

Sommerschule, école d'été 2017

26.08.17

Workshop

«well-differentiated thyroid cancer»

PD Dr. Gerhard F. Huber, USZ

gerry.huber@usz.ch

historical background

„If a surgeon should be so foolhardy as to undertake a thyroid removal, every step of the way will be environed with difficulty, every stroke of his knife will be followed by a torrent of blood, and lucky will it be for him if his victim lives long enough to enable him to finish his horrid butchery. No honest and sensible surgeon would ever engage it.“

Gross, 1866

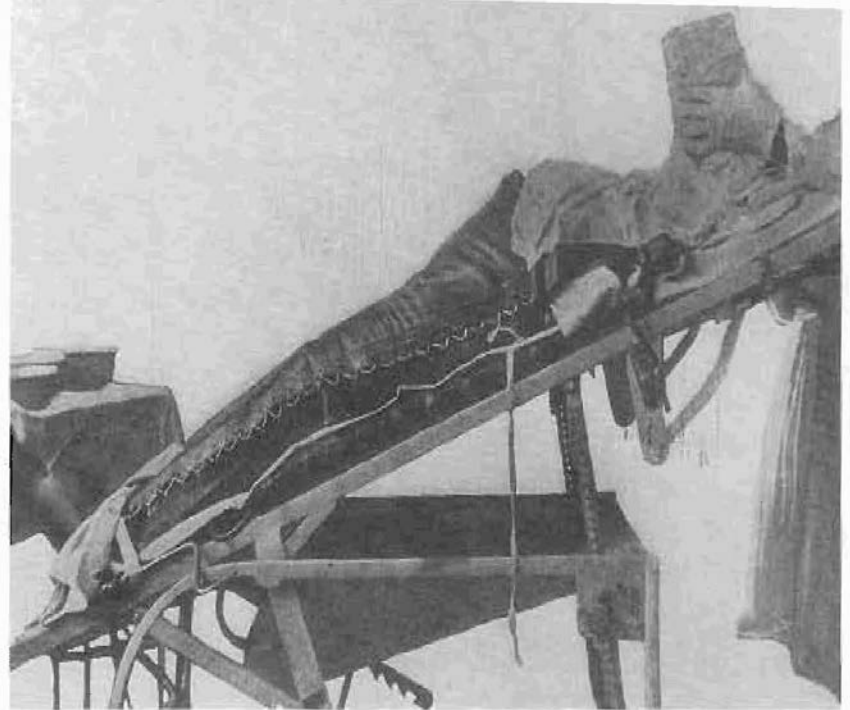
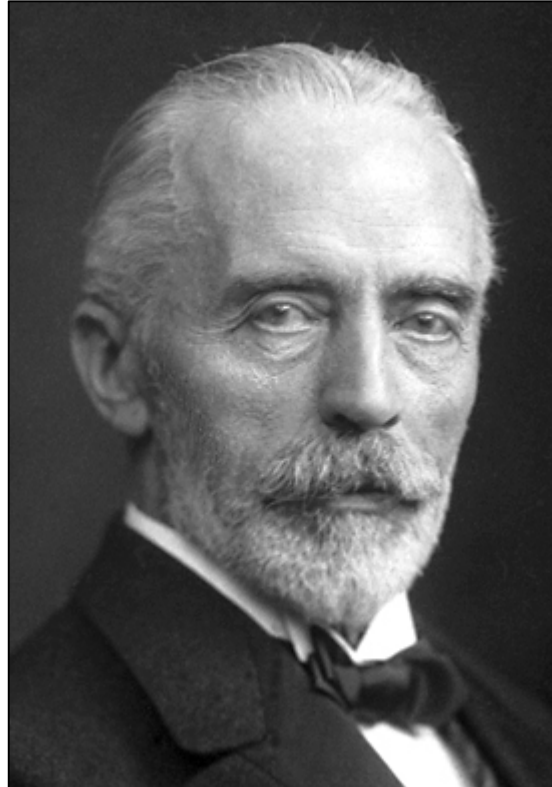


Figure 1-6. Criles pneumatic suit used to prevent shock in thyroid operations. (From Shedd DP: *Historical landmarks in head and neck cancer surgery*, Pittsburgh, 1999, American Head and Neck Society. With permission.)

historical background



Marie Bichsel before and 9 years after thyroid sx



recommended Guidelines

Well differentiated thyroid cancer

THYROID Volume 26, Number 1, 2016 © American Thyroid Association	SPECIAL ARTICLE
THYROID Volume 25, Number 7, 2015 © American Thyroid Association DOI: 10.1089/thy.2014.0460	SPECIAL ARTICLES
<h3>Management Guidelines for Children with Thyroid Nodules and Differentiated Thyroid Cancer</h3> <p>The American Thyroid Association Guidelines Task Force on Pediatric Thyroid Cancer</p> <p>Gary L. Francis,^{1,*} Steven G. Waguespack,^{2,*} Andrew J. Bauer,^{3,4,*} Peter Angelos,⁵ Salvatore Benvenga,⁶ Janete M. Cerutti,⁷ Catherine A. Dinauer,⁸ Jill Hamilton,⁹ Ian D. Hay,¹⁰ Markus Luster,^{11,12} Marguerite T. Parisi,¹³ Marianna Rachmiel,^{14,15} Geoffrey B. Thompson,¹⁶ and Shunichi Yamashita¹⁷</p>	

learning objectives

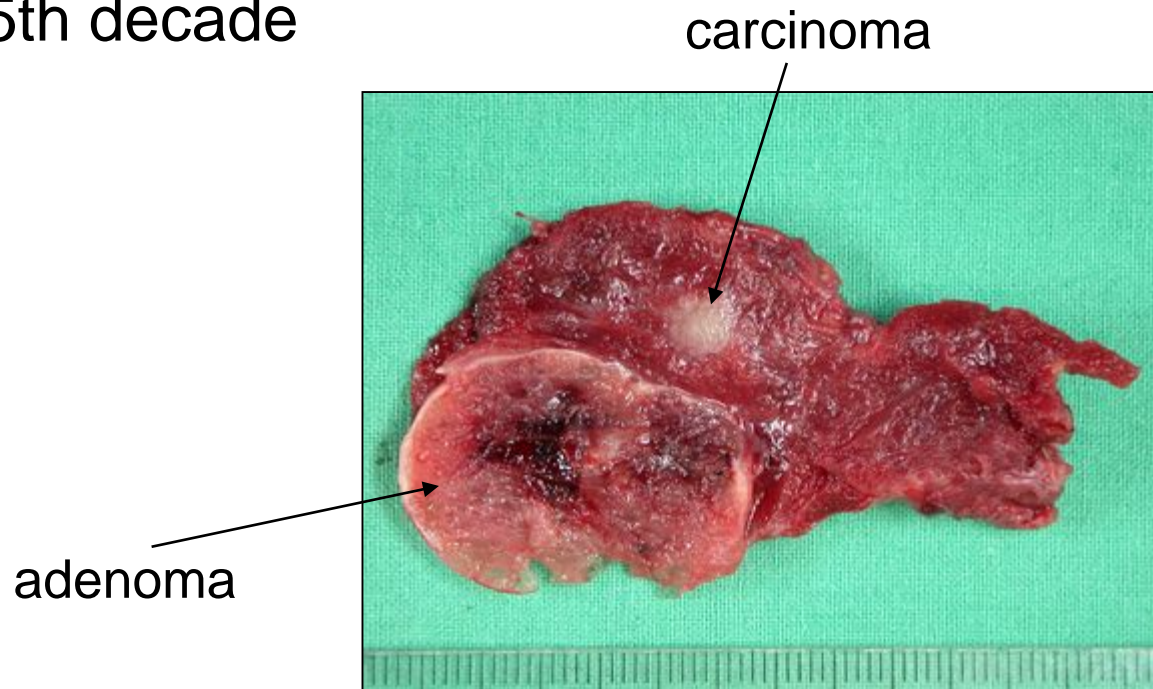
- focus on papillary thyroid carcinoma
- importance of US in FNAC in initial staging
- extent of initial surgery for PTC
- is there a role for initial «prophylactic» lymph node dissection?
- impact of initial surgery on outcome and subsequent surveillance
- surgeon's role in management of PTC recurrences
- limitations of radioiodine therapy & EBRT

thyroid cancer

- 1% of all malignant tumours
- 94% differentiated (85% papillary, 15% follicular)
- diagnostic workup
 - US & FNAC mandatory
 - MRI in case of + In (incl. mediastinum)
 - Calcitonin, CEA
 - diagnostic workup (exclude MEN IIa, IIb)

papillary thyroid cancer

- predisposing factors: RT, f:m = 2:1,
- 5-10% hereditary
- peak: 5th decade

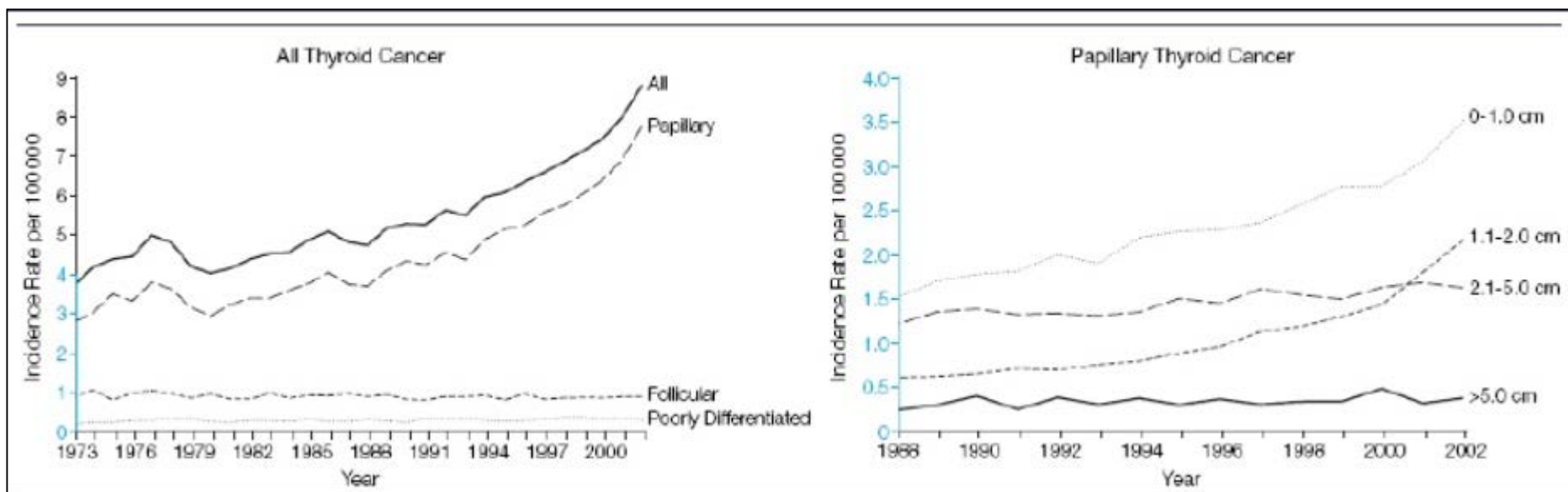




What is known so far?

- PTC incidence is rising
- survival remains excellent
- PTC <1cm is not associated with DSD
- recurrences are still common (~30%)
- 80 of recurrences occur within 10 yrs of initial dx
- in general, locoregional lymph node mets
- «recurrences» may actually represent persistent disease
- microscopic (occult) mets of PTC are the rule
- most micrometastases remain quiescent

rising thyroid cancer incidence is driven by PTC



Davies L. Increasing incidence of thyroid cancer in the United States, 1973-2002, JAMA 2006

prognosis

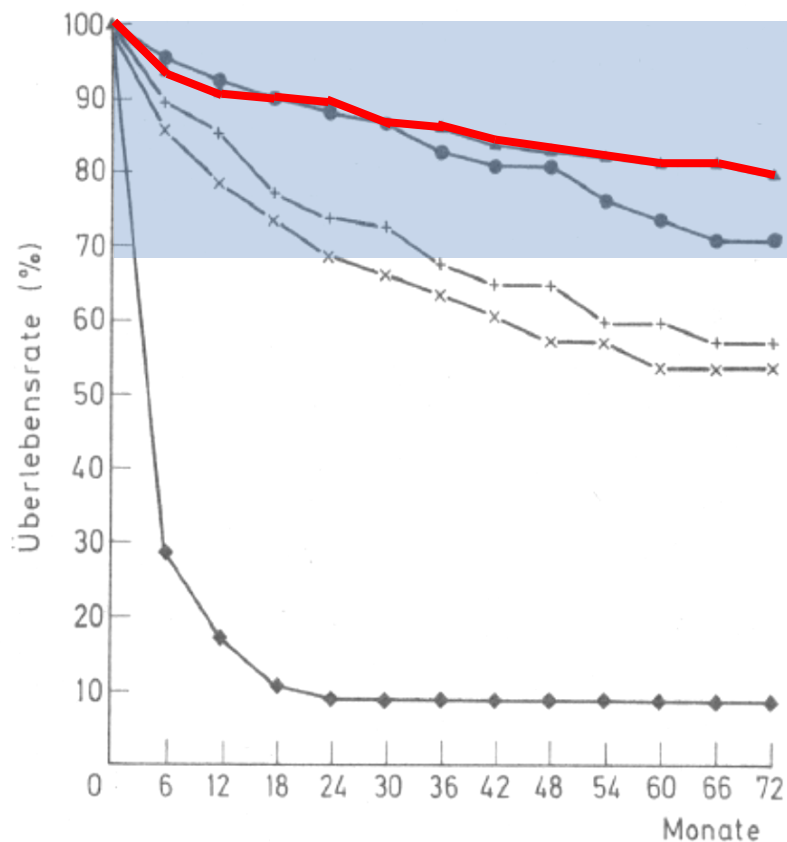


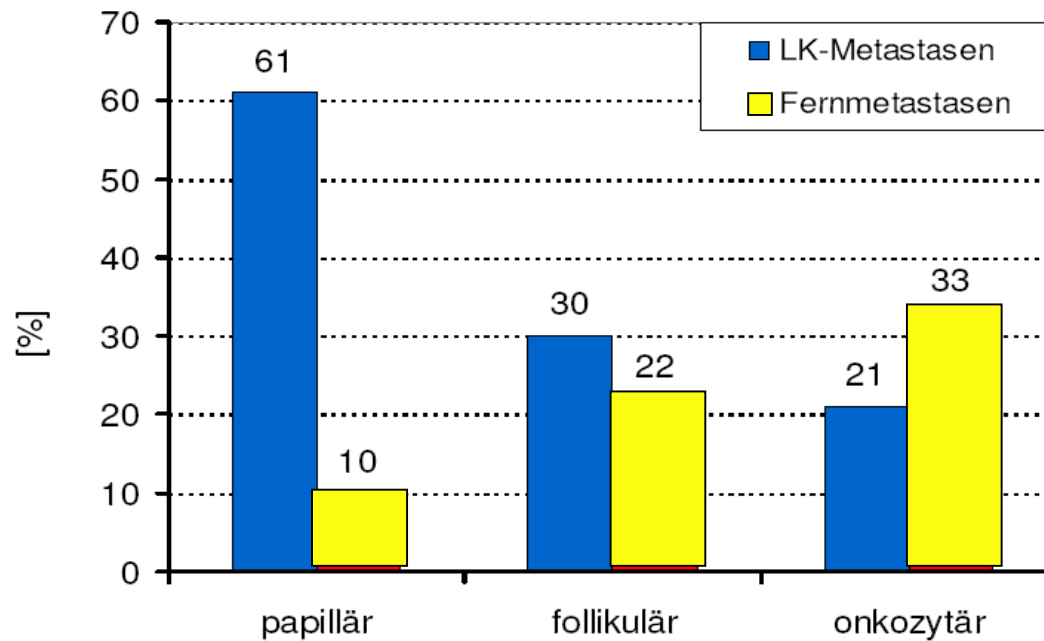
Abb. 8.6. Histologische Differenzierung und Überlebensrate beim Schilddrüsenkarzinom. Hauptsächliche Zelltypen: ● = follikulär (gut differenziert) ($n = 131$); ▲ = papillär ($n = 227$); + = follikulär (weniger differenziert) ($n = 106$); × = medullär ($n = 43$); ◆ = anaplastisch ($n = 77$). (Nach [5])

prevalence of lymph node metastasis

Relationship between tumor size and central lymph node metastasis			
Tumor size	Node metastasis (%)		Total
	Absent	Present	
≤ 1 cm*	82 (61.7)	51 (38.3)	133
1.1–2 cm	109 (40.8)	158 (59.2)	267
2.1–4 cm	73 (16.3)	205 (73.7)	278
> 4 cm	17 (21.0)	64 (79.0)	81
Total	281 (37.0)	478 (63.0)	759
*P < 0.0001.			

Relationship between tumor size and lateral lymph node metastasis			
Tumor size	Node metastasis (%)		Total
	Absent	Present	
≤ 1 cm*	51 (55.4)	41 (44.6)	92
1.1–2 cm	115 (46.6)	132 (53.4)	247
2.1–4 cm	81 (29.6)	193 (70.4)	274
> 4 cm	17 (21.0)	64 (79.0)	81
Total	264 (38.0)	430 (62.0)	694
*P < 0.0001.			

metastasizing pattern





exams of thyroid nodules

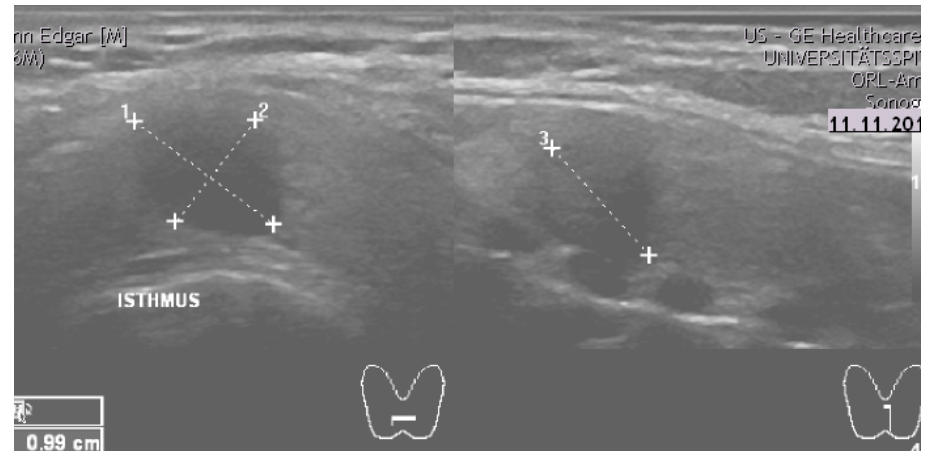
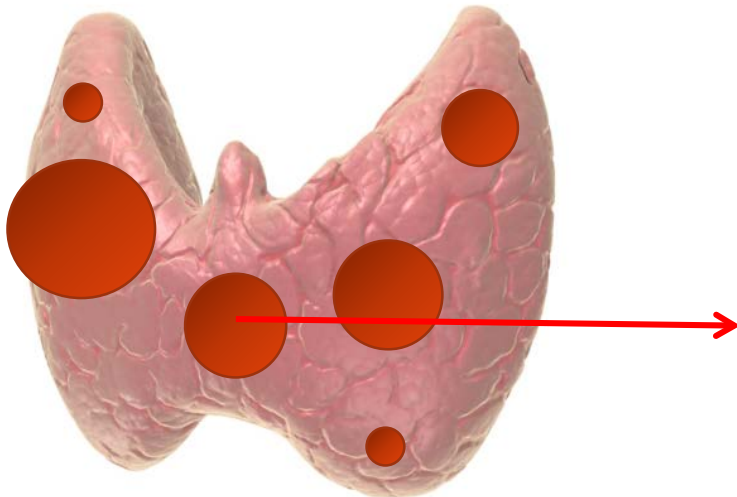
Risk factors depending on patient hx and clinical exam

- Family history
- Male sex
- <20y / >70y
- Solitary nodule >4cm / (rapidly growing nodule)
- Symptoms: Hoarseness, pain, Dysphagia, Dyspnoea
- Cervical metastatic disease
- Radiation exposure



exams of thyroid nodules

- **how** many nodes ?
- location
- criteria of malignancy
 - patient history / ultrasound / cytology





exams of thyroid nodules

which nodes have to be removed ?

- symptomatic node (?)
- node causing aesthetic impairment
- node > 4cm
- rapidly growing lymph node*
- retrosternal nodes

criteria for malignancy in US

TABLE 3 Independent risk of malignancy for different US criteria in Bethesda III nodules calculated with multivariable binary logistic regression

US criteria	OR (95 % CI)	<i>p</i>
Hypoechoic	4.8 (1.4–16)	0.013
Irregular margin	3.3 (1.1–10)	0.038
Microcalcifications	4.0 (1.3–12.4)	0.018

US ultrasound, *OR* odds ratio, *CI* confidence interval

Only criteria significantly associated with malignancy in univariate analysis are included

FNAC Classification

Bethesda diagnostic category		British Thyroid Association		American Thyroid Association
I	Non-diagnostic or unsatisfactory	Thy1	Non-diagnostic	Non-diagnostic/unsatisfactory
II	Benign	Thy2	Non-neoplastic	Benign 0-3%
III	Atypia of undetermined significance or follicular lesion of undetermined significance	Thy3a	Atypical features present	Indeterminate or suspicious for malignancy 15-40%
IV	Follicular neoplasm or suspicious for a follicular neoplasm	Thy3f	Follicular neoplasm suspected	Indeterminate or suspicious for malignancy
V	Suspicious for malignancy	Thy4	Suspicious of malignancy	Indeterminate or suspicious for malignancy 60-75%
VI	Malignant	Thy5	Diagnostic of malignancy	Malignant 97-100%

risk for malignancy

...to think about

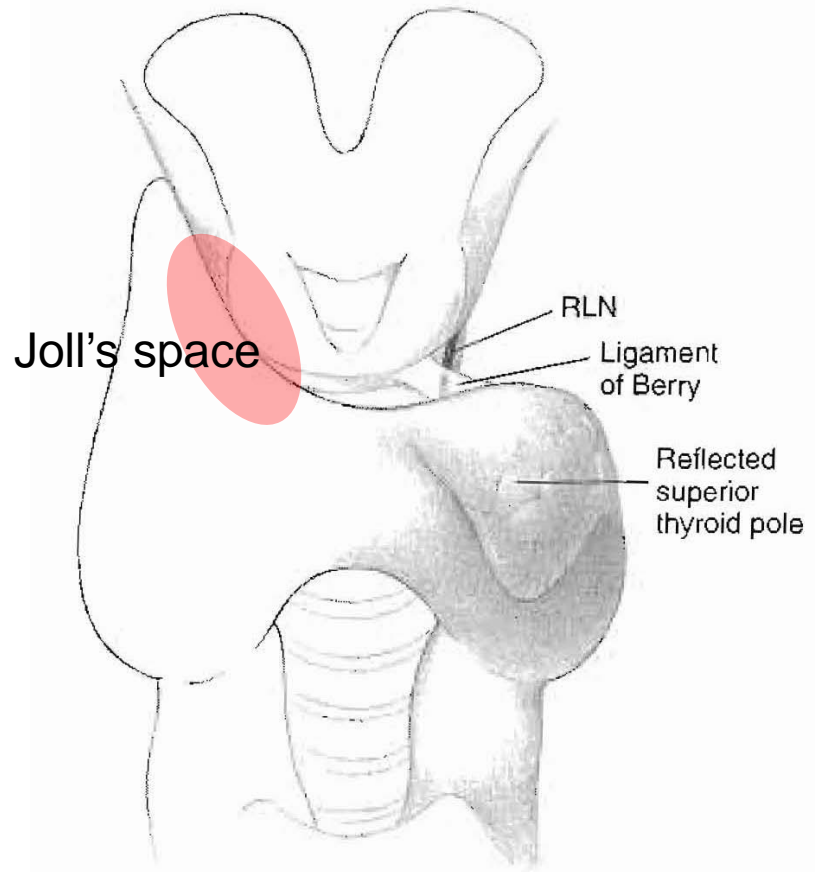
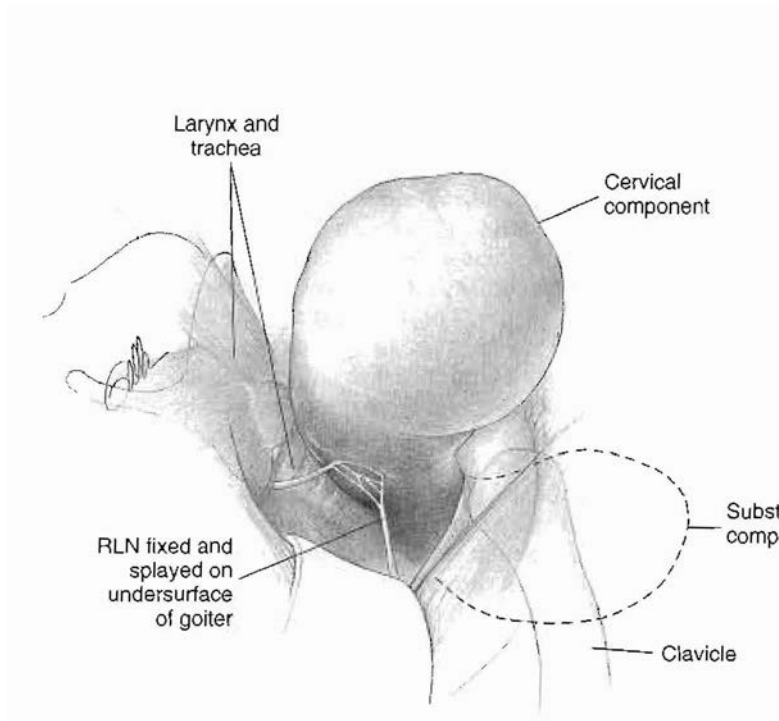


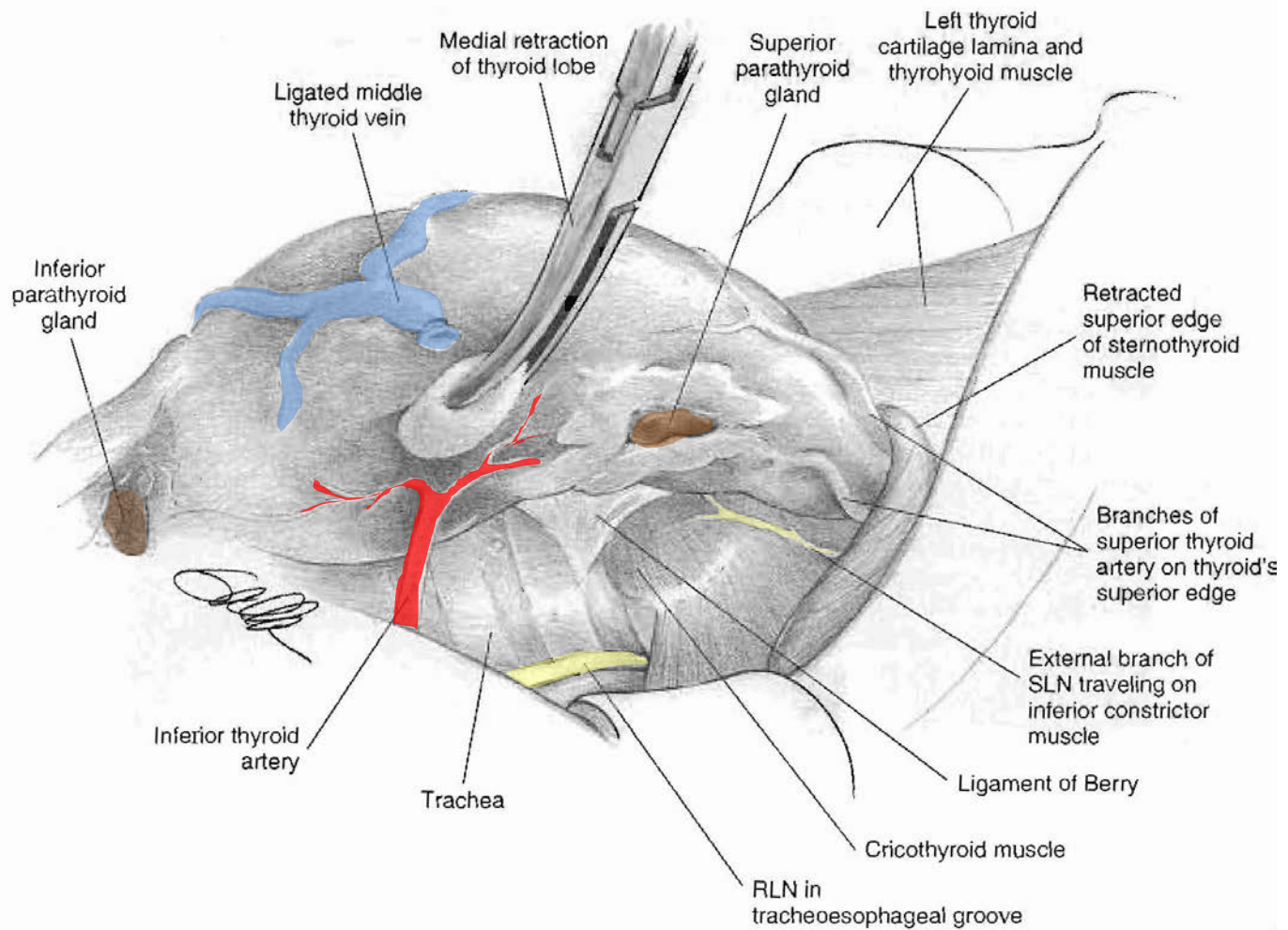
- H&N surgeon: “no matter how good I operate, eventually, after few years only half of my patients are still alive”
- thyroid surgeon: “no matter how bad I operate, eventually, after many, many years all of my patients are still alive”

anonymus

surgical procedures

- hemithyroidectomy
- total thyroidectomy
- isthmectomy
- ((subtotal thyroidectomies))





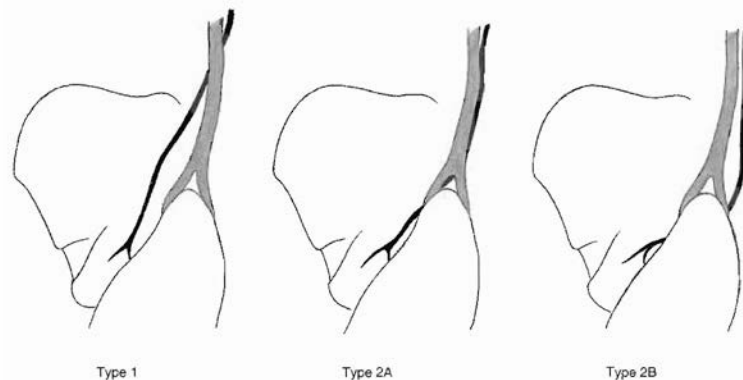
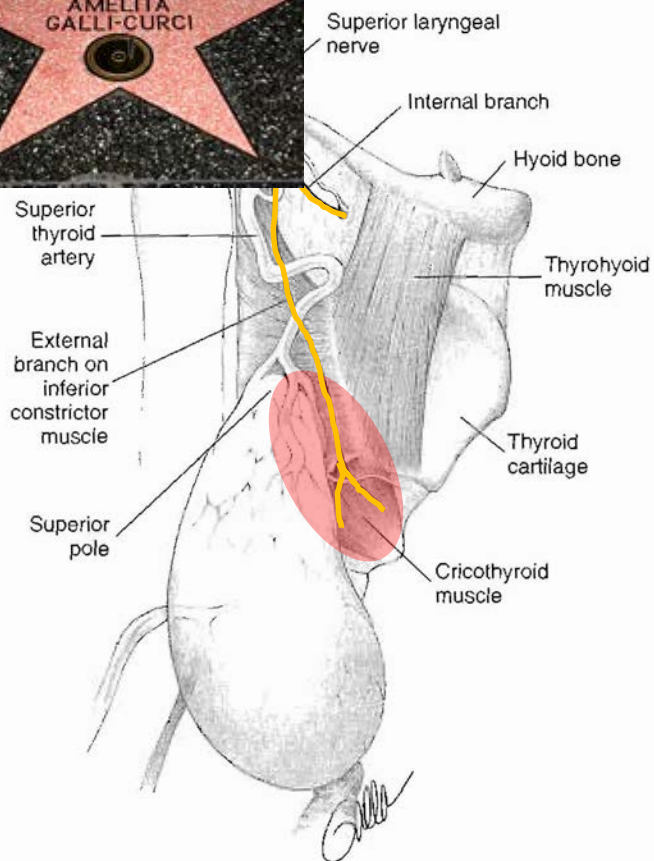
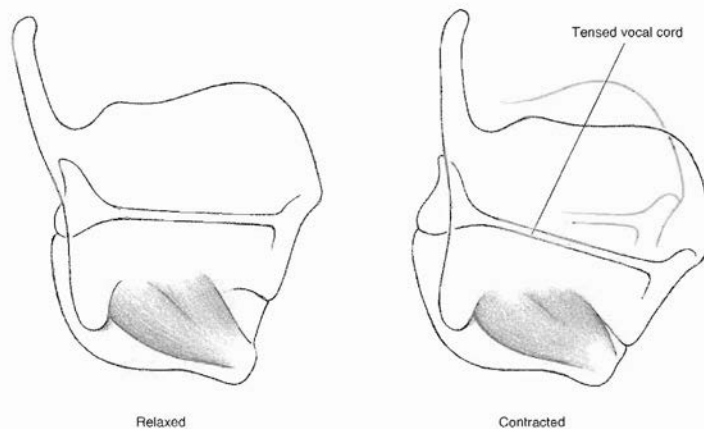


Figure 24-3. Surgical anatomical classification of EBSLN.



complications

	primary sx	revision sx
RLN palsy	0.5-3%	10-20%
hypocalcemia	0.1-1%	1-5%
hemorrhage	1-4%	1-4%
wound infection	1-2%	1-2%
lethality	0%	0-1%

complications

	n	transient %	permanent %
Seiler 1996	1815	k.A.	1.5
Joosten 1997	1556	6.6	1.6
Thermann1998	2100	k.A.	0.6
Steinert 1998	725	2.6	0.7
Nielsen 1998	457	2.7	0.7
Bergamschi 98	604	3.1	0.7
Röher 1998	4742	2.4	0.6
Steinmüller 2000	1727	3.9	0.6
total	13726	2.6	0.7

recent / future developments

- minimally invasiv Sx
- Harmonic scalpell
- robotic approaches
- thermoablation

Up to 39% of re-operations for thyroid cancer are a direct result of incomplete initial surgery

Table IV. Preventability of reoperation in 72 patients with persistent or recurrent PTC

	<i>No. of Patients</i>
I. Group 1 (persistent PTC)	17
A. Reoperation preventable	14 (82%)
1. Inadequate preoperative imaging*	12 (71%)
a. Ultrasonography not performed before surgery	4
b. Ultrasonography of thyroid performed without assessment of levels II to V	8
2. Incomplete initial surgery	11 (65%)
a. Known lateral neck disease not dissected	3
b. Node plucking (from lateral neck) at initial surgery with persistent disease in the same compartment	2
c. Incomplete resection of the primary thyroid neoplasm	2
d. Bulky central compartment disease not completely resected	4
B. NCCN guidelines not followed	11 (65%)
1. Less than total or less than near-total thyroidectomy performed	8
2. Gross lymph node metastases but neck dissection not performed	6†

II. Group 2 (recurrent PTC)	55
A. Reoperation preventable	27 (49%)
1. Incomplete initial operation	14 (25%)
a. Node plucking at initial surgery with recurrence in the same compartment	9
b. Gross lymph node metastases not removed	5
2. Inadequate TSH suppression (>0.5 µU/mL)	17 (31%)
B. NCCN guidelines not followed	22 (40%)
1. Less than total or near-total thyroidectomy performed	4
2. Completion total thyroidectomy not performed	1‡
3. Gross lymph node metastases but neck dissection not performed	17

Kouvaraki, Preventable reoperations for persistent and Recurrent papillary thyroid carcinoma. Surgery 2004

Impact of PTC regional metastatic disease

n=5123 / DTC

Occurrence of Lymph Node and Distant Metastases in Patients with Differentiated Thyroid Carcinoma, Demonstrating Univariate and Multivariate ORs of Dying from Thyroid Carcinoma with 95% CIs										
Metastases	Cases		Controls		Univariate analysis ^a		Multivariate analysis ^b		Multivariate analysis ^c	
	Total	%	Total	%	OR	95% CI	OR	95% CI	OR	95% CI
Lymph node metastases ^d	196	33	127	21	2.5	1.6–4.1	3.2	1.7–6.0	1.9	1.1–3.6
No lymph node metastases ^d	116	19	179	30	1.0	Reference	1.0	Reference	1.0	Reference
Initial distant metastases ^e	146	25	29	5	6.6	4.1–10.5	5.0	2.9–8.5	2.9	1.2–7.4
No initial distant metastases	427	72	547	92	1.0	Reference	1.0	Reference	1.0	Reference
Late distant metastases ^f	394	66	93	16	15.3	9.8–24.0	14.8	8.5–25.6	14.7	9.0–24.0
No late distant metastases	122	21	456	77	1.0	Reference	1.0	Reference	1.0	Reference

OR: odds ratio; 95% CI: 95% confidence interval.
The percentages were calculated from the total number of cases and controls, including those with incomplete information.
^a Adjusted for matching variables (age, gender, and calendar period).
^b Adjusted for histopathologic subgroup (follicular thyroid carcinoma and papillary thyroid carcinoma) and tumor differentiation.
^c Adjusted for TNM stage.
^d Included only those patients in whom lymph node surgery was performed; 572 patients lacked information regarding lymph node status or surgery.

Lundgren CI et al. Clinically significant prognostic factors for differentiated thyroid carcinoma: a population-based, nested case-control study. Cancer. 2006 Feb 1;106(3):524-31



Surgeon's role in optimizing PTC care

- management over the life span
- personal investment in long term outcome
- prevent recurrences: survival impact, cost, risk of reoperation, emotional toll
- partner with endocrinologist, nuclear medicine specialist, pathologist, sometimes radiation oncologist (high risk patients)



Surgeon's role in optimizing PTC care

- for PTC>1cm
- total thyroidectomy: multilocality, RAI, follow TG
- clear all clinically and sonographically detectable adenopathy @ initial surgery
- surgeon's responsibility to obtain high-quality pre-op US for all FNA+ PTC
- prophylactic «initial lymph node dissection»
- concept of compartment-orientated LN-Dissection



2015 ATA guidelines

- Recommendation 36C. Thyroidectomy without prophylactic central neck dissection may be is appropriate for small (T1 or T2), noninvasive, clinically node-negative PTC (cN0) and for most follicular cancers.

(Strong Recommendation, Moderate-quality evidence)



support for initial CND in PTC

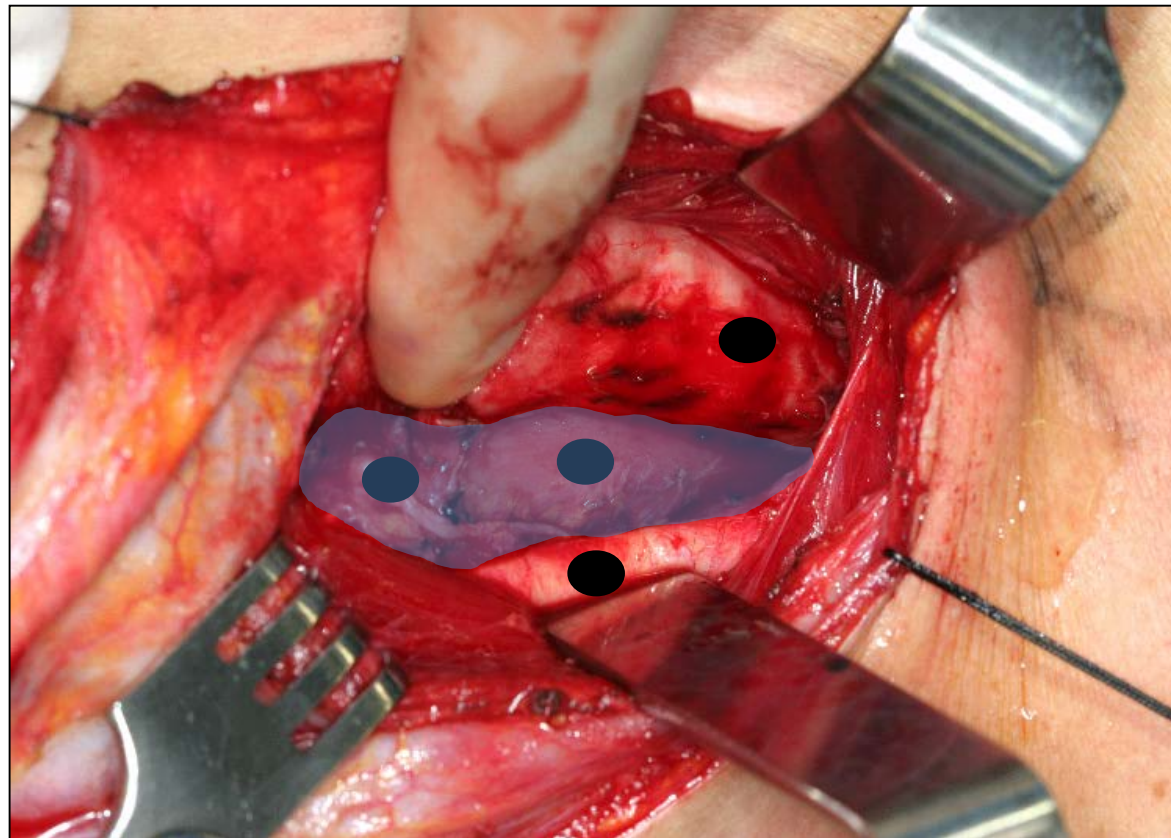
- Goteborg study: 195 PTC patients prospectively analysed patients
- Mean f/u 13 yrs
- routine, meticulous bilateral central neck clearance
- RAI used thriftily
- much lower DSM compared to controls

City of the study	Study period	No. of patients	Stage III (% of patients)	Lymph node dissection	¹³¹ I treatment (% of patients)	Median follow-up (years)	Death due to thyroid cancer ^a (%)
Helsinki [22]	1956–1979	199	19	No information	?	11.5	11.1
Göteborg	1970–1989	195 ^b	37	Microdissection	6	13	1.6
Bergen [14]	1971–1989	167	28	“Node-Picking”	41	10	8.4

^aPatients with distant metastases at diagnosis excluded.
^bPatients with tumors less than 5 mm are excluded.



CND technique





CND: Technique and complications

- space confined by hyoid, thoracic inlet, carotid sheaths
- auto-transplantation of inferior parathyroid gland (**Cave: auto-transplantation of tumor affected LN!**)
- ipsilateral CND generally sufficient – no additional benefit of bilateral in terms of post-op TG
- permanent hypoparathyroidism ~3%
- permanent RLN palsy (0.5%)
- temporary RLN dysfunction higher
- no Δ in long-term complication rate when performed by experienced surgeons



radioactive-iodine: Myth & truth

- **Myth:** RAI “cleans up” residual disease after surgery
- **Truth:** ineffective in treatment of macroscopic remnants and nodes
- post-op RAI mainly for ablation of residual normal thyroid tissue => set TG to 0
- RAI is no substitute for (excellent) = complete surgery





RAI and lymph node mets of PTC

- PT reduced ability to take up RAI
- 25% of WDTC are **initially** resistant to RAI
- cells in many nodal mets of PTC do not express NIS
- RAI no effect on nodal mets >1cm in diameter



Sx vs RAI

- most PTC patients in the low risk category
 - for patients undergoing complete initial surgical treatment, RAI shows no additional benefit
 - in patients without complete surgical clearance, post-OP RAI will not improve situation, these patients need further Sx
-
- RAI benefits a small subset of high-risk PTC patients
 - reasonably well effect on pulmonary mets
 - poor impact on lymph node disease

What is of importance?

- **RAI negative** thyroid cancers often also **not EBRT sensitive**
- often surgical treatment as the only curative treatment option (consider «extended» operation)



Take home messages:

- US is essential: **ALL** cancer cases
- clear the neck of disease
- **do it right the first time!**
- no node picking; **compartment dissection**
- consider routine initial “prophylactic” ipsilateral Level VI dissection for FNA positive PTC>1cm
- have **realistic expectations** for what **RAI** can do
- be vigilant for recurrences: **US and TG**