



PTC and lymph node dissection: when, how extensive, technical pitfalls

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overview

- issues and philosophy
 - recommendations
 - therapeutic vs prophylactic dissection
 - surgical techniques
-



introduction - philosophy

- # the surgical management of regional lymph nodes in papillary thyroid carcinoma has long been controversial.
 - those who promote a very conservative approach to lymph nodes, ie local excision only of clinically involved nodes, point to the apparent lack of any impact on survival in previous studies for patients with positive nodes.
 - on the other hand, there have been a number of significant changes in relation to our approach to papillary thyroid carcinoma and its long term management that challenge such conservative philosophy.
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new paradigms

New Paradigms in the Management of Thyroid Cancer

Orlo Clark

Department of Surgery, University of California, San Francisco, U.S.A.

With the advent of blood thyroglobulin levels (basal and TSH stimulated) and improvements in ultrasound scanning patients who were formerly considered to be cured of their thyroid cancer are now being identified with persistent or recurrent cancer usually in cervical nodes with an increased frequency post thyroidectomy. An ultrasound suspicious node can be confirmed by FNA cytology under ultrasound guidance.

Considerable discussion has previously occurred regarding the extent of a thyroidectomy to obtain an optimal outcome. Total or near total thyroidectomy is generally recommended if post thyroidectomy treatment with ^{131}I is to be considered. Controversy also continues regarding the clinical significance of lymph node metastases, but virtually all investigations document that such metastases are associated with an increased rate of recurrent thyroid cancer.

A new paradigm must be used to address patients with papillary thyroid cancer (PTC) since clinically occult nodal metastases occur in up to 80% of these patients. Although these involved nodes usually remain dormant, they are now being identified and cytologically confirmed when 5 mm in size or larger by thyroglobulin testing and ultrasound scanning. Numerous investigations document that the presence of lymph node metastases correlate with primary tumor size, multifocal primary PTC, an irregular occult primary tumor, distant metastases and perhaps familial PTC.

Retrospective investigations have documented that unsuspected nodal metastases are present by ultrasound examinations in about one-third of patients with thyroid cancer. Clinically, Kouvaraki MA (*Surgery* 134: 946, 2003) reported that preoperative ultrasonography changed the surgical approach for patients with thyroid cancer to include more extensive dissection of the central nodes, the ipsilateral jugular nodes and also, although less frequently, the contralateral nodes. SKIP metastases also occur in about 20% of patients with thyroid cancer (Machins A et al. *Arch Surg* 135:43, 2004).

To conclude:

- 1) Occult nodal metastases are present in most patients with PTC
- 2) Preoperative ultrasound scanning of the thyroid and cervical nodes is essential and is more sensitive and accurate than physical examination
- 3) Therapeutic nodal dissection is recommended for ultrasound documented abnormal or enlarged nodes
- 4) Prophylactic neck dissection in clinically and ultrasonography negative necks is not necessary in patients with PTC

**10th Congress of
the Asian Association of
Endocrine Surgeons**

12 - 15 March 2006
Hong Kong Convention and Exhibition Centre



the new paradigms for PTC

lymph node involvement of no clinical consequence



lymph node involvement impacts outcome

radioiodine scans on regular basis for follow-up



ultrasound and thyroglobulin for follow-up

focus on “survival” data for patients



focus on disease free status for patients



former attitude to lymph nodes

“Everyone who works with papillary thyroid cancer knows that most of the patients have lymph node metastases. We also know that they do not have any bearing on outcome”

■ *Blake Cady – invited commentary. World J Surg 1994;18:558-9*

AGES	age	grade		extent	size	
AMES	age		dist mets	extent	size	
DAMES	age		dist mets	extent	size	diploid
GAMES	age	grade	dist mets	extent	size	
MACIS	age		dist mets	(invas)	size	completeness



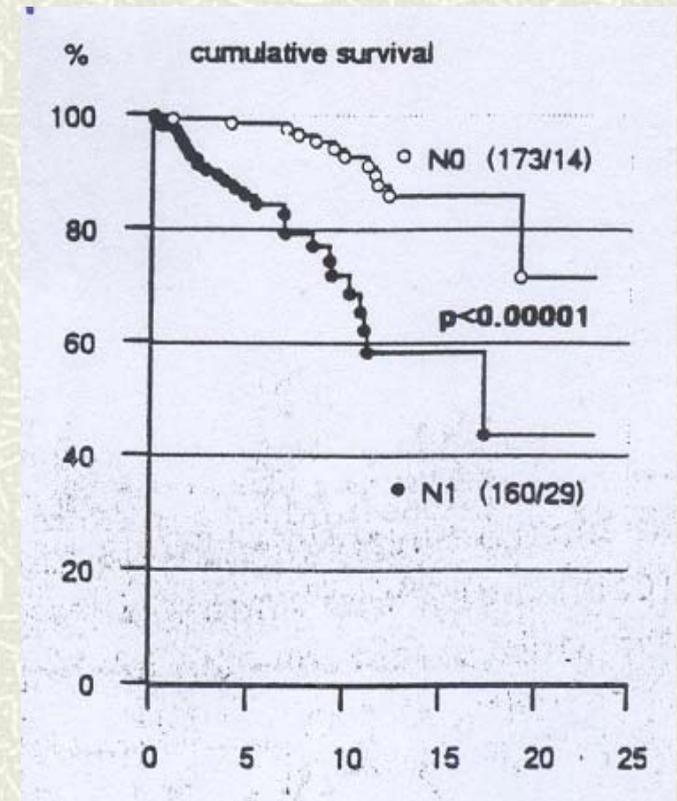
lymph node involvement

considerable Japanese data demonstrating impact of nodal involvement in selected groups (needs to be understood in the context of ^{131}I ablation not being generally used in Japan)

■ *Ohshima A Yamashita H, Noguchi S et al. Arch Surg 2000;135:1194-8*

German data (342 patients) - N1 status significantly influenced survival in patients – effect most pronounced in T1-T3 tumors

■ *Scheumann GFW, Gimm O ... Dralle H. World J Surg 1994;18:559-68*





recent Swedish data

- # Swedish population data (n=5,123) - nested case control study matched for age, sex and calendar year
- # patients with lymph node metastases more likely to die (OR, 2.5; 95% CI, 1.6-4.1)
- # still significant after adjustment for TNM (OR, 1.9; 95% CI 1.1-3.6)
 - *Lundgeren CI, Hall P Zedenius J. Cancer 2006;106:524-31*



2. changing follow-up

- # the routine inclusion of cervical ultrasound as part of the follow-up protocol of patients with thyroid cancer has meant that significantly greater numbers of patients are being diagnosed with lymph node involvement that was not previously suspected clinically.
-



ATA guidelines

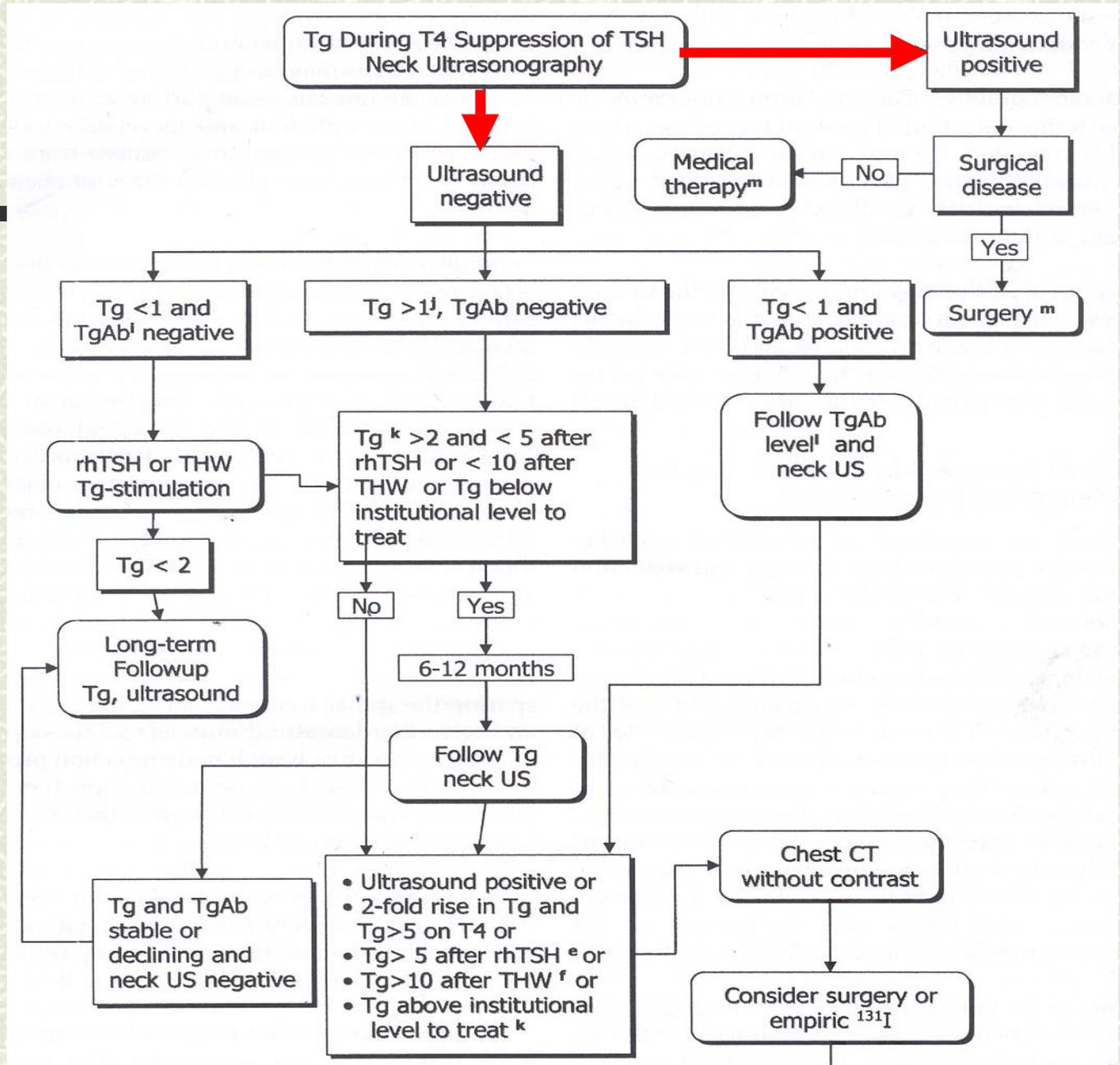
RECOMMENDATION 48

“after surgery, cervical ultrasound to evaluate the thyroid bed and central and lateral cervical nodal compartments should be performed at 6 and 12 months and then annually for at least 3-5 years, depending on the patient’s risk for recurrent disease and thyroglobulin status”

■ *Thyroid 2006;16:1-33*



ATA flow chart for thyroid cancer follow-up





3. survival vs disease free

- # the aims of treatment have also changed – young patients with papillary cancer are no longer prepared to simply accept that any residual disease has a less than 5% chance of leading to their death in the next 20 years – rather the aim of treatment should be to render patients disease-free as assessed by undetectable thyroglobulin levels and negative ultrasound, provided that such an approach does not lead to increased morbidity.
-



the game has changed

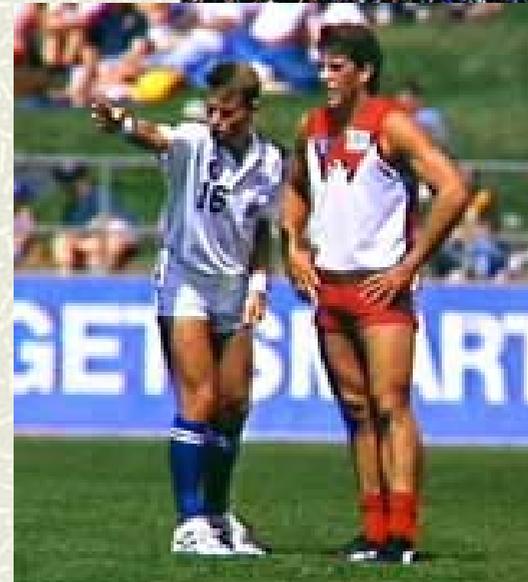
- # playing technique has improved with time
- # berry picking has been replaced by selective neck dissection focused on involved levels





the game has changed ...

- # the goal posts have moved
 - athyroglobulinemia vs survival
- # there is better scrutiny of results of decisions
 - routine ultrasound pre and post-operatively vs scans





current approach - ATA guidelines

- # R27: routine central compartment (level VI) dissection should be considered for patients with papillary thyroid carcinoma and suspected Hurthle cell carcinoma....
- # R28: lateral neck compartment dissection should be performed for patients with biopsy proven metastatic cervical lymphadenopathy detected clinically or by imaging...
 - *Thyroid 2006;16:1-33*



why – (1) local recurrence

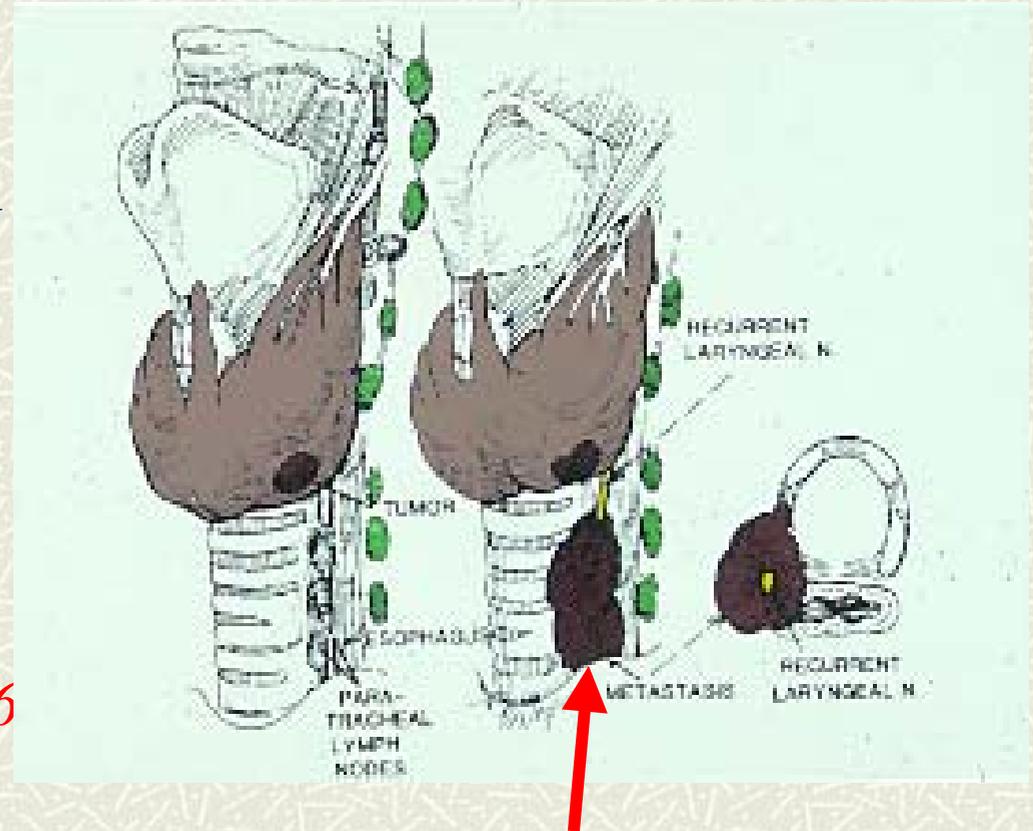
- # many studies show that lymph node involvement is associated with significantly higher risk of local and regional recurrence as well as distant metastases
 - *Mazzaferri EL, Kloos RT. J Clin Endocrinol. Metab 2001;86:1447-63*
 - # formal lymph node dissection compared to berry-picking reduces local recurrence rates (10% vs 25%) at 20 years
 - *Hay ID, Bergstrahl EJ, Grant CS et al. Surgery 1999;126:1173-81*
-



“local recurrence”

- most “local recurrence in the thyroid bed” is in fact nodal involvement of level VI paratracheal nodes
- very significant increased risk of death with loco-regional recurrence
OR 5.3 (3.9-7.1)

■ *Lundgeren CI, Hall P...
Zedenius J. Brit J Surg 2006
(in press)*

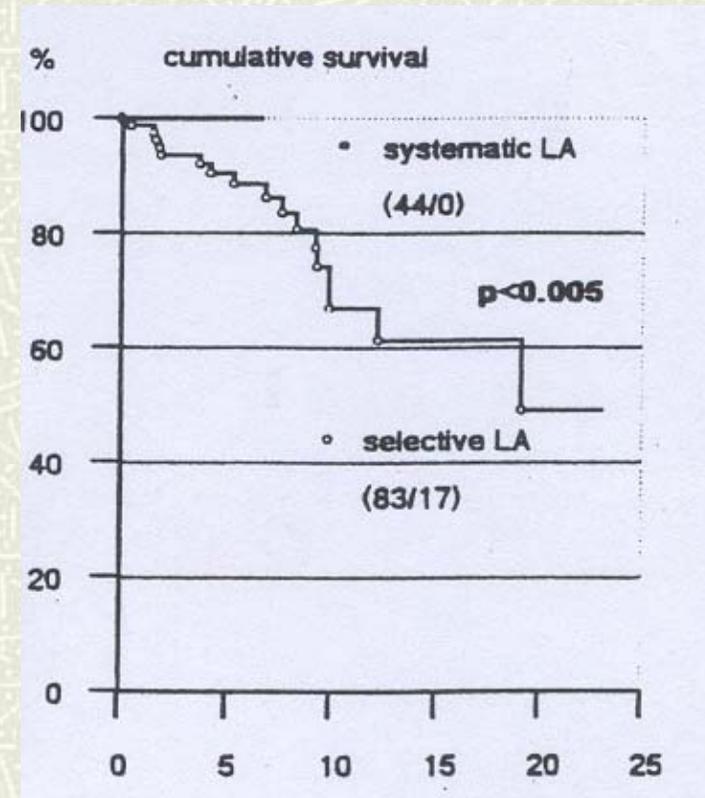


picture courtesy J Shah, MSKCC



why – (2) survival

- # Japanese data: evidence of improved survival for poor risk groups (although needs to be interpreted in context of absence of radioiodine)
 - *Noguchi S, Murakami N, Yamashita H, Toda M, Kawamoto H. Arch Surg 1998;133:276-80*
- # German data: systematic lymphadenectomy superior to local node removal
 - *Scheumann GF, Gimm O ... Dralle H. World J Surg 1994;18:559-68*





survival

- # Swedish data – lymph node dissection did not impact survival significantly however techniques included the range of procedures from berry-picking to modified radical neck dissection by surgeons of varying experience
 - *Lundgeren CI, Hall P... Zedenius J. Brit J Surg 2006 (in press)*
 - # *lymph node involvement impacts survival but data to support the role of surgery in improving survival still lacking*
-

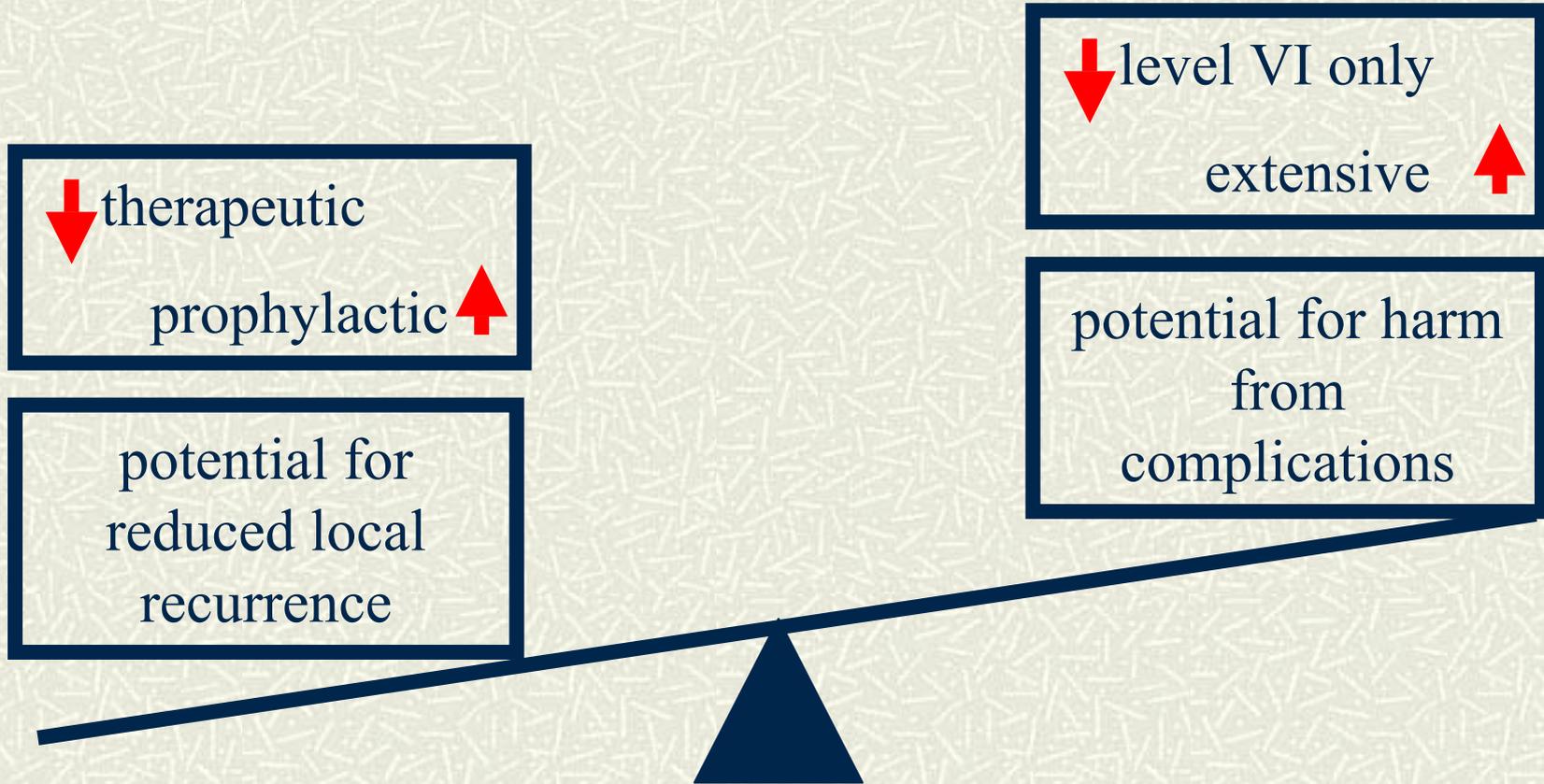


at what cost?

- # some reports of high rate of complications - 50% permanent hypoPTH following Level VI/VII dissection
 - *Khoo ML, Freeman JL. Head Neck 2003;25:10-14*
- # other reports more acceptable – 363 total thyroidectomies with 147 routine bilateral Level VI dissection - 1.9% permanent hypoparathyroidism
 - *Watkinson JC. in. Mazzaferi EL, Harmer C, Mallick UK, Kendall-Taylor P (eds) Practical management of thyroid cancer. Springer London 2006:149-64*
- # University of Sydney data – no increase in permanent complications with selective dissection
 - *Palazzo FF, Gosnell R ... Delbridge L. Eur J Surg 2006;32:340-4*



cost vs benefit



decision for surgery a balance



(1) therapeutic dissection options

- “berry-picking”- local excision of enlarged or clinically involved nodes - generally involves shelling out palpable nodes
 - formal modified radical neck dissection – entire lymph node bearing compartment on one side
 - “selective” neck dissection – dissection of only those levels specifically involved by tumor
-



“berry picking”

- # berry picking is effective in dealing with clinically apparent nodes, however normal lymph nodes or nodes with micrometastases remain intact in the surgical field
 - # higher documented local recurrence rates
 - # long-term follow-up in some young patients consists of repeated removal of enlarged lymph nodes - often “reactionary”
-



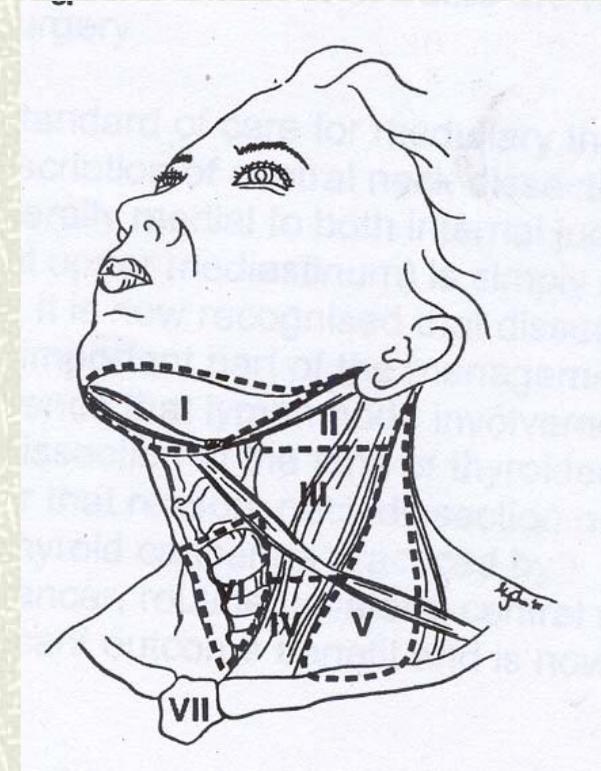
modified radical neck dissection

- # formal modified radical neck dissection is unnecessary for all but patients with extensive nodal involvement
 - # significant potential morbidity in relation to accessory and hypoglossal nerves, stiffness and paraesthesia, as well as thoracic duct injury
 - # no data to show that results any better than selective neck dissection
-



selective neck dissection

- # selective neck dissection based on concept that cervical lymph nodes are aggregated in groups, not spread throughout the neck in a continuous sheet
- # metastases generally spread in an orderly manner from visceral nodes to more peripheral groups
- # therapy individualized and targeted to those levels that are specifically involved or likely to be involved if the dissection is prophylactic





concepts - selective neck dissection

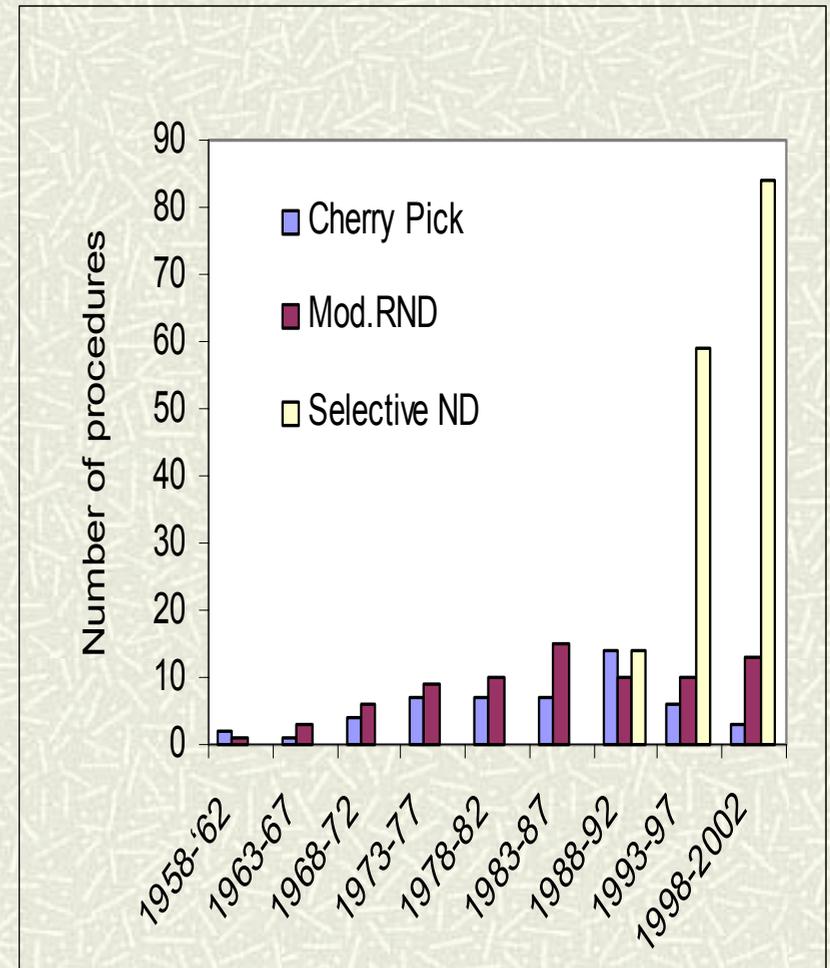
- # is Level I, II, V dissection always necessary?
- # retrospective review of 106 patients undergoing neck dissection
- # recurrence at Levels I and V very uncommon
- # Level II recurrence not related to previous dissection
 - *Caron NR, Tan YY... Clark OH. Selective modified radical neck dissection for papillary thyroid cancer – is level I, II, and V dissection always necessary. World J Surg 2006;30:833-840*



University of Sydney data (n=900)

■ dramatic increase in both the overall use of lymphadenectomy increased in past 2 decades as well as a shift to selective lymph node dissection

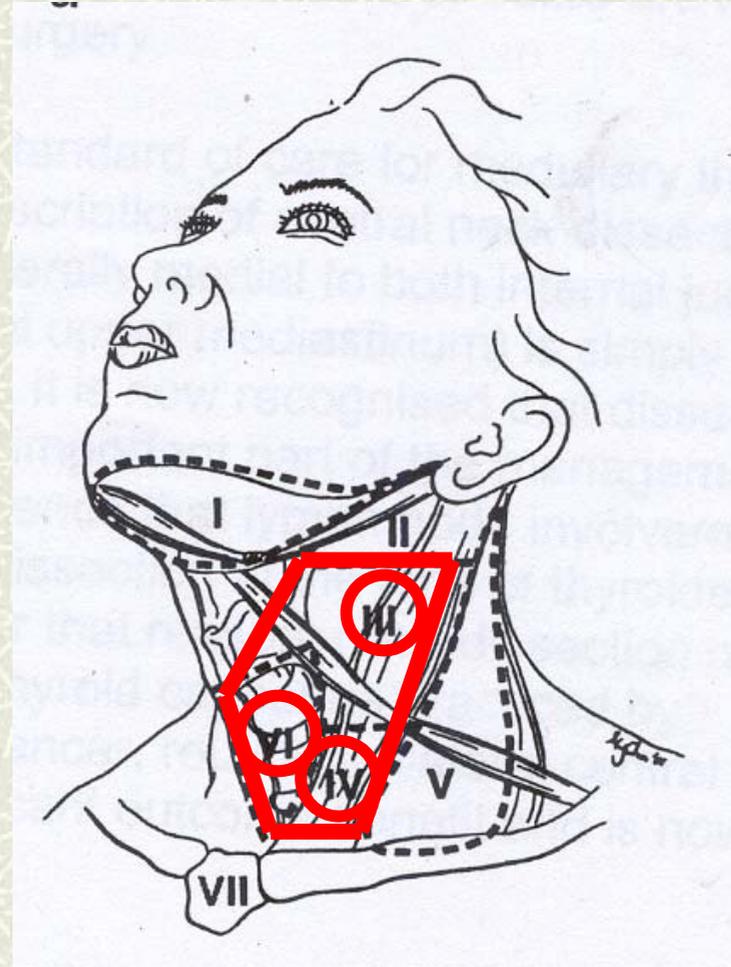
■ *Palazzo FF, Gosnell R ...
Delbridge L. Eur J Surg
2006;32:340-4*





levels dissected last 5 years

I	2%
II	35%
III	57%
IV	65%
V	27%
VI	81%
VII	5%





complications last 5 years (n=208)

	selective dissection (n=100)	no dissection (n=108)
permanent hypoPTH	13	15
temp RLN neuropraxia	6	1* (P=0.05)
permanent RLN palsy	2	1
re-op for bleeding	1	1
Horner's syndrome	2	0
XI nerve palsy	0	0



(2) prophylactic dissection: options

- 
- A large, dark blue arrow pointing downwards, indicating a sequence or progression of options.
- # OPTION 1: no prophylactic dissection and rely on radioiodine ablation for treating non-palpable nodal disease
 - # OPTION 2: unilateral level VI dissection – minimal procedure directed to the most likely site of involvement
 - # OPTION 3: bilateral central neck dissection – comprehensive clearance of likely involved nodes but higher potential for complications
-



still controversial

OPTION 1: *Orlo Clark, 2006*

- # “prophylactic neck dissection in clinically and ultrasonography negative necks is not necessary in patients with PTC”

OPTION 3: *John Watkinson, 2006*

- # “in the N0 neck within the central compartment (level VI), routine dissection should be considered as part of a total thyroidectomy”
-



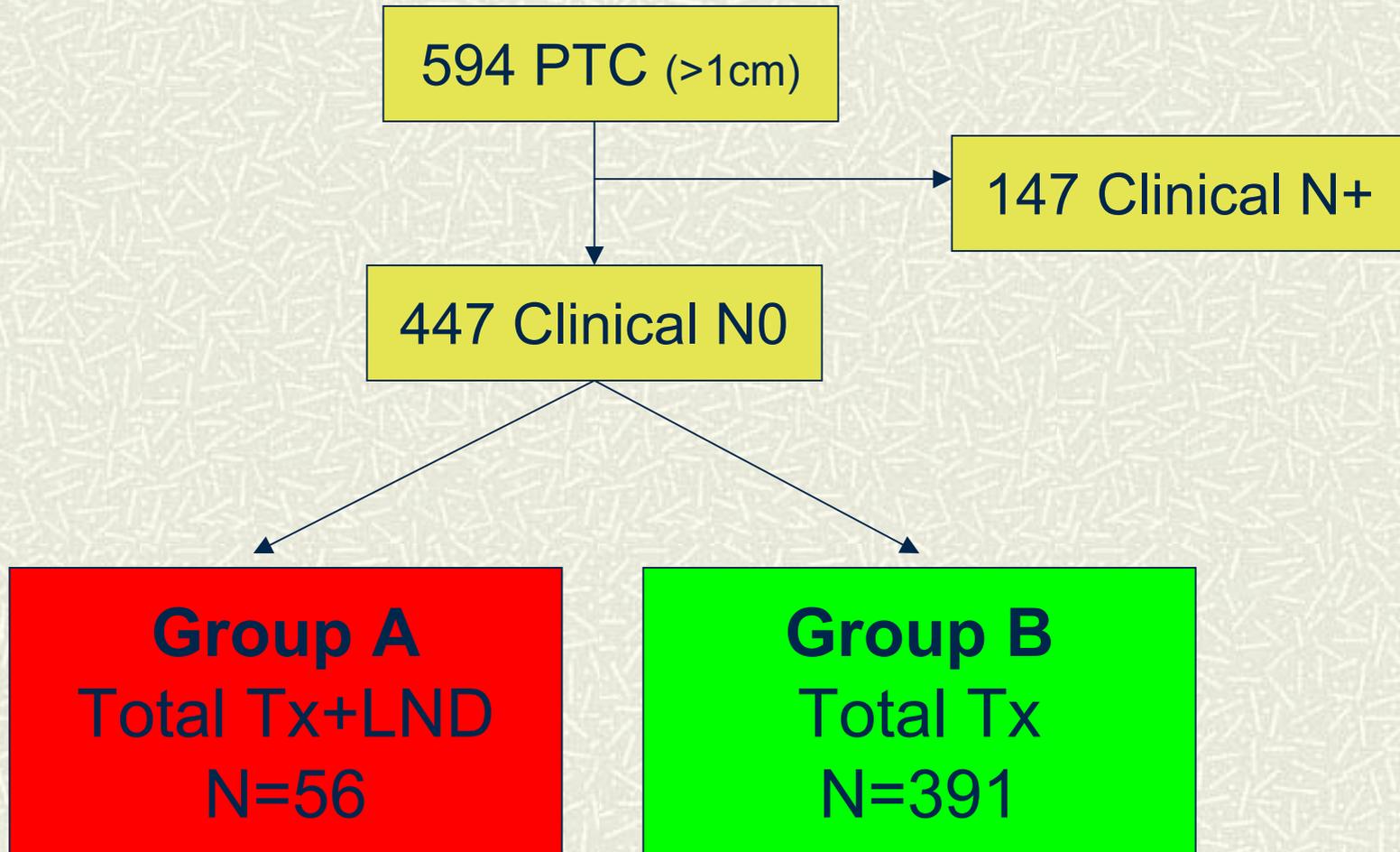
University of Sydney: OPTION 2

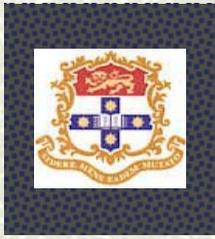
- # retrospective cohort study Dec 1995 to April 2005 of:
 - total thyroidectomy alone vs total thyroidectomy plus level ipsilateral VI LND

 - # histologically proven PTC >1cm
 - # pre-op node negative neck clinically and on routine ultrasound
 - # no difference in tumor size of MACIS score
 - # outcomes:
 - thyroglobulin
 - radioiodine doses
-



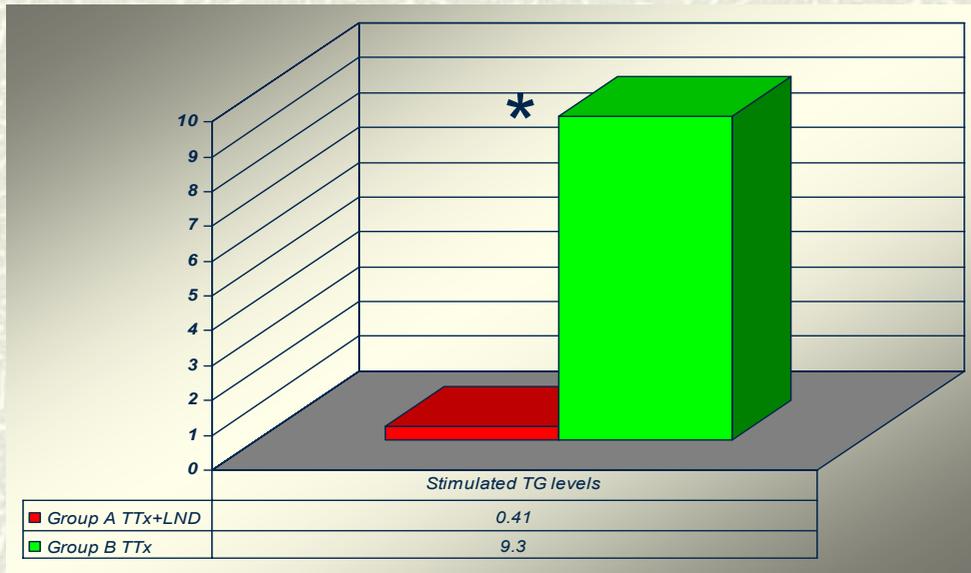
study population





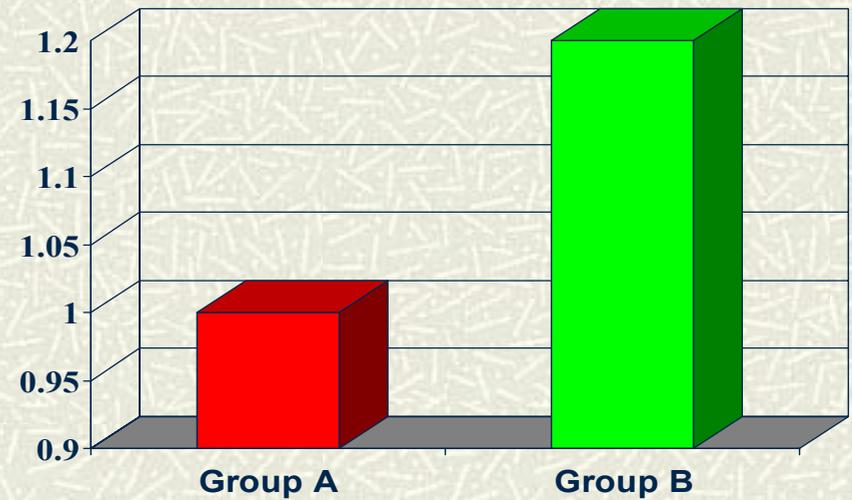
post-ablative serum TG levels

Serum TG ug/L
6-12 months

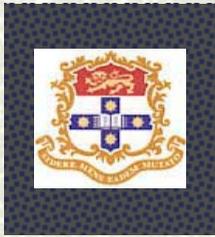


* P=0.02

No of ¹³¹I treatments

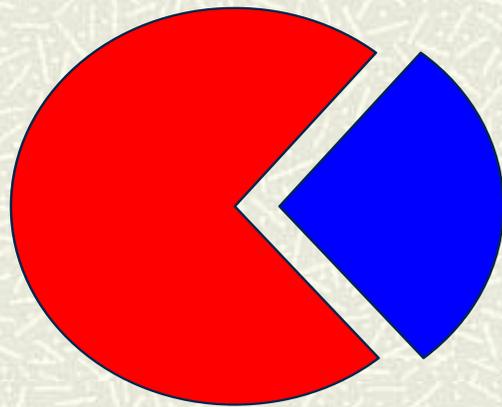


P=0.51



stimulated serum TG (6-12mth)

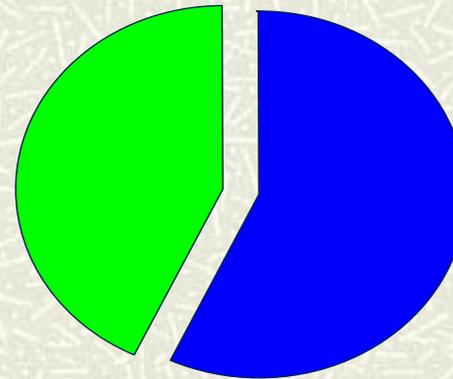
Group A



■ TG undetectable
■ TG > 0.8 ug/L

72%*

Group B



■ TG >0.8ug/L
■ TG undetecatable

43%*

*p=0.001



operative complications

	Group A TTx + LND	Group B TTx	p value
wound infection	1.8%	1.3%	0.76
hemorrhage	1.7%	1%	0.6
temp hypocalcemia	17%	8%	0.03**
permanent hypoparathyroidism	1.6%	1%	0.3
permanent RLN injury	0	1%	0.4



study conclusion

- # routine LND of the ipsilateral level VI compartment for PTC can be performed with low complication rates.
 - # LND VI is associated with significantly lower levels of stimulated thyroglobulin following ^{131}I ablation.
 - # routine ipsilateral LND VI combined with total thyroidectomy results in higher rates of “athyroglobulinemia” when compared with total thyroidectomy alone
-



?ultrasound/palpation for Level VI

- # ultrasound notoriously unreliable for detecting paratracheal nodal involvement
- # sensitivity only 10% (compared to over 80% for other levels)
 - *Ito Y, Tomoda C, Uruno T et al. Worl J Surg 2006;30:91-9*
- # intra-operative palpation of groove also unreliable – clinically involved nodes often not detected until after dissection commenced



summary

therapeutic dissection

- general consensus for selective neck dissection guided by clinical assessment and pre-operative ultrasonography

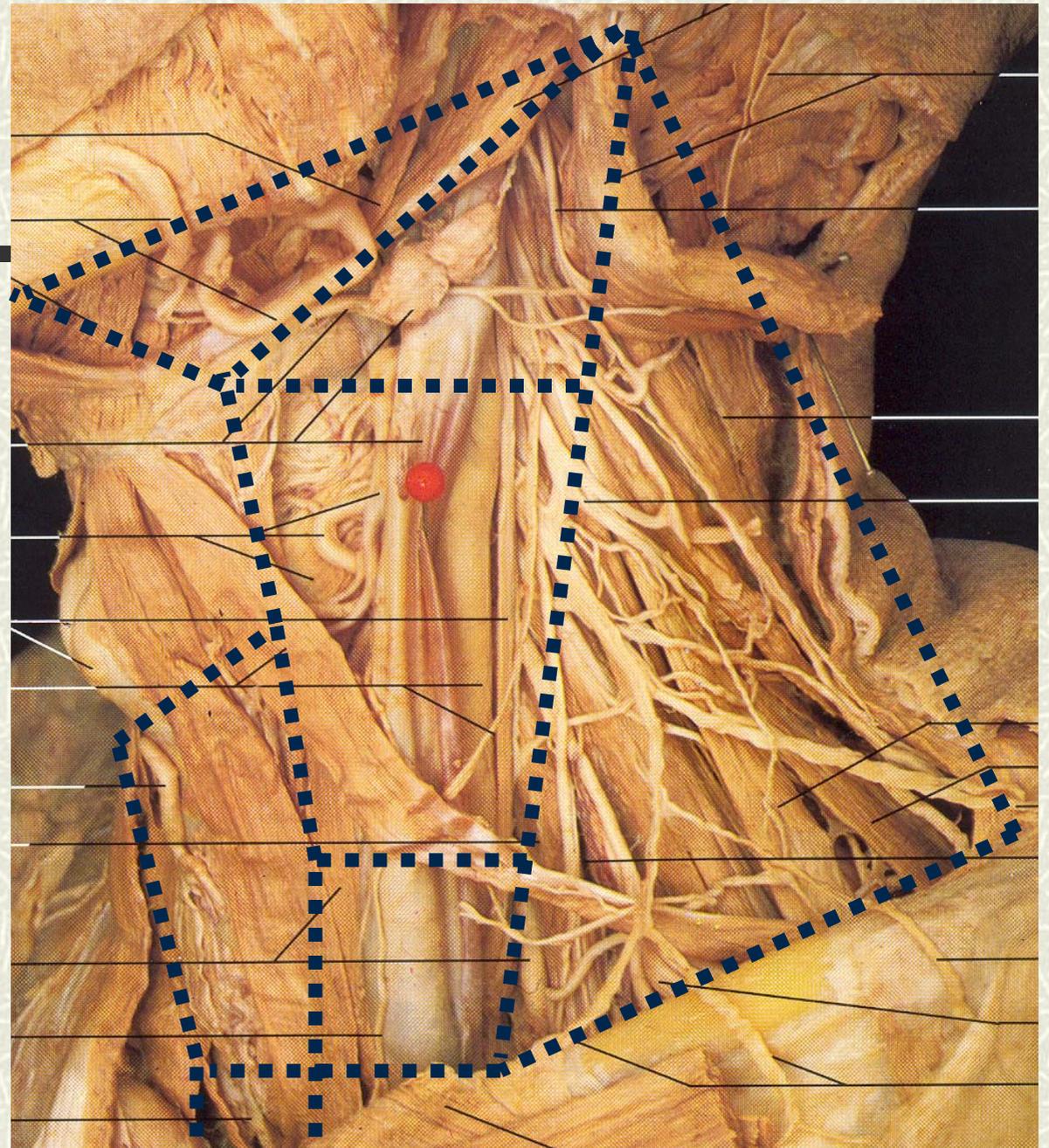
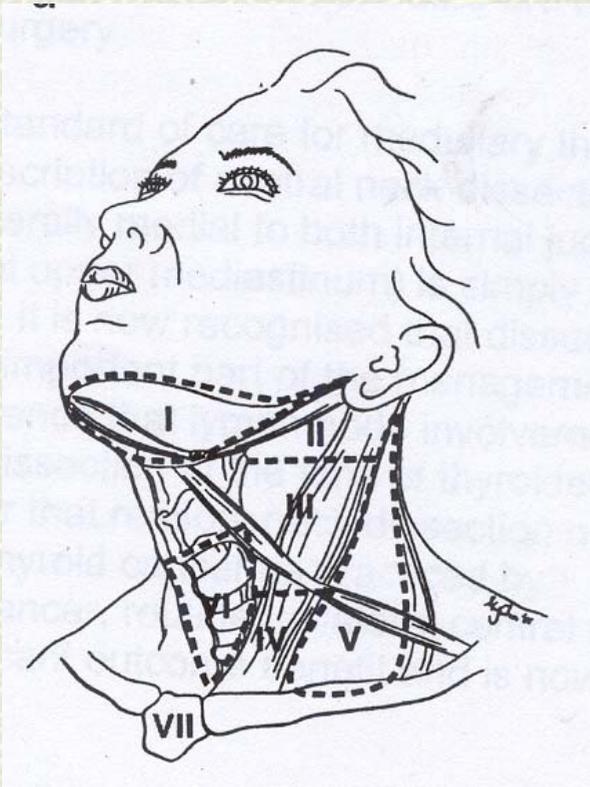
prophylactic dissection

- no overall consensus but consider ipsilateral Level VI dissection as a safe and effective to either bilateral central neck dissection or no dissection
-



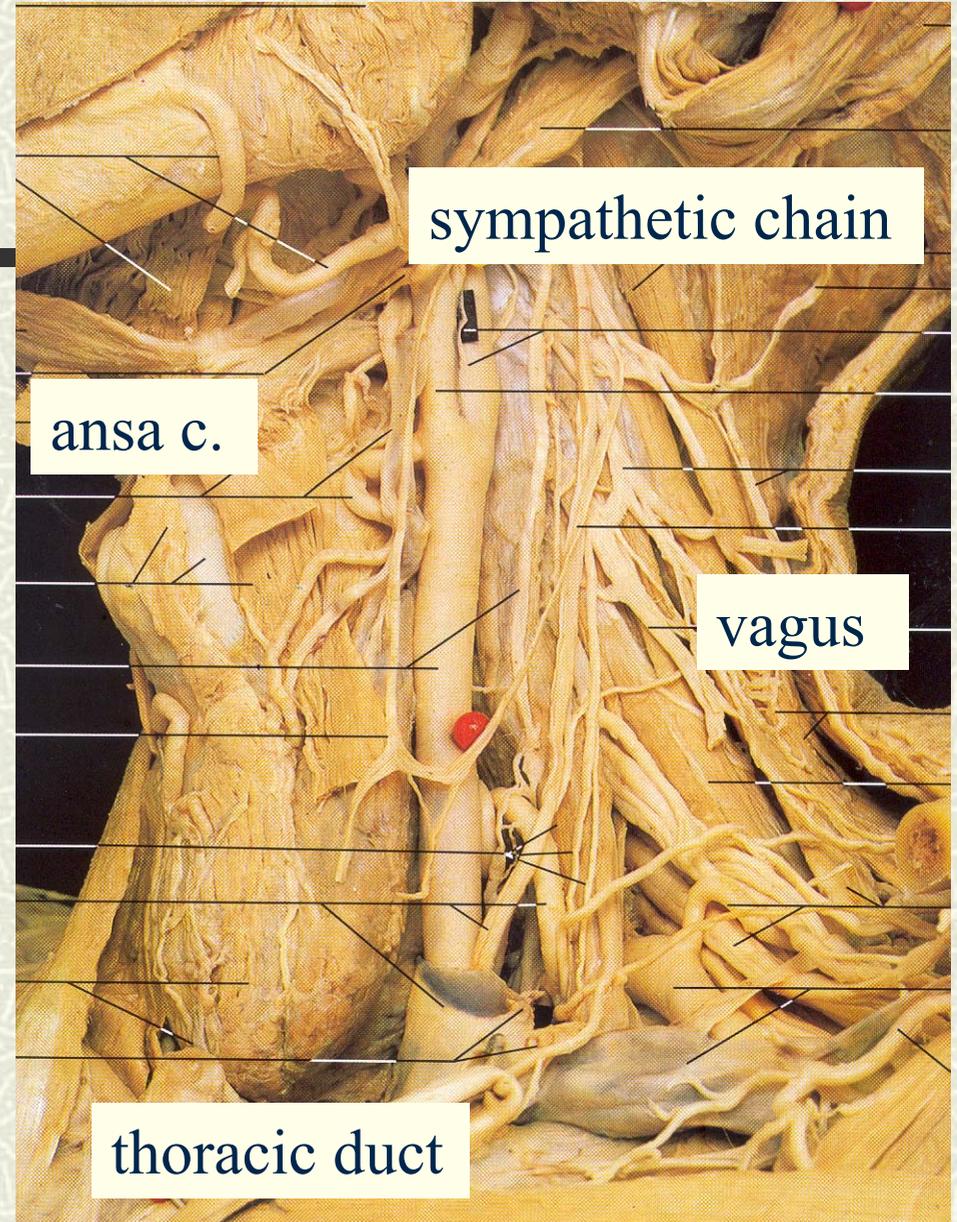
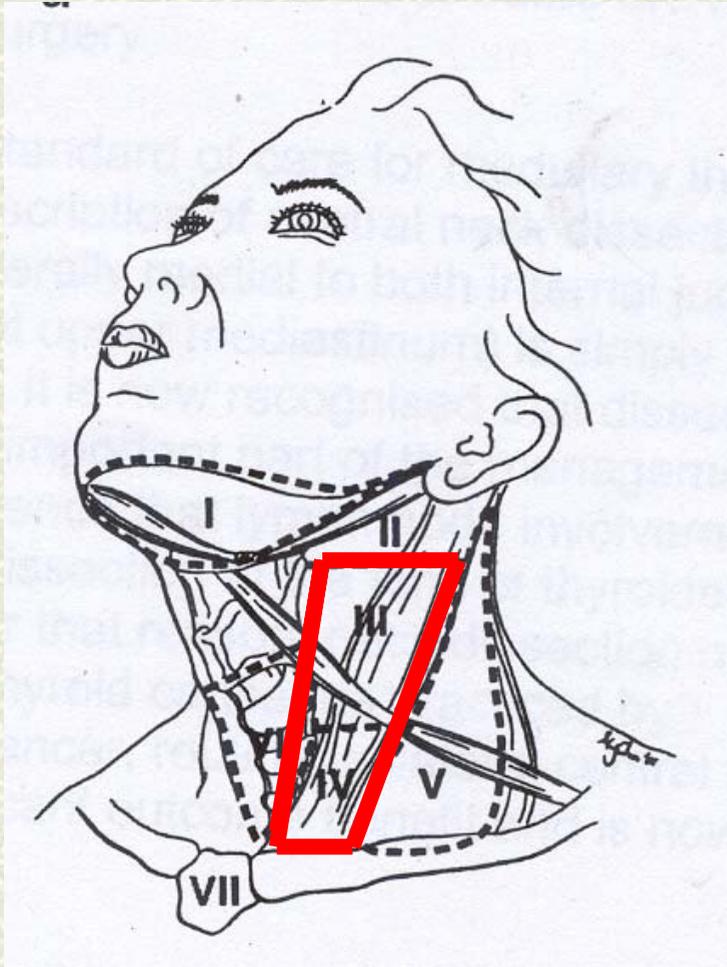
therapeutic

technical aspects



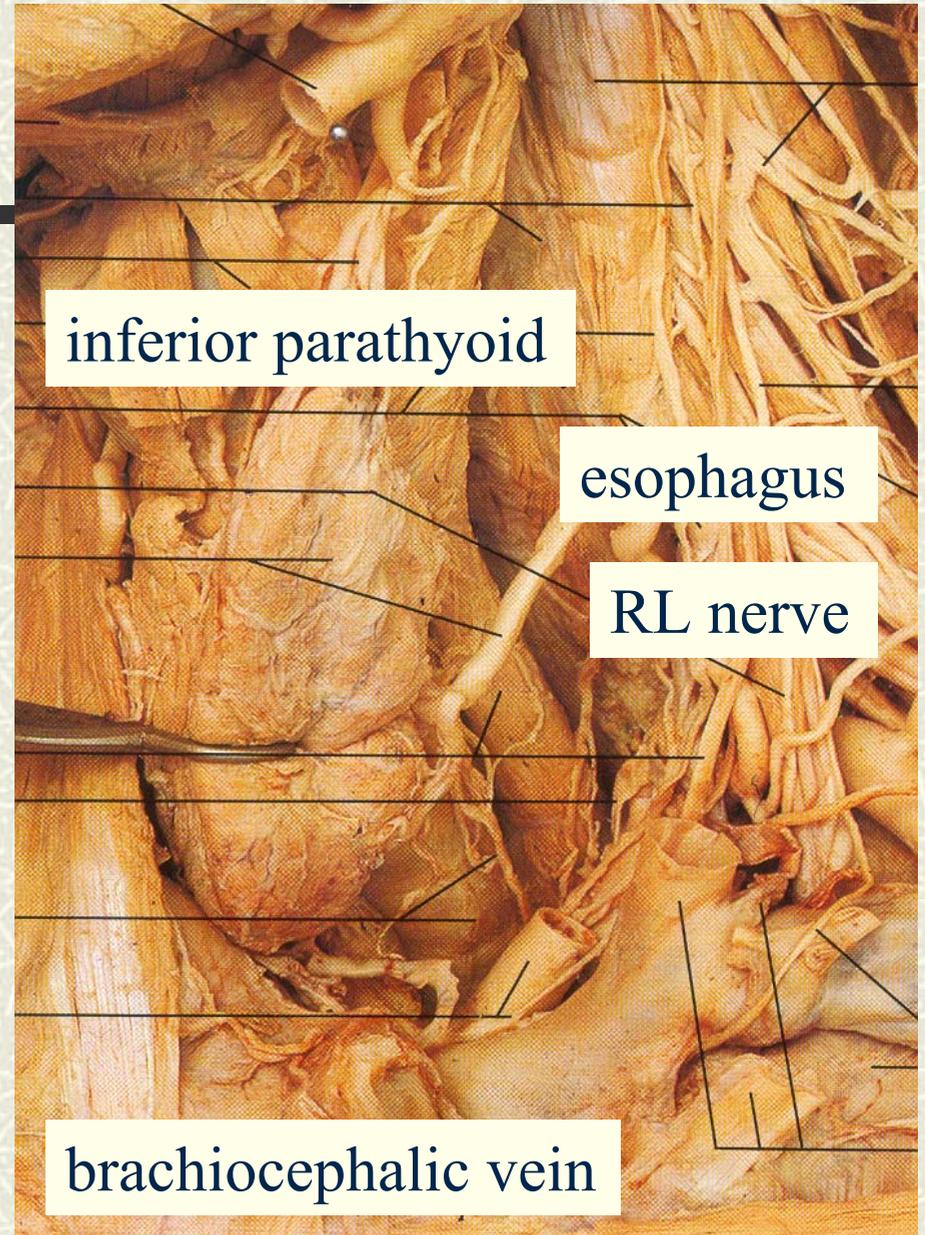
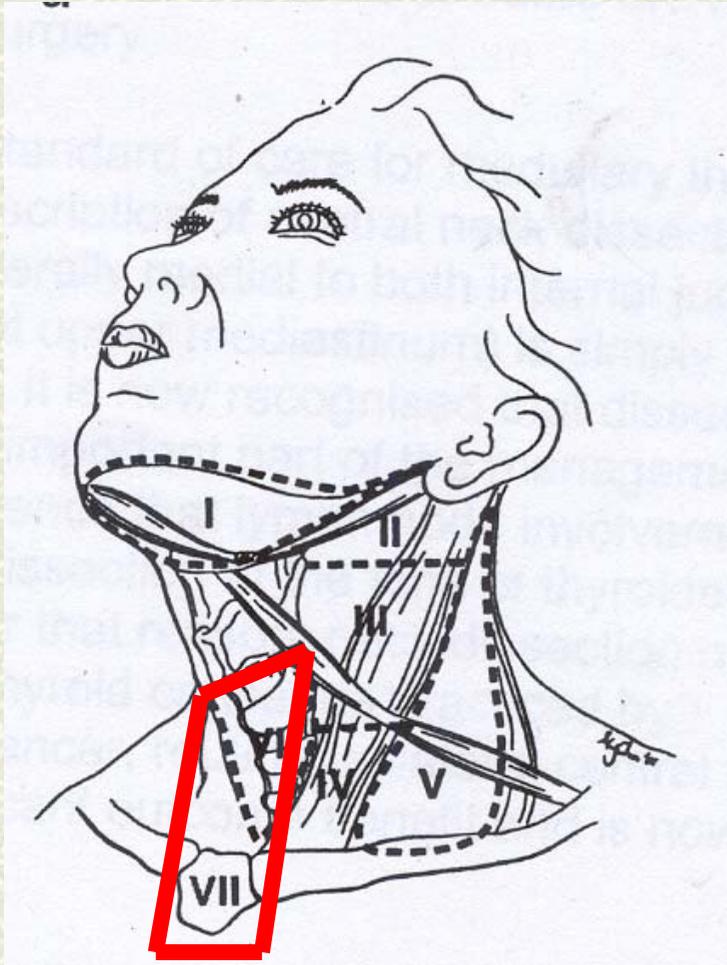


Levels III/IV



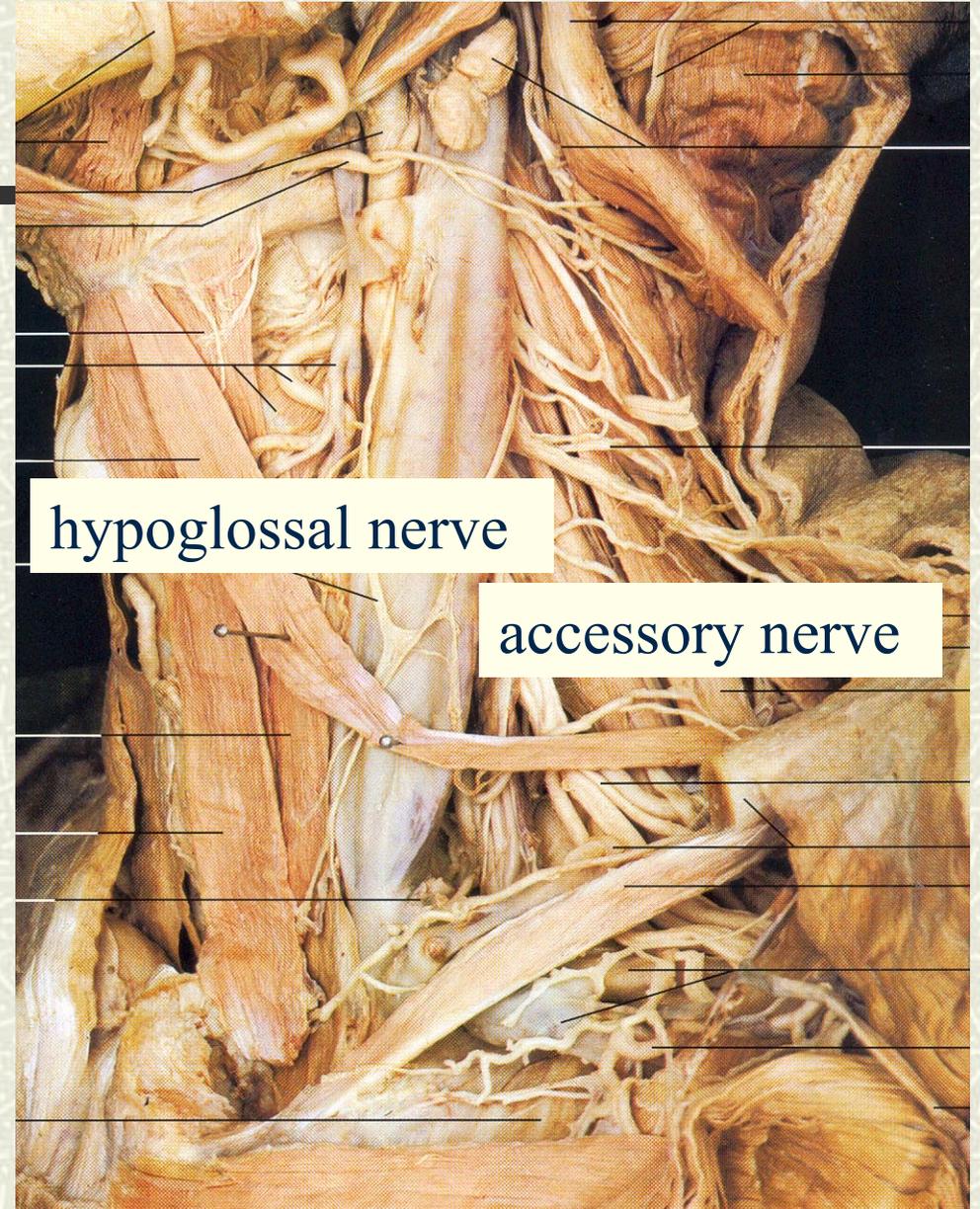
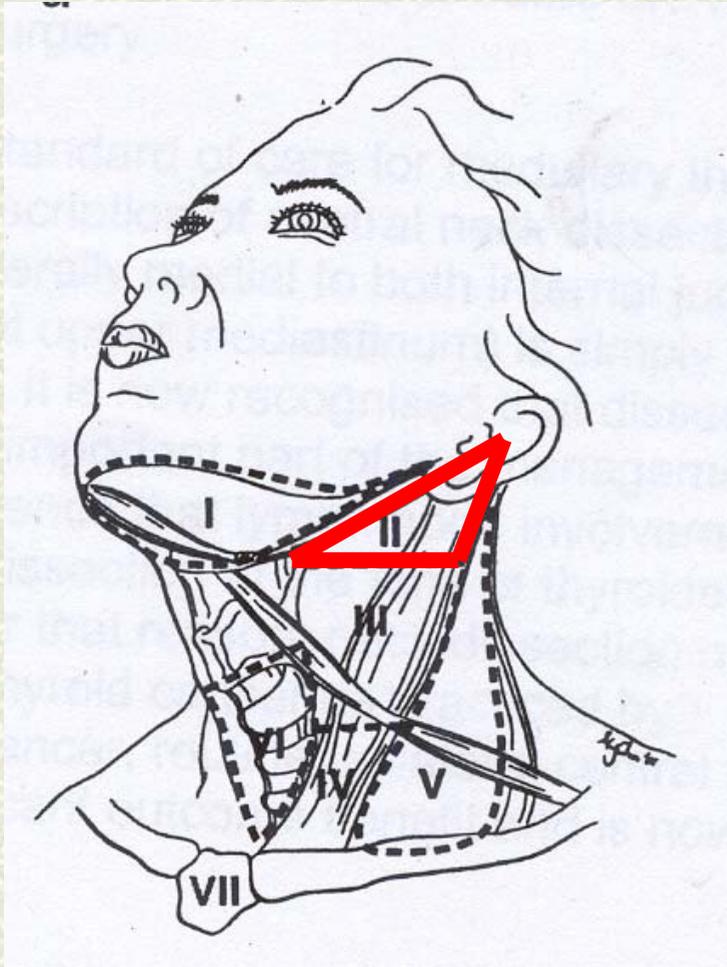


Levels VI/VII





Level II

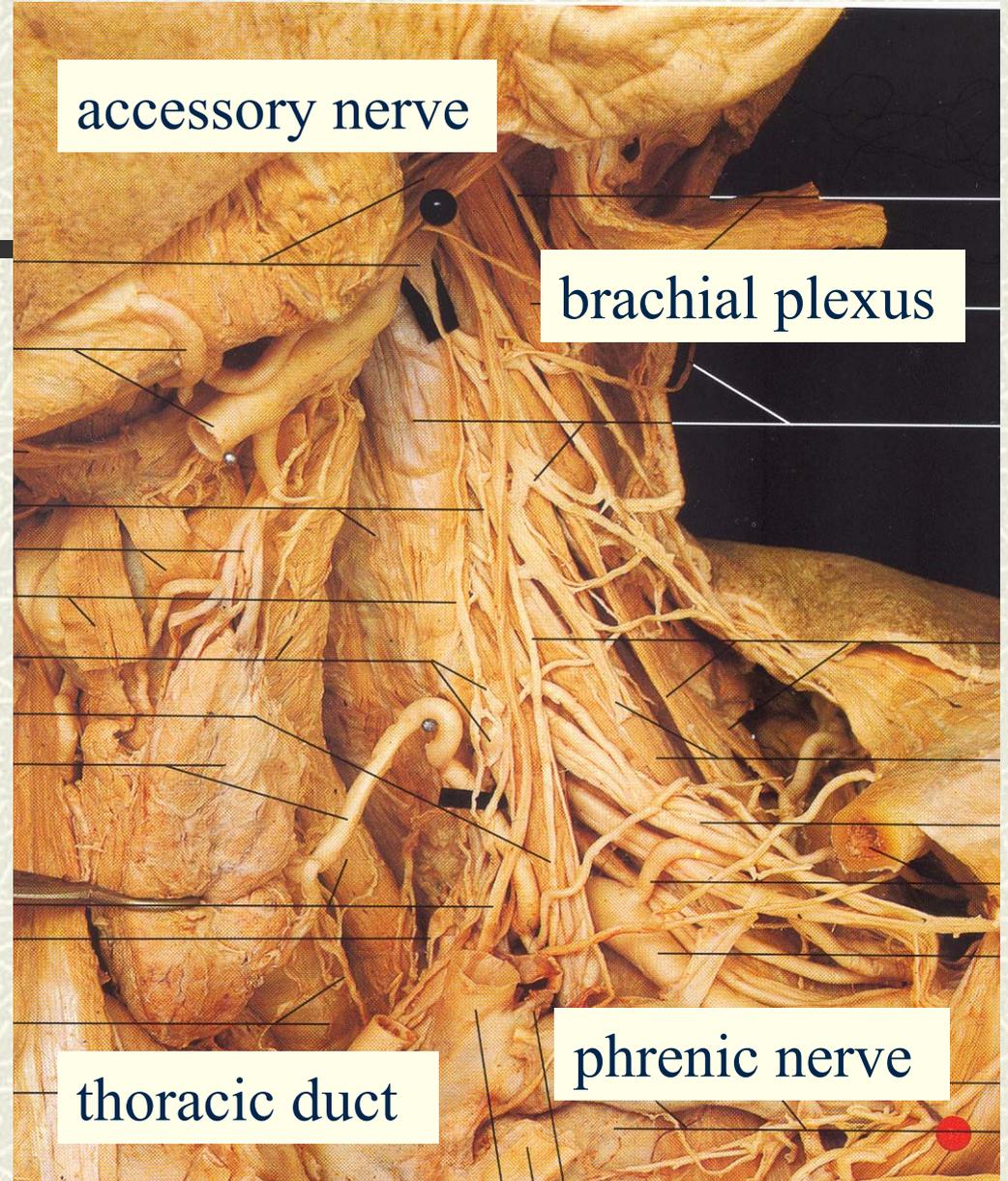
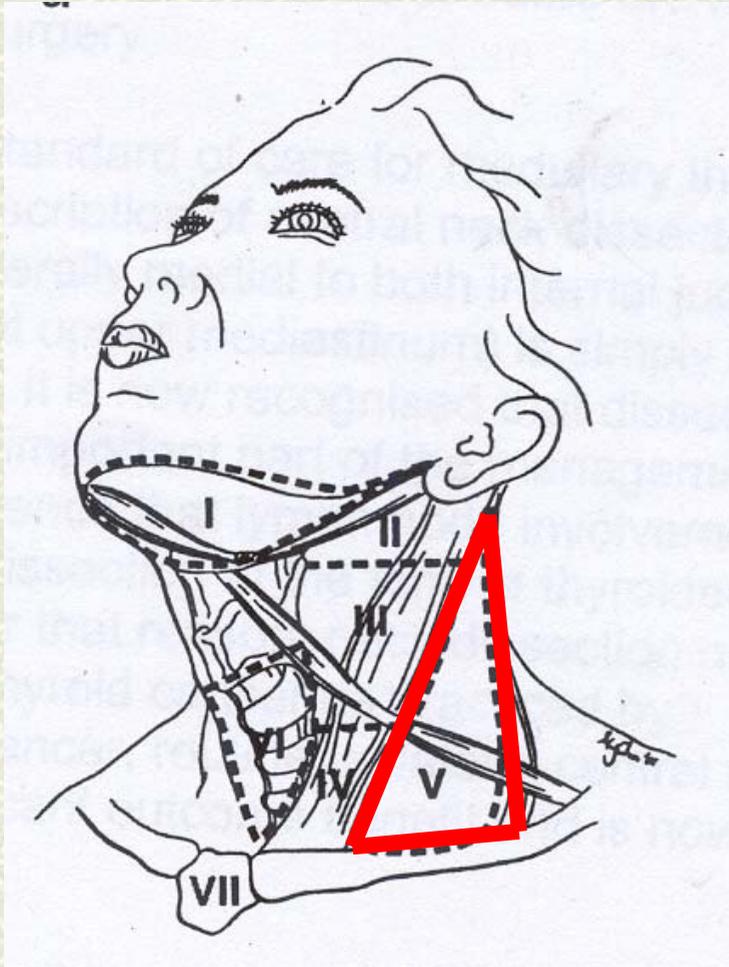


hypoglossal nerve

accessory nerve



Level V

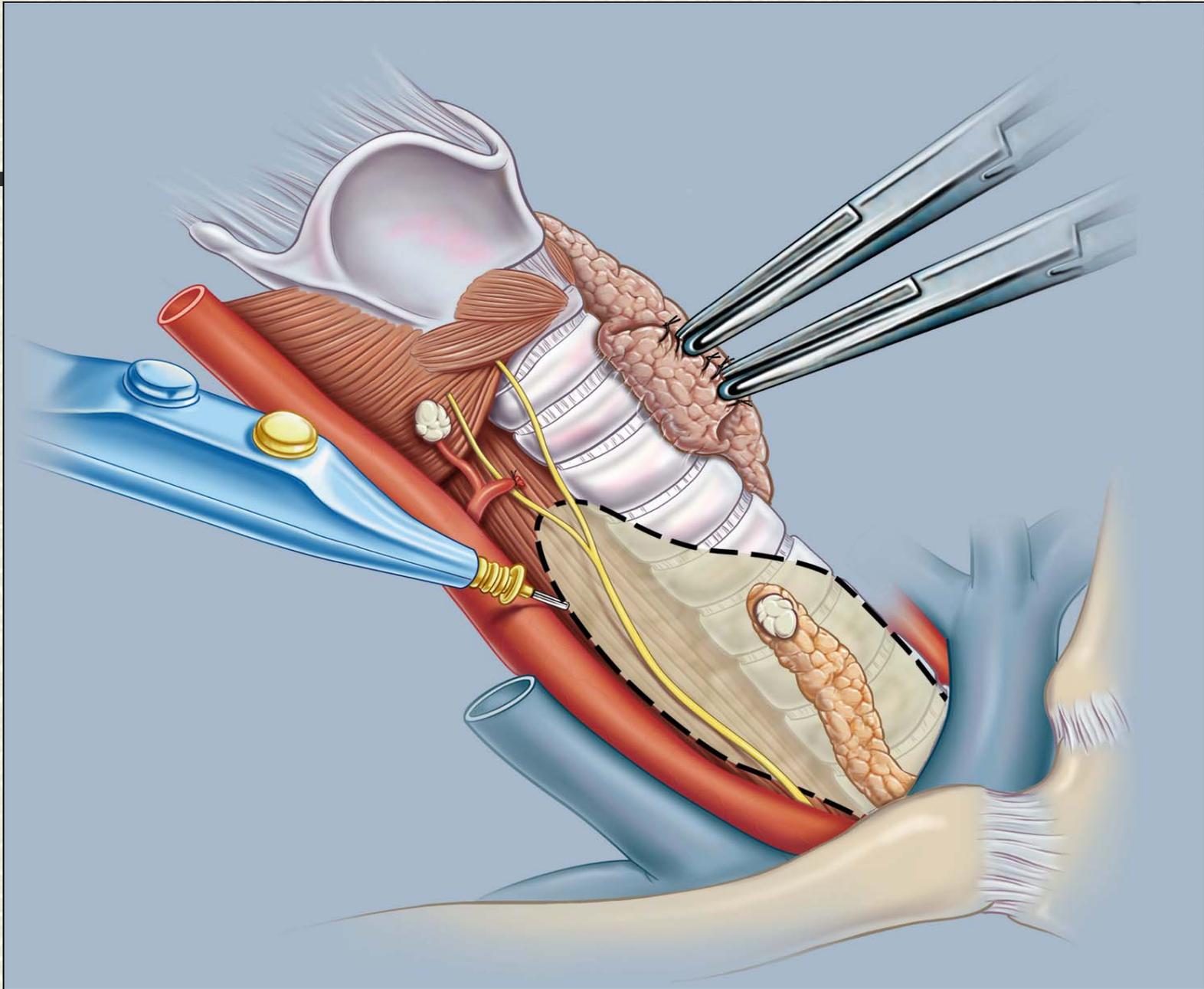


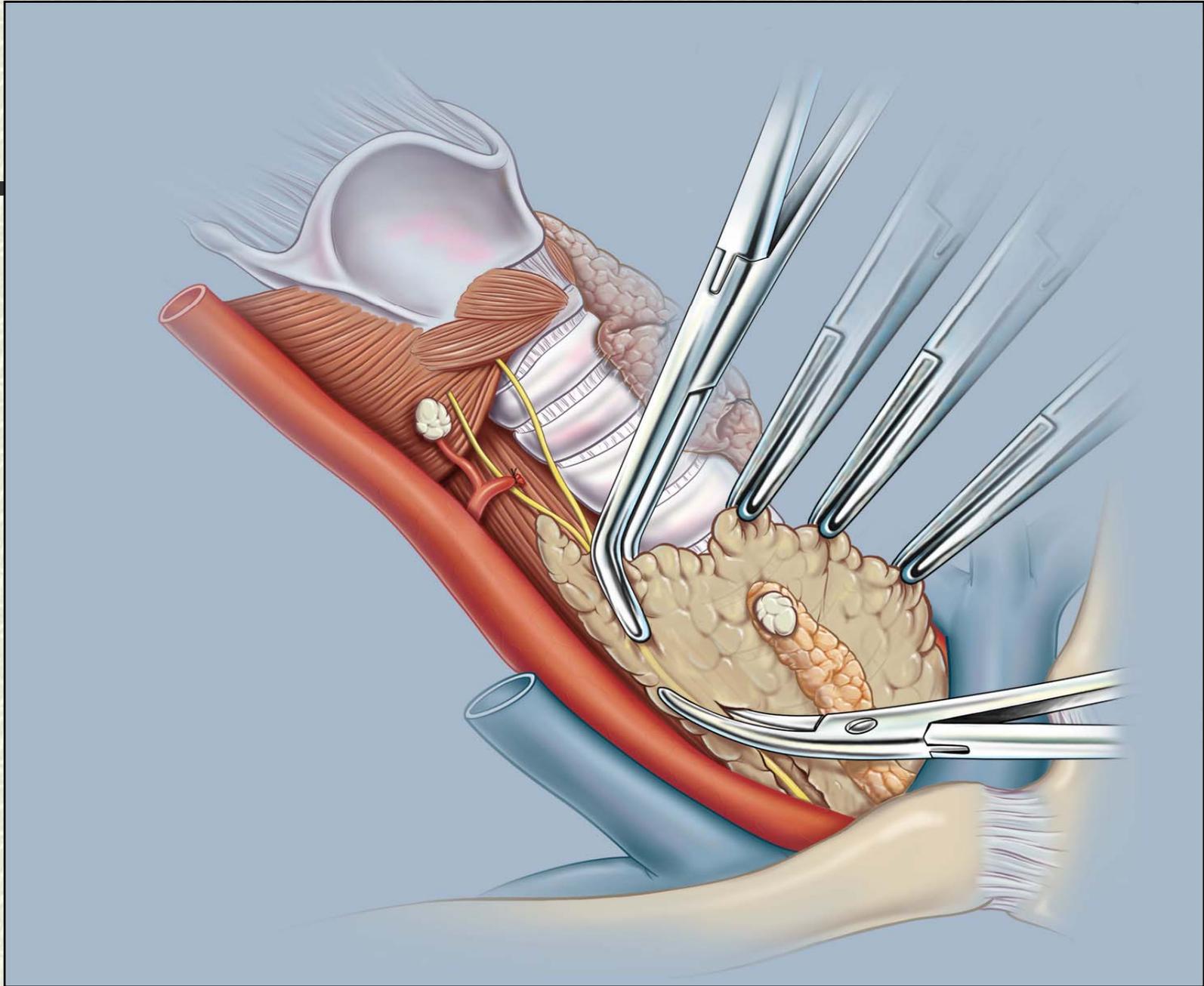


prophylactic level VI dissection

technical aspects

- # performed after total thyroidectomy (at which perithyroidal, pre-laryngeal (delphic) nodes will have been removed)
 - # clearance of tracheo-esophageal groove
 - dissection of RLN to root of neck
 - removal and autotransplantation of inferior parathyroid either within thyro-thymic region or on thyroid gland surface
-

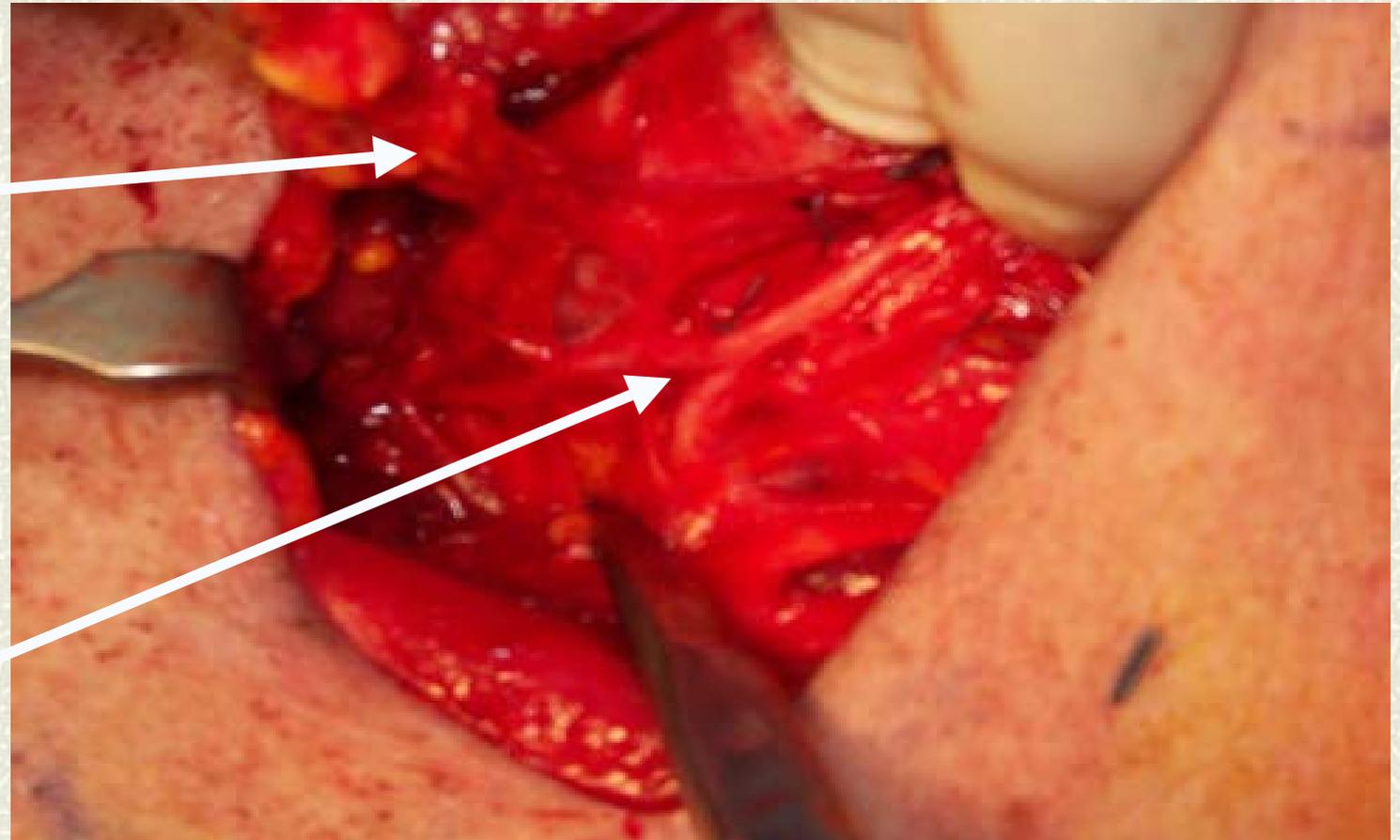




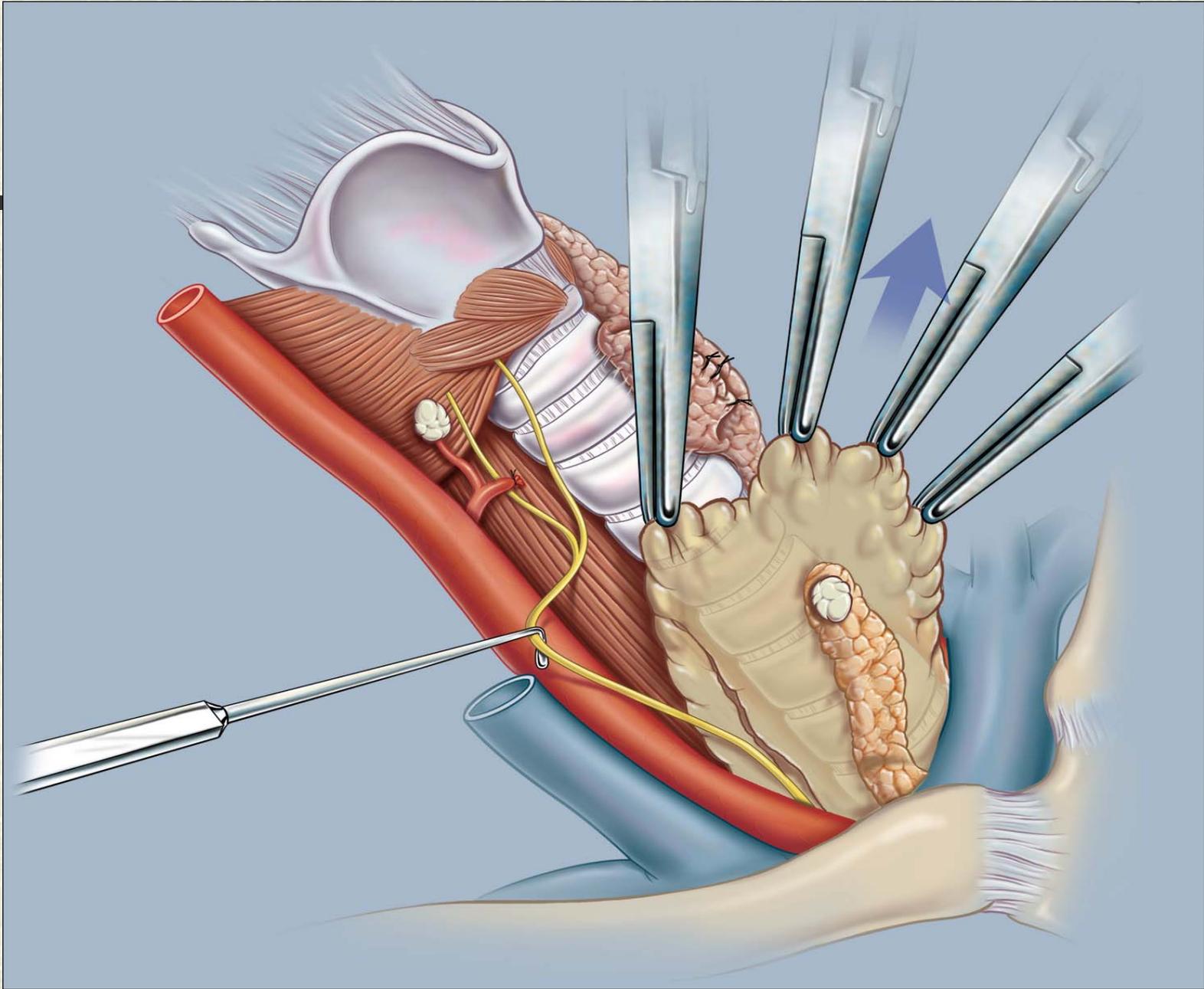


Level VI dissection

paratracheal
(Level VI)
nodes



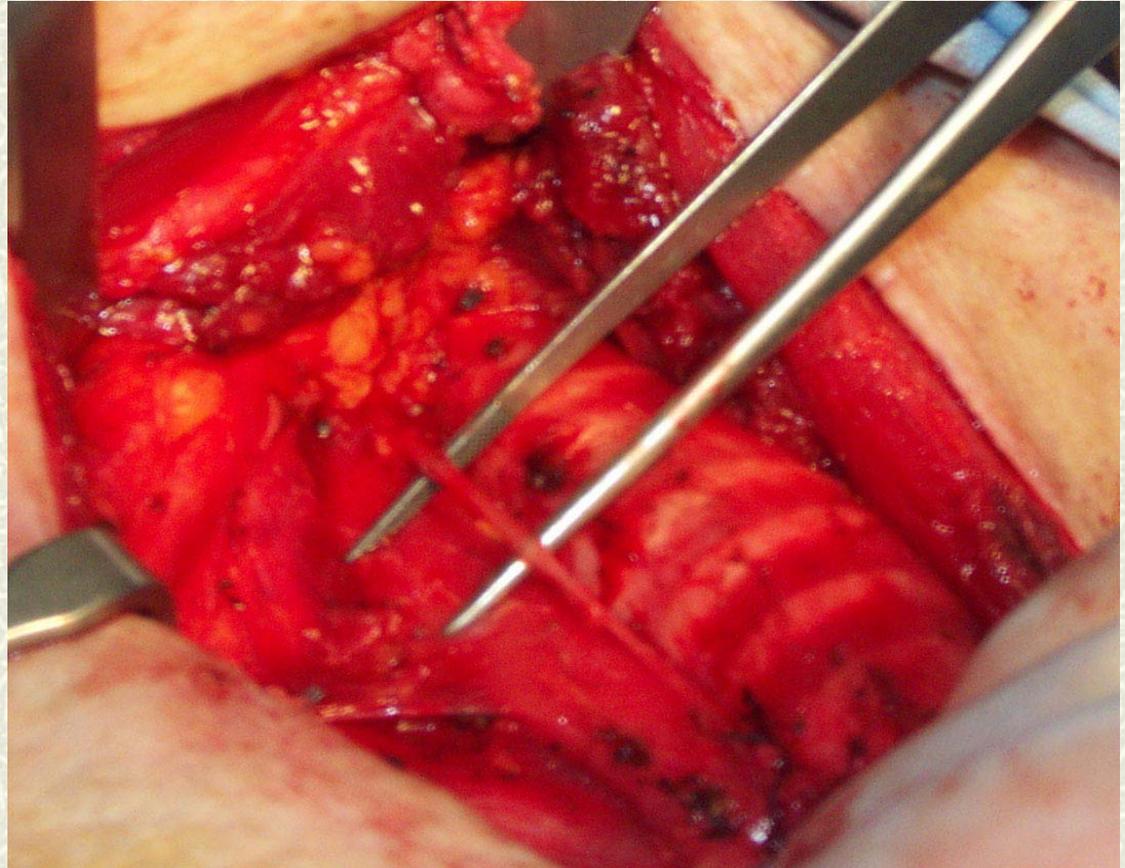
recurrent nerve





tracheo-esophageal groove

clearance of
tracheo-esophageal
involves complete
mobilisation of
recurrent laryngeal
nerve





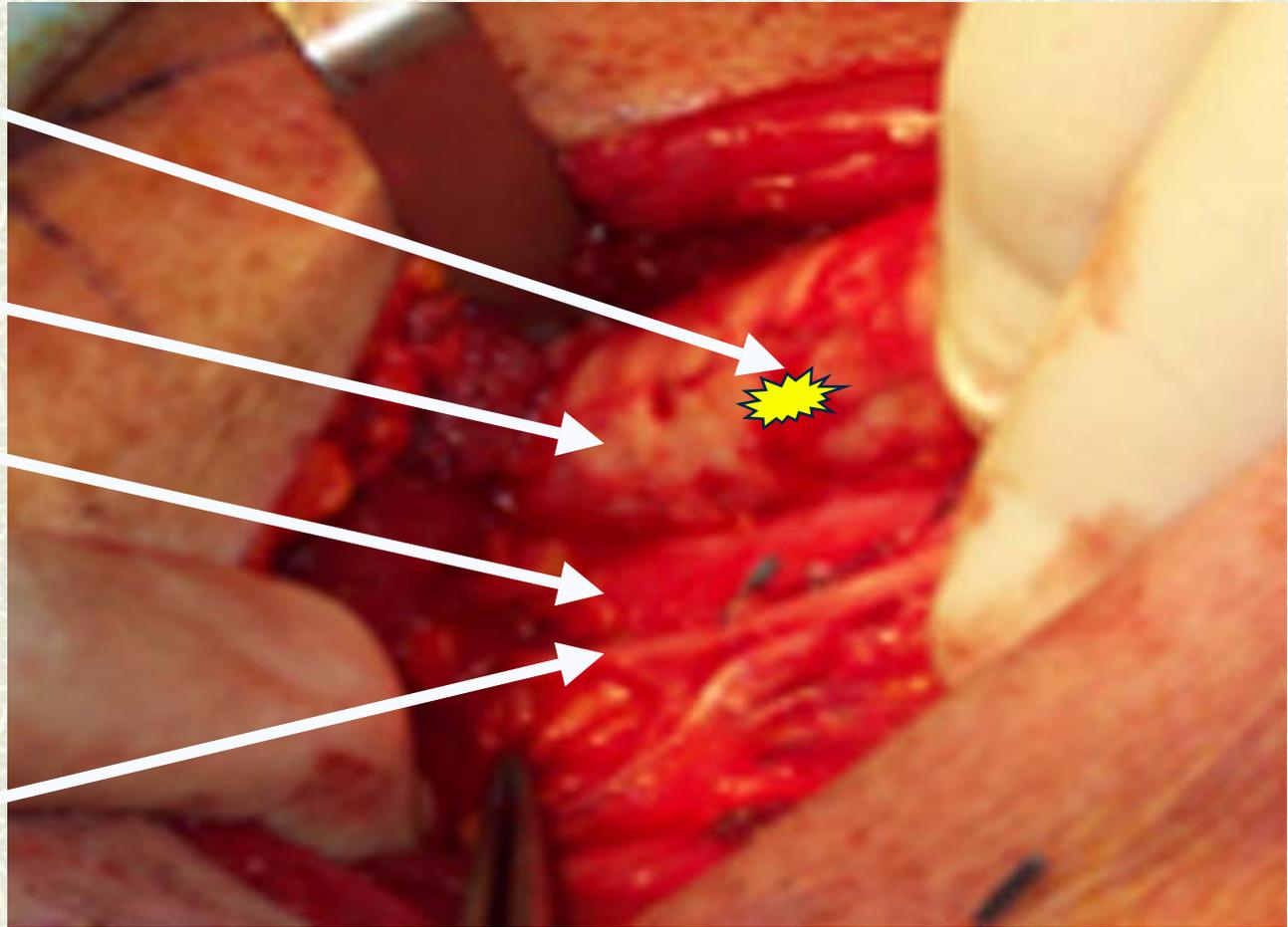
Level VI dissection

inf parathyroid site

trachea

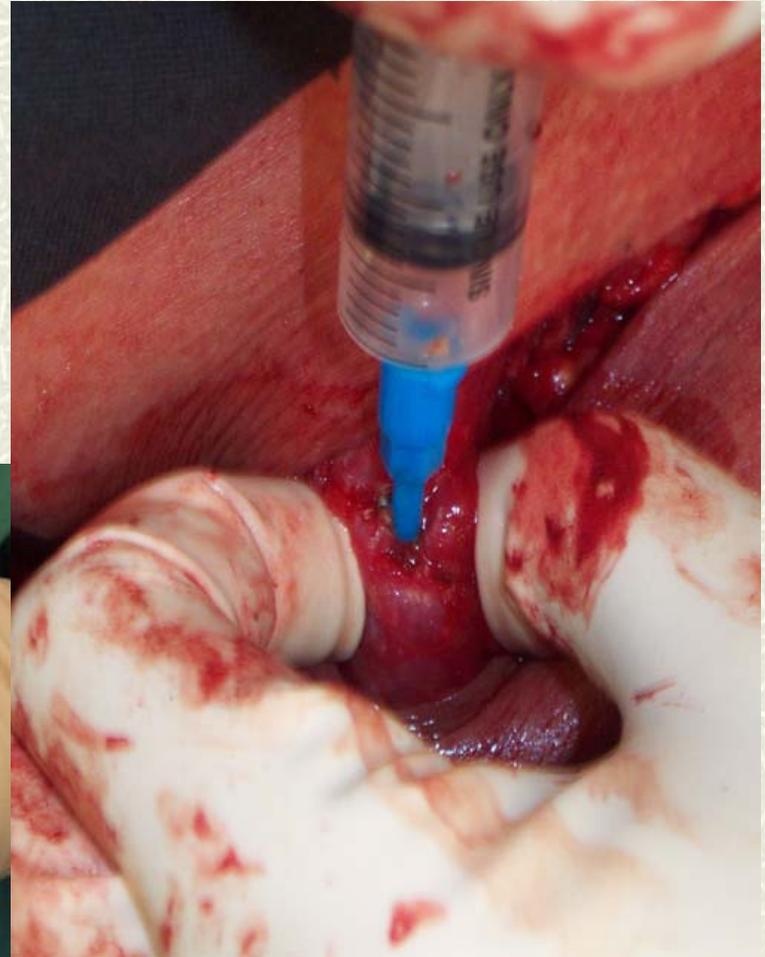
esophagus

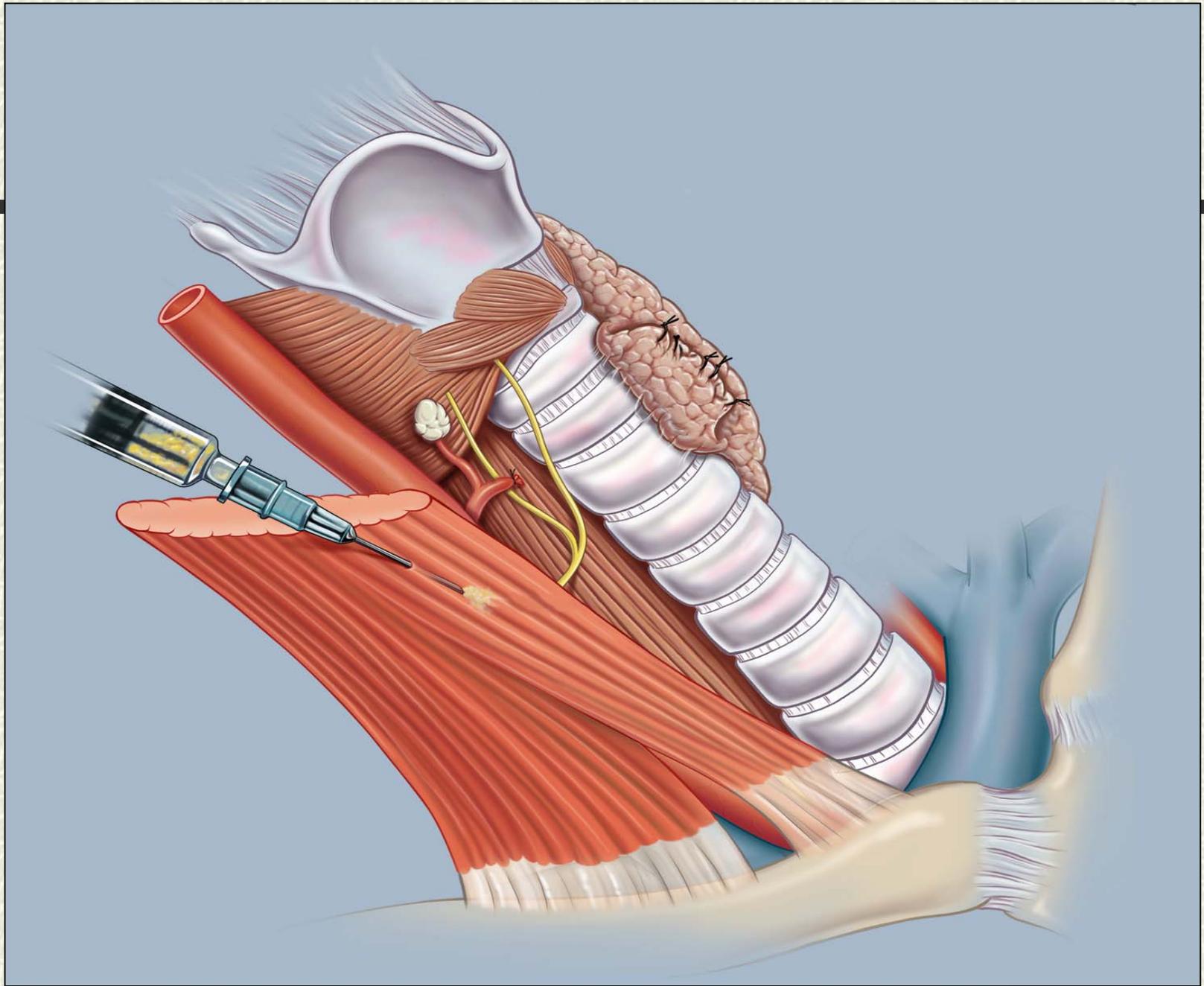
recurrent
nerve





injection technique







sentinel lymph node dissection ?

- # sentinel node biopsy for PTC is feasible
 - *Dixon E, McKinnon G, Pasiaka J World J Surg 2000;11:1396-401*
 - # studies have demonstrated accuracy with identification rates up to 92%
 - *Dzodic R. World J Surg 2006;30:841-6*
 - # technique looking for a role – does it pass the “why bother” test?
 - # SLND finds its place where formal nodal dissection is associated with significant morbidity eg axillary dissection for breast cancer and groin dissection for melanoma
 - # central compartment dissection for PTC can be performed through the same incision with minimal (if any) added morbidity
-



conclusion

- # the management of papillary thyroid cancer should now clearly be tailored to the individual patient, taking into account available clinical and imaging data and risk-stratification, but should also include pre-operative assessment, and consideration of surgical management, of the regional lymph nodes.
-





PMCT incidence

- # overall incidence up to 36% of autopsy specimens
 - *Harach HR, Franssila KO, wasenius VM. Cancer 1985;56:531-538*
- # cervical lymph node metastases do however occur
 - 34 cases of PMCT presenting with cervical lymph nodes
 - 4/34 developed distant metastases and died
 - poor outcome associated with nodes > 3cm, non-encapsulated or sclerosing primary tumors
 - *Sugitani I, Yanagisawa A, Shimizu A et al. World J Surg. 199822:31-3*
- # tumor size not a reliable predictor of biologic behaviour



management of PMCT

- # establish philosophical aim of therapy with patient:
 - if the goal is to eliminate all disease and reduce to a minimum the likelihood of recurrence then total thyroidectomy, node dissection and radioiodine ablation is recommended
 - if the goal is to keep intervention to a minimum while accepting some degree of risk of recurrence the careful follow-up is all that is required
 - *Drucker WD, Robbins RJ. in. Mazzaferi EL, Harmer C, Mallick UK, Kendall-Taylor P (eds) Practical management of thyroid cancer. Springer London 2006:149-64*
-