Science of ^{131}I Therapy in the Molecular Theranostics Paradigm

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Active Surveillance vs ^{131}I Therapy (Watchful Waiting vs Why Wait?) for Low Risk Thyroid Cancer

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Financial Disclosures

Jubilant Draximage: **Adivsor**

Esai: **Advisor**

Slide:ology[1] Disclaimer

- I have broken the first rule of Slide:ology, which is using a significant amount of text.
- The reason is that the slides will be available to you through e-mail, and you will need more text to help understand the slides.
- My e-mail is: douglasvannostrand@gmail.com

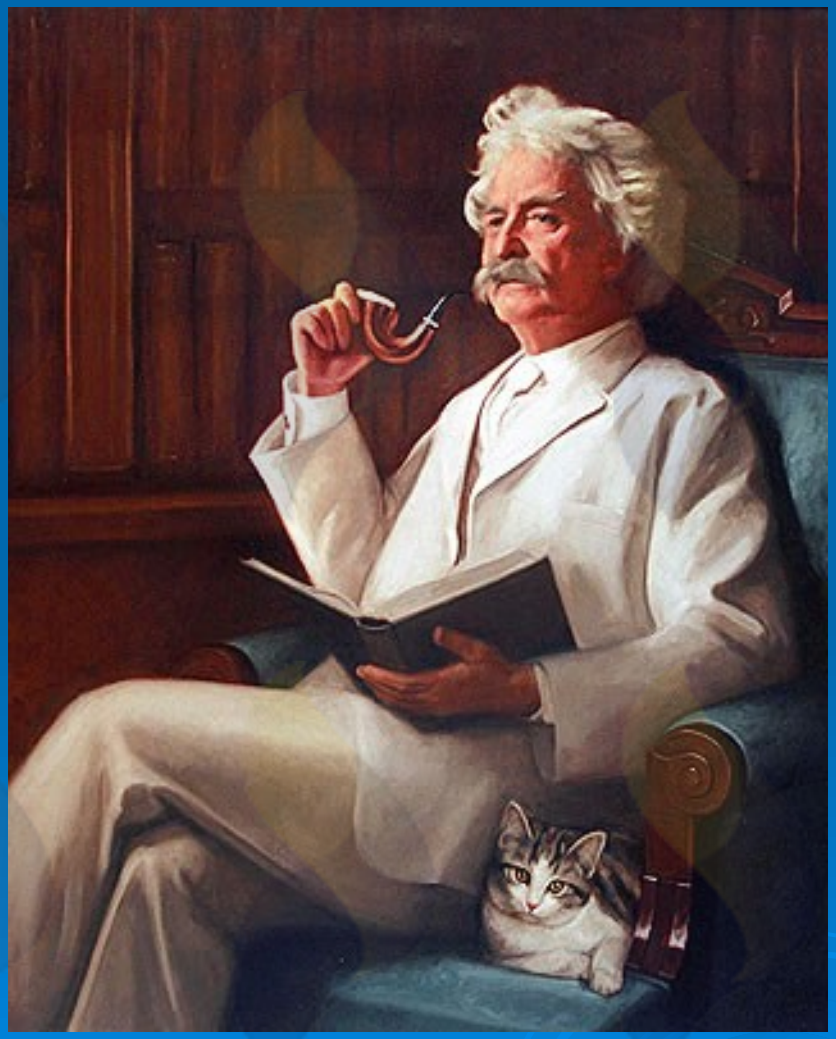
[1] **Sllde:ology, Nancy Duarte, 2008, O'Reilly Media, Sebastopol, Ca**

Objectives

After attending this session, an attendee will be able to:

- List the two major management approaches to low-risk patients
  - Active surveillance (3.g., “Watcful waiting?”)
  - vs
  - ^{131}I Therapy (e.g., “Why wait?”)
- Discuss the limitations, reservations, and lamentations of articles supporting “less-is-more” and “more-is-less.”
- “Resolve” the controversy.
- Describe future initiatives.

Words of Wisdom From the Past



"It ain't what you don't know that gets you into trouble.
It's what you know for sure that just ain't so"

Mark Twain

Words of Wisdom From the Past

"We have more areas in common than differences."

Words of Wisdom From the Past

"We all should celebrate our differences"

Anonymous

Words of Wisdom From the Past

"Differences should be the 'Workbench' of Progress"

Anonymous

Objective #1

List the two major management approaches to low risk patients:

- Active Surveillance

  (e.g., Watchful waiting or “Less-is-More”)

- ^{131}I Adjuvant Treatment

  (e.g., Why wait? or “More-is-less.”)

Articles supporting “Less is More”

Active Surveillance (Watchful Waiting) from 2015 ATA Guidelines

- Tuttle et. al., Thyroid 2010;20:1341–1349.
- Vaisman et al., Clin Endocrinol (Oxf) 2012;77:132–138.
- Castagna et al., Eur J Endocrinol 2011;165:441–446.
- Pitoia et. al., Thyroid 2013;23:1401–1407.
- Schvartz et al.. J Clin Endocrinol Metab 2012;97:1526–1535. 545.
- Durante et al., J Clin Endocrinol Metab 2012;97:2748–2753.

Articles supporting “More is Less”

^{131}I Therapy (“Why Wait?”)

- Verburg FA, et al., Eur J Endocrinol. 2005;152: 33–37. 12.
- Verburg FA, et al., Clin Endocrinol (Oxf). 2009;71:291-297.
- Handkiewicz-Junak D, et al., Mol Cell Endocrinol. 2010;322: 8-28.
- Verburg, et al., JCEM 2014;99:4487
- Donohoe, et al. SNMMI Appropriate Use Criteria. JNM. 2020;61:375-96.

But rather than discussing the pros and cons of each article, I want to move to Objective #2.

Objective #2

2. Discuss the limitations, reservations, and lamentations of articles supporting "less-is-more" and "more-is-less."

At least 9 items

Limitations, Reservations, and Lamentations

1. No conclusive prospective study

No randomized, controlled, prospective trial has been published with long enough follow up comparing any postoperative therapeutic strategy with vs without ^{131}I adjuvant treatment for patients with the many categories of low risk differentiated thyroid cancer.

Limitations, Reservations, and Lamentations

2. "Absence of Evidence is Not Evidence of an Absence."

- **Non-inferiority studies are required.**
- **Power is to be a non-inferiority study and to reach statistical significance.**
- **Power means higher numbers of observations.**
- **No non-inferiority study has been published regarding the effectiveness of ^{131}I adjuvant treatment vs active surveillance in low risk DTC**

Limitations, Reservations, and Lamentations

3. Not Enough Follow up

Limitations, Reservations, and Lamentations

Metaanalysis of I-131 Effectiveness

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
Mexico	229	5		NS
Pisa	964	12	NS	P<0.001

Sawka JCEM 2004 and slide courtesy of Dr. Marcus Luster, MD, Germany

Limitations, Reservations, and Lamentations

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Limitations, Reservations, and Lamentations

3. Not Enough Follow up

4. Promulgation of incorrect conclusions

Limitations, Reservations, and Lamentations

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

Recurrent disease , Biochemical disease, metastasis, persistent disease, or death	30 mCi	100 mCi	*p*
All patients	40% (20)	40% (39)	NS
T3NO-X	25.6%	27.8%	NS
T1-2N1 and T1-2NO	47.4%	40%	NS
T3N1	40.9%	52.9%	NS

Limitations, Reservations, and Lamentations

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T1-2N1 and T1-2NO	47.4%	40%	NS
T3N1	40.9%	52.9%	NS

"Our study provides the first evidence that in . . . patients at intermediate risk , high RAI activities have no major advantage over low activities."

Limitations, Reservations, and Lamentations

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30 mCi is equally as effective as 100 mCi.

Limitations, Reservations, and Lamentations

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30 mCi is equally as ineffective as 100 mCi.

Limitations, Reservations, and Lamentations

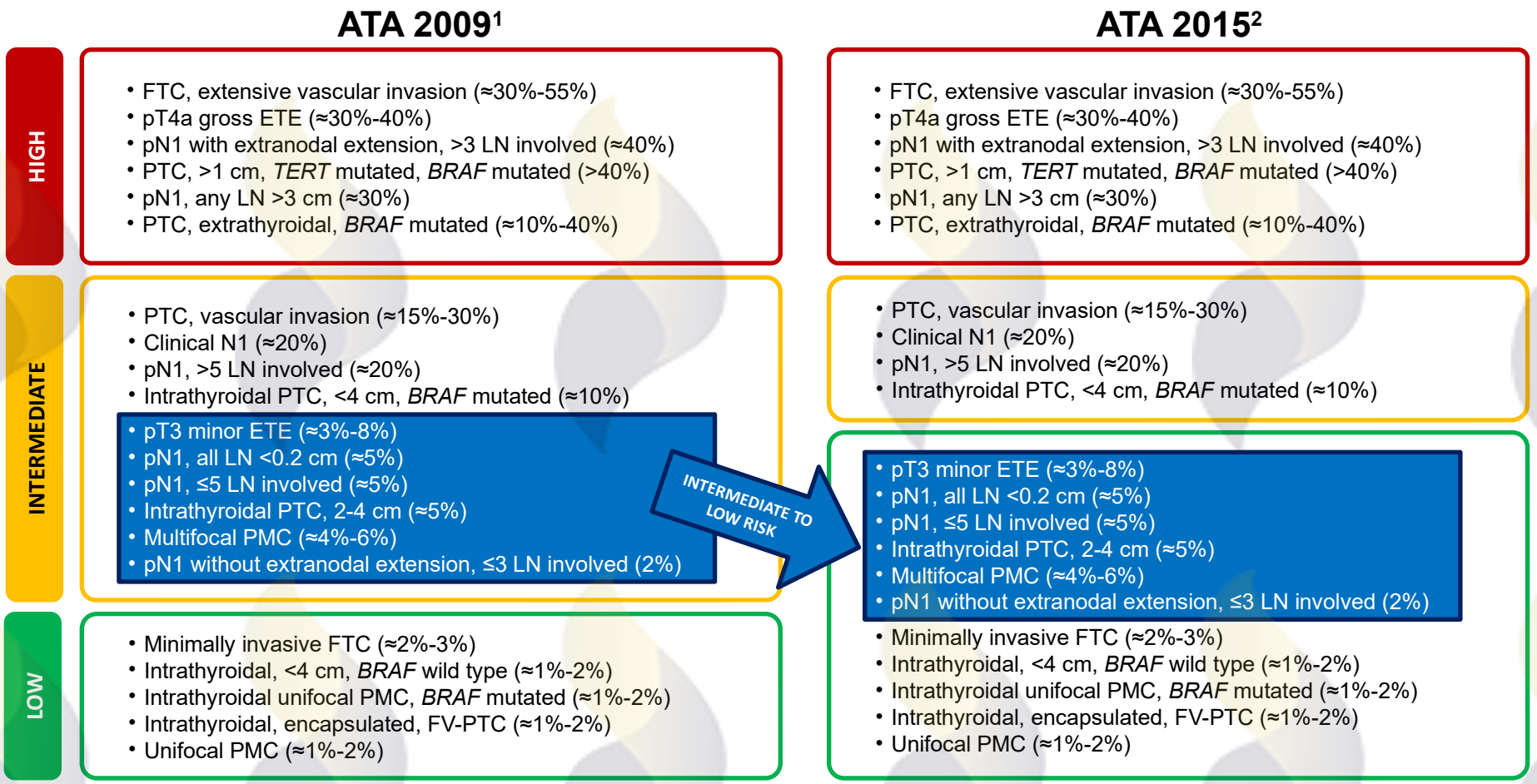
4. Promulgation of incorrect conclusions

- This article has been referenced by more than 13 other articles that “30 mCi is as effective as 100 mCi.”

Limitations, Reservations, and Lamentations

5. Moving patients that were staged as intermediate risk to low risk.

Risk of Recurrence: Stratification



1. Adapted from Cooper DS, et al. *Thyroid.* 2009;19:1167-1214.
2. Adapted from Haugen BR, et al. *Thyroid.* 2016;26:1-133.

ATA, American Thyroid Association; ETE, extrathyroidal extension; FTC, follicular thyroid cancer; FV, follicular variant; LN, lymph node; PMC, papillary microcarcinoma; PTC, papillary thyroid cancer; TERT, telomerase reverse transcriptase.

Limitations, Reservations, and Lamentations

6. What is really “low risk?”

- 10%, 5%, 1% , <1% recurrence rate or distant mets?
- By whose standard?

Risk of Recurrence: Stratification

	ATA 2009[1]	ATA 2015[2]
HIGH	• FTC, extensive vascular invasion (≈30%-55%) • pT4a gross ETE (≈30%-40%) • pN1 with extranodal extension, >3 LN involved (≈40%) • PTC, >1 cm, *TERT* mutated, *BRAF* mutated (>40%) • pN1, any LN >3 cm (≈30%) • PTC, extrathyroidal, *BRAF* mutated (≈10%-40%)	• FTC, extensive vascular invasion (≈30%-55%) • pT4a gross ETE (≈30%-40%) • pN1 with extranodal extension, >3 LN involved (≈40%) • PTC, >1 cm, *TERT* mutated, *BRAF* mutated (>40%) • pN1, any LN >3 cm (≈30%) • PTC, extrathyroidal, *BRAF* mutated (≈10%-40%)
INTERMEDIATE	• PTC, vascular invasion (≈15%-30%) • Clinical N1 (≈20%) • pN1, >5 LN involved (≈20%) • Intrathyroidal PTC, <4 cm, *BRAF* mutated (≈10%)	• PTC, vascular invasion (≈15%-30%) • Clinical N1 (≈20%) • pN1, >5 LN involved (≈20%) • Intrathyroidal PTC, <4 cm, *BRAF* mutated (≈10%) • pT3 minor ETE (≈3%-8%) • pN1, all LN <0.2 cm (≈5%) • pN1, ≤5 LN involved (≈5%) • Intrathyroidal PTC, 2-4 cm (≈5%) • Multifocal PMC (≈4%-6%) • pN1 without extranodal extension, ≤3 LN involved (2%)
LOW	• Minimally invasive FTC (≈2%-3%) • Intrathyroidal, <4 cm, *BRAF* wild type (≈1%-2%) • Intrathyroidal unifocal PMC, *BRAF* mutated (≈1%-2%) • Intrathyroidal, encapsulated, FV-PTC (≈1%-2%) • Unifocal PMC (≈1%-2%)	• Minimally invasive FTC (≈2%-3%) • Intrathyroidal, <4 cm, *BRAF* wild type (≈1%-2%) • Intrathyroidal unifocal PMC, *BRAF* mutated (≈1%-2%) • Intrathyroidal, encapsulated, FV-PTC (≈1%-2%) • Unifocal PMC (≈1%-2%)

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Limitations, Reservations, and Lamentations

- pN1 without extranodal extension, ≤3 LN involved (2%)
- Multifocal PMC (≈4%-6%)
- Intrathyroidal PTC, 2-4 cm (≈5%)
- pN1, all LN <0.2 cm (≈5%)
- pN1, ≤5 LN involved (≈5%)
- pT3 minor ETE (≈3%-8%)

Limitations, Reservations, and Lamentations

6. What is really “low risk?”

- 10%, 5%, 1% , <1% recurrence rate or distant mets?
- By whose standard?
  - Your standard
  - My standard?
  - Consensus?
  - The patient’s standard?

Limitations, Reservations, and Lamentations

- **The European Consensus Conference and the Latin American Thyroid Society classify patients as either being at very low risk or low risk.**
  - Very low risk (unifocal, intrathyroidal T1a N0M0),
  - Low risk (T1b N0M0, T2N0M0, or multifocal T1N0M0,)
- **These would be classified by ATA as low risk.**
- **However, how a patient "perceives" these percentages may be very different.**

Pacini et al., . Eur J Endocrinol 2006: 154:787–803. 541.
Camargo et al. Arq Bras Endocrinol Metabol 2008; 52:1167–1175.

Limitations, Reservations, and Lamentations

7. "You can always treat later."

i. Be wary of this premise.

ii. You can always treat later, but not necessarily as well.

iii. You can always treat better if you cure now rather than if you treat metastases later.

Limitations, Reservations, and Lamentations

8. Consensus

- In the absence of good evidence, 'consensus' is one surrogate that is used.

- Be wary of a consensus.

Limitations, Reservations, and Lamentations

8. Consensus

- In the 1920s, the consensus was that the " 'Roaring 20s' would roar on!".

Limitations, Reservations, and Lamentations

8. Consensus

- In the 1920s, the consensus was that the " 'Roaring 20s' would roar on!"

Limitations, Reservations, and Lamentations

8. Consensus

- In the late 1500 and earlier 1600s, the universal consensus was that

  "the *sun rotated around the earth.*"

- Galileo

Limitations, Reservations, and Lamentations

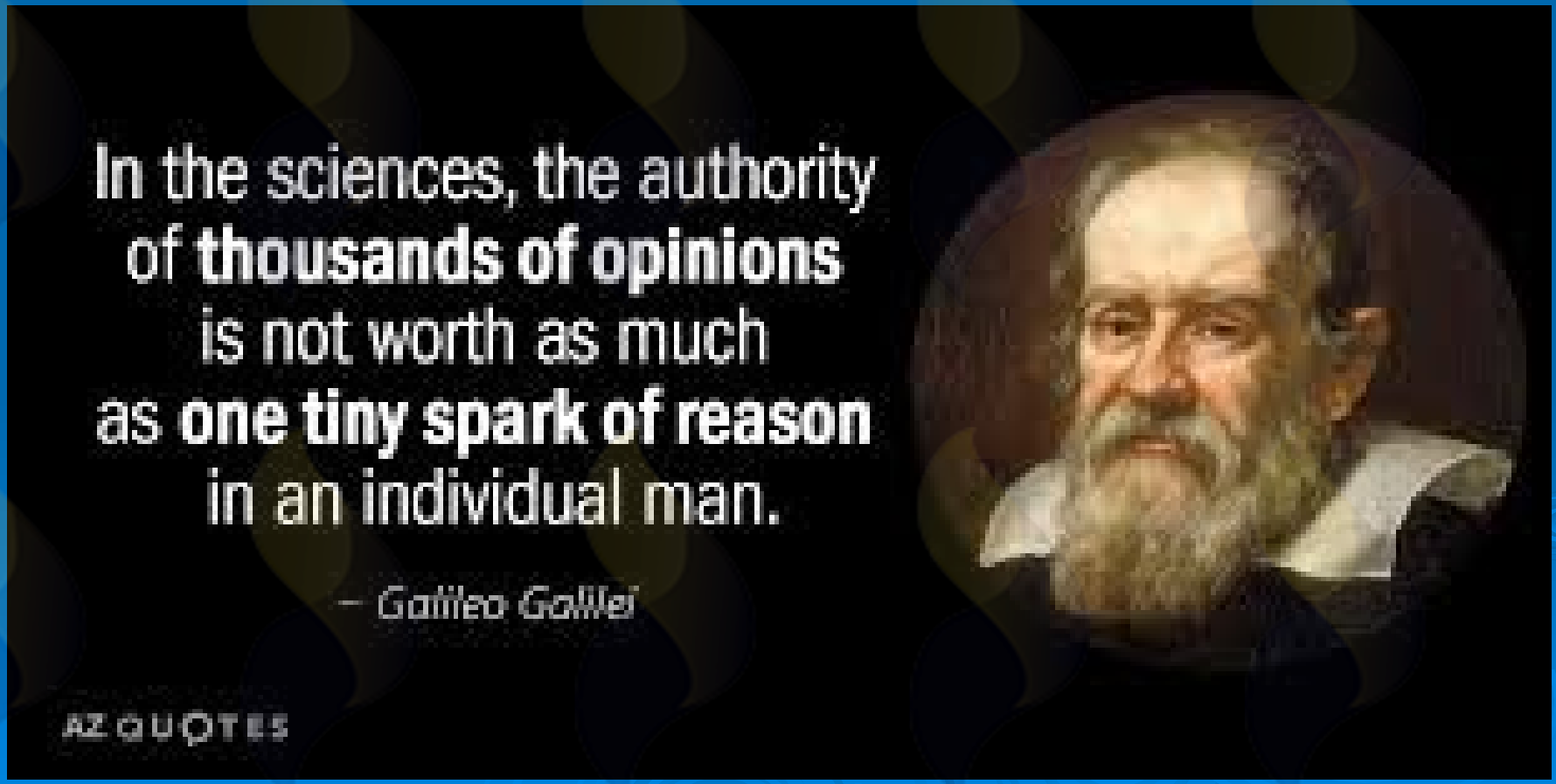
8. Consensus

- He was sentenced to be executed!!!
- So much for consensus!

- Galileo

Limitations, Reservations, and Lamentations

8. Consensus



Limitations, Reservations, and Lamentations

8. Consensus

- This is not just in the 1500/1600 or 1920s.
- It has been throughout history.
- Just look at our own last century, present day politics, and even COVID-19.
- Be wary of consensus.

Limitations, Reservations, and Lamentations

8. Consensus

- But you say this does not happen within the science of differentiated thyroid cancer?
- Remember the Castagna article and the 13+ articles that referenced it– a consensus.

Limitations, Reservations, and Lamentations

9. "A simple falsehood is better than a complex truth."

- Does this cliché creep into our practice of medicine?
- I am confident that no one does this consciously.
- However, the forces from many facilities, practices, and HMOs are increasing "**EFFICIENCY**" (and RVUs), which directly or indirectly affect our practices.
- And this can subtly or subconsciously affect our favoring recommendations that are easy—e.g., active surveillance.

Limitations, Reservations, and Lamentations

"A simple falsehood is better than a complex truth."

- How?
- Less time spent on patient education.
- Discourages patient questions.
- No informed consent.
- And you can think of other mechanisms.

- Results in:
- Increases productivity with increased RVUs.
- Less liability.
- Rightly or wrongly, the patient "senses" that his/her problem is not that concerning.
- Less apparent confusion within the patient.

Limitations, Reservations, and Lamentations

In Summary

- **Limitations, Reservations, and Lamentations.**
  1. No conclusive prospec
  2. "An absence of evidence is not evidence of an absence."
  3. Following up is not long enough.
  4. ~~You can always treat later.~~
  5. Promulgation of incorrect conclusions.
  6. Moving patients that were staged as intermediate risk to one large low risk category.
  7. What is really "low risk?"
  8. Consensus and Galileo
  9. Be cautious of the forces that encourage "a simple falsehood is better than a complex truth."

Objective #3

3. Resolving the controversy of the management of “low” risk differentiated thyroid cancer.

Resolving the Controversy

If you guessed that my position favors

"More-is-Less"

Resolving the Controversy

If you guessed that my position favors

~~"More-is-Less"~~

Resolving the Controversy

My position is:

Personalized Medicine

Resolving the Controversy

Personalized Medicine

1. Staging.
2. Adequate Staging.
3. Performance of a pe-therapy-diagnostic scan to maximize staging

Author	Reference	Altered staging, indeterminates, management, and/or outcomes
Aide	J Clin Endocrinol Metab 2009;94:2075-2084.	22%
Barwick	Eur J Endocrinol 2010;162:1131-1139.	42%
Ciappuccini	Eur J Endocrinol 2011;164:961-969.	Sole prognostic variable
Geerlings	Nuc Med Comm 2010; 31:417-422.	27%
Grewal	J Nucl Med 2010;51:1361-1367.	20%
Kohlfuerest	Eur JNMMI 2009;36:886-893.	36%
Maruoka	Radiology 2012;265:902-909.	22%

Author	Reference	Altered staging, indeterminates, management, and/or outcomes
Mustafa	Eur JNMMI 2010;37:1462-1466.	25%
Ruf	Nuc Med Comm 2004;25:1177-1182.	25%
Schmidt	J Nucl Med 2009;50:18-23.	35%
Spanu	JNMMI 2009;50:184-190.	36%
Tharp	Eur J Nucl Med Mol Imaging 2004;31:1435-1442.	41%
Wang	Clinical Imaging 2009;33:49-54.	23%
Yamamato	J Nucl Med 2003;44:1905-1910.	88%

Resolving the Controversy

Personalized Medicine

1. Staging.
2. Adequate Staging.
3. Performance of a pe-therapy-diagnostic scan to maximize staging
4. Appropriate preparation of the patient for pre-therapy diagnostic scan .

Adequate elevation of TSH

Low iodine diet

Confirming low iodine in urine

Resolving the Controversy

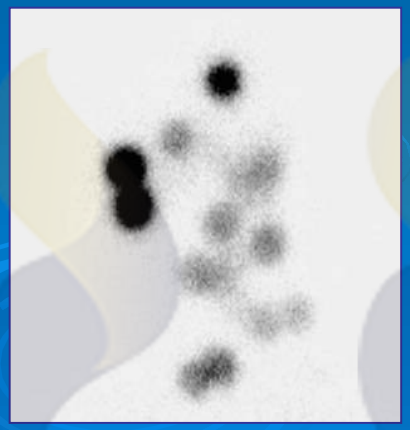
Personalized Medicine

1. Staging.
2. Adequate Staging.
3. Performance of a pre-therapy-diagnostic scan to maximize staging
4. Appropriate preparation of the patient for pre-therapy diagnostic scan .
5. Appropriate performance of the pre-therapy diagnostic scan.

Not all Radioiodine Scans are Created Equal

Standard Whole Body Scan

Pinhole Collimator Spot Image



- Thyroid. 2019;29:901-9.

Resolving the Controversy

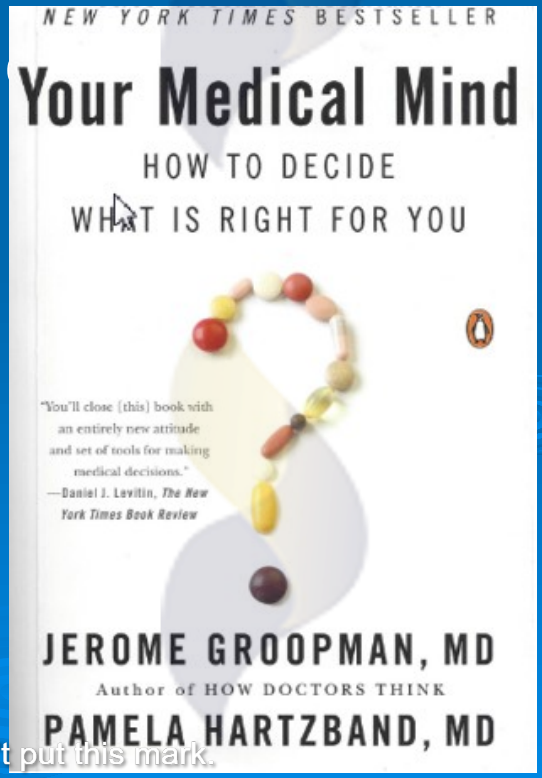
Personalized Medicine

1. Staging.
2. Adequate Staging.
3. Performance of a pe-therapy-diagnostic scan to maximize staging
4. Appropriate preparation of the patient for pre-therapy diagnostic scan .
5. Appropriate performance of the pre-therapy diagnostic scan.
6. Genomic/molecular testing
7. Comorbidities.
8. Benefit vs Risks.

Resolving the Controversy

Personalized Medicine

1. Staging.
2. Adequate Staging.
3. Performance of a pe-therapy-diagnostic scan to maximize staging
4. Appropriate preparation of the patient for pre-therapy diagnostic scan .
5. Appropriate performance of the pre-therapy
6. Genomic/molecular testing
7. Comorbidities.
8. Benefit vs Risks.
9. Patient's desires:
    - Is the patient a "minimalist" or "maximalist"?



Resolving the Controversy

Personalized Medicine

1. Staging.
2. Adequate Staging.
3. Performance of a pe-therapy-diagnostic scan to maximize staging
4. Appropriate preparation of the patient for pre-therapy diagnostic scan .
5. Appropriate performance of the pre-therapy diagnostic scan.
6. Genomic/molecular testing
7. Comorbidities.
8. Benefit vs Risks.
9. Patient's desires .
    - Is the patient a "minimalist" or "maximalist"?
    - Is the patient comfortable with "treating later"?
10. Patient compliance?
11. The ability to follow the patient?

For 10 to 20 years?

Personalized Medicine

12. Physician work environment:
    - Facility forces are "at work" on physician practices:
        - The facility "pushes" "RVUs first" vs "patient first".
        - You should be able to treat this even though you only treat a couple of patients per year.
        - You should not refer a patient to competing a institution.
    - Capabilities of your clinic or medical facility:
        - Only can give 30 mCi and not 100 mCi ?
13. Insurance coverage?
14. Specific issues of various country health care systems?

Objective #4

- **Describe future initiatives.**

Future Initiatives

- **ESTIMABL2 (France)**
- **IoN (Great Britian)**

Just published
Leboulleux S, NEJM 2020;386;10:923-932

ESTIMABL 2

Inclusion criteria:

pT1a (m) Nx Mx

pT2 Nx Mx

1.1 GBq (30 mCi)/active stimulation versus surveillance

5 years

750 patients

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

Courtesy Frederick Verburg

Future Initiatives

- **ESTIMABL2 (France)**

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

Future Initiatives

- **ESTIMABL2 (France)**

- Prospective
- Open-label randomized phase III trial
- Multi-instutional
- Non-inferiority comparison
- Randomization to post-operative radioiodine ablation versus followed-up without postoperative radioiodine ablation [active surveillance].
- Published in the NEJM

Future Initiatives

- **ESTIMABL2 (France)**

The conclusion verbatim:

"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 a

Future Initiatives

- **ESTIMABL2 (France)**

- However, I have three (3) reservations involving:

- ^{131}I Activity administered,
- Low-risk classifications, and
- Duration of follow up.

Future Initiatives

- **ESTIMABL2 (France)**

The conclusion verbatim:

“In patients with low-risk thyroid cancer undergoing thyroidectom a follow-up strategy that did not involve the use of radioiodine wa noninferior to an ablation strate with radioiodine regarding the occurrence of functional, structural, and biologic events a

Future Initiatives

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1.1 GBq (30 mCi)/active stimulation versus surveillance

5 years

750 patients

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

Future Initiatives

- **ESTIMABL2 (France)**

^{131}I Activity Administered

- Their use of 30 mCi is not sufficient for their conclusion of . . .

  “. . . a strategy of active surveillance was non-inferior to the use of radioiodine.”

- 30 mCi is not enough to make such a broad misleading statement about all activities of radioiodine.

Just published
Leboulleux S, NEJM 2020;386;10:923-932

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pT1a (m) Nx Mx

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1.1 GBq (30 mCi)/active stimulation versus surveillance

5 years

750 patients

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Inclusion criteria:

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~~pT2 Nx Mx~~

1.1 GBq (30 mCi)/active stimulation versus surveillance

5 years

750 patients

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

Future Initiatives

- **ESTIMABL2 (France)**

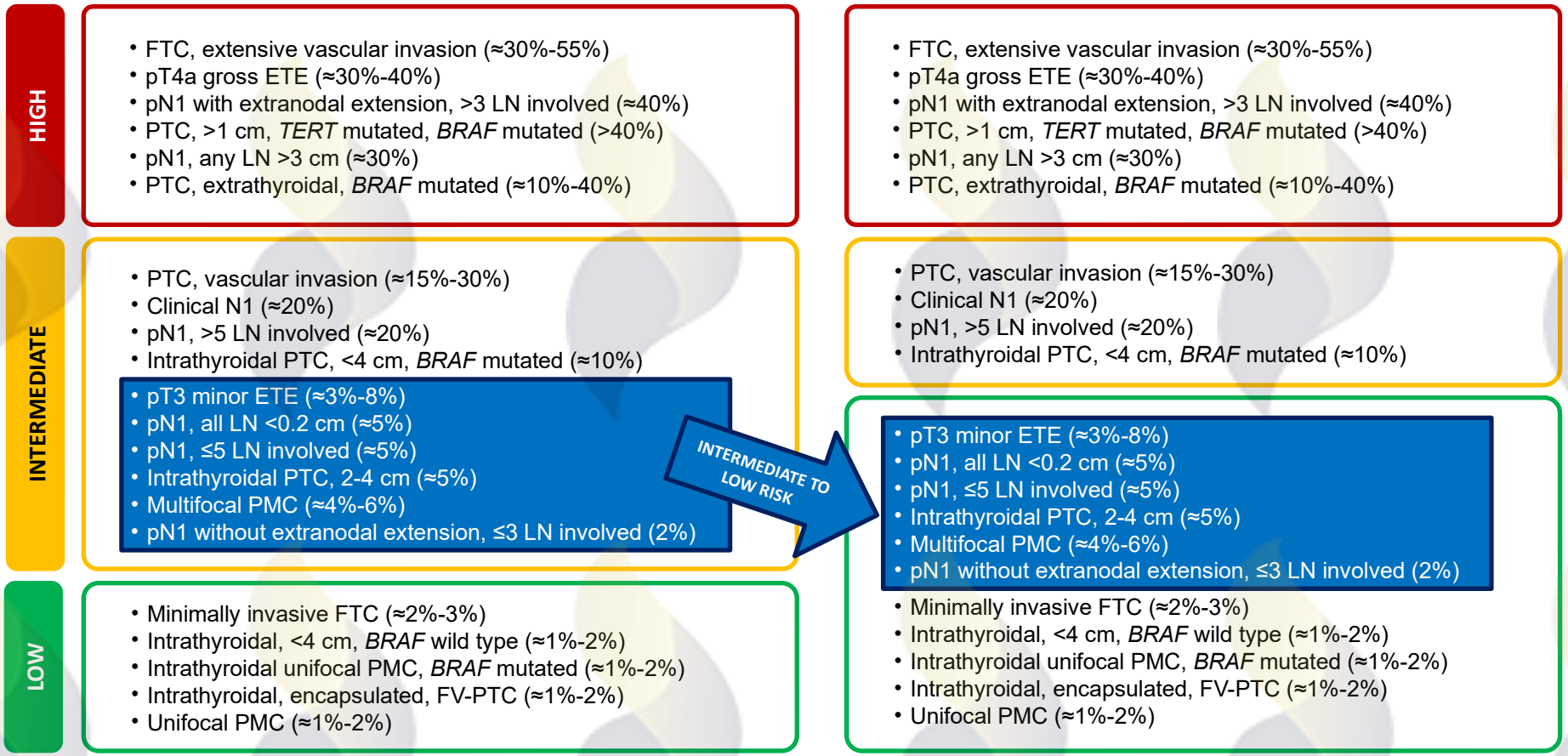
"In patients with low-risk thyroid cancer undergoing thyroidectom a follow-up strategy that did not involve the use of radioiodine wa noninferior to an ablation strate with radioiodine regarding the occurrence of functional, structural, and biologic events at 3 years."

Future Initiatives

- **ESTIMABL2 (France)**

"In patients with low-risk thyroid cancer undergoing thyroidectom a follow-up strategy that did not involve the use of radioiodine wa noninferior to an ablation strate with radioiodine regarding the occurrence of functional, structural, and biologic events at 3 years."

Risk of Recurrence: Stratification



1. Adapted from Cooper DS, et al. *Thyroid.* 2009;19:1167-1214.
2. Adapted from Haugen BR, et al. *Thyroid.* 2016;26:1-133.

ATA, American Thyroid Association; ETE, extrathyroidal extension; FTC, follicular thyroid cancer; FV, follicular variant; LN, lymph node; PMC, papillary microcarcinoma; PTC, papillary thyroid cancer; TERT, telomerase reverse transcriptase.

• ESTIMABL2 (France)

Low-Risk Disease

- Their use of the term *"low-risk" disease* in the conclusion of their abstract may mislead individuals that any one classified as "low-risk" should do as well with or without any radioiodine treatment.

- They only studied pT1a, pT1b, N0 \ NX, M0 \ MX

- This does not encompass all of the so-called "low-risk" group.

Just published
Leboulleux S, NEJM 2020;386;10:923-932

ESTIMABL 2

Inclusion criteria:

pT1a (m) Nx Mx

pT2 Nx Mx

1.1 GBq (30 mCi)/active stimulation versus surveillance

5 years

750 patients

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

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• ESTIMABL2 (France)

Duration of Follow-up:

- Leboulleux et al. submits two articles in support of 3 years. But three years is not enough.
  - Durante et al.
  - Dong et al.

Future Initiatives

• ESTIMABL2 (France)

Duration of Follow-up:

- Lebeulloux et al. submited two articles in suppor of 3 years. But three years is not enough.
  - Durante et al. JCEM 2013 1;98(2):636-42.
    - Median follow up of 10.4 yrs
    - All relapses within 8 or fewer yrs after treatment
    - Evaluated 1020 patients
    - However, 908 had radioiodine therapy.
  - Leboulleux did not even use 5 yrs, but instead reduced the follow up to 3 yrs.
  - Three yrs of follow up is not enough.

Future Initiatives

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    - Mean time to initial cancer recurrence was 9.41 + 7.69 years.

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  - Durante et al.
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    - 466
    - Mean time to initial cancer recurrence was 9.41 + 7.69 years.
    - Specifically, the mean time to recurrenc for local recurrence was 10.60 + 7.80 years, regional recurrence was 7.87 + 7.71 years, and distant metastases was 13.49 + 7.80 years.

Future Initiatives

- **ESTIMABL2 (France)**

Metaanalysis of I-131 Effectiveness

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
Mexico	229	5		NS
Pisa	964	12	NS	P<0.001

Sawka JCEM 2004 and courtesy of Dr. Markus Luster, MD, Germany

Future Initiatives

- **ESTIMABL2 (France)**

Thus, three major problems that may mislead practitioners, patients and third-party payors by :

1. **Extrapolating a non-response to 30 mCi to higher ^{131}I activities for adjuvant treatment,**
2. **Extrapolating data from very select low-risk patients to all patients within the low-risk category, and**
3. **Extrapolating data of only 3 years**

Future Initiatives

- **ESTIMABL2 (France)**

In my opinion:

1. **If you are going to treat with ^{131}I for suspected but unproven remaining cancer,**
2. **Then perform ^{131}I adjuvant treatment with ^{131}I administered activities of 100 to 150 mCi.**
2. **30 mCi administered activity is for remnant ablation to destroy normal residual tissue with no**

Zero Dose Concept ...

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Example: "Heart attack" AND "Los Angeles"
Search for studies: Search
Advanced Search | Help | Studies by Topic | Glossary

Find Studies | About Clinical Studies | Submit Studies | Resources | About This Site

Home > Find Studies > Study Record Detail

Text Size

IoN- Is Ablative Radio-iodine Necessary for Low Risk Differentiated Thyroid Cancer Patients

This study is currently recruiting participants. (see Contacts and Locations)

Verified December 2013 by University College, London

Sponsor:
University College, London

Collaborator:
Cancer Research UK

Information provided by (Responsible Party):
University College, London

UCL

NCRI

IoN

IoN– Is ablative radio-iodine Necessary for low risk differentiated thyroid cancer patients

Courtesy of Dr. F Verburg

Future Initiatives

ION

- The problem with this study is it will tell you that doing nothing is the same as administering 30 mCi.
- And 30 mCi is for remnant ablation.
- It says nothing about whether or not high activities will have better outcomes for ^{131}I adjuvant treatment to reduce recurrence

In Summary

- "It ain't what you don't know that gets you into trouble. It's what you know for sure that just ain't so."
- "We have more things in common than differences."
- "Celebrate Our Differences"
- "Differences are the 'workbench' of progress."
- "In the sciences, the authority of thousands of opinions is not worth as much as one tiny spark of reason in an individual person."

Limitations, Reservations, and Lamentations

Summary

1. No conclusive prospective studies
2. "Absence of evidence is not evidence of an absence."
3. Follow up has not been long enough.
4. Be careful moving a patient that was previously staged as intermediate risk to low risk disease.
5. Be wary of unjustified conclusions.
6. What is really "low risk?" <1%? 1%? 5%? 8%?
7. "Can you really treat later—as well as if you had treated earlier?"
8. Be wary of consensus.
9. Be wary of "A simple falsehood is more efficient than a complex truth."

Active Surveillance (Watchful Waiting?)
vs
^{131}I Therapy (Why Wait?)

For "Low" Risk Thyroid Cancer

My position is: "Less and More"

Less

Interpreting Guidelines as Sacrosanct

and

More

Special thanks to my past staff of the MedStar Washington Hospital Center Division of Nuclear Medicine

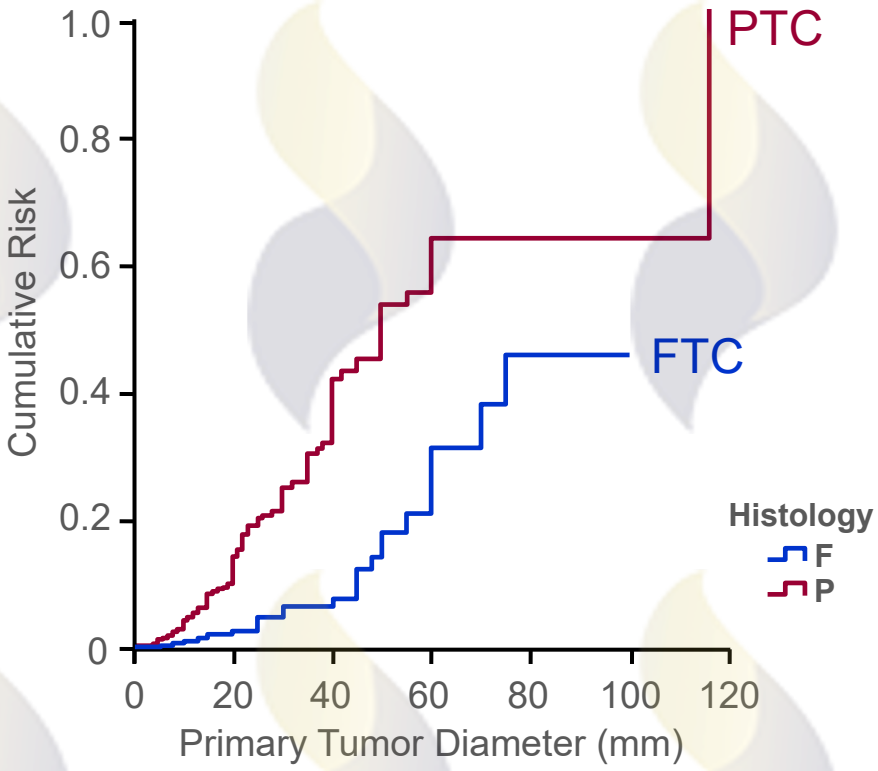
douglasvannostrand@gmail.com

Special thanks to my MedStar Health research staff

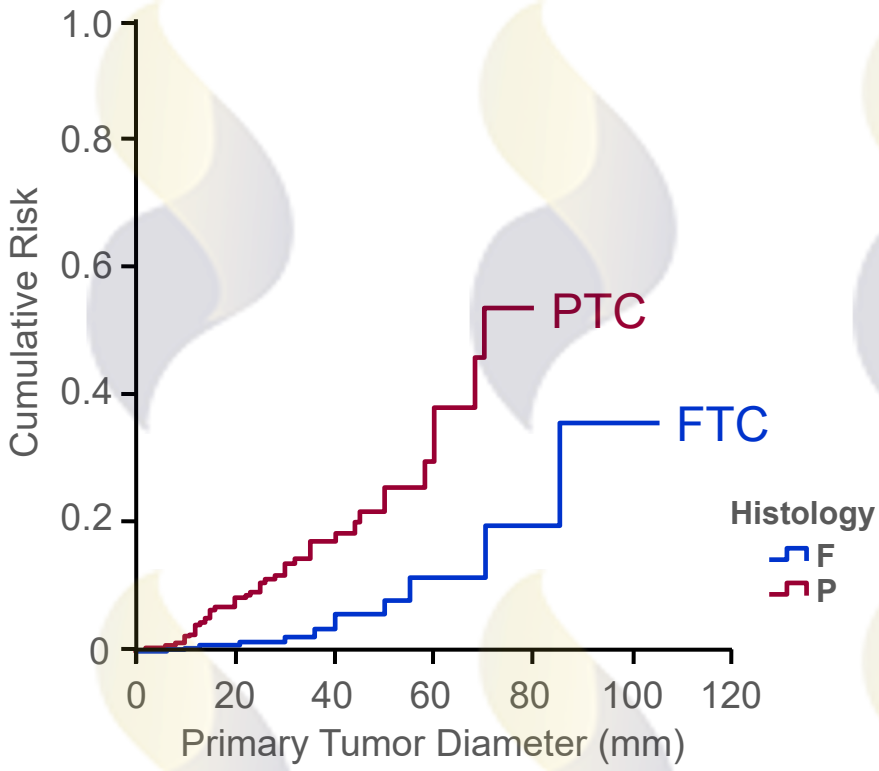
douglasvannostrand@gmail.com

≤54 mCi
>54 mCi

Low Risk ≠ No Risk



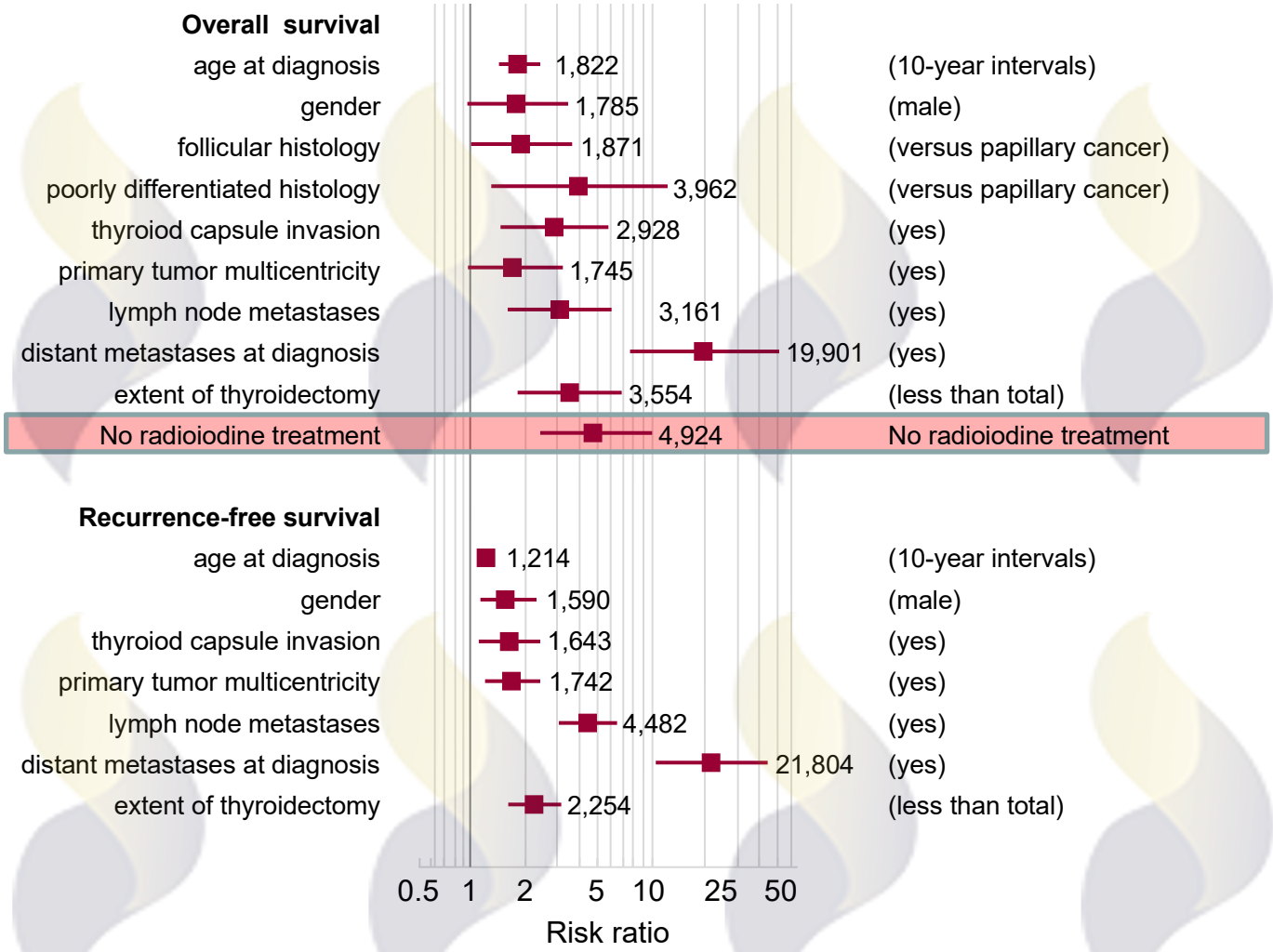
Tumour diameter and risk of local invasion



Tumour diameter and risk of N1

Verburg FA, et al. *Clin Endocrinol (Oxf).* 2009;71:291-297.

Negative Prognostic Factors



Handkiewicz-Junak D, Czarniecka A, Jarzab B.
Mol Cell Endocrinol. 2010;322:8-28.

Articles Supporting "More-is-Less:

Verburg et al. JCEM 2014;99:4487

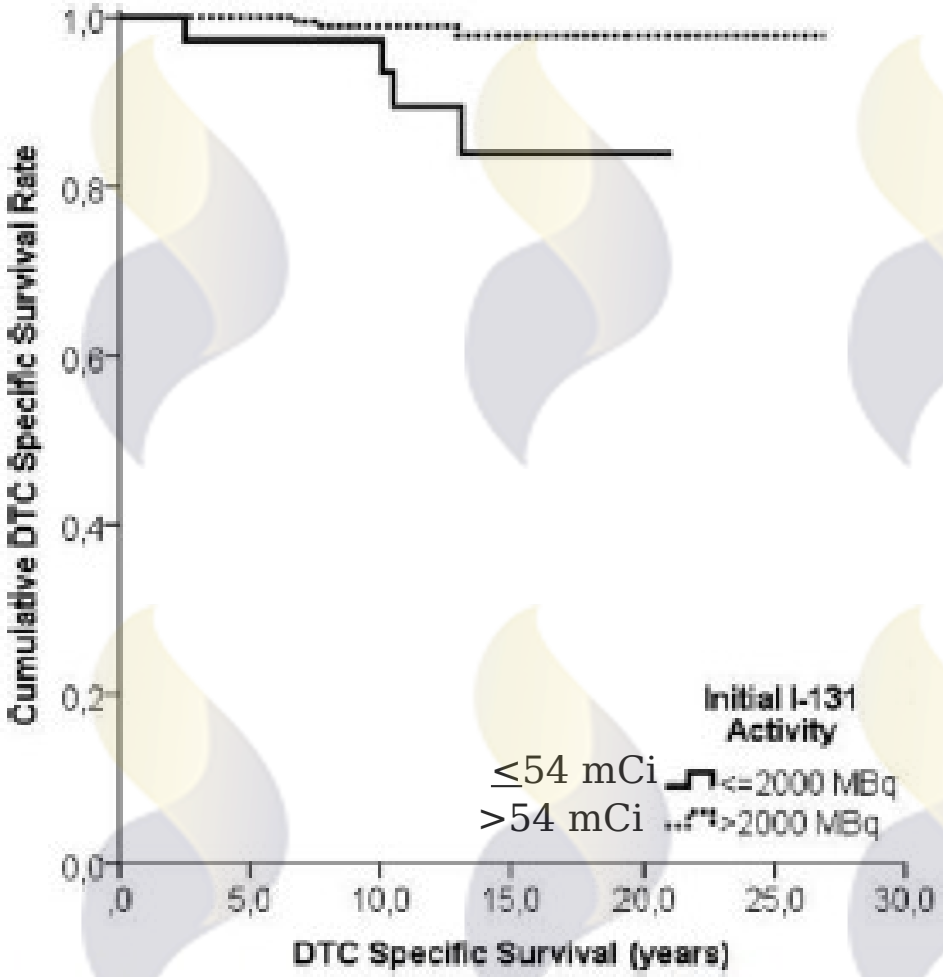


Figure 1. DTC-specific survival in low-risk patients ≥45 years at [illegible] stratified remnant ablation activity.