Treating Thyroid Cancer using I-131 Maximum Tolerable Dose Method

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Thyroid Carcinoma

- New cases and deaths in the U.S., 2007
  - New Cases - 33,550
  - Deaths - 1,530

- Risk factors that increase chances
  1) White female, over 40 y.o.
  2) Genetic (for medullary thyroid carcinoma)
  3) Not enough iodine in the diet
  4) Radiation and/or radioactive fallout

National Cancer Institute, http://www.cancer.gov/
Thyroid Cancer Incidence Rates

Trends in SEER Incidence Rates by Primary Cancer Site
1995-2004

Ages Less Than 65

Thyroid
Liver & IBD
Kidney & Renal Pelvis
Prostate
Testis
Pancreas
Melanoma of the Skin
Corpus & Uterus, NOS
All Except Lung
Hodgkin Lymphoma
All Cancer Sites
Colon & Rectum
Brain & ONS
Myeloma
Breast (Female)
Oral Cavity & Pharynx
Eosophagus
Leukemia
Ovary
Stomach
Non-Hodgkin Lymphoma
Urinary Bladder
Lung & Bronchus (Female)
Cervix Uteri
Lung & Bronchus (Male)
Larynx

Ages 65 and Over

Thyroid
Melanoma of the Skin
Hodgkin Lymphoma
Kidney & Renal Pelvis
Non-Hodgkin Lymphoma
Liver & IBD
Esophagus
Urinary Bladder
Lung & Bronchus (Female)
Pancreas
Brain & ONS
Testis
Myeloma
All Cancer Sites
All Except Lung
Leukemia
Prostate
Breast (Female)
Ovary
Lung & Bronchus (Male)
Stomach
Colon & Rectum
Oral Cavity & Pharynx
Corpus & Uterus, NOS
Larynx
Cervix Uteri

Source: SEER 13 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry and Rural Georgia). For sex-specific cancer sites, the population was limited to the population of the appropriate sex.

Underlying rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).
The APC is the Annual Percent Change over the time interval.

* The APC is significantly different from zero (p<0.05).

Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.
Methods of Treatment

- Depending on type and stage of the cancer:
  1) surgery
  2) radioactive iodine
  3) hormone therapy
  4) external radiation
  5) chemotherapy

Maxon, HR. J Nuclear Med, 1992; 33:1132-1136
Radioactive Iodine Therapy

1. post surgery for thyroid removal
2. related to tumor’s future capacity to concentrate iodine
3. positive relationship between total I-131 uptake per tumor mass and outcome – but not proven for maximal doses

** doses < 35 Gy to tumor likely will not respond to I-131 therapy need 300 Gy to thyroid remnant, 120 Gy to metastatic foci
Radioiodine Uptake Ranges

- Radioiodine is used to determine thyroid uptake.
- Isotopes used include I-123 and I-131.
- Normal uptake: 15-25%
- Hypo: <10%
- Hyper: >30%
Images of Thyroid Cancer

WB PET Scan with FDG

WB Nuclear Med Scan with TI-201

Surgical Tumor Removal
Iodine Kinetics (simplified)

\[
\begin{align*}
K_{13} &= 0.56 \\
K_{21} &= 0.114 \\
K_{12} &= 0.005 \\
K_{14} &= 0.1 \\
K_{01} &= 2 \\
K_{32} &= 0.002 \\
K_{42} &= 0.007 \\
K_{04} &= 0.018
\end{align*}
\]
Estimated % of Administered $^{131}$I

MIRD Dose Estimate Report No. 5  (Maximum thyroid uptake of 15%)
I-131 Review

- physical half-life of 8.06 days

- **Beta emitter**
  - max energy 610 KeV; avg energy 193 KeV
  - tissue range of 0.8 mm

- **Gamma emitter**
  - principal energy 365 KeV (81%)

94% of radiation dose is from the beta emissions
# Iodine-131 Decay Data

Half life: 8.06 days

<table>
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<th>Emissions</th>
<th>No.</th>
<th>Energy (Mev)</th>
<th>Yield</th>
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<td>gamma</td>
<td>6</td>
<td>0.03</td>
<td>4.6%</td>
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<td>0.08</td>
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<td>0.284</td>
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<td>0.364</td>
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<td>0.637</td>
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<td>0.723</td>
<td>2.6%</td>
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<td>beta</td>
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<td>0.248</td>
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<td>0.334</td>
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<td>0.606</td>
<td>89.3%</td>
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</table>
General Guidelines for Thyroid Cancer patients

- For postoperative ablation of thyroid bed remnants depending on the amount of functioning tissue present
  
  \( (75 - 150 \text{ mCi}) \)

- For treatment of presumed thyroid cancer in the neck or mediastinal lymph nodes
  
  \( (150 - 200 \text{ mCi}) \)

- For treatment of distant metastases
  
  \( (> 200 \text{ mCi}) \) *Candidate for MTD*
Maximal Dose Therapy
Considered When

- Patients with life-threatening disease
- Patients with progressive disease but little response to previous treatments
- Patients with bone mets
- Patients with nodal disease

Goal is to treat but not to cure disease
Why Perform Maximal Dose Therapy?

- Standard treatment using empiric guidelines is only a “best guess” and not truly tailored for each patient

- Better outcome if treated with one rather than multiple I-131 treatments
Common Side Effects from >200 mCi Dose I-131 Therapy

- 60-70% radiation sickness
- 10-15% sialoadenitis
- 10% leukopenia for up to one year
- 70% transient azoospermia
- Cystitis, radiation thyroiditis, gastritis, transient loss of taste
Absorbed Dose Calculations
Uses Modification to the MIRD System

“Practical Determination of Patient-Specific Marrow Dose Using Radioactivity Concentration in Blood and Body”

Shen, Denardo Sgouros, et. al
UC Davis/Memorial Sloan-Kettering Cancer Institute
Journal of Nuclear Medicine, Vol 40, No. 12 December 1999
Critical Factors in Calculating Patient Dose

- Dose to red marrow
  - Red marrow self dose
  - Total body to red marrow dose
- Dose to lungs
  - Whole body retention at 48 hours
Limiting Factors for Maximal I-131 Dose Therapy

- Whole Body Retention at 48 hours
  - 80 mCi if lung metastases are present
  - 120 mCi if lung mets not present

Requires: WB counting using dual head Gamma Camera

- 200 cGy (200 Rads) absorbed dose to the red BM

Requires:

- WB counting
- blood sampling
- mathematical modeling
General Principles for Calculating Absorbed Dose

Give amount of radioactivity which will reside in a particular organ

Must determine total # nuclear transformations that occur within that organ

1) activity (transition rate or decay rate) \( \text{Physical characteristics} \)
2) time that nuclide is resident in that organ \( \text{Biologic characteristics} \)

Cumulated Activity (mCi-hrs) = Activity (mCi) in organ x time = (mCi-hrs)

Divide the Cumulated Activity in the organ / Total given Activity to body
= total # nuclear transitions in organ per unit activity

This is also known as the Residence Time in the organ of interest
Phantom Models in OLINDA-EXM

- 70 kg adult (reference male)
- 57 kg (reference female)
- 57 kg 15 year old
- 32 kg 10 year old
- 19 kg 5 year old
- 9.2 kg 1 year old
- 3.4 kg newborn
<table>
<thead>
<tr>
<th></th>
<th>Adrenals</th>
<th>Brain</th>
<th>Liver</th>
<th>Lungs</th>
<th>Muscles</th>
<th>Ovaries</th>
<th>Pancreas</th>
<th>Red Mar.</th>
<th>Thymus</th>
<th>Thyroid</th>
<th>U.B. Cont.</th>
<th>Uterus</th>
<th>Total Body</th>
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<tbody>
<tr>
<td>Dose Conversion Factors (Gy/mCi/h), Nuclide: 131 I, 0.02900 day, Adult Female</td>
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</table>

**Note:** The table contains dose conversion factors for various organs and body parts in Gy/mCi/h for the nuclide 131 I, with a decay time of 0.02900 days. The table includes columns for Adrenals, Brain, Liver, Lungs, Muscles, Ovaries, Pancreas, Red Marrow, Thymus, Thyroid, U.B. Cont., Uterus, and Total Body. Each column represents the conversion factor for the respective body part or system, measured in Gy/mCi/h.
Biodistribution of I-131

- For most radiopharmaceuticals, the activity in a given organ does not remain constant throughout the period of interest
  - radioactive (physical) decay
  - ongoing biologic processes of uptake and removal of metabolites
Problems with Biodistribution

Patients have very different rates of metabolism, especially older or sicker patients.

Patients with Thyroid Cancer have had their thyroids removed.

Each lesion will have its own uptake and biological removal rate.
Performing Maximal Dose I-131 Therapy

- Administer tracer dose of I-131 (~2-3 mCi)
- Obtain blood samples at specific time intervals
- Obtain whole body images (gamma camera) at specific time intervals
I-131 Dosimetry Chronological Steps

1. Patient is booked for the procedure HP needs name, medical record number, DOB, weight and recent hematocrit

2. Work must begin on a Monday, dosimetry done Monday-Friday

3. Patient gets dosed with the I-131 treatment the following Monday

4. Patient must stay in the hospital post treatment, usually up to five days
Day One

BACKGROUND
IV inserted
Blood draw
Whole Body Count

Administer Iodine

0  1  2  3  4  5  6
HOURS

NO VOID
Blood draw
Whole Body Count

VOID
Blood draw
Whole Body Count

VOID
Blood draw
Whole Body Count
Days 2 through 5

Day 2 (24 hr) – Blood draw and whole body count
Day 3 (48 hr) – Blood draw and whole body count
Day 4 (72 hr) – Blood draw and whole body count
Day 5 (96 hr) – Blood draw and whole body count
Dosimetry calculations
Review with MD
Order dose
Room Preparation for I-131 Radiotherapy Patient on 7W

Room 7W-26
**Patient #1**

43 yo female with Papillary Thyroid Cancer

<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
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<tbody>
<tr>
<td>01/28/2005</td>
<td>I-123 uptake focal nodal disease, four distinct areas within neck region; total neck uptake 0.26 %</td>
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<tr>
<td>02/04/2005</td>
<td>I-131 Therapy Dose 196 mCi</td>
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<tr>
<td>02/11/2005</td>
<td>WB scan, 7 days post I-131 therapy</td>
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<tr>
<td>09/20/2005</td>
<td>I-131 WB dosimetry (five days)</td>
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<tr>
<td>09/27/2005</td>
<td>I-131 Therapy Dose 450 mCi</td>
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<tr>
<td>10/07/2005</td>
<td>WB scan, 7 days post I-131 therapy</td>
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</table>
90 minutes post ingestion intake
3 hours post ingestion intake
5 hours post ingestion intake
24 hours post ingestion intake
48 hours post ingestion intake
72 hours post ingestion intake
96 hours post ingestion intake
<table>
<thead>
<tr>
<th>Date</th>
<th>Event Details</th>
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<tr>
<td>06/06/2006</td>
<td>I-131 WB dosimetry (five days)</td>
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<tr>
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<td>Intense uptake in the thyroid bed; patchy uptake in both mid lung bases</td>
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<tr>
<td>06/28/2006</td>
<td>WB scan, 15 days post I-131 therapy</td>
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<td>Findings similar to previous dosimetry scans;</td>
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<tr>
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<td>In addition, iodine avid focus in right mid neck</td>
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</tbody>
</table>

60 yo female with metastatic papillary thyroid cancer to the lungs
Two hours post tracer dose
Four hours post tracer dose
24 hours post tracer dose
48 hours post tracer dose
72 hours post tracer dose
Dosimetry Results

Blood Activity per Gram vs Time Post Administration

- **Exponential fit to all data**
  \[ y = 0.0689e^{-0.061x} \]
  \[ R^2 = 0.9632 \]

- **Exponential fit to last 3 data points**
  \[ y = 0.278e^{-0.0738x} \]
  \[ R^2 = 0.9664 \]
Exponential fit to all data

\[ y = 2.6148e^{-0.0274x} \]

\[ R^2 = 0.9318 \]

Exponential fit to last three data points

\[ y = 1.4122e^{-0.0163x} \]

\[ R^2 = 0.9659 \]
## Dose to Red Marrow

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<td>90</td>
<td>Blood</td>
<td>Using Exponential Fit to all data</td>
<td>Whole Body</td>
<td>Using Exponential Fit to all data</td>
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<td>91</td>
<td>0.3237 uCi-hrs/gm</td>
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<td>113.18 mCi-hrs</td>
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<td>Dose to Red Marrow</td>
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<td>99</td>
<td>S1</td>
<td>1.88E-01 cGy/mCi-hr</td>
<td>Red Marrow Sell Dose</td>
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<td>100</td>
<td>S2</td>
<td>1.03E-02 cGy/mCi-hr</td>
<td>Total Body to Red Marrow</td>
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<td>0.6</td>
<td>Red marrow to Blood activity concentration ratio</td>
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<td>102</td>
<td>M</td>
<td>57000 gms</td>
<td>MIRD Standard Adult Phantom Total Body Mass (g)</td>
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<td>1220 gms</td>
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<td>C_{exp}</td>
<td>0.00000237 mCi-hrs/gm</td>
<td>Blood cumulative activity (mCi-hrs/gm) using exponential fit to curve</td>
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<td>105</td>
<td>A_{w,b}</td>
<td>113.16 mCi-hrs</td>
<td>Whole body cumulative activity (mCi-hrs) using exponential fit to curve</td>
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<td>S3</td>
<td>6.41E-03 cGy/mCi-hr</td>
<td>S2<em>M/(M-m) - S1</em>m/(M-m)</td>
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<td>107</td>
<td>A_{w,b}</td>
<td>0.68 mCi-hrs</td>
<td>Using C_{exp}</td>
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<td>A_{w,b}</td>
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<td>D_{red}/A_{o}</td>
<td>0.274 cGy/mCi</td>
<td>[S1<em>A_{RM} + S3</em>(A_{w,b}/A_{RM})]A_{o}</td>
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<td>731 mCi</td>
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<td>Exponential Curve Max dose to not exceed 200 cGy to Red Marrow</td>
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</table>
Whole Body Cumulative Activity

Exponential fit to all data to $a = \ldots$

113.16 mCi·hrs

Exponential fit to last three points

190.22 mCi·hrs

Whole Body Retention at 48 Hours

Exponential fit to all data

$y(48) = 0.2270839$

as % 22.71%

120 mCi 528 mCi
80 mCi 352 mCi

Exponential fit to last three points

$y(48) = 20.92%$

120 mCi 574 mCi
80 mCi 382 mCi

Days. Time Post Administration
Administered 352 mCi
THYROID ANTERIOR COUNTS

AVG CNTS/PIXEL

TIME
LEFT LUNG POSTERIOR VIEW COUNTS

AVG CNTS/PIXEL

TIME (HOURS)
RIGHT LUNG POSTERIOR VIEW COUNTS

AVG CNTS/PIXEL

TIME (HOURS)
8 days post therapy dose
15 days post therapy dose
As of October 17, 2007

- Both patients are doing very well
- No recurrence of cancerous cells
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