



From active surveillance to total thyroidectomy... offering your early stage thyroid cancer patient the best option for them

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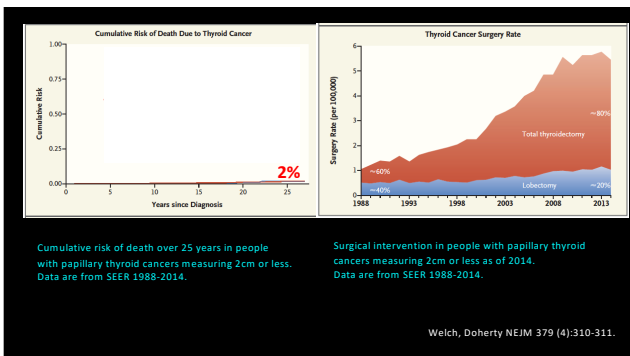



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Disclosures

- No commercial relationships to disclose

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For most patients, the fact that a cancer was found 'incidentally' – that is – in the absence of symptoms - is not meaningful. Cancer is cancer.

They are right. Overdiagnosis – identification of cancers unlikely to go on to become clinically evident - is an epidemiologic phenomenon, not an individual one.

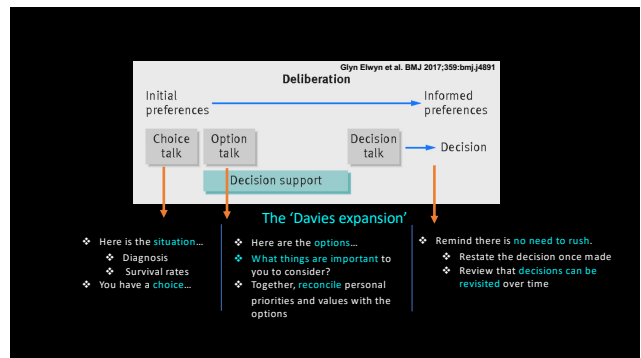
Deciding that you are (or are not) overdiagnosed is a personal decision you make with your doctor.

Davies, et al. A thyroid incidentaloma registry: lessons learned and the path forward. *Thyroid* 2016

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Having a Conversation


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For tumors greater than 1.5cm in diameter...

Hemithyroidectomy or Total thyroidectomy?



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Which of these patients is eligible for hemithyroidectomy as first line management?

A. Patient with a contained 3cm papillary thyroid cancer and a cNO neck
 B. Patient with a contained 2cm papillary thyroid cancer and a cN1b neck

With which of these patients might completion thyroidectomy be discussed?

A. On pathology: Multifocal disease in the resected lobe that is >1cm
 B. On pathology: 3 central nodes positive, metastatic foci are all <5mm in size
 C. On pathology: hob nail variant


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Who is eligible for a hemithyroidectomy?

All follicular cell derived cancers <4cm

Clinically NO neck

* 1cm or less thyroid cancers with a clinically NO neck should not undergo total thyroidectomy (2015 ATA Guidelines)



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Why the change?

Recognition that radioactive iodine often not needed – so total thyroidectomy not necessary

Survival “in properly selected patients” about the same

Move from whole body iodine scanning to:
 Neck ultrasound
 Tg measurement – even after lobectomy

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Who should have a total thyroidectomy?

Patients with:

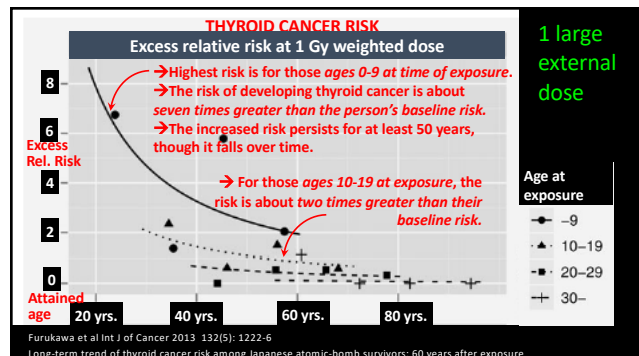
- Follicular cell derived cancer >4cm
- Clinically apparent extrathyroidal extension
- cN1 disease
- M1 disease

If the cancer is <4cm:

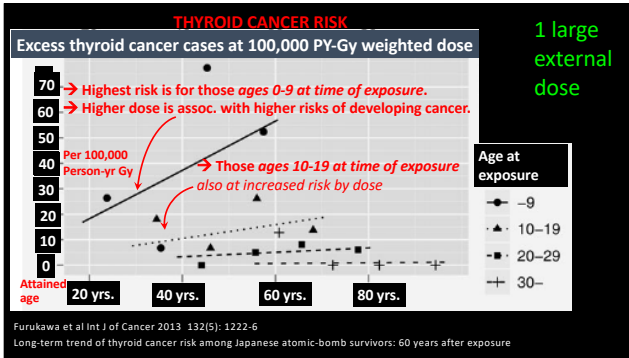
- Older age (>45 – ATA, or >55 more recent data)
- Contralateral thyroid nodules
- ATA says ‘history of head and neck radiation’*
- Familial DTC (DTC in 3 or more 1st degree relatives)



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Are thyroid cancers more aggressive that develop after medical radiation exposure?

- Single institution cohort of patients diagnosed with differentiated thyroid cancer 1986-2010
- 116 patients exposed to external beam radiation, 3509 unexposed
- Similar characteristics overall, except XRT exposed were more often:
 - male (39% vs 27%)
 - Older than age 45 (67% vs 54%)
- No difference in five year disease specific survival
- No difference in five year recurrence rates

Previous External Beam Radiation Treatment Exposure Does Not Confer Worse Outcome for Patients with Differentiated Thyroid Cancer Shaha, MA et al Thyroid 2018 27(3):412-418

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What about completion thyroidectomy?

...If radioactive iodine will be indicated

Risk of Structural Disease Recurrence
(In patients without structurally identifiable disease after initial therapy)

High Risk Gross extrathyroidal extension, incomplete tumor resection, distant metastases, or lymph node >1 cm	FTC, extensive vascular invasion (≥ 30-55%) pT4 gross ETE (≥ 30-40%) pN1 with extranodal extension, >3 LN involved (≥ 40%) FTC, >1 cm, TERT mutated & BRAF mutated* (≥ 40%) pN1, any LN > 3 cm (≥ 20%)
Intermediate Risk Aggressive histology, minor extrathyroidal extension, vascular invasion, or >5 involved lymph nodes (R2-3 cm)	FTC, extrathyroidal, BRAF mutated* (≥ 10-40%) FTC, vascular invasion (≥ 15-30%) Clinical N1 (≥ 20%) >1cm Multifocality pN1, > 8 LN involved (≥ 20%) (NCCN) Intrathyroidal FTC, < 4 cm, BRAF mutated* (≥ 10%) pT3 minor ETE* (≥ 5-15%)
Low Risk Intrathyroidal FTC < 5 LN micro-metastases (≤ 0.2 cm)	pN1, all LN < 0.2 cm (5%) pN1, ≤ 8 LN involved (≤ 5%) Intrathyroidal FTC, < 4 cm (≥ 5%) Multifocal PTMC (≥ 4-6%) pN1 without extranodal extension, < 3 LN involved (2%) Minimally invasive FTC (≥ 2-3%) Intrathyroidal, < 4 cm, BRAF wild type* (≥ 1-2%) Intrathyroidal unifocal PTMC, BRAF mutated*, (≥ 1-2%) Intrathyroidal, nonpapillary, PV-PTC (≥ 1-2%) Unifocal PTMC (≥ 1-2%)

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Surgery – known side effect

- **Need for thyroid hormone replacement**
- **34% after hemithyroidectomy**
 - 1,240 pts, Kaiser Southern California, benign disease
 - Said et al World J. Surg 2013
- **100% after total thyroidectomy**

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Surgery – potential harms

- Major morbidity rate = (return to the operating room + medical complications)
 - 3.8%
 - NSQIP data by CPT code, 10,000 cases, 2005-2007 Goldfarb et al Annals Surg. Onc 2011
 - Hematoma
 - 1.25%
 - Nationwide Inpatient Sample data from 1998-2010, Weiss et al. Surgery 2014

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Surgery – potential harms

- **Vocal cord paralysis**
 - ~1% permanent & 10% temporary; or 8.2%
 - 1% is from Prospective multi institutional trial of nerve monitoring – highly select group
 - Mirallic et al, Surgery 2018
 - 8.2% is from SEER Medicare data on total thyroidectomy - broad surgical community
 - Francis et al, AAOHNS 2014

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Surgery – potential harms


- **Hypocalcemia (after total thyroidectomy):**
 - temporary **16%**, permanent **1.3%**
 - Meta analysis of **16 trials – selected surgeons**
 - Shan *et al* Laryngoscope 2012



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Should I be your surgeon?

- “High Volume” surgeons have better outcomes
 - 23 cases per year
 - NIS data 1993-2008. >871,000 patients
 - Loyo *et al* Laryngoscope 2013
- 20 cases per year is the cutpoint
- Kaiser northern California data 2008-2015. 10,548 patients
- Meltzer *et al*, JAMA Ota 2019
 - Absolute decrease in VCP and hypoparathyroidism for 10 vs 40 cases annually: 0.6% (1.6% → 1%)



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Which of these patients is eligible for hemithyroidectomy as first line management?

A. Patient with a contained 3cm papillary thyroid cancer and a cN0 neck **ELIGIBLE**

B. Patient with a contained 2cm papillary thyroid cancer and a cN1b neck **NOT ELIGIBLE**

With which of these patients might completion thyroidectomy be discussed?

A. On pathology: Multifocal disease in the resected lobe that is >1cm **DISCUSS**

B. On pathology: 3 central nodes positive, metastatic foci are all <5mm in size **LOW RISK**

C. On pathology: hob nail variant **DISCUSS**

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For tumors 1.5cm in diameter or smaller...

Active surveillance or Hemithyroidectomy?

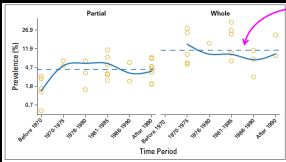



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Why should we consider active surveillance?

The subclinical reservoir

Meta analysis of autopsy studies demonstrating the prevalence of undiagnosed thyroid cancer in people who died of other causes:



No difference over time in the autopsy prevalence of thyroid cancer

Furuya-Kanamuri *et al.*, Journal of Clinical Oncology, 2016

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What does active surveillance entail?

Kuma Hospital, Japan

- **1 cm or less PTC, cN0**
- **Baseline:** ultrasound of thyroid and lateral necks, TSH, Tg, TPO Ab, Calcium
- **Protocol:**
 - Ultrasound thyroid and lateral neck 6 months after baseline, then annually
 - Labs as above
 - Laryngoscopy if voice change

Mem. Sloan Kettering


- **1.5cm or less PTC, cN0**
- **Baseline:** ultrasound of thyroid and lateral necks, TSH
- **Protocol:**
 - Ultrasound thyroid and lateral neck every 6 months for 2 years, then annually



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Who is eligible for active surveillance?


- Tumor / Neck US characteristics
- Medical team characteristics
- Patient characteristics



Brito et al Thyroid 2016

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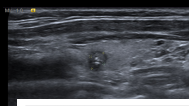
- Which of these patients would be a candidate for both active surveillance and a hemithyroidectomy using U.S.A. Guidelines?
 - A 32 year old woman who plans a pregnancy in the next few years and has a 9mm papillary thyroid cancer located in the middle of the affected lobe.
 - A 68 year old man with a 1.3cm thyroid cancer located in the lower right pole, up against the posterior border of the thyroid capsule.
 - A 50 year old woman with a 1.4cm papillary thyroid cancer in a background of other thyroid nodules and a strong family history of papillary thyroid cancer
 - A 56 year old man with a 1.1cm BRAF positive, PET positive papillary thyroid cancer



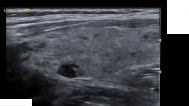
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Tumors


IDEAL



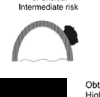
APPROPRIATE




Acute angle
Low-risk



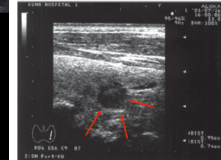
Nearly right angle or unclear
Intermediate risk



Obtuse angle
High-risk



INAPPROPRIATE



Brito et al Thyroid 2016
Upper Case pictures courtesy of Dr. Michael Tuttle
Lower case picture from Miyauchi et al Thyroid 2018, 28(1):23-31

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Medical Team

IDEAL

- Experienced thyroid cancer multidisciplinary management team
- High quality neck ultrasonography
- Prospective data collection
- Tracking/reminder system for follow up

APPROPRIATE

- Experienced endocrinologist or thyroid surgeon
- Neck ultrasound routinely available

INAPPROPRIATE

- Little experience with Thyroid cancer management
- Reliable Neck ultrasound not available

Brito et al Thyroid 2016

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Patient

IDEAL

- Age >60
- Agreeable to approach
- OK if surgery needed later
- Plans to come for visits
- Supportive family/HC team
- Competing illnesses

APPROPRIATE

- Age >18-59
- Strong family hx of papillary thyroid cancer
- Childbearing potential

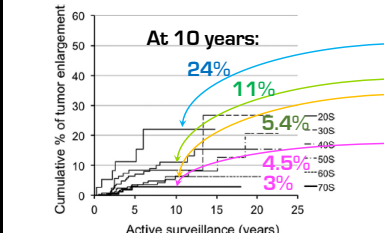
INAPPROPRIATE

- Age <18
- Unlikely to be able to follow up
- Not interested in monitoring approach
- Transplant candidates*
- Military service*
- Concerns about healthcare coverage*

Brito et al Thyroid 2016

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How likely is it my cancer will grow?

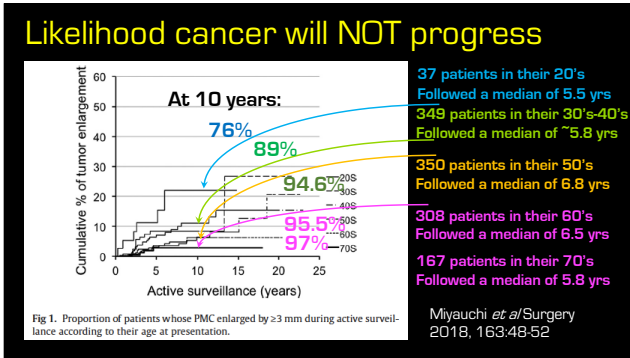


Age Group	Cumulative % of tumor enlargement
20s	24%
30s	11%
40s	5.4%
50s	4.5%
60s	3%
70s	3%

- 37 patients in their 20's Followed a median of 5.5 yrs
- 349 patients in their 30's-40's Followed a median of ~5.8 yrs
- 350 patients in their 50's Followed a median of 6.8 yrs
- 308 patients in their 60's Followed a median of 6.5 yrs
- 167 patients in their 70's Followed a median of 5.8 yrs

Miyauchi et al/Surgery 2018, 163:48-52

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How would we decide about surgery?

- Every visit is a re-evaluation of appropriateness
- Increase of 3mm in one dimension or doubling in volume
- Increased rate of change over time
- Biopsy proven positive lymph nodes
- Patient preference

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- Which of these patients would be a candidate for both active surveillance and a hemithyroidectomy using U.S.A. Guidelines?
 - A 32 year old woman who plans a pregnancy in the next few years and has a 9mm papillary thyroid cancer located in the middle of the affected lobe. **YES**
 - A 68 year old man with a 1.3cm thyroid cancer located in the lower right pole, up against the posterior border of the thyroid capsule. **NO**
 - A 50 year old woman with a 1.4cm papillary thyroid cancer in a background of other thyroid nodules and a strong family history of papillary thyroid cancer. **YES**
 - A 56 year old man with a 1.1 cm BRAF positive, PET positive papillary thyroid cancer. **YES**

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Will surgery relieve the burden of living with cancer?

<p>Kuma Monitoring Cohort 33%: worry "sometimes" (or more) about their cancer</p> <p>Davies <i>et al</i> JAMA Oto 2019</p>	<p>Treated low risk patients: >33%: somewhat or very concerned - long-term side effects / disease recurrence.</p> <p>Sawka <i>et al</i> Acta Oncol. 2016</p>
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Trading one kind of worry for another

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Questions? Discussion...

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