Imaging in Thyroid Cancer

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University of Pennsylvania School of Medicine
Philadelphia, PA
I-123

Ultrasound

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Background

- Radioiodine ablation of thyroid remnants after surgery is a generally accepted treatment in many patients with differentiated thyroid cancer (DTC).
- Diagnostic I-131 scanning is usually performed prior to I-131 therapy to demonstrate remnant or metastases.
- Diagnostic I-131 scanning is subsequently used as surveillance for residual/recurrent DTC.
- Although remnant visualization is improved with higher diagnostic I-131 doses, “stunning” may occur with doses between 3-10 mCi.
Definition of Stunning:

A sub-lethal effect by diagnostic doses of I-131 on differentiated thyroid tissue causing reduced uptake of the subsequent therapeutic I-131 dose.
What is the ideal radionuclide for imaging?

✓ concentrated by normal thyroid tissue and by thyroid cancer
✓ energy emitted by the radionuclide should be within the range of the camera so that pictures can be of good quality
✓ minimal radiation exposure to the patient
✓ does not inhibit the effect of subsequent I-131 therapy
I-123 versus I-131
Comparative Properties

<table>
<thead>
<tr>
<th></th>
<th>I-123</th>
<th>I-131</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>159 keV</td>
<td>364 keV</td>
</tr>
<tr>
<td>Emission</td>
<td>γ</td>
<td>γ and β</td>
</tr>
<tr>
<td>Stunning</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Half-life</td>
<td>13 hours</td>
<td>8 days</td>
</tr>
<tr>
<td>Expense</td>
<td>2mCi-$250</td>
<td>3mCi-$100</td>
</tr>
<tr>
<td>Availability</td>
<td>Less</td>
<td>More</td>
</tr>
<tr>
<td></td>
<td>(cyclotron, transport)</td>
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</table>

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I-123 Diagnostic WBS compared to post-I-131 WBS

• Pre-ablation patients
  – Low dose I-123 (300-600 µCi) ~90% concordant
  – High dose (1-15 mCi) ~94% concordant

• Surveillance patients
  – Dx WBS+ ➔ 80% concordant
  – Dx WBS- ➔ 60% concordant; 40% with new positive findings

**5 and 24-Hour I-123 Scintigraphy**

Comparison of 5hr and 24hr diagnostic images after 1.5mCi I-123 in DTC patients either prior to thyroid remnant ablation or during surveillance for residual/recurrent cancer.

Comparison of diagnostic I-123 imaging with scans obtained 7 days after I-131 therapy.

Scintigraphy
99 consecutive DTC patients (70 remnant ablation, 29 surveillance)

Day 1:
- Oral administration of 1.5 mCi I-123
- **5 hours**: Whole body and head/neck planar imaging

Day 2:
- **24 hours**: Whole body and head/neck planar imaging

Day 2 PM or Day 3:
- I-131 Rx for remnant ablation or metastasis

Post-therapy scans—whole body planar images obtained 7 days after I-131 treatment
Remnant Ablation Scans (70)
5 hour vs. 24 hour

• Concordance in 47/70 (67%)

• 24 hour scans superior in 21/70 (30%)
  – additional or equivocal thyroid bed foci imaged in 18
  – better delineation of multifocal pulmonary uptake in 3

• 5 hour scans superior in 2/70 (3%)
  – count poor thyroid remnant at 24 hrs (technical)
  – faint mediastinal focus at 24 hrs
Case: BO

I-123 at 5 hours

I-123 at 24 hours

Esophageal uptake
Esophageal uptake

I-123 at 24 hours
Case: JP

I-123 at 5 hours

I-123 at 24 hours
Case: JP

I-131 Post-Therapy Scan

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Surveillance Scans (29)

5 hour vs. 24 hour

23 negative, 6 positive scans

• Concordance in 25/29 (86%)
• 24 hour scans superior in 4/29 (14%),
  4/6 with positive scans (66%)
  – additional/equivocal thyroid bed foci imaged in 2
  – equivocal pulmonary metastases confirmed in 2
Case: LS

I-123 at 5 hours  I-123 at 24 hours

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Post-therapy imaging
74 patients received I-131 therapy

• Concordance with 24hr I-123 scans in 69/74 patients (93%)
• Demonstrated 1-2 additional foci within the thyroid bed in 5 (7%) remnant patients
  – Did not demonstrate any metastases not previously seen on diagnostic scans
Case: PK

I-123 at 5 hours

I-123 at 24 hours

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Case: PK

I-131 Post-Therapy scan
University of Pennsylvania
326 pts with diagnostic I-123 and post-therapy scans

<table>
<thead>
<tr>
<th></th>
<th>Scans</th>
<th>Concordant w/post-Rx</th>
<th>Discordant w/post-Rx</th>
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<tbody>
<tr>
<td><strong>Initial ablation</strong></td>
<td>256</td>
<td>244</td>
<td>95%</td>
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University of Pennsylvania
326 pts with diagnostic I-123 and post-therapy scans

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<td><strong>Initial ablation</strong></td>
<td>256</td>
<td>244 95%</td>
<td>12 5% 10 thyroid bed 2 LN</td>
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University of Pennsylvania
326 pts with diagnostic I-123 and post-therapy scans

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<tr>
<td>Positive I-123</td>
<td>70</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>median Tg 8.1ng/ml</td>
<td>41</td>
<td>88%</td>
<td>30 neck</td>
</tr>
<tr>
<td>range &lt;1.0-16,000</td>
<td></td>
<td></td>
<td>3 lung</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 bone</td>
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University of Pennsylvania
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<td>36&lt;br&gt;88%&lt;br&gt;30 neck&lt;br&gt;3 lung&lt;br&gt;3 bone</td>
<td>5&lt;br&gt;12%&lt;br&gt;3 LN&lt;br&gt;1 ovary&lt;br&gt;1 add’l lung</td>
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University of Pennsylvania
326 pts with diagnostic I-123 and post-therapy scans

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<tr>
<td>Negative I-123</td>
<td>70</td>
<td>29</td>
<td>19</td>
</tr>
<tr>
<td>median Tg 56.3ng/ml range 12-530</td>
<td>66%</td>
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University of Pennsylvania
326 pts with diagnostic I-123 and post-therapy scans

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<tr>
<td>Negative I-123</td>
<td>70</td>
<td>19 66%</td>
<td>10 34%</td>
</tr>
<tr>
<td>median Tg 56.3ng/ml range 12-530</td>
<td>29</td>
<td>6 LN</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 diffuse lung</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 discrete lung</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 thymus</td>
<td></td>
</tr>
</tbody>
</table>
Case: EB

I-123 at 24 hours

Anterior

Posterior

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Case: EB

I-131 Post-Therapy scan

Anterior

Posterior
Case: RS

I-123 at 24 hours

**T-spine**

**skull**

**pelvis**

**L-spine**

123 I IMAGES 24 HRS.
Case: RS
I-131 Post-Therapy scan

Anterior

Posterior
Case: RB

I-123 at 24 hours

Anterior

Posterior

Slides are not to be reproduced without permission of author
Case: TH

I-123 at 24 hours

Anterior

Posterior
Case: TH

I-131 Post-Therapy scan

Anterior

Posterior
Case: TH

I-131 Post-Therapy scan

Anterior

Posterior
Case: TH

I-131 Post-Therapy scan
Right lateral pelvis
Case: TD

I-123 at 24 hours

I-131 Post-Therapy scan
Case: BW

Anterior

Posterior

I-123 at 24 hours

I-131 Post-Therapy scan
Case: SB

3.0mCi I-123 at 24 hours

Anterior

Posterior
Case: SB

3.0mCi I-123 at 30 hours

Anterior  Posterior
Case: SB

I-131 Post-Therapy scan

Anterior

Posterior
Concordance of Diagnostic I-123 and Post-therapy Scintigraphy

- Shankar
- Gulzar
- Berbano
- Yaakob
- Mandel
- Gulzar
- Mandel
- Siddiqi
- Alzahrani
- Gerard

I-123 Dose (mCi) vs. Concordance with Post-Therapy Scans (%)

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How do diagnostic I-123 and I-131 scans compare?

Concordance with post-therapy scans
# New Metastases on Post-therapy Scans

## Diagnostic I-131 vs. Post-therapy scans

<table>
<thead>
<tr>
<th>Study</th>
<th>I-131 Dose (mCi)</th>
<th>New Sites of Metastases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nemec (207)</td>
<td>0.5</td>
<td>32 LN, 16 distant</td>
<td>23%</td>
</tr>
<tr>
<td>Balachandran (43)</td>
<td>1-3</td>
<td>7 LN, 7 lung</td>
<td>31%</td>
</tr>
<tr>
<td>Spies (39)</td>
<td>5</td>
<td>12 LN or lung</td>
<td>31%</td>
</tr>
<tr>
<td>Sherman (143)</td>
<td>2-5</td>
<td>7 LN, 9 lung, 1 bone</td>
<td>10%</td>
</tr>
<tr>
<td>Fatourechi (117)</td>
<td>3</td>
<td>9 LN, 5 lung, 2 bone, 1 adrenal</td>
<td>13%</td>
</tr>
<tr>
<td><strong>OVERALL (549)</strong></td>
<td></td>
<td>LN 16%, Distant 7%</td>
<td><strong>18%</strong></td>
</tr>
</tbody>
</table>
# New Metastases on Post-therapy Scans

<table>
<thead>
<tr>
<th>Study</th>
<th>I-123 Dose (mCi)</th>
<th>New Sites of Metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yaakob (12)</td>
<td>1</td>
<td>none</td>
</tr>
<tr>
<td>Mandel (13)</td>
<td>1.5</td>
<td>LN (1)</td>
</tr>
<tr>
<td>Shankar (74)</td>
<td>1.5</td>
<td>none</td>
</tr>
<tr>
<td>Mandel (326, <em>unpublished</em>)</td>
<td>2.0</td>
<td>LN(14), lung(3), ovary(1)</td>
</tr>
<tr>
<td>Gerard (12)</td>
<td>1-5</td>
<td>LN (3)</td>
</tr>
<tr>
<td>Gulzar (27)</td>
<td>5</td>
<td>LN (1)</td>
</tr>
<tr>
<td>Siddiqi (18)</td>
<td>5</td>
<td>LN (1)</td>
</tr>
<tr>
<td>Berbano (16)</td>
<td>10</td>
<td>none</td>
</tr>
<tr>
<td>Alzahrani (238)</td>
<td>5-15</td>
<td>LN (13), lung (2)</td>
</tr>
</tbody>
</table>

**OVERALL (724)**  
LN 5%  Distant 1%
Ultrasound for detection of metastatic lymph nodes in patients with thyroid cancer
A case to start:

43 y.o. woman with 3.2cm R pap CA, 5/7 paratracheal LNs+

W/D: TSH 72, Tg 34; WBS thyroid bed uptake 1.4%

Rx with 125 mCi I-131, post-Rx scan thyr bed only

On 0.137mg T4, TSH 0.08, Tg <1.0

W/D: TSH 93, Tg 14: WBS negative

Rx with 150mCi I-131, post-Rx scan negative
What is producing the serum thyroglobulin?
Localization of nodal mets in 119 pts after thyroidectomy and bilateral cervical neck dissection

- Level VI: 85%
- Level VI + Lateral: 63%
- Level VI alone: 22%
- Lateral alone: 15%

Contralateral node involvement in 18% of patients with unilateral tumors

But, less than 20% of patients have been found to have clinically apparent nodal recurrence*

*This estimate predates the use of ultrasound!!
Cumulative occurrence during 25 years of post-op events, 2370 patients 1940-2000

Hay, Trans Amer Clin Assoc 2002
Some basic facts about cervical LNs

- Normal cervical LNs detected in healthy people
  - Up to 300 present in neck
  - No age, gender, ethnic difference
  - Decreased detection with older age
- Size of normal LNs varies with location, age
  - Upper neck (submandibular) larger—oral cavity inflammation causing reactive hyperplasia
  - Smaller in younger than older patients; fatty infiltration occurs with age
Neck Node Classification

Som et al, AJR 2003
US of normal cervical lymph nodes

• **Shape**
  – **OVAL** assessed by short to long (S:L) axis ratio
  – S:L is < 0.5 → oval; S:L ≥ 0.5 → round
  – HOWEVER, normal submandibular LN (95%) may be round!

• **Echogenic hilus (hypoechoic cortex)**
  – consists of fatty tissue, sinuses, intranodal vessels
  – visualized in larger nodes (90% with transverse > 5mm) and older patients (more fat!)

• **Vascularity**
  – hilar vascularity (90% with transverse > 5mm) or avascular (smaller nodes, usually posterior triangle)
How commonly are normal cervical LNs visualized on US?

1000 healthy volunteers in Nice, France

<table>
<thead>
<tr>
<th>Frequency of LNs</th>
<th>Entire pop</th>
<th>Male</th>
<th>Female</th>
<th>Younger than 50</th>
<th>50 or older</th>
<th>Recent ENT infection (&lt;3months)</th>
<th>No recent ENT infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>68%</td>
<td>69%</td>
<td>67%</td>
<td>72%</td>
<td>64%</td>
<td>65%</td>
<td>68%</td>
</tr>
<tr>
<td>Bruneton, J Ultrasound Med 1994</td>
<td></td>
<td></td>
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<td></td>
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</table>

Slides are not to be reproduced without permission of author.
Normal lymph node

Transverse

Sagittal

Fatty hilus

Slides are not to be reproduced without permission of author
Normal lymph node

Sagittal

short:long 0.375
Normal lymph node

Sagittal

Fatty hilus

Hilar vasularity
US of abnormal cervical lymph nodes

- **Shape:** $S:L \geq 0.5 \rightarrow$ round
- **Echogenicity:** Hyperechoic compared to muscle
- **Absence of echogenic hilus**
- **Cystic change**
- **Calcifications**
- **Peripheral vascularity**

Ying, J Ultrasound Med 1998
Malignant 9 mm right lateral cervical LN hyperechoic, rounded shape,

S 7mm
L 11mm
S:L 0.64

Transverse

sternocleidomastoid
carotid
Malignant 9 mm right lateral cervical LN hyperechoic, rounded shape, micro Ca^{2+}
Hyperechogenic lymph node, hypervascularity on color Doppler

Sagittal
3 lymph nodes with papillary cancer

Sagittal

superior

inferior
So, how does Ultrasound compare with Radioiodine imaging for lymph node detection?
Detection of LN mets in 51 patients with neck recurrences

- 494 patients DTC followed for mean 55 months
- All were post thyroidectomy and I-131 Rx
- Underwent withdrawal I-131 WBS and US

Frasdolti et al, Cancer 2003
Detection of LN mets in 51 patients with neck recurrences

Frasdolti et al, Cancer 2003
So, how does Ultrasound compare with PET imaging for lymph node detection?

- No direct comparisons between PET and US
- I-131 non avid patients reported to be PET+ ~70% of time
- AND, cervical lymph nodes are the most common location
- These can be visualized with US!

Alnafasi J Nuc Med, 2000;
What do we do when US detects an abnormal LN?

US guided FNA

- cytology
- Tg measurement
- ?Tg mRNA
US FNA of right cervical LN, sent for Tg

jugular

carotid
Routine use of pre-op US changed surgery in 39%

- Retrospective study of 212 pts (pap and MTC) who had surgery for primary, persistent or recurrent disease
- US detected ABNORMAL LNs not on PE in
  - 20% primary
  - 39% persistent (< 6months after primary surgery)
  - 68% recurrent (> 6 months after primary surgery)
- Pattern of LN+
  - 56% paratracheal, 31% ipsilateral, 13% contralateral

Kouvaraki Surgery 2003
Future Directions

- Optimal dose of I-123 for withdrawal imaging
- Optimal time for scan acquisition
- Future therapeutic rhTSH use for I-131 remnant ablation and metastatic disease may benefit from rhTSH imaging with I-123 rather than with I-131 to avoid potential stunning
- Is sensitivity of US improved with TSH stimulation?
Collaborators

Abass Alavi
Lalitha Shankar
Stephanie Fish
Simin Dadapavar
Jill Langer
The Piranha Club

32 CARAT GOLD?!  
PURE GOLD IS 24 CARAT...  
HOW CAN THIS BE 32 CARAT?!  

IT'S AN ISOTOPE*

*NOTE: THIS GAG IS VERY FUNNY IF YOU HAPPEN TO BE A NUCLEAR PHYSICIST
Comparison of diagnostic I-123 and I-131 Images

- 12 patients (9 initial therapy, 3 second therapy)
- I-123 scans: 24 hours after 2-3.5mCi
  I-131 scans: 72-96 hours after 3-5mCi
- Diagnostic I-131 scans reported better than I-123 in 4 patients
  - 2 pts: new cervical LN and lung metastases
  - 1 pt: “in retrospect” bone metastases seen on I-123
  - 1 pt: new axillary and faint mediastinal metastases
- Post-therapy scans not shown

Sarkar, J Nuc Med, 2002
Diagnostic I-123 and I-131 scans:

I-131 scan reported to show left cervical LN and pulmonary metastases

Sarkar, J Nuc Med, 2002
Diagnostic I-123 and I-131 posterior views.

96 hr I-131 posterior view reported to show left cervical LN and pulmonary metastases

~3mCi I-123 at 24 hours
~4mCi I-131 at 24 hours
~4mCi I-131 at 96 hours

Sarkar, J Nuc Med, 2002