Low Risk Differentiated Thyroid Cancer

Verona - October 27, 2006

Definition of Risk in the Management of Differentiated Thyroid Carcinoma

Andrea Frasoldati

Unità Operativa di Endocrinologia

Arcispedale S. Maria Nuova Reggio Emilia

Prognostic indicators in differentiated thyroid carcinoma

The biology of thyroid cancer represents a spectrum of behavior ranging from well differentiated thyroid lesions with an excellent prognosis to anaplastic carcinoma....It is important that clinicians have methods at their disposal to assess the behavior of a patient's thyroid malignancy.

DS Dean & ID Hay, Cancer Control 2000

Accurate prognostic assessment of DTC patients is fundamental, in order to:

- **Define an appropriate treatment strategy**
  conservative vs extensive surgery
  indication to ^{131}I ablation treatment

- **Define an appropriate follow-up strategy**

Avoid potentially harmful and morbid measures

Avoid waste of resources

The practical problems associated with risk management

- **Two basic questions: who is at risk and risk of what?**
- **Obtaining current data useful to calibrate models and doing actual risk comparisons**
- **Persuading people to balance risks, rather than passively assume traditional concepts, habits, procedures**

From data analysis to operational models

- **1. Obtaining data to calibrate models.**

Large retrospective studies → univariate and multivariate analysis of different risk factors → elaboration of scoring systems

- **2. Doing actual risk comparisons**

Validation and comparison of different scoring systems in DTC patient populations

Risk assessment in the patient with DTC: the available scoring systems

EORTC	European Organization for Research and Treatment of Cancer, 1979
AGES	Mayo Clinic, Rochester, 1987
MACIS	Mayo Clinic, Rochester, 1993
AMES	Lahey Clinic Foundation, Boston,1988
EOD	Extent of Disease; University of Chicago, 1990
OSU	Ohio State University, Columbus, 1994
MSKCC	Sloan Kettering Centre, New York, 1995
NCTCS	National Cancer Treatment Cooperation Study, 1998

AMES

312 DTC patiernts

(Lahey Clinic Foundation, Boston 1960-1981)

Low risk	High risk
Younger patients (men ≤40, women ≤ 50) M0 Older patients if intrathyroid PTC, minimally invasive FTC Primary cancer <5 cm No distant metastases	All patients M+ Older patients if - Extrathyroid PTC - FTC major capsular invasion - Primary cancer ≥ 5 cm

Risk class	Low	High
20 yr Survival	**99.2%**	**46%**

Cady & Rossi Surgery 104: 947, 1988

MACIS SCORE

1779 PTC patients
(Mayo Clinic 1940-1989)

distant Metastasis:	yes = 3 no = 0
Age at diagnosis	<40 years = 3.1 ≥ 40 = 0.08 x age
inComplete resection:	yes = 1 no = 0
Invasion:	yes = 1 no = 0
Size of tumor	0.3 x size in cm

MACIS Score	**< 6.0**	**6.0 - 6.99**	**7.0 - 7.99**	**> 8.0**
20 yr Survival	**99%**	**89%**	**56%**	**24%**

Hay et al., Surgery 1993; 114:1050-1058

MSKCC (Games)

n = **1038 DTC patients**

(Memorial Sloan Kettering 1930-1985)

	LOW	**Intermediate**		**High**
Age	<45	<45	>45	>45
M0/M1	M0	M1	M0	M1
T (size/extracaps)	T1/T2	T3/T4	T1-T2	T3/T4
Histology and Grade	PTC	FTC and/or high grade	PTC	FTC and /or high grade

Risk class	**Low**	**Intermediate**	**High**
20 yr Survival	**99%**	**85%**	**57%**

Shaha et al., Surgery 1994; 116:1036-1041

UICC/AJCC (TNM) Staging System
n = 700 DTC patients
(University of California, 1970-1995)

	Age< 45 years			Age ≥45 years		
Stage	**T**	**N**	**M**	**T**	**N**	**M**
I	anyT	any N	M0	T1	N0	M0
II	any T	any N	M1	T2	N0	M0
III				T3	N0	M0
				T1-T3	N1a	M0
IV				T4 or N1b or M1		

Stage	I	II	III	IV
Survival rate follow-up 11.3 year	**98.3%**	**84.2%**	**70.0%**	**38.1%**

Loh et al., JCE&M 1997, 82:3553-62

Comparing the Performance of different DTC Scoring Systems

Criterium	Best performing scoring systems
Selectivity in detecting high-risk population	MACIS, AMES, TNM, EORTC
Mortality rate in high vs. low-risk patients	MACIS AMES, EORTC, Ohio, TNM, EOD
Survival rate among different risk classes	TNM, Ohio, EORTC, EOD

Brierley et al., Cancer 1997

RISK OF DEATH IN DTC PATIENTS

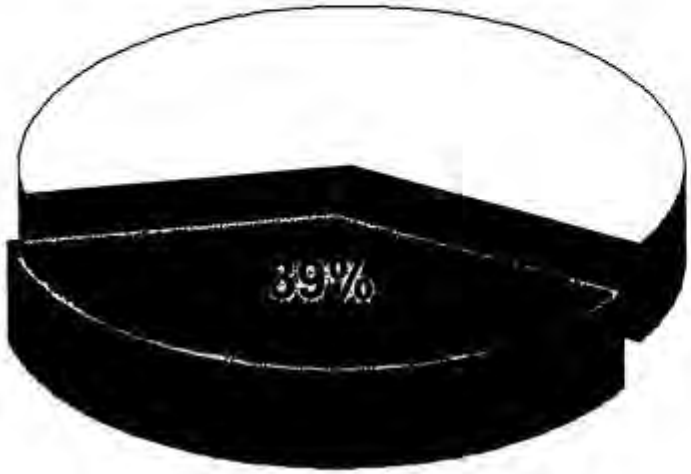
TABLE II.
Differentiated Carcinoma of Thyroid: Impact of Risk Groups on Survival.

Risk Group	No. (%)	Death Rate (%)
Memorial[9]		
Low risk	403 (39)	1
Intermediate risk	403 (39)	13
High risk	232 (22)	54
Mayo[7]		
Low risk	737 (86)	2
High risk	121 (14)	46
Lahey[6]		
Low risk	277 (89)	1.8
High risk	33 (11)	46

Shaha et al., Laryngoscope 2004, 114:393-402

Risk group distribution for low-risk thyroid cancer

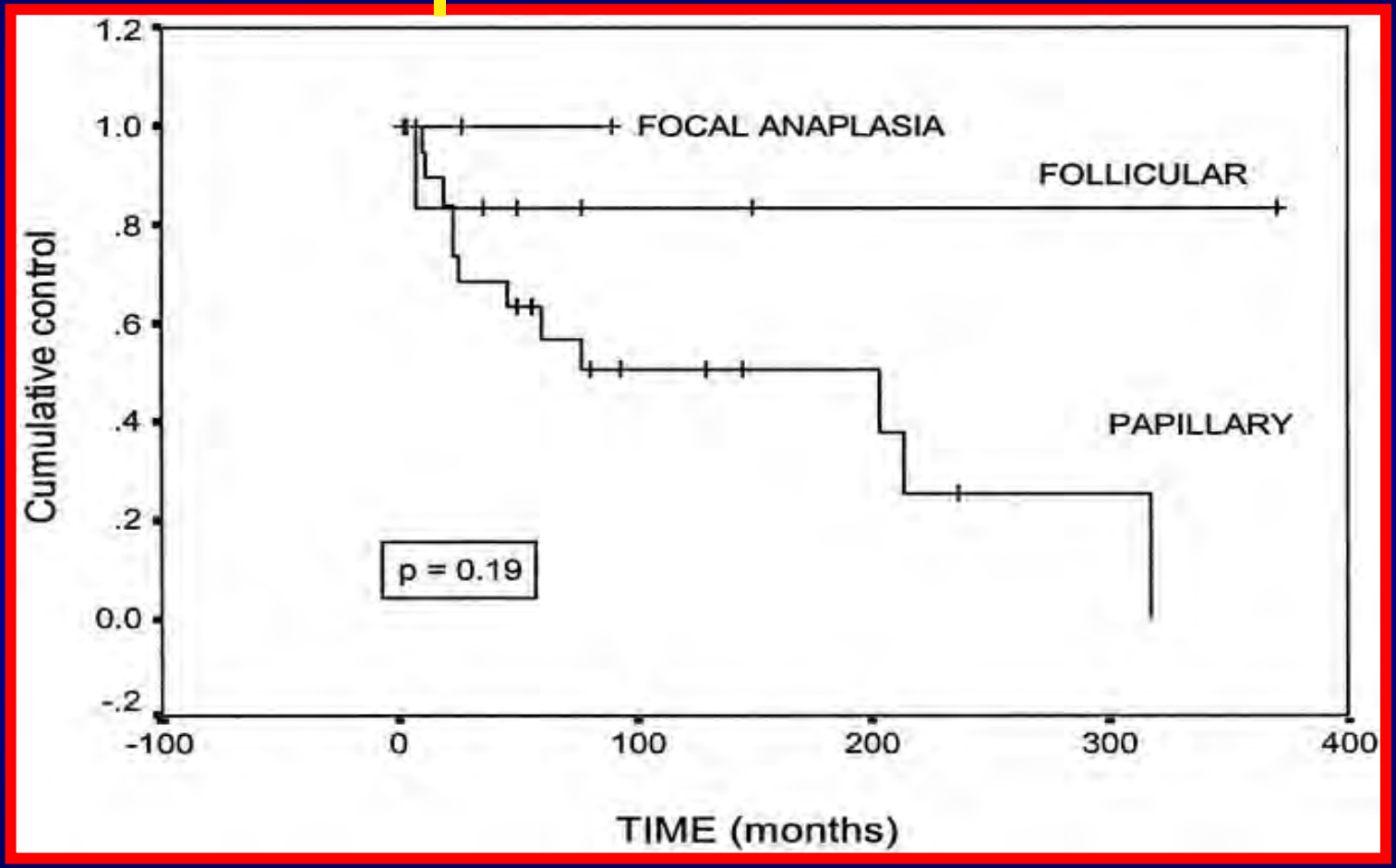
Low Risk Thyroid Cancer



Local rec:	5%
Reg rec:	10%
Dist mets:	2%
5 yr surv:	100%
20 yr surv:	99%
DOD:	1%

Shaha, Laryngoscope, 2004; 114:393-402

Lower locoregional control in patients with PTC



(difference not statistically significant – p = 0.19)

Clark et al. Laryngoscope 2005, 115:661-667

Some Limitations of the available scoring systems 1.

- Definition of low vs. high risk patients is not always consistent among different scoring systems
- Scoring systems may not reflect the actual clinical presentation of patients with DTC
- they do not consider the impact of early diagnosis and therapy on DTC outcome:

↓

Most DTC patients nowadays have a stageI/stage II disease and the proportion of high risk patients is supposed to be small

Some Limitations of the available scoring systems 2.

- Insufficient "***risk of what?***" definition

Risk of loco regional metastasis

Risk of distant metastasis

↓

Risk of disease recurrence

Risk of death

Towards a dynamic definition of Low-risk DTC: the pyramid paradygm

HIGH-RISK patients

LOW RISK

Post ablative setting

Post-surgical setting

Pre-surgical setting

Definition of risk in DTC: operational settings

1. Pre-surgical setting

Patient-related factors: Age/sex – clinical history

Tumor-related factors: US and cytological findings

2. Post surgical setting

Tumor-related factors: Histological findings

Thyroglobulin levels

Negative US imaging

3. Post ^{131}I ablative setting

Thyroglobulin levels

WBS and other imaging studies

Defining of Low-risk DTC in the pre-surgical setting

≤ 1 cm ∅ tumor (cytological pattern of PTC or follicular neoplasm) without US evidence of capsular involvement, multifocality and neck node metastasis

1. Pre-surgical setting
US findings

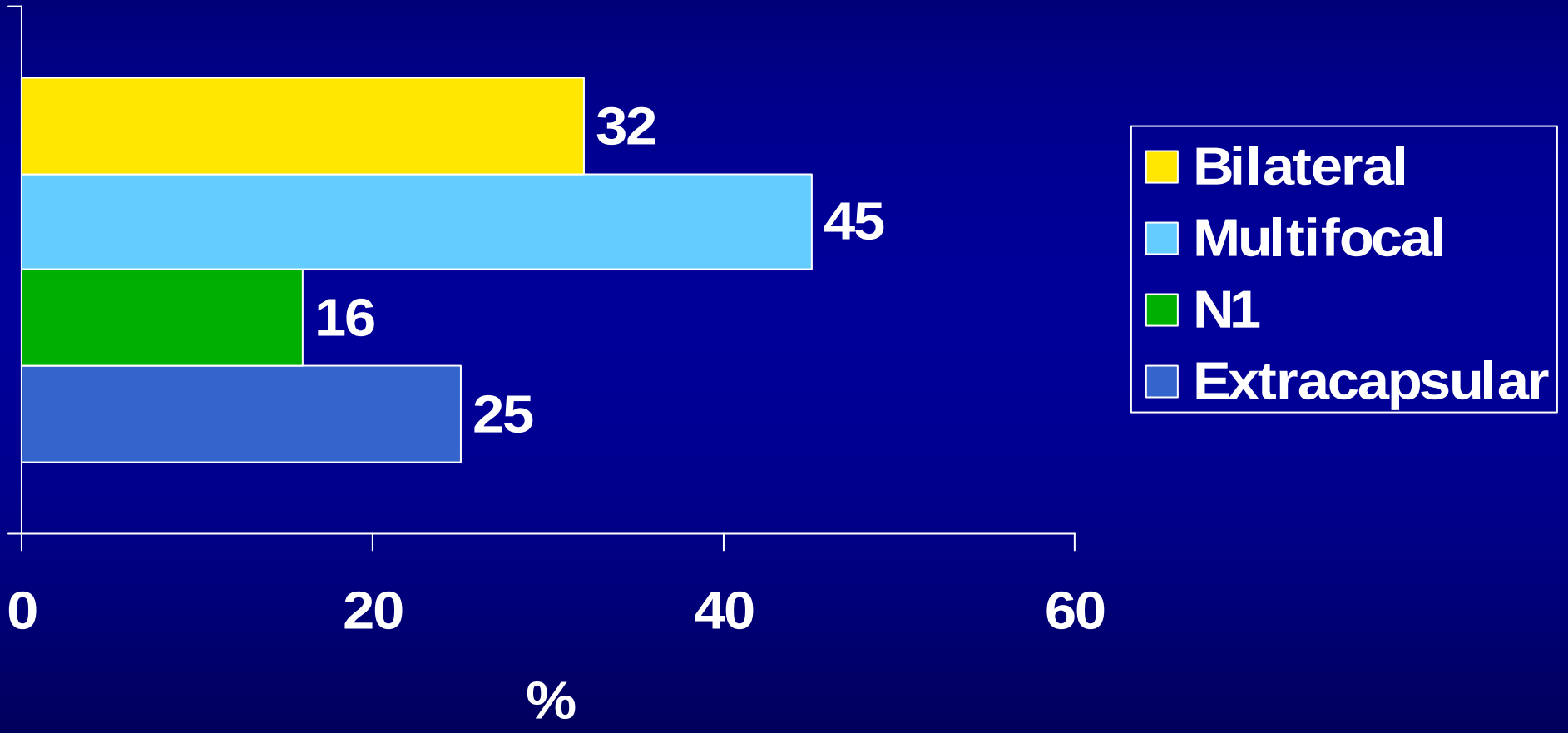
Size

Multifocality/Bilaterality ?

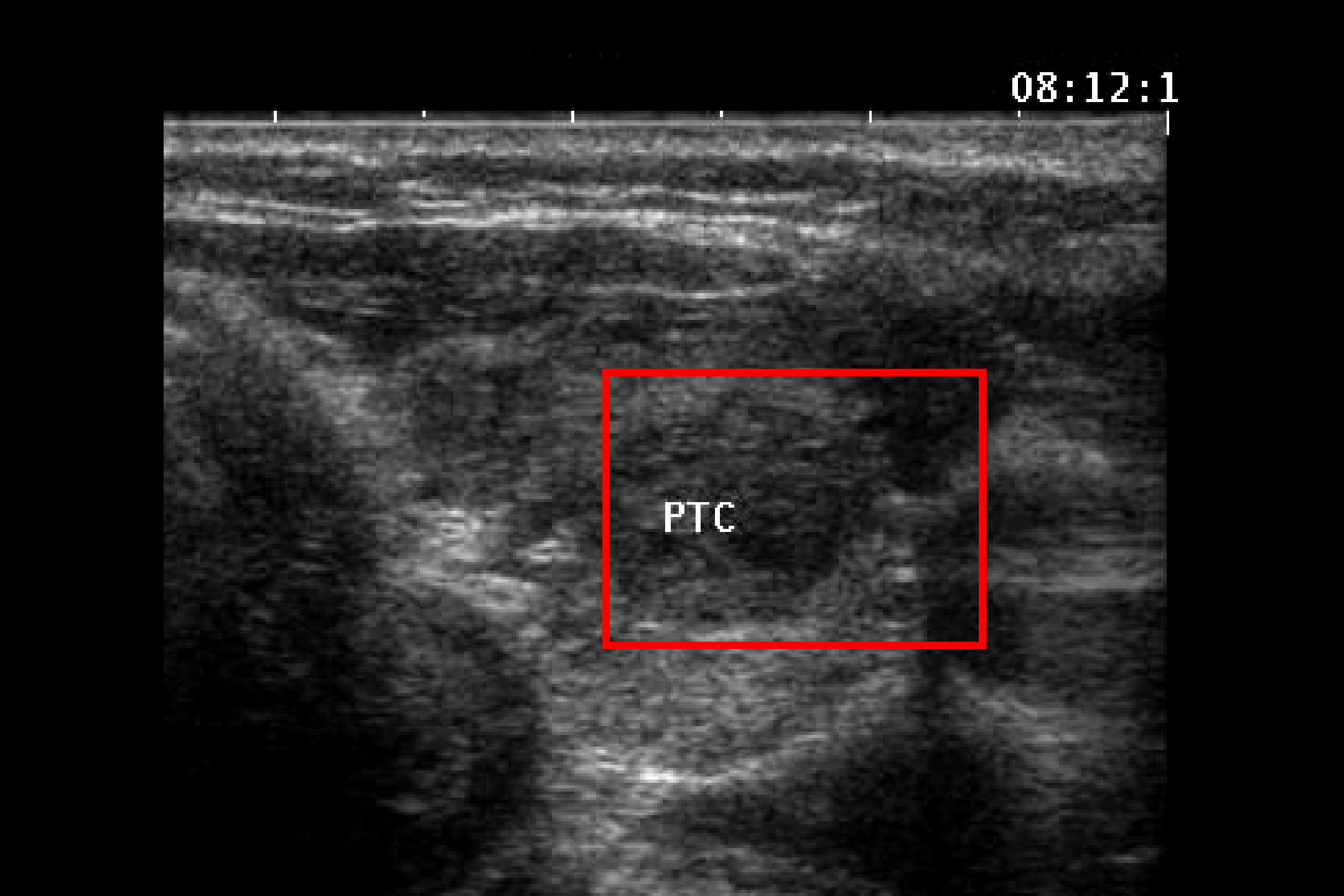
Extracapsular extension/invasiveness ?

Neck lymph node metastases ?

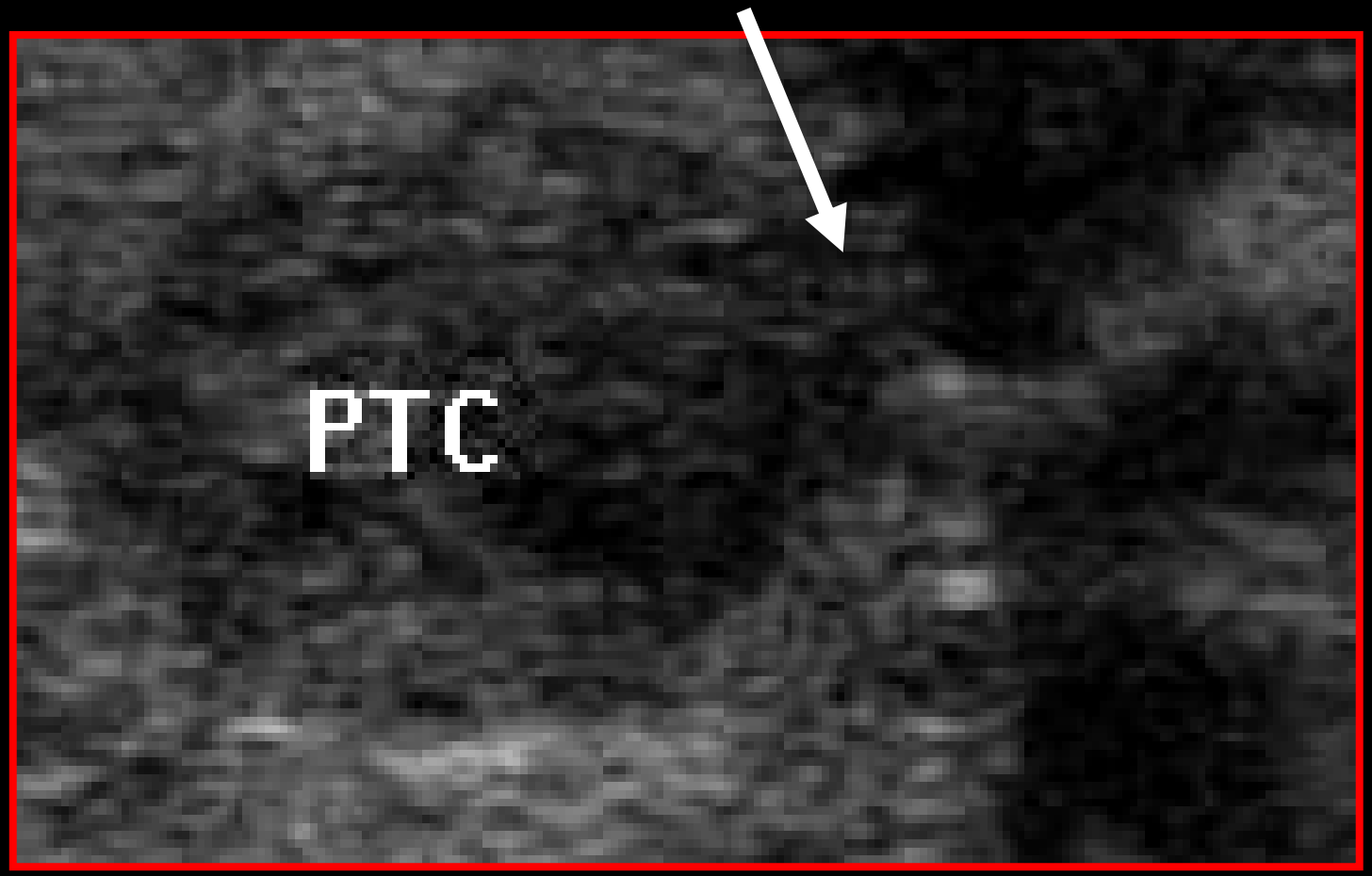
Histological indexes of aggressiveness in a series of ≤ 1 cm ∅ DTC




nm / G 110
08:12:43 AM
PTC


08:12:1
PTC

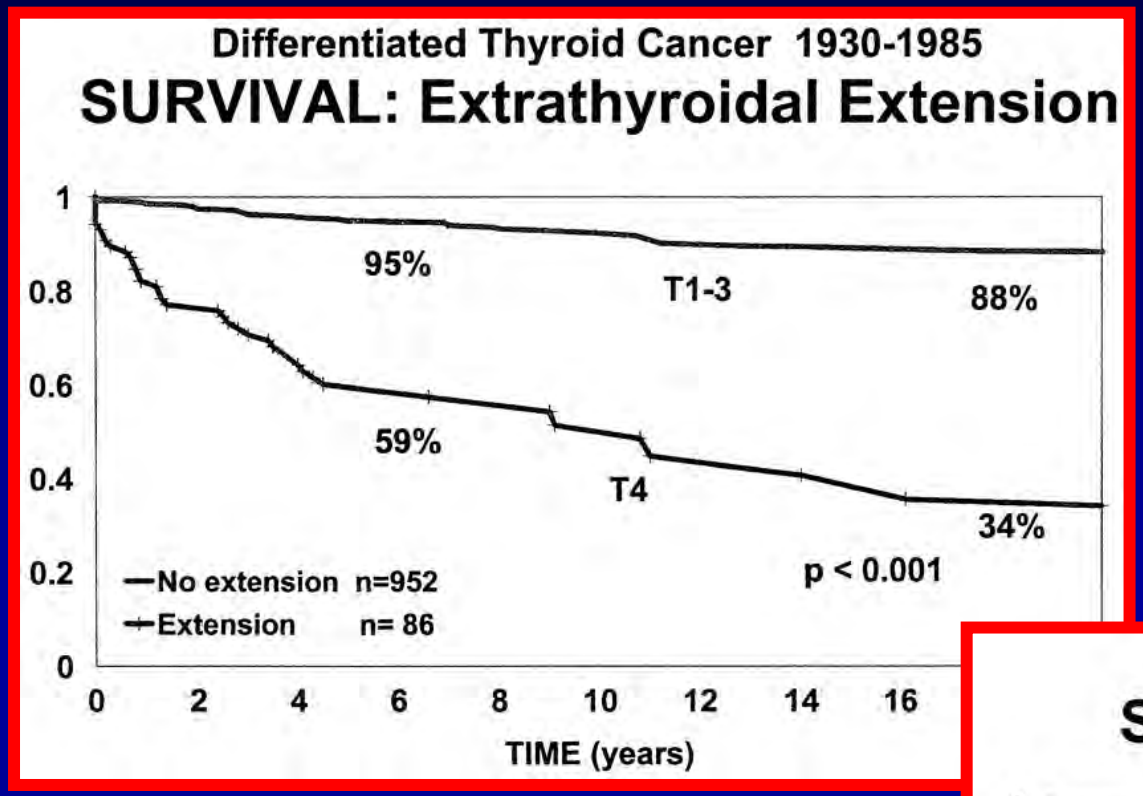
Capsular invasion?



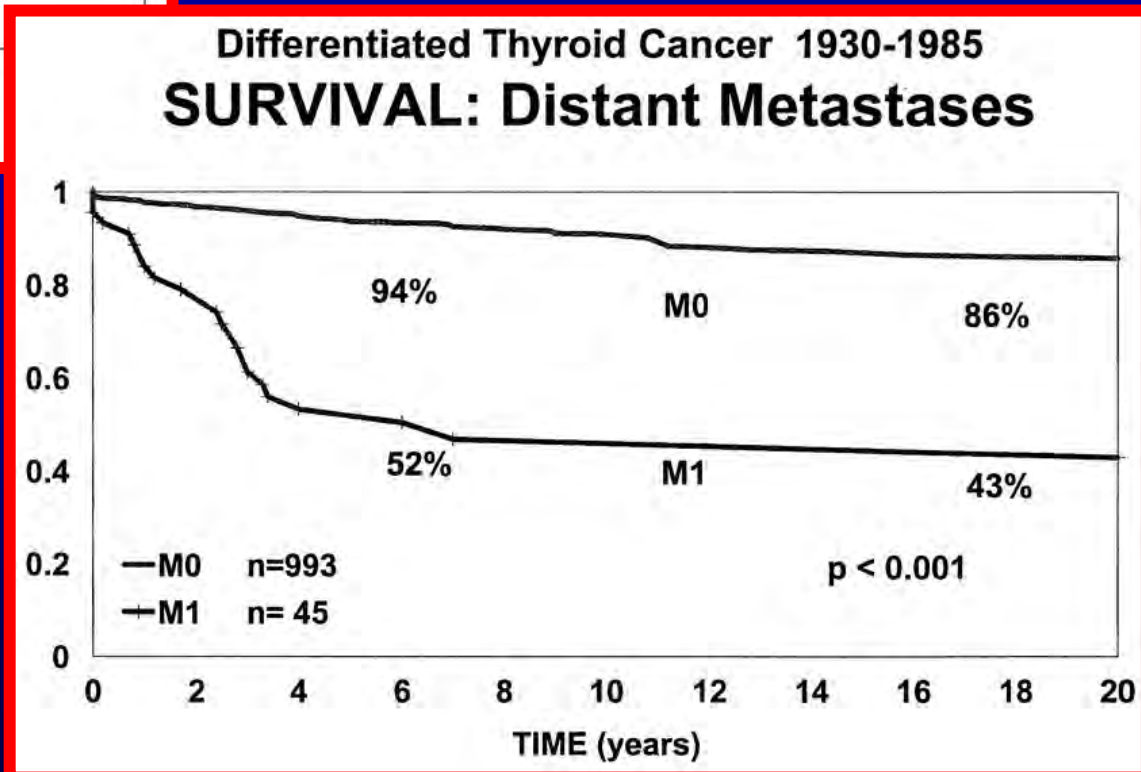
Tumor-related factors in M1 vs. M0 patients

	M1	M0	Significance
PTC:FTC	76:24	85:15	NS
Histol. var.	23.5%	(5-10%)	n.a.
Size	38±32 mm	22±13mm	0.003
% Multifocal	50	38	NS
% ETE	57%	7.2%	<0.001
%N1	57%	26%	<0.001
Tg level	141±119	24.8±62.3	<0.001

Clark et al., Laringoscope 2005, 115:661



DTC Survival by different prognostic factors



Shaha, Laryngoscope 2004, 114:393-402

Pre-surgical lymph node assessment in DTC: false negative US results

Site of FN US	DTC
All pts	151
FN US	47
Central	43
Ipsilateral	5
Controlateral	3

US sensitivity in detecting central compartment lymph node metastases = 52%

Kouvaraki et al., Surgery 2003 134:946-954

Pitfalls in the pre-surgical prognostic assessment

- US cannot reliably detect extracapsular extension
- US/FNA cannot reliably detect mutifocality
- US cannot reliably detect metastatic lymph nodes in the central compartment
- Cytological examination cannot identify more aggressive DTC variants

Towards a dynamic definition of Low-risk DTC: the pyramid paradygm

HIGH-RISK patients

LOW RISK

Post ablative setting

Post-surgical setting

Pre-surgical setting

Defining Low-risk DTC in the post-surgical setting

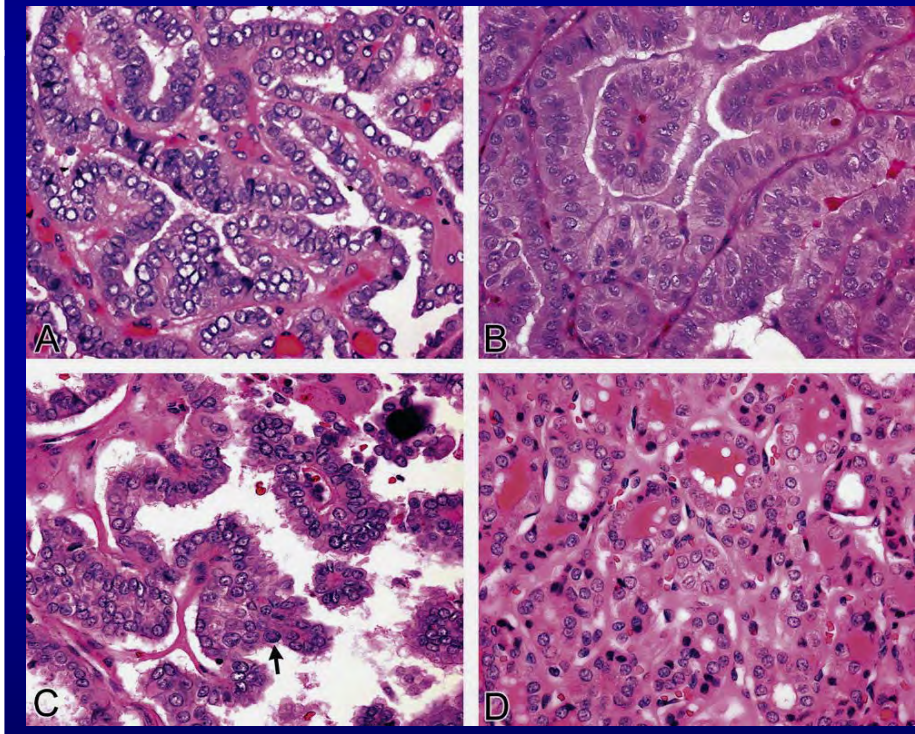
T1N0 DTC without histological clues of possible aggressiveness (PTC variants, FTC angioinvasivity)

Low (≤2 vs. ≤10 vs. ≤30 ng/ml ?) post-surgical off T4 Tg levels

Negative US imaging

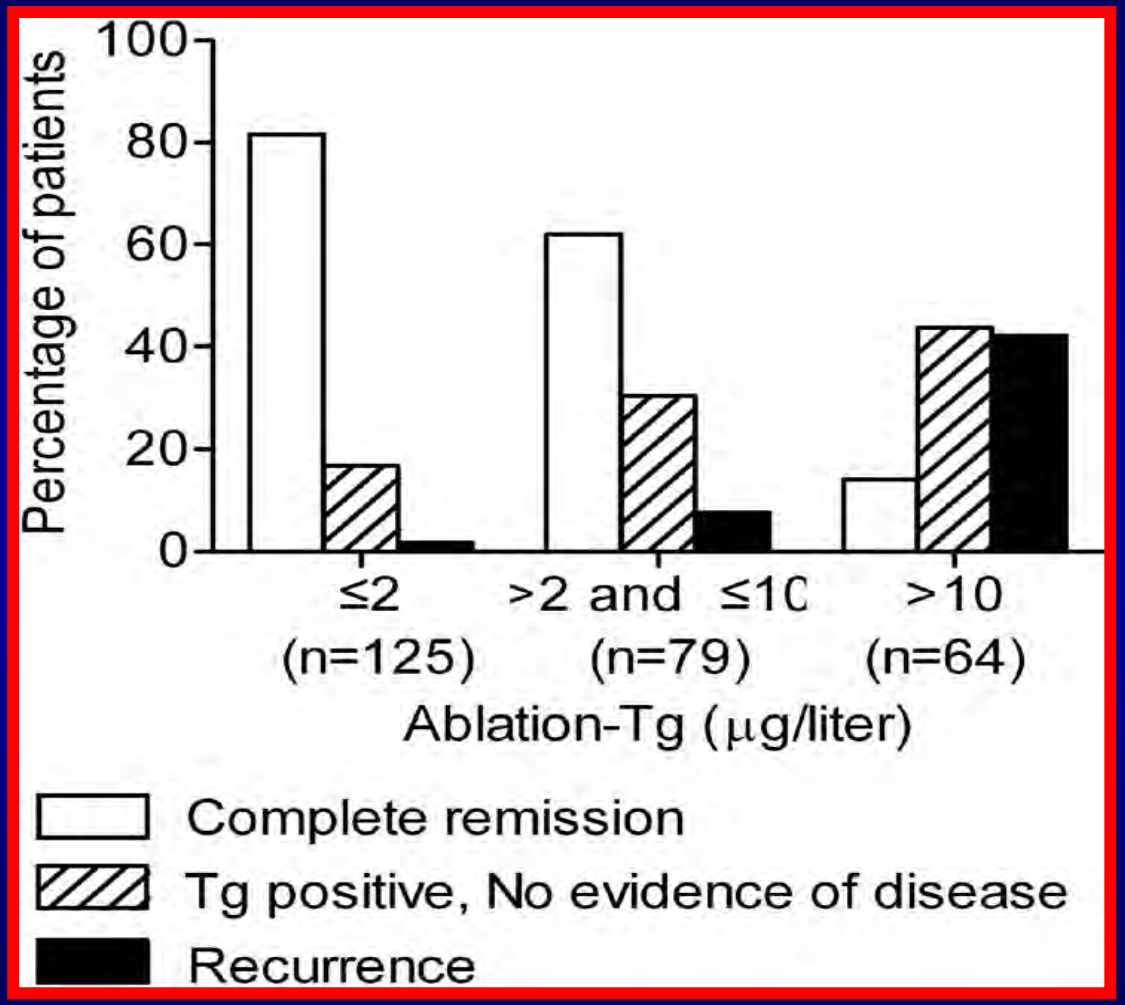
Papillary thyroid carcinoma: histological variety and prognosis

Histologic variant	Tumor disease mortality (%)
Well-differentiated	3.8
Follicular	4.4
Diffuse sclerosis	-
Solid	66.7
Tall cell	55.6
Poorly differentiated	83.3



Ortiz Sebastian et al., Arch Surgery, 2000

Clinical outcome according to serum Tg at the time of remnant ablation



Kim T. Y. et al. J CE&M, 2005;90:1440-1445

Serum Tg levels measured at the time of ^{131}I ablation: predictive value for DTC recurrence

	PPV	NPV
Tg ≤ 2ng/ml		98.4%
Tg ≥2 ng/ml	23.1%	
Tg ≤ 10 ng/ml		96.1%
Tg ≥ 10 ng/ml	42.2%	

Kim T. Y. et al. J CE&M, 2005;90:1440-1445

Pitfalls in the post-surgical prognostic assessment

- In case of conservative surgery, risk of missing bilaterality (30%)
- In case of Total Thyroidectomy without central neck dissection, risk of missing N1a
- Post-surgical Tg levels: which cut-off? what if ↑↑aTG?
- US limitations in the evaluation of thyroid remnants

Towards a dynamic definition of Low-risk DTC: the pyramid paradygm

HIGH-RISK patients

LOW RISK

Post ablative setting

Post-surgical setting

Pre-surgical setting

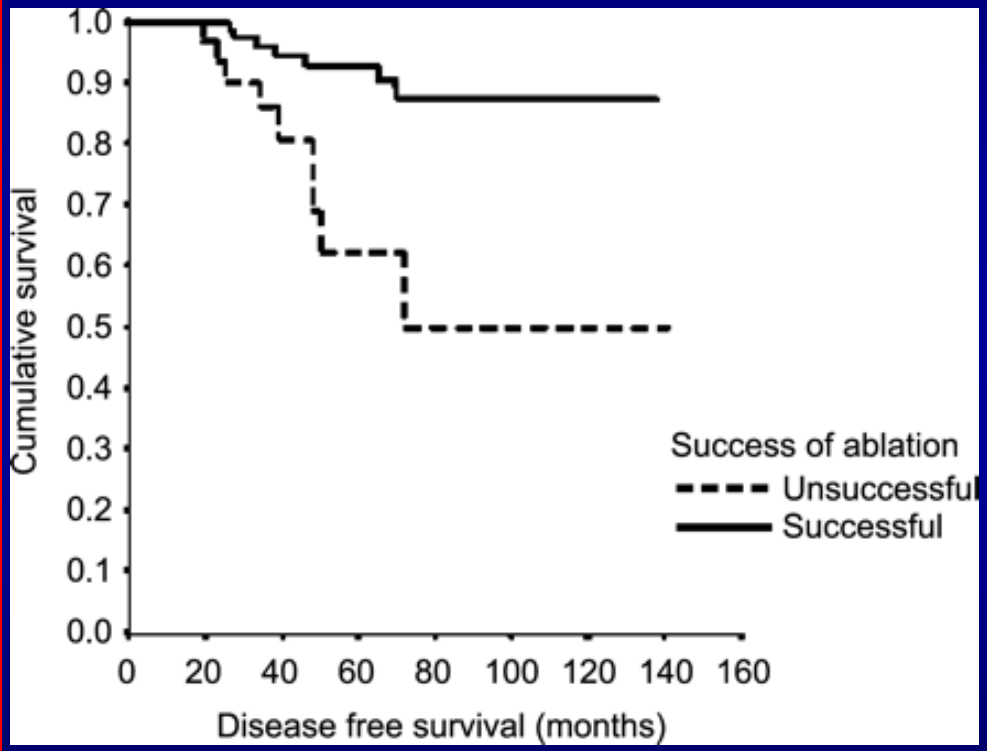
Defining Low-risk DTC in the post-ablative setting

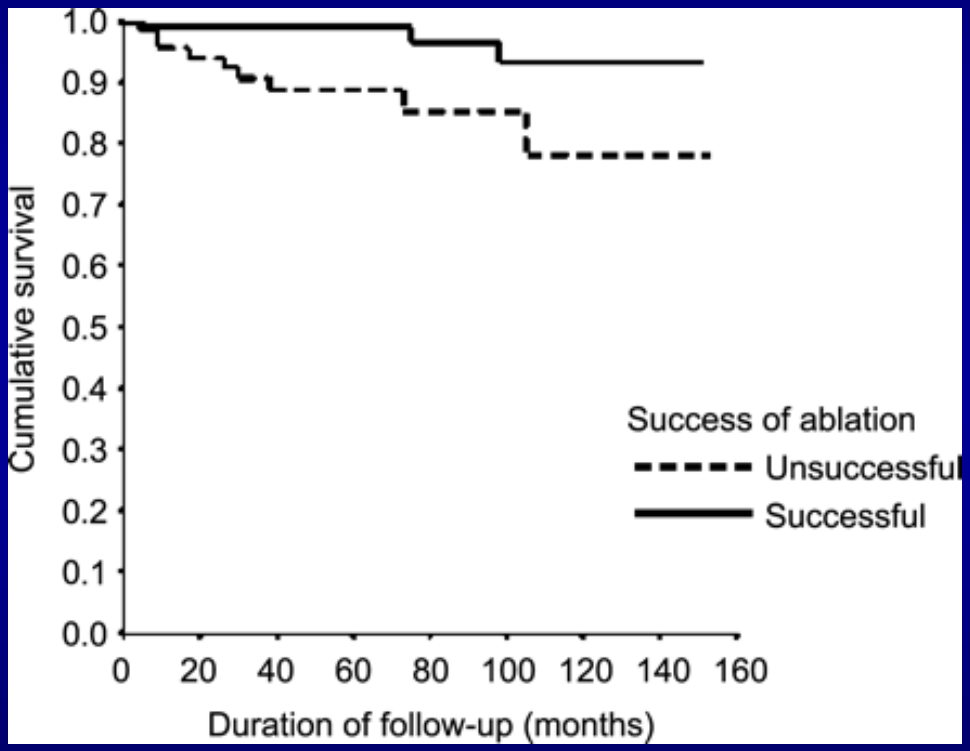
Younger (< 45 trs.) patients with T1-3 N0-1 DTC
Older patients (≥ 45 yrs.) patients with T1-2 N0 DTC

No histological clues of possible aggressiveness (PTC variants, FTC angioinvasivity)

Undetectable/Very low post- ^{131}I ablation TG levels
Negative US imaging
Negative WBS

Prognostic significance of successful ^{131}I ablation in DTC patients





Verburg FA et al., Eur J Endocrinology, 2005, 152: 33-37

Distribution of Clinical Events according to Tg Level after ^{131}I ablation (Tg2) and Lymph Node Status

Tg2 level and lymph node status	No events	Events
N– and Tg2 $\leq$ 10 ng/mL	72	2
N+ or Tg2 $>$ 10 ng/mL	21	14

N– = node invasion absent; N+ = node invasion present.

Toubeau et al., J Nucl Med, 2004 , 45(:988-94.

Low-risk DTC: towards a dynamic definition

…"The definition ***"low risk"*** *is no longer based on initial staging but rather now refers to patients treated by adequate surgery and, when indicated, adjuvant radioiodine treatment, who have* ***no evidence of disease*** *in evaluation performed* ***in the 6-12 months following initial treatment****."…*

Schlumberger et al, Eur J Endocr 2004, 151:539-48

Towards a dynamic definition of Low-risk DTC: the pyramid paradygm

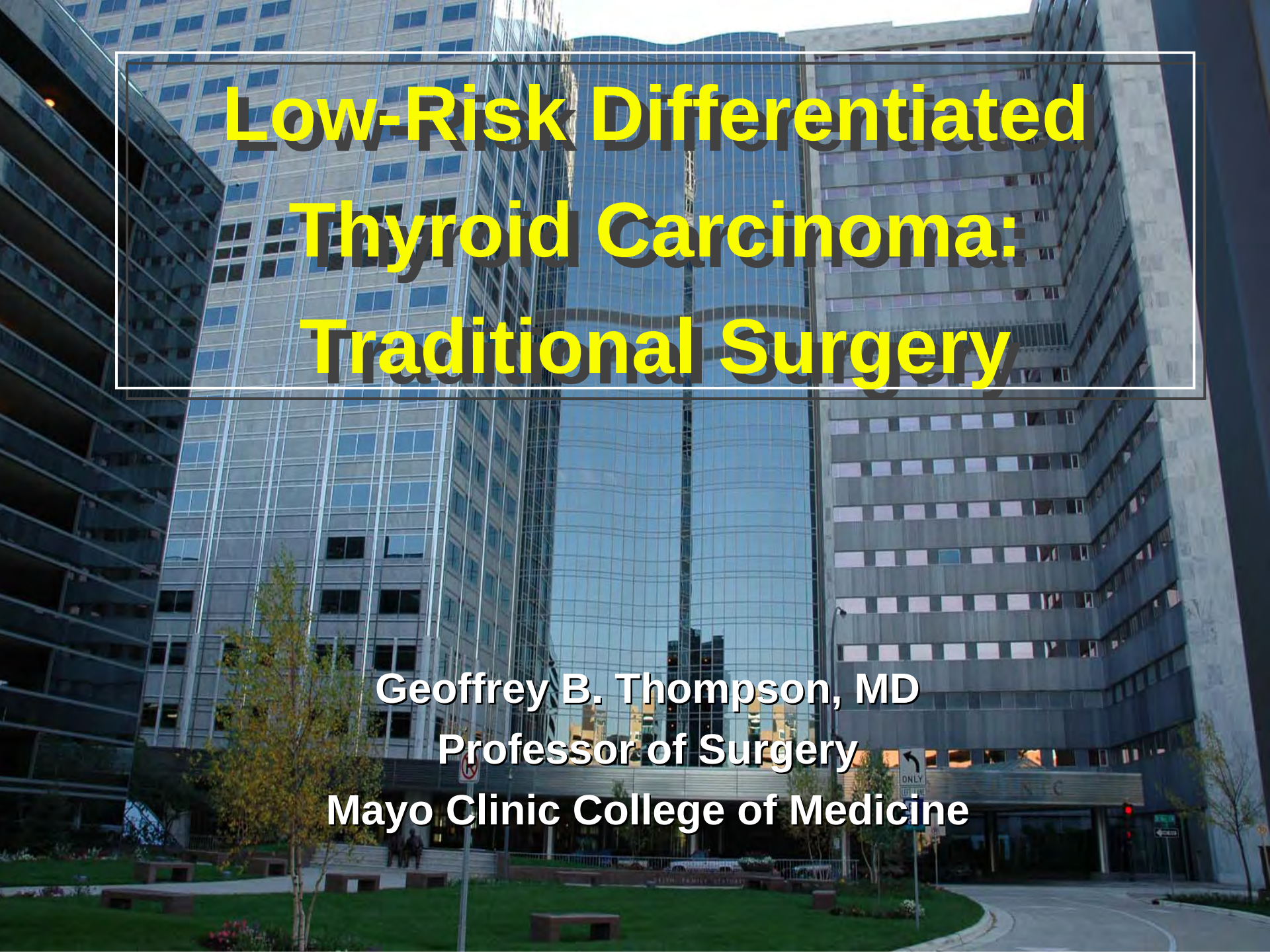
HIGH-RISK patients

LOW RISK

Post ablative setting

Post-surgical setting

Pre-surgical setting



Low-Risk Differentiated Thyroid Carcinoma: Traditional Surgery

Geoffrey B. Thompson, MD
Professor of Surgery
Mayo Clinic College of Medicine

Papillary Thyroid Cancer (PTC)

- Most common endocrine malignancy
- 80% of new cases worldwide
- Extent and type of therapy → controversial
- No long-term prospective controlled trials

Extent of Thyroidectomy (PTC)
Recommendations (Late 90's)

- **American Thyroid Association**
  Near-total or Total
- **AACE**
  Near-total or Total
- **Society of Surgical Oncology**
  Low Risk: Unilateral Lobectomy
  High Risk: Total thyroidectomy

Papillary Thyroid Cancer (PTC)

- Societal recommendations
  - Bilobar resection (BLR) = Near total / Total thyroidectomy
  - Radioiodine remnant ablation (RRA)

Papillary Thyroid Cancer (PTC)

- **Why? (Multicentric Cancer)**
  - Improves cause-specific mortality (CSM)
  - Reduces tumor recurrence (TR)
  - Facilitates radioiodine scanning and use of therapeutic RAI
  - Improves effectiveness of thyroglobulin (Tg) screening

Differentiated Thyroid Carcinoma

MACIS (PTC)

Metastasis (distant)

Age (at diagnosis)

Completeness of primary tumor resection

Invasion of extrathyroidal structures

Size (of primary tumor)

MACIS Prognostic Scoring System

Score = 3.1 (if age = 39 yrs) or 0.08 X age (if age = 40 yrs)

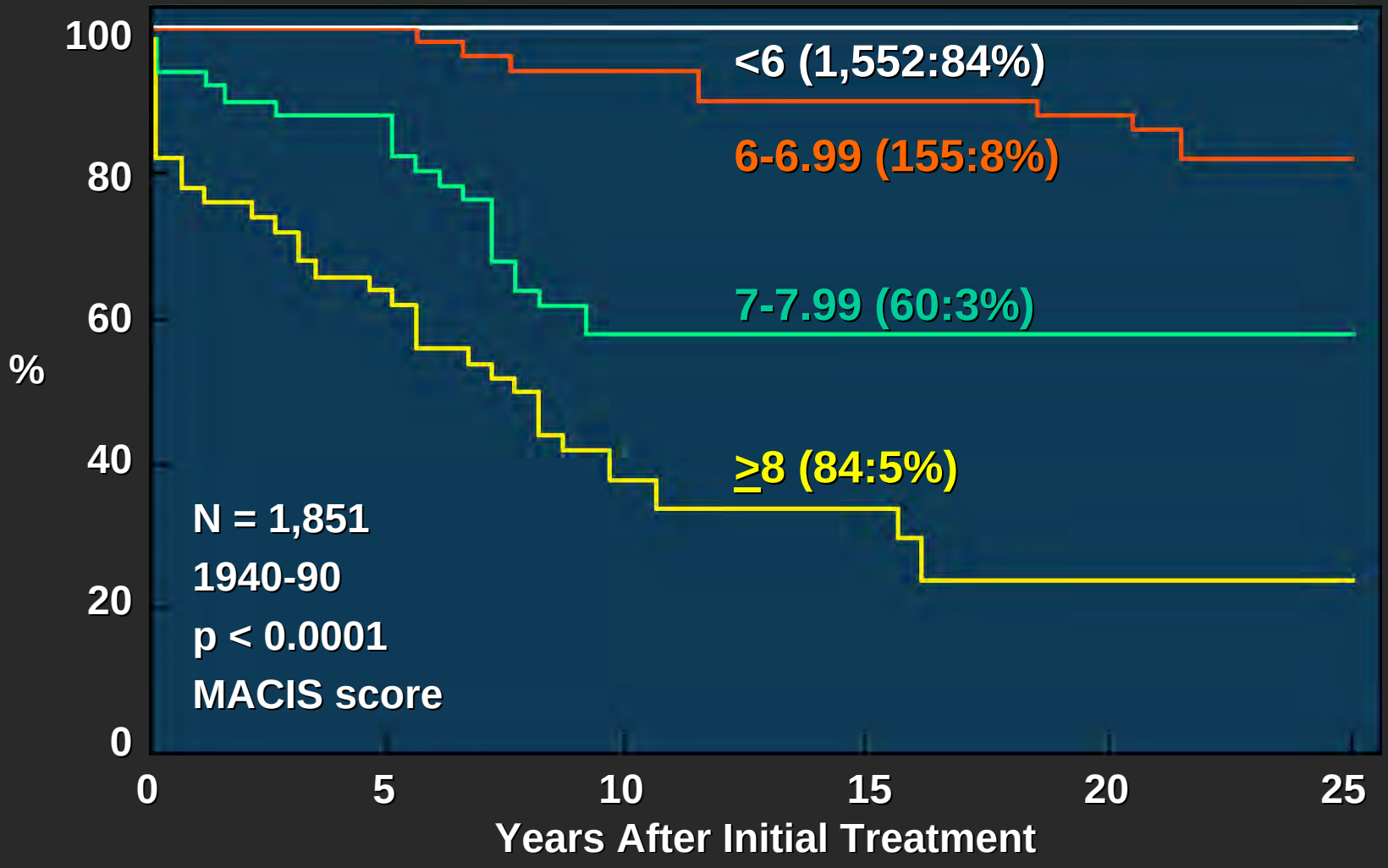
+ 0.3 X tumor size (cm-max diameter)

+ 1 (if incompletely resected)

+ 1 (if locally invasive)

+ 3 (distant spread)

Influence of MACIS Score on Survival from PTC



Survival by MACIS Score @ 20 yrs

- <6 99%
- 6.00-6.99 89%
- 7.00-7.99 56%
- >8 24%

PTC

In low-risk patients:

- No survival benefit: unilateral lobectomy vs bilobar resection
  - Hay et al 1987
- TR higher with unilateral procedure
  - Grant et al 1988, Hay et al 1988

Risk of Locoregional Recurrence

Unilateral Lobectomy

4x-7x higher compared to BLR @ 20 years

Low-Risk DTC Patients: Limited Surgery?

Local Recurrence

- ⇑ Patient anxiety
- ⇑ Physician anxiety
- ⇑ Surgeon anxiety
- ⇑ Need for reoperation
- ⇑ Time away
- ⇑ Cost

PTC

In high-risk patients

- CSM and TR rates higher: unilateral lobectomy vs BLR
  - Hay et al 1987

Low-Risk DTC Patients: Limited Surgery?

Total Thyroidectomy (Morbidity)

- The risk of permanent hypoparathyroidism is significantly greater than lesser resections in many series
- 3% vs 1.4% @ Mayo Clinic (Total vs NT)
- Rates as high as 15-20% have been reported

Hay et al. Surgery 1998; 124:958-966

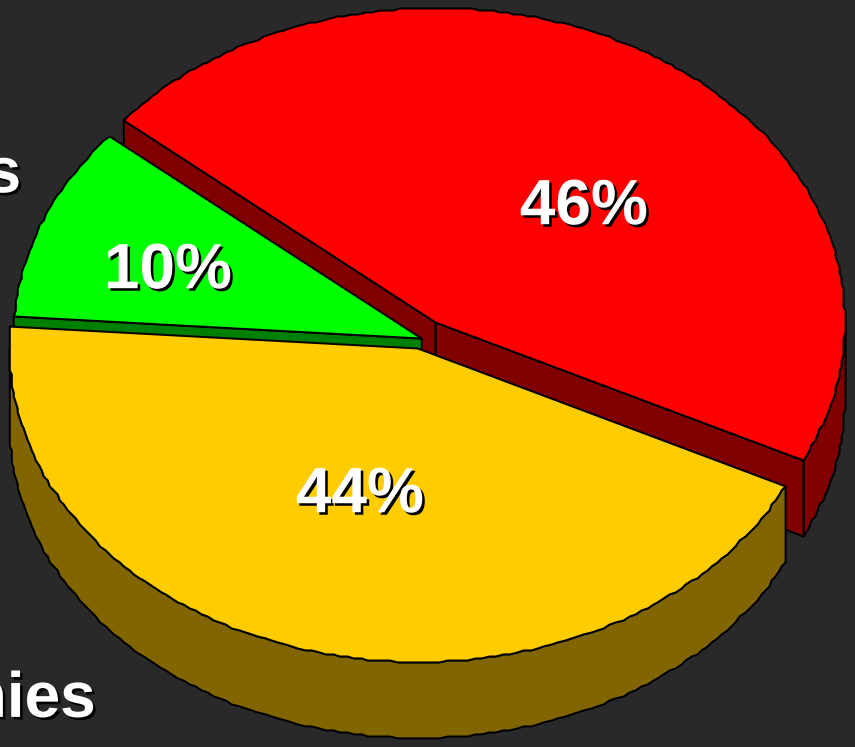
PTC

Near-Total vs Total Thyroidectomy (BLR)

- **No difference** in **CSM or TR** in either **low-** or **high-risk** groups
  - Hay et al 1987

First-Time Operations for Low-Risk PTC

1999-2000 (24 months)
124 patients



Permanent Vocal Cord Paralysis

None

Permanent Hypoparathyroidism

- 3 patients (Total) 5.3%
- 1 patient (NT) 1.9%

3.2%

Low-Risk DTC Patients: Limited Surgery?

These additional local recurrences can be nearly eliminated without a significant increase in permanent hypoparathyroidism

Low-Risk DTC Patients: Limited Surgery?

How?

Near-Total Thyroidectomy

Not routine Total Thyroidectomy or Unilateral Lobectomy

PTC

- Mayo Clinic: 1940-2000
- 2,512 consecutive patients
- 43,095 person-years of follow-up
- Median follow-up: 14 years (60 years)

Hay et al, 2002

PTC

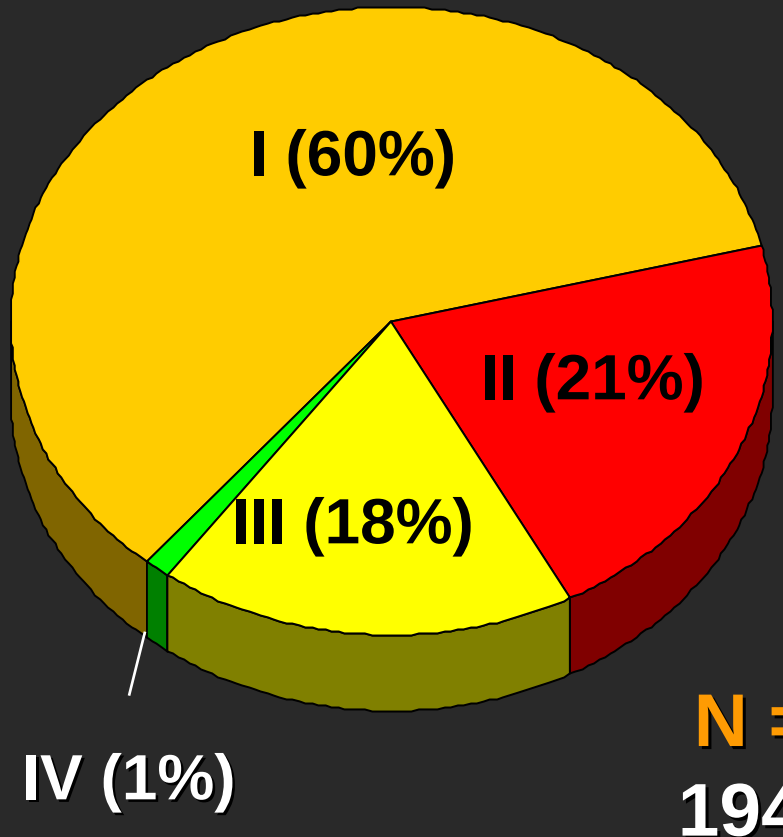
- Death from PTC: 106 patients (4%)
- Excluded (TR):
  - Distant mets within 30 days
  - Incomplete resection

Hay et al, 2002

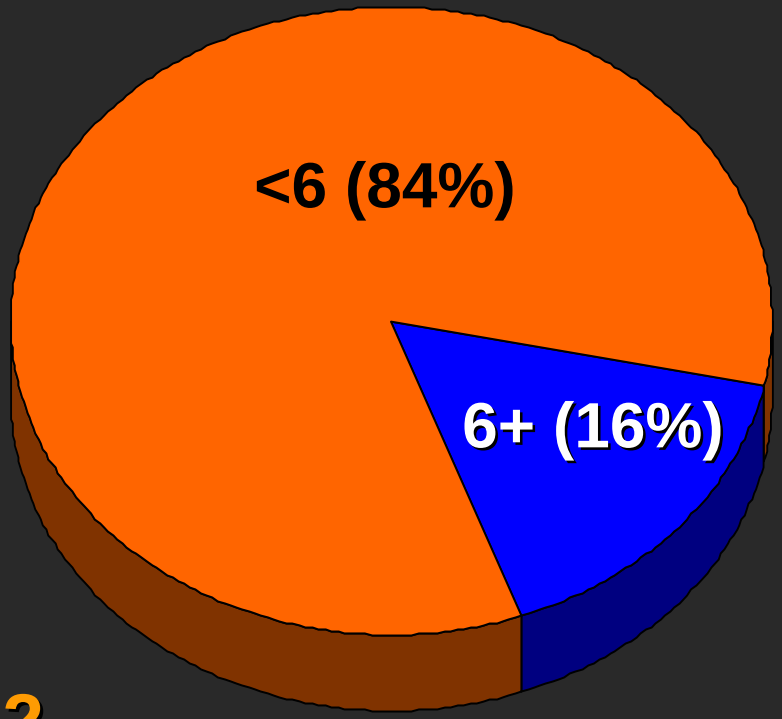
Papillary Thyroid Carcinoma 1940-2000

Presenting Disease

p TNM Stages



MACIS Scores



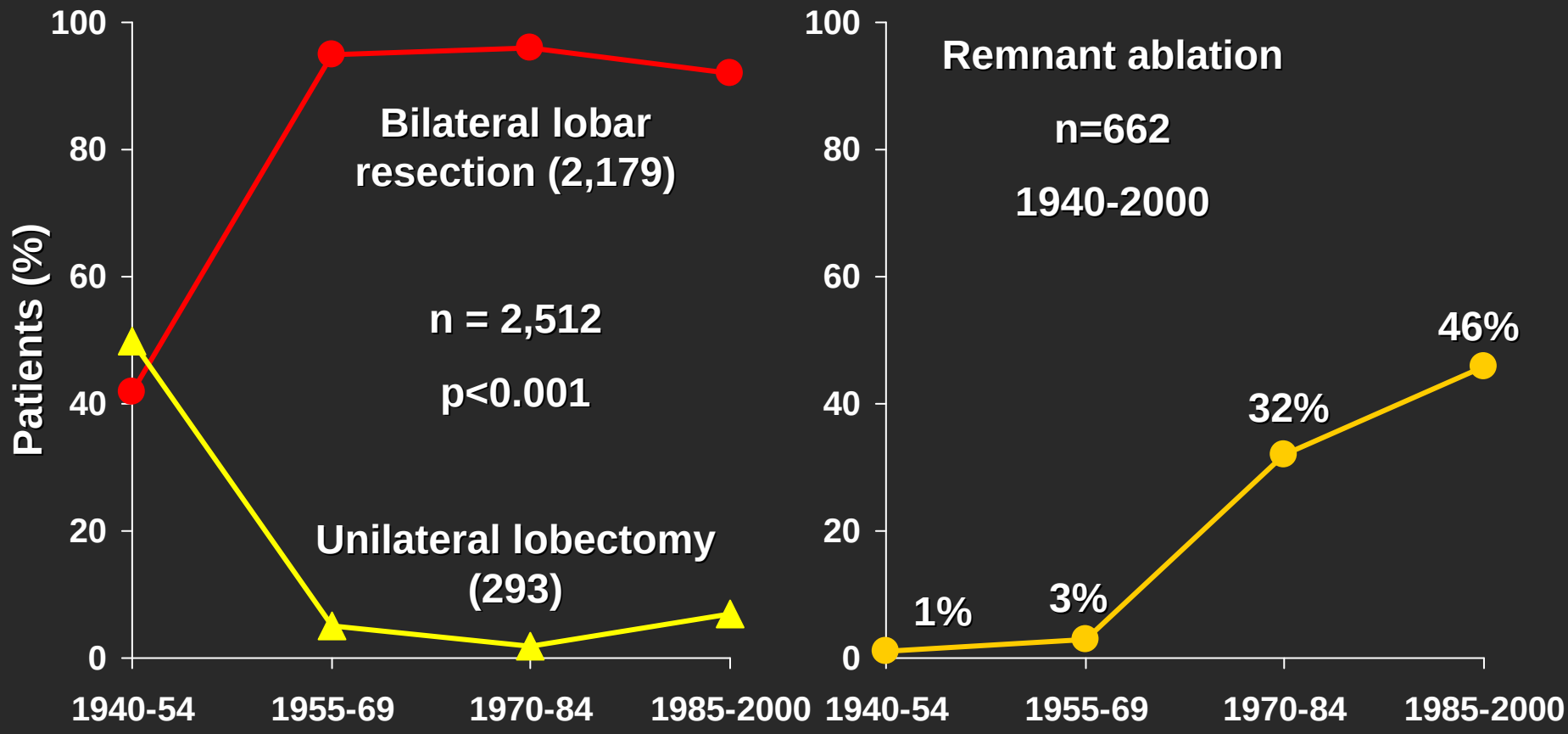
N = 2,512

1940-2000

Hay et al, 2002

Papillary Thyroid Carcinoma 1940-2000

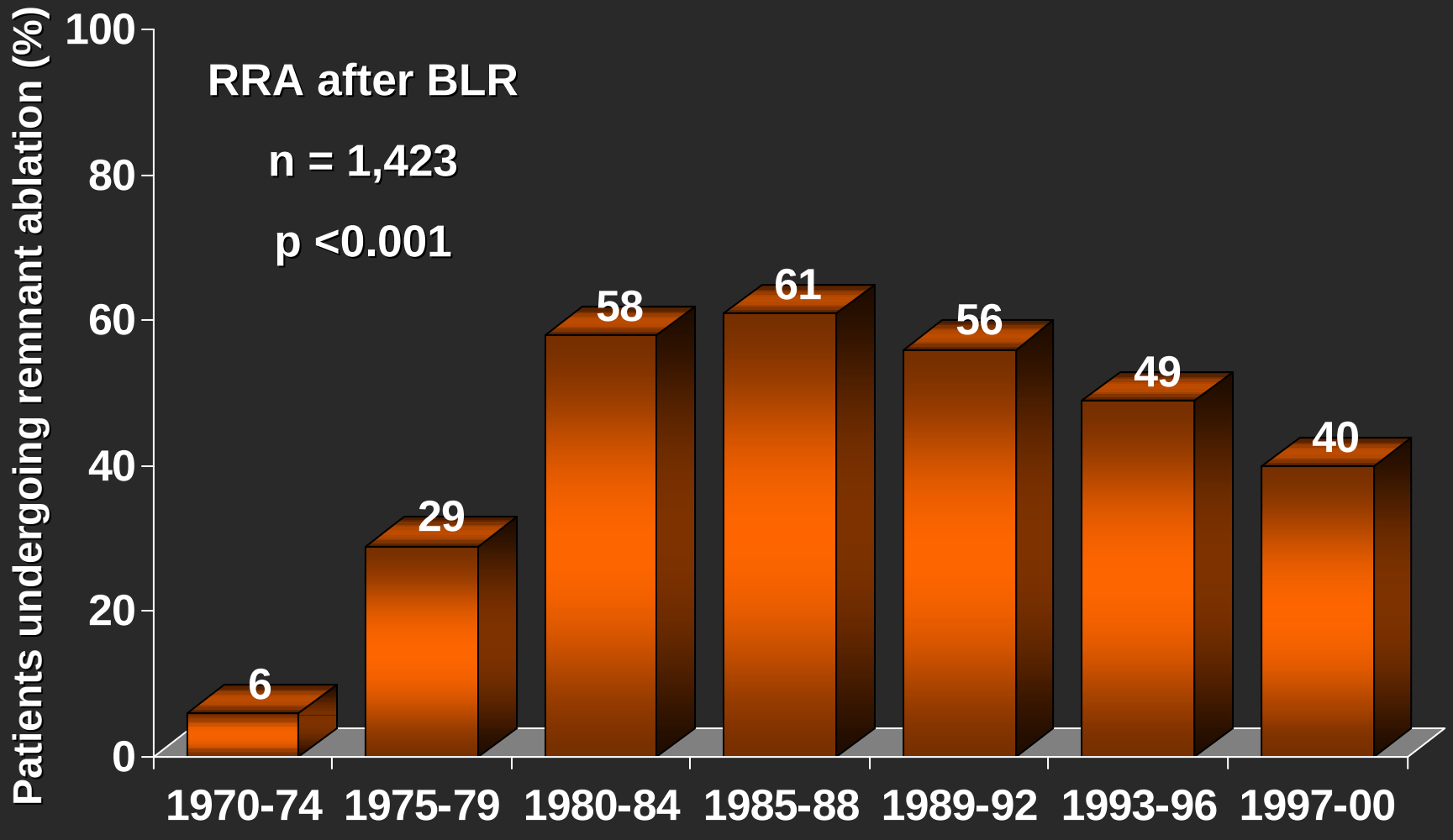
Trends in Extent of Surgery & RRA



Hay et al, 2002

Papillary Thyroid Carcinoma 1970-2000

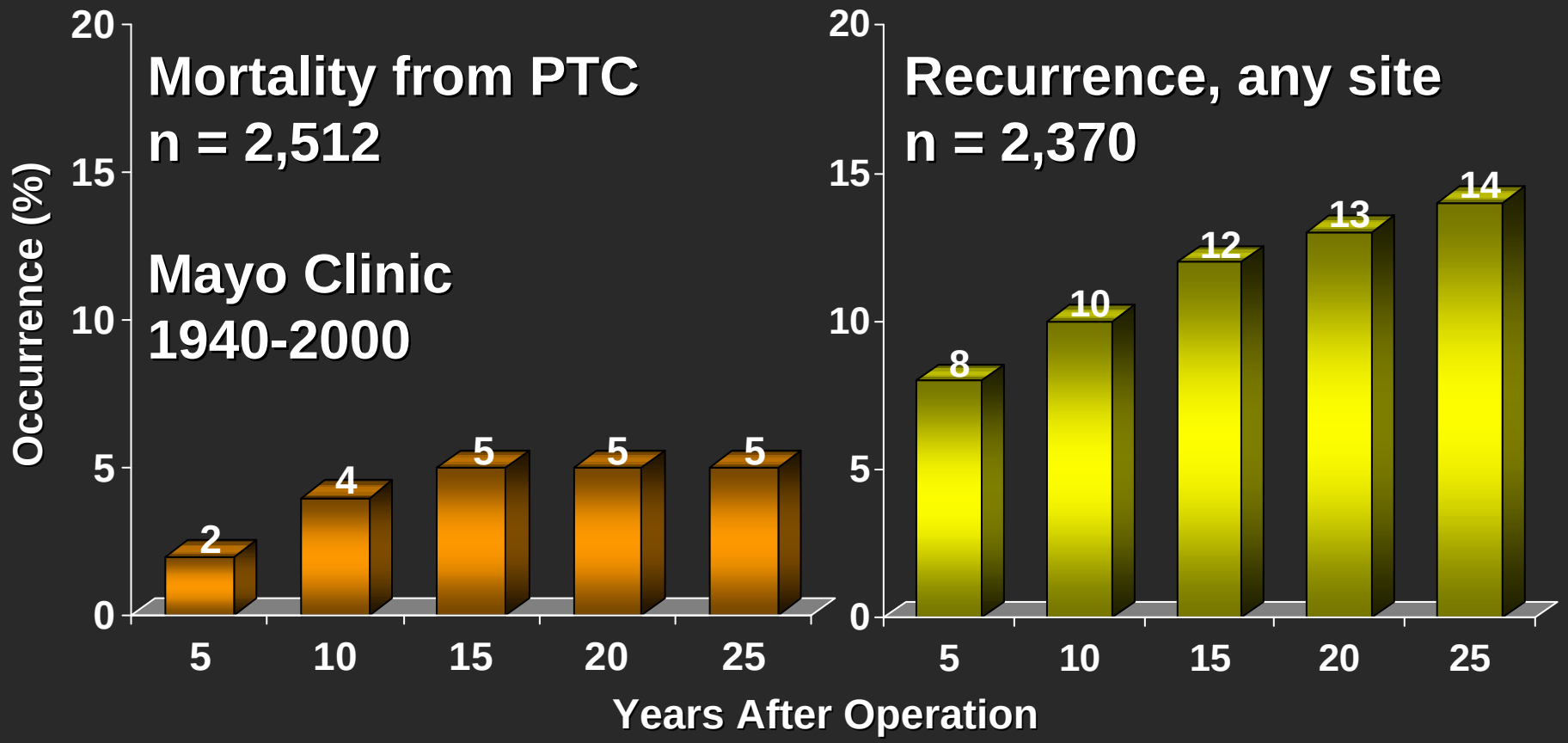
Changing Frequency of Remnant Ablation



Hay et al, 2002

Papillary Thyroid Carcinoma 1940-2000

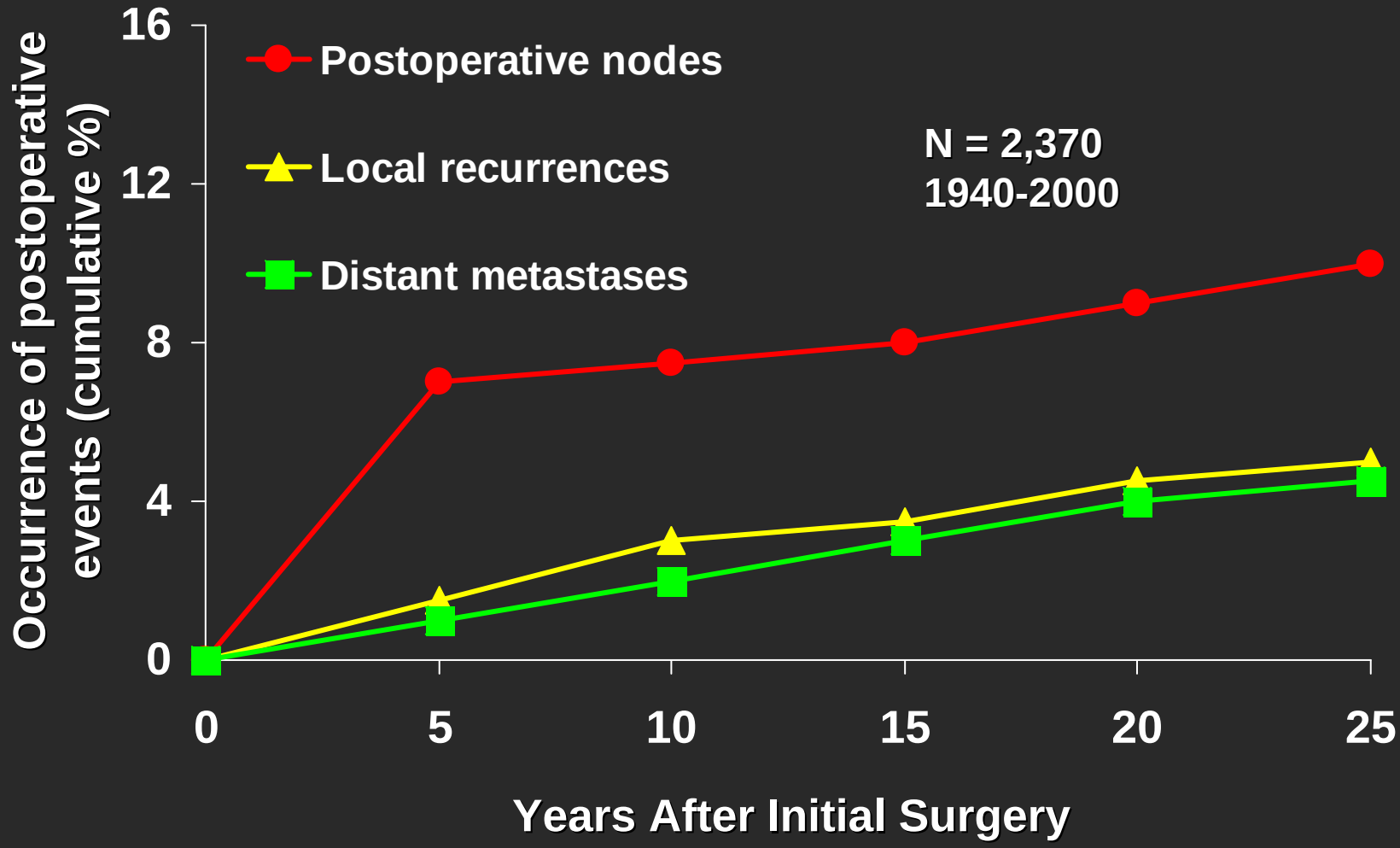
Overall Outcome



Hay et al, 2002

Papillary Thyroid Carcinoma 1940-2000

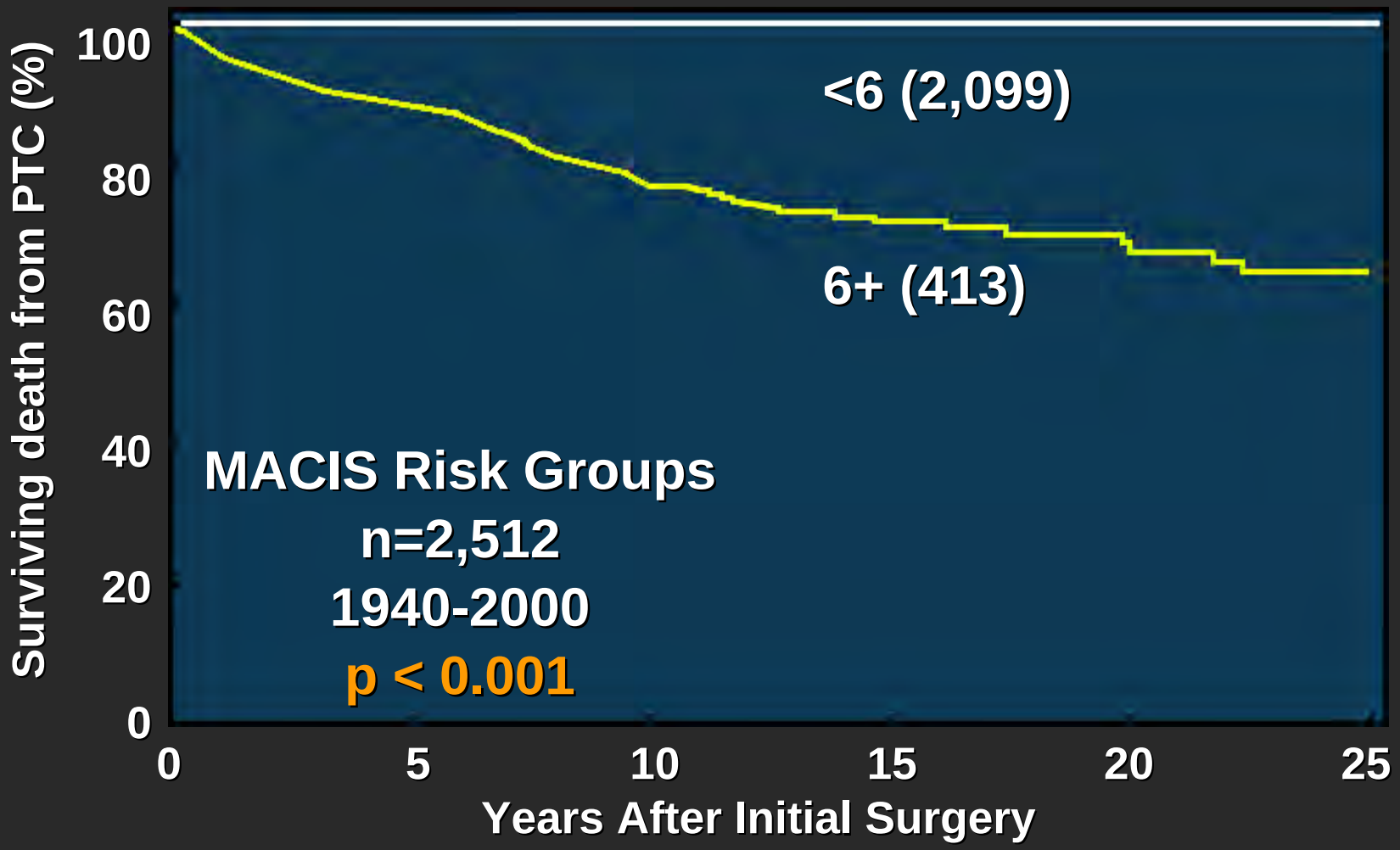
Overall Outcome



Hay et al, 2002

Papillary Thyroid Carcinoma 1940-2000

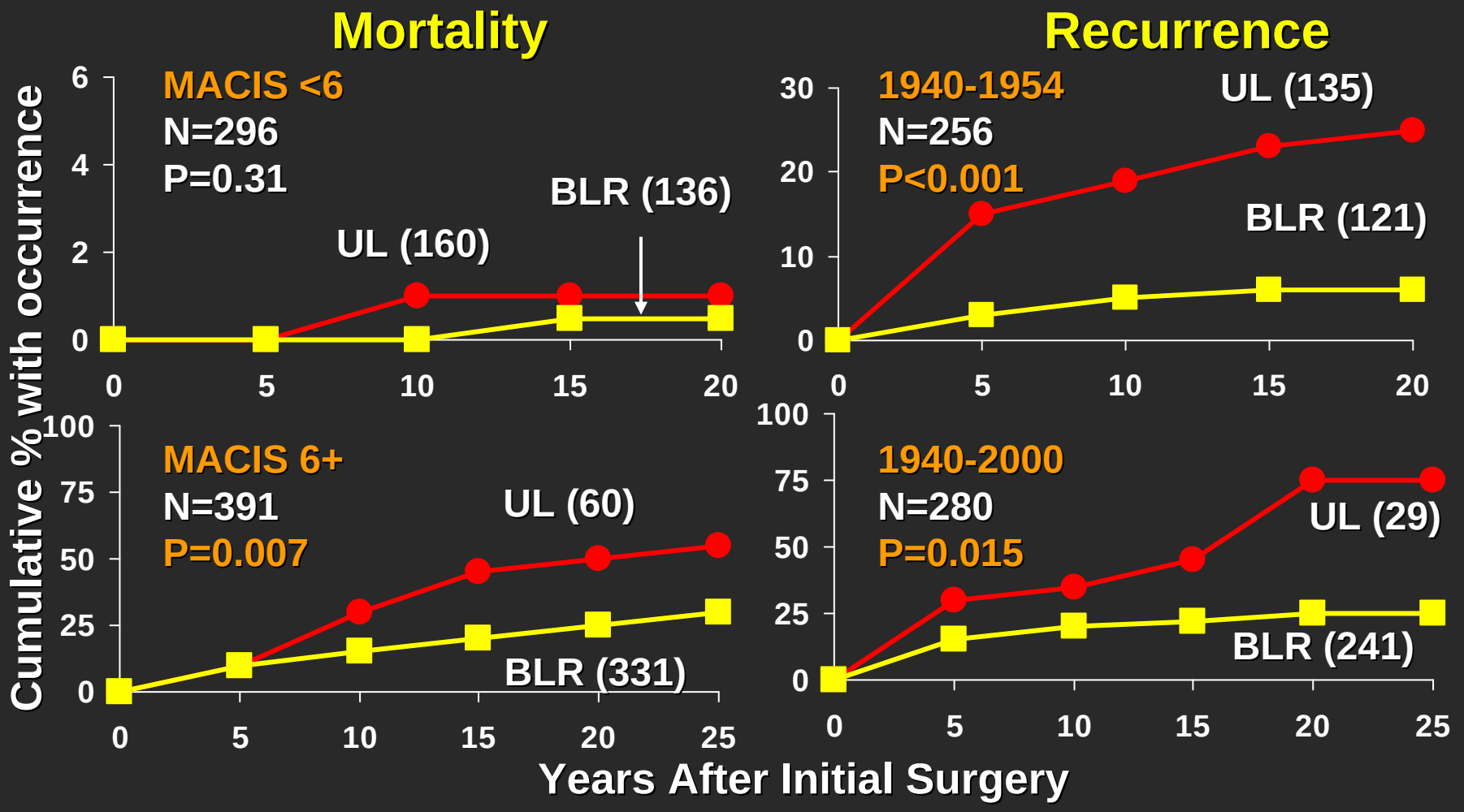
Survival to Death



Hay et al, 2002

Papillary Thyroid Carcinoma

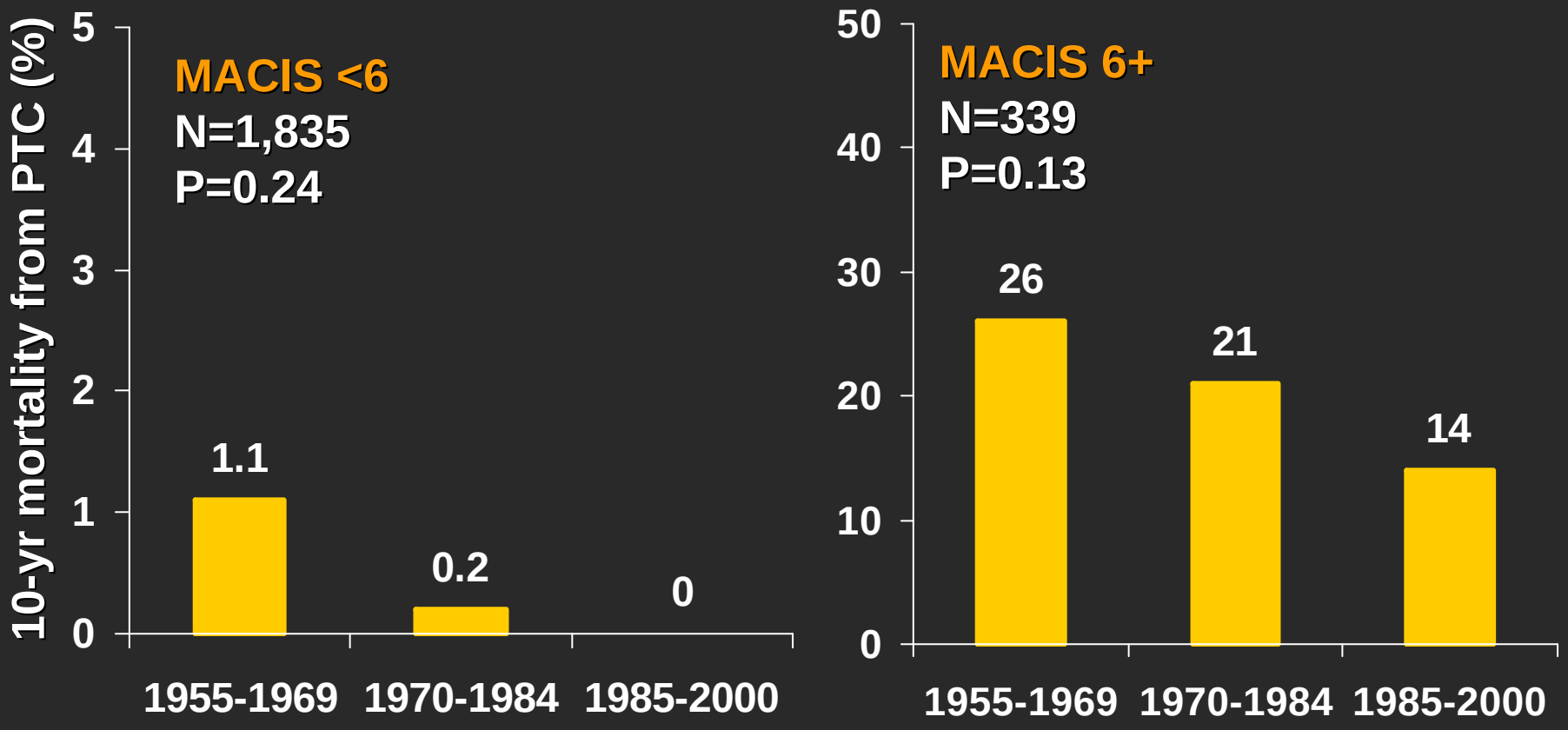
Comparison of Outcome



Hay et al, 2002

Papillary Thyroid Carcinoma 1955-2000

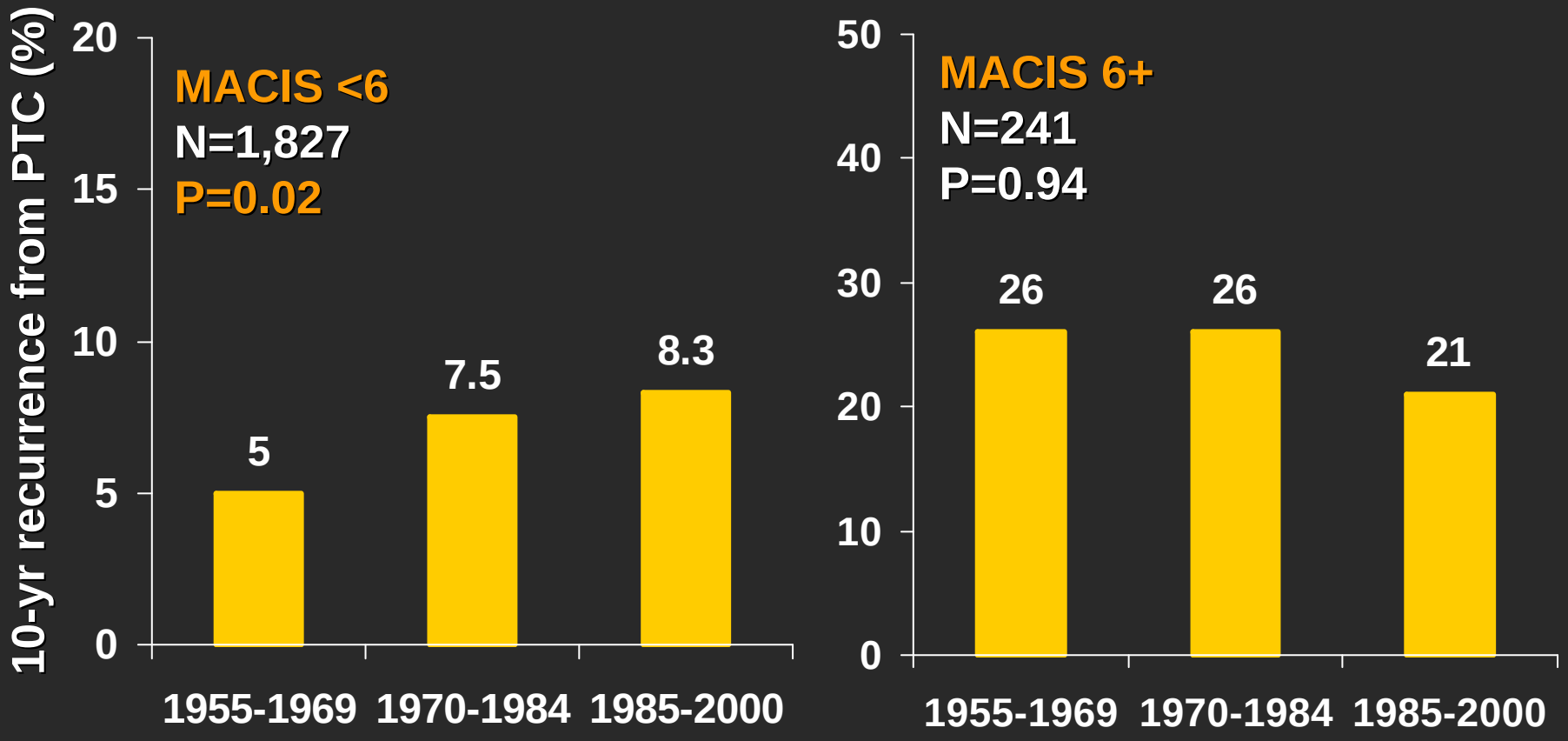
Cause Specific Mortality



Hay et al, 2002

Papillary Thyroid Carcinoma 1955-2000

Tumor Recurrence



Hay et al, 2002

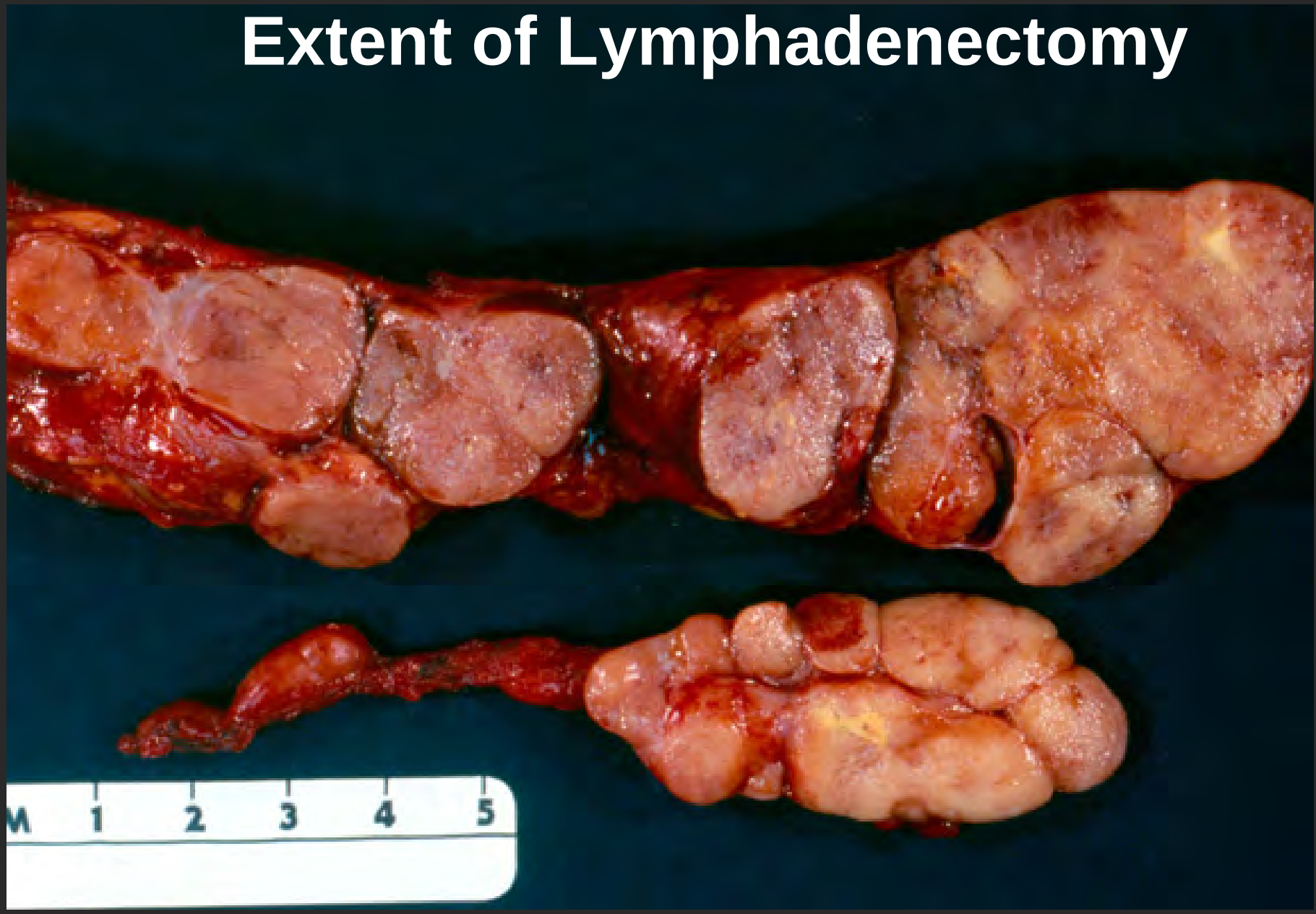
Papillary Thyroid Carcinoma 1970-2000

Low-Risk (MACIS <6) 1970-2000	20-yr Mortality NT/TT Alone	20-yr Mortality NT/TT and RRA	20-yr Recurrence NT/TT Alone	20-yr Recurrence NT/TT and RRA
Node-negative (n=636)	0%	0% P=NA	3.4%	4.3% P=0.80
Node-positive (n=527)	1.2%	0.9% P=0.99	19.5%	19.9% P=0.19

Hay et al, 2002

Scar @ 3 months

Extent of Lymphadenectomy



Value of Preoperative Ultrasound in PTC

- Mayo Clinic: 770 pts (1999-2004)
- US identified nonpalpable lateral nodes: 15% in first time operations
- Reops-NLLN's: 64% ; NCLN's: 28%
- US altered extent of operation in 41% of initial and 43% of reoperative pts. with palpable nodes

Stulak et al. Arch of Surg, 2006

Why Perform Cervical Lymphadenectomies

- Thyroglobulin levels (withdrawal, Thyrogen® stimulated)
- High resolution ultrasound
- Radioiodine and PET scans
- Tg mRNA

Endocrinologists

PTC

Lymph Node Dissection (PTC)

- Children
  - 80-90% clinically positive
- Adults
  - 10-20% clinically positive
- Extensive prophylactic dissections
  - 80% positive
- Therapeutic dissections
  - 7-8% develop positive nodes
- Immune surveillance very effective

PTC

"Berry-Picking" vs Formal Nodal Dissection

- Nodal recurrences increased in all series
- Reoperations more difficult
  - Increased morbidity
- Metastatic carcinoma in lymph nodes > 3 mm always associated with disease in smaller lymphatics
  - Noguchi et al 1970, 1987

PTC

Choice of Nodal Dissection

- **Central compartment** (ipsilateral paratracheal, pretracheal, upper mediastinal) in virtually all cases
- **Modified or Selective Neck Dissection** for clinically detectable nodes (ultrasound, palpation, biopsy)

PTC

Do Lymph Nodes Affect Survival?

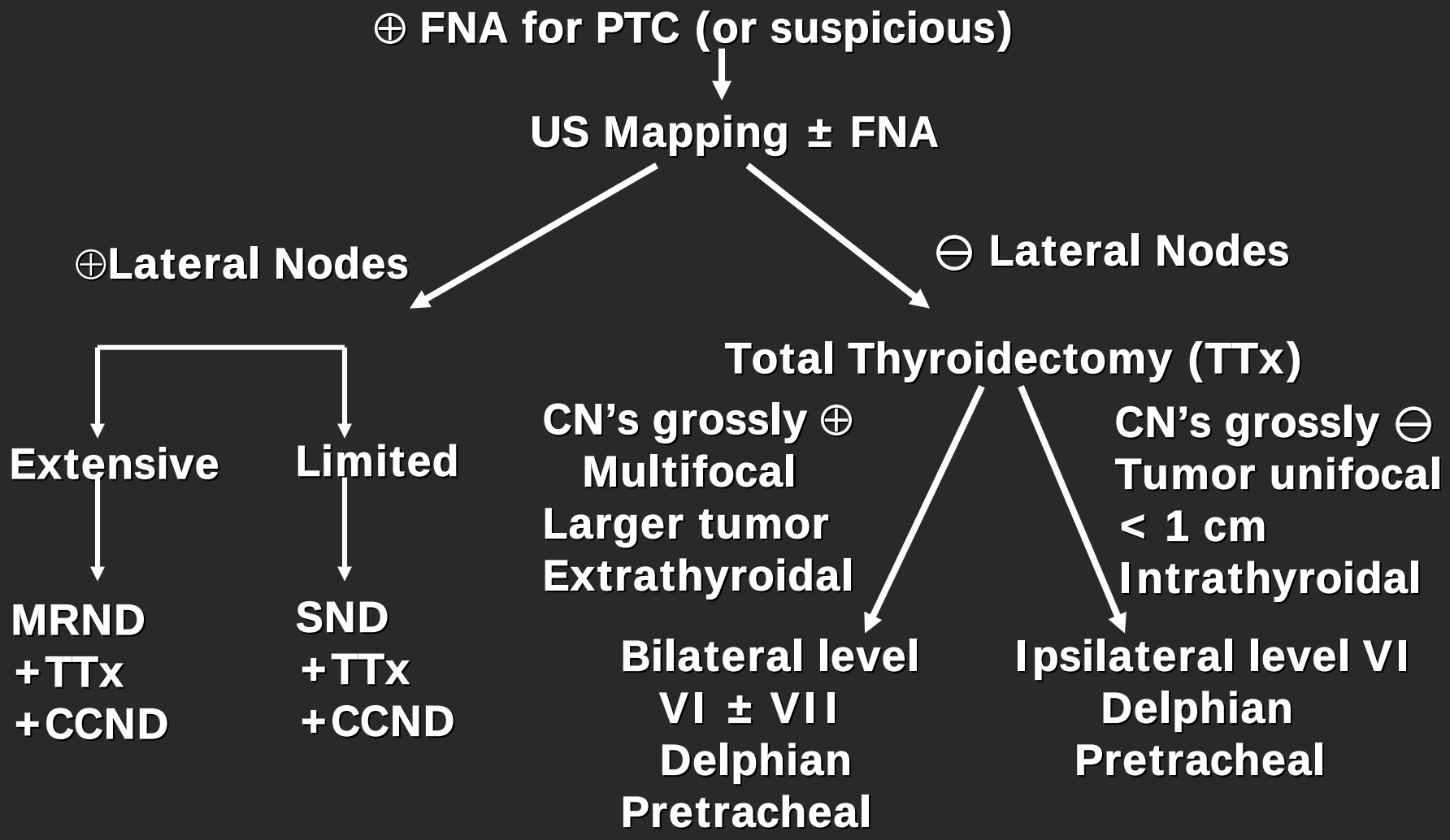
- **Probably not** in most cases
- Nodes beget nodes **(not death)**

PTC

Exceptions:

- Bulky, matted nodes ?
- Extracapsular spread ?
- ⊕ nodes in stage III disease yes

Practical Algorithm



MRND = modified radical neck dissection
SND = selective (lateral) neck dissection

PTC

Radical Neck Dissections:

- Never
- Increased complications (esp. wound)
- No survival or TR benefit

Conclusion (1)

- BLR and conservative nodal dissection (CND) reduces TR in low-risk patients
- BLR and CND reduces TR and CSM in high-risk patients
- RRA does not further reduce CSM or TR in MACIS low-risk patients

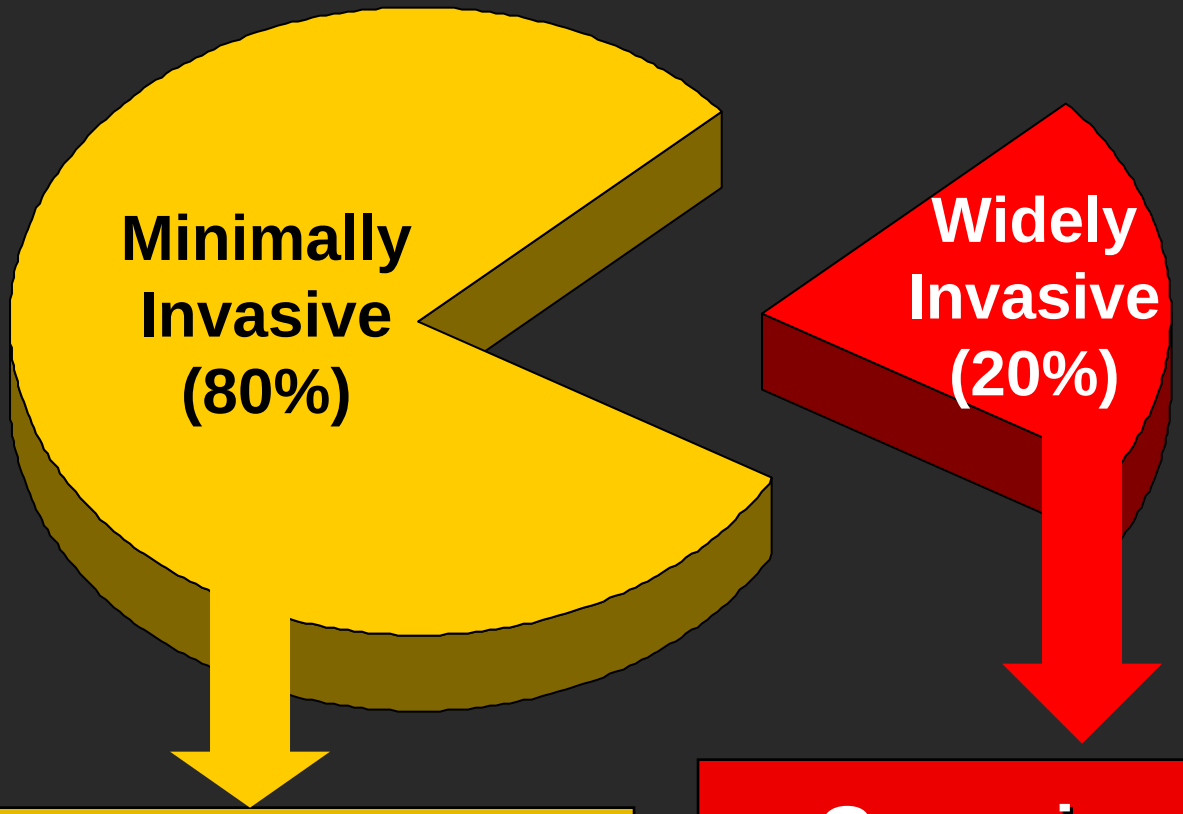
Follicular Thyroid Cancer (FTC)

- 10-15% of thyroid malignancies
- Cytology insufficient
- Capsular / vascular invasion
- 90% unifocal
- Hematogenous spread
- Lung and bone metastases: 15%
- Nodal metastases: FCC 5%

Follicular Thyroid Cancer

- Lymph node metastases (< 5%)
  - Usually associated with locally advanced tumor
  - Worse prognosis

FTC



Microscopic vascular and capsular invasion

Gross involvement of vessels and contiguous structures

FTC

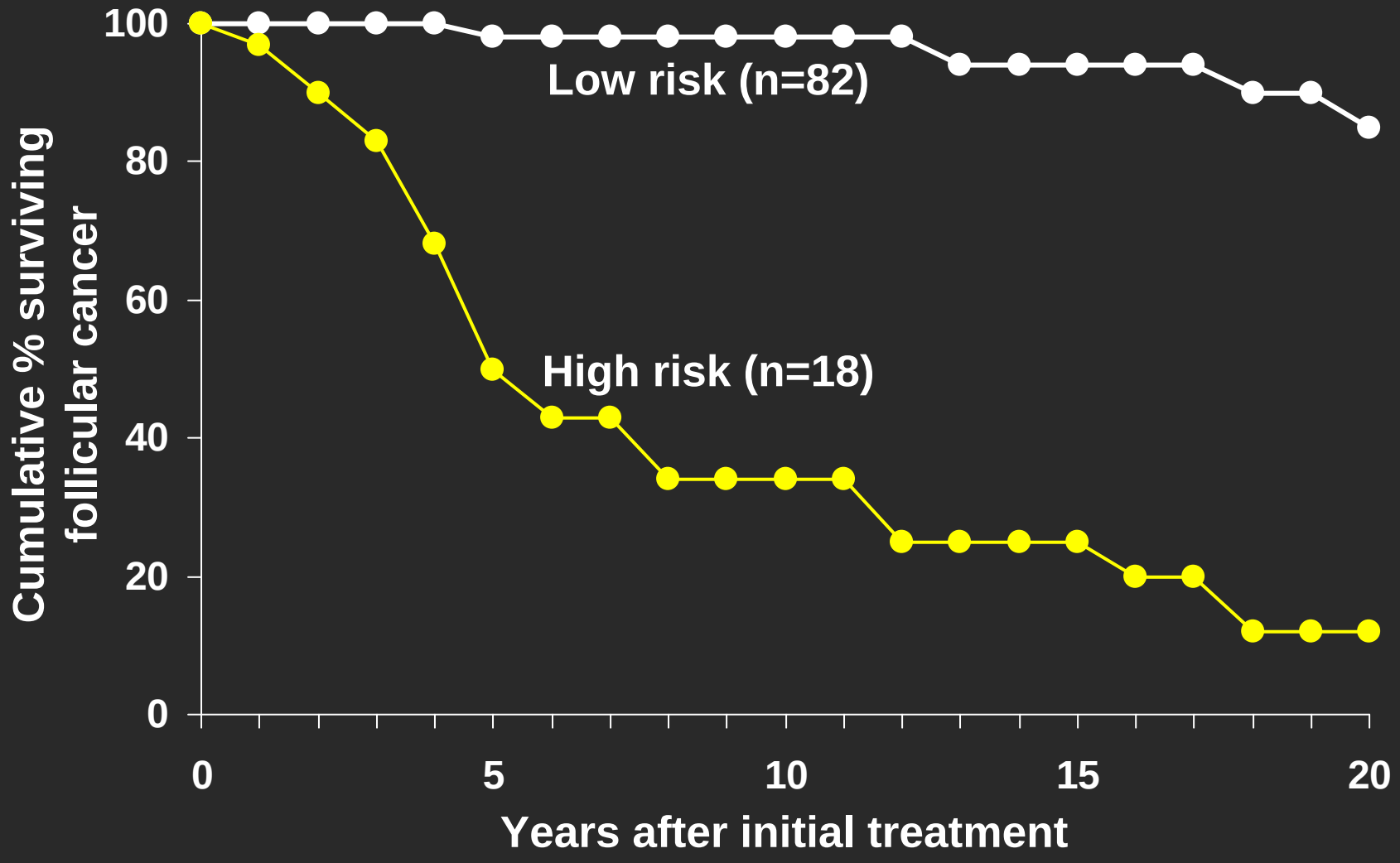
- Prognostic indicators
  - Age > 50
  - Marked vascular invasion
  - Metastatic disease

Brennan et al, 1991

FTC

- **High risk** (2/3 risk factors)
  - Survival: 47% and 8% @ 5 and 20 years
- **Low risk** (0-1/3 risk factors)
  - Survival: 99% and 86% @ 5 and 20 years

FTC



Brennan et al, 1991

FTC

- Tumors < 2 cm with
  - minimal capsular invasion alone
    - √ No metastases or deaths
    - √ Recent 10-year follow-up
    - Lobectomy Alone

van Heerden et al, 1992

Hurthle Cell Cancer

- <5% of all thyroid cancers
- More locally aggressive
- Less avidity for RAI
- Nodal metastases in 1/3

Follicular and Hurthle Cell Carcinoma

- Lymph node mets from FTC rare (<5%); if present consider FVPTC
- Routine CCND and LND for FTC not necessary unless positive nodes are present grossly or by US
- HCC has positive nodes in up to 30%; manage nodes like PTC

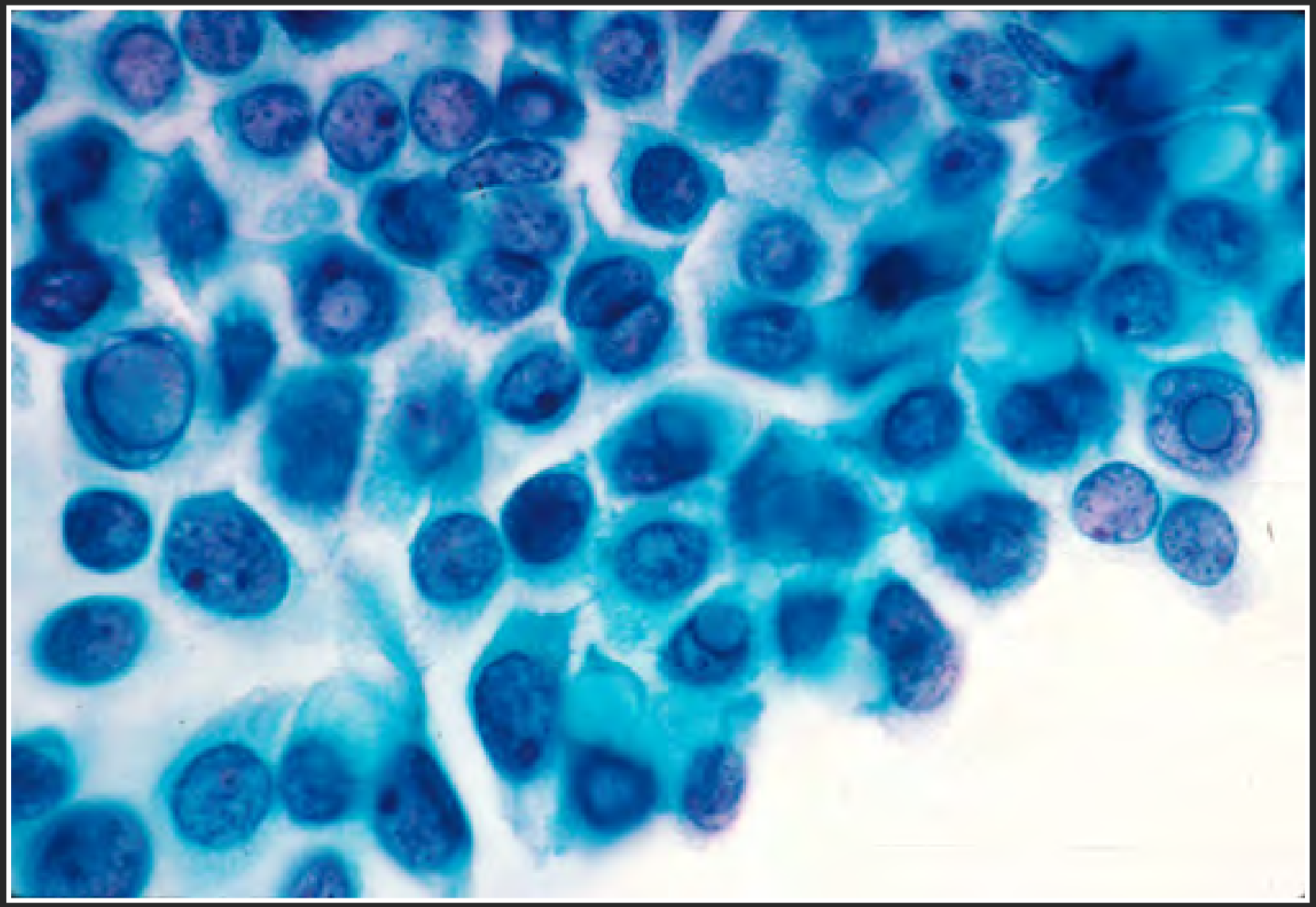
FTC/HCC

Treatment:

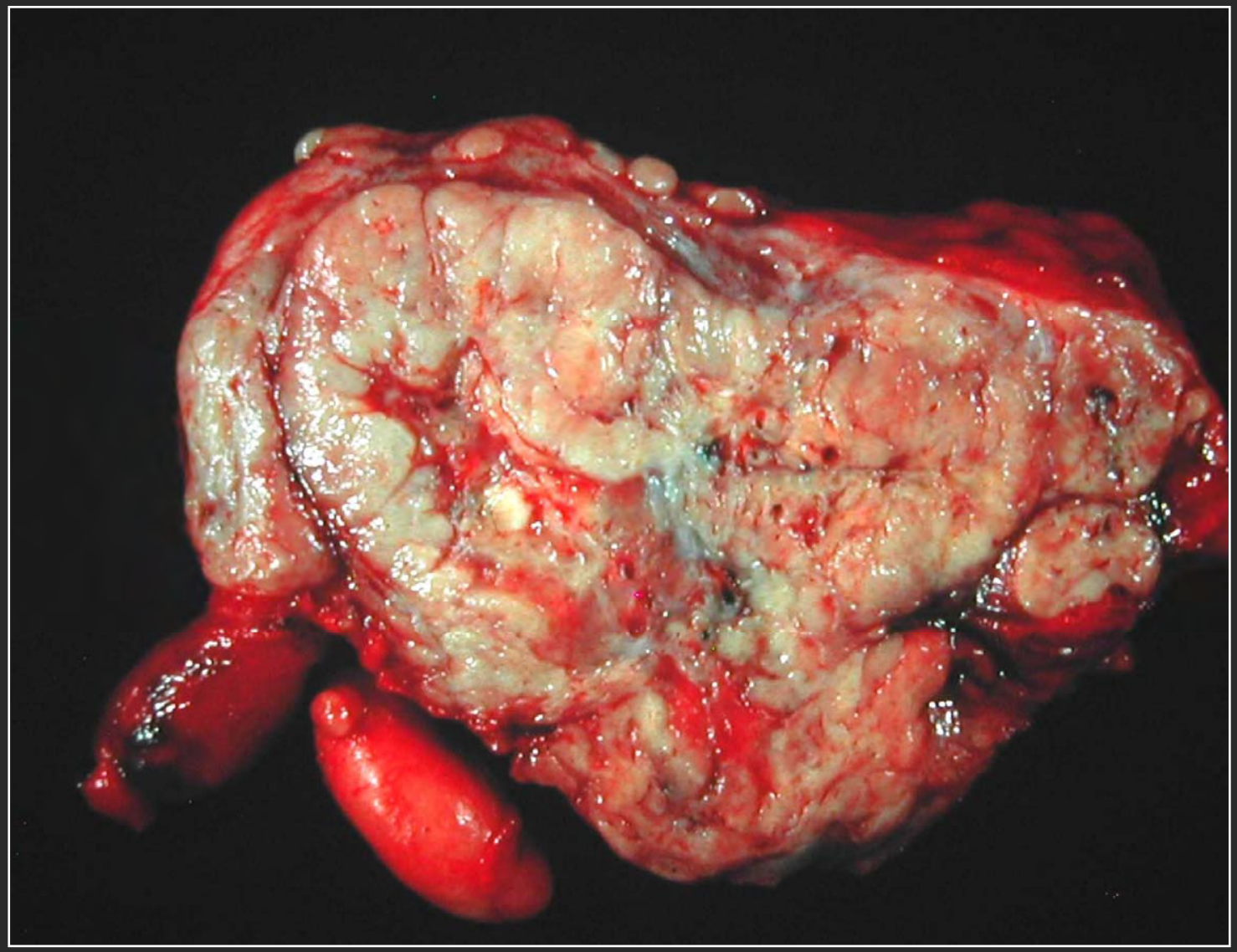
- Total / NT Thyroidectomy
- Sample central nodes*
- Formal node dissection when nodes ⊕
- CCND for HCC
- RRA, THST except in small tumors with minimal capsular invasion

*may be only indication of FVPTC

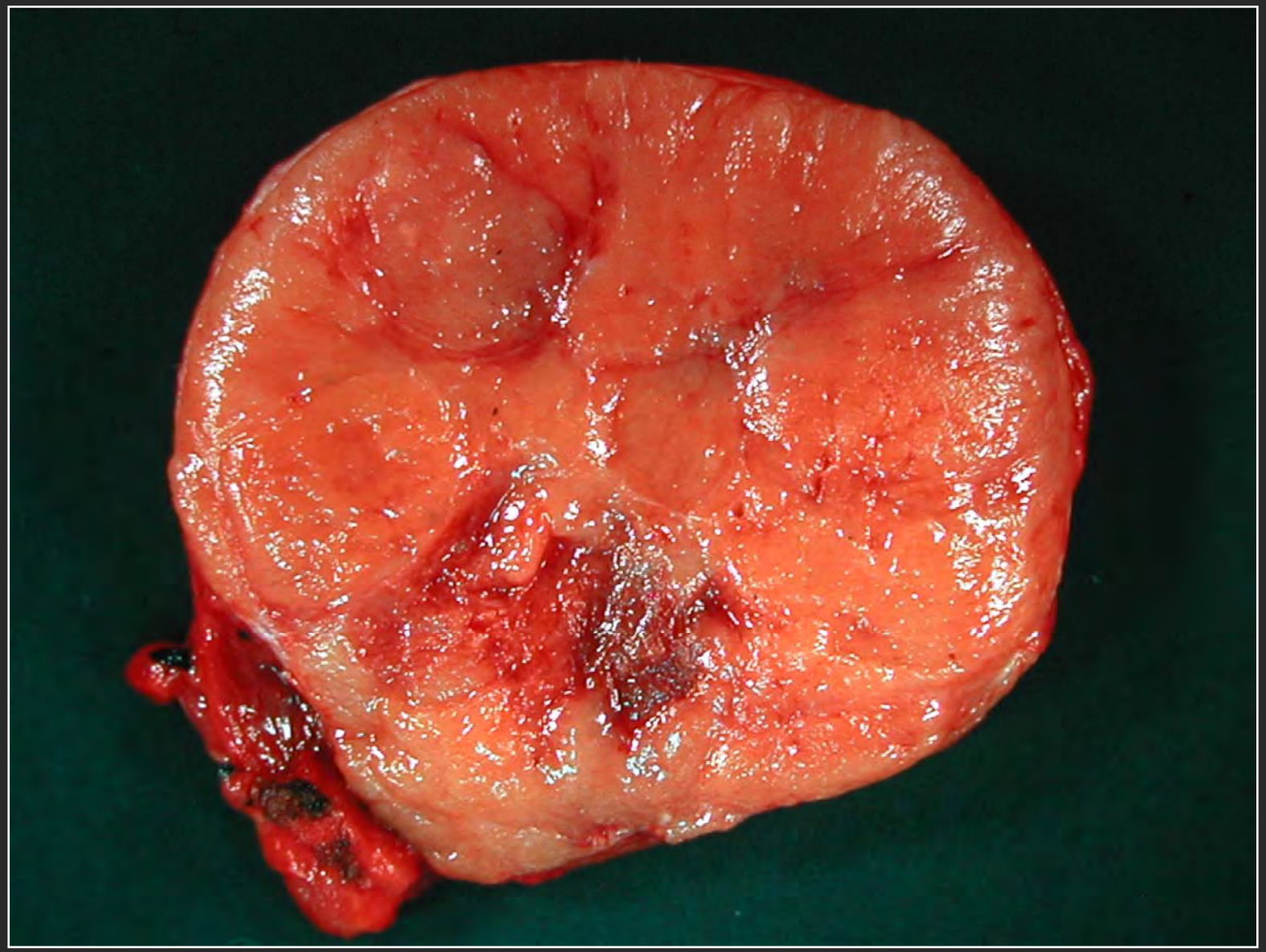
Papillary Thyroid Carcinoma-FNAB



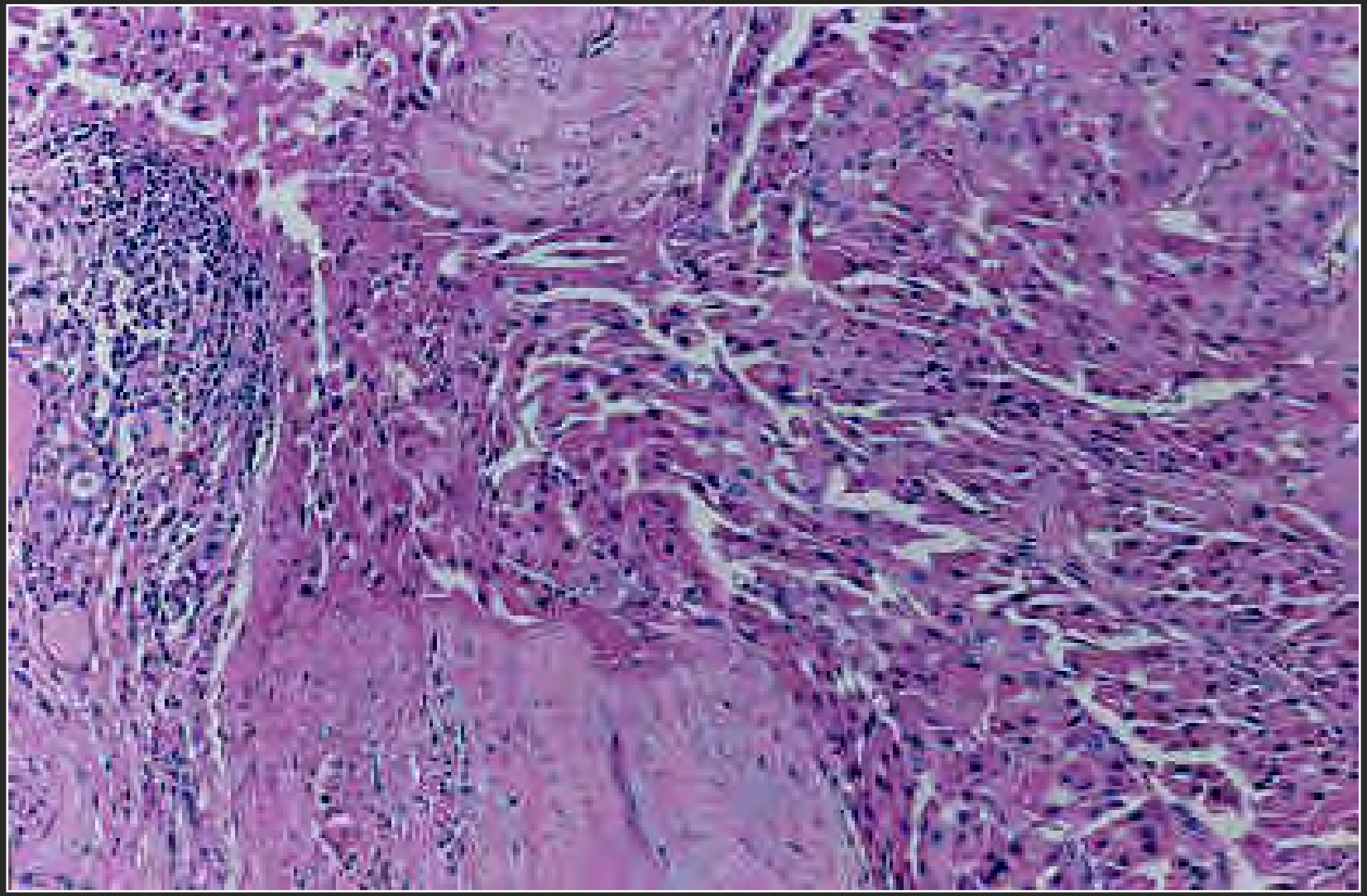
Widely Invasive Follicular Carcinoma



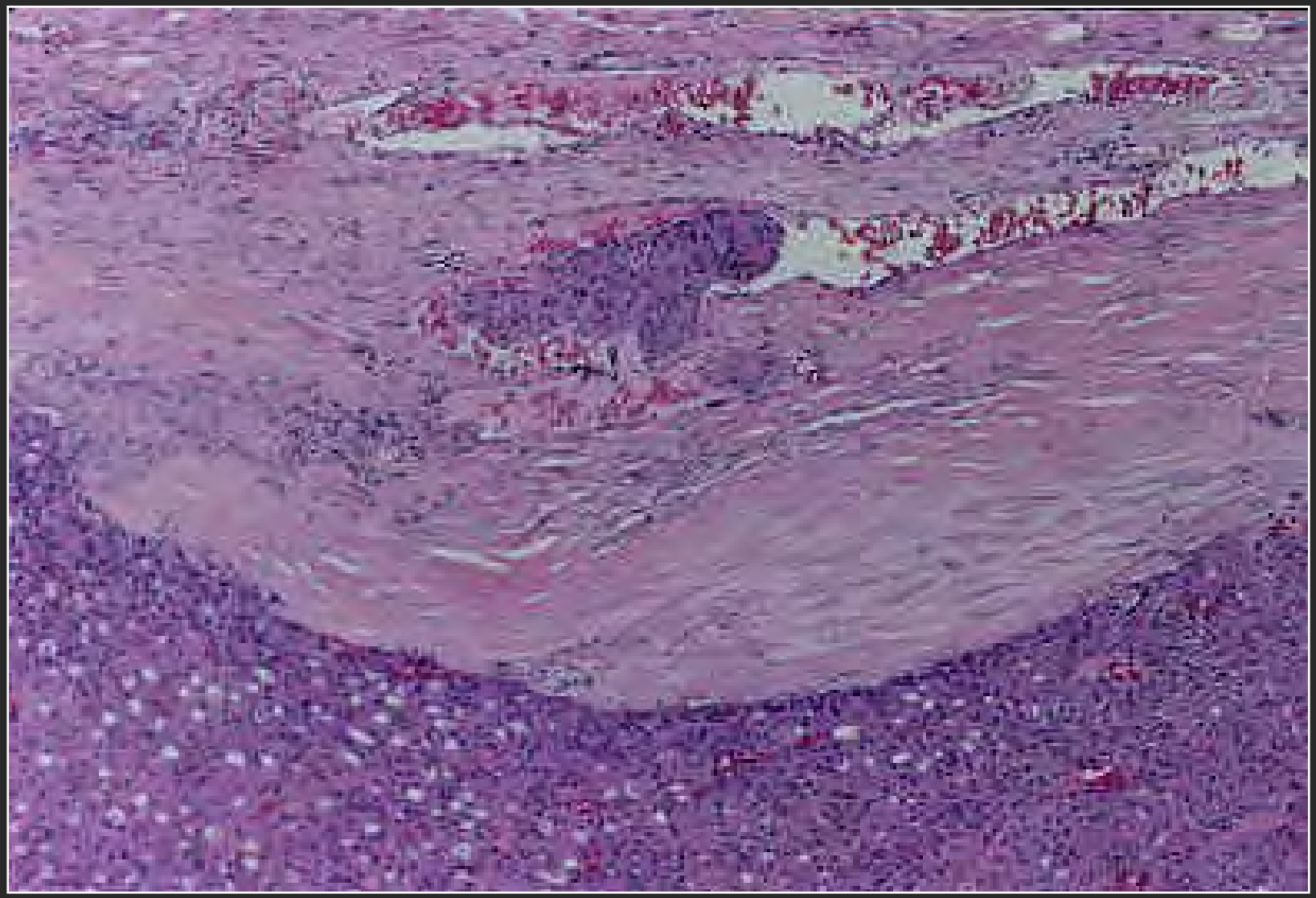
Hurthle Cell Adenoma or Carcinoma ?



Follicular Carcinoma-Capsular Invasion



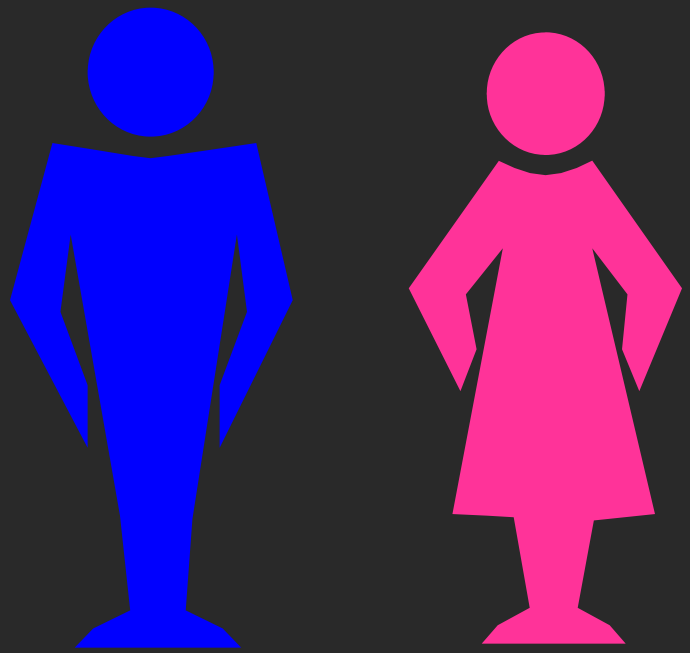
Follicular Carcinoma-Vascular Invasion



Follicular Neoplasms: Frozen Section

Results: 1023 Patients

286 (28%)



737 (72%)

Mean age: 52.1 years

Follicular Neoplasms: Pathology

		Frozen Section		
		Ca	Non-Ca	Total
Perm	Ca	65 TP	18 FN	83
Section	Non-Ca	7 FP	933 TN	940

65/83 (78%) Ca Dx by FS

Follicular Neoplasms:
Frozen Section Dependent Upon:

- Good pathologists
- Significant exposure to frozen section, especially thyroid
- Superb support system

Low-Risk differentiated thyroid cancer

Mini-invasive video-assisted thyroidectomy (MIVAT)

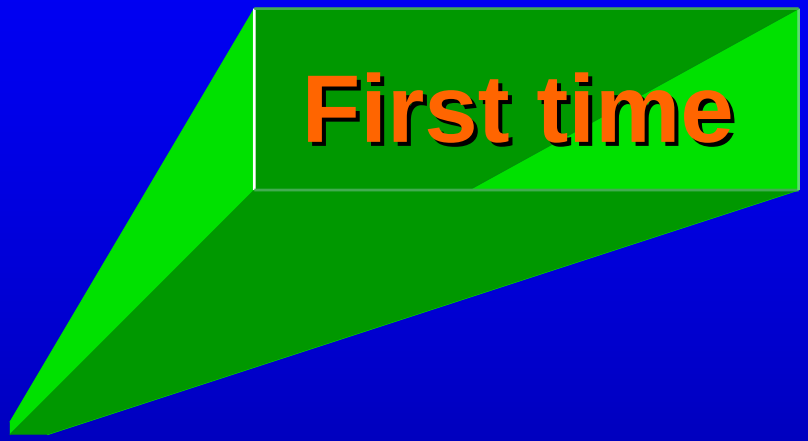
Maurizio Bagarani

C. Morano, F. Cilurso, U. Basile, A. Cardillo

Departement of General Surgery
Endocrine Surgery Unit
Regina Apostolorum Hospital
Albano Laziale, Rome

Verona 2006

Video-assited neck surgery



M. Gagner

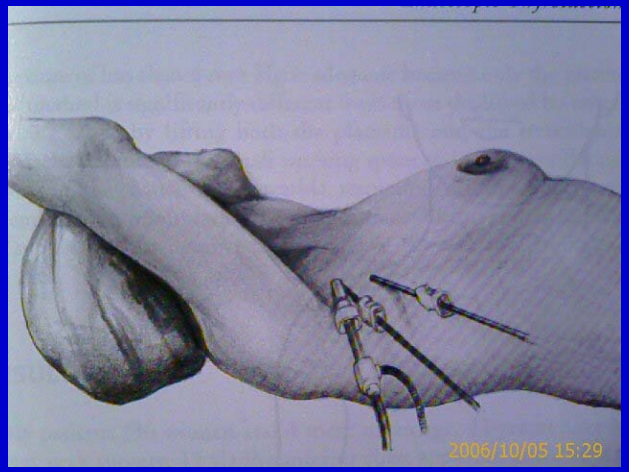
Endoscopic subtotal parathyroidectomy in patients with primary hyperparathyroidism

Br. J. Surg. 1996; 83 : 875

Endoscopic thyroidectomy

Extracervical approach

anterior chest

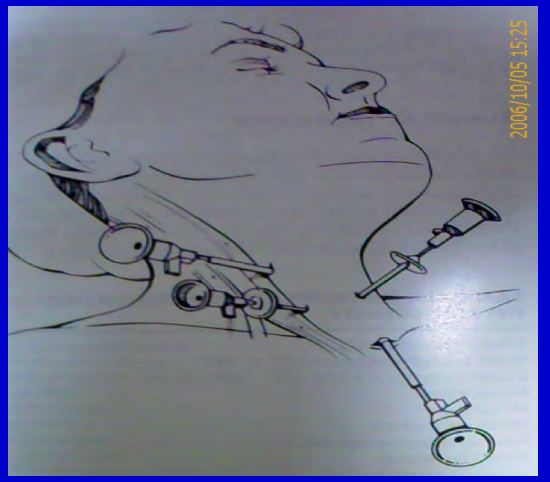


axillary

Takami, J.Am.Coll.Surg. 2000;191:336

Cervical approach

Total video

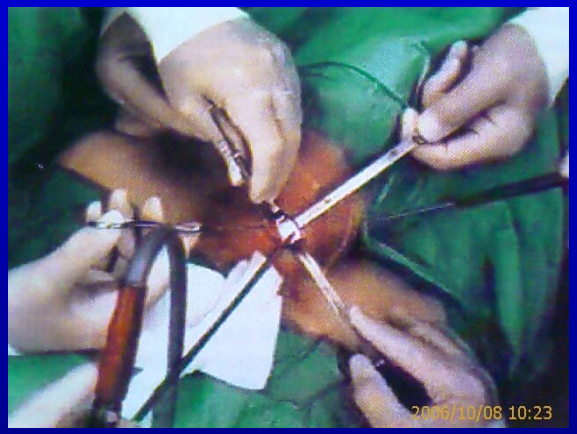


Gagner, Thyroid 2001;11:161

MIVAT
(minimally invasive videoassisted thyroidectomy)

- Video-assisted thyroid lobectomy has been introduced since 1998 by Miccoli at University of Pisa

- This technique uses a gasless video-assisted approach with a small central incision (1.5 cm)



Miccoli P. Surgery 2001;130:1039

Multiinstitutional experience

Miccoli P. Bellantone R. World J Surg 2002;26:972

- The mivat technique is safe and feasible.
- The complication rate is not different from that of standard thyroidectomy.
- The operating time appears longer than with conventional procedure and the number of patients eligible remains low.
- The advantages in terms of cosmetic results and postoperative distress are evident.

Established Indications

- Single nodule
- Nodule largest diameter < 3.5 cm
- Benign or low-grade follicular tumor
  (low-risk papillary carcinoma)
- Thyroid volume < 20 ml

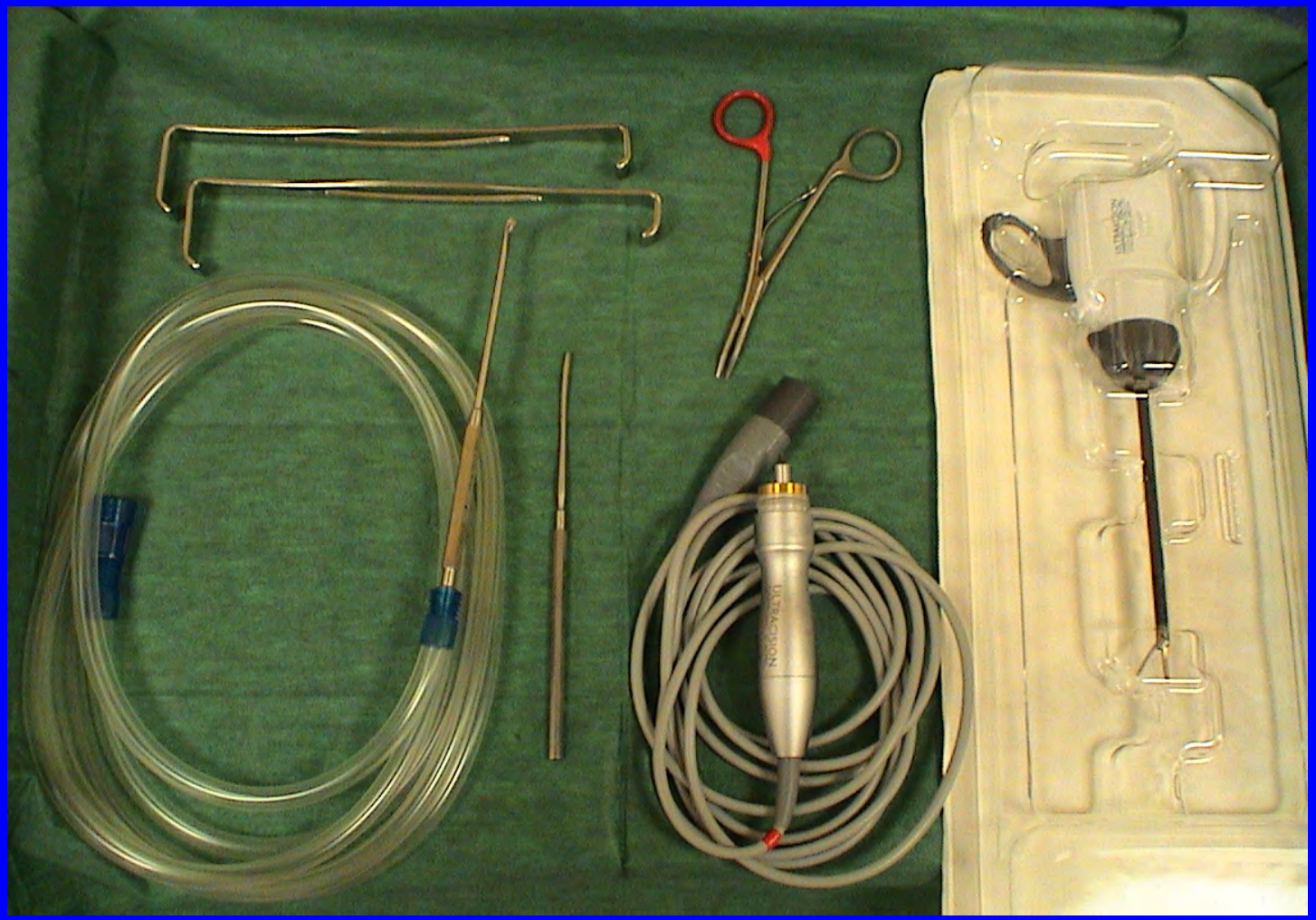
Contraindications

Absolute	Relative
Previous neck surgery	Previous neck irradiation
Large goiter	Hyperthyroidism
Local advanced cancer	Thyroiditis
Lymph node metastases	Severe obesity

Preparation for intervention

- **Position of patient** — neck hyperextension not needed
- **Surgical staff** — 3-4 surgeons
- **Monitor** — better two at the top of the the patient

instrumentations



Video-assisted technique

Personal experience

33 patients

2005	15 out of 315	4.7%
2006	18 out of 225	8.0%

Mean age

47.7

F/M

29/4

Diameter of main nodule

Mean	15.8 mm
Range	6-40

Thyroid volume (22 pat.)

Mean	31 ml
Range	12-68

8 pat. > 30

Pathology

- Papillary carcinoma 9
- Follicular carcinoma 2
- Nodular hyperplasia 10
- Follicular adenoma 10
- Thyroiditis 2

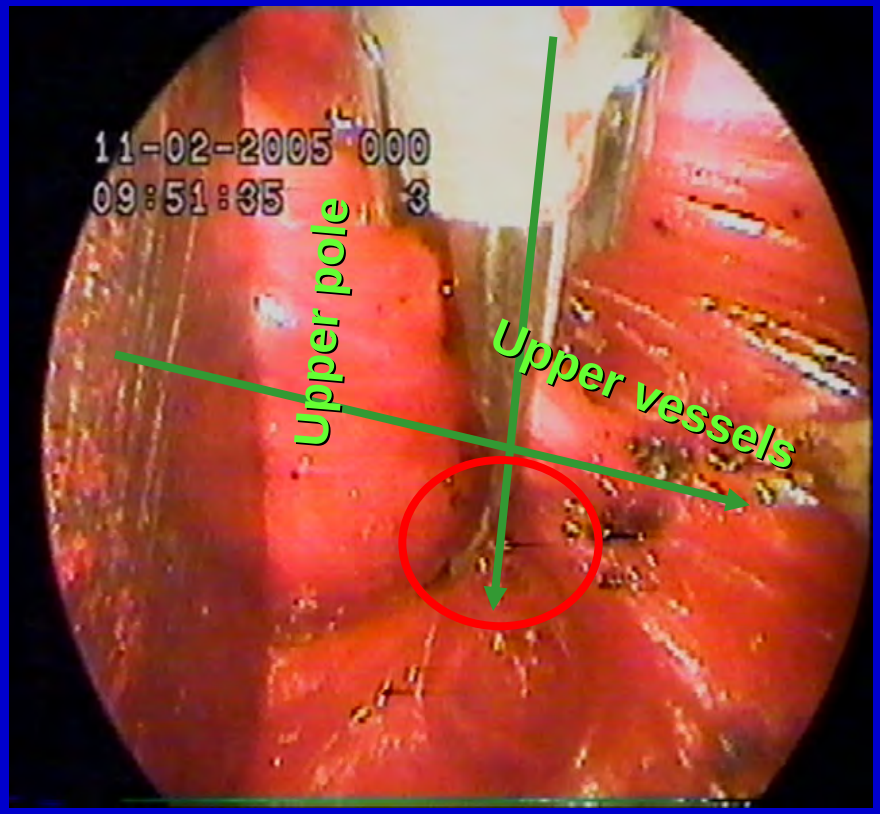
Type of surgery

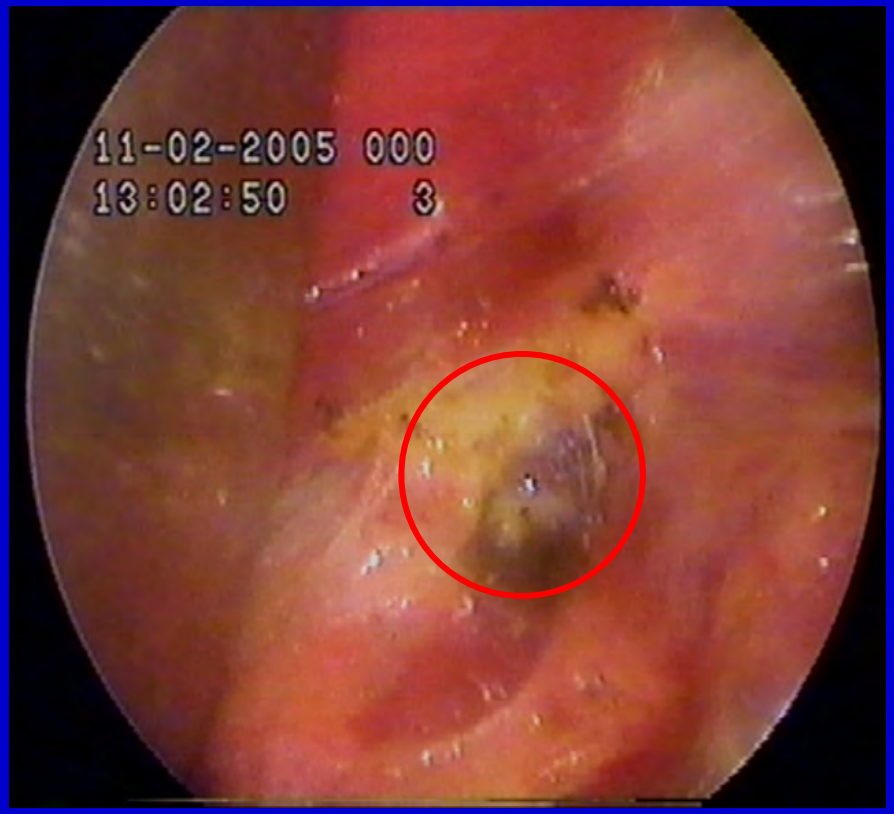
Total thyroidectomy	26
Emithyroidectomy	7

Results

- Mean Hospital stay 3.5 gg
- Majors complications 0
- Conversion 1
- Laringeal nerve palsy 0
- Mild transient dysphonia 3
  permanent 0
- Transient hypocalcemia 3
  permanent 0

Possible causes of dysphonia first training phase



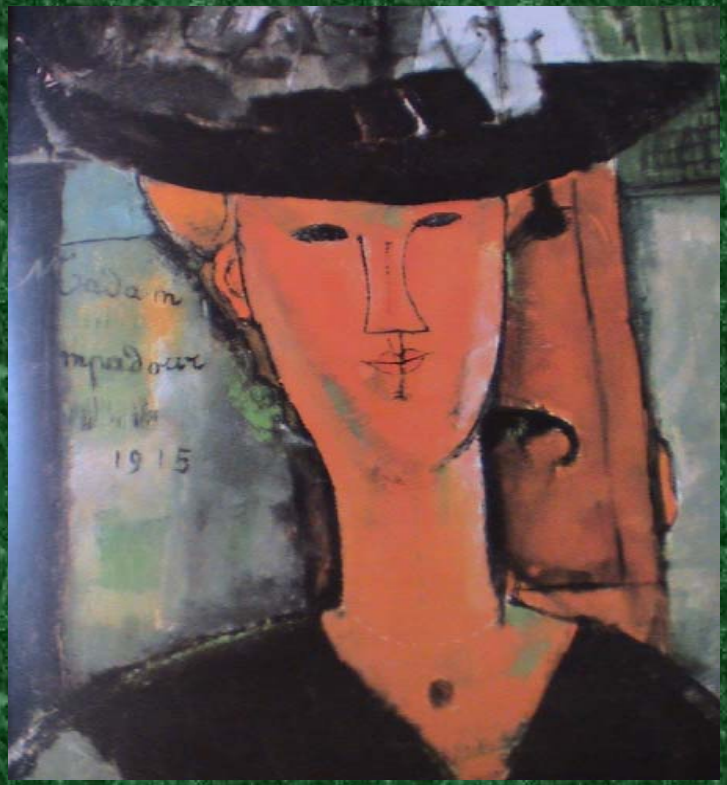


two opposite techniques ?

conventional

S. Giovanni “decollato”, Caravaggio
La Valletta , Malta

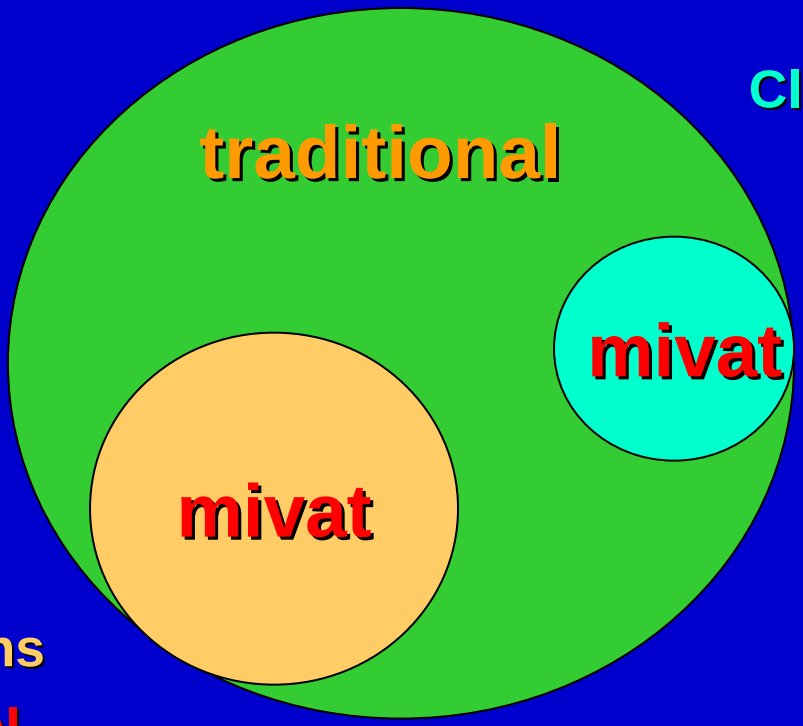
video-assisted



Madame Pompadour , Modigliani
Art Institute Chicago

Mivat and conventional thyroidectomy

Two integrated techniques



Classical Indications

Volume < 20 ml

10%

Wider Indications

Volume < 30 ml

15-20%

Bellantone WJS 2006

the future ?

Is it possible to widen the indication between videoassisted and conventional incision ?

Miccoli	**1998**	**1.5 cm (vol.<20)**
Bellantone	**2000**	**2.0 cm (vol.<30)**
Conventional		**5.0 cm**

probably yes by a

2.5-3.0 cm neck incision

Smaller than conventional incision

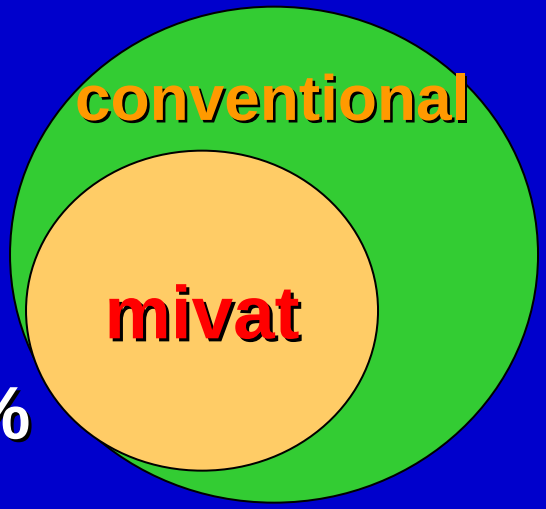
2.5 cm (vol.<50)

5.0 cm

Without beeing too invasive

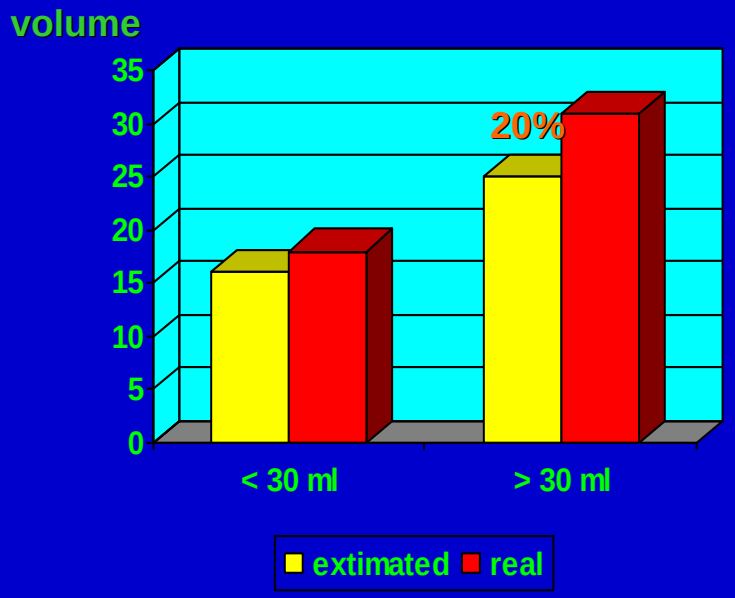
rationale for larger incision

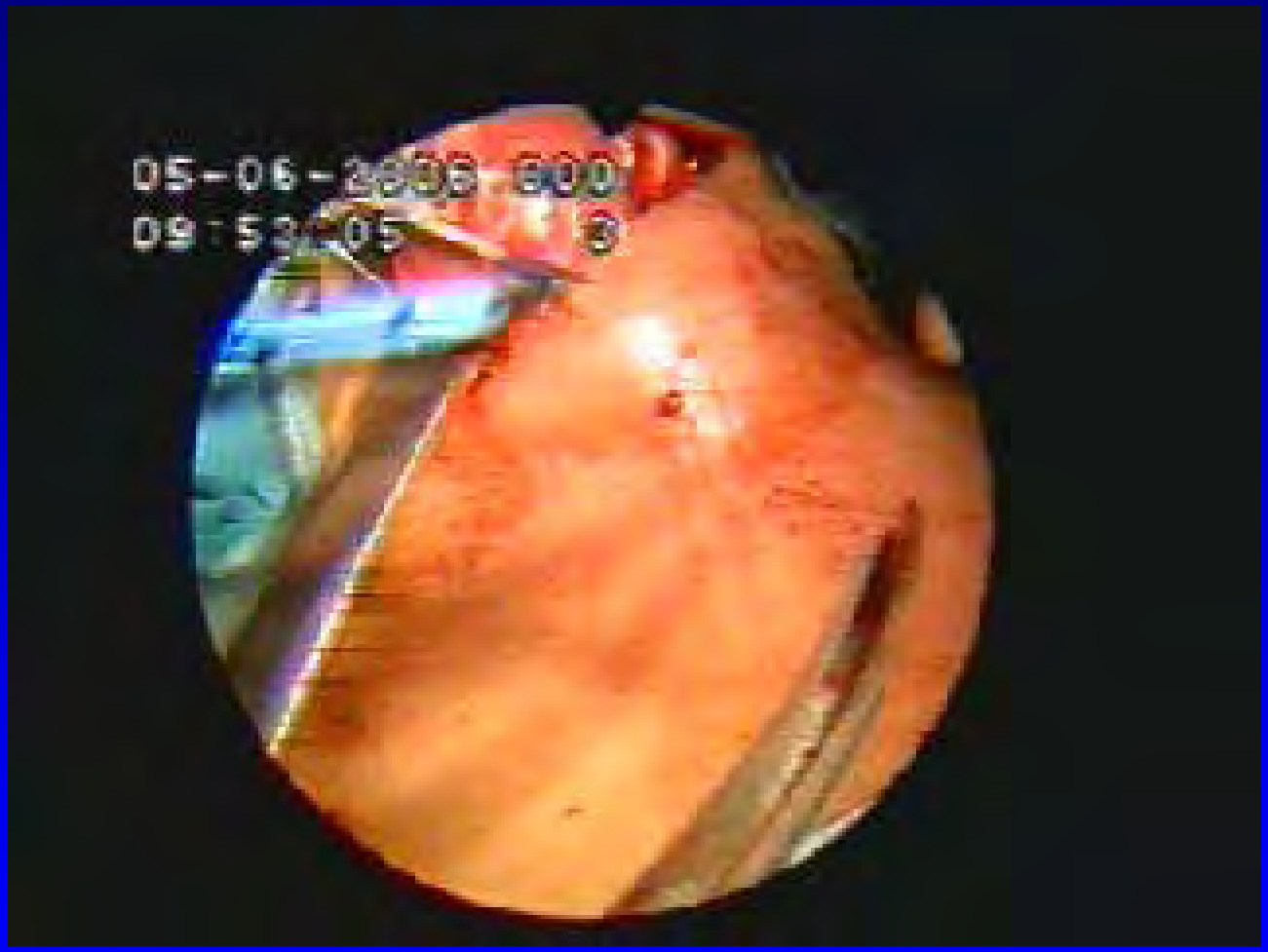
- Increased number of treated patients



30-40%

- Treatment of patients with underestimated volume





advantages

Mivat with enlarged incision 2.5-3.0 cm

Conventional minimal incision 4.0-6.0 cm

Prospective controlled study

Patients with thyroid volume between 20-50 ml

Conventional minimal Cervical incision 4.0-6.0 cm

Video-assisted technique Cervical incision 2.0-3.0 cm

Main evaluation criteria

- Postoperative complications
- Mean hospital stay
- Cosmetic evaluation
- Patient's satisfaction
- Volume of residual gland

Conclusions

- Mivat is a safe technique which provides excellent cosmetic results and decreases patients' discomfort
- It is not an alternative to the conventional surgical technique but integrates with it
- It requires particular attention in the preparation of upper pole especially during the learning curve.

Conclusions 2.

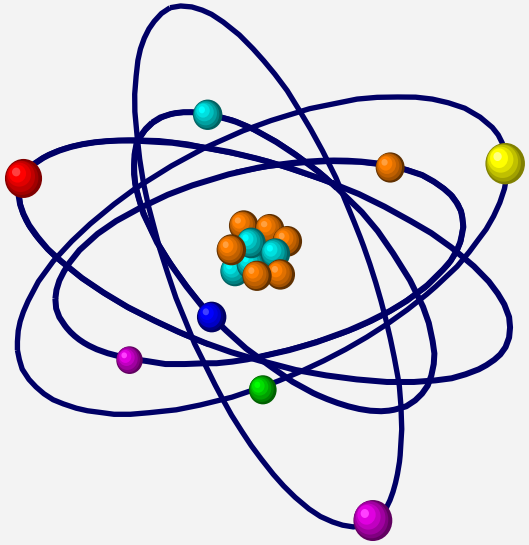
- Lymph node dissection requires skilled operators; hence, a careful preoperative US neck assessment is mandatory
- Currently, MIVAT seems the procedure of choice when performing thyroidectomy for a solitary nodule with cytological diagnosis of follicular lesion
- In the future, the indications might be extended to larger thyroid glands (up to 30 ml): the advantages must be verified in controlled studies

6th AME National Meeting – 3rd Joint Meeting with AACE

Update in Clinical Endocrinology

Low-risk Differentiated Cancer

Ablative Treatment: Always or "à la demande" or with rhTSH



Marco Ferdeghini – Chiara Colato – Claudio Traino

Dipartimento di Scienze Morfologico-Biomediche e di Patologia
Università degli Studi di Verona
Fisica Medica Azienda integrata Universitaria Ospedaliera - Pisa

Verona - 27 ottobre 2006

A multidisciplinary team with expertise and interest in the management of DTC

Endocrinologist/Oncologist, Surgeon, Pathologist, Nuclear Medicine Physician, Medical Physicist, Radiologist, Radiotherapist, Biochemist, Specialist Nurse

To decrease

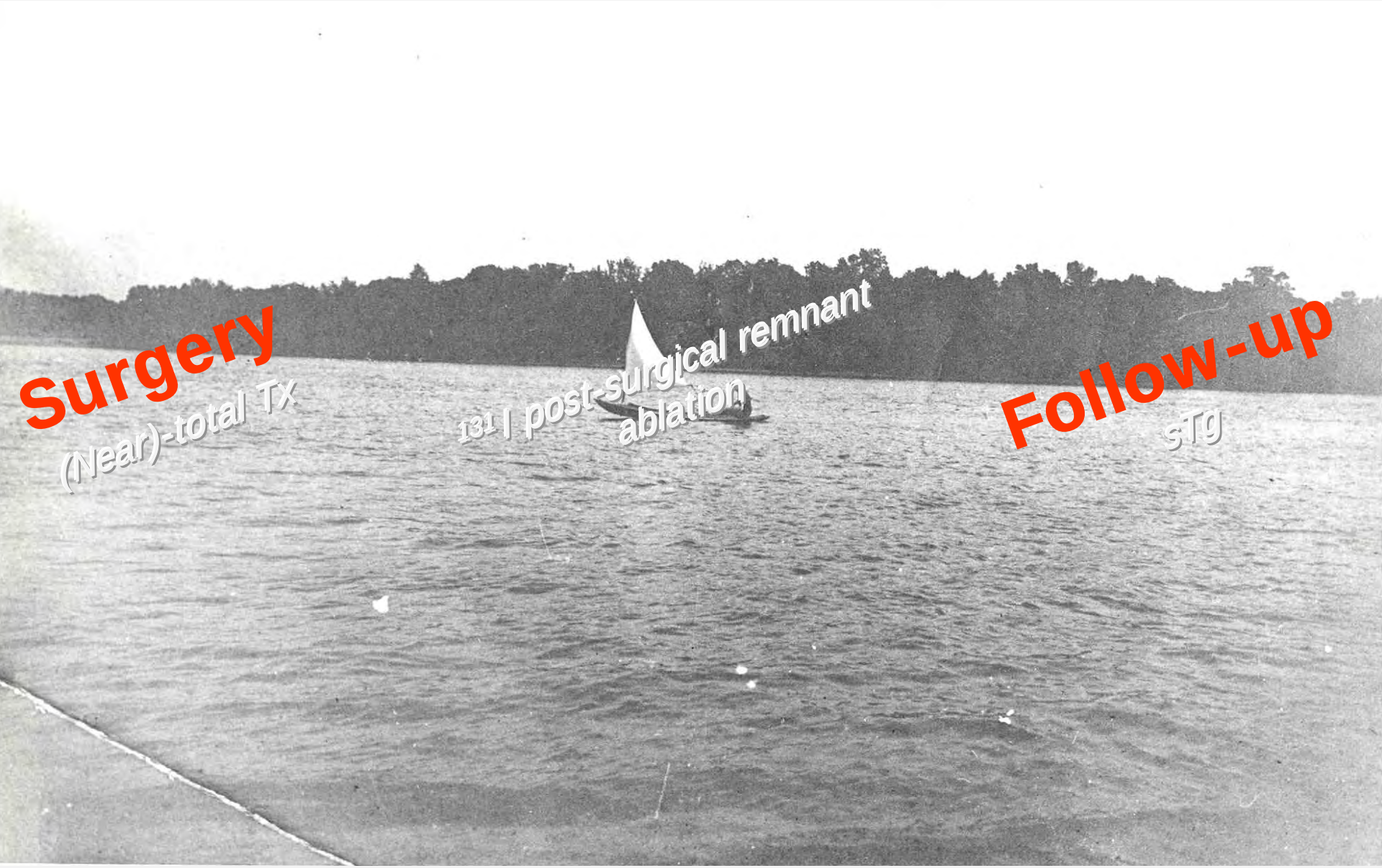
- **the recurrence rate and possibly the mortality rate**

To improve

- **sTg assessment as cornerstone tumor marker**
- **post-therapy and follow-up ^{131}I-WBS sensitivity and specificity**
- **Tg-Abs assessment as tumor markers when present**

Differentiated Thyroid Carcinoma

Differentiated Thyroid Carcinoma



^{131}I ablation and the decrease of DTC recurrence and mortality rates

Series	N	Follow-up (yrs)	^{131}I Effectiveness cancer mortality	^{131}I Effectiveness cancer recurrence
Mayo Clinic	2444	>25	NS	NS
Illinois Registry	2282	6.5	NS	
MD Anderson	1599	11		P<0.001
Ohio State	1510	16.6	P<0.0001	P<0.016
Pisa	964	12	NS	P<0.001
Hong Kong	587	9.2	NS	
Toronto	382	10.8	NS	
Gustave Roussy	273	7.3		NS
Mexico	229	5		NS
Gunderson/Lutheran	177	7.2		NS
UCSF	187	10.6	NS	P<0.0001

Sawka JCEM 2004 Metanalysis of ^{131}I effectiveness

Comment by Bryan R Haugen ***JCE&M 2004***

Taken together, these data would suggest that patients with low-risk DTC may benefit from radioiodine remnant ablation by decreased risk of locoregional recurrence (69%) and decreased risk of distant metastatic disease (50%).

Comment by Ernest Mazzaferri ***JCE&M 2004***

The main conclusions are that it may be beneficial in decreasing recurrence of DTC, but the results are inconsistent and the benefit of remnant ablation remains unclear in low risk patients treated with bilateral thyroidectomy and thyroid hormone suppression of TSH.

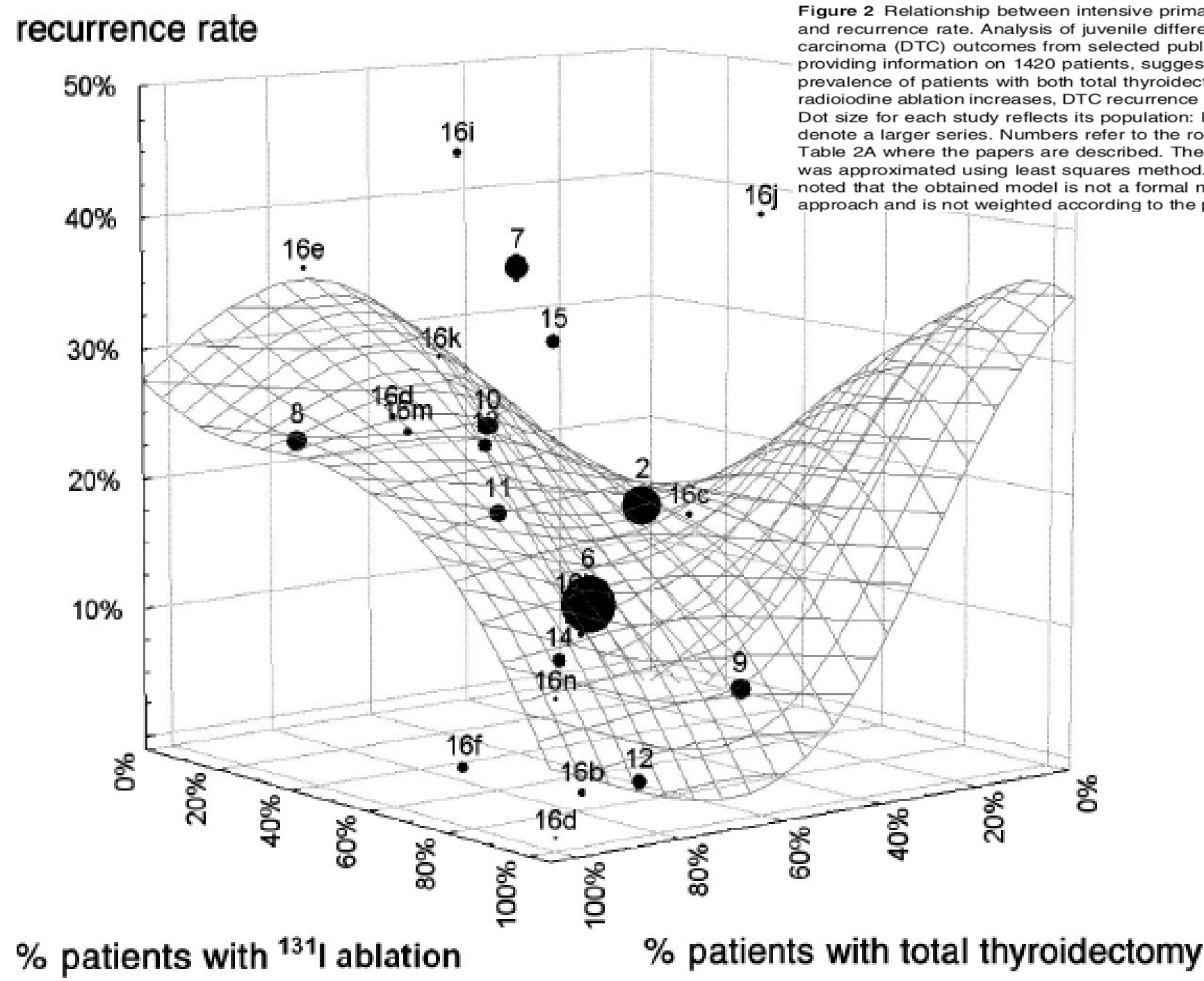


Figure 2 Relationship between intensive primary treatment and recurrence rate. Analysis of juvenile differentiated thyroid carcinoma (DTC) outcomes from selected published studies, providing information on 1420 patients, suggests that as the prevalence of patients with both total thyroidectomy and radioiodine ablation increases, DTC recurrence rate decreases. Dot size for each study reflects its population: larger dots denote a larger series. Numbers refer to the row numbers in Table 2A where the papers are described. The fitted surface was approximated using least squares method. It should be noted that the obtained model is not a formal meta-analysis approach and is not weighted according to the population size.

Jarzab B Endocrine-Related Cancer 12:773–803;2005

AACE/AAES MEDICAL/SURGICAL GUIDELINES FOR CLINICAL PRACTICE: MANAGEMENT OF THYROID CARCINOMA

ENDOCRINE PRACTICE Vol. 7 No. 3 May/June 2001 203

Radioiodine Remnant Ablation

lack of evidence of improved outcome. The issue of RRA in low-risk patients remains unsettled; a case-by-case decision is recommended, guided by clinical judgment and experience.

^{131}I ablation: indications

European Journal of Endocrinology (2006) **154** 787–803 ISSN 0804-4643

CONSENSUS STATEMENT

European consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium

Furio Pacini, Martin Schlumberger[1], Henning Dralle[2], Rossella Elisei[3], Johannes W A Smit[4], Wilmar Wiersinga[5] and the European Thyroid Cancer Taskforce

Section of Endocrinology and Metabolism, University of Siena, Via Bracci, 53100 Siena, Italy, [1]Service de Médicine Nucléaire, Institut Gustave Roussy, Villejuif, France, [2]Department of General, Visceral and Vascular Surgery, University of Halle, Germany, [3]Department of Endocrinology, University of Pisa, Italy, [4]Department of Endocrinology and Metabolic Disease, Leiden University Medical Center, The Netherlands and [5]Department of Endocrinology and Metabolism, University of Amsterdam, The Netherlands

THYROID
Volume 16, Number 2, 2006

Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association Guidelines Taskforce*

Members: David S. Cooper,[1] (Chair), Gerard M. Doherty,[2] Bryan R. Haugen,[3] Richard T. Kloos,[4] Stephanie L. Lee,[5] Susan J. Mandel,[6] Ernest L. Mazzaferri,[7] Bryan McIver,[8] Steven I. Sherman,[9] and R. Michael Tuttle[10]

Guidelines for the management of thyroid cancer in adults

British Thyroid Association

Royal College of Physicians

March 2002

Indications (!)

UK GL 2002 III, B

- The majority of **adult** Pts with tumour size **Ø ≥ 1 cm** following total Tx

EU Guidelines 2006 - High-risk group

Consensus: recommended

Reduces the recurrence rate, possibly prolongs survival,
permits early detection of persistent disease

- Documented persistent disease: **M_1, R_{1-2}**
- Complete tumor resection **stages III and IV disease or N1**, at high risk of persistent or recurrent disease

ATA GL 2005 R32 – Recommendation B fair evidence

- All stages **III and IV disease** (AJCC 6th edition)
- All stage II disease <45 years

Indications (!?)

EU Guidelines 2006 - Low-risk group

No consensus: controversial benefits

Uncertainties: administered to all Pts or only to ***selected*** Pts

- less than total Tx or *no lymph node dissection*
- Age <18 yrs
- T1 >1 cm N0 M0 or **multifocal** ***T1*** N0 M0
- **T2** N0 M0
- Unfavorable **histology**
  - PTC: tall cell, columnar cell, diffuse sclerosing
  - FTC: widely infiltrating follicular

ATA GL 2005 R32 – Recommendation B fair evidence

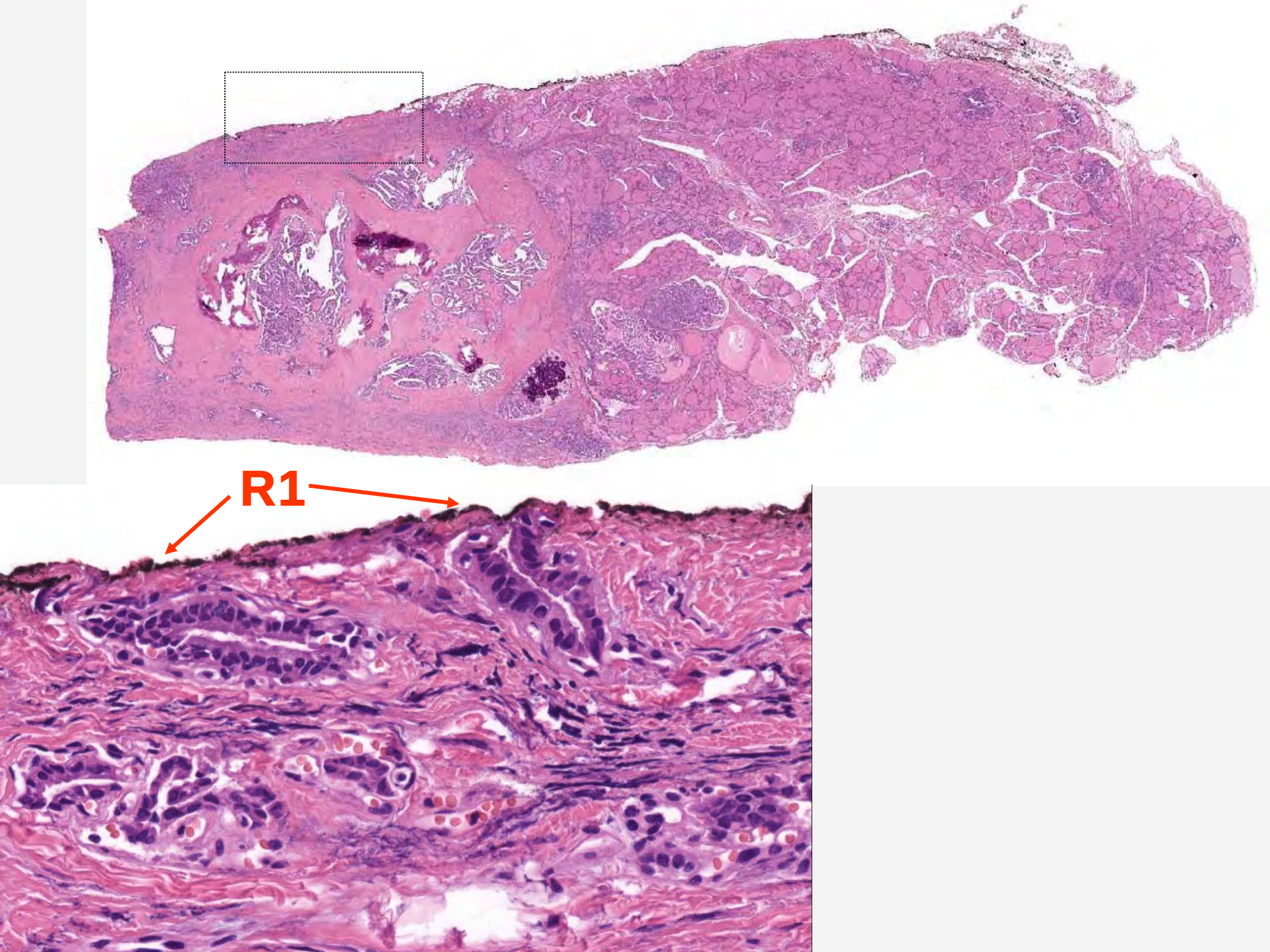
- Most **stage II** disease **≥45 years**
- ***Selected stage I disease***, ... ***multifocal*** disease, ***nodal metastases***, ***extrathyroidal or vascular invasion***, and/or more ***aggressive histologies***

Indications (?)

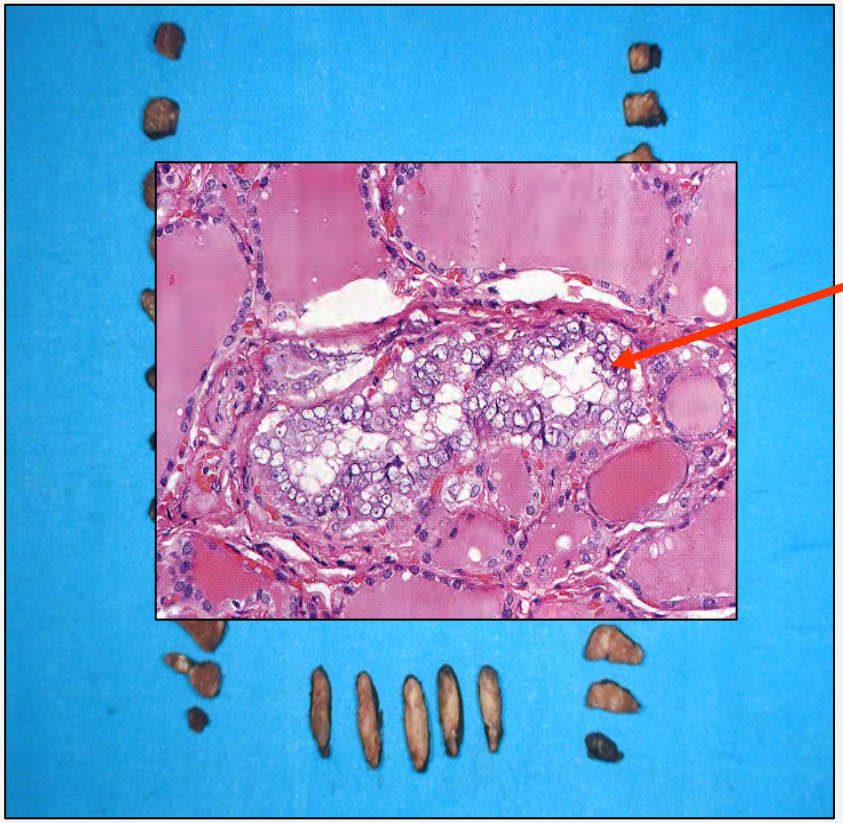
EU Guidelines 2006 - Very low-risk group

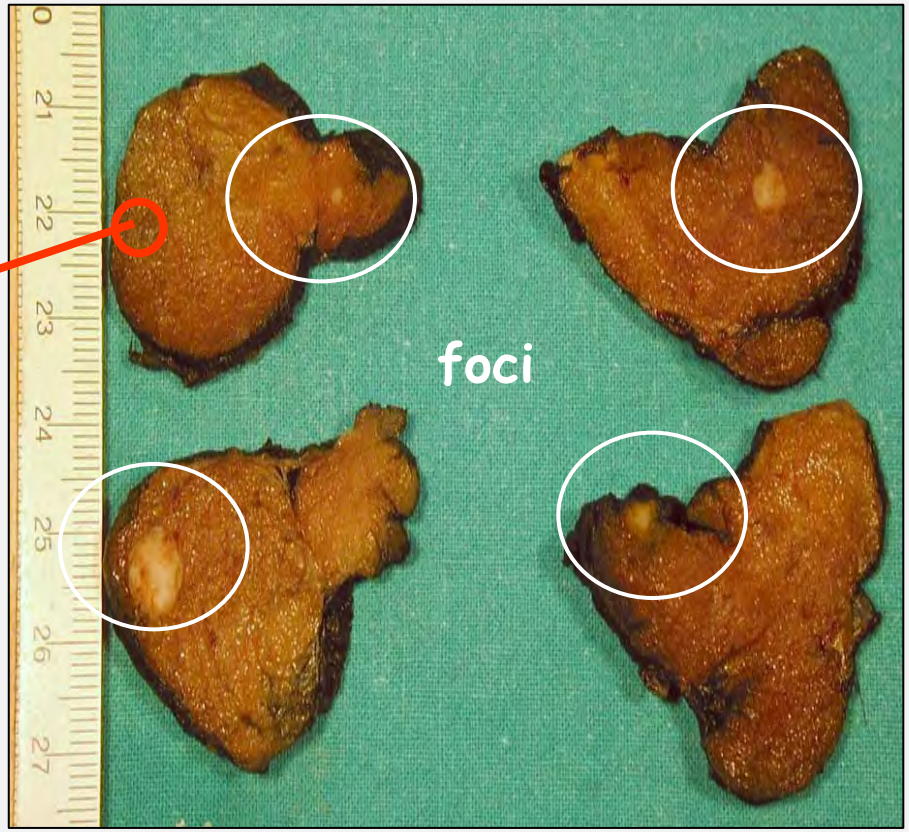
Consensus: no benefits, no indication

- Complete surgery
- Unifocal T1 ≤1 cm N0 M0
- Favorable histology
- No extrathyroidal extension
- No lymph node metastases

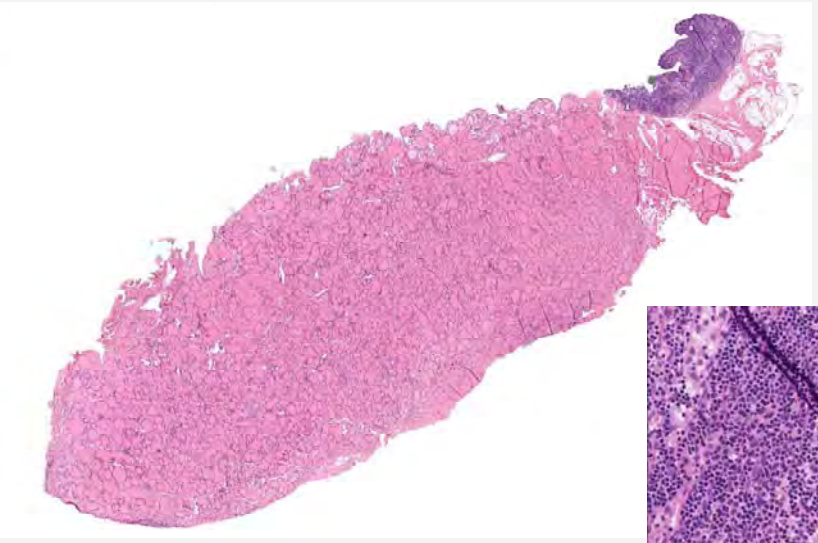

R1

Multifocality, bilaterality

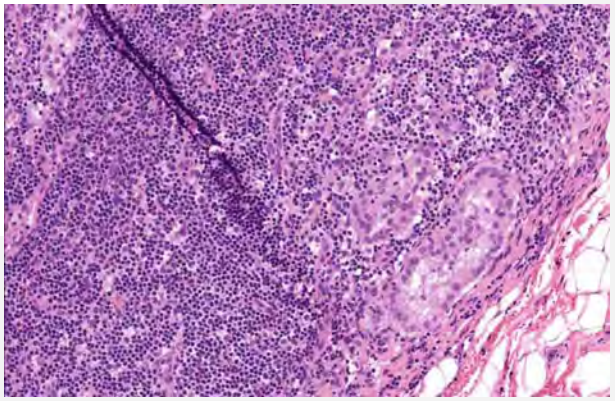


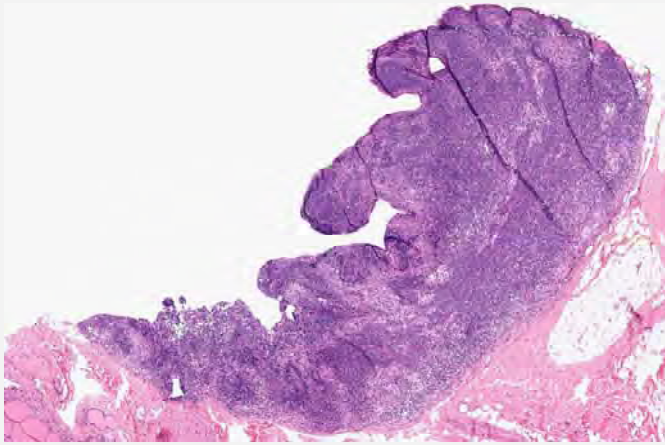


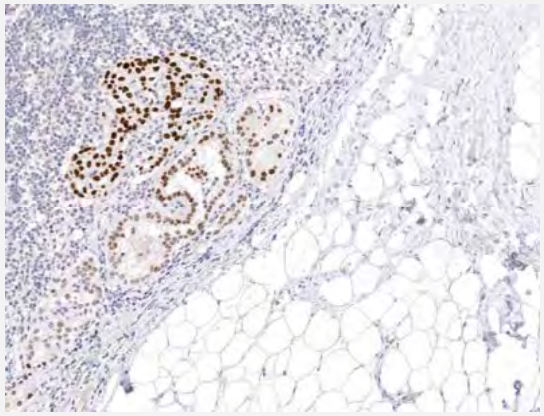
Lymph node occult metastases



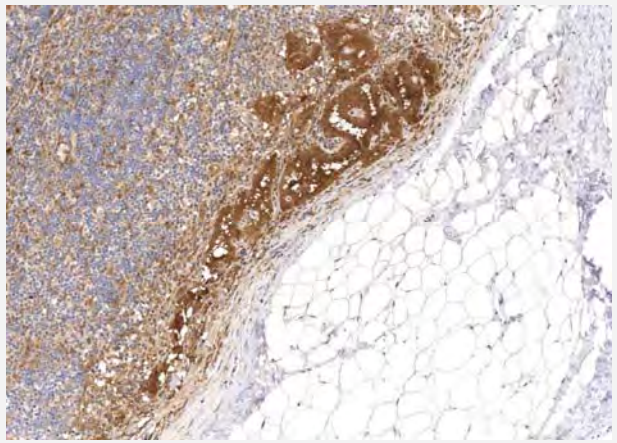
E&H



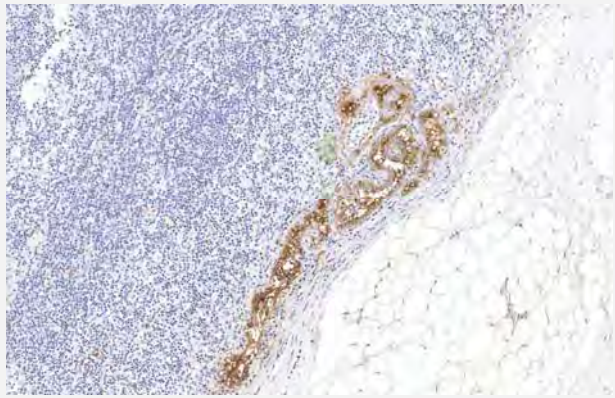




TTF-1

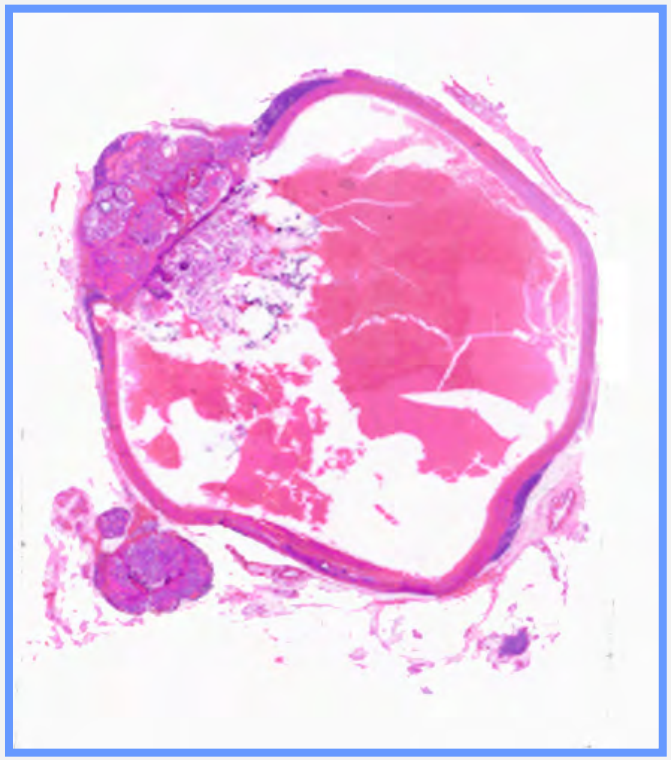


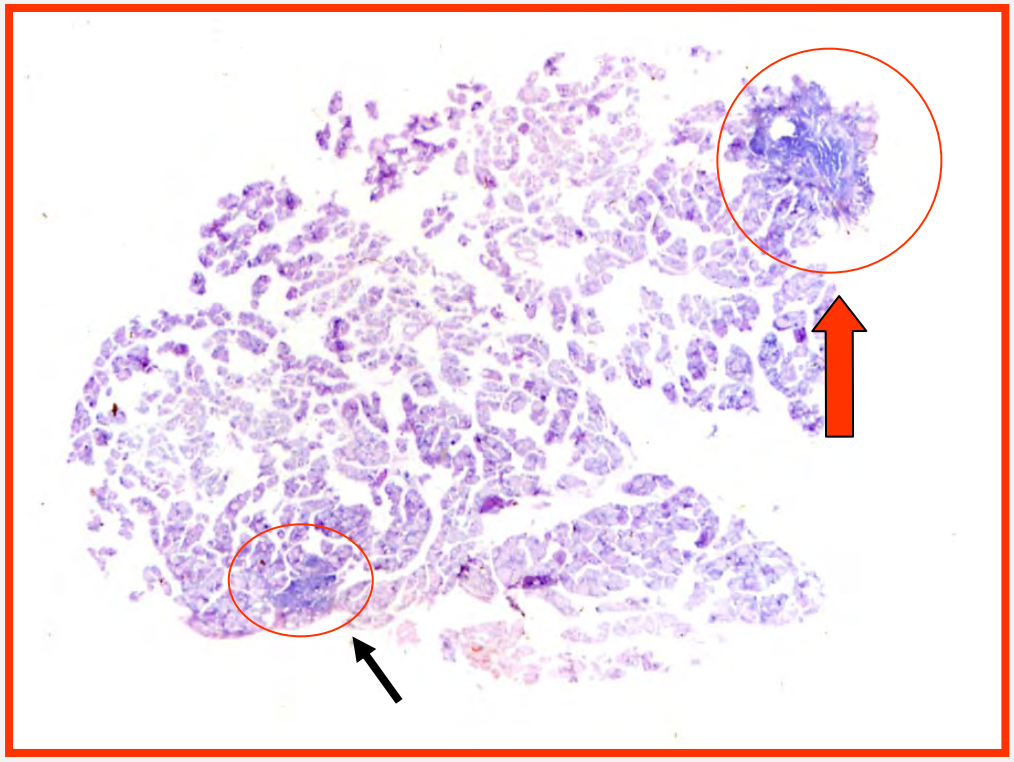
Galectin-3



HBME

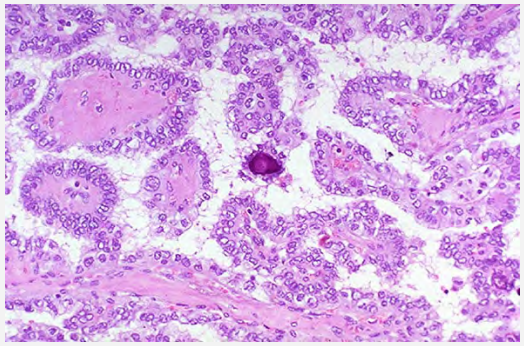
Multifocality & node metastasis



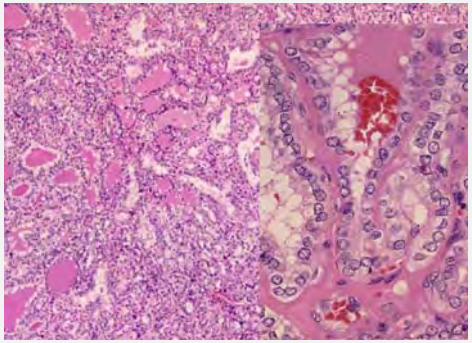


DTC Histology

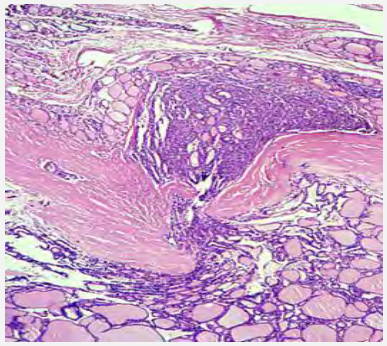
- *Favorable histology*



Papillary

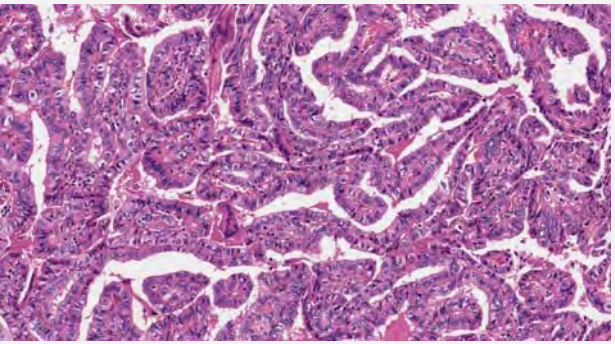


Follicular variant of Papillary

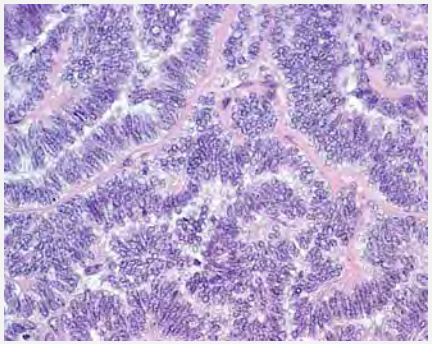


Minimally Invasive Follicular

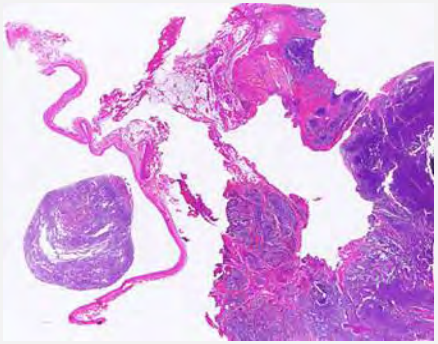
- *Unfavorable histology*



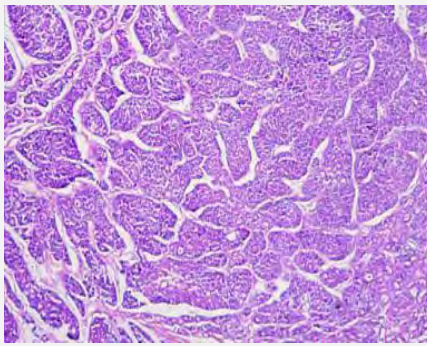
"Tall cell"



Columnar



Widely Invasive Follicular



Insular


OPORTO
LA CIUDAD MÁS BONITA
DEL MUNDO

Renaming Papillary Microcarcinoma of the Thyroid Gland

J. Rosai, V.A. LiVolsi, M. Sobrinho-Simoes and E.D. Williams

Int J Surg Pathol 2003; 11:249-51

the term **papillary microtumor (PMiT)** was chosen... (*specifically for)* a **single focus** of papillary carcinoma measuring <1 cm in diameter contained **within the thyroid** gland of an **adult** patient found **incidentally** at thyroidectomy done for some other reason**.**

...where **2 or more** lesions are present, each **individually <1 cm**, but **>1 cm when taken together**;... it would be safer **not to use** the term **PTiM** under these circumstances

... excludes ... those rare instances in which the tumor has features that may be indicative of a potential for an aggressive behavior... cases accompanied by invasion of the thyroid capsule, blood vessel permeation, or tall cell features

If a papillary carcinoma of <1 cm Ø incidentally found at *US, CT, or MRI* examination performed for some other reason, ... should still be classified as **PMiT.** Conversely, the use of the term is not recommend if the tumor were to be found in the presence or suspected presence of metastases

Patient preparation

A low-iodine diet before remnant ablation?

ATA Guidelines 2006 R38 - **Recommendation B**

- A low-iodine diet for 1–2 weeks is recommended particularly for Pts with high iodine intake

Ablation success rates after a stringent low-iodine diet

- significantly improved in Dutch DTC (Plujmen 2003)
- + instruction to avoid salt, seafood iodine-containing multivitamins compared to a regular diet not improved in an American study (Morris 2001)

ATA Guidelines 2006 R38

- Measurement of iodine excretion may be a useful way to identify iodine intake that could interfere with ^{131}I uptake

Pre-ablation diagnostic WBS before remnant ablation?

Procedure avoided without loss of information

- Low clinical utility
- Post-therapy WBS performed 3–8 days after ^{131}I administration is much more sensitive
- Possibility of a stunning effect on the subsequent therapeutic activity of ^{131}I

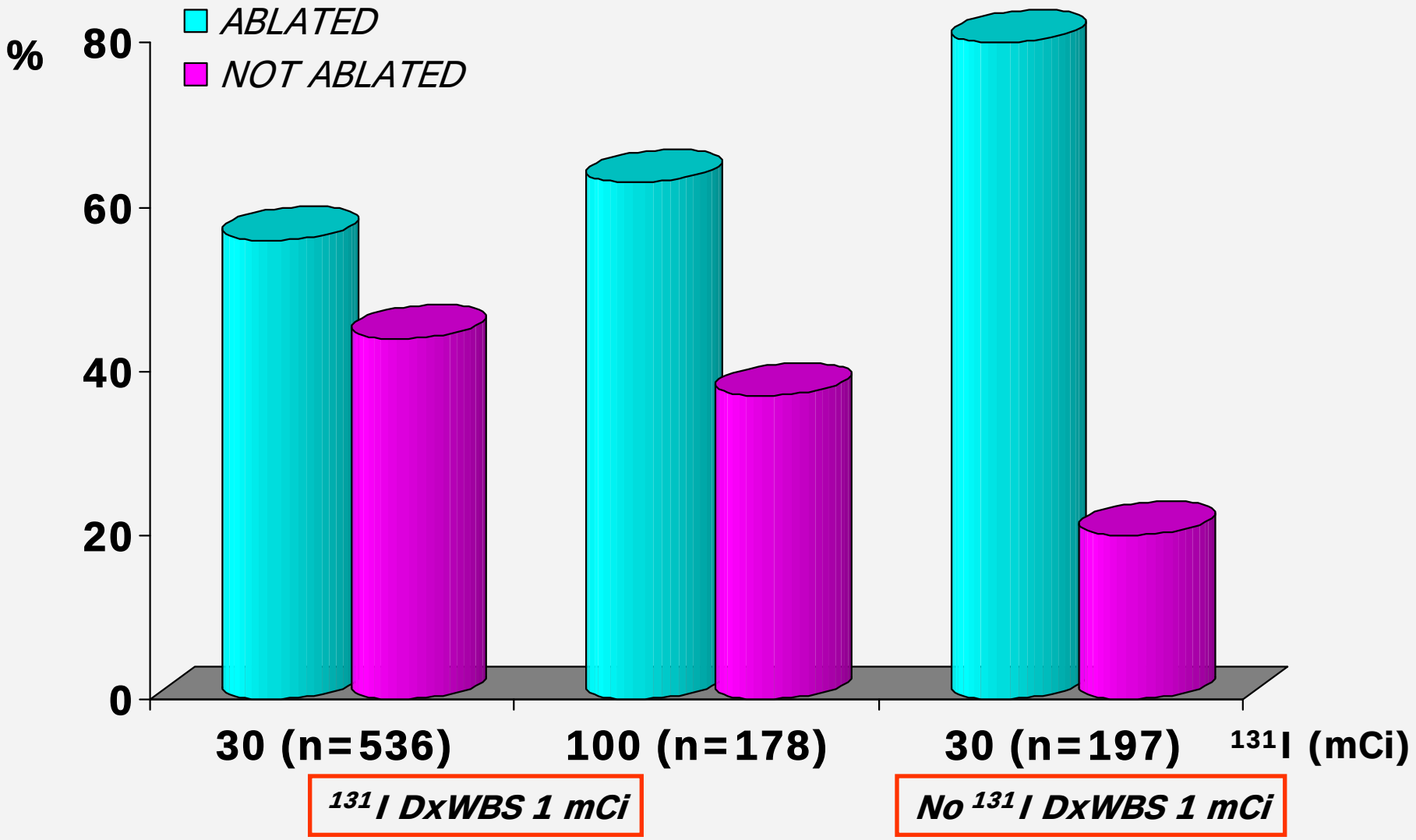
^{131}I Low activity (3.7 MBq, 100 µCi)

- to reduce stunning
- to perform dosimetric studies

^{123}I-WBS (2 to 5 mCi 74-185 MBq) or **^{99m}Tc-WBS**

- in uncertainty concerning the extent of Tx
- to reduce the risk of stunning
- at 24 h comparable but not superior images to both ^{131}I diagnostic and post-ablation scans *(Sarkar 2002 - Siddiqi 2001)*

Pre-ablation diagnostic WBS before remnant ablation?



Bianchi 2005

Remnant mass

Inversely correlated with the success of ^{131}I ablation

Maxon HR, et al., J Nucl Med 1992; 33: 1132–36

Van Wyngaarden M, McDougall IR Nucl Med Commun 1996; 17: 199–207.

Doi SA, Woodhouse NJ. Clin Endocrinol 2000; 52: 765–73

Rosario PW, et al. Nucl Med Commun 2004; 25: 1077–81

Studies comparing different activities of ^{131}I for thyroid remnant ablation

	^{131}I activity mCi	Pts N.	'Successful ablation' %	
McCowen, 1976	≤30 80-100	36 28	Recurrence Free Survival & Actuarial Survival Rate	NS
DeGroot & Reilly, 1982	26-30 50-60 >60	18 21 9	83 100 100	
Ramacciotti, 1982	30 50 75	20 10 14	40 30 71	
Creutzig, 1987	30 100	10 10	50 60	
Johansen,1991	29 100	36 27	81 84	
Mazzaferri & Jhiang, 1994	29-50 51-100	59 79	Recurrence Rate	NS
Hodgson, 1998	29 50	20 5	80 80	
Sirisalipoch, 2004	50 100	63 75	65 89	

Studies comparing different activities of ^{131}I for thyroid remnant ablation

	^{131}I activity *mCi*	Patients *N.*	'Successful ablation' *%*
Bal, 1996	25-34 (30±1.5) 35-64 (50.6±5.4) 65-119 (88.6±14) 120-200 (155±28.7)	27 54 38 30	63 78 74 78
Bal, 2004	15 20		59,6 63,6
	25 30 35 40 45 50	509	81,4 83,6 79,4 78,3 84,4 81,8

Dosimetric approach

Maxon HR, et al.

Radioiodine-131 therapy for well differentiated thyroid cancer – a quantitative radiation dosimetric approach: outcome and validation in 85 patients

J Nucl Med 1992;33:1132-6

Aim: 300 Gy delivered to the thyroid remnant

173–374 Gy

120 Gy
Successful ablation

600 Gy
Unsuccessful ablation

Post-therapy WBS after remnant ablation?

ATA GL 2005 R32 - **Recommendation B**

- Recommended 5–8 days after ^{131}I remnant ablation to visualize metastases
- Published data supporting this time interval are lacking

After high ^{131}I activity

- Additional metastatic foci (most often in the neck, lungs and mediastinum) in 10%–26% of Pts compared to the diagnostic WBS
- Altered the disease stage in ~ 10% of the Pts
- Affected clinical management in 9%–15%

TSH elevations to provide sufficient thyroid stimulation

- *>25 or 30 mIU/L* *(Schlumberger, 1998)*
- *≥30–50 mIU/mL* *(McDougall & Weigel 2001)*

TH withdrawal

and consequent hypothyroidism

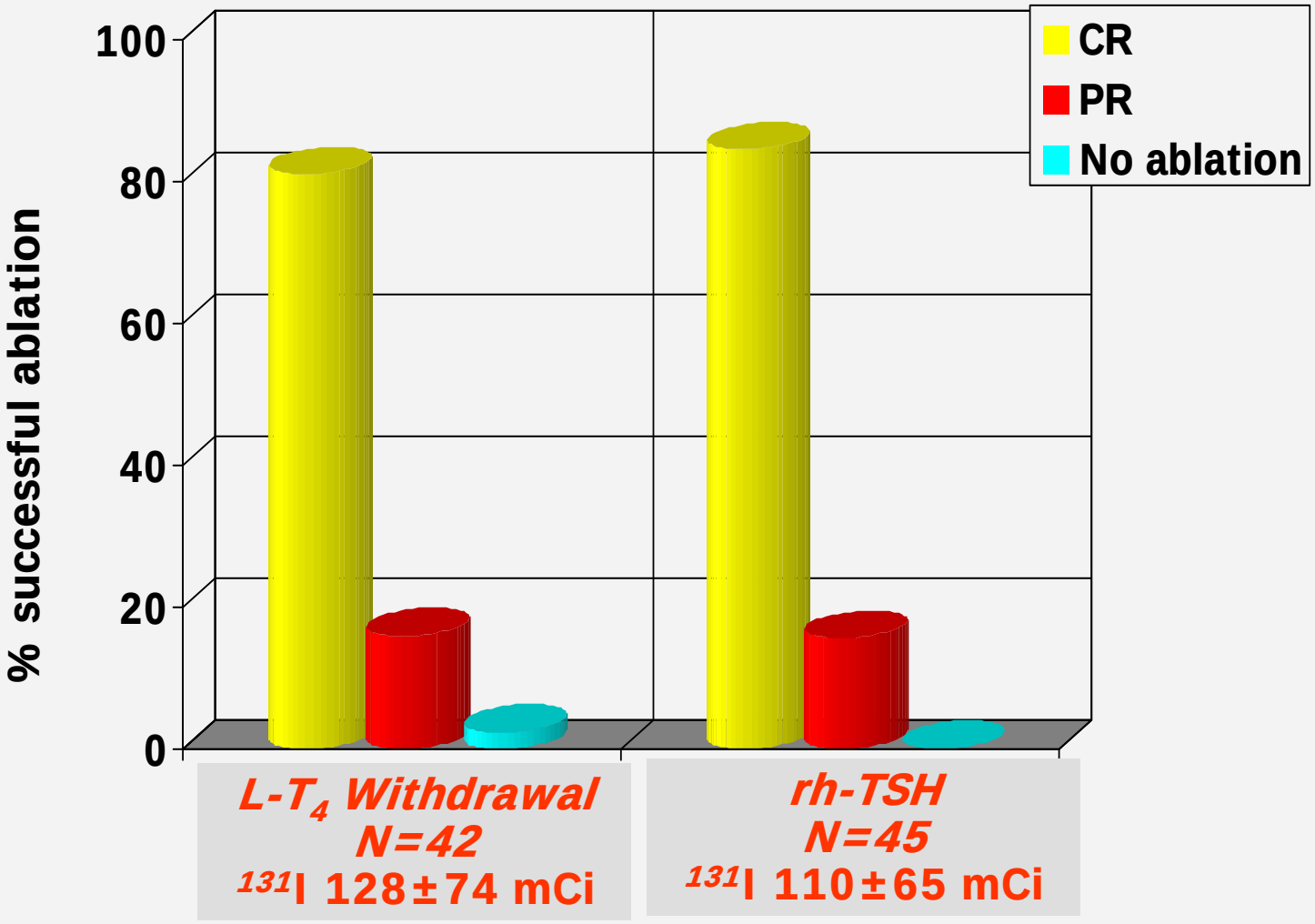
vs

rhTSH on L-T_4 therapy

preserving quality of life

Robbins

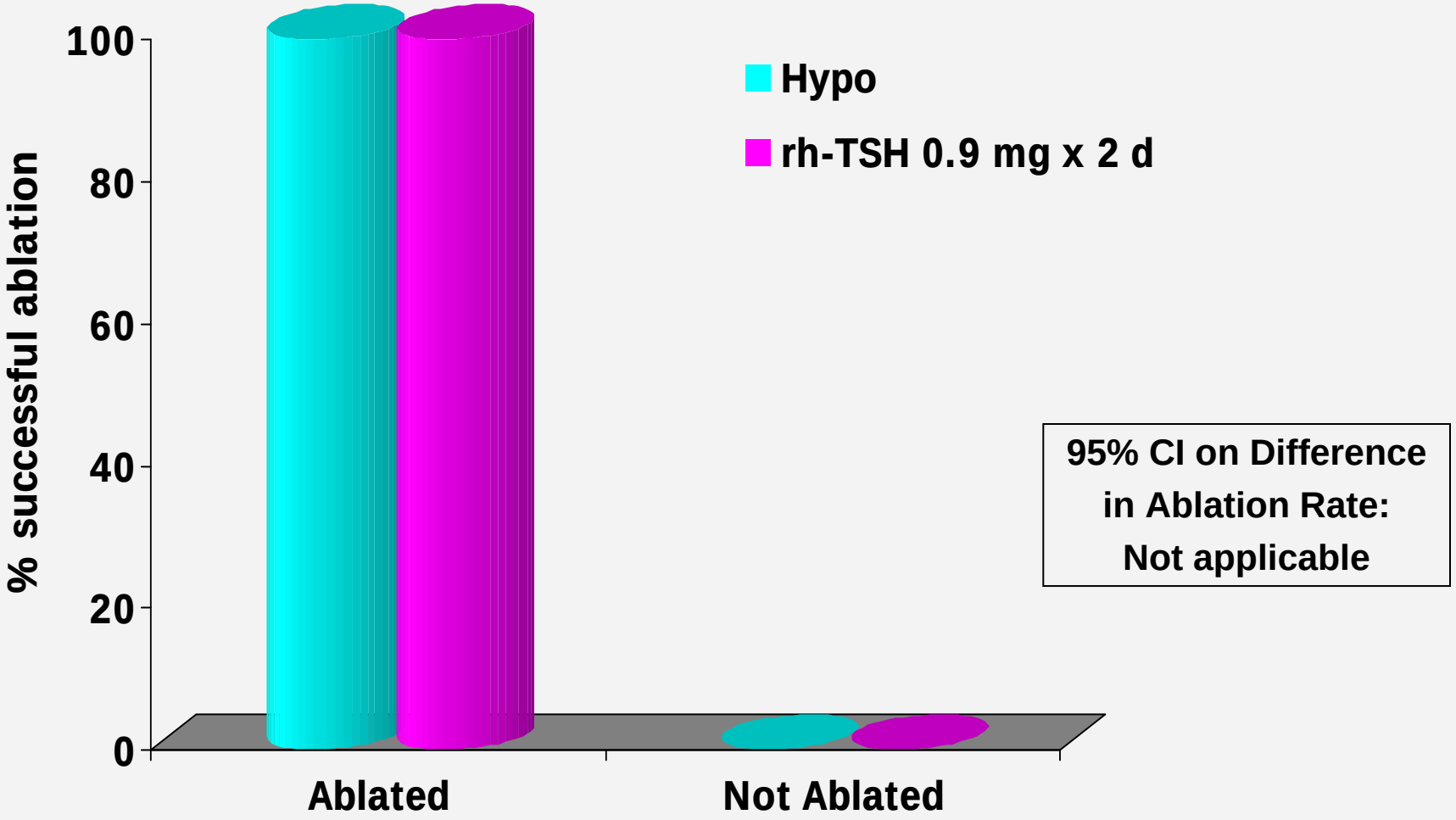
Dosimetric approach



rhTSH-aided ablation using a ^{131}I activity of 100 mCi

A Randomized, Controlled, Multi-National Pilot Study

(Pacini F et al, JCEM 2006)

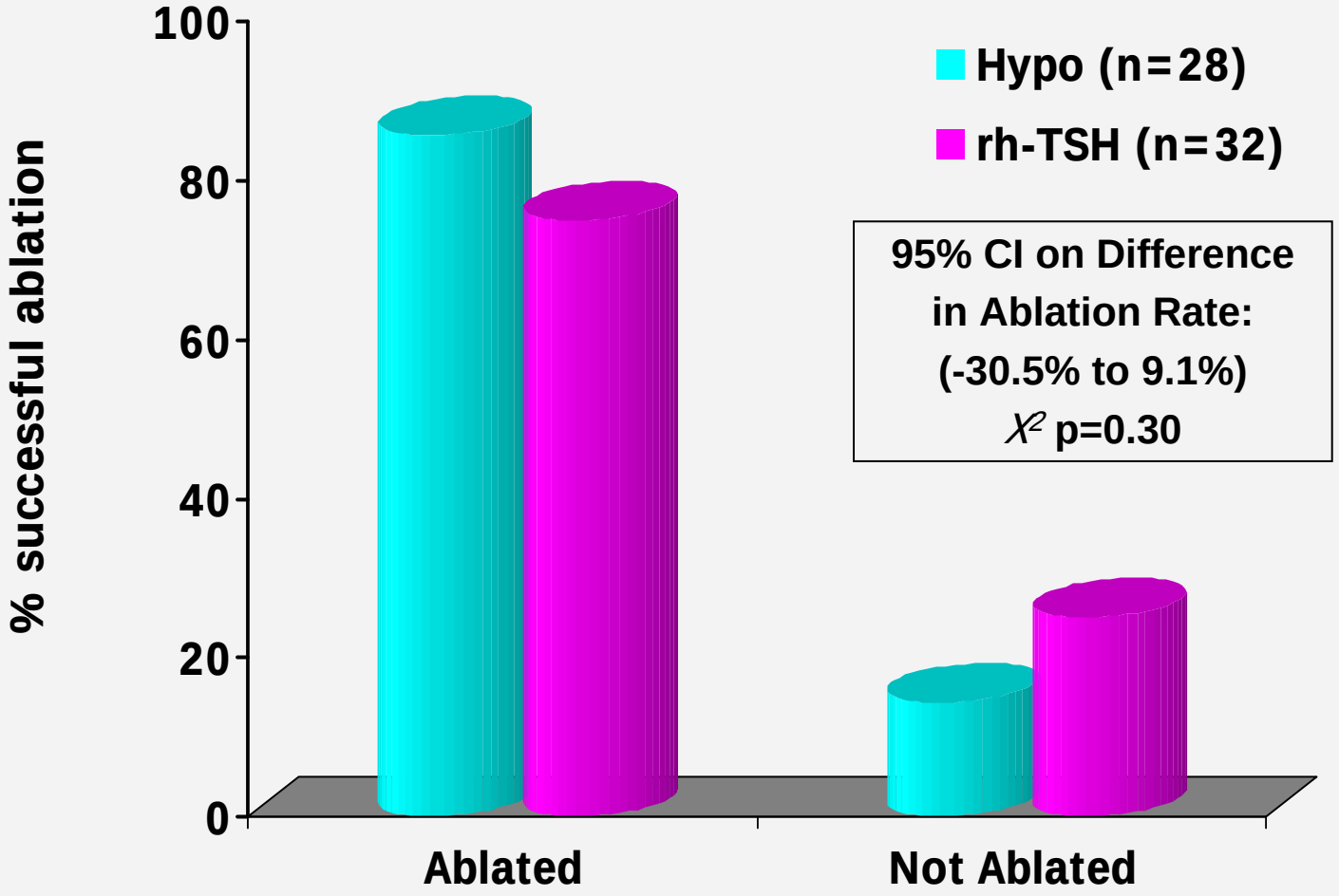


Ablation = no visible uptake or, if visible, <0.1% at the 8 mo rhTSH-WBS

rhTSH-aided ablation using a ^{131}I activity of 100 mCi

A Randomized, Controlled, Multi-National Pilot Study

(Pacini F et al, JCEM 2006)

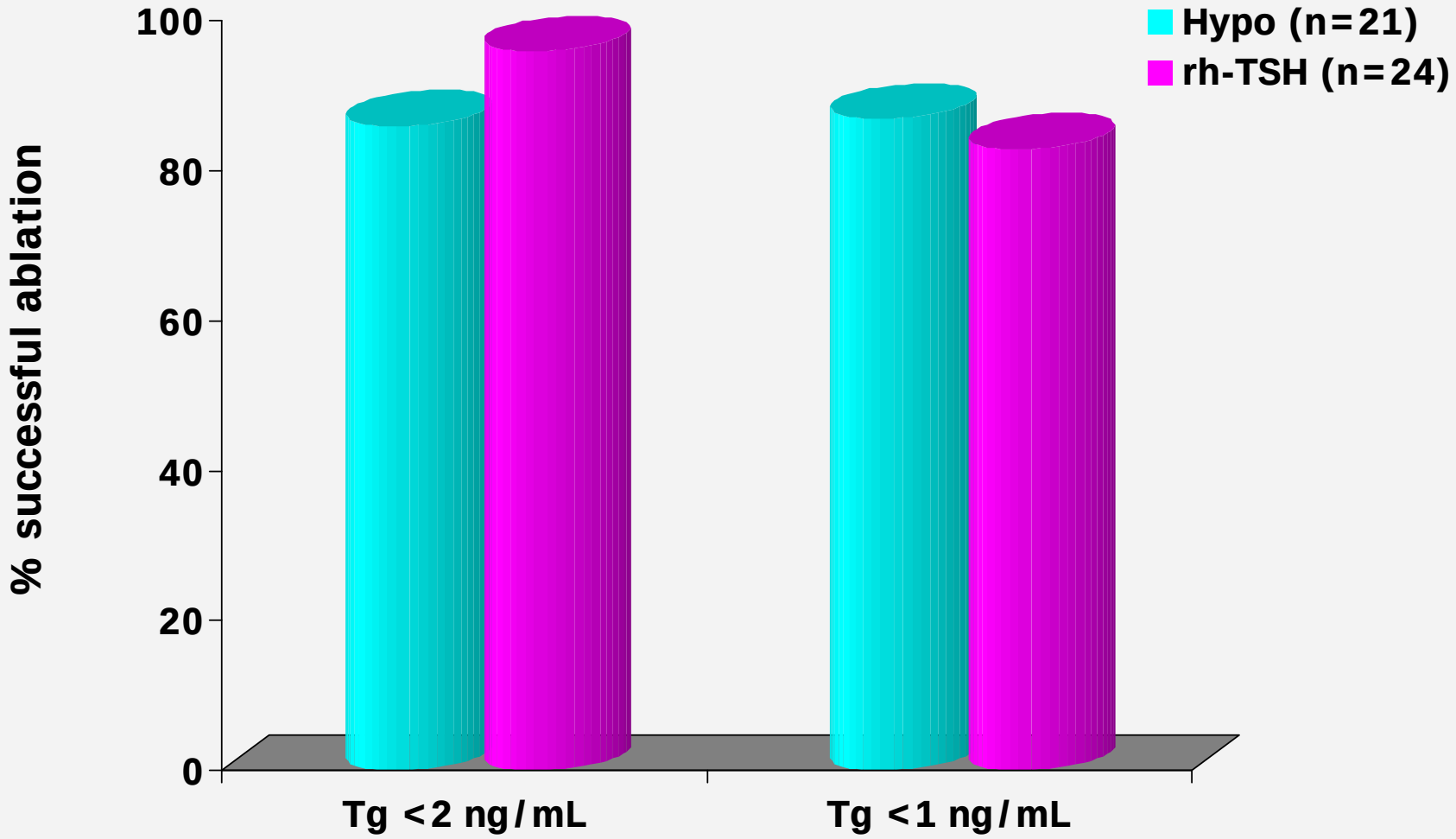


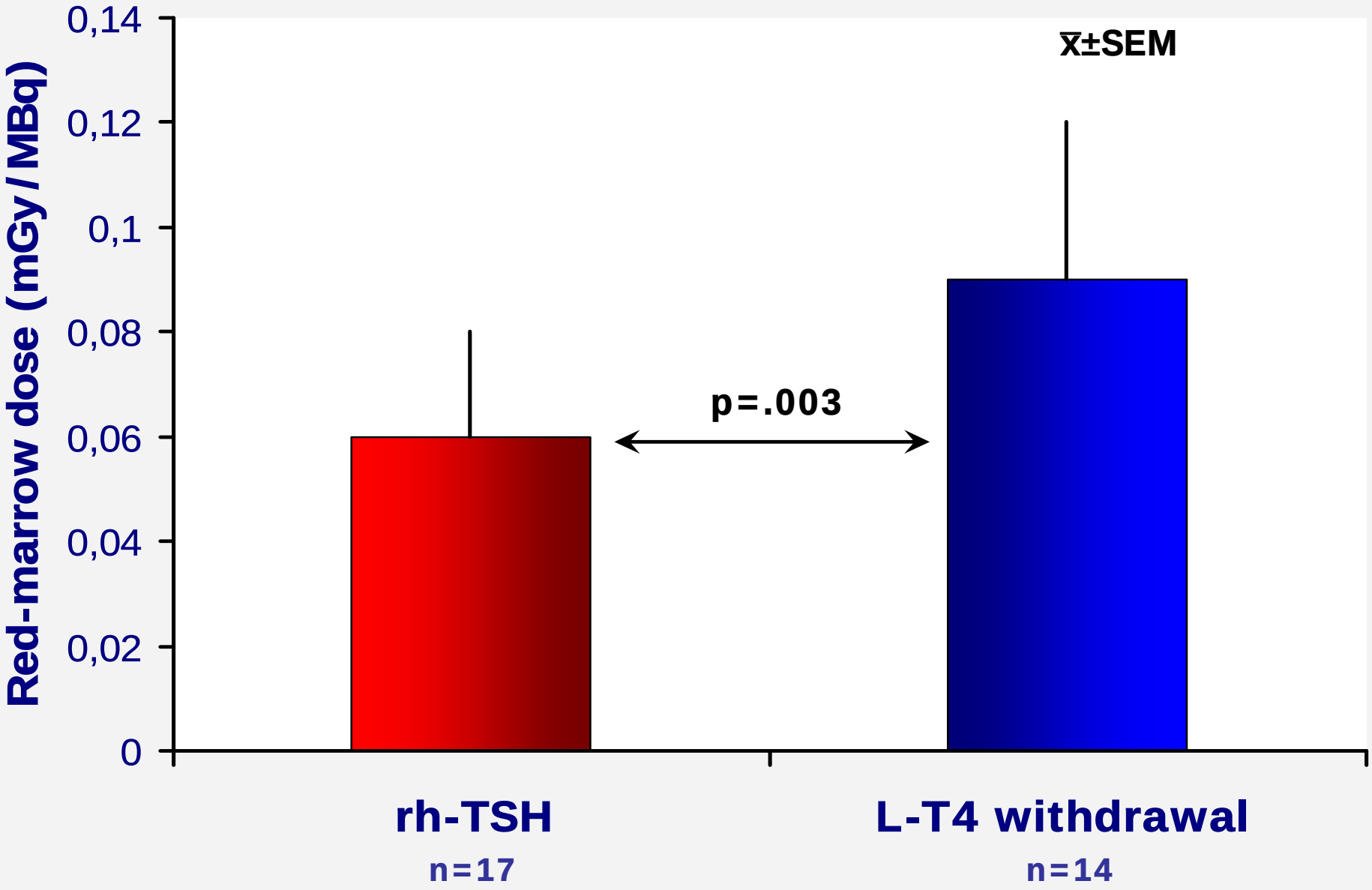
Ablation = no visible thyroid bed uptake at the 8 mo rhTSH-WBS

rhTSH-aided ablation using a ^{131}I activity of 100 mCi

A Randomized, Controlled, Multi-National Pilot Study

(Pacini F et al, JCEM 2006)





This result is in good agreement with those reported in rh-TSH pretreated Pts (Luster, M, et al. Eur J Nucl Med Mol Imaging 2003; 30: 1371; Menzel, C et al. J Nucl Med 2003;44:1065)

Remnant cumulated activity per unit administered activity (h)

The thyroid-remnant absorbed dose can be calculated by equation (MIRD):

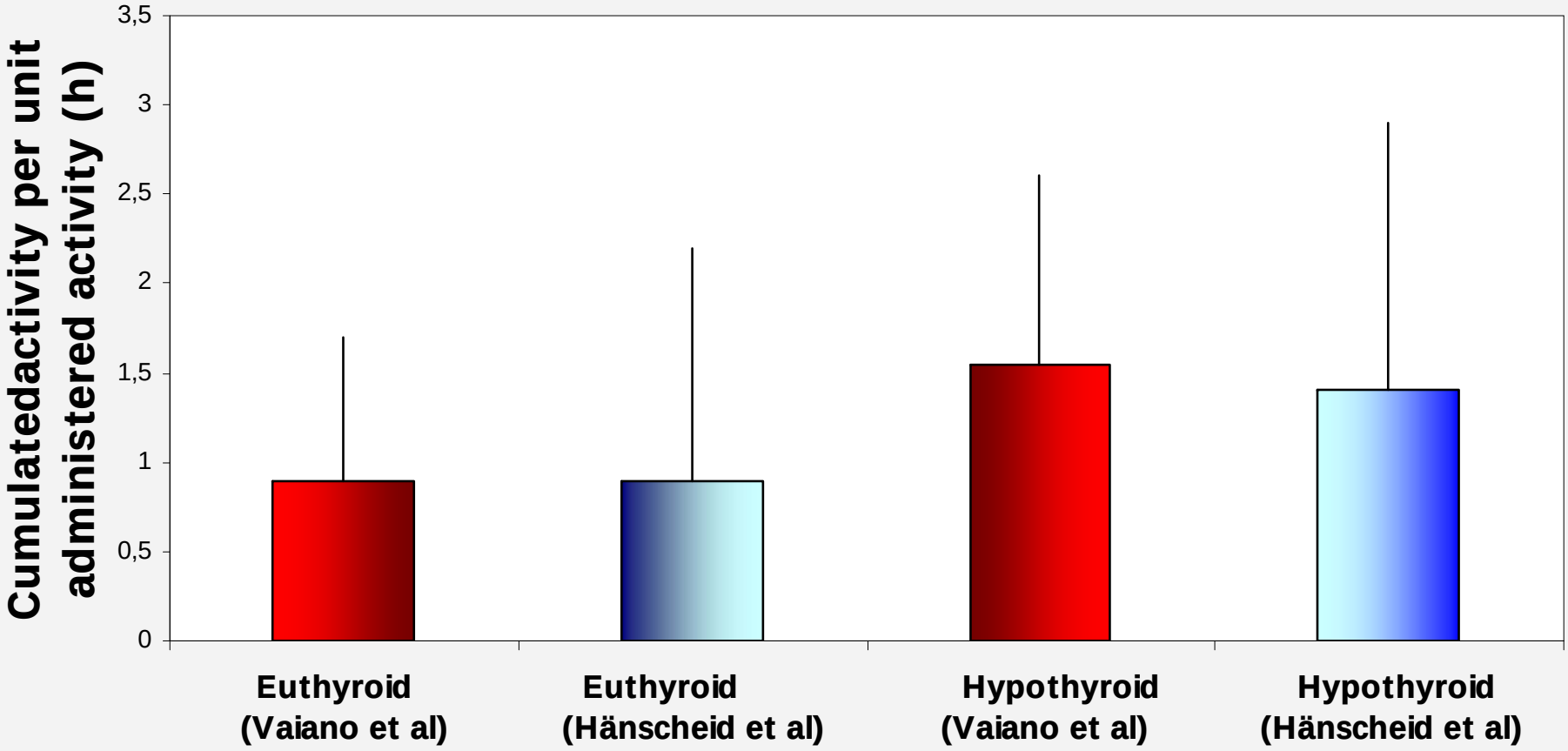
$$D_R = \tilde{A}_R S_{T \leftarrow T} \frac{m_T}{m_R}$$

where $\tilde{A}_R$ is the cumulated ^{131}I activity in thyroid post-surgical remnant; $S_{T \leftarrow T}$ is the MIRD-defined S-values for thyroid irradiating itself (constant); m_T is the reference man thyroid mass (constant) and m_R is the post-surgical remnant mass.

TWO CONSEQUENCES:

- The remnant absorbed dose depends strongly from the remnant mass
- For Pts whose remnant mass is the same the remnant absorbed dose depends on the cumulated activity in the remnant

Comparison between cumulated activities per unit administered activities

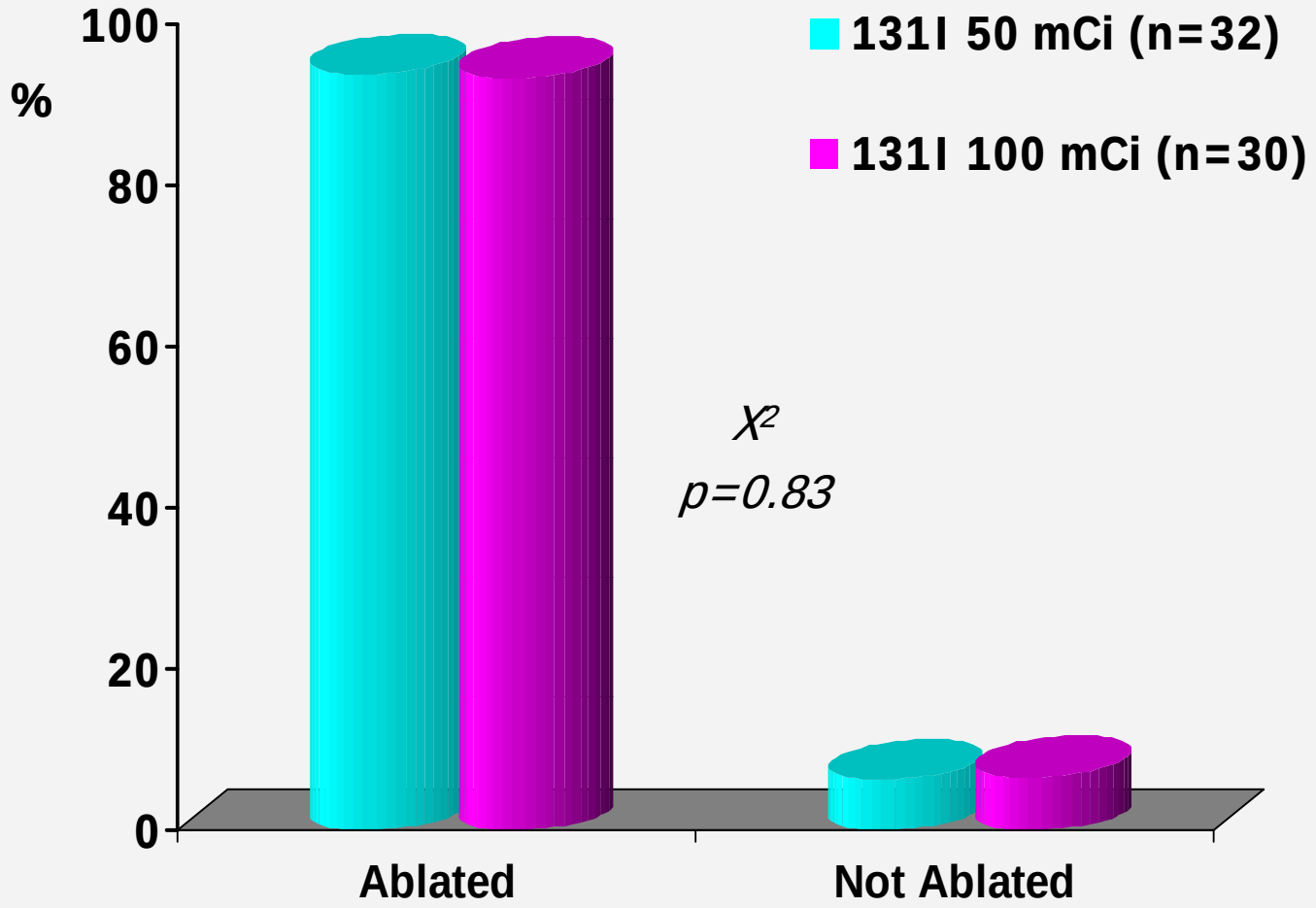


CONSEQUENCES: If one wants the same remnant absorbed dose for Pts with the same remnant mass, the administered activity must be ~ 1.5 times higher for rh-TSH Pts

rhTSH-aided ablation using a ^{131}I activity of 50 vs 100 mCi

A Randomized Pilot Study

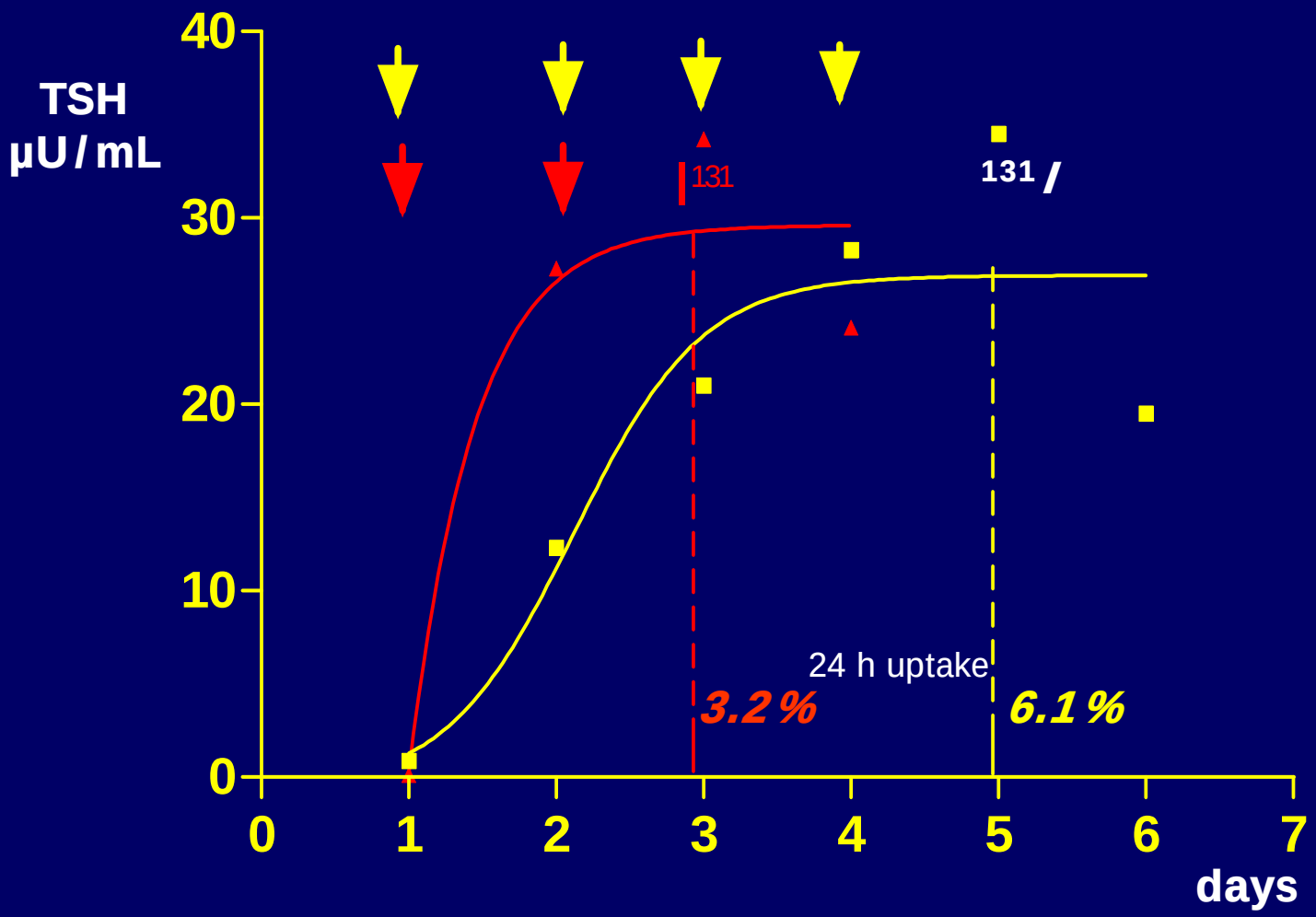
(Pacini F et al)



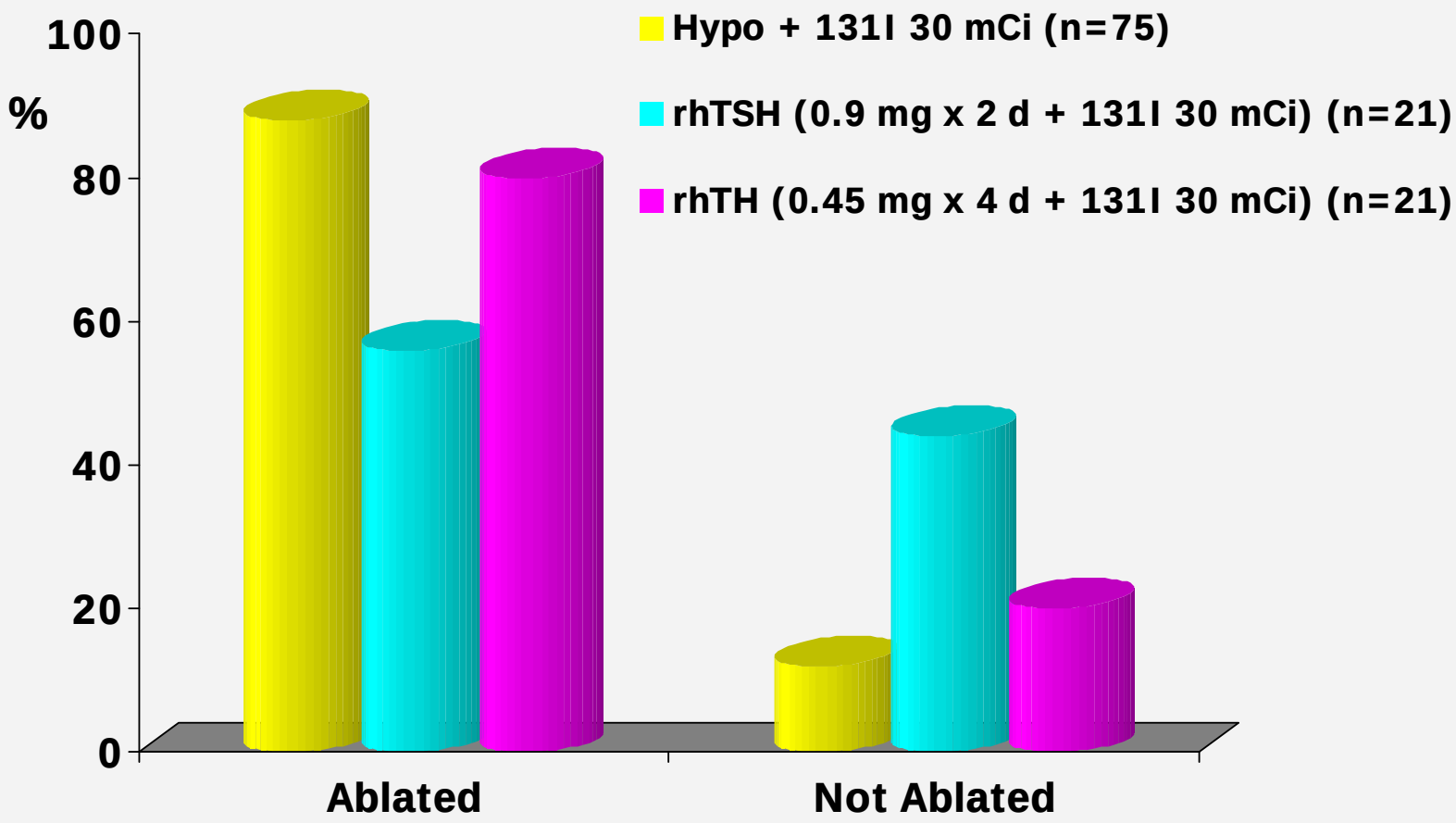
Ablation = no visible thyroid bed uptake or,
if visible, <0.1% at the 8 mo rhTSH-WBS

Post-surgical remnant uptake after rh-TSH

0.9 mg x 2 d *vs* 0.45 mg x 4 d



Elisei R



Ablation = no visible uptake at the 8 mo rhTSH-WBS

Castagna 2005

^{131}I ablation: indications

- Surgery: complete ?
- T1: ≤1 cm >1 cm ?
- Unifocal ? ⇔ Assessment of Multifocality ?
- Favorable histology
- Lymph node metastases ? ⇔ Level VI ?
- Extrathyroidal extension ?

^{131}I ablation: protocol

- **Surgery: complete YES**
- **T1: ≤1 cm YES**
- **Unifocal YES**
  ⇔ Assessment of Multifocality YES
- **Favorable histology YES**
- **Lymph node metastases NO ⇔ Level VI YES**
- **Extrathyroidal extension NO**

Very low-risk

^{131}I ablation: when indicated

- Low-iodine diet YES / NO
- ^{131}I diagnostic WBS NO
  ⇔ Assessment of uptake for dosimetry YES / NO
- rhTSH YES
- ^{131}I activity the lowest useful
- ^{131}I posttherapy WBS YES

6th AME National Meeting
Update In Clinical Endocrinology
Verona October 27-29, 2006

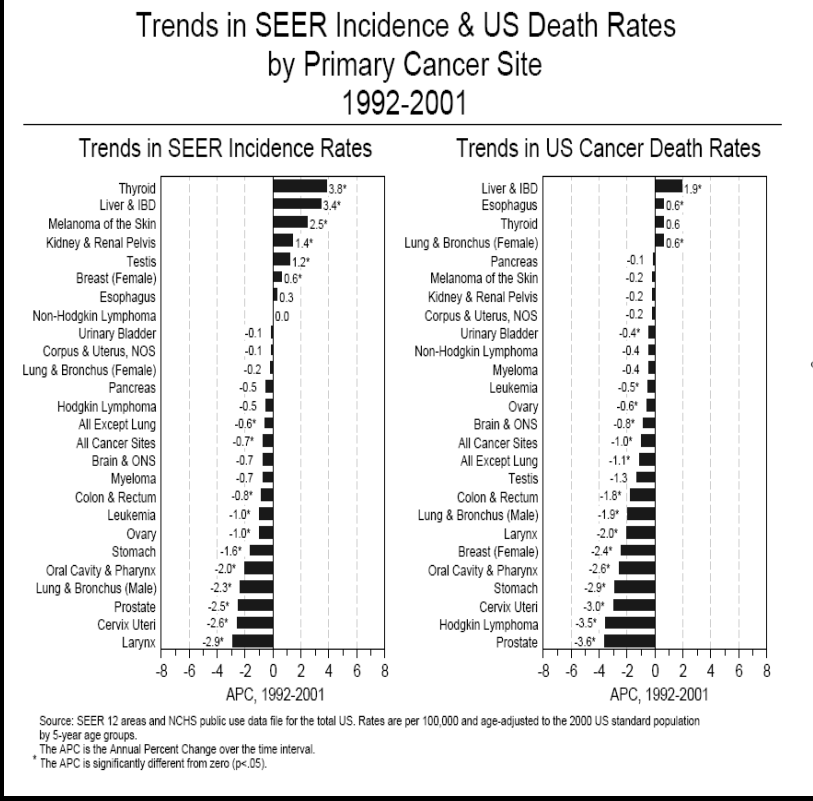
Low Risk Differentiated Thyroid Cancer

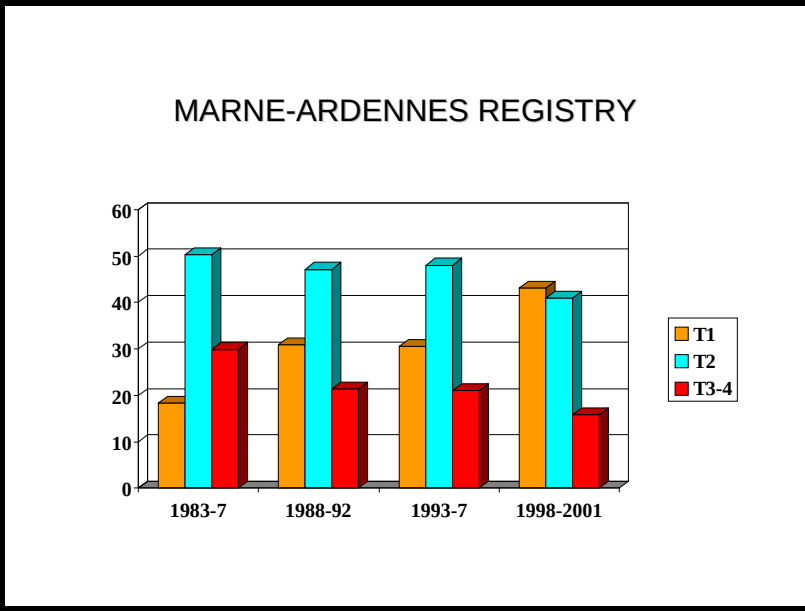
What Kind of Follow-up?

Furio Pacini
Department of Endocrinology
University of Siena, Italy

Thyroid cancer

- Thyroid nodules may approach 20% of the population;
- 5-7% of thyroid nodules is cancer (the most frequent endocrine cancer);
- Thyroid cancer is among the three human cancers at increase;
- The clinical presentation has been changing in recent years: >80% are at low risk
- Long term survival is the rule, but recurrences may appear even 20 years from the diagnosis.
- Thus, it has strong socio-economical implication





European Journal of Endocrinology (2006) 154 787–803 ISSN 0804-4643

CONSENSUS STATEMENT

European consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium

Furio Pacini, Martin Schlumberger[1], Henning Dralle[2], Rossella Elisei[3], Johannes W A Smit[4], Wilmar Wiersinga[5] and the European Thyroid Cancer Taskforce

Section of Endocrinology and Metabolism, University of Siena, Via Bracci, 53100 Siena, Italy, [1]Service de Médicine Nucléaire, Institut Gustave Roussy, Villejuif, France, [2]Department of General, Visceral and Vascular Surgery, University of Halle, Germany, [3]Department of Endocrinology, University of Pisa, Italy, [4]Department of Endocrinology and Metabolic Disease, Leiden University Medical Center, The Netherlands and [5]Department of Endocrinology and Metabolism, University of Amsterdam, The Netherlands

Definition of risk

- **Very low risk patients: T1<1cm, unifocal and intra-thyroid; favorable histology; N0**
- **High risk patients: T2-4, N1, M1, persistent disease**
- **Low risk patients: all the other patients.**

FOLLOW-UP

Depending from initial treatment:

Lobectomy:

- **Serum Tg poorly sensitive**
- **Neck ultrasound: most sensitive**

Replacement, not suppressive l-T4 therapy

FOLLOW-UP

Depending from initial treatment:

Total thyroidectomy:

- **Serum Tg highly sensitive**
- **Neck ultrasound highly sensitive**
- **13I diagnostic WBS poorly sensitive**

FOLLOW-UP: 3 months after ablation

On l-T4 therapy: Measurements of

- Serum Tg and anti-Tg antibodies

- Thyroid hormones and TSH: to assess the appropriate dose of l-T4

SERUM Tg LEVELS SOON AFTER INITIAL TREATMENT

- Some months after initial treatment, detectable serum Tg (<5-10ng/mL) may be produced by:
  - irradiated cells that will disappear in 2/3 of cases (Baudin, Pacini, Torlontano, Toubeau), and serum Tg will decrease
  - neoplastic cells that will progress, and serum Tg will increase.
- A control TSH-stimulated Tg obtained some months (or years) later will differentiate these two groups of patients.
- The most relevant parameter is the trend of Tg level, rather than its level.

FOLLOW-UP: 8-12 MONTHS AFTER ABLATION

- Clinical examination: poorly sensitive
- Neck ultrasonography
- Serum Tg determination following TSH stimulation
- (^{131}I-total body scan)

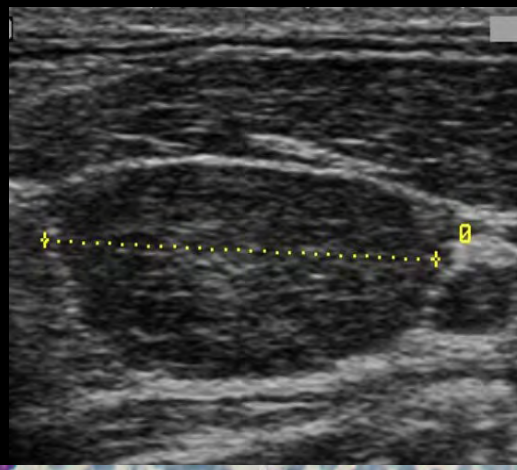
NECK ULTRASONOGRAPHY

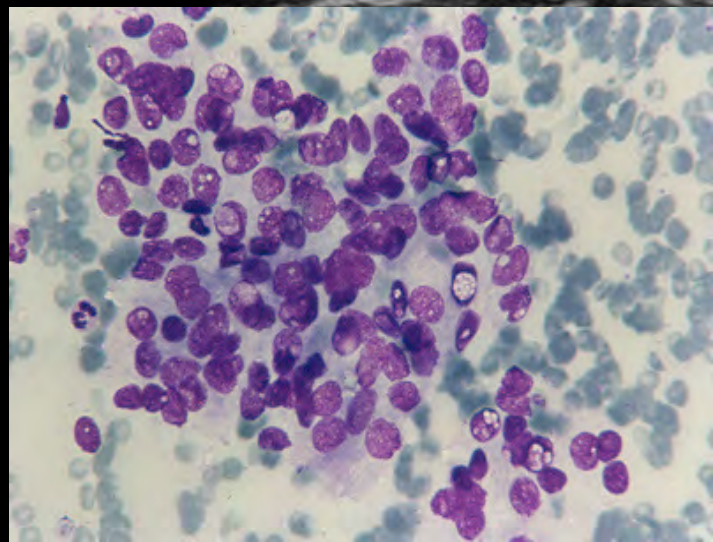
The most sensitive tool for detecting neck lymph node metastases.

Benign lymph nodes are frequent, and specificity should be improved by:

- – Careful definition of US criteria of suspicion
- – FNA: cytology + Tg in the aspirate fluid

Strongly recommended





SERUM Tg DETERMINATION

- Serum Tg is a marker of disease (Van Herle, 1975), not a disease
- Measurement:
  - Immunometric assay (IMA)
  - Standardization: CRM-457
  - Functional sensitivity < 1ng/mL. Supersensitive methods (<0.1ng/mL): improved sensitivity but decreased specificity.
  - Search for interferences:
    - Measurement of anti-Tg antibodies.

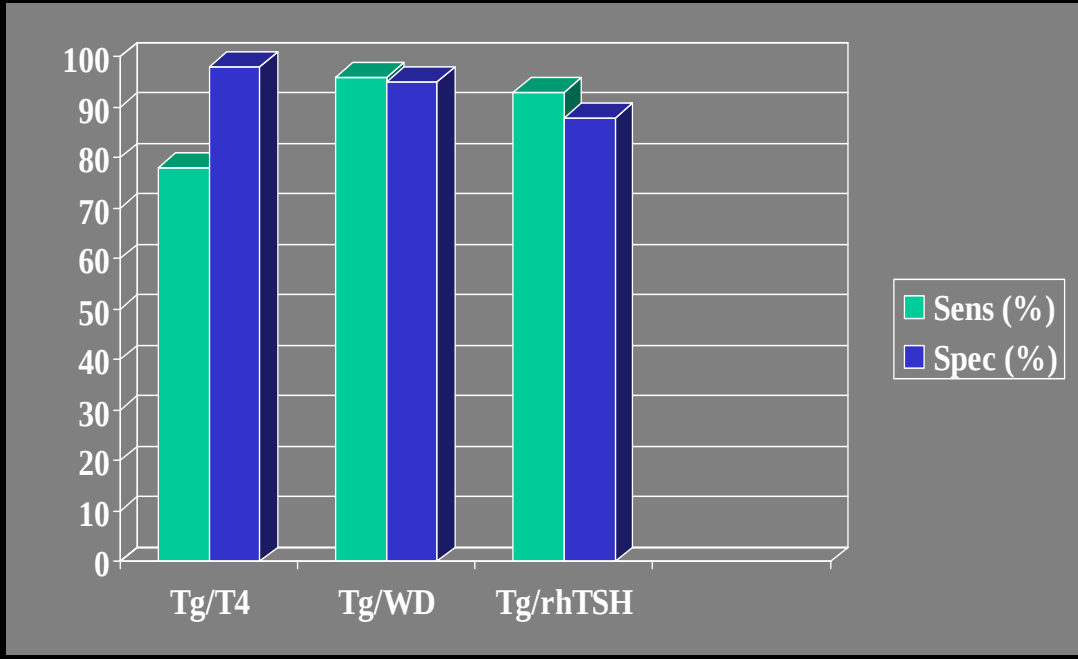
USE OF rhTSH.

- The benefits in terms of QOL of rhTSH over withdrawal are obvious.
- Is the sensitivity of serum Tg similar following rhTSH and withdrawal?

DETECTABLE Tg LEVEL AFTER THYROID ABLATION.

Eustatia-Rutten, Clin Endocrinol, 61: 61, 2004

The sensitivity of serum Tg determination is improved by 15-20% following TSH stimulation.



SIGNIFICANCE OF DETECTABLE Tg/TSH AT 1 YEAR

	Hauge n2002	Mazzaferri 2002	Robbins 2002	Torlontano 2003	Pacini 2003	Baudin 2003
n	83	107	109	92	294	256
Tg/TSH <1 ng/ml (%)	83	81	83	85	85	86
No disease (%)	98	98	92	99	98	98
Tg/TSH >1 ng/ml(%)	17	19	17	15	15	14
Disease detected	6	8.4	8.2	3.3	7.8	3.5
Neck / Distant	4.8/1.2	3.7/4.7	4.6/3.7	3.3/0	6.1/1.7	1.9/1.6
NED	9.6	10.3	9.2	12	7.1	10.9

OUTCOME OF LOW RISK PATIENTS WITH Tg ≤ 1ng/mL FOLLOWING THYROID HORMONE WITHDRAWAL

- 219 patients
- Mean follow-up: 10 years
- Neck lymph node recurrence at US: **1 (<0.5%).**
- TSH in the normal range (0.5-2.5 µU/mL) in > 90%.
- Cailleux, JCEM, 2000

- 315 patients
- Mean follow-up: 12 years
- Neck lymph node recurrence at US: **2 (0.6%).**
- Pacini, JCEM, 2002.

Excellent NPV of Tg/TSH
Diagnostic 131-I WBS useless

DETECTION OF NECK RECURRENCES

STUDY INFORMATION:

Reference	Pacini	Frasoldati	Torlontano
N_1/Pts	27/340	51/494	38/456

METHOD:

Tg/TSH	85% (rhTSH)	57% (WD)	82% (WD)
^{131}I TBS	21%	45%	34%
Neck US	70%	94%	100%
Neck US+Tg/TSH	96%	99.5%	100%

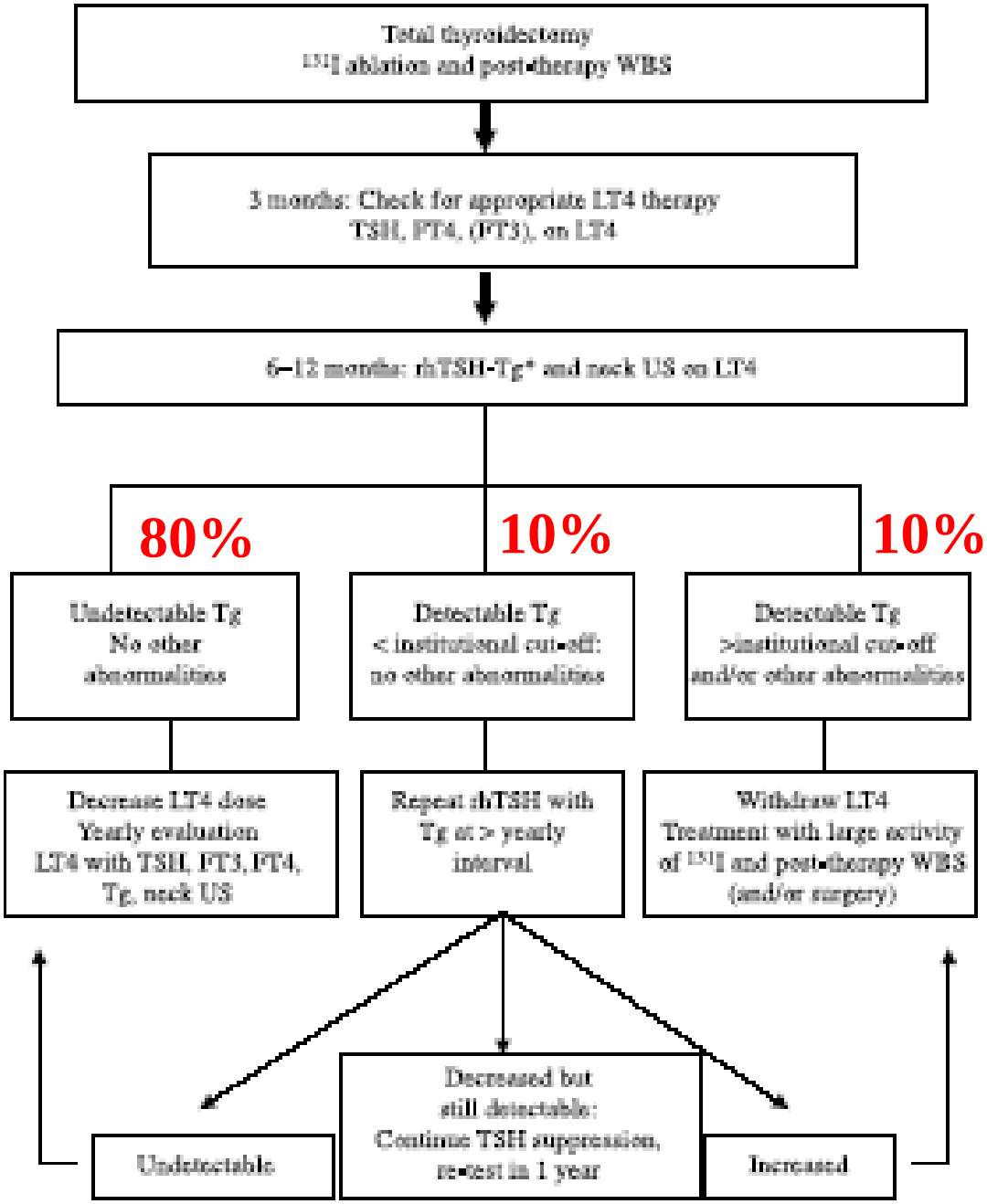
Combination of neck US and Tg/TSH determination.

LOW RISK PATIENTS: UNDETECTABLE SERUM stimulated Tg AT 8-12 MONTHS

- False negative results are rare (excellent NPV)
- LT4 dose can be decreased to achieve a low-normal serum TSH level (0.5-2.5 µU/mL)
- Patients are followed up on a yearly basis on replacement L-T4 treatment.
- In the absence of abnormalities, no other testing is warranted.
- The need for another TSH stimulation test needs further studies.

Patients with positive anti-Tg antibodies

- Serum Tg unreliable if undetectable
- Follow the changes in anti-Tg antibodies
- Neck Ultrasound
- Diagnosic WBS may be informative


Total thyroidectomy
^{131}I ablation and post-therapy WBS
3 months: Check for appropriate LT4 therapy
TSH, FT4, (FT3), on LT4
6–12 months: rhTSH-Tg* and neck US on LT4
80%
10%
10%
Undetectable Tg
No other abnormalities
Detectable Tg
< institutional cut-off:
no other abnormalities
Detectable Tg
>institutional cut-off
and/or other abnormalities
Decrease LT4 dose
Yearly evaluation
LT4 with TSH, FT3, FT4,
Tg, neck US
Repeat rhTSH with
Tg at > yearly
interval
Withdraw LT4
Treatment with large activity
of ^{131}I and post-therapy WBS
(and/or surgery)
Undetectable
Decreased but
still detectable:
Continue TSH suppression,
re-test in 1 year
Increased

"A consensus report of the role of serum thyroglobulin as a monitoring method for low-risk patients with papillary thyroid carcinoma"

Mazzaferri EL, Robbins RJ, Spencer CA, Braverman LE, Pacini F, Wartofsky L, Haugen BR, Sherman SI, Cooper DS, et al.

J Clin Endocrinol Metab, 2003, 88: 1433-2003

"Follow up of low risk patients with differentiated thyroid carcinoma: an European prospective"

Schlumberger M, Berg G, Cohen O, Duntas I, Jamar F, Jarzab B, Limbert E, Lind P, Pacini F, Reiners C, Sanches Franco F, Toft A, Wiersinga WM

European Journal of Endocrinology, 2004, 150: 105-112

CONCLUSIONS

- Follow up based on neck US and Tg/TSH
- Routine control ^{131}I-TBS in most patients can be avoided: low uptake in the thyroid bed: no relevance
- Use of rhTSH improves the QOL and does not decrease the quality of follow up
- No interest of other scintigraphy markers
- FDG PET scanning in selected patients

- *Shift from suppressive to replacement therapy as soon as your patient is defined as complete remission*