled from urine
- Cases of up to 42% elimination through sweat!
- Exposure from dose to public from fractional uptake is a manageable risk.
Cancer Ablation: Patient Instructions

- Isolation 1-2 days: sole use of bedroom and bathroom
- Thorough cleaning of area.
- Wash clothes and linens.
- Act as if you have the flu for 1 week.
Justification

• Cormack and Shearer dose calculator
• NCRP 155 – Zanzonico spreadsheet
Patient Calculation: No Big Deal

100 mCi, 2% retention
2 days of isolation

- Co-Worker: 14 mrem
- Spouse: 174 mrem
- Child: 11 mrem
- Infant: 110 mrem
Cancer Ablation: Patient Experience

• Metastatic, 200 mCi, in-patient
• Initial reading at 1m: 29 mR/hr
  – 24 hrs: 17.2 mR/hr
  – 48 hrs: 12.7 mR/hr
  – 72 hrs: 9.2 mR/hr
  – 96 hrs: 6.2 mR/hr
Cancer Ablation: Patient Experience

• Metastatic, 200 mCi, in-patient
• After 4 days patient was released, thorough cleaning by nuclear medicine and room was wrapped
• Day 5 wipe tests (200 dpm/100 cm² is clean)
  – Sink: 1700
  – Phone: 10900
  – Toilet Handle: 17800
  – Toilet Paper Holder: 38600
Lessons Learned?

• Physical health of patient prevented them from being an outpatient
• Standard restriction conventions underestimated exposure risk due to fractional uptake
• A team of experienced technicians were unable to prevent and remove contamination from a restricted area effectively

• Health risk? $10^6$ dpm $\approx 0.5$ μCi
Patient Specific Factors

• Ablation cases tend to be more uniform, with contamination being the higher risk.
• Ability to properly isolate oneself is the major risk factor.
  – Do patients fully comply?
• Assumptions of patient interactions with family and co-workers have huge implications
Patient Calculation: Spouse

200 mCi, 5% retention
8 hrs sleeping, 6 hours within 1 m
2 days of isolation

Sleep within 0.3 m
• Sleep alone for 5 days after isolation

Sleep within 0.5 m
• 2 days of isolation sufficient

If pregnant, sleep alone for 2 weeks vs 5 days for 200 mrem
Patient Calculation: Child

200 mCi, 5% retention
4 hrs held, 4 hours within 1 m
2 days of isolation

100 mrem
• No holding child for 2 weeks post isolation

200 mrem
• No holding child for 1 week post isolation

Are these assumptions even reasonable?
Balancing Risk

• Conservative interaction models may give reassurance that procedure is safe for majority of patients.
• These same assumptions give unreasonable expectations to patients that have the most difficult circumstances.
• Guidelines that are impossible to comply with will compromise adherence or ability to participate in treatment.
Hyperthyroidism

- Much higher fraction of I-131 retained
  - Very large range of uptake 30–80%

Controversy regarding treatment of thyrotoxicity
- Multiple treatments: hyperthyroid to euthyroid
- One treatment: hyperthyroid to hypothyroid

Range of prescribed doses: 5–30 mCi

<table>
<thead>
<tr>
<th>RADIONUCLIDE</th>
<th>COLUMN 1 ACTIVITY AT OR BELOW WHICH PATIENTS MAY BE RELEASED</th>
<th>COLUMN 2 DOSE RATE AT 1 METER, AT OR BELOW WHICH PATIENTS MAY BE RELEASED</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(GBq)</td>
<td>(mCi)</td>
</tr>
<tr>
<td>Ag-111</td>
<td>19</td>
<td>520</td>
</tr>
<tr>
<td>Au-198</td>
<td>3.5</td>
<td>93</td>
</tr>
<tr>
<td>Cr-51</td>
<td>4.8</td>
<td>130</td>
</tr>
<tr>
<td>Cu-64</td>
<td>8.4</td>
<td>230</td>
</tr>
<tr>
<td>Cu-67</td>
<td>14</td>
<td>390</td>
</tr>
<tr>
<td>Ga-67</td>
<td>8.7</td>
<td>240</td>
</tr>
<tr>
<td>I-123</td>
<td>6.0</td>
<td>160</td>
</tr>
<tr>
<td>I-125</td>
<td>0.25</td>
<td>7</td>
</tr>
<tr>
<td>I-125 implant</td>
<td>0.33</td>
<td>9</td>
</tr>
<tr>
<td>I-131</td>
<td><strong>1.2</strong></td>
<td><strong>33</strong></td>
</tr>
</tbody>
</table>
Hyperthyroidism

- Risk of contamination relatively low.
  - Eliminated I-131 largely evacuated during first urination
  - Sole use of a bedroom and bathroom for 2 days still recommended
- No need for total patient isolation
- No need for hospitalization
- Impression: “not as big of a deal”
Hyperthyroidism: Patient Instructions

• Sleep alone for 1-2 days
• Use separate bathroom for 1-2 days if possible
• Act as if you have the flu for 1 week
• Be mindful of time and space you occupy with others
Patient Calculation: No Big Deal

15 mCi, 30% uptake
No restrictions

- Co-worker 95 mrem
- Spouse 198 mrem
- Child 72 mrem

Held infant with no restrictions 539 mrem
Patient Specific Factors

• Combination of uptake values, prescription values, and patient specific $t_{1/2}$ result in a wide range of safety risks.
• Understanding patient interaction patterns is crucial to properly consulting them.
• Held children are at the most risk.
  – Single mothers?
  – NICU nurses?
## Worst Case Scenario

30 mCi, 80% uptake  
No restrictions

<table>
<thead>
<tr>
<th>Relationship</th>
<th>Radiation Dose</th>
<th>Restrictions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-worker</td>
<td>465 mrem</td>
<td>30 mCi, 80% uptake</td>
</tr>
<tr>
<td>Spouse</td>
<td>966 mrem</td>
<td>14 days - 490 mrem</td>
</tr>
<tr>
<td>Child</td>
<td>352 mrem</td>
<td>7 day no contact, no holding for 60 days</td>
</tr>
</tbody>
</table>

Held infant with no restriction 2627 mrem
7 day no contact, no holding for 60 days 200 mrem

Centura Health®
Patient Experience: Hyper with Infants

30 mCi, 40% uptake
Working mother with infant – 200 mrem

• Don’t hold child 28 days
• No contact Days 0-2
• 30 min holding, 2 hours at 1m Days 3-16
• 1 hour holding, 4 hours at 1m Days 17-30
• 2 hours holding, 4 hours at 1m Days 31+
Patient Specific Factors

• Acquiring 24 hour uptake values is crucial to accurate consultation
• Consulting the patient long before treatment will allow them to assess their own contact patterns
• Measuring patient exposure several days post therapy will allow for adaptations to consultation
Consulting: New Direction

• Uniform consultation processes have been the end-goal
• Consensus very difficult to achieve, wide arrange of experience
  – Too many what ifs
• Consultation of every patient by a physicist not standard or even possible
• Templating approaches for all patients have been unsuccessful
Consulting: New Direction

• Identify patient groups that DO fit templated constraints
  – Formulating custom plans for all patients is time consuming and will lead to unnecessary variation
  – Can allow nuclear medicine to handle patient interactions
  – Thorough patient questionnaire necessary for success
  – Identify answers that flag a physicist’s response
Consulting: Triage

- Separate patients into different risk groups that require varying degrees of physicist intervention
  - Low risk – templated solution, no physicist needed
  - Intermediate risk – templated solution, physics consult still warranted
  - High risk – consult from physicist with good understanding of risk planning, command of spreadsheet
Cancer Ablation: Triage

- Evaluated dose risks based on common range of prescription and uptake values.
  - No mets: 2% uptake
  - Mets: 5% uptake
  - 50, 100, and 200 mCi
- Nearly all patients will fall within this range.
Cancer Ablation: Risk Analysis

100 mCi, 5% uptake

<table>
<thead>
<tr>
<th>Category</th>
<th>POI</th>
<th>Interaction</th>
<th>Time</th>
<th>Restriction</th>
<th>Exposure (mrem)</th>
<th>Total (mrem)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Co-Worker</td>
<td>3 ft</td>
<td>8 hours</td>
<td>2 days</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spouse and family</td>
<td>Spouse</td>
<td>Sleeping</td>
<td>8 hours</td>
<td>2 days</td>
<td>398</td>
<td>425</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 ft</td>
<td>6 hours</td>
<td>2 days</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children</td>
<td>3 ft</td>
<td>6 hours</td>
<td>2 days</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Spouse - Pregnant</td>
<td>Spouse</td>
<td>Sleeping</td>
<td>8 hours</td>
<td>16 days</td>
<td>73</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 ft</td>
<td>6 hours</td>
<td>2 days</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Father and spouse/co-worker pregnant</td>
<td>Pregnant</td>
<td>3 ft</td>
<td>6-8 hours</td>
<td>2 days</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Parent with infants</td>
<td>Infant</td>
<td>3 ft</td>
<td>6 hours</td>
<td>2 days</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Holding</td>
<td>4.8 hours</td>
<td>12 days</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>* 192</td>
</tr>
<tr>
<td>Works with children</td>
<td>Children</td>
<td>3 ft</td>
<td>8 hours</td>
<td>10 days</td>
<td>10</td>
<td>101</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Holding</td>
<td>4.8 hours</td>
<td>10 days</td>
<td>91</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children</td>
<td>3 ft</td>
<td>8 hours</td>
<td>3 days</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Holding</td>
<td>1 hour</td>
<td>3 days</td>
<td>44</td>
<td></td>
</tr>
</tbody>
</table>

* 5 day
* 165
Cancer Ablation: Risk Analysis

• Sole access to bedroom and bathroom
  – No infants
  – Patient must have ability to care for oneself
  – Must have good understanding of risks
  – Templated solution!

• Apart from managing infant exposure, hospitalization is the only solution
Hyperthyroid: Triage

• Using the same approach, evaluated dose risks over wide range of possibilities.
  – 10 – 30 mCi
  – 30 – 70% uptake
• Analyzed different potential interaction patterns
# Hyperthyroid: Risk Analysis

<table>
<thead>
<tr>
<th>General Restrictions</th>
<th>24 hr Uptake (%)</th>
<th>Work</th>
<th>24 hr Uptake (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30</td>
<td>50</td>
<td>70</td>
</tr>
<tr>
<td>Dose (mCi)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>25</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sleeping Partner</th>
<th>24 hr Uptake (%)</th>
<th>Pregnant Women/Children</th>
<th>24 hr Uptake (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30</td>
<td>50</td>
<td>70</td>
</tr>
<tr>
<td>Dose (mCi)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>15</td>
<td>0</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>20</td>
<td>1</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>25</td>
<td>4</td>
<td>11</td>
<td>18</td>
</tr>
<tr>
<td>30</td>
<td>6</td>
<td>14</td>
<td>21</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>200 mrem limit</th>
<th>24 hr Uptake (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Held Child - 1 hr/day</td>
<td>30</td>
</tr>
<tr>
<td>Dose (mCi)</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>25</td>
<td>9</td>
</tr>
<tr>
<td>30</td>
<td>14</td>
</tr>
</tbody>
</table>

---

[^Centura Health]: [Image - 14x0 to 734x540]
Hyperthyroid: Risk Analysis

• Can sleep alone – bed or couch
• Not living in extremely close quarters
• Mostly templated solutions
• Exposure risk to children and pregnant women largest risk factor
  – Too many variables to template, must assess interactions on a patient by patient basis
  – May take multiple phone calls and interactions to determine risk
  – Measuring patient at different time points post therapy will help guide instructions
Hyperthyroid: Reality Check

- Even with these models we have only a general idea of actual risk
- 24 hour uptake values from “tracer” doses not the same as treatment uptake
- Clearance rates can be affected by medication and diet
- Measurement of patient exposure is the only way to be certain
Interesting Cases

• Patients receiving dialysis
  – Possible contamination of unit
  – Patient’s spend considerable time in close quarters with other patients

• Prisoner receiving dose for cancer ablation
  – Contamination of cell
  – Other prisoners in close contact (concrete block shielding?)
  – Special handling instructions for guards
Interesting Cases

• Medical emergency, patient covered in own bodily fluids. EMS is called, doesn’t recognize patient’s radioactive bracelet or its removed.

• Emergency room visits in general, difficult to enforce quarantine of room in busy ER clinic.
Conclusion

• Iodine 131 cases present a multitude of challenges.
• We are accustomed to patient specific needs
  – Anatomy
  – Physiology
  – Lifestyle? – Impossible to template
• Focus energies on high risk patients, filter out low risk individuals
• Don’t underestimate complexity and needs of the individual
References

• NRC Regulatory Guide 8.39
• NRC Regulatory Guide 8.23