Salute to Dr. Saul Hertz
Diagnostic and Therapeutic Uses of Radioiodine

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Availability of slides

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Financial Disclosures

The usual CME commercial financial disclosures:

• Genzyme: Speaker bureau
• Advisor to Jubilant Draximage

• The atypical financial disclosures:
  • Not fee for service, and
  • Not incentivized by my hospital in any way regarding volumes or revenues generated,
  • In fact, I work pro bono.
Objectives

In addition to the Salute to Dr. Hertz and the specific objectives presented in the meeting program,
I have two additional objective

• To discuss what has developed as a result of the initial administration of $^{130}$I by Dr. Hertz, and
• To present to you some “pearls” to help you determine when radioiodine imaging and therapies are not necessarily “equal.”

One of the Important Sequele of Dr. Hertz is Radioiodine Imaging
The Utility of Pre-ablation Radioiodine Scans Differentiated Thyroid Cancer

Final 2016 ATA Guidelines

- **Useful**
  - “… may be useful when the extent of the thyroid remnant or residual disease cannot be accurately ascertained from surgical report or neck ultrasonography, and
  - When the results may alter the decision to treat or the [amount of prescribed] activity of RAI that is to be administered. “

- “[… has been reported to yield information that could alter clinical management … in 25 to 53% of patients.”

- **Concern for stunning with $^{131}$I.**

- **Identification and localization of uptake foci may be enhanced by concomitant SPECT-CT.**

- **When performed, utilize $^{123}$I or low-activity of $^{131}$I (1-3 mCi) with the therapeutic activity optimally administered within 72 h of the diagnostic activity**
The Utility of Pre-ablation Radioiodine Scans in Differentiated Thyroid Cancer

Personal Comments

Remains controversial

Radioiodine Scanning

A rarely, if ever, spoken factor of radioiodine imaging is:

Imaging Technique
List several items that you can ask your nuclear medicine physician in order for you to help assess the quality of the radioiodine thyroid imaging your patients are receiving:

1.  
2.  
3.  
4.  
5.  
6.  
7.  
8.  
9.  
10.  

Technique 1: Superiority of spot image to whole body image.

From a whole body image  Spot image
Technique 2: Superiority of pinhole images to spot images
Technique 2: Superiority of pinhole images to spot images

6 mm aperture  4 mm aperture
Technique 1 and 2: Spot and pinhole collimator images
Technique 3:  ?????????????????

48 hour vs 72 hour spot image

Technique 2:  Delayed Imaging

48 hour vs 72 hour spot image
Technique 3: Delayed imaging

48 hour vs 72 hour spot image

All time points have a tumor to background ratio of 2:1

Tumor to background ratio of 2:1

Series 1
Series 2

Tumor to background ratio of 2:1

The Tumor to Background ratio frequently keeps increasing, because the background frequently clears faster than the tumor.

Tumor to background ratio now > 10:1

48 hour vs 72 hour spot image
Technique 3: Delayed imaging

The Tumor to Background ratio frequently keeps increasing, because the background frequently clears faster than the tumor.

48 hour vs 72 hour spot image
Technique 4: ????????????????

Same images as before, but different mechanism.

What is the mechanism?

Technique 4: ????????????????

The image on right was acquired for twice as long as image on the left.
Technique 4: Longer acquisition time

The image on right was acquired for twice as long as image on the left.

Counting Statistics!!!!!
**Technique 4: Longer acquisition time**

**Example: Lesion to background ratio of 1.2 to 1***

<table>
<thead>
<tr>
<th></th>
<th>Counts/ X min/pixel</th>
<th>Standard deviation</th>
<th>Counts/2X min/pixel</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion</td>
<td>120</td>
<td>( \sqrt{120} = 10.9 )</td>
<td>240</td>
<td>( \sqrt{240} = 15.4 )</td>
</tr>
<tr>
<td>Background</td>
<td>100</td>
<td>( \sqrt{100} = 10 )</td>
<td>200</td>
<td>( \sqrt{200} = 14.1 )</td>
</tr>
</tbody>
</table>

*Very simplified example.

**Technique 5:** ?????????????? ???

![Anterior view](image1)

![Posterior view](image2)
Technique 5: Adjust contrast/brightness

Anterior view

Posterior view

Technique 6: ???????????????
Technique 6: ????????????

1. If there is a focal hot spot, the physician has to go talk to the patient or exam the patient, or

Technique 6: ????????????

2. If the physician doesn’t to it, then he/she can teach their technologists how to do that.
3. One doesn’t need to know all the reported cases of false positive uptake. One only has to ask and inspect, and if necessary, take an additional modified view to confirm.
Technique 7: Use a large prescribed activity

- Do they administer a higher prescribed activity of $^{131}$I or $^{123}$I?
- Stunning
- Iodine refractory

Technique 8: Patient preparation TSH

- Making sure endogenous TSH is over 30 units when preparing patient with thyroid hormone withdrawal (THW).
- If preparing with rhTSH, measurements of TSH typically not necessary.
- Choosing THW vs rhTSH for patients with distant metastases remains controversial.
• Yes,
• Explore history of high iodine exposure,
• 1-2 weeks,
• Although optimal stringency not known, commonly studied diet is ≤ 50 ug/day.

(Weak recommendation, Low-quality evidence)

What are the threshold for urine iodine values?

• No thresholds for urine iodine values or spot $U_{I}/Cr$ (urine-iodine-to-creatinine) ratios given.
Although the effects of stringent compliance of a low iodine diet on the sensitivity of radioiodine scan is not known, it may help add that “slight edge” for detection.

<table>
<thead>
<tr>
<th>Thyroxine (µg)</th>
<th>Iodine by % of weight</th>
<th>µg</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>0.6534</td>
<td>16</td>
</tr>
<tr>
<td>50</td>
<td>0.6534</td>
<td>33</td>
</tr>
<tr>
<td>75</td>
<td>0.6534</td>
<td>49</td>
</tr>
<tr>
<td>100</td>
<td>0.6534</td>
<td>65</td>
</tr>
<tr>
<td>125</td>
<td>0.6534</td>
<td>82</td>
</tr>
<tr>
<td>150</td>
<td>0.6534</td>
<td>98</td>
</tr>
<tr>
<td>200</td>
<td>0.6534</td>
<td>131</td>
</tr>
<tr>
<td>250</td>
<td>0.6534</td>
<td>163</td>
</tr>
</tbody>
</table>
What about thyroid hormone and iodine?

Simple mnemonic

2/3

- Consider spot $U_{I/Cr}$ (urine-iodine-to-creatinine ratio) to better normalize for unknown status of hydration.

Technique 10: SPECT-CT

Images from the same patient.

Planar

SPECT-CT


Xue, EJNMMI 2013;40:768-78
### Technique 10: SPECT-CT

<table>
<thead>
<tr>
<th>Author</th>
<th>Reference</th>
<th>Altered staging, indeterminates, management, and/or outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aide</td>
<td>J Clin Endocrinol Metab 2009;94:2075-2084.</td>
<td>22%</td>
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<tr>
<td>Barwick</td>
<td>Eur J Endocrinol 2010;162:1131-1139.</td>
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<tr>
<td>Ciappuccini</td>
<td>Eur J Endocrinol 2011;164:961-969.</td>
<td>Sole prognostic variable</td>
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<td>Geerlings</td>
<td>Nuc Med Comm 2010; 31:417-422.</td>
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<tr>
<td>Grewal</td>
<td>J Nucl Med 2010;51:1361-1367.</td>
<td>20%</td>
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<tr>
<td>Kohlfuerest</td>
<td>Eur JNMMI 2009;36:886-893.</td>
<td>36%</td>
</tr>
<tr>
<td>Maruoka</td>
<td>Radiology 2012;265:902-909.</td>
<td>22%</td>
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<tr>
<td>Mustafa</td>
<td>Eur JNMMI 2010;37:1462-1466.</td>
<td>25%</td>
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<td>Ruf</td>
<td>Nuc Med Comm 2004;25:1177-1182.</td>
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<td>Schmidt</td>
<td>J Nucl Med 2009;50:18-23.</td>
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<tr>
<td>Spanu</td>
<td>JNMMI 2009;50:184-190.</td>
<td>36%</td>
</tr>
<tr>
<td>Tharp</td>
<td>Eur J Nucl Med Mol Imaging 2004;31:1435-1442.</td>
<td>41%</td>
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<tr>
<td>Wang</td>
<td>Clinical Imaging 2009;33:49-54.</td>
<td>23%</td>
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<tr>
<td>Yamamato</td>
<td>J Nucl Med 2003;44:1905-1910.</td>
<td>88%</td>
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<tr>
<td>Avram</td>
<td>JCEM 2015 online early release</td>
<td>29%</td>
</tr>
</tbody>
</table>

Personal Comments

No evidence based medicine??????

Plenty of evidence based medicine for the value of pre-ablation scans and SPECT-CT when performed well.
The Utility of Pre-ablation Radioiodine Scans Differentiated Thyroid Cancer

Find out what technique(s) your imaging facility is using.

Future Techniques: PET and $^{124}$I

Positron Emission Imaging (PET-CT)
Future Techniques: PET and $^{124}$I

One of the Important Sequelae of Dr. Hertz is Radioiodine Imaging

"Pearls" to help you determine when radioiodine images are not necessarily "equal."
Several Pearls that 
$^{131}$I Therapy 
of 
Differentiated Thyroid Cancer 
are not necessarily 
“Equal.”

Interpretation 
of the Literature 
is not “equal.”
Prescribed Activity of $^{131}$I

Adjuvant Treatment of Suspected but Unproven Residual Lymph Node Metastases from Differentiated Thyroid Cancer

Castagna et al., Eur J Endo 2013;169:23-29

<table>
<thead>
<tr>
<th>Recurrent disease, Biochemical disease, metastasis, persistent disease, or death</th>
<th>30 mCi</th>
<th>100 mCi</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>40% (20)</td>
<td>40% (39)</td>
<td>NS</td>
</tr>
<tr>
<td>T3NO-X</td>
<td>25.6%</td>
<td>27.8%</td>
<td>NS</td>
</tr>
<tr>
<td>T1-2N1 and T1-2NO</td>
<td>47.4%</td>
<td>40%</td>
<td>NS</td>
</tr>
<tr>
<td>T3N1</td>
<td>40.9%</td>
<td>52.9%</td>
<td>NS</td>
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Prescribed Activity of $^{131}$I for Adjuvant Treatment of Thyroid Cancer
“Our study provides the first evidence that in ... patients at intermediate risk, high RAI activities have no major advantage over low activities.”

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30 mCi is equally as effective as 100 mCi.
30 mCi is equally as ineffective as 100 mCi.

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Castagna et al., Eur J Endo 2013;169:23-29

Festina Lente
Fundamentals of Radiation Therapy

1. “Determining and delivering radiation to the tumor for control,” and

2. “Determining and minimizing the radiation dose to the normal tissues.”

None of the various empiric approaches are based on either one of these fundamental principles of radiation therapy planning.

THYROID
Volume 7, Number 4, 1997
Mary Ann Liebert, Inc.

Dosimetric Considerations in the Radioiodine Treatment of Macrometastases and Micrometastases from Differentiated Thyroid Cancer

HARRY R. MAXON,1 STEPHEN R. THOMAS,2 and RANASINGHAGE C. SAMARATUNGA2

• Demonstrated that one needed 8,000 rads to destroy lymph nodes.

• If less than 4,000 rads, than low likelihood of successful treatment of lymph nodes.
• It isn’t whether or not you agree with their numbers of rads one must deliver.

• Rather, the article confirmed that you must reach a certain threshold in order to destroy metastases in a lymph node.

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30 mCi is equally as ineffective as 100 mCi.
Progress with Lesional Dosimetry

**Dosimetry**

- 3D-RT
- Uses
  - The 3D-RT $\text{BED}$
  - Add
  - The object dose
- Object dose

**Dosimetry**

- 3D-RD (Bogues and Hobbs, Johns Hopkins)
  - The rate at which it is delivered:
    - (Biologically Effective Dose [BED] def. on a per-voxel basis.)

**Future Techniques: PET and $^{124}$I**

**Positron Emission Imaging (PET-CT)**

**$^{124}$I PET Image**
Fundamentals of Radiation Therapy

1. “Determining and minimizing the radiation dose to the normal tissues.”

None of the various empiric approaches are based on either one of these fundamental principles of radiation therapy planning.
Whole Body Dosimetry

Do I want to hear a talk on “Dosimetry?”
• Maximum Tolerated Activity based on 200 rads to the blood (bone marrow).

• Without pulmonary mets, do not exceed 120 mCi whole body retention at 48 hours.

• With pulmonary mets, do not exceed 80 mCi whole body retention at 48 hours.
This is a Typical Full Dosimetry Protocol

• Dose day 1
• Blood samples every day
• Short scan every day
• Whole body scan day 3.

Imaging dose
1-2 mCi of I-131 po
Following standard preparation (e.g. withdrawal of thyroid hormone, low iodine diet, etc.)

Blood
Optional

K-Scans
Optional

Whole Body Scans

Simplified Dosimetry

• Atkins, et al. Thyroid, 2015;25:1347.
This is a Typical Full Dosimetry Protocol

**Imaging dose**
- 1-2 mCi of I-131 po
- Following standard preparation (e.g. withdrawal of thyroid hormone, low iodine diet, etc.)

**Simplified Dosimetry**
- **Dose day 1**
- **Blood samples every day**
- **Short scan every day**
- **Whole body scan day 3.**

<table>
<thead>
<tr>
<th></th>
<th>Mon</th>
<th>Tues</th>
<th>Wed</th>
<th>Thurs</th>
<th>Fri</th>
<th>Sat</th>
<th>Sun</th>
<th>Mon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K-Scans</td>
<td>2-4 hours</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Whole Body Scans</td>
<td>Optional</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
This is the curve of the %48-hour Whole Body Retention data from which the equation is obtained.


Simplified Dosimetry is Simple
And can be done in any nuclear medicine facility with a gamma camera.
So, I just heard a presentation on Dosimetry

One Final Thought regarding $^{131}$I prescribed activity for lymph nodes and distant metastases
A small change can make a big difference in outcomes.

To help visualize this concept, here are some hopefully memorable images of that concept.
A small change can make a big difference in outcomes.
A small change in $^{131}\text{I}$ prescribed activity may make a big difference in outcomes.

*Special Thanks to the Staff of the Washington Hospital Center Division of Nuclear Medicine*
Not all Nuclear Medicine Radioiodine Imaging and Therapy of Differentiated Thyroid Cancer are Created Equal

Douglas Van Nostrand, MD, FACP, FACNM
Director, Nuclear Medicine Research
MedStar Research Institute and Washington Hospital Center
Professor of Medicine, Georgetown Univ School of Medicine

A small change in $^{131}$I prescribed activity may make a big difference in outcomes.

Douglas Van Nostrand, MD, FACP, FACNM
Director, Nuclear Medicine Research
MedStar Research Institute and Washington Hospital Center
Professor of Medicine, Georgetown Univ School of Medicine
Thank You

Availability of slides

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