1st Annual UT Southwestern Endocrine Tumor Symposium

Radioiodine treatment for Thyroid Cancer: Why, When and How

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Disclosures

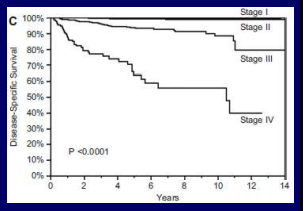
- None

Objectives

1) Address WHY 131-I is administered for DTC treatment
2) Address WHEN 131-I is administered for DTC treatment
3) Address HOW 131-I is administered for DTC treatment

Thyroid Cancer Prognosis

- Patients with stage I-II disease have favorable prognosis (mortality < 1% at 20 years) (low risk group)
- Mortality increases to 25-40% among patients at stages III and IV (high risk group)



Jonklaas J et. al. Thyroid. 2006 (12):1229-42 - **NTCTCS**
National Thyroid Cancer Treatment Cooperative Study Group
- initiated in 1987
- multicenter Registry at 11 North American Institutions
- central data repository at MD Anderson, Texas

National Thyroid Cancer Treatment Cooperative Study Group

Registry Staging Classification

		Papillary carcinoma	
		Age < 45	*Age ≥ 45*
Primary Tumor Size (cm)	< 1	I	I
	1–4	I	II
	> 4	II	III
Primary Tumor Description	Microscopic multifocal	I	II
	Macroscopic multifocal or macroscopic tumor capsule invasion	I	II
	Microscopic extraglandular invasion	I	II
	Macroscopic extraglandular invasion	II	III
	Poor differentiation	n/a	n/a
Metastases	Cervical lymph node metastases	I	III
	Extracervical metastases	III	IV

Stages I and II = Low Risk **Stages III and IV = High Risk**

WHY 131-I ?

There is evidence of improved overall survival and disease-specific survival in patients with advanced tumors and regional and/or distant metastatic disease who received postoperative ^{131}I therapy

National Thyroid Cancer Treatment Cooperative Study Group
Jonklaas J et. al. Thyroid. 2006: 2936 DTC patients

Outcomes following RAI Rx

	Disease-Specific Survival		
	RR	95% CI	p
Stage I	0.00063	*	0.1
Stage II	1.21	0.26–3.92	0.76
Stages III & IV	1.46	1.13–1.87	0.0045

no RAI/RAI; RR>1 indicates a better outcome associated with RAI

National Thyroid Cancer Treatment Cooperative Study Group
Jonklaas J et. al. Thyroid. 2006 (12):1229-42

Outcomes following RAI Rx

	Disease-Free Survival		
	RR	95% CI	p
Stage I	0.64	0.47–0.85	0.0013
Stage II	1.03	0.75–1.39	0.84
Stages III & IV	1.32	1.02–1.68	0.035

no RAI/RAI; RR>1 indicates a better outcome associated with RAI

Carhill et al J. Clin Endocrinol Metab, Sept. 2015
NTCTCS: Updated Analysis 1987-2012: 4941 pts.
Median F/U 6 yrs, longest 25 yrs; total 34,631 person-yrs.

RAI Rx

- improved **OS** in Stage III – **RR 0.66, p = 0.04**
- improved **OS** Stage IV – **RR 0.7, p = 0.049**
- improved **DFS** in Stage II – **RR 0.7, p = 0.05**

TSH Suppression Therapy (TSHT)

Moderate TSH suppression improved OS and DFS across ALL Stages (I - IV) – **RR 0.13, p = 0.09**

*** Unexpected for Low-Risk patients (Stages I-II), c/w with residual ds.**

Sawka et al. JCEM 2004, 89(8):3668–3676

A Systematic Review and Meta-analysis of the Effectiveness of RAI for DTC

Goal: to determine whether RAI Rx decreases the risk of Death or Recurrence in DTC

- **1543 papers reviewed; 31 Cohort Studies selected**

statistically significant effect for 10-yr outcomes:

- **Decreased Risk of Locoregional Recurrence**
  RR 0.31 (CI 0.2, 0.49)
- **Decreased Risk for distant metastases**
  Absolute Risk reduction 3%

Adjuvant Treatment: Prescribed Activity

Meta-analysis of I-131 Effectiveness

Sawka JCEM 2004

Courtesy of Dr. Marcus Luster, MD, Germany

Series	N	Follow-up (yr)	I-131 effectiveness Cancer mortality	I-131 effectiveness Cancer recurrence
Ohio State	1510	16.6	P<0.0001	P<0.016
UCSF	187	10.6	NS	P<0.0001
Hong Kong	587	9.2	NS	
Toronto	382	10.8	NS	
Illinois Reg	2282	6.5	NS	
Gundersen	177	7.2		NS
MD Anderson	1599	11		P<0.001
Gustave R	273	7.3		NS
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Pisa	964	12	NS	P<0.001

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Adjuvant Radioactive Iodine Therapy Is Associated With Improved Survival for Patients With Intermediate-Risk Papillary Thyroid Cancer

Ewa Ruel, Samantha Thomas, Michaela Dinan, Jennifer M. Perkins, Sanziana A. Roman, and Julie Ann Sosa

Department of Medicine (E.R., J.M.P.), Division of Endocrinology, Metabolism, and Nutrition, Department of Surgery (J.A.S.), Section of Endocrine Surgery, Duke University Medical Center, and Duke Cancer Institute (J.A.S.), Durham, North Carolina 27710; Department of Biostatistics (S.T.), Duke University , Durham, North Carolina 27708; and Duke Clinical Research Institute (M.D., J.A.S.), Durham, North Carolina 27705

- **National Cancer Data Base (NCDB)**
- **21,870 pts -** Follow-up: Mean 6.8 yrs; Median 6.6 yrs
  - Longest 14.9 yrs.
- **Intermediate risk (2009 ATA guidelines)**

➢ **T3, N0, M0 or Mx**
- Tumor > 4 cm
- Tumor of any size with minimal ETE

➢ **T1-3, N1, M0 or Mx**

Ruel et al. , JCEM 2015;200;1529-1536.

Adjuvant RAI Rx.

Improved OS in All patients (p< 0.001)

- ➢ Patients < 45 yrs (p < 0.002)
- ➢ Patients ≥ 45 yrs (p < 0.008)

➢ 29% reduction in the risk of death for all patients
- HR 0.71 (CI 0.62-0.82), p < 0.001

➢ 36% reduction in the risk of death for pts. < 45 yrs.
- HR 0.64 (CI 0.45-0.92), p = 0.016

Ruel et al. , JCEM 2015;200;1529-1536.

RAI treatment of Known Disease

11,832 pts. (PTC: 91.24%; FTC: 8.76%)

All-cause mortality:

PTC cohort:
- ➢ 5y mortality: 22.7% w/o RAI vs 11.0% w. adjuvant RAI
- ➢ 10y mortality: 25.5% w/0 RAI vs 14.0% w. adjuvant RAI

FTC cohort:
- ➢ 5y mortality: 45.5% w/o RAI vs 29.2% w. adjuvant RAI
- ➢ 10y mortality: 51% w/o RAI vs 36.8% w. adjuvant RAI

Yang et al. Thyroid 2017;27(7):944-52
Comparison of Survival Outcomes Following Postsurgical RAI vs. EBRT in Stage IV DTC

WHEN 131-I

When 131-I is administered depends on the therapeutic intent:

1) Remnant ablation
2) Adjuvant treatment
3) Treatment of known disease

Remnant ablation

✓ Elimination of postoperative normal thyroid tissue remnants in order to achieve an undetectable Tg level

✓ **Aim:**
- facilitating follow-up and early detection of relapse.
- enable high-sensitivity post-Rx WBS to diagnose unsuspected regional or distant metastases.

✓ It is performed for patients with **low-risk** pathology

✓ Low 131-I activity for Remnant Ablation ~ **30 mCi 131-I**

Adjuvant RAI administration

✓ Elimination of occult infra-radiologic residual disease in patients with suspected microscopic metastatic disease based on histopathologic risk factors that predict tumor spread beyond thyroid gland

✓ **Aim:** to decrease recurrence risk and improve survival

✓ **Practical point: these patients are NOT Low Risk**

✓ **They are Medium –risk & High –risk for recurrence**

RAI Treatment of Known Disease

- ✓ To treat iodine-avid regional and/or distant metastases in patients with known residual or metastatic disease
- ✓ **Aim:** achieve cure or remission, reduce persistent or recurrent disease, and improve survival
- ✓ ± Whole Body/Blood Dosimetry Calculations
- ✓ ± Lesional Dosimetry Calculations
- ✓ Radiological and biochemical follow-up to assess response

HOW 131-I

Radioiodine therapy planning (Theragnostics)

Patient-individualized 131-I therapy prescription:

1) Integration of clinical data (patient's age and clinical presentation: with/without palpable lymphadenopathy)
2) Surgical pathology report: defining **T** and **N** – depending on the extent of surgical dissection
3) Post-operative Tg levels (suppressed/stimulated; Thyrogen vs. hypothyroid stimulation)
4) Diagnostic imaging findings: Diagnostic RAI scans (planar ± SPECT/CT imaging)

Avram AM. J Nucl Med. 2012 May;53(5):754-64.

RAI Scintigraphy

- completes staging and risk stratification
- guides therapeutic management decisions

➢ Diagnostic RAI scans (Dx WBS)

and/or

➢ Post-therapy RAI scans (PostRx WBS) performed with diagnostic intent

- **Identification of regional and distant metastases**
- **Tumor biology characterization**
  (the capacity of metastatic deposits to concentrate radioiodine, and their likelihood to respond to RAI therapy)

Functional Thyroid Cancer Imaging

Dx. Scans and PostRx. Scans are performed for ALL pts referred for RAI Rx.

Good Technique is essential for high quality imaging

Scans performed at [1-2 days Post-Dx] and 2-5 days **Post Rx. Whole Body (WB)** + Static planar view (Neck & Chest)

(Table speed: 5 cm /min; Static images acquired for 20 min, 256x256 matrix

Routine SPECT-CT imaging for:

- ➢ characterization of central neck activity:
  Thyroid Remnant vs. Nodal metastases
- ➢ anatomic localization of distant disease
- ➢ rapid exclusion of suspected physiologic mimics

SPECT Technique: 64 projections (20 s/stop); 128x128 matrix

Avram AM et al. J Clin Endocrinol Metab. 2013 Mar;98(3):1163-71.

Dx WBS Scans Complete Staging

Characterization of N status and M status

320 consecutive pts. (47 ± 16 yrs, range 10 – 90)

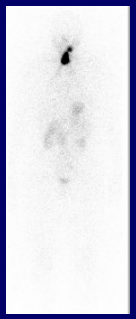
- ➢ **detected regional mets. in 35% pts.**
- ➢ **detected distant mets. in 8% pts.**

Changes TNM staging:

- ➢ **4% of young pts. (age <45 yrs)**
- ➢ **25% of older pts. (age ≥45 yrs)**

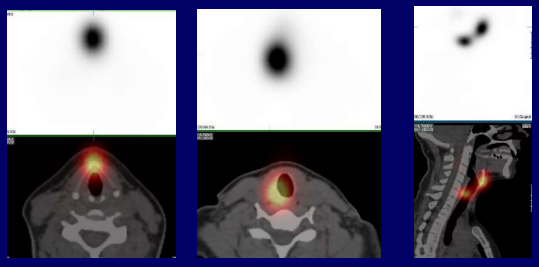
Avram AM et al. J Clin Endocrinol Metab 2013; 98(3):1163-71

34 year old woman with follicular carcinoma, well differentiated, 2.8 cm, with several foci of capsular invasion and one focus of lymphovascular invasion, margins negative.



Component Ref Range & Units	6/7/2019
Thyroglobulin (ng/mL)	1.4
Thyroglobulin Antibody <4 IU/mL	<1
Free T4 0.76 - 1.70 ng/dL	0.17 (L)
TSH 0.30 - 5.50 mIU/L	114.36 (H)
Calcium 8.6 - 10.3 mg/dL	9.4

34 year old woman with 2.8 cm FTC (one focus of lymphovascular invasion)



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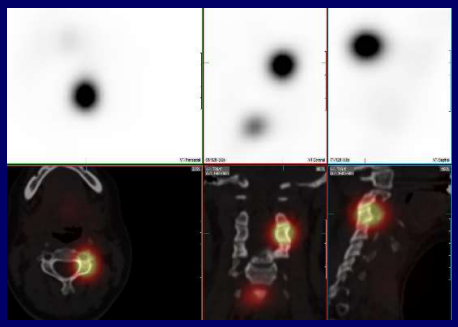


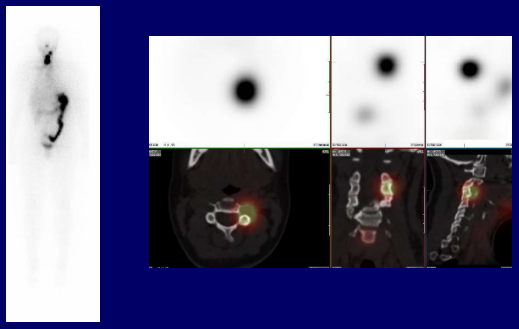
Dosimetry

- 24 hour neck iodine uptake: 4.7%
- 48 hour whole body retention: 10%

WHOLE BODY DOSIMETRY: 0.24 cGy/mCi adm activity
BLOOD DOSIMETRY: 0.38 cGy/mCi adm activity

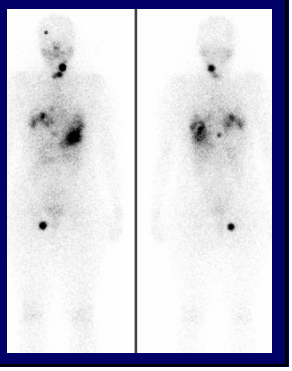
The patient was administered 370 mCi (13.7 GBq) 131-I Rx.

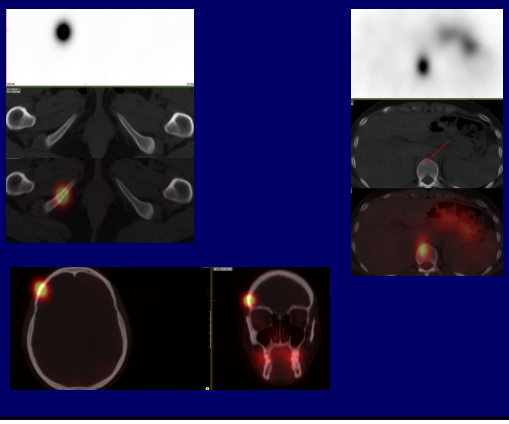
34 year old woman with 2.8 cm FTC (one focus of lymphovascular invasion) – **PostRx 370 mCi 131-I Scan**

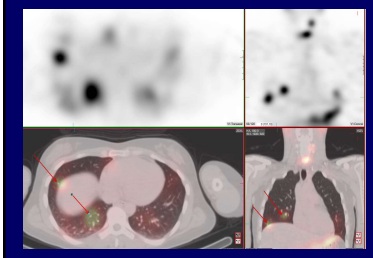


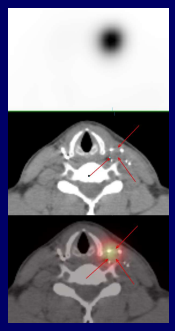
Identification of Distant Metastases lead to dosimetrically guided RAI Rx.

32 year old woman
1.8 cm follicular-variant PTC left lobe; + margins
- 15+/27 nodes central neck
- 6+/46 nodes left neck
- TSH 118 mU/L
- Tg 862 ng/mL









Dosimetry Calculations

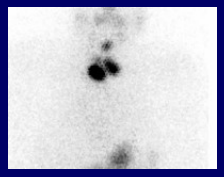
- Whole Body Dosimetry: 0.56 cGy/mCi adm. activity
- Blood Dosimetry: 0.62 cGy/mCi adm. activity

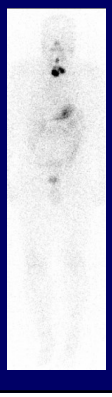
RAI Rx. 320 mCi (11.8 GBq) 131-I therapy

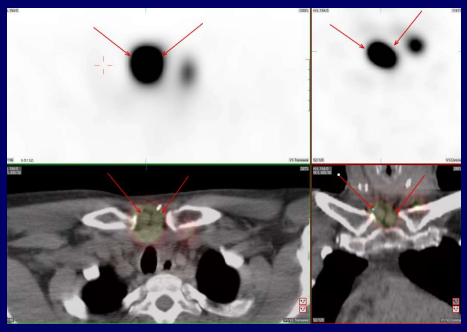
Identification of large residual nodal metastases led to surgical referral

45 year old man with 3.5 cm PTC

- 30+/58 bilateral metastatic lymph nodes:
  - central neck : N1a 17+/17
  - right neck (9+/26)
  - left neck (4+/15) N1b 13+/41
  - Total Nodes resected: 30+/58



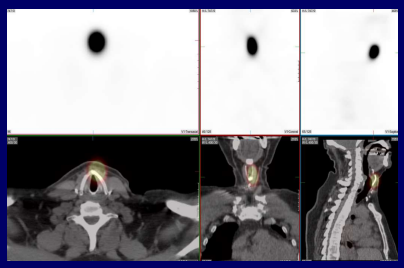




3 large residual metastatic lymph nodes (~ 1 x 1.2 cm) at the sternal notch and in the left supraclavicular area.

Surgical referral prior to 131-I therapy

Detection of non-iodine avid disease on SPECT/CT



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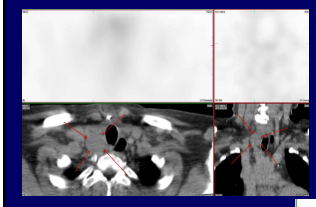
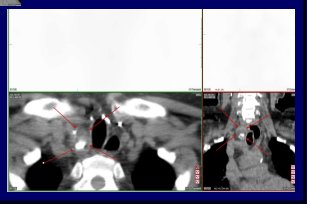


3 cm cystic lesion with internal calcifications in the right thyroid bed

US-guided FNA:

- Non-diagnostic, acellular
- Aspirated fluid contained
- Tg >300 ng/mL



Dx RAI Scans Complete Risk Stratification

Univ. of Michigan experience in 320 patients

Risk Stratification performed by **Endocrinologist** before and after information from pre-ablation scans was made available:

- **15% pts.** (48/320) changed risk stratification after imaging information on nodal and distant metastatic status

- **Management changed in 31% pts. (99/320 pts)**

Avram AM et al. J Clin Endocrinol Metab 2015 May;100(5):1895-902

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