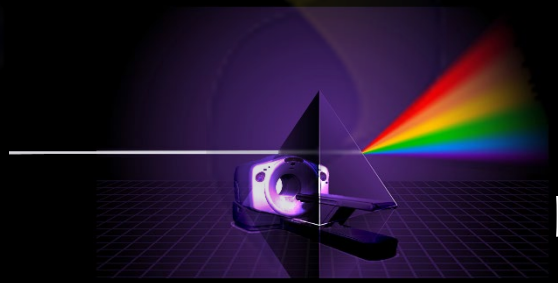
5TH ANNUAL Miami Thyroid Oncology Symposium

March 18-19 2022



Post thyroidectomy RAI imaging and Ablation

Seza Gulec

March 18, 2022

RAI Ablation

- Surgical total thyroidectomy (even meticulous extracapsular technique by expert surgeons) is never complete in the most strict sense. “Beta-knife” completes total thyroidectomy!
- Remnant ablation refers to the use of I-131 to destroy post-operatively residual benign thyroid tissue to facilitate initial staging and follow-up studies
  - Thyroglobulin
    - Improves specificity of Tg as a tumor marker
    - Sensitivity is dependent on tumor differentiation/TSH/TgAb
  - RAI Imaging
    - Clears atypical and ambiguous findings, facilitates f/u image interpretations
    - Improves sensitivity for EOD evaluation for RAI-avid disease
  - Ultrasound

RAI Ablation

- Ablation activity debate is not resolved (30mCi vs 100+mCi)
  - Mallick ,2012,NEJM and Schlumberger,2012,NEJM: non-inferiority of 30mCi
  - Historical retrospective reports with mixed results
  - Remnant activity determination has nothing to do with risk stratification
    - Activity is linked to dose. Dose is linked to remnant volume and kinetics
- Ablation success is dependent on absorbed dose (D [Rads] = Ã x S)
  - Goolden,1962: 50K | Hurley & Becker: 1982: 100K | Maxon 1992: 30K
    - Remnant volume and kinetics are highly variable
    - Remnant volume determination is imprecise. An error of ∓ 0.5g changes the estimate by 100%
    - Remnant volumes are inconsistent, particularly in community settings
    - Remnant RAI clearance is under-appreciated, typically not determined
- Low-activity ablation equivalency (non-inferiority) is due to the relatively consistent remnant volume in academic centers

100mCi is better

An Analysis of "Ablation of Thyroid Remnants" with I-131 in 511 Patients from 1947–1984: Experience at University of Michigan

William H. Beierwaltes, Roya Rabbani, Carl Dmuchowski, Ricardo V. Lloyd, Patti Eyre, and Shirley Mallette

University of Michigan Medical Center, Ann Arbor, Michigan

Between January 1947 and June 1983, 511 patients were given treatment doses of I-131 after surgery for thyroid cancer in the presence of I-131 uptake in thyroid remnants. Thirty-four patients were removed from the study leaving 462 patients with a 99% follow-up at 1 or more yr, with a mean follow-up of 15 yr. Of 267 patients with radioiodine uptake confined to the thyroid bed, 233 (87%) had ablation from the first dose of I-131 ranging from 100 to >200 mCi. The higher the percent uptake, the more difficult it was to achieve ablation. In the percentages of successful ablation, there were no significant differences between I-131 doses of: 100–149 mCi, 150–174 mCi, 179–199 mCi, and 200 mCi or more. The 100–149 mCi ablative dose may furnish "adjuvant" therapy for occult metastases.

J Nucl Med 25: 1287–1293, 1984

The original advocates of the use of 29.9 mCi of I-131 to ablate uptake in normal thyroid-gland remnants from a normal thyroid gland after surgical thyroidectomy, for treatment of well-differentiated thyroid cancer, believed that this dose would ablate the uptake in a normal remnant (*1*). Presumably, therefore, the 39% of their patients whose remnant was not ablated with 29.9 mCi and who required an additional 100-mCi dose later had thyroid cancer in a remnant previously judged "normal."

than normal thyroid tissues. Wollman found that the most active I-131-concentrating thyroid cancer contained <40% of the I-131 concentration in normal thyroid tissue in the same individual (*4*).

Data are lacking relating the following parameters to the success rate in "ablating" the uptake in the remnant, as followed up to 37 yr: the sex and age of the patient, the dose range for the first "ablating" dose, the number of doses, the total administered dose, or the presence or absence of known metastases before or after treatment.

29mCi is not inferior to 100mCi

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ablation with Low-Dose Radioiodine and Thyrotropin Alfa in Thyroid Cancer

Ujjal Mallick, F.R.C.R., Clive Harmer, F.R.C.P., Beng Yap, F.R.C.P., Jonathan Wadsley, F.R.C.R., Susan Clarke, F.R.C.P., Laura Moss, F.R.C.P., Alice Nicol, Ph.D., Penelope M. Clark, F.R.C.Path., Kate Farnell, R.C.N., Ralph McCready, D.Sc., James Smellie, M.D., Jayne A. Franklyn, F.Med.Sci., Rhys John, F.R.C.Path., Christopher M. Nutting, M.D., Kate Newbold, F.R.C.R., Catherine Lemon, F.R.C.R., Georgina Gerrard, F.R.C.R., Abdel Abdel-Hamid, F.R.C.R., John Hardman, F.R.C.R., Elena Macias, M.D., Tom Roques, F.R.C.R., Stephen Whitaker, M.D., Rengarajan Vijayan, F.R.C.R., Pablo Alvarez, M.Sc., Sandy Beare, Ph.D., Sharon Forsyth, B.Sc., Latha Kadalayil, Ph.D., and Allan Hackshaw, M.Sc.

CONCLUSIONS

Low-dose radioiodine plus thyrotropin alfa was as effective as high-dose radioiodine, with a lower rate of adverse events. (Funded by Cancer Research UK; ClinicalTrials.gov number, NCT00415233.)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

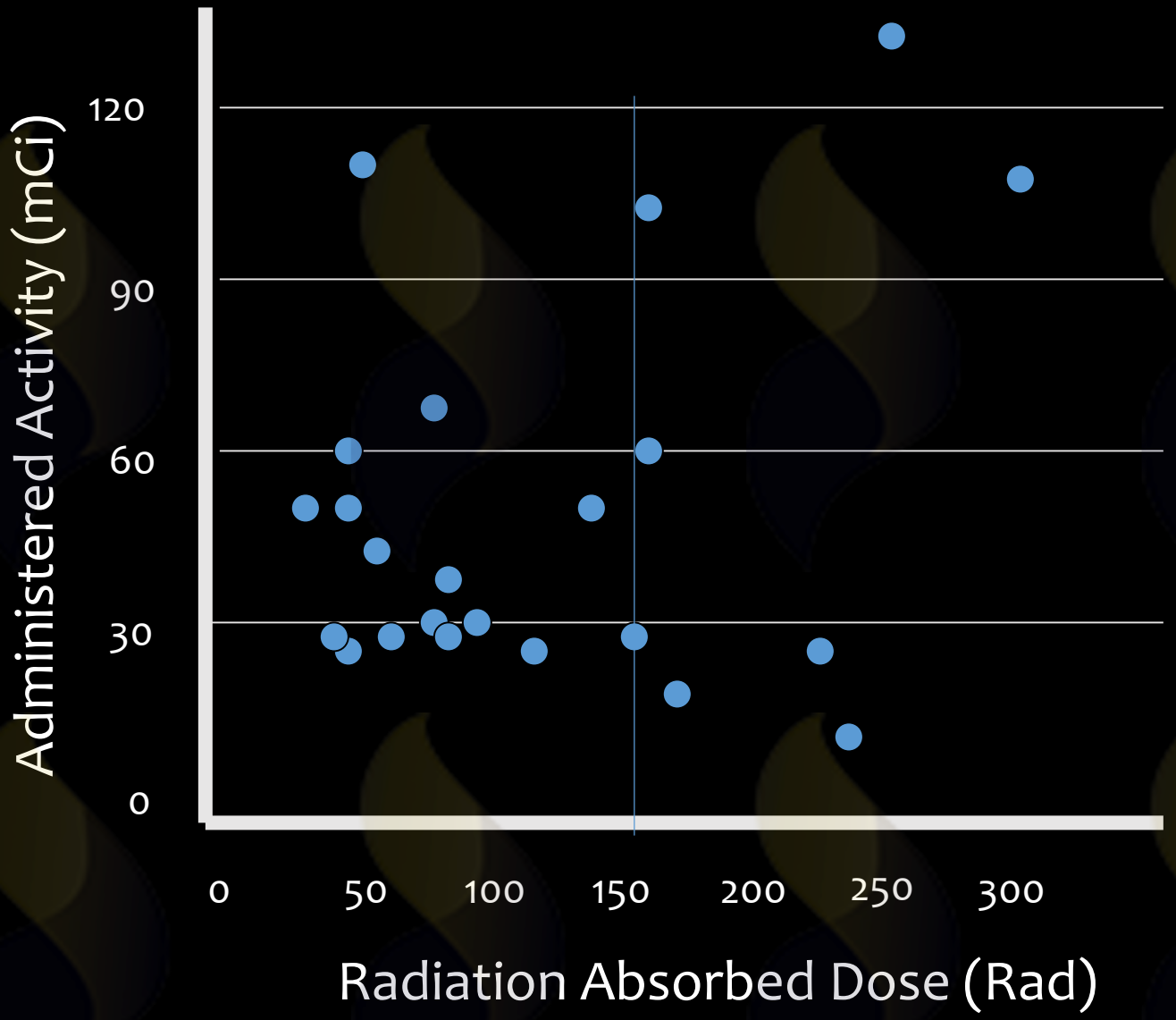
Strategies of Radioiodine Ablation in Patients with Low-Risk Thyroid Cancer

Martin Schlumberger, M.D., Bogdan Catargi, M.D., Ph.D., Isabelle Borget, Pharm.D., Ph.D., Désirée Deandreis, M.D., Slimane Zerdoud, M.D., Boumédiène Bridji, M.D., Ph.D., Stéphane Bardet, M.D., Laurence Leenhardt, M.D., Ph.D., Delphine Bastie, M.D., Claire Schvartz, M.D., Pierre Vera, M.D., Ph.D., Olivier Morel, M.D., Danielle Benisvy, M.D., Claire Bournaud, M.D., Françoise Bonichon, M.D., Catherine Dejax, M.D., Marie-Elisabeth Toubert, M.D., Sophie Leboulleux, M.D., Marcel Ricard, Ph.D., and Ellen Benhamou, M.D., for the Tumeurs de la Thyroïde Refractaires Network for the Essai Stimulation Ablation Equivalence Trial*

CONCLUSIONS

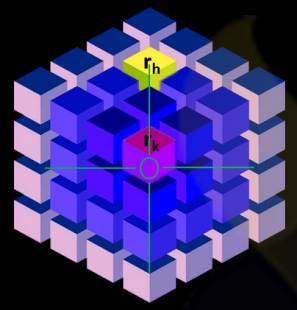
The use of recombinant human thyrotropin and low-dose (1.1 GBq) postoperative radioiodine ablation may be sufficient for the management of low-risk thyroid cancer. (Funded by the French National Cancer Institute [INCa] and the French Ministry of Health; ClinicalTrials.gov number, NCT00435851; INCa number, RECF0447.)

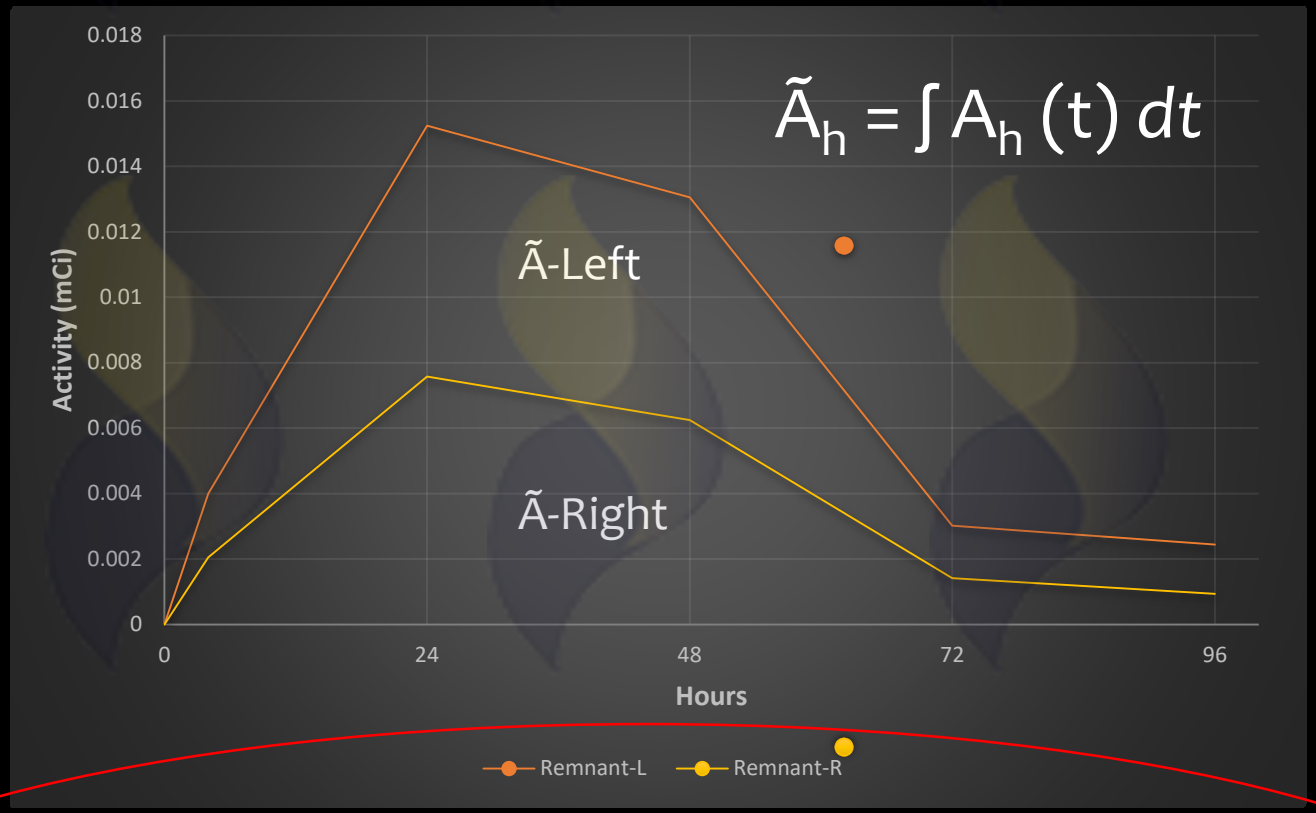
A categorical objection to the “low dose” vs “high Dose” reference



Remnant volumes and kinetics in a multi-institutional community setting

$$D = \tilde{A} \times S$$



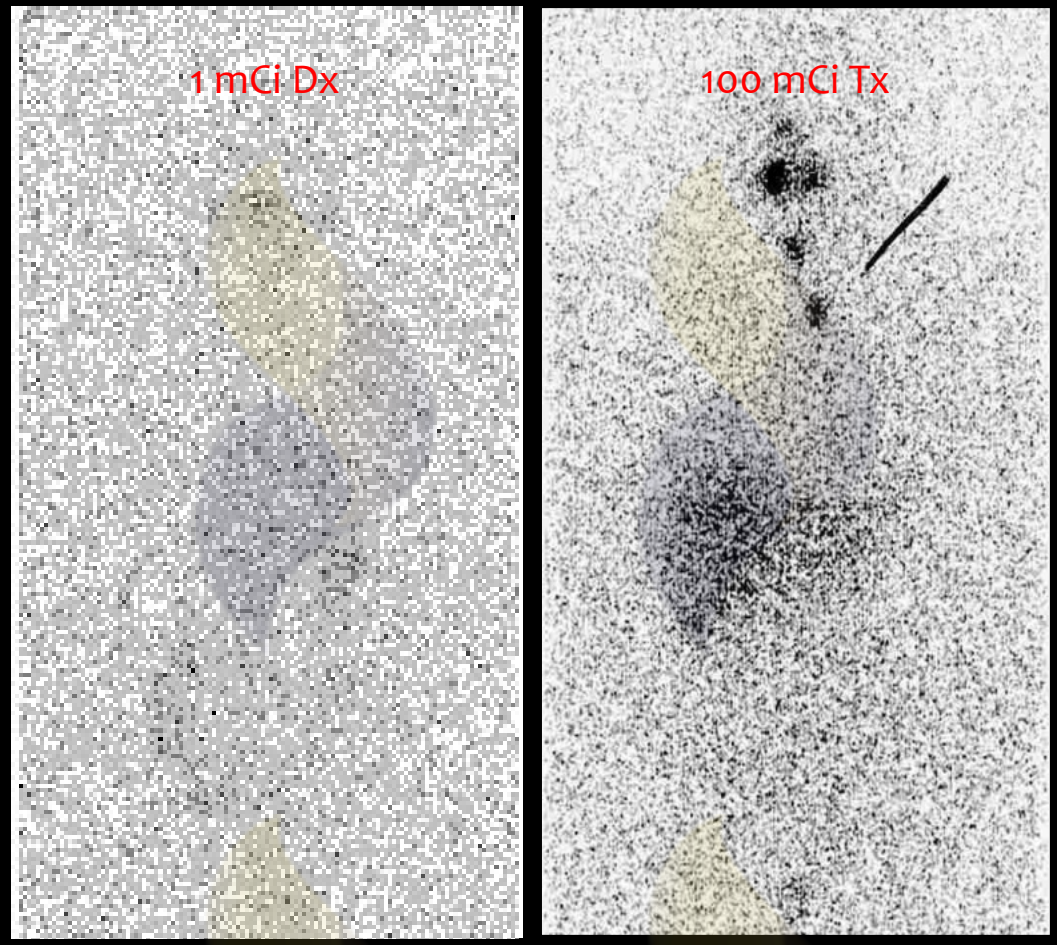


	Minimum	Maximum
Maximum Total Remnant Activity (μCi)	1.2	215.9
Functional Total Remnant Volume (ml)	1	60
Activity per ml Total Remnant Volume (μCi/ml)	0.036	11.265
Total Remnant Cumulated Activity (μCi-hr)	68	12757.3

RAI Ablation Rationale and Recommendations

- No RAI ablation has been advocated in low-risk patients
  - RAI ablation is indicated when total thyroidectomy is intended
  - Surgical total thyroidectomy is complete only with RAI ablation
  - It is total or not total!
- 29mCi activity has been advocated in low risk patient
  - Risk category has no bearing on activity determination
  - It is to ablate or not to ablate
- When a preoperative decision to perform a total thyroidectomy, RAI ablation should be performed for a complete thyroidectomy

Pre-ablation RAI imaging, I-131

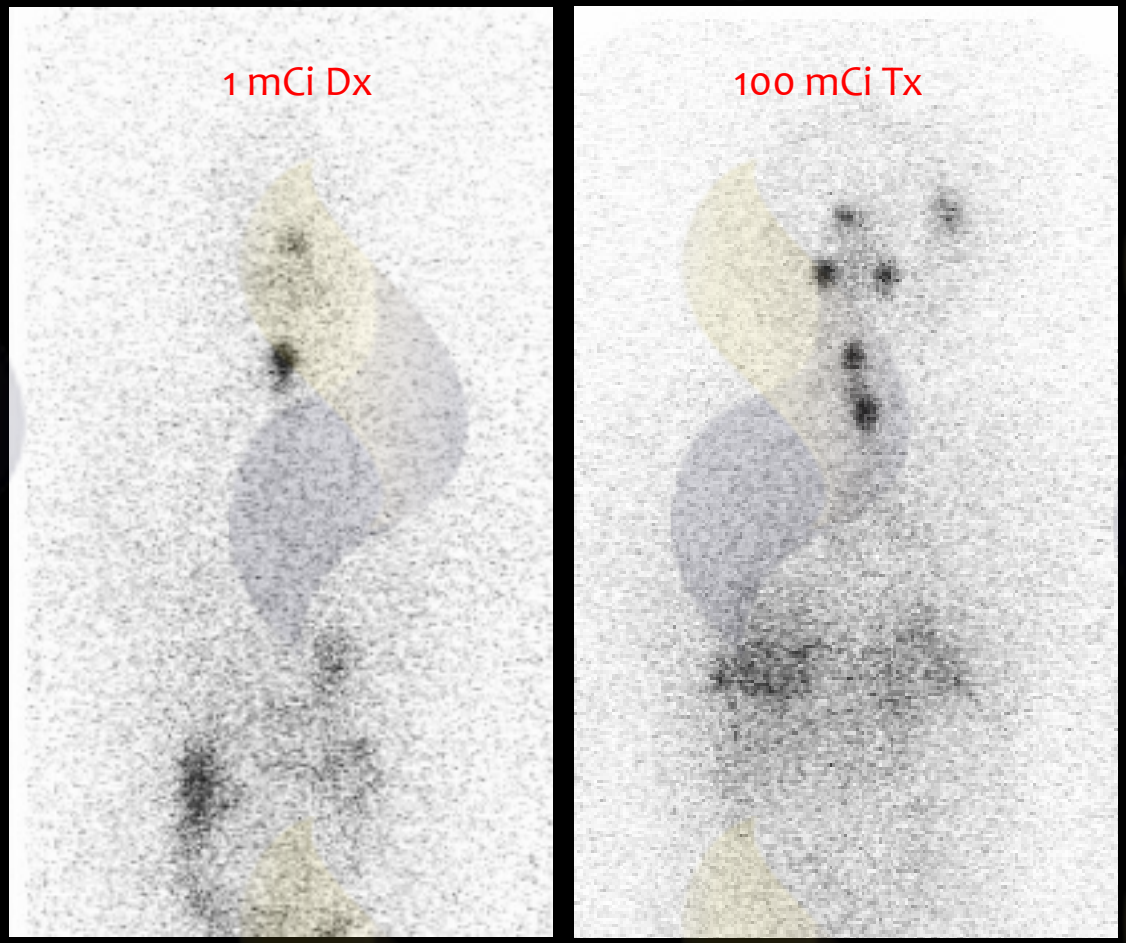


Pre-ablation diagnostic RAI imaging is **sub-theranostic**

More so with BRAF-like tumors which have nodal metastases

Small-volume nodal disease is below the detection sensitivity

Pre-ablation RAI imaging, I-131



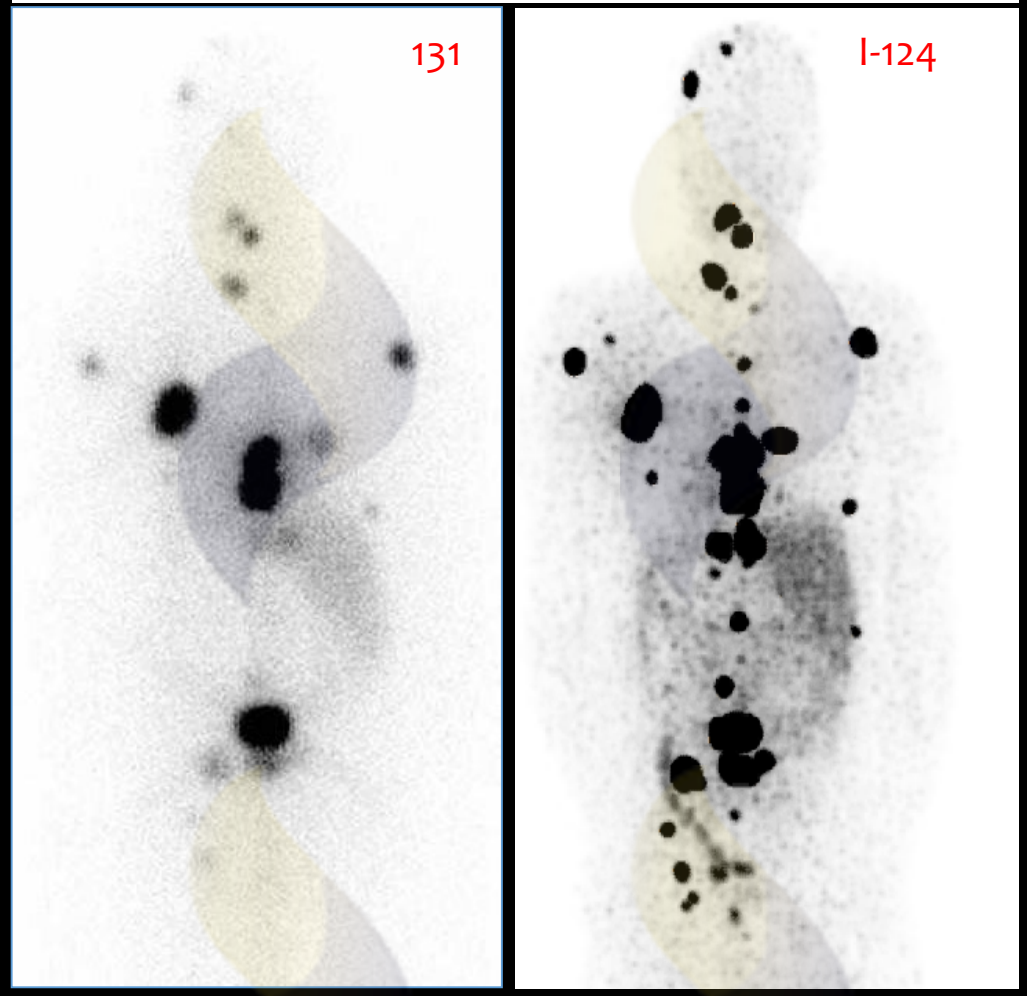
Pre-ablation diagnostic RAI imaging is **sub-theranostic**

More so with BRAF-like tumors which have nodal metastases

Small-volume nodal disease is below the detection sensitivity

Pre-ablation RAI imaging, I-124

Van Nostrand D et al. **Thyroid.** 2010; 20(8): 879-83



Improved detection sensitivity

Improved spatial resolution

Pre-ablation RAI imaging, I-124

Gulec S et al. Thyroid. 2016 Mar;26(3):441-8

Improved detection sensitivity

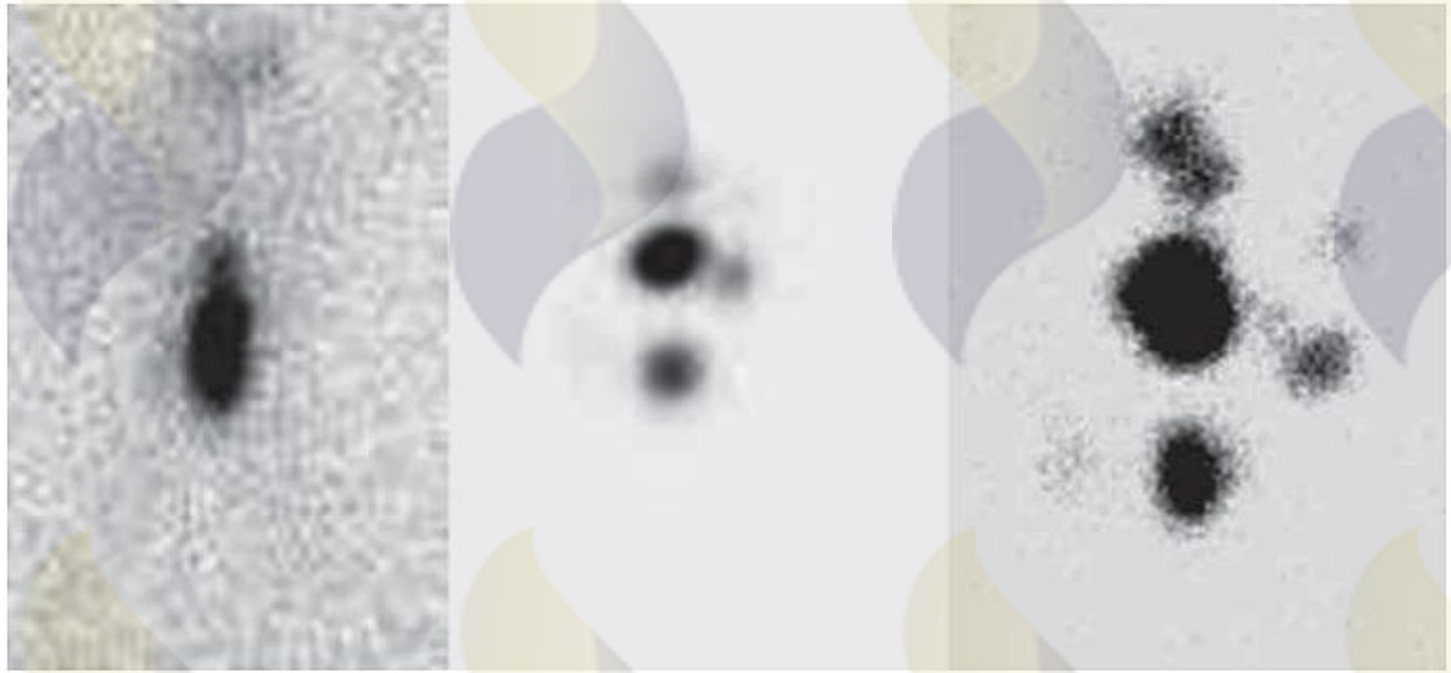
Improved spatial resolution

Potential challenge in diagnostic accuracy

Optimizing Theranostic Technique

Radioiodine Imaging for Differentiated Thyroid Cancer: Not All Radioiodine Images Are Performed Equally

Van Nostrand THYROID 2019; 29 (7): 901

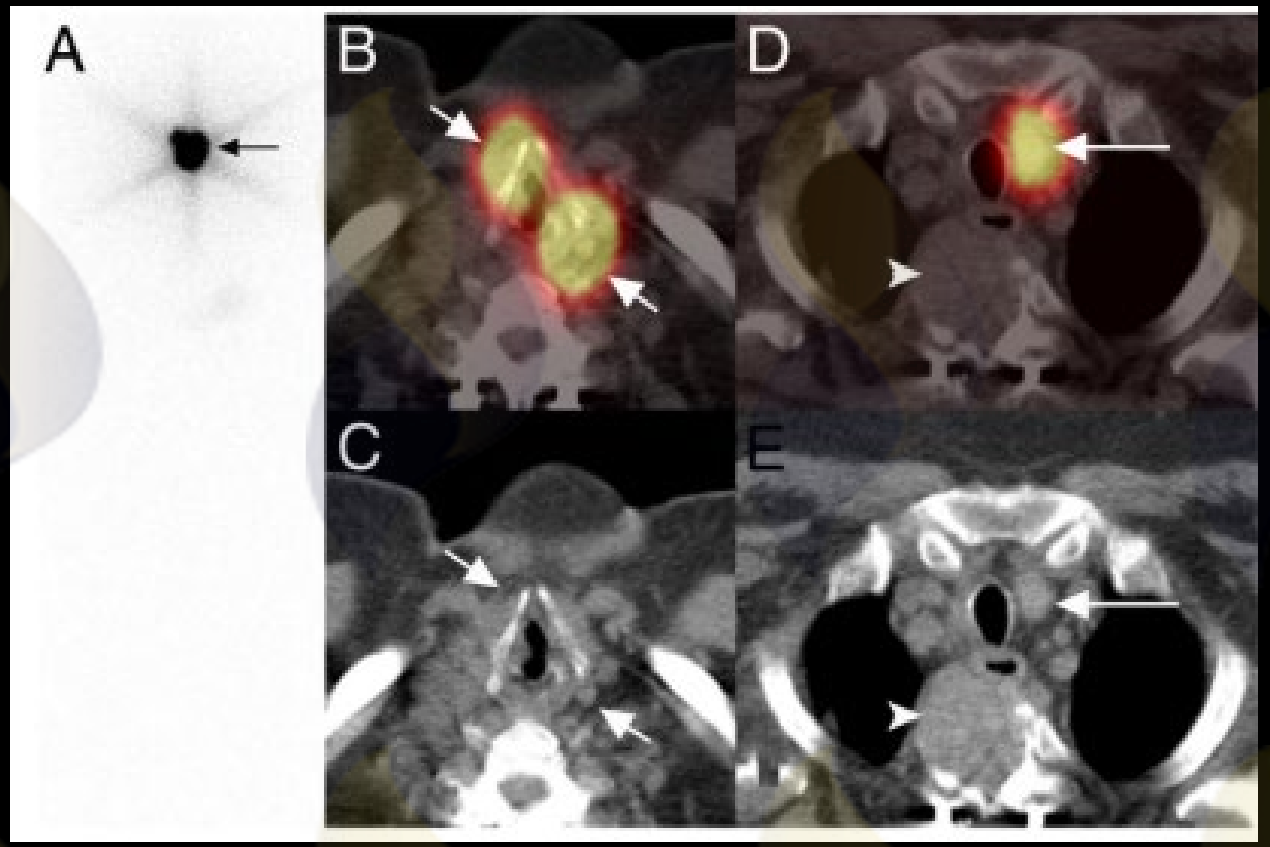


Spatial resolution may or may not improve specificity

Not all the areas of paramedian focal uptake are nodal metastases

Pre-ablation RAI imaging, I-131 SPECT/CT

Avram A et al. J Clin Endocrinol Metab, March 2013, 98(3):1163–1171

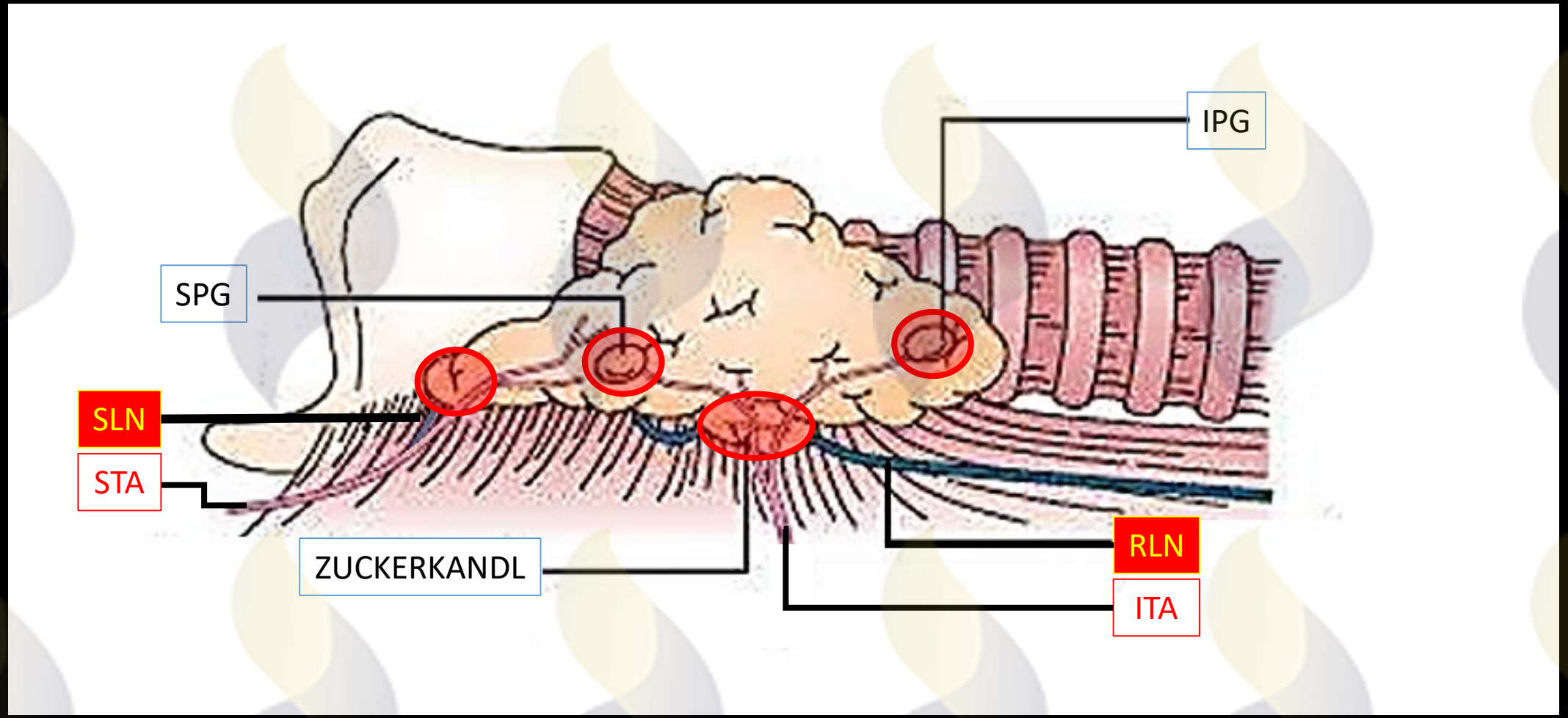


Improved detection sensitivity

Improved spatial resolution

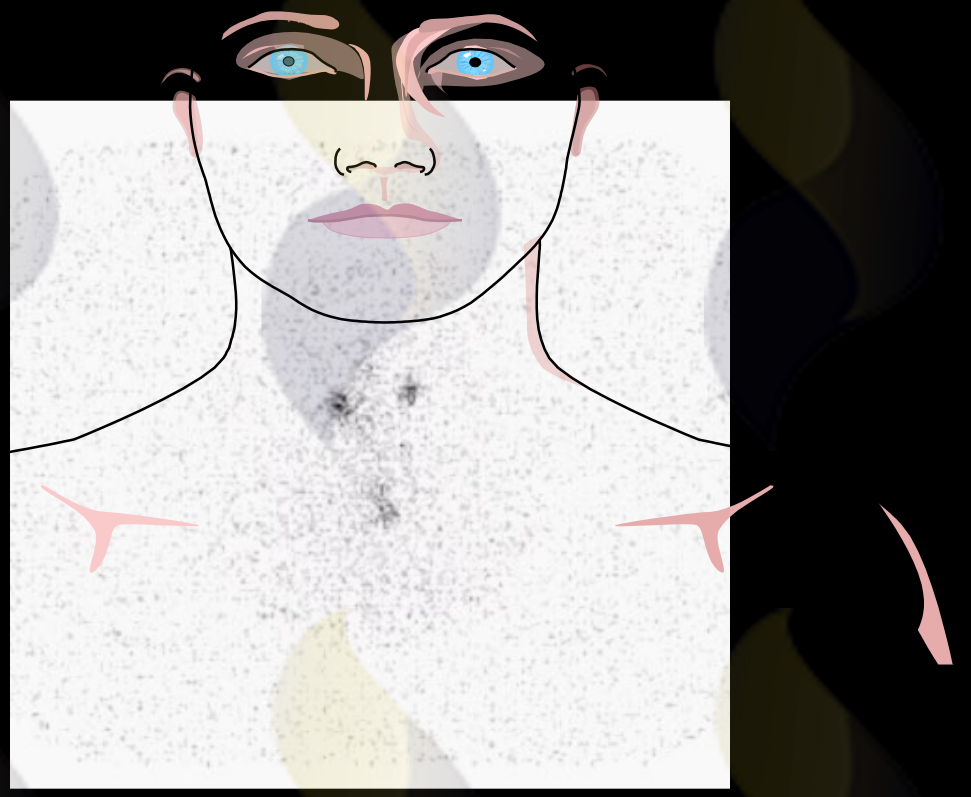
Potential challenge in diagnostic accuracy

Critical surgical anatomy



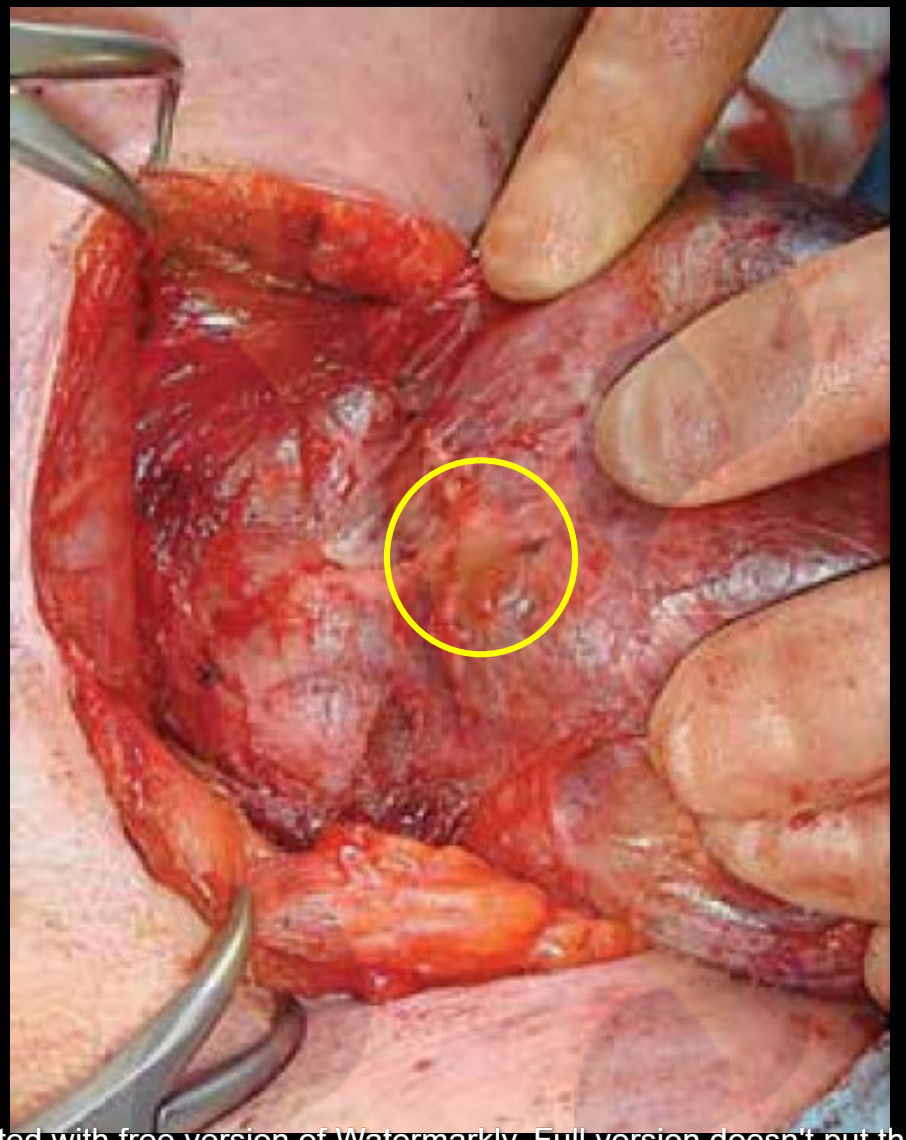
Nuclear surgical anatomy

Upper pole



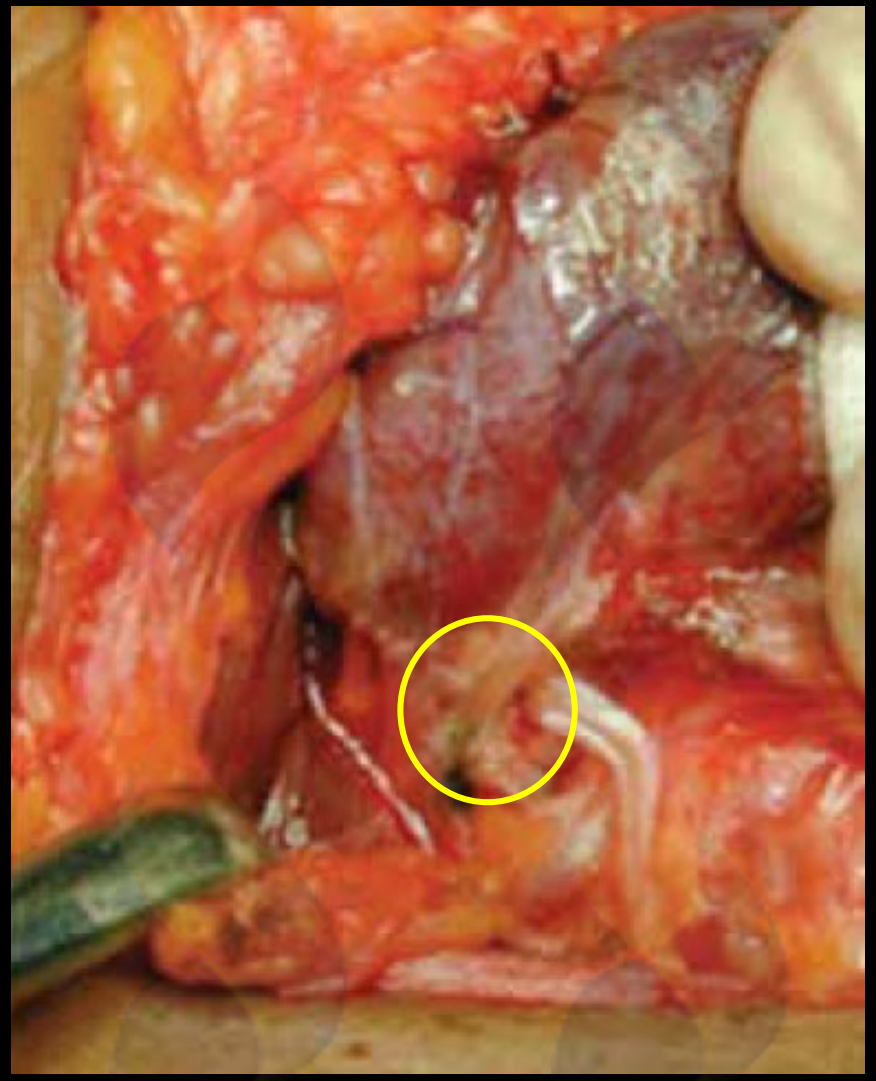
Critical surgical anatomy

Parathyroids



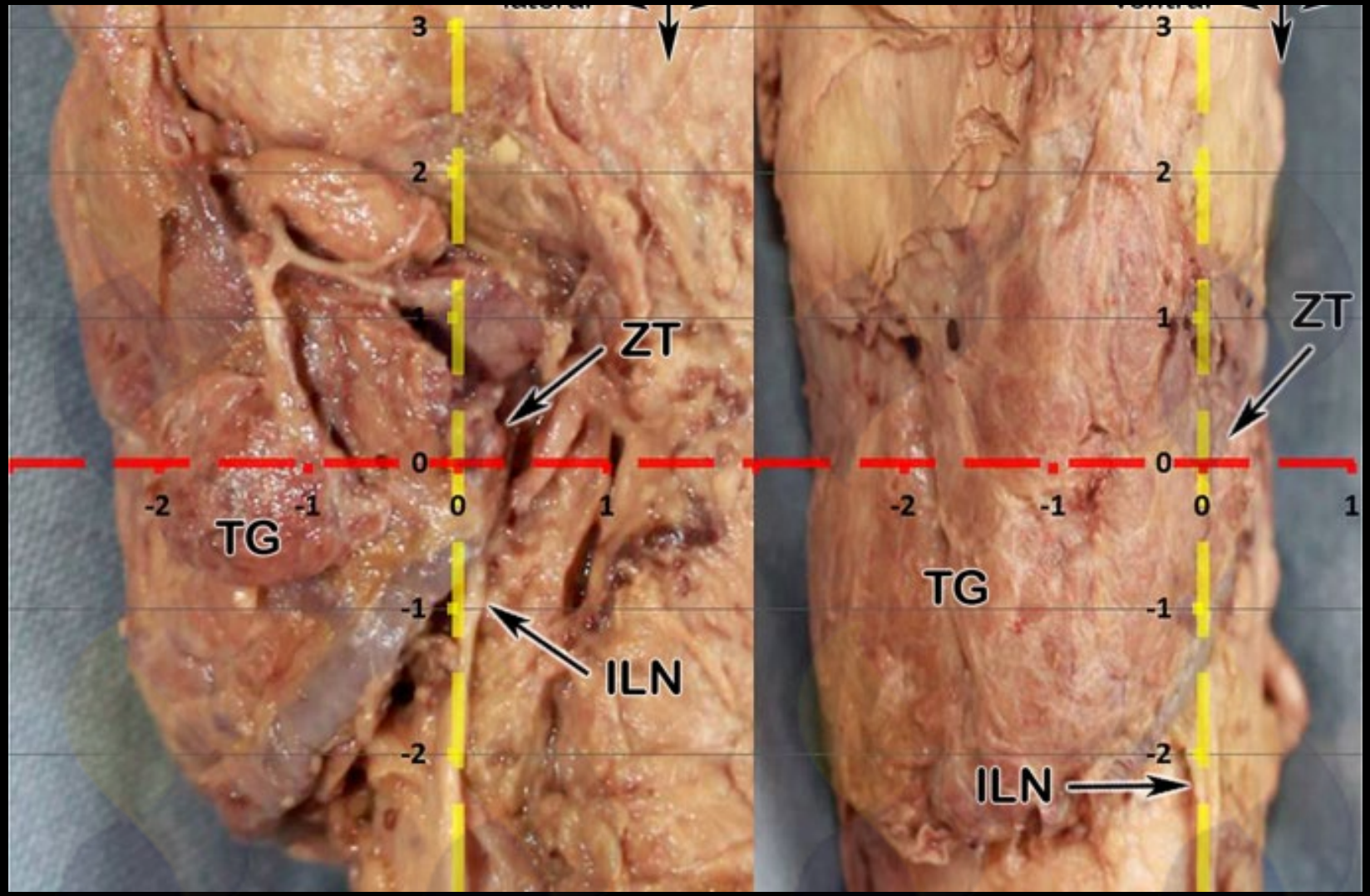
Critical surgical anatomy

Ligament of Berry



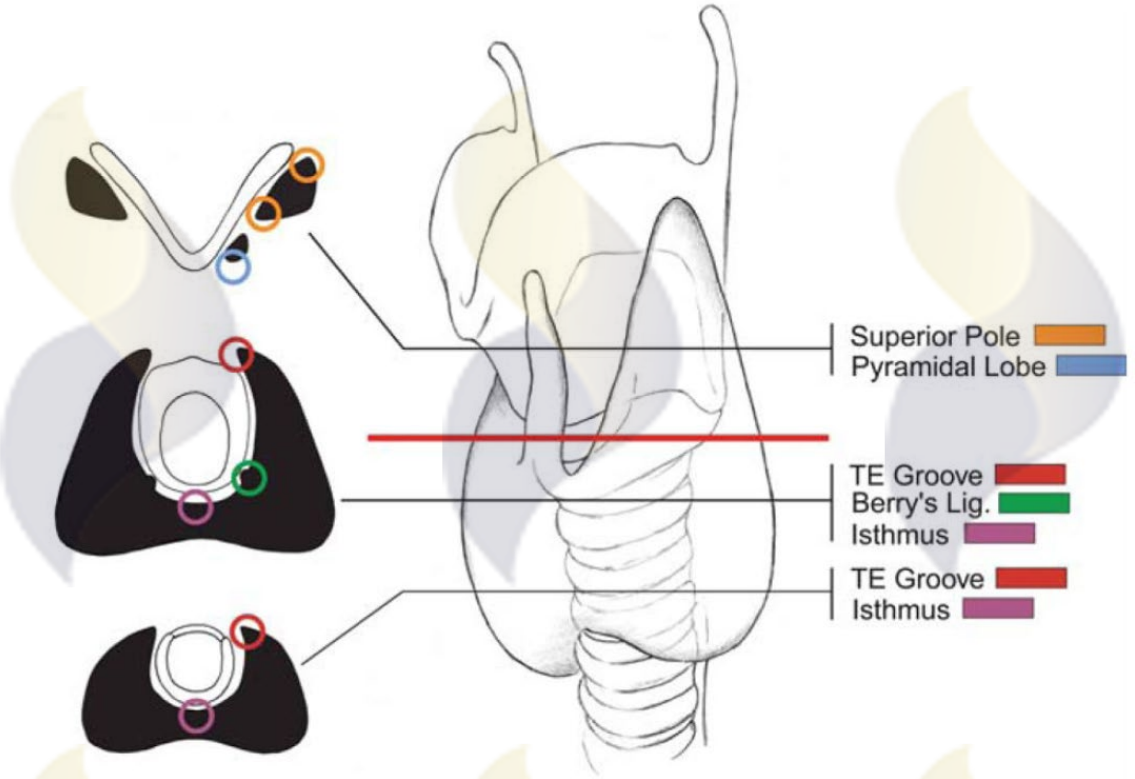
Critical surgical anatomy

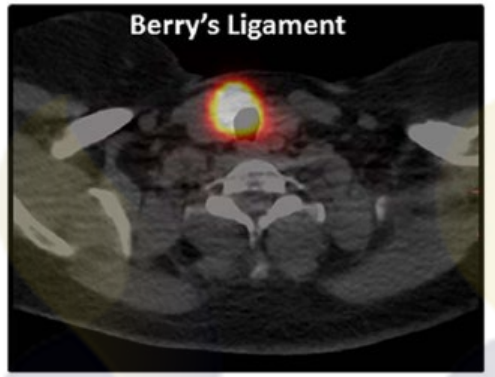
Zuckerkandl Tubercle

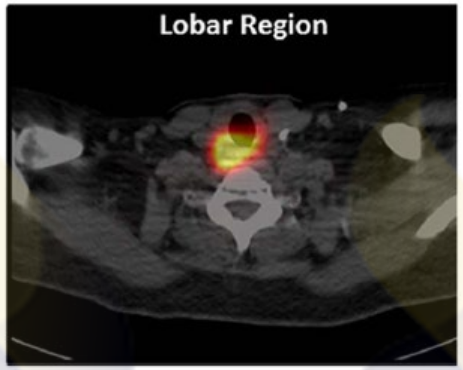


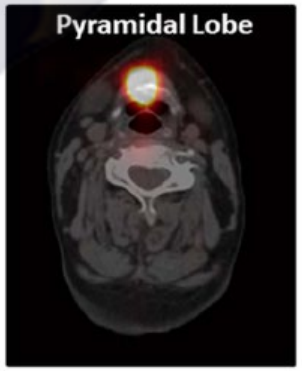
Nuclear surgical anatomy, I-131 SPECT/CT

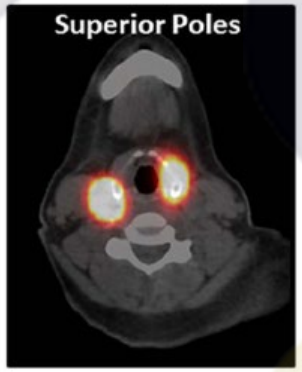
141 DTC patients with total thyroidectomy MSKCC, MGH/Harvard











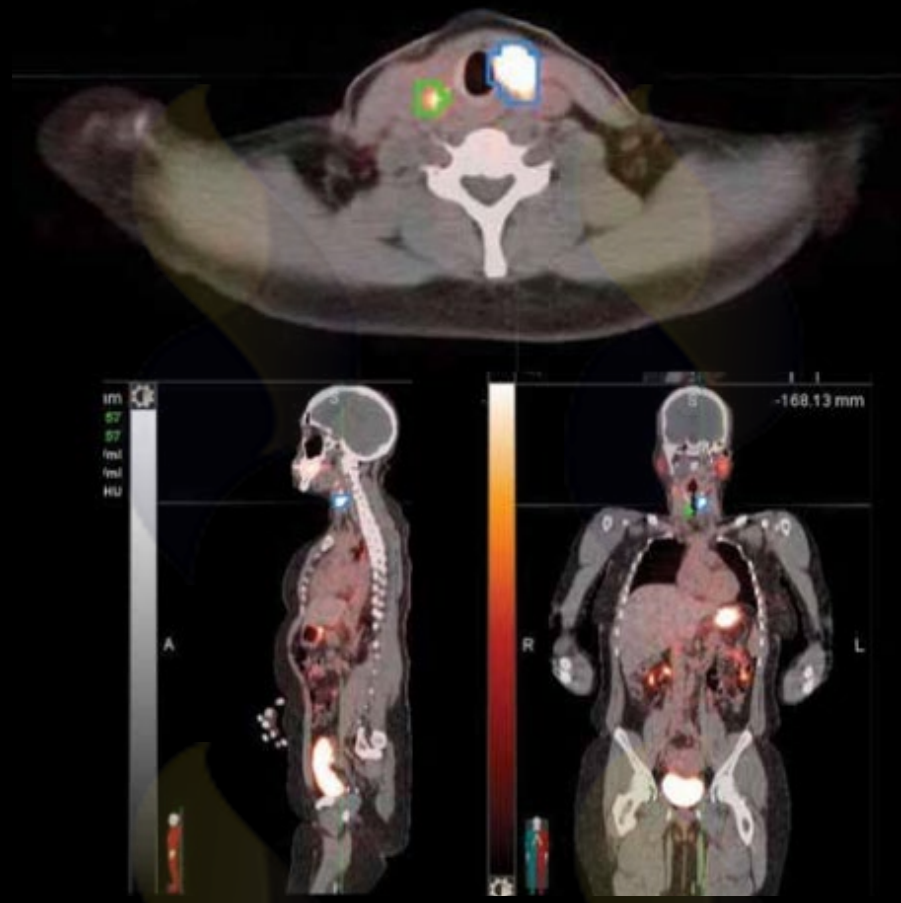
Median 24h neck uptake 0.3%

Remnant uptake: 93% diagnostic planar imaging, 99% post-treatment SPECT/CT

Ligament of Berry:87%, Superior pole(s): 79%, Paratracheal: 67%, Isthmus: 54%, Pyramidal lobe: 46%

Zeuren R et al. Laryngoscope 2015; 125: 2417

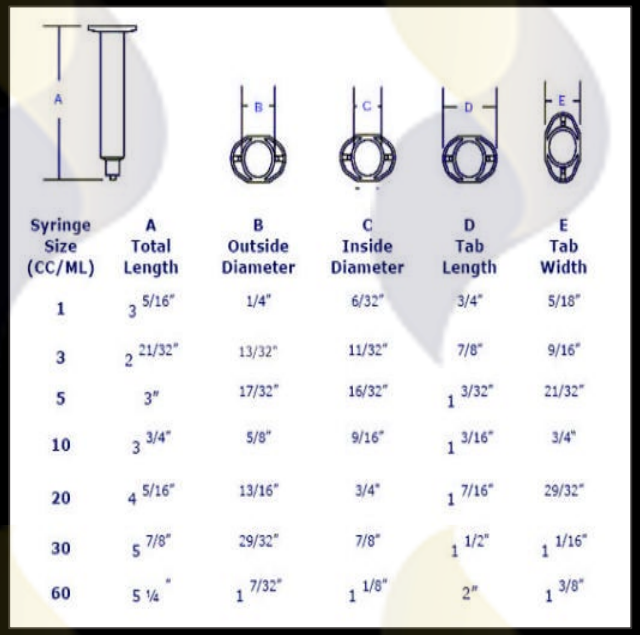
Nuclear surgical anatomy, I-124 PET/CT



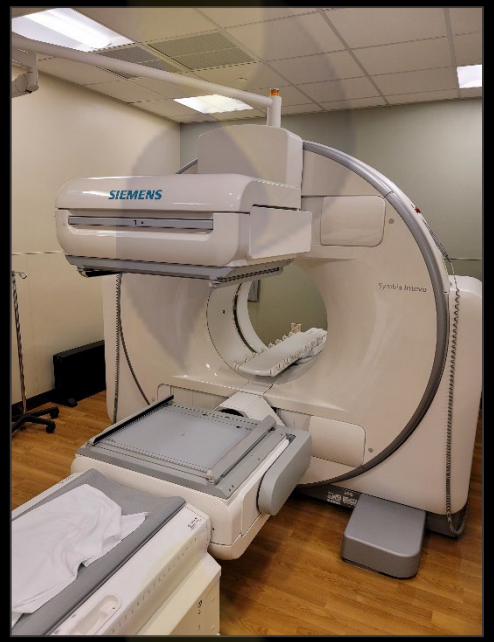
Gulec et al. Mol Imaging Radionucl Ther 2017; 26: 16-23

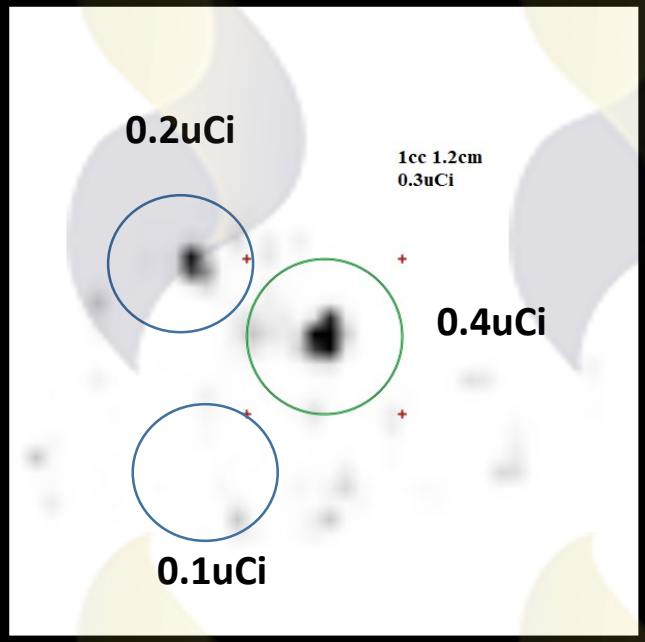
Minimal Detectable Activity [Best Case Scenario]

Modeling based on 1mCi activity distribution in remnant tissue and malignant tissues
No soft tissue background, Minimum attenuation



Syringe Size (CC/ML)	A Total Length	B Outside Diameter	C Inside Diameter	D Tab Length	E Tab Width
1	3 5/16"	1/4"	6/32"	3/4"	5/18"
3	2 21/32"	13/32"	11/32"	7/8"	9/16"
5	3"	17/32"	16/32"	1 3/32"	21/32"
10	3 3/4"	5/8"	9/16"	1 3/16"	3/4"
20	4 5/16"	13/16"	3/4"	1 7/16"	29/32"
30	5 7/8"	29/32"	7/8"	1 1/2"	1 1/16"
60	5 ¼"	1 7/32"	1 1/8"	2"	1 3/8"





Minimum Detectable Activity
0.15uCi

Theranostic Power-Dependent Minimal Detectable Size by SPECT/CT

Minimal Detectable Activity

Modeling based on 1mCi activity distribution in remnant tissue and malignant tissues
No soft tissue background, Minimum attenuation

Target diameter (cm)	Activity (µCi), TP-100 Remnant	Activity (µCi), TP-040 RAS-like node met	Activity (µCi), TP-003 BRAF-like node met
0.3cm	0.14	0.06	0.004
0.4cm	0.34	0.13	0.01
0.5cm	0.65	0.26	0.02
0.8cm	2.68	1.07	0.08
1.0cm	5.24	2.09	0.16
1.2cm	9.05	3.62	0.27
1.5cm	17.67	7.07	0.53
1.6cm	21.45	8.58	0.64

Theranostic Power-Dependent Minimal Detectable Size by SPECT/CT

Pre-ablation | Post-ablation RAI imaging

- Clinical value of Pre-ablation RAI imaging is limited
  - Low theranostic power
    - Attenuated RAI avidity | RAI indifference
    - More so with BRAF-like tumors which have nodal metastases
    - Small-volume nodal disease is below the detection sensitivity
  - Focal remnants can be misinterpreted for nodal disease
    - False upstaging
  - Logistical issues if rhTSH is used
- Post-ablation imaging is an absolute!

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thyroidectomy without Radioiodine in Patients with Low-Risk Thyroid Cancer

S. Leboulleux, C. Bournaud, C.N. Chougnet, S. Zerdoud, A. Al Ghuzlan, B. Catargi, C. Do Cao, A. Kelly, M.-L. Barge, L. Lacroix, I. Dygai, P. Vera, D. Rusu, O. Schneegans, D. Benisvy, M. Klein, J. Roux, M.-C. Eberle, D. Bastie, C. Nascimento, A.-L. Giraudet, N. Le Moullec, S. Bardet, D. Drui, N. Roudaut, Y. Godbert, O. Morel, A. Drutel, L. Lamartina, C. Schvartz, F.-L. Velayoudom, M.-J. Schlumberger, L. Leenhardt, and I. Borget

CONCLUSIONS

In patients with low-risk thyroid cancer undergoing thyroidectomy, a follow-up strategy that did not involve the use of radioiodine was noninferior to an ablation strategy with radioiodine regarding the occurrence of functional, structural, and biologic events at 3 years. (Funded by the French National Cancer Institute; ESTIMABL2 ClinicalTrials.gov number, NCT01837745.)

The Evolving Role of ^{131}I for the Treatment of Differentiated Thyroid Carcinoma

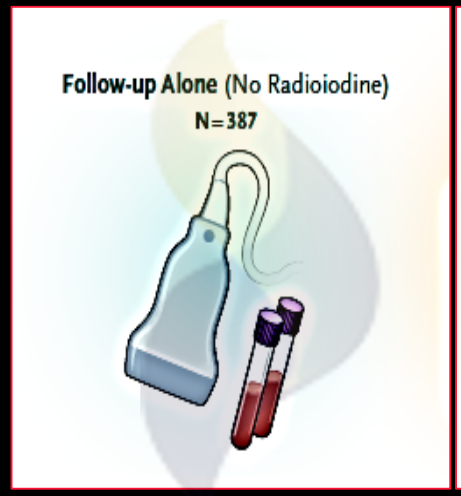
Richard J. Robbins, MD[1]; and Martin J. Schlumberger, MD[2]

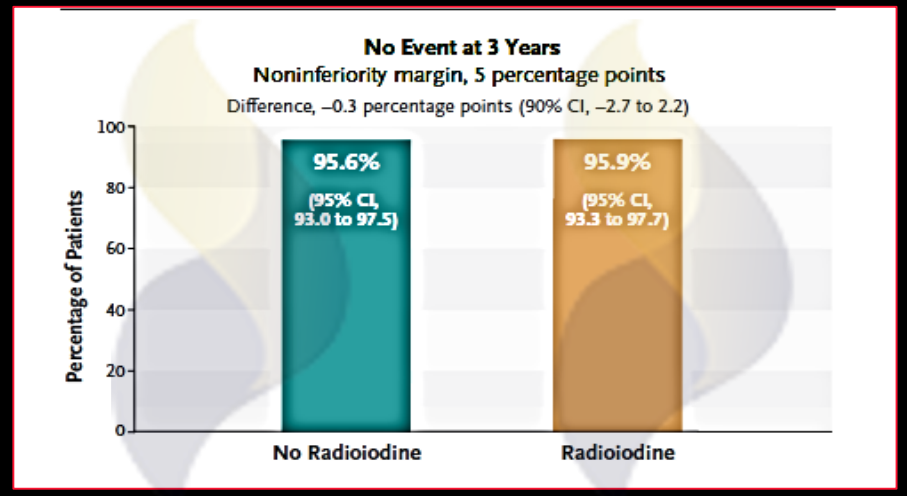
[1]*Endocrine Service, Division of General Medicine, Department of Medicine, Memorial Sloan–Kettering Cancer Center, New York, New York; and* [2]*Service de Medecine Nucleaire, Institut Gustave Roussy, Villejuif, France*

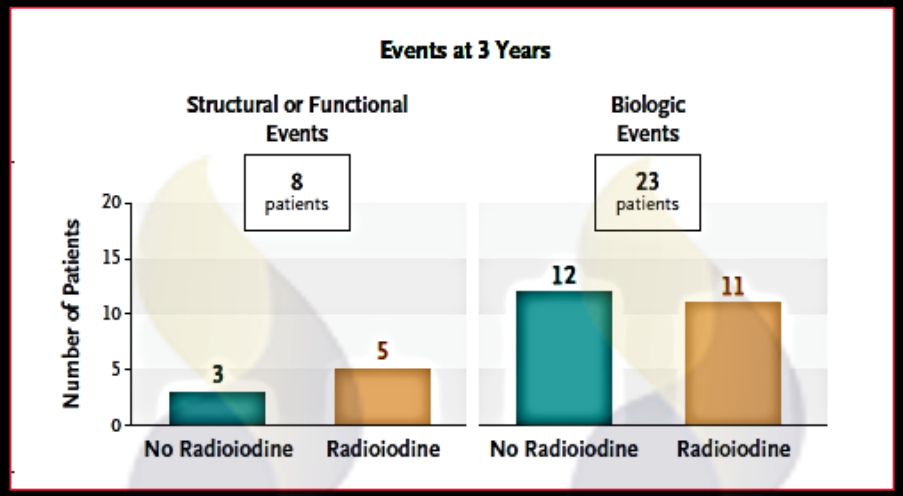
survival was examined. Although they found cohort studies to be inconsistently designed, in pooled analyses the evidence did support the reduction of relative risk of local and distant metastases (*36*). The studies were somewhat biased, however, in risk stratification, so that patients at higher risk were more likely to have had RRA. Only one study, which followed a cohort for more than 30 y, found that RRA resulted in a significant reduction in mortality (*37*). A comparison with similar patients treated at the Mayo Clinic suggested that these benefits may reflect differences in completeness of surgical excision (*38*). It appears that there is less need for RRA in low-risk patients who have had a

In general, we suggest that RRA can be omitted in low-risk patients who have well-differentiated solitary carcinomas <1.5 cm in greatest diameter without lymph node involvement and who have undergone a complete resection of the tumor. We recommend RRA for any individual with a carcinoma >1.5 cm or with a thyroid carcinoma of any size with obvious lymph node involvement, extrathyroidal extension, or multicentricity. We also recommend RRA for all individuals who have undergone incomplete surgical resection. All individuals who have RRA should have a whole-body scan after therapy to screen for unexpected metastatic lesions.

Thyroidectomy without Radioiodine in Patients with Low-Risk Thyroid Cancer







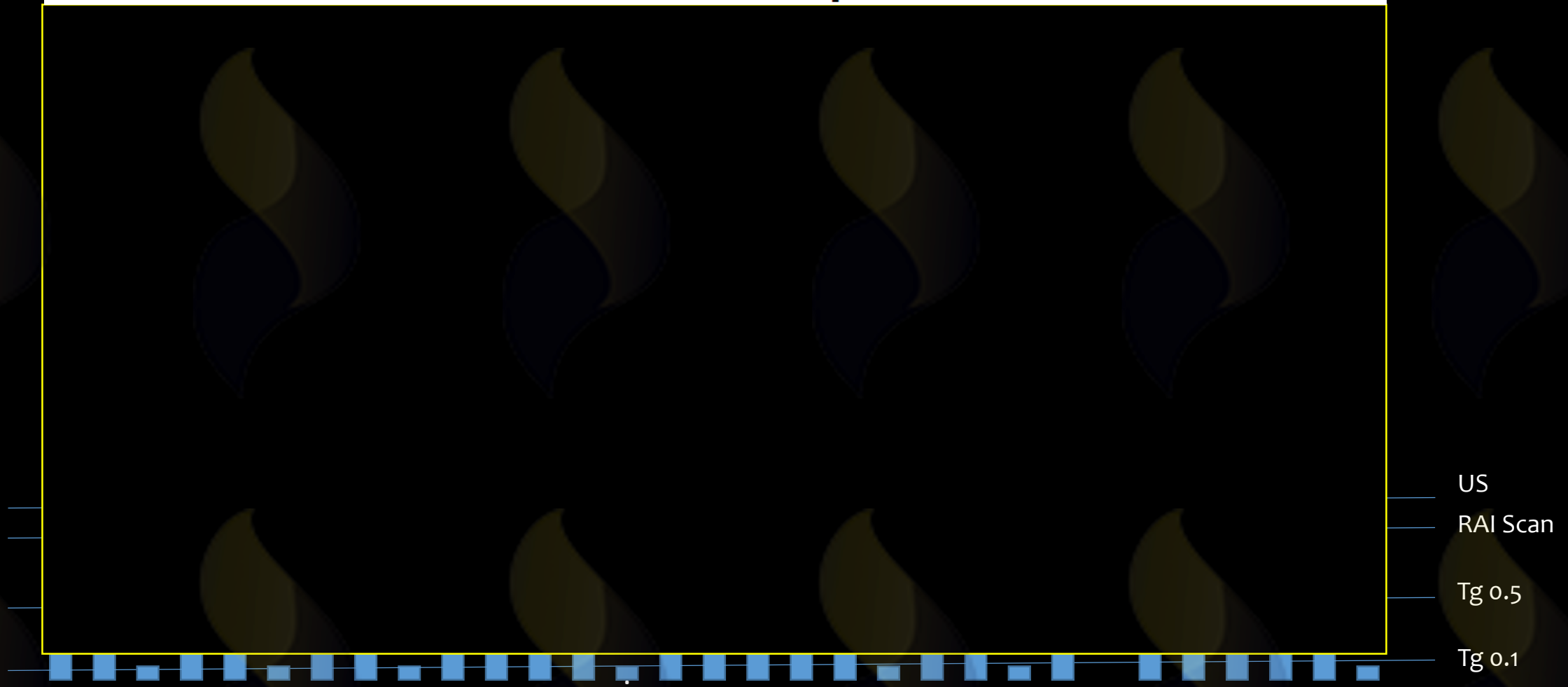
Cancer thyroïdien différencié à faible risque : le traitement ablatif par iode 131 est-il utile ?

NON INCLUSION CRITERIA:

1) Patients having undergone less than a total thyroidectomy
2) Patients with aggressive histotype (poorly differentiated, tall-clear-cylindric cell, diffuse sclerosing, or with an anaplastic component)
3) Patients having undergone surgery less than 2 months or more than 4 months before inclusion
4) Patients with cancer classified as pT1a unifocal (in which ablation is not necessary), or pT1N1, pT2, pT3, pT4 or N1 (who have a higher risk of recurrence) (classification TNM 2010)
5) Patient with known distant metastasis
6) Abnormal post-operative neck ultrasound of the lateral lymph node compartments
7) Patients with another malignancy not in remission for at least 2 years (except for in situ cervix uterine cancer, basocellular skin cancer)
8) Patients with a recent history of drugs affecting thyroid function, including injection of radio-contrast agents during the last 8 weeks.
9) Patients previously treated with radioactive iodine or who previously underwent a whole body scan with radioactive iodine
10) Pregnant or breast feeding women
11) Subject with any kind of disorder that may compromise his/her ability to give written informed consent and/or to comply with study procedures

10) Women of childbearing age should have a negative pregnancy test before any radioiodine administration
11) Both patients with or without thyroglobulin antibodies are eligible

Differentiated thyroid cancer: is there a need for radioiodine ablation in low risk patients?



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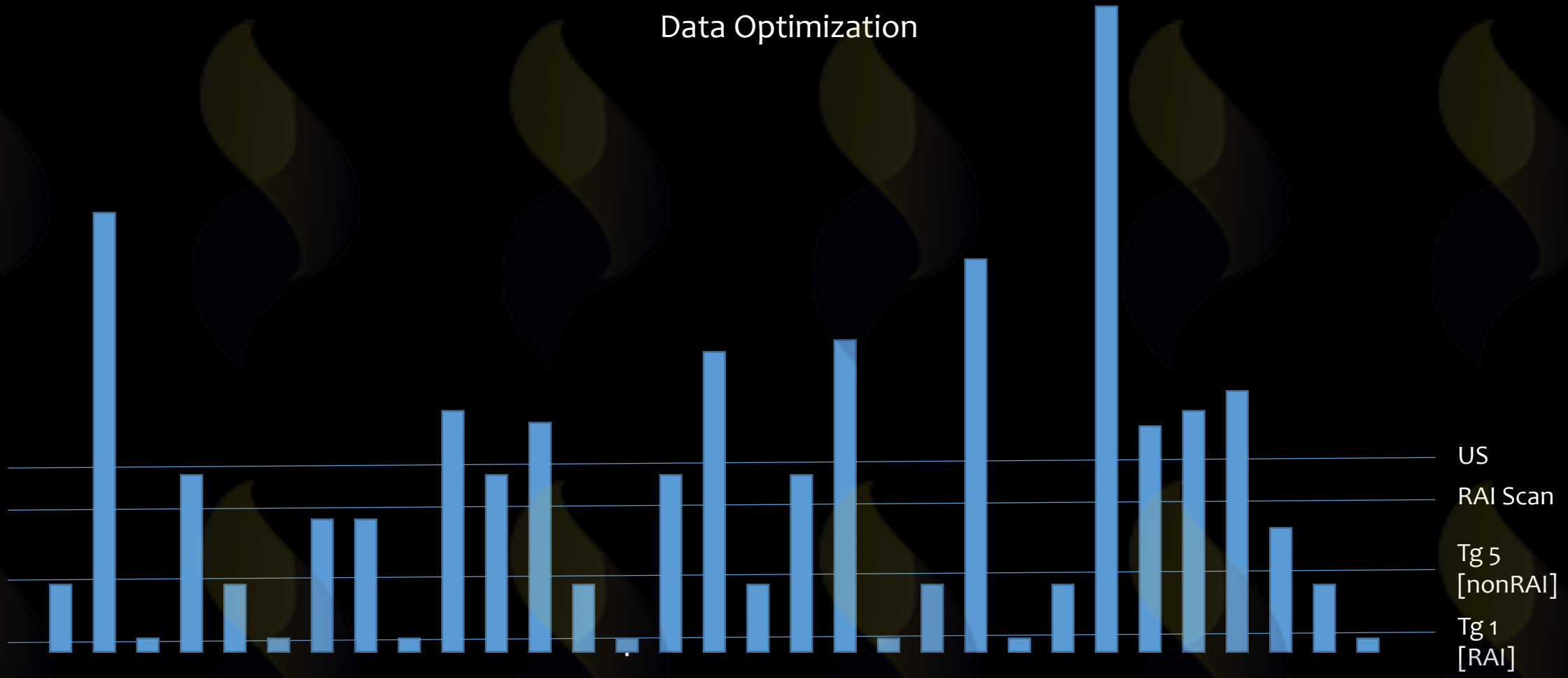

Differentiated thyroid cancer: is there a need for radioiodine ablation in low risk patients?