The Role of Nuclear Medicine in Thyroid Cancer

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Outline of Presentation

• Basis for use of radioiodine (RAI)
• Physical characteristics of RAI
• Imaging modalities for diagnosis, treatment, and patient monitoring
• Controversies in the use of RAI
• Patient Selection and Dosing
• Clinical examples
Basis for Use of RAI

$^{131}$Iodine is processed similarly and the beta emissions result in tissue necrosis.
Physical Characteristics of RAI

^{131}\text{Iodine} \quad ^{123}\text{Iodine}

- Physical $½$-life: 8.06 days 
- Mode of Decay: Beta particles and gamma radiation (364 keV)  
- Radiation Absorbed Dose:  
  ~130 rads/100 $\mu$Ci 
- Activity administered:  
  30-200+ mCi

- Radiated 13.2 hours  
- Electron capture (159 keV)
- $\sim$3 rads/100 $\mu$Ci 
- 0.2-5 mCi
# Imaging Modalities

<table>
<thead>
<tr>
<th>Modality</th>
<th>Diagnosis</th>
<th>Therapy</th>
<th>Monitor</th>
<th>Misc</th>
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<tbody>
<tr>
<td>US</td>
<td>✓</td>
<td></td>
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<tr>
<td>CT</td>
<td>✓</td>
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<td>✓</td>
<td>Chest and bone</td>
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<tr>
<td>MRI</td>
<td>✓</td>
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<td>✓</td>
<td>Bone and brain</td>
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<tr>
<td>PET/CT</td>
<td>✓</td>
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<td>✓</td>
<td>FDG, FDOPA, $^{124}$Iodine</td>
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<td>SPECT/CT</td>
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<td></td>
<td>✓</td>
<td>Better localization compared to planar</td>
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<tr>
<td>$^{123}$Iodine</td>
<td>✓</td>
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<td>✓</td>
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<tr>
<td>$^{131}$Iodine</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>DMSA, SSRI, MIBG, NaF bone</td>
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Controversies in the Use of RAI

Issues We Can All Agree On

Doctor. I’ve eaten something that disagrees with me.

No you haven’t.
Example of Disagreement

Is a pre-ablation WBS necessary?

- European Thyroid Association: No
- American Thyroid Association: Selected patients if it might change management
- NCCN (National Comprehensive Cancer Network): Yes
There is a near-zero role for scintigraphy in the initial evaluation of a patient with suspected thyroid cancer.

If cytology reading is indeterminate (e.g., “suspicious”, “follicular lesion”, “follicular neoplasm”), consider scan.
Imaging Studies

1-123 Uptake and Scan

$^{99m}$Tc-pertechnetate Scan

Ultrasound
I-123 Scan for "Goiter"

- Note uptake in lower, anterior chest
- These are metastases from thyroid cancer
What is your Diagnosis?

This is a pertechnetate scan in a dog with hyperthyroidism; note that thyroid carcinomas in canines will concentrate pertechnetate (unlike humans)
Remnant Ablation

• The destruction of residual macroscopically normal thyroid tissue after surgical thyroidectomy
• Recommended for patients with known distal metastases, gross extrathyroidial extension of tumor, primary tumor size >4 cm
Objectives of Ablation

- Ablating residual thyroid tissue ↑ sensitivity for detecting metastases on I-131 WBS
- Ablating residual thyroid tissue facilitates interpretation of serum thyroglobulin levels
- Potentially treating residual postoperative microscopic tumor foci (tumoricidal, adjuvant therapy)
- Decreasing rate of recurrence
- Increasing survival
Ablation
(patients < 45 yrs old)

• Stage I: Those with multifocal disease, nodal metastases, extrathyroidal or vascular invasion, aggressive histology

• Stage II: Any T, any N, M1
Ablation (patients > 45 yrs old)

• Essentially all stages (I-IV)
Is a Pre-Ablation Scan Necessary?

- Delineation of pattern and percent uptake in the thyroid bed/neck
- Demonstration of distant metastases (may be especially helpful in the lungs, bone, and brain)
- May use I-123 (1.5-3 mCi)
- Treat patient within 72 hours of scan
I-131 for Ablation

- Preparation: low iodine diet for 1-2 weeks (i.e., <50 micrograms/day)
- TSH >30 mIU/L
- Withdrawal or Thyrogen™
- Dose: 30-100 mCi
- Inpatient or outpatient
Successful Ablation

- Absence of uptake on WBS 6-12 months after ablation, non-measurable Tg level, no suspicious findings on US

- Guidelines from the European Journal of Nuclear Medicine, 2008
RAI Therapy

A Gift from Above
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<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>I-131</td>
<td>.75</td>
<td>Near Perfect</td>
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<tr>
<td>TI-201</td>
<td>.68-.90</td>
<td>.88</td>
</tr>
<tr>
<td>MIBI</td>
<td>.73</td>
<td>.85</td>
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<tr>
<td>FDG</td>
<td>.83</td>
<td>.96</td>
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DMSA, MIBG, Octreotide
Patient with Hurthle Cell Carcinoma; negative I-131; given 4 mCi of Thallium

- This is a thallium-201 image of the head and neck. Note the two sites of metastases, corresponding to the skull and the posterior neck.
Sestamibi

- This is a $^{99m}\text{Tc}$-sestamibi study in a patient who is I-131 negative with an elevated thyroglobulin level. Note the cardiac activity and the extensive uptake below the diaphragm.
Hurthle Cell CA; Iodine Negative
Octreotide Image
Clinical Examples
Patient Selection and Dosing
Hierarchy of Therapy for Metastases

Surgical excision of locoregional disease (in potentially curable patients) → I-131 → external beam radiation therapy → watchful waiting if patient is stable → experimental chemotherapy trials
Methods of Diagnostic Scanning

Conventional
- Discontinue thyroid
- Low iodine diet
- Measure serum TSH, Tg, and anti-thyroglobulin antibodies
- 2-5 mCi of RAI
- Image at 48 hours
- Resume thyroid vs. immediate treatment

rh-TSH-mediated
- Continue on thyroid
- Follow Thyrogen protocol
- Measure Tg and anti-thyroglobulin antibodies
- 4 mCi of RAI
Methods of Administration of RAI

- Empiric: nodal metastases = 100-175 mCi; distant metastases 200 mCi
- Determined by upper bound limit of blood and body dosimetry: maximum 200 rads to the blood, < 80 mCi retention in the lungs at 48 hrs if diffuse pulmonary uptake
- Quantitative tumor dosimetry: based upon estimated tumor uptakes
- Brain: add glucocorticoid
Administration of RAI

- Empiric therapy justified if Tg > 10 ng/mL or if Tg doubling time 12 months or less*
- No randomized controlled studies to confirm increased survival (even if Tg goes down)
- If using in combination with external beam RT, give RAI first if possible (this is debated in the literature)

* Mazzaferri
Negative Study
Minimal Disease

ANTERIOR

POSTERIOR
Distant Disease
The Importance of a Post-Therapy Scan

Diagnostic Study

Post-Therapy Study
Widespread Metastases

This is an I-131 whole body scan, following 150 mCi of radioactive iodine.
Side Effects of RAI Administration

- Nausea +/- emesis
- Sialadenitis
- Dental caries
- Nasolacrimal duct obstruction
- Gonadal dysfunction
- Secondary malignancies
Monitoring

• 2009: 37,200 new cases in the U.S.

• 1,630 deaths

• 10-30% of patients thought to be disease free after initial therapy will develop recurrence and/or metastases

• WBS may be of value 6-12 months after ablation in intermediate and high-risk patients
Low-Risk Patients
(after initial surgery and remnant ablation)

- No local or distant metastases
- All microscopic tumor resected
- No tumor invasion of locoregional tissues or structures
- Tumor has no aggressive histology (e.g., tall cell, insular, columnar cell) or vascular invasion
- No I-131 uptake outside the thyroid bed on the first post-treatment WBS
Monitoring Low-Risk Patients

- ~85% of post-operative patients
- TSH-suppressed Tg and cervical US
- May follow with TSH-stimulated Tg if suppressed Tg is undetectable (~20% of patients will have a suppressed Tg level <1ng/ml but a stimulated level >2 ng/ml)
Intermediate-Risk Patients

- Microscopic invasion of tumor into the peri-thyroidal soft tissues at initial surgery or tumor with aggressive histology or vascular invasion
High-Risk Patients

- Macroscopic tumor invasion
- Incomplete tumor resection
- Distant metastases
- I-131 uptake outside the thyroid bed on the post-treatment scan done after thyroid remnant ablation
RAI: Special Issues

- Children and Adolescents: base activities in consideration of age, body weight, body surface area, 24-hour uptake in the thyroid bed

- Utilize rhTSH in patients with hypothalamic or pituitary disease, functioning metastases, risks with hypothyroidism, patient preference
Special Issues

• Lithium: inhibits iodine release from the thyroid without impairing uptake; no outcome data
• Pulmonary metastases: pneumonitis and fibrosis are rare
• Macronodular pulmonary metastases: RAI if demonstrated to be iodine-avid
• FDG-Positive patients: likely will not respond to RAI
Special Issues

- Bone metastases: consider resection if isolated and symptomatic (↑ survival)
- RAI for iodine-avid metastases
- If skeletal lesions identified in locations where acute swelling may produce severe pain, fracture, or neurologic complications (e.g., spine) consider EBRT + steroids
Special Issues

• Secondary malignancies: low-risk
• Gonadal function: temporary amenorrhea or oligomenorrhea; ↓ sperm count + ↑ FSH
• PET imaging: TSH may enhance the PET scan
• Post-Therapy RAI scan: 10-26% of patients show additional metastases after high dose RAI
Stunning

• The tissues concentrating I-131 are sufficiently harmed by the scanning dose so that subsequent uptake of therapeutic RAI may be diminished

• Can use lower dose for diagnostic study, treat immediately, or use I-123
Challenges for RAI

- Overall risk of recurrence for differentiated thyroid cancer is ~20%
- $^{131}$I-positive recurrence ~60-67%
- Reduced sensitivity in medullary thyroid carcinoma and Hurthle cell carcinoma
- $^{131}$I-negative tumors show impaired Na$^+$/I$^-$ pumps, a sign of dedifferentiation
Indications for $^{18}$F FDG-PET

- Tg + (some debate as to level) with negative WBS
- Initial staging + F/U in patients with poorly differentiated thyroid cancers
- Invasive or metastatic Hurthle cell carcinoma
- Prognostic tool to identify patients with distant metastases at high-risk for disease-specific mortality
- Identify patients unlikely to respond to RAI
- Measurement of post-treatment response to external beam radiation therapy, surgery, embolization, or systemic therapy
PET in Thyroid Cancer

• The higher the Tg → the greater the number of tumor cells → the larger the tumor size → the more likely to be seen on PET

• Report: sensitivity of FDG-PET for detecting metastases; 11% if Tg <10, 50% if 10-20, 93% if >100
PET in Thyroid Cancer

- PET may find an unsuspected malignancy
- Probable that the higher the SUV the poorer the prognosis
- PET/CT can assess the volume of disease; >125 ml → reduced survival
- Thyroid incidentalomas have a high rate of malignancy
Thyroid Cancer

- 80 year old female with thyroid carcinoma. Diagnosed >30 years ago; s/p thyroidectomy and RAI. Recent biopsy of right neck mass showed papillary carcinoma, felt to be thyroidal in origin.
This is her PET study after a negative I-131 whole body scan.
Positive PET in I-131 Negative Patient
Correlative MRI
PET: large tumor burden
Poorly differentiated cancer
Patient with NHL; referred for restaging

Patient had multiple hypermetabolic lymph nodes, reported as consistent with NHL recurrence

Biopsy was benign; patient had Kikuchi-Fujimoto’s Disease
Shortly thereafter the patient was operated upon for thyroid cancer; 12/22 lymph nodes were positive. The study below is her I-131 scan post ablation.

ERGO
Positive study for NHL (no lymphoma)
Negative study for thyroid cancer (present)