

THE THYROID NODULE

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THE THYROID NODULE (Abstract): Nodular disease of the thyroid is common; however, malignancy of the thyroid occurs in only 0.004% of the American population annually (12,000 new cases per y). About 5% of thyroid nodules are malignant; the remainder represent a variety of benign diagnoses, including colloid nodules, degenerative cysts, hyperplasia, thyroiditis, or benign neoplasms. A rational approach to management of a thyroid nodule is based on the clinician's ability to distinguish the more common benign diagnoses from malignancy in a highly reliable and cost-effective manner. A comprehensive history and physical examination provides the foundation for decision making in the management of thyroid nodules. The diagnosis algorithm includes lab tests, ultrasound exam, scintigraphy and fine-needle aspiration biopsy. This paper also presents the technique of thyroidectomy and the risks factors for recurrent nerve palsy. It is also discussed the indications of the total versus subtotal thyroidectomies in different thyroid pathology. Conclusions: Thyroid nodular is still a frequent disease. All "cold" nodules are potentially malignant. Unilateral isthmo-lobectomy or bilateral thyroidectomy are the treatments of choice. Careful search to identify recurrent nerve is advisable, and mandatory in bilateral disease. Neuromonitoring may be promising tool to prevent the recurrent nerve palsy. Bloodless surgery reduces the risk of nerve lesion.

KEY WORDS: THYROID NODULAR DISEASE, THYROIDECTOMY, RECURRENT NERVE PALSY

Thyroid nodular disease

- How did it begin? : History
- Is it frequent? : Epidemiology
- What are the complaints? : Symptoms of nodules
- Is it dangerous? : Anatomic-Pathologic findings
- How to detect? : Diagnostic methods
- When to operate?: Indications for surgery
- How to operate? : Types of surgery
- To speak or not to speak? : Postoperative problems
- What to do about it? : Prevention of complications
- Specific items: I* treatment; Retrosternal goiter
- Take home message: Conclusions

History

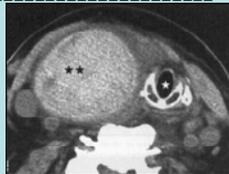
Theodor Kocher (Bern 1841- Bern 1917)
Professor of Surgery in 1872
Performs first thyroidectomy in 1876
Adheres to Lister's principles of asepsis
Reduces mortality from 16% to 0.5%
Observes cretinism after total thyroidectomy
Obtains Nobel Prize in 1909

Epidemiology of Thyroid Nodular Disease

- Prevalence:- palpable : 4-7% of population
- detected at autopsy or imaging: 20 – 60% of population!
- Types: - one or some nodules in thyroid
- multinodular goiter (MNG)
- Sex ratio: 4 ♀ / 1 ♂
- Importance: ± 10 % are malignant

Symptoms of nodular thyroid disease

- Cause: Thyroid enlargement
 - visible
 - invisible (too small / retrosternal)
- Results:
 - Compressive symptoms
 - Dyspnoea (trachea) *
 - Difficult swallowing (oesophagus)
 - Hoarseness (recurrent nerve) **
 - Horner syndrome (cervical nerve) ***
 - Venous (internal jugular or innominate vein)
 - Cosmetic complaints



*Gitsoos et al. BMJ 1996; 312: 484
** Abboud et al. J. Laryngol. Otol. 1999; 113: 473-4
*** Van Doorn & Kranendonk. Neth. J. Med. 1996; 48: 216-9.

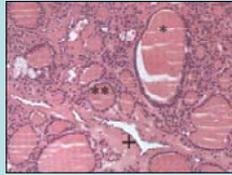
Risk of malignancy in thyroid nodules

- ± 5% in MNG
 - mostly in dominant nodule
 - mostly in longstanding disease (> 10 years)
- ± 10 % in solitary nodule:
 - > early diagnosis necessary!

Pathology of thyroid nodules

- Cystic and mixed cystic: 19 and 12 %*

- Follicular adenoma('s):
50 %
(solitary or in MNG)



- Papillary/Follicular carcinoma: 10 %
- Hürtle cell adenoma: 2 %
- Other: 8 %

*Ashcraft & Van Herle. Head & Neck Surg. 1981, 3:216-230 & 297-322.

Thyroid function in nodular disease

- Euthyroidism : 92,5 % (normal T4 / T3 / TSH)
- Hyperthyroidism : 7,5 % (T4 ↑ / T3 ↑ / TSH ↓)

(L.P. Bron & C.J. O'Brien. Br. J. Surg. 2004, 91: 569-74)

Diagnostic imaging in thyroid nodular disease

- Anatomical
 - Ultrasound
 - CT scan
 - [MRI]
 - >tumour size / tumour location / compression of organs / possible pathologic lymph nodes
- Functional
 - Scintigraphy I¹³¹ or Th²⁰¹
 - > "hot", "warm" or "cold" nodule!

Diagnostic puncture of solitary nodule or suspicious nodule in MNG

- F(ine) N(eedle) A(spiration) B(iopsy)
 - generally performed under ultrasound
 - Sensitivity: 90-95% / Specificity: 70-80%
- Three results: positive / negative / inconclusive
- Excellent technique, but:
 - sometimes bleeding !!
 - possibly false negative !!
 - every "cold" nodule with negative FNAB should have scrupulous follow-up !!
 - if inconclusive → risk of malignancy doubled (± 20%)

Treatment



Is there any indication for conservative treatment in thyroid nodular disease? *

- Yes: if nodules are
- small (< 2cm Ø)
 - functional (not "cold" nor "hot", but "warm" at scintigraphy)
 - clearly negative at FNAB (not + or inconclusive)
 - slowly growing
 - not compressing other organs
 - esthetically accepted by patient

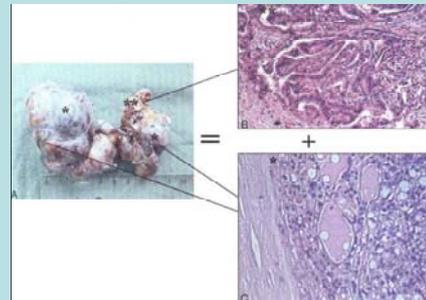
- How: low dose levothyroxine (50-100 ug/day)
- reduces TSH production
 - diminishes thyroid stimulation, hence nodular growth

* Berghout et al. Lancet 1990, 336: 193-197.

When is SURGERY indicated for Nodular Thyroid Disease?

1. Suspected or proven malignancy in a solitary nodule or in a dominant nodule of MNG
2. Thyreotoxicosis (treatment-resistant hyperthyroidism)
3. Significant compressive symptoms
4. Retrosternal location
5. Inacceptable cosmetic deformity (e.g. larger tumours!)

A: Multinod.goiter B: Papillary cancer



C: Follicular adenoma

Type of surgery in nodular disease

Different for

- solitary nodule
- multinodular goiter

Surgery for solitary thyroid nodule

- in one lobe: total lobectomy (TL)
(= hemithyroidectomy)
--> includes isthmus !
- in isthmus:
 - small (< 2 cm) but cosmetically important :
isthmectomy
 - larger (> 2 cm) and encroaching on one of the lobes: isthmolobectomy (TL)

Surgery for multinodular disease

- confined to one lobe (or with not suspicious small nodule(s) in other lobe < 2cm Ø)
→ **isthmolobectomy**
[NEVER PARTIAL or SUBTOTAL LOBECTOMY: recurrence rate is 15-42%]
- present in both lobes (bilateral nodules > 2cm Ø)
→ **total thyroidectomy** or **subtotal thyroidectomy** =
TL on most affected site + STL on other side
→ still controversial issue !

* Rojdmarm & Jarhult Eur J. Surg. 1995, 161: 725-7.

Why is there controversy in treatment for MNG?

- Rates of complications of surgery variable!

Acute complications of thyroid surgery (1)

- Bleeding (frequency 3%)
 - superficial:
 - careful dissection of right planes (beware of superficial and jugular veins)
 - careful positioning of suction drains
 - deep:
 - double suture or transfixing suture of main arterial trunks (superior and inferior thyroid artery)
 - limited and careful use of electrocoagulation
 - eventual Valsalva manoeuvre (PEEP to 30 mmHg)

Acute Complications of thyroid surgery (2)

- Respiratory distress
 - after extubation in tracheomalacia
 - trachea collapse and insufficient respiration
 - prevention: controlled extubation on next morning in case of reduction of Ø of trachea more than ¾ of circumference
 - treatment: tracheotomy

Postoperative Complications of Thyroid Surgery

Nervous lesions!

Superior and recurrent laryngeal nerve

- Vagal nerve
 - Superior laryngeal nerve
 - internal branch
 - external branch
 - Inferior (or recurrent) laryngeal nerve
- Right recurrent nerve
 - Branches off below subclavian artery
 - Climbing behind common carotid artery
 - Lying in tracheo-oesophageal groove
 - Enters larynx at posterior cricothyroidal junction

Left Recurrent Nerve (anatomy)

- Left Recurrent Nerve
 - > below aortic arch
 - under aortic arch cranially → trachea
 - in tracheo-oesophageal groove, then into trachea
- Recurrent nerve function
 - Intrinsic laryngeal muscles
 - Except:
 - » Cricothyroid muscle
 - » Mucosa distal of vocal cords
 - Aberrant position
 - Adherence / elongation in cases of goiter

Postoperative Complications of thyroid surgery (1)

- Recurrent nerve lesion
 - elongation
 - minimal fibre section or coagulation lesion
 - vocal cord paresis (= heals within 6 months)
 - total section → vocal cord paralysis
 - unilateral: partial or total compensation of voice deficit possible
 - bilateral: permanent voice deficit (various degrees dependent on logopedic treatment)

Frequency dependent on size of nodular disease: 1-7%

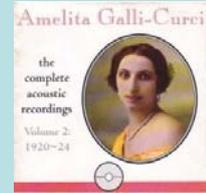
* Thomusch et al World J Surg. 2000, 24: 1335-41.
Hockauf & Sailer. Head Neck Surg, 1982, 4: 380-4.

Postoperative Complications of thyroid surgery (2)

- Lesion of external branch of the superior laryngeal nerve
 - lesion frequency 0,1 – 2,6% depending on anatomy*
 - higher frequency in large upper pole MNG
 - effect: paralysis of cricothyroid muscle
 - voice deficit of high tones
 - quick tiredness of speech



* Lorre et al. Am Otol Rhinol Laryngol. 1998, 107: 1015-22.
Lennquist et al. Surgery 1987, 102: 999-1008.



EBSLN ?

In 1935, « the surprising voice is gone forever: she had specter of a ghost replaced the velvet softness » After thyroidectomy (170gr), her vocal registry dramatically diminished... She had to give up singing.

Postoperative Complications of thyroid surgery (3)

- Hypoparathyroidism
 - temporary (< 6 months): in case of excision or lesion of most but not all parathyroids: present in ± 6% *
 - permanent: only in case of total extirpation of all parathyroids: present in ± 1,5% *
- only in bilateral thyroid operation

* Thomisch et al. World J Surg 2000, 24: 1335-41.

Importance of complications in discussion on MNG surgery

- Question: Is there higher frequency of recurrent nerve palsy or hypothyroidism in total vs subtotal thyroidectomy?
- Answer:
 - dependent on expertise (and surgical technique) of surgeon : controversial !!*
 - variable in literature reports (0 – 14%)
 - early reports (before 1990) in favour of TL + STL
 - later reports (after 1990) in favour of TT
 - first in USA
 - later also in Europe / Australia **

*pro: Sosa et al. Ann Surg. 1998, 228: 320
contra: Thomusch et al. World J Surg. 2000, 24: 1335-41.
** Bron & O'Brien. Br. J. Surg. 2004, 91: 569-574.

Complications in the series of Bron & O'Brien (n=834)(BJS 2004)

Table 3 Complications of total thyroidectomy

	Indication for surgery			All patients
	MNG	Toxic MNG	Graves' disease	
Wound infection	4	0	0	4 (0.5)
Haemorrhage	11	4	0	15 (1.8)
RLN palsy				
Temporary	15	3	1	19 (2.3)
Permanent	8	0	1	9 (1.1)
Hypoparathyroidism				
Temporary	106	8	6	120 (14.4)
Permanent	19	1	0	20 (2.4)
Total	163	16	8	187 (22.4)

Values in parentheses are percentages. MNG, multinodular goitre; RLN, recurrent laryngeal nerve.

Recurrent Nerve lesions:

Effects of nerve exposure and resection (Wagner & Seiler, BJS 1994)

Table 3 Recurrent laryngeal nerve palsy after subtotal and total lobectomy: effect of nerve exposure

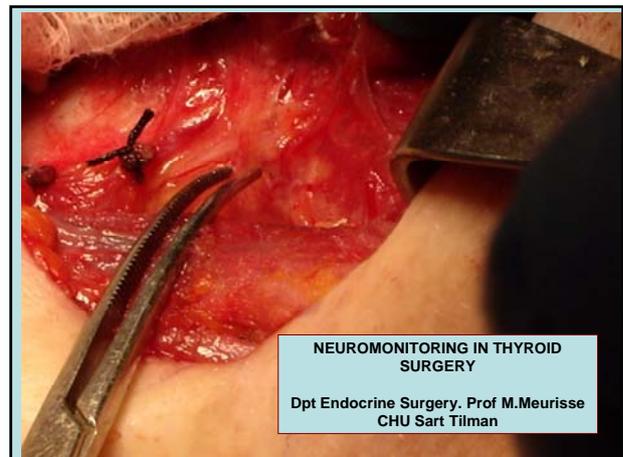
	Nerves at risk			P*
	Exposed	Not exposed	Total	
	Subtotal lobectomy	558 (49.5)	569 (50.5)	
RLN palsy rate				
Transient	11 (2.0)	10 (1.8)	21 (1.9)	n.s.
Permanent	8 (1.4)	4 (0.7)	12 (1.1)	
Total	19 (3.4)	14 (2.5)	33 (2.9)	
Total lobectomy	318 (91.6)	29 (8.4)	347 (100.0)	
RLN palsy rate				
Transient	10 (3.1)	4 (14)	14 (4.0)	<0.01
Permanent	12 (3.8)	2 (7)	14 (4.0)	
Total	22 (6.9)	6 (21)	28 (8.1)	

RLN, recurrent laryngeal nerve. Values in parentheses are percentages. *p, test with Yates' correction. †P<0.001, (subtotal versus total lobectomy) n.s., not significant

Recurrent Nerve lesions:

Effects of nerve exposure and resection (Wagner & Seiler, BJS 1994)

- Conclusions:
 1. Total thyroidectomy has a fourfold incidence of Recurrent Nerve Palsy vs subtotal resection
 2. Exposure of the nerve reduces lesions, especially in total resection



Risk factors recurrent nerve lesion

- Friedrich T. et al. Incidence of damage tot RLN in surgical therapy of various thyroid gland diseases – a retrospective study. Zentrabl Chir 1998, 123(1):25-9.
- N= 725
 - RLN paresis/paralysis: 7,6%
 - Paralysis (>6 months)
 - » Euthyroid nodular goiter: 2,1%
 - » Recurrent goiter: 11,7%
 - » Thyroid carcinoma: 10,1%
 - Exposure vs. Non-exposure
 - RLN paresis: significant difference
 - Experience
 - Residents (6,7%) vs
 - Registrars and consultants (0%)



Most important factor for RLNPalsy: REDO's.

	Temporary %	Permanent %
Primary benign N=359	17 (4%)	1 (0.2%)
T Cancer N= 103	3 (2%)	1 (0.7%)
Graves N=46	11 (12%)	1 (1.1%)
Redo N=29	4 (10.8%)	3 (8.1%)

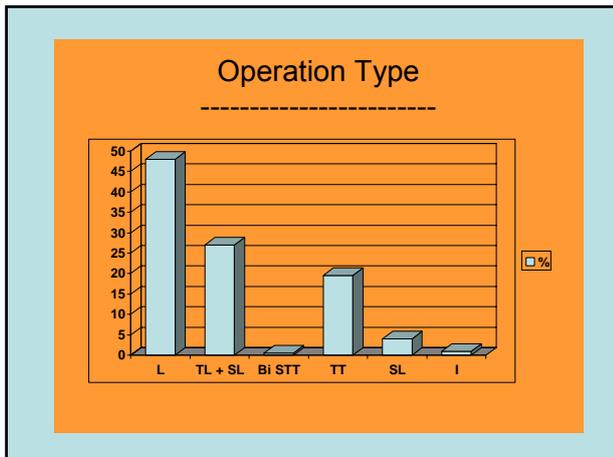
Recurrent laryngeal nerve palsy after thyroidectomy with routine identification of the recurrent laryngeal nerve.
Chiang FY et al . 2005; *Surgery* 137 (3).

Own Series of Thyroid operations

- N = 154
 - Men: n = 31
 - Women: n = 123
 - Age: 18 – 84 yr (mean: 60 yr)
- Not followed: 4

Anatomopathologic Results

- N = 150
 - Functional adenoma: n = 40 (27%)
 - Not-functional (cyst): n = 3 (2%)
 - Unilateral multiple nodules: n = 36 (24%)
 - MNG: n = 46 (30%)
 - Hashimoto: n = 3 (2%)
 - Graves: n = 4 (3%)
 - Riedel: n = 1 (0,5%)
 - Hyperplasia: n = 6 (4%)
 - Papillary Thyroid CA: n = 10 (7%)
 - Medullary Thyroid CA: n = 1 (0,5%)



Results: recurrent nerve lesion

- N = 154 (own series)
 - No lesion: n = 147 (95%)
 - Unilateral paresis: n = 5 (4%)
 - Bilateral paresis: n = 1 (0,5%)
 - Unilateral paralysis: n = 1 (0,5%)
- Paresis : means recovery within 6 months

Patients with recurrent nerve lesion

- Operation
 - Total lobectomy : n = 5
 - Total thyroidectomy : n = 2 (MNG, Thyroid Ca)
- APD
 - Functional adenoma: n = 1
 - Unilateral multiple nodules: n = 2
 - MNG: n = 1
 - Hashimoto: n = 2
 - Papillary Thyroid CA: n = 1
- Recurrent nerve
 - Unilateral paresis: n = 5
 - Bilateral paresis: n = 1
 - Unilateral paralysis: n = 1

General factors determining extent of resection: personal views

1. Nodular disease completely invading both lobes : **best TT** (STT would leave nodular adenomatous tissue in place)
2. Dependence on hormone substitution of **non compliant patient** is risky [whether due to financial problems (absence of drug reimbursement) or compliance problems (migrant population / availability of medication)] : **best STT**
3. General surgery teams with insufficient or **borderline expertise** in endocrine surgery (< 50 thyroid op./year) * [controversial]: **best STT**
4. **Specific expertise of surgical team** in endocrine surgery (better anatomical dissection / lower bleeding rate / low complication rate): **best TT** **

* Thomusch et al. World J Surg. 2000, 24: 1335-41.
** Tartaglia et al. Chir. Ital. 2003, 55: 499-510.

Table 4. Morbidity and mortality.

Morbidity/mortality	Total (no.)	Hospital operative volume 1998		
		<50	50-150	>150
Morbidity				
Transient hypoparathyroidism	464 (6.4)	23 (8.9)	133 (6.8)	308 (6.1)
Permanent hypoparathyroidism	108 (1.5)	2 (0.8)	6 (0.3)	100 (2.0)
Transient RLN palsy*	279 (2.1)	10 (2.1)	91 (2.6)	178 (1.9)
Permanent RLN palsy*	144 (1.1)	4 (0.9)	42 (1.2)	98 (1.0)
Seroma/hematoma	199 (2.7)	14 (5.4)	79 (4.0)	106 (2.1)
Cardiac morbidity	52 (0.7)	1 (0.4)	12 (0.6)	39 (0.8)
Wound infection	44 (0.6)	2 (0.8)	22 (1.1)	20 (0.4)
Pulmonary morbidity	37 (0.5)	3 (1.2)	11 (0.6)	23 (0.5)
Wound dehiscence	8 (0.1)	0	3 (0.2)	5 (0.1)
Thromboembolic morbidity	8 (0.1)	0	3 (0.2)	5 (0.1)
Cerebral morbidity	9 (0.1)	0	0	9 (0.2)
Miscellaneous	86 (1.2)	2 (0.8)	30 (1.5)	54 (1.1)
Mortality	3 (0.04)	0	1 (0.1)	2 (0.04)

Number in parentheses are percents.
RLN: recurrent laryngeal nerve.
*RLN palsies were adjusted to nerves at risk (13,436).

Specific factors determining extent of resection: personal views

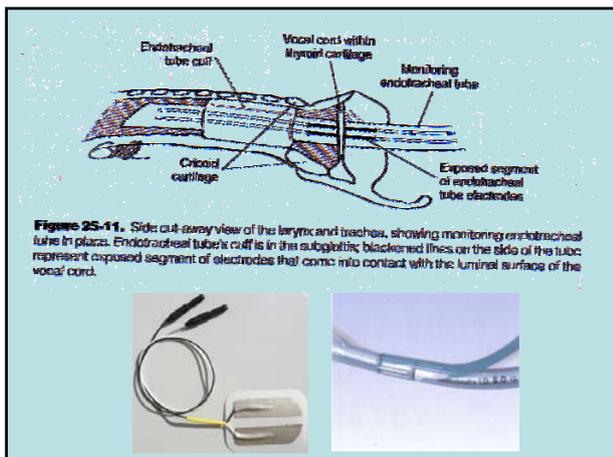
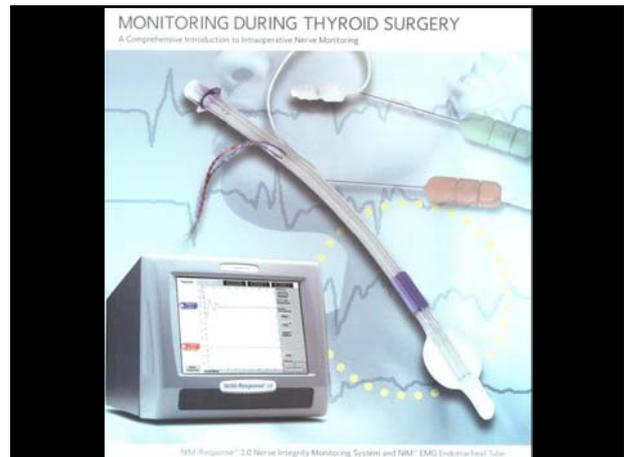
1. In case of programmed unilateral lobectomy (TL), do not touch or open other side *
2. In case of programmed TL on one side and small (< 2cm) but suspicious nodule in other lobe, do perform a subtotal lobectomy of that lobe, with concomitant frozen section (and eventually followed by totalisation)

* Chao et al World J. Surg 1997, 21: 644-7.

Role of RLN monitoring to reduce RLN palsy in thyroid surgery

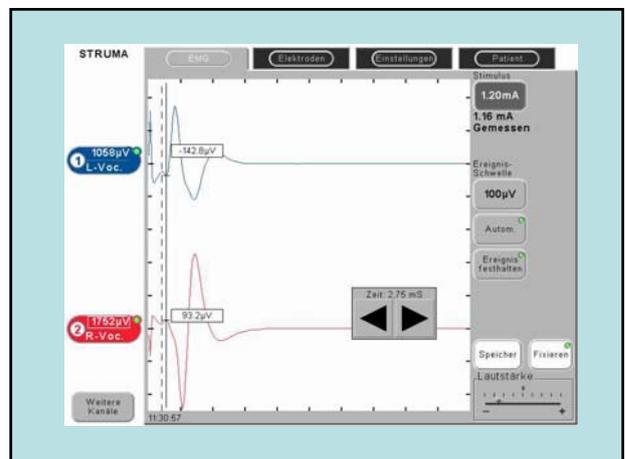
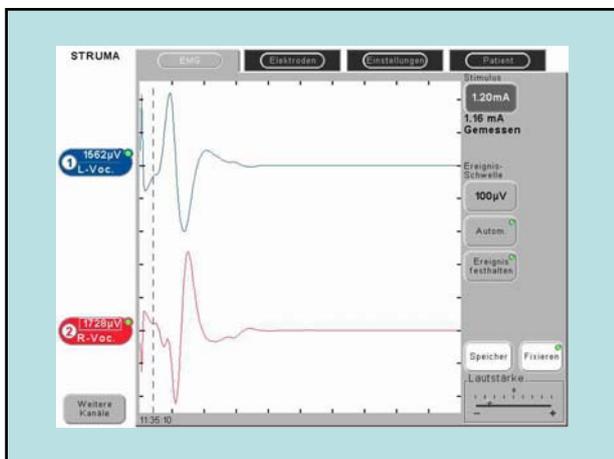
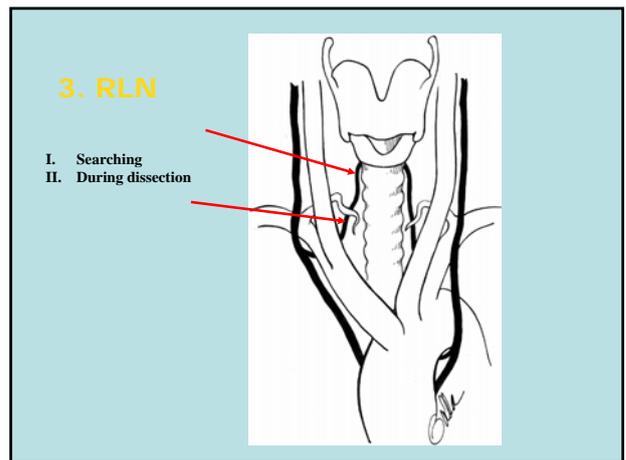
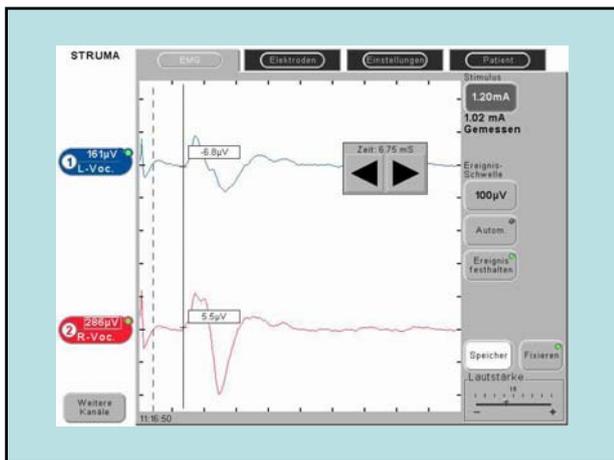
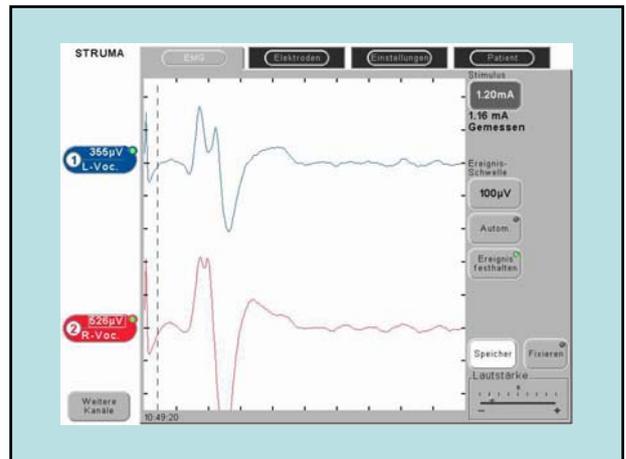
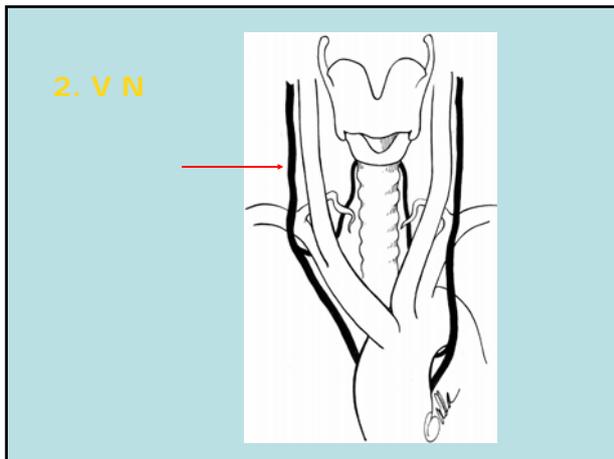
- **Technique:** laryngeal post-cricoid electrode placement and registration of intra-operative nerve stimulation
- **Results:** Identification of nervous activity with stimulation treshold of 0,57 mA. *

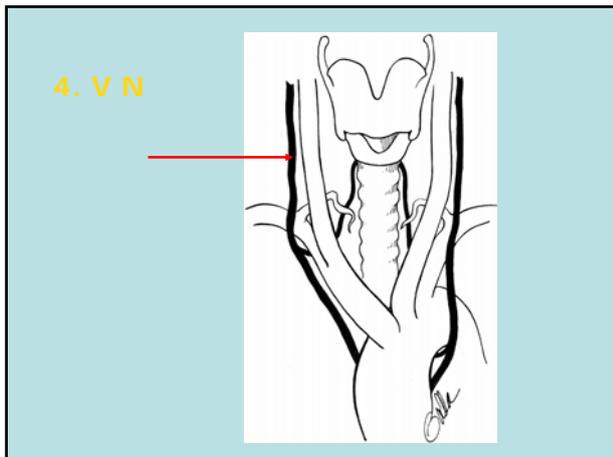
* Mareus et al. Laryngoscope 2003, 113: 356-61.



1. EBSLN







Neuromonitoring: conclusions

- Interesting tool to detect and identify the nerves (vagal/superior laryngeal/recurrent)
- Too large series are necessary to prove outcome difference with or without its use
- Possible medicolegal repercussions in the future

Should an operated patient have hormone treatment?

1. Substitution treatment in case of TT
 - levothyroxine 1,6 ug/kg/day or generally 100 ug/day * (= normal T4 secretion in a 70 kg person [vs 6 ug/day T3])
2. Suppressive treatment against recurrence in case of TL or TL+STL
 - levothyroxine dose aiming at reducing TSH < 0,4 mU/l (generally between 50 and 150 ug/day) [controversial **]
 - Personal view: maintenance of a low-normal TSH: 0,5 – 2 mU/l, high-normal T4 > 20 mU/l

* Wiersinga. Horm. Res. 2001, 56 Suppl. 1: 74-81.
 ** pro: Berghout et al: Lancet 1990, 336: 193-7.
 contra: Hegedus et al. Endocrin. Rev. 2003, 24: 102-132.

Is there any indication for I¹³¹-treatment in nodular goiter?

- Two indications:
 1. In case of hyperthyroidism and thyroid nodular disease in normovolaemic thyroid
 2. In case of absolute contra-indication for surgery
- Results:
 1. Can give a volume reduction up to 40% in 1 year *
 2. Risk of secondary cancer in irradiated thyroid **
 3. Possible enhancement by means of recombinant human TSH (rhTSH) ***

* Huysmans et al. Ann Int. Med. 1994, 121: 757-62.
 ** Rubino et al. Br. J. Cancer 2003, 89: 1638-44.
 *** Albino et al. J. Clin. Endocrin. Metab. 2005, 90: 2775-80.

Retrosternal Goiter

- Mostly symptomatic with growing volume
- Compressive symptoms on trachea and in lesser degree on esophagus or recurrent nerve
- In +/- 80% resectable via cervicotomy

Conclusions

- Thyroid nodular is still a frequent disease
- All cold nodules are potentially malignant
- Unilateral isthmo-lobectomy or bilateral thyroidectomy are the treatments of choice
- Careful search to identify recurrent nerve is adviseable, and mandatory in bilateral disease
- Neuromonitoring may be promising tool
- Bloodless surgery reduces risk of nerve lesion