



Mariano Provencio

Servicio de Oncología Médica

Hospital Universitario Puerta de Hierro

Estadificación del cáncer de pulmón

Agenda

- Estadificación
 - Orientación al diagnóstico
 - Histología
 - Novedades
 - Métodos de diagnóstico
 - Especialmente ... PET
 - TNM
-
- Estadificación: piedra angular

Cáncer de pulmón

Métodos diagnósticos

Confirmación

- Citología de esputo
 - La rentabilidad depende del tipo histológico, tamaño y localización
 - Mejor “calidad”: 3 muestras de expectoración matinal
 - Sensibilidad del 69%
 - Especificidad del 96%
 - Correlación citológica e histología:
 - 96% en SCLC
 - 95,3% para ca epidermíode
 - 87,8% para adenocarcinoma
 - 81,4% para ca de células grandes

Cáncer de pulmón

Métodos diagnósticos

Sugieren la existencia del tumor

- Rx de tórax, proyecciones PA y L.,
- TAC de tórax y hemiabdomen superior

Confirmación

- Citología de esputo
- Broncoscopia con biopsia
 - Después de TAC
 - 90% de éxito si combinada con citología
 - 60% si lesiones periféricas de < 2 cm
- Biopsia trans-bronquial
- PAAF trans torácica de lesiones pulmonares
- Mediastinoscopia con biopsia

Cáncer de pulmón

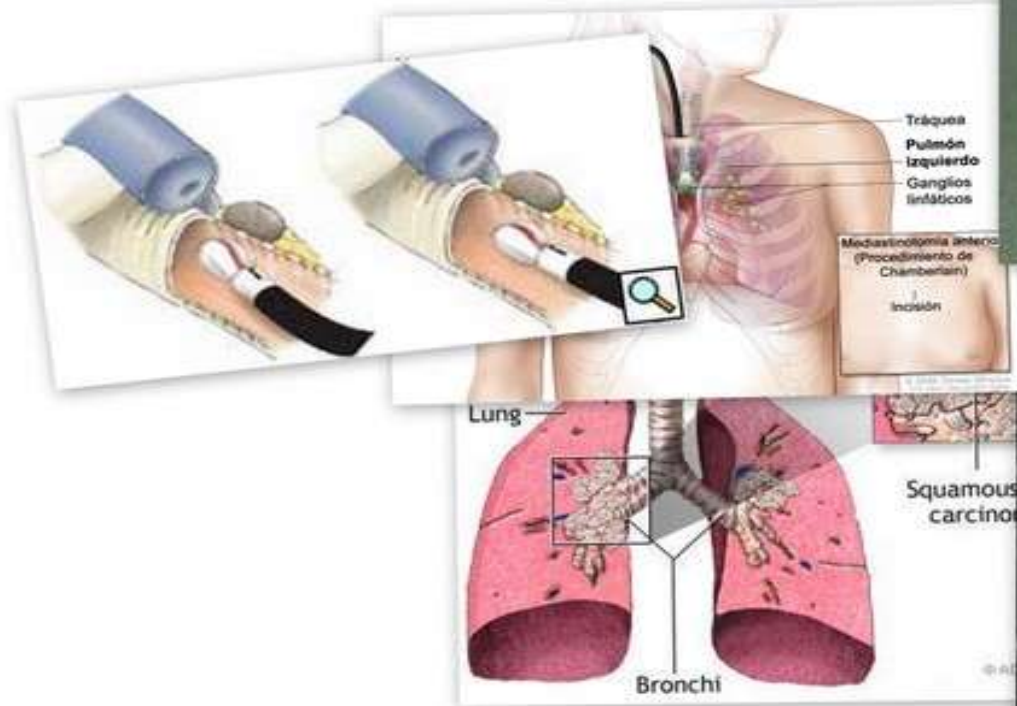
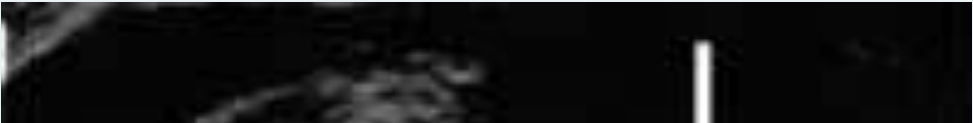
Métodos diagnósticos

Sugieren la existencia del tumor

- Rx de tórax, proyecciones PA y L,.
- TAC de tórax y hemiabdomen superior

Confirmación

- Citología de esputo
- Broncoscopia con biopsia
- Biopsia trans-bronquial
 - Éxito en 79-95%
- PAAF trans torácica de lesiones pulmonares
 - Sensibilidad del 95-100%
 - Complicaciones: neumotórax en el 15%
- Mediastinoscopia con biopsia
 - No más del 3% se debe llegar a otras pruebas o no dx previo cirugía



Mariano Provencio

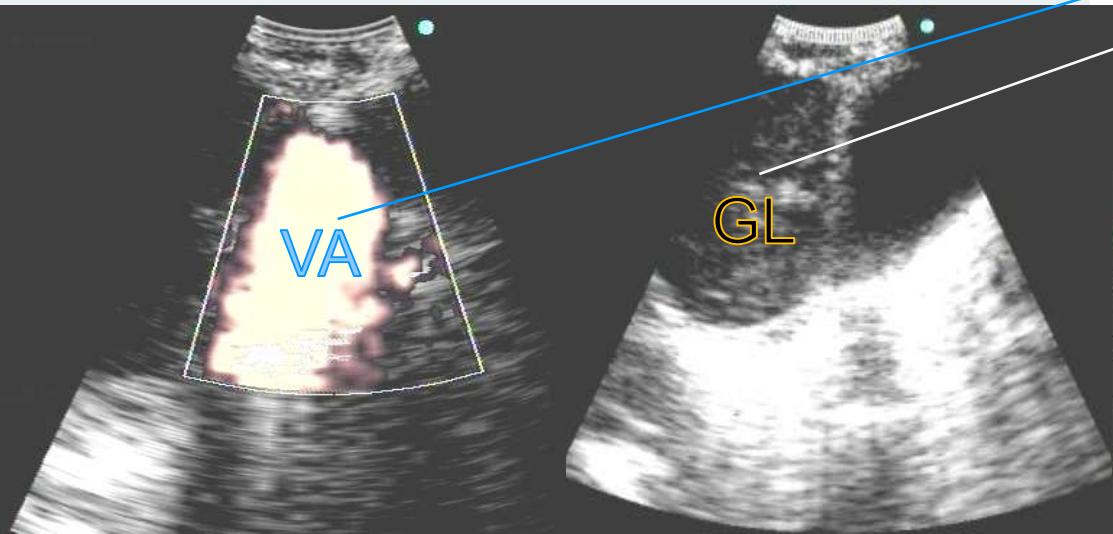
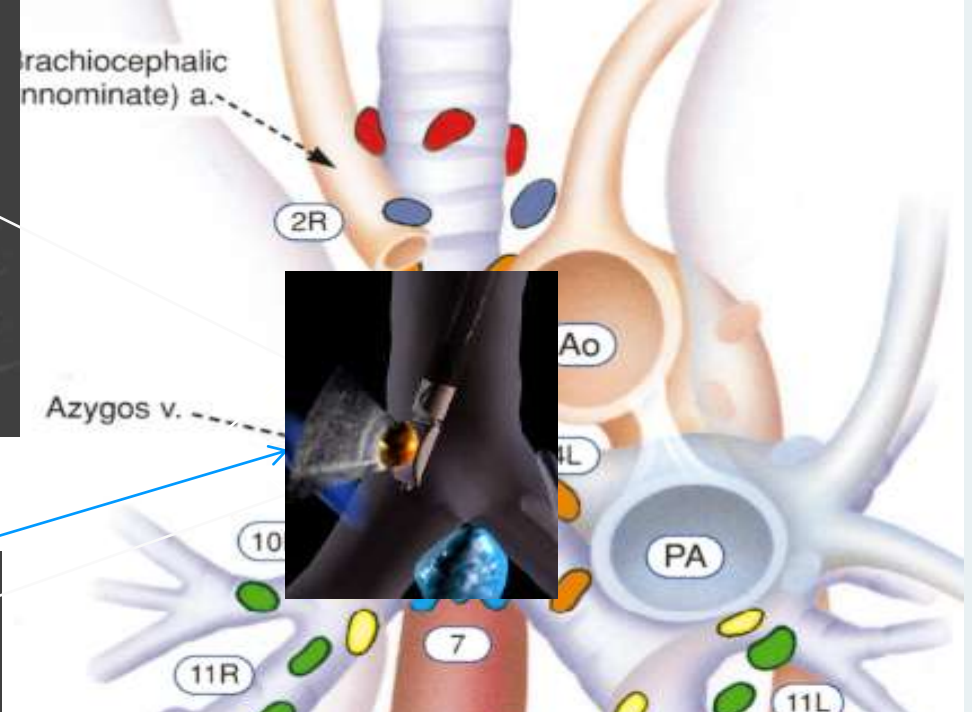
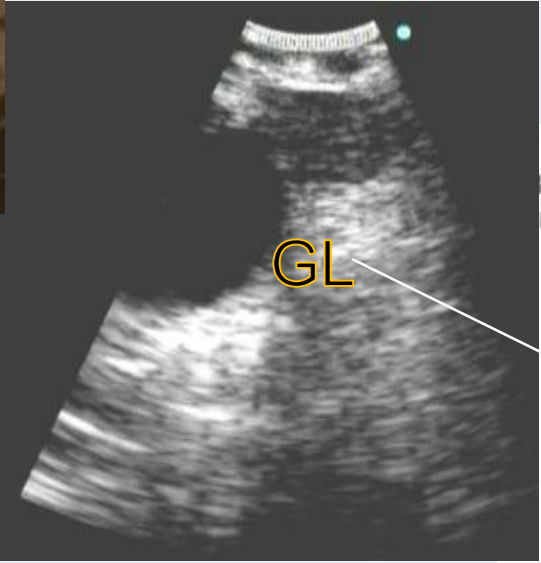
Punción TB ciega en estadificación CPNM

Study	Year	No.	Stage	Prev	Sens	Spec ^a	PPV ^a	NPV
Fernandez-Villar ²⁷⁷	2010	280	cN1-3	...	68	(100) ^a	(100) ^a	10
Utz ²⁹⁴	1993	61	cN0/N2	100	56	(100) ^a	(100) ^a	...
Selcuk ²⁹¹	2003	26	cN2-3	100	100	(100) ^a	(100) ^a	...
Wilsher ²⁹⁸	1996	24	cN2-3	96	90	(100) ^a	(100) ^a	...
Katis ²⁷⁹	1998	76	cN2-3	95	74	(100) ^a	(100) ^a	(20) ^b
Bilaceroglu ²⁷³	1998	134	cN1-3	88	75	(100) ^a	(100) ^a	(36) ^b
Melloni ²⁸²	2009	51	cN2-3	88	76	(100) ^a	(100) ^a	(33) ^b
Shannon ²⁹³	1996	24	cN2-3	88	90	(100) ^a	(100) ^a	(60) ^b
Stratakos ²⁹⁴	2008	77	cN1-3	86	88	(100) ^a	(100) ^a	(58) ^b
Schenk ²⁸⁸	1993	64	cN2-3	86	56	(100) ^a	(100) ^a	(82) ^b
Wang ²⁹⁷	1983	39	cN2-3	86	76	(100) ^a	(100) ^a	(71) ^b
Schenk ²⁹⁰	1989	29	cN2-3	86	80	(100) ^a	(100) ^a	(44) ^b
Medford ²⁸¹	2010	79	cN2-3	84	79	(100) ^a	(100) ^a	(58) ^b
Mak ²⁸⁰	2004	24	cN1-3	83	60	(100) ^a	(100) ^a	(33) ^b
Vansteenkiste ²⁷⁶	1994	80	cN2	79	79	(100) ^a	(100) ^a	55
Rodriguez de castro ²⁸⁶	1997	80	cN2-3	78	66	(100) ^a	(100) ^a	45
Harrow ²⁷⁸	2000	264	cN1-3	72	93	99	99	80
Shah ²⁹²	2006	129	cN1-3	71	68	(100) ^a	(100) ^a	56
Rodriguez de castro ²⁷⁵	1995	56	cN2-3	70	77	(100) ^a	(100) ^a	70
Patelli ²⁸³	2002	182	cN2	67	98	(100) ^a	(100) ^a	83
Rong ²⁸⁷	1998	49	cN1-3	66	100	(100) ^a	(100) ^a	100
Rakha ²⁸⁴	2010	182	cN1-3	57	84	(100) ^a	(100) ^a	70
Garpestad ²⁷⁴	2001	32	cN1-3	57	83	(100) ^a	(100) ^a	67
Schenk ²⁸⁹	1986	88	cN2-3	39	50	96	89	75
Bernasconi ¹⁷⁶	2006	113	cN2-3	31	54	(100) ^a	(100) ^a	91
Wallace ²⁹⁶	2008	138	cN2-3	30	36	(100) ^a	(100) ^a	78
Ratto ²⁸⁵	1988	47	cN2	30	14	(100) ^a	(100) ^a	73
Summary: median		2,408		81	78	(100)^a	(100)^a	77

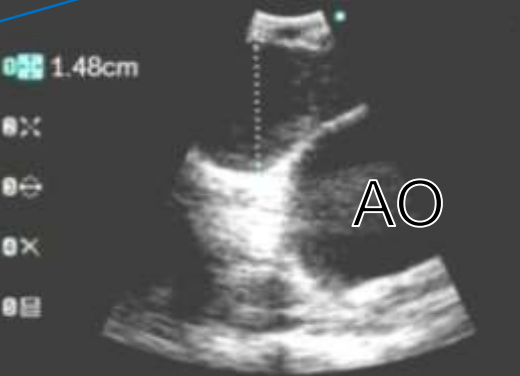
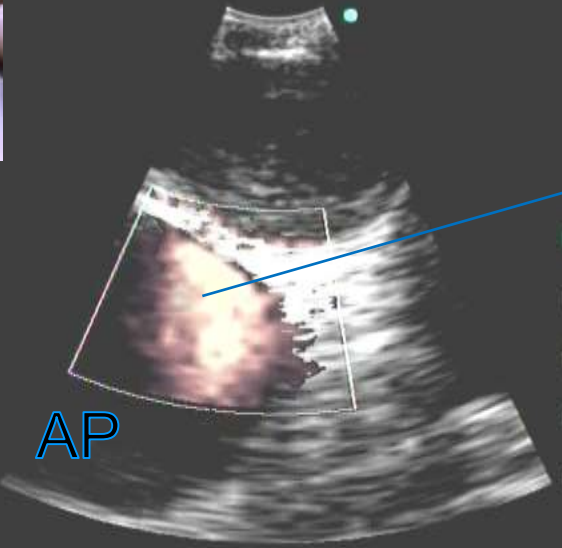
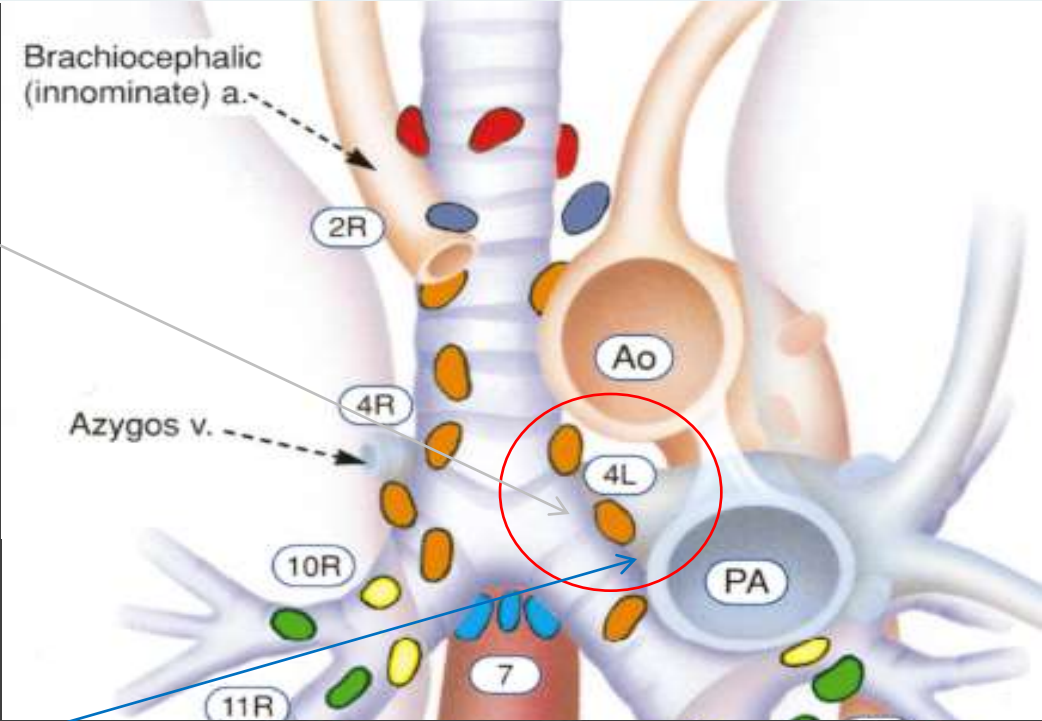
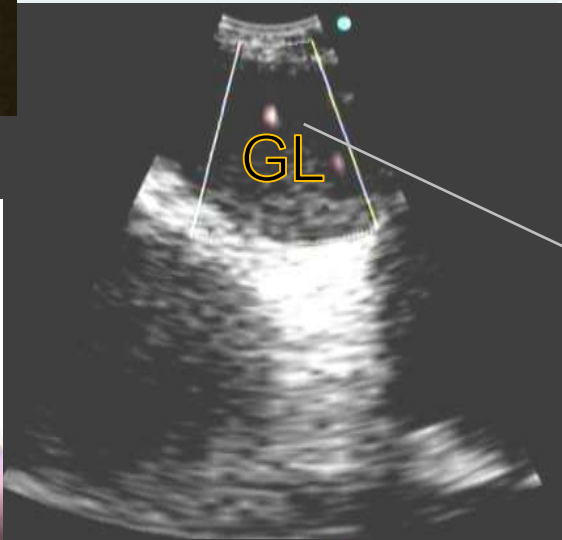
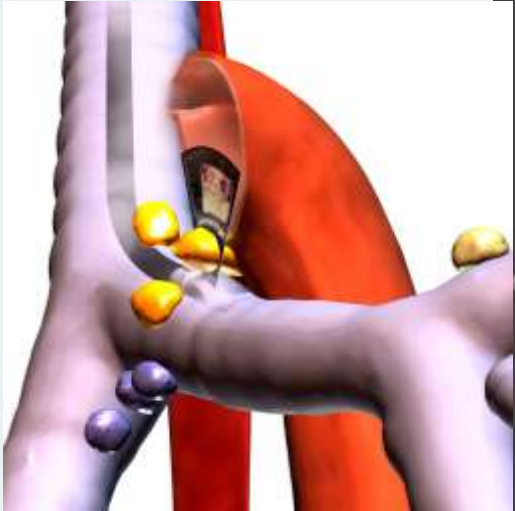
- Dependiente de explorador y tamaño de la adenopatía
- Limitaciones acceso a determinadas estaciones
- Validez y seguridad insuficiente
- Muestras limitadas



4R



4L

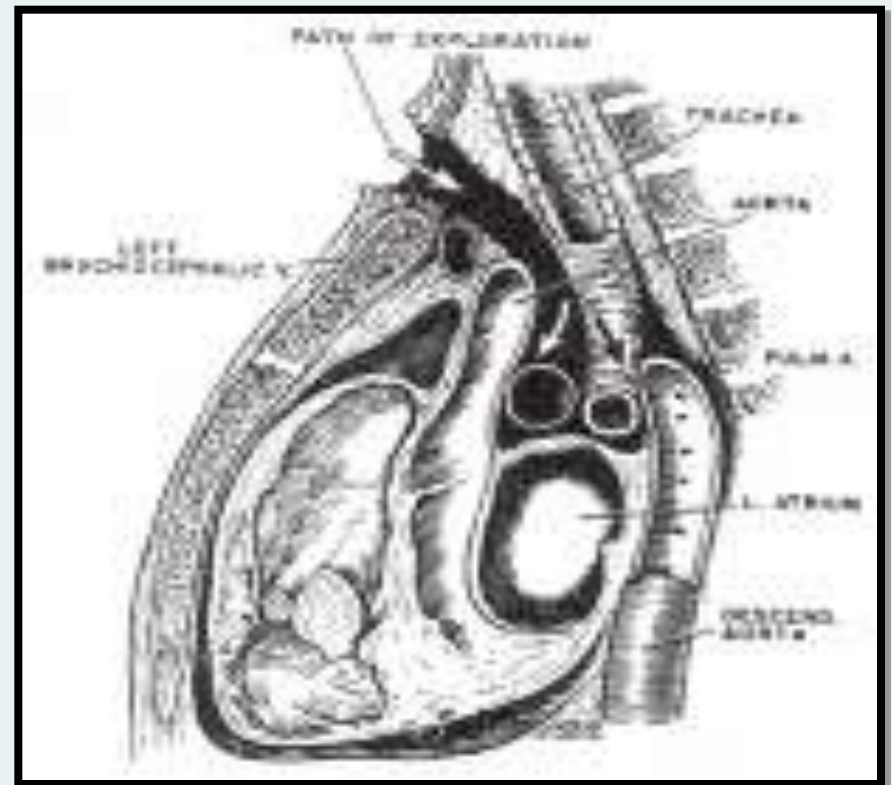
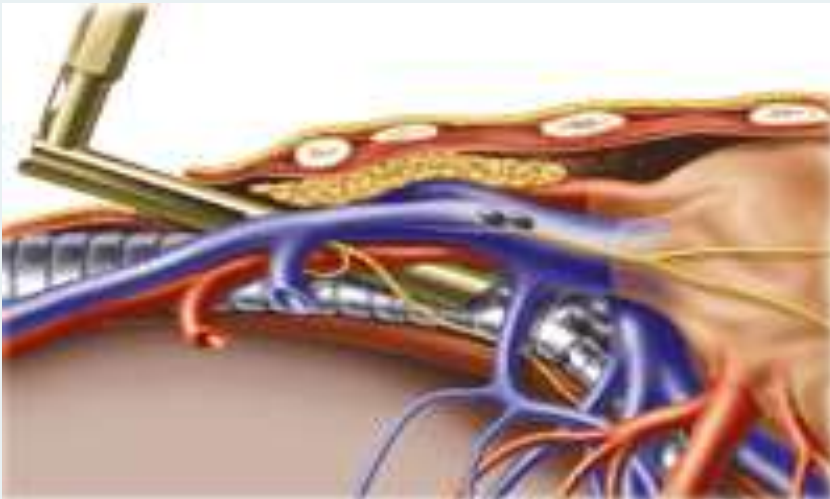


Estadificación invasiva

- **La punción-aspiración transbronquial** positiva en el 90% de las subcarinales
- **Mediastinoscopia cervical:** adenopatías paratraqueales derechas e izquierdas, altas y bajas, así como las subcarinales anteriores; la sensibilidad global es del 81%
- **Mediastinoscopia cervical extendida** (mediastinotomía paraesternal): adenopatías de la ventana aorto-pulmonar y prevasculares con sensibilidades globales cercanas al 50 y 70%, respectivamente

Abordajes

- Mediastinoscopia Cervical Estándar
 - Carlens en 1959.
 - SUPRAESTERNAL 3 cm
 - Plano de disección digital. Pretraqueal ,paratraqueal, subcarinal
 - S 80%, E 90%,



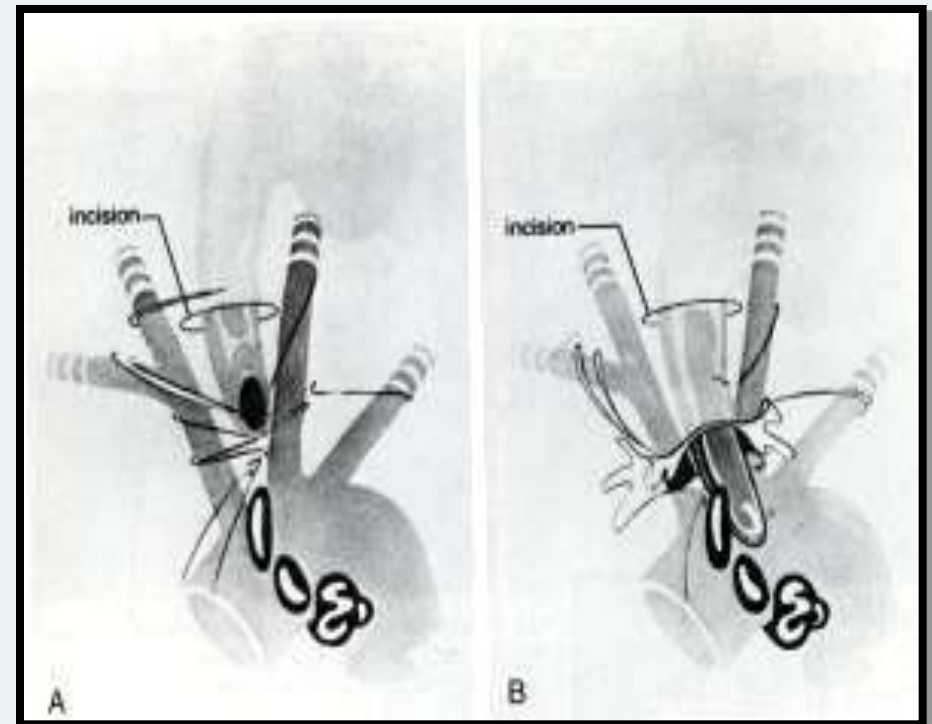
Mediastinoscopia Cervical Extendida

Disección entre la arteria innominada y la carótida

El endoscopio por delante del arco aórtico



Ann Thorac Surg 2002;73:250-256
Curr Opin Pulm Med 2001;7:226-233



Para : Adenopatías ventana aorto-pulmonar, subaortica y paraorticos.

Mediastinoscopia infraesternal...

Kido 1999

No selectividad pulmonar.

Baja reserva pulmonar.

Tumores por debajo de Vena Innominate.

T 2-9 cm.

Visualiza ambas pleuras.

4 cm por debajo xifoides..

Permite realizacion extendida.

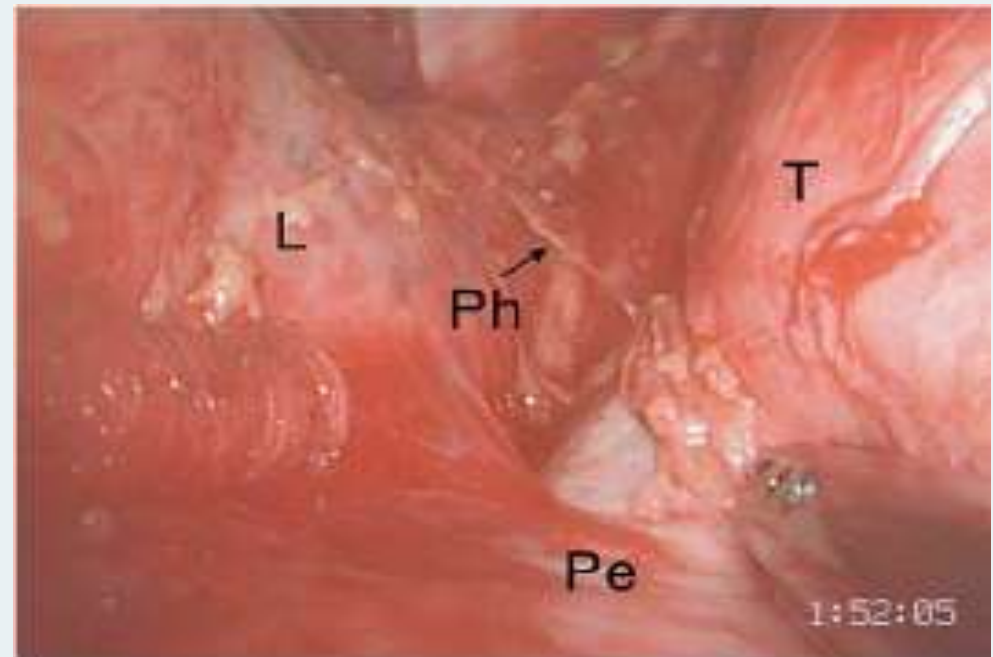
20 Ptes.

Tiempo qx 270 min.

Morbilidad 0%

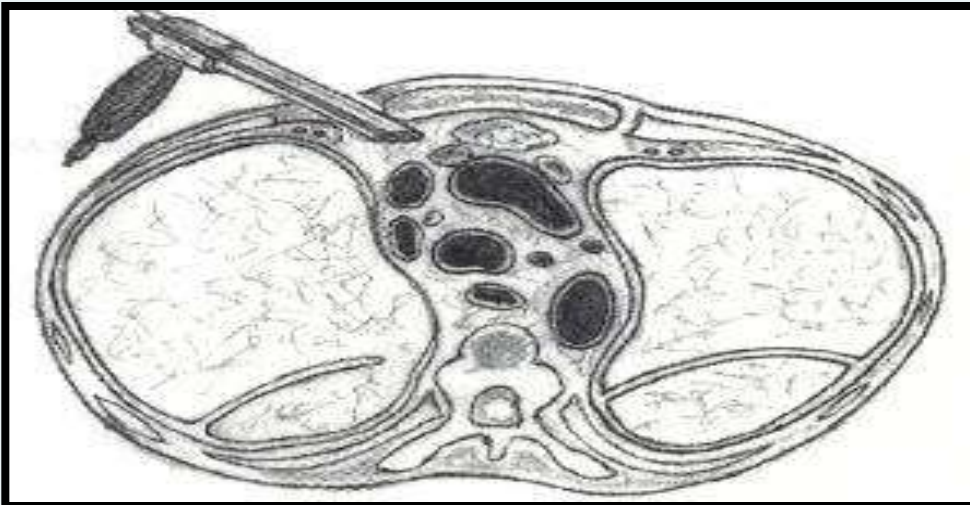
Conversion: 10%

Mortalidad 0.5%

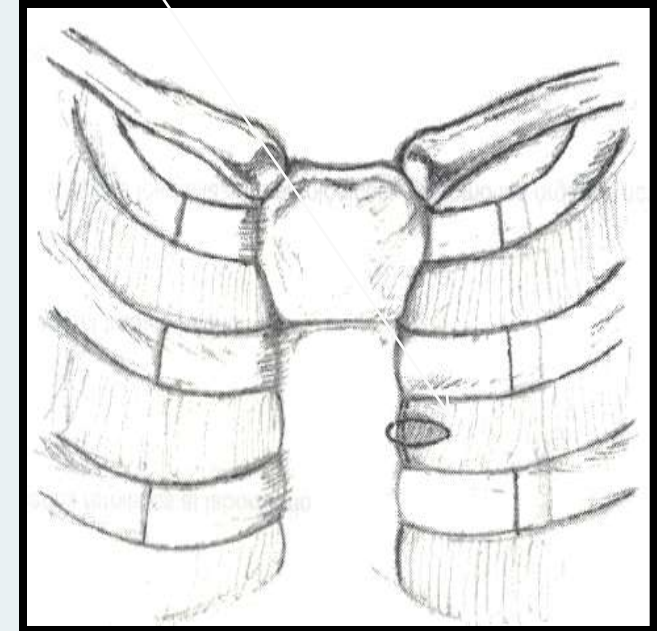


Abordaje Paraesternal

- Descrito en 1966 (Maxwell Chamberlain)
- Dos modalidades
 - Mediastinoscopio
 - Cielo abierto
 - anestesia local
 - Adenopatías parahiliares
 - Tumores por debajo del hilio pulmonar
 - Complemento de la mediastinoscopia



insición 2 do y 3er. EIC izq.



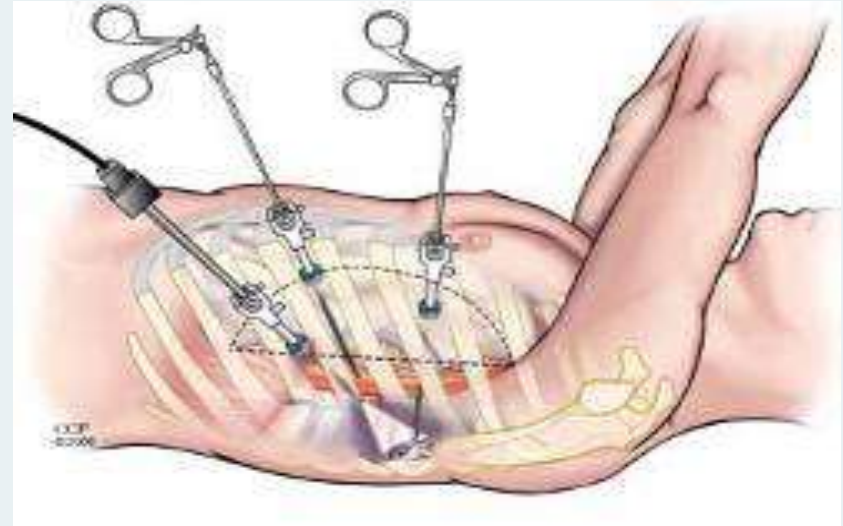
Toracoscopia video-asistida (VATS)

Diagnóstico y terapéutico

Diagnóstico definitivo 96%

■ Indicaciones

- Biopsia de ganglios
- Biopsia de TM
- Resección de T. pequeños
- Resección de quistes
- Información adicional: Invasión, carcinomatosis, derrame

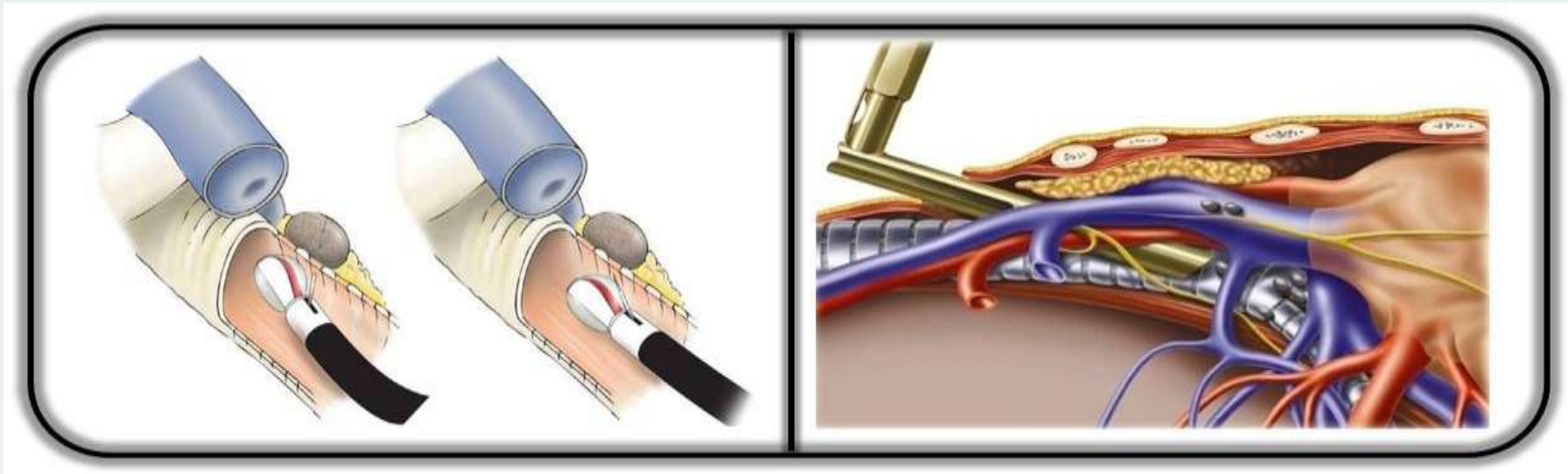


EBUS vs. Mediastinoscopia

Estudio	N	Sensibilidad		VPN		Prevalencia
		EBUS	MED.	EBUS	MED.	
Ernst*	66	87%	68%	78%	59%	89%
Yasufuku**	190	81%	79%	91%	90%	35%

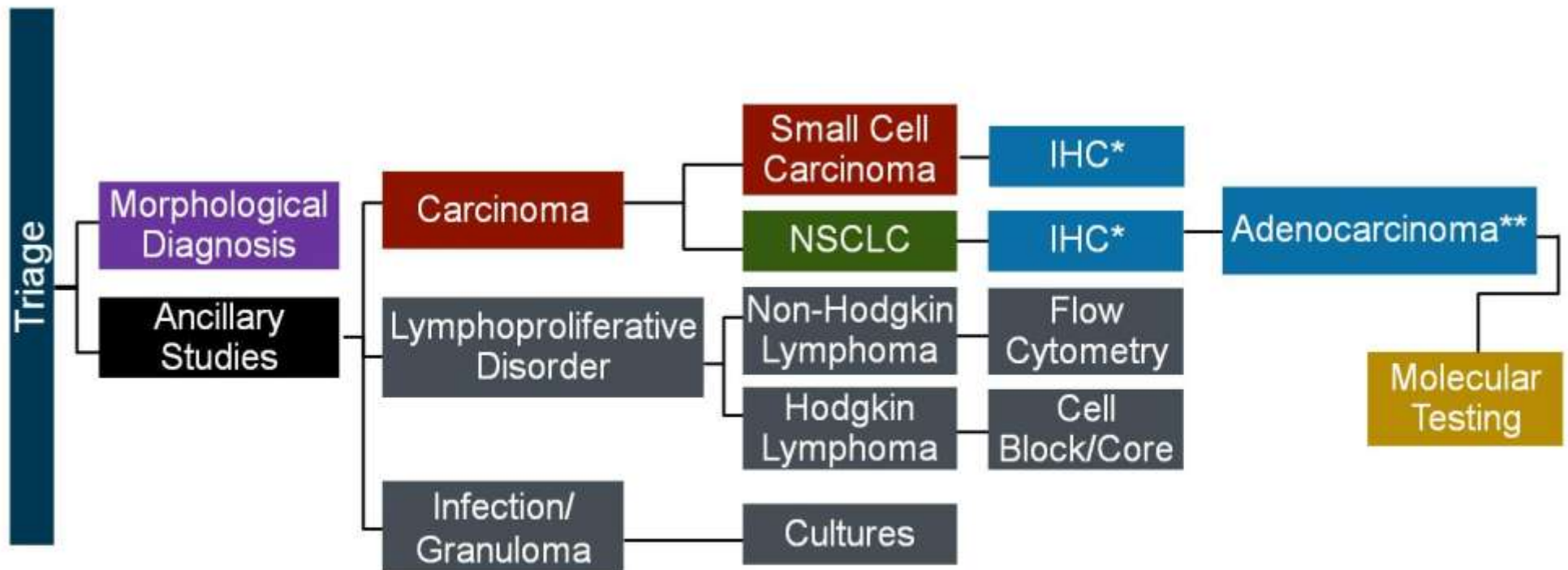
*Diferencias significativas

**Diferencias no significativas



Ernst A et, al. J Thorac Oncol 2008;3:577

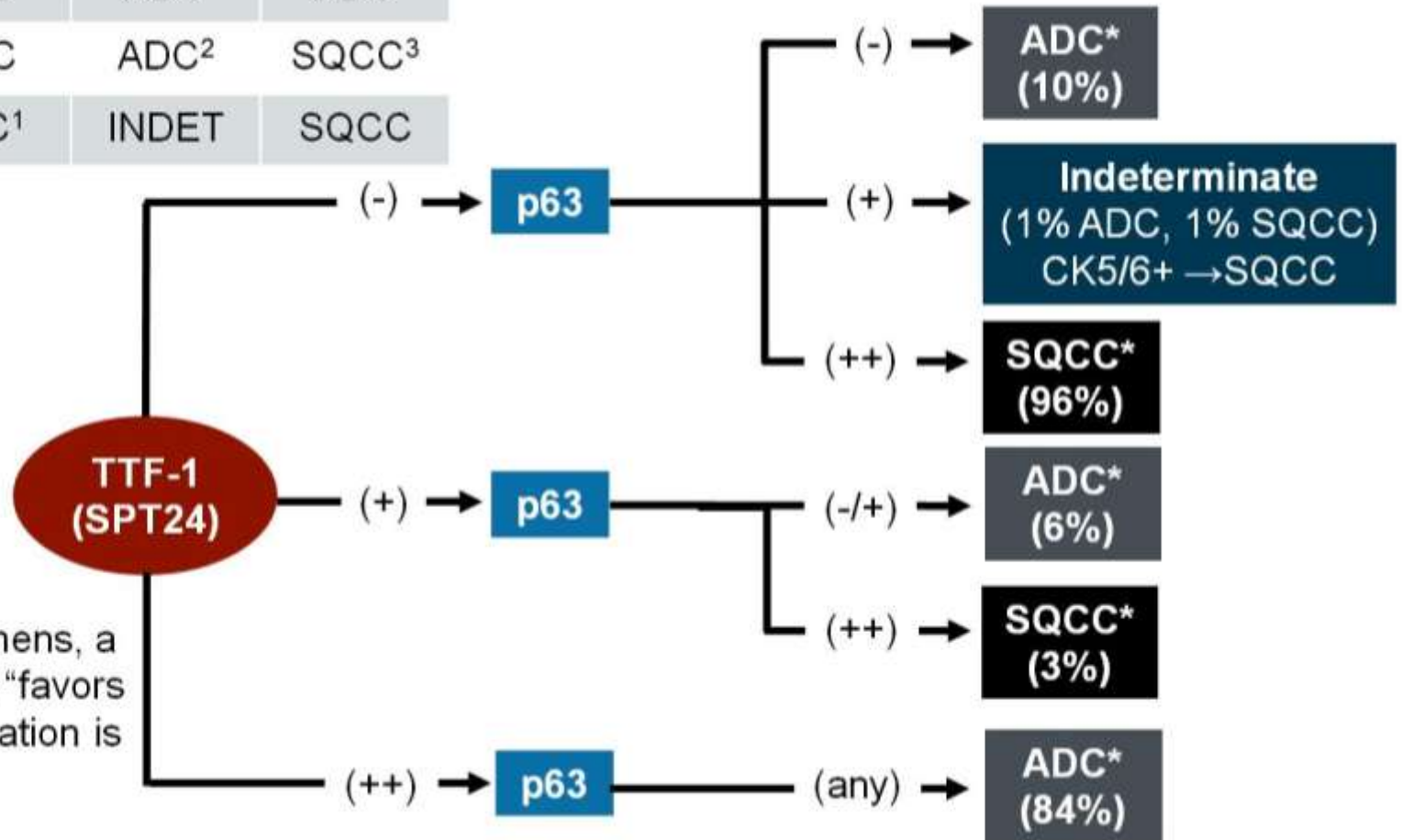
Yasufuku K, et al. J Thorac Cardiovasc Surg 2011;142:1393



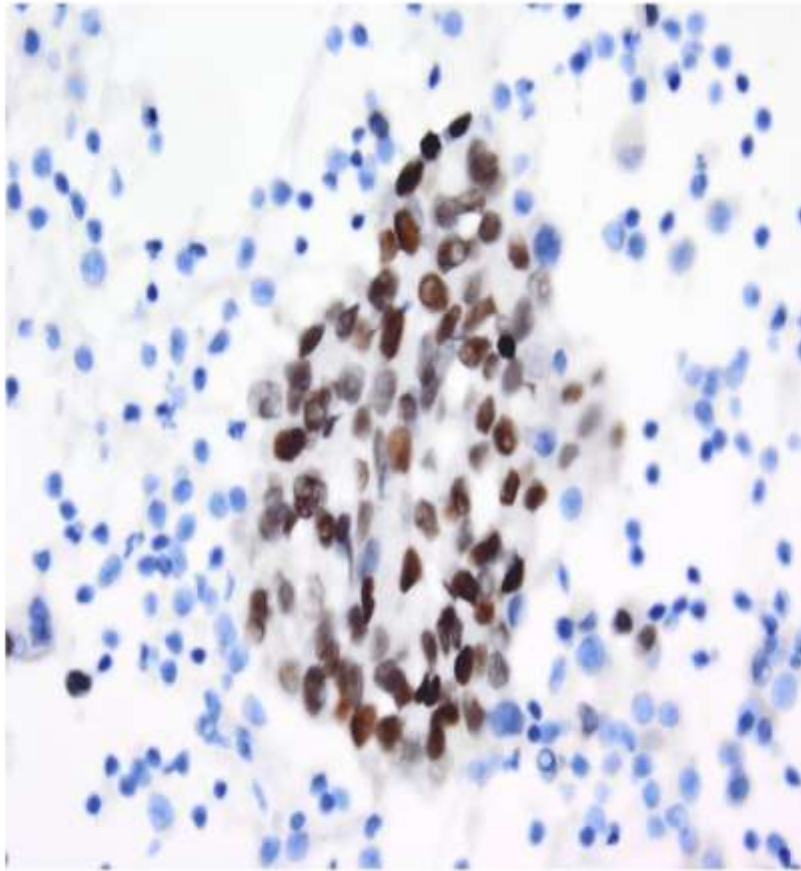
*Perform immunohistochemistry (IHC) to confirm diagnosis if necessary.

**Perform molecular testing on carcinomas with adenocarcinoma or when a component of adenocarcinoma cannot entirely be excluded.

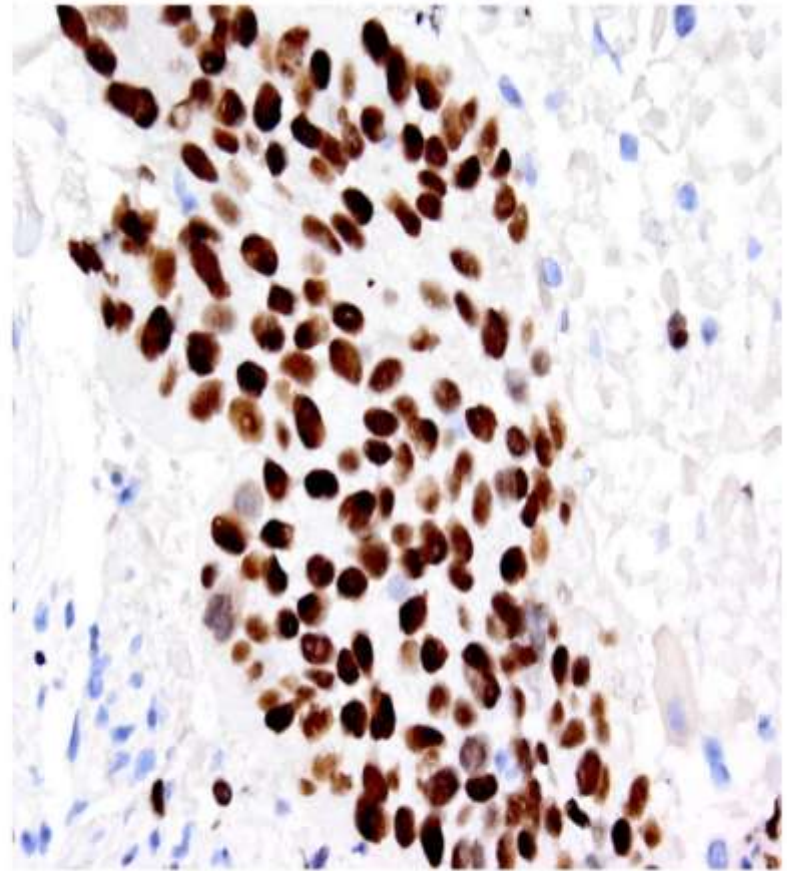
	p63-	p63+	p63++
TTF-1++	ADC	ADC	ADC
TTF-1+	ADC	ADC ²	SQCC ³
TTF-1-	ADC ¹	INDET	SQCC



*In small specimens, a "favors ADC" or "favors SQCC" classification is preferred.



NSCLC, favor ADC with
TTF-1-positive staining



NSCLC, favor SQCC with
p63-positive staining

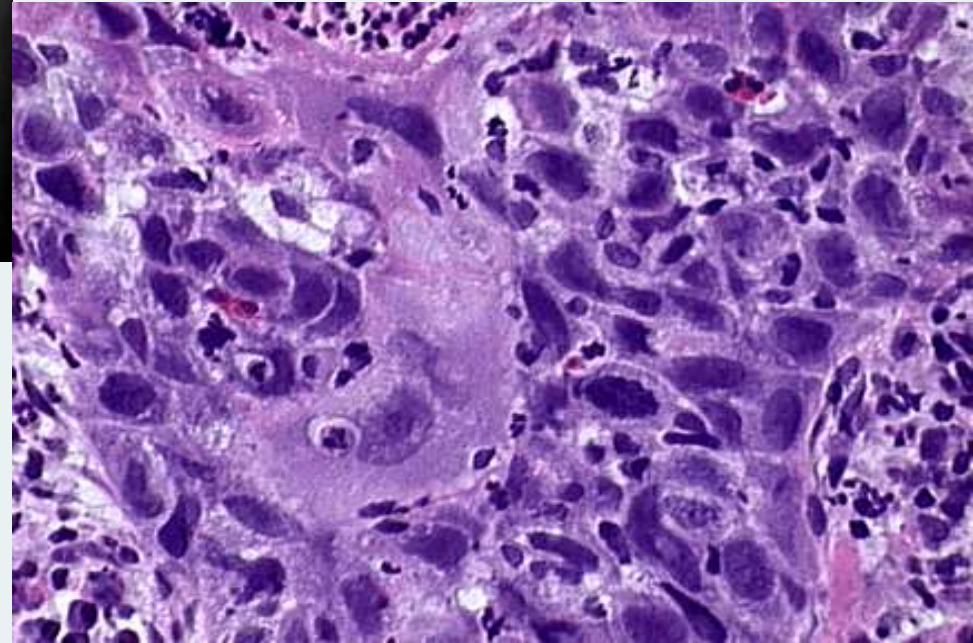
Carcinoma escamoso

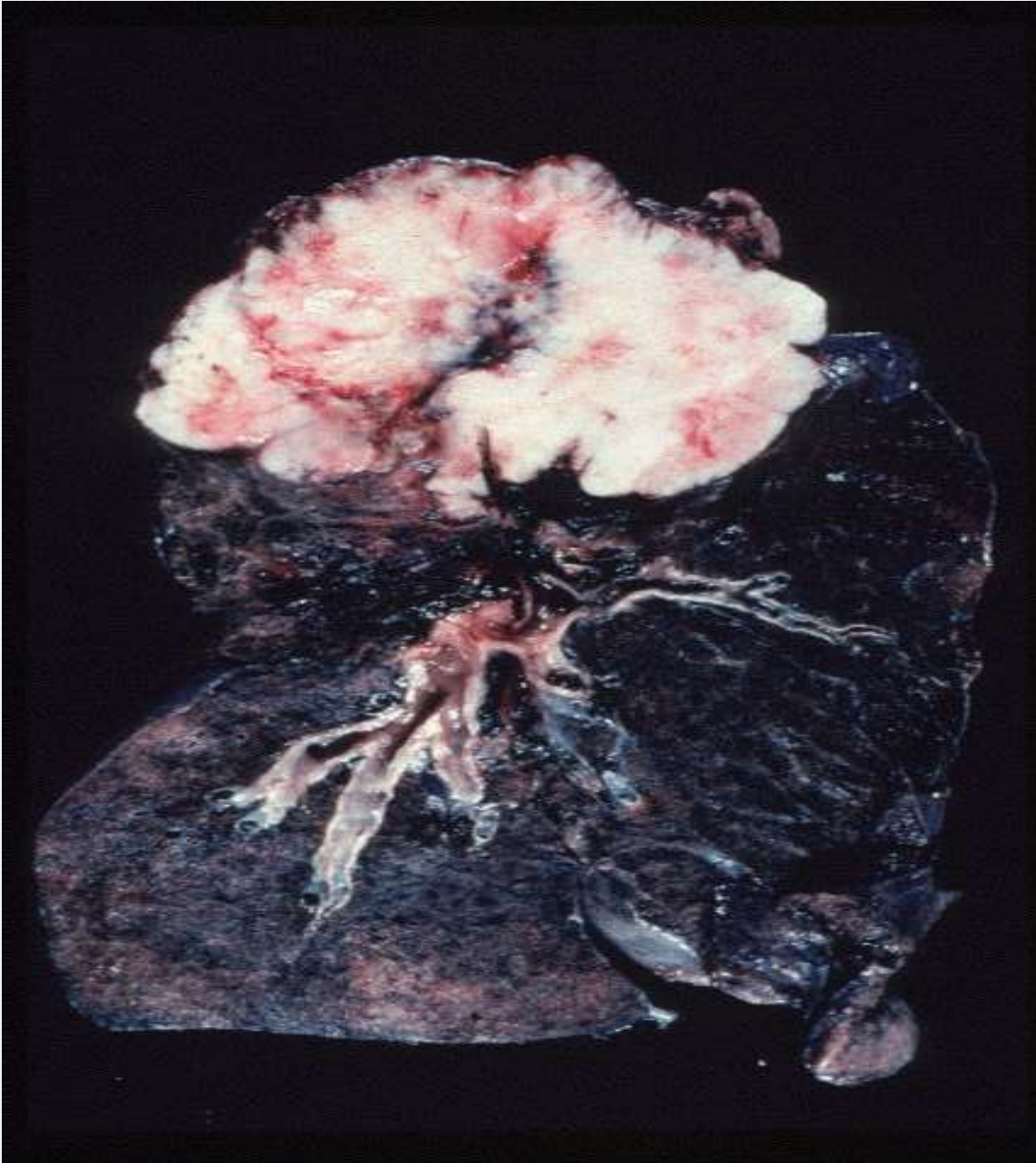


75% Central

P 63 +

CEA +





Adenocarcinoma

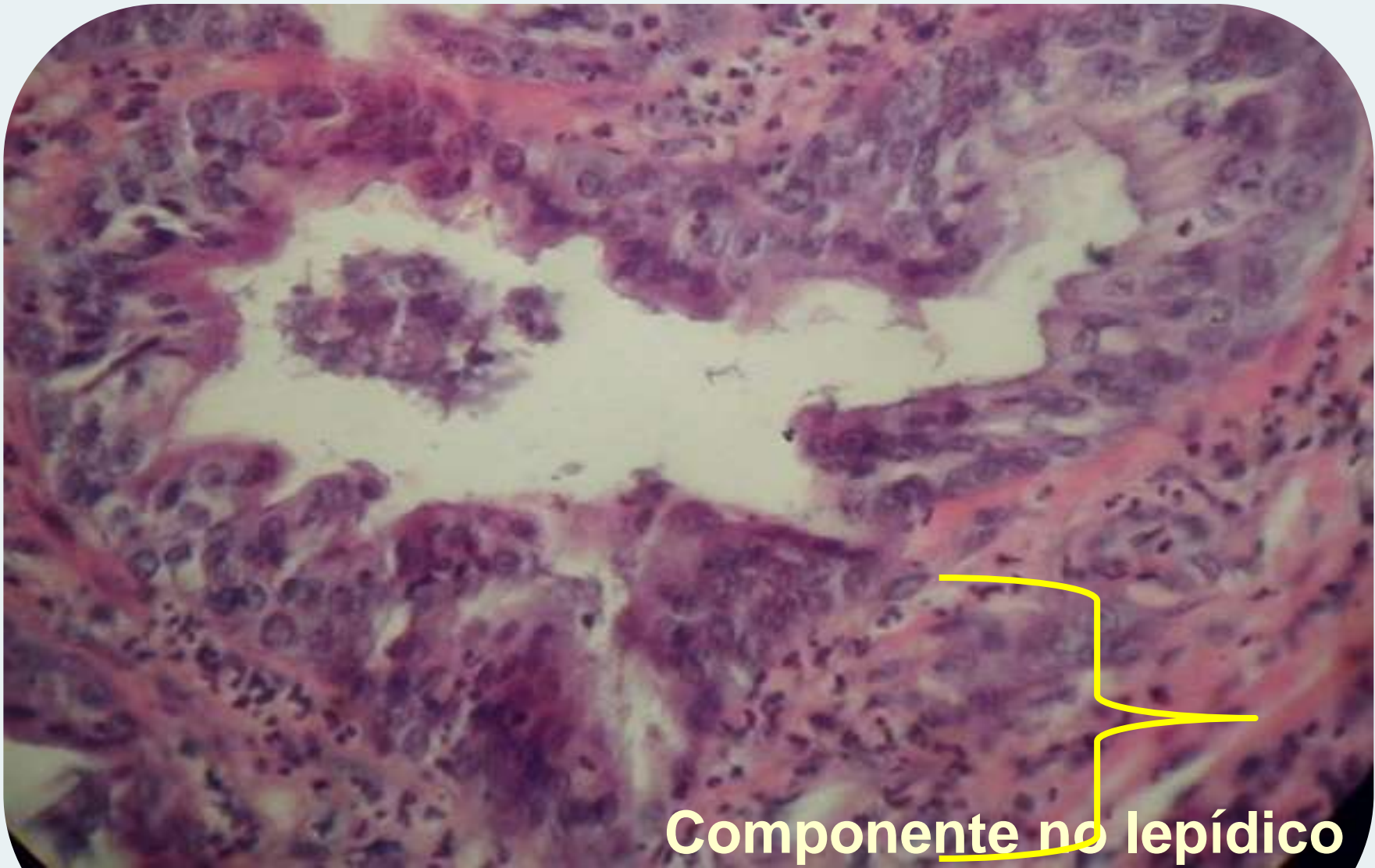
Más tamaño sin síntomas

Apariencia gris-blanquecina

No áreas de fibrosis

Sí fibrosis

Sí afectación pleural



Componente no lepidico

Estadificación

- TNM

Subgrupos de estadios TMN 2007 y supervivencia a los 5 años						
Cualquier T Cualquier N	IV (2%)					M1a
N3	IIIB (7%)					M1b
N2	IIIA (19%)				IIIB	M0
N1	IIA		IIB	IIIA	IIIA	
N0	IA (50-80%)	IB (47%)	IIA (36%)	IIB (26%)		
	T1a	T1b	T2a	T2b	T3	T4

Cambios en T:

T1a (< 2 cm), T1b (2-3 cm)

T2a (3-5 cm), T2b (5-7 cm)

T3 (> 7 cm)

T3 (nódulos en mismo lóbulo) (antes T4)

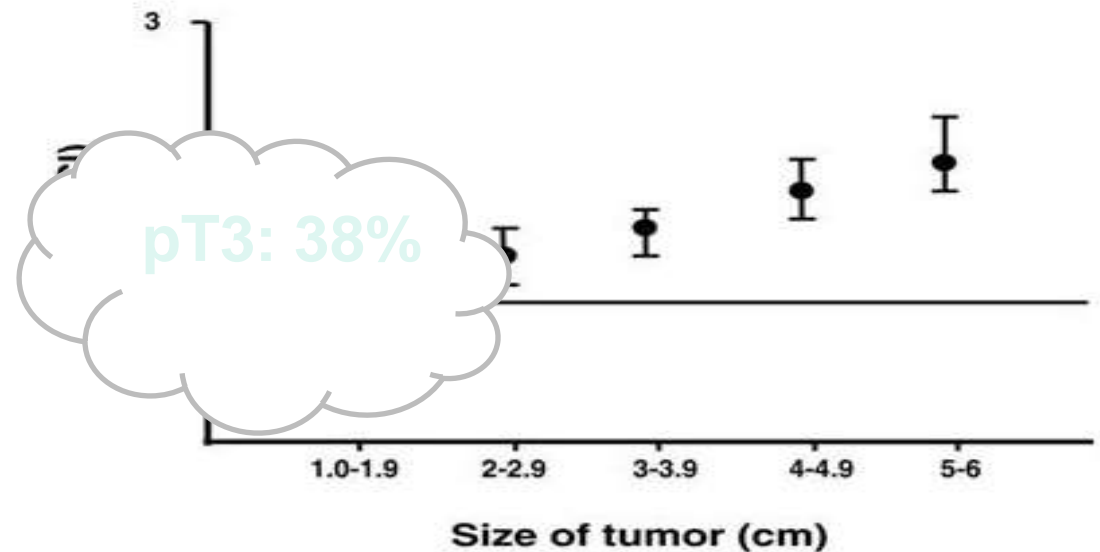
T4 (nódulos en distinto lobulo, ipsilateral) (antes M1)

No cambios en N

pT1-T2N0M0 (tamaño cm)	Supervivencia 5 años
≤2	77%
2-3	71%
3-5	58%
5-7	49%
➤7	35%

RR Death as a Function of Size

C.M. Mery, et al. Chest 28:3255, 2005



TNM, no es una tabla para aprender de memoria

T: dificultades para el T

- **T1 y T2 :**
 - suele valer por TC o endoscopia
 - La diferencia entre ambos, si se produce es intrascendente para tto
- **Entre cT3 y cT4 es muy importante**
 - Precisión para determinar la afectación mediastínica del TAC no muy buena (falsos positivos del 33%)
 - Si extensa afectación mediastínica (irresecable) no necesario confirmar esta afectación

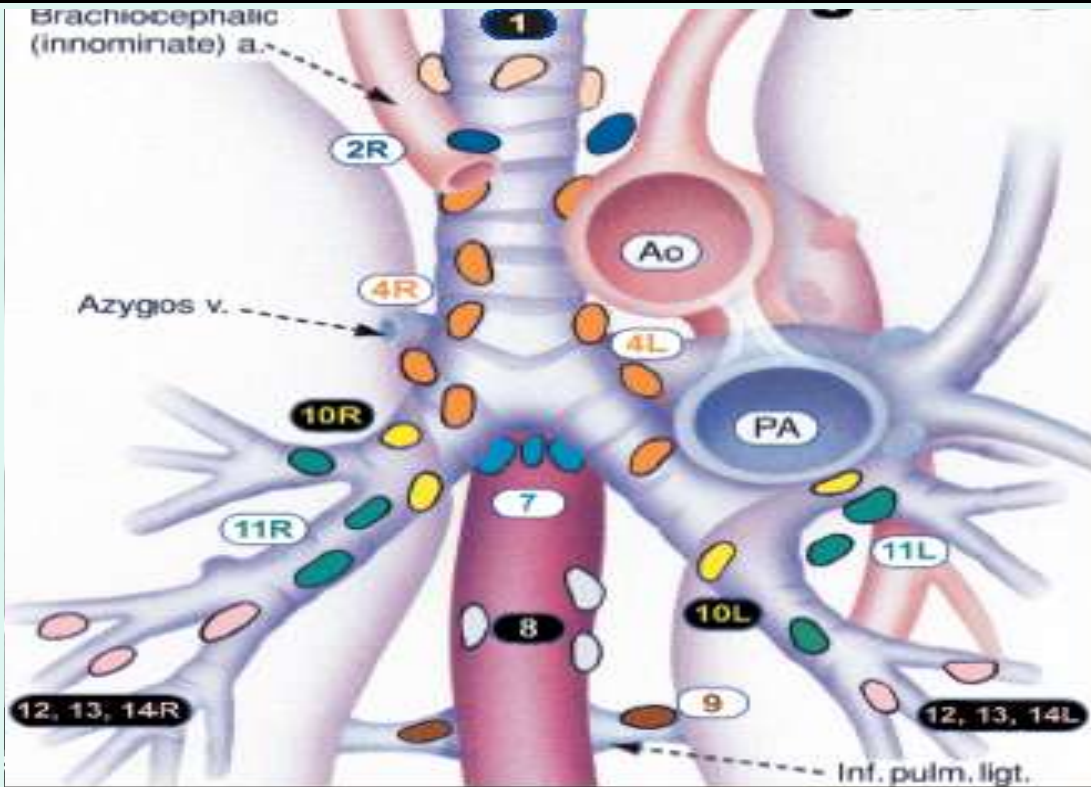
TNM, no es una tabla para aprender de memoria

- **T: dificultades para el T**
 - **Si Tumor de Pancoast**
 - MRI preferible a CT
 - Visualiza plexo y subclavia
 - Falso negativo: 6%, **falso positivo del 0% con MRI**
 - Falso negativo. 19%, **falso positivo del 19% con TAC**
- » **Goldstraw P, Lung Cancer 1994, 11: 1-4**

TNM, no es una tabla para aprender de memoria

- Factor N
 - Diámetro de 1 cm es el utilizado como límite
 - Con 1,5cm, el 50% son tumor
 - CT
 - Alto valor predictivo negativo para N
 - Entre 0,82 y 0,84
 - Bajo valor predictivo positivo
 - Entre 0,51-0,78
 - **El 18% de los pacientes considerados por criterios de TC como N² son realmente N⁰.**
 - **CONFIRMAR AP**

Diámetro ganglionar máximo Normal



<u>Región</u>	<u>Diámetro menor</u>
2R	7mm
2L	7mm
4R	10mm
4L	10mm
5	9mm
6	8mm
7	11mm
8R	10mm
8L	7mm
10R	10mm
10L	7mm

R= derecha
L= izquierda

A= anterior
P= posterior

PET Scan

- ▣ Staging:
 - ▣ Tumor
 - ▣ Locoregional lymph nodes
 - ▣ Extra thoracic Staging

- ▣ Impact on staging and management

PET staging: T factor

- ▣ Usually assessed by thoracic CT
 - ▣ Occasionally supplemented by magnetic resonance imaging:
 - ▣ Superior sulcus extension
 - ▣ Relationship with the heart or large vessels
 - ▣ **PET offers little** extra benefit
 - ▣ **T < 2 cm, 45% negative PET**
 - ▣ *Port JL. J Thorac Cardiovasc Surg 2005, Dec 1611.*
 - ▣ **PET may be more** beneficial in **evaluating** pleural effusions
 - ▣ Sensitivity: 89%; specificity: 94%; accuracy: **91%**
 - ▣ *Gupta NC. Chest 2002; 122: 1918-1924*
 - ▣ Primary tumor standardized uptake value measured on PET
 - ▣ Systematic review and meta-analysis. *J Thorac Oncol 5, 2010*

PET staging: N factor

(!!) Meta-analysis of PET and CT in mediastinal lymph node metastases

- ▣ Dwamena 1999
- ▣ Fisher 2001
- ▣ Hellwing 2001
- ▣ Bradbury 2002
- ▣ Toloza 2003
- ▣ Gould 2003
- ▣ Birim 2005
- ▣ Yang Y 2011

PET staging: N factor

- ▣ Methodological quality: Standards for reporting of diagnostic accuracy (STARD)
- ▣ Birim O *Ann Thorac Surg* 2005; 79:375-81
 - ▣ After search and exclusions (abstracts, duplications,...)
 - ▣ **49 potentially relevant studies**
 - ▣ 6 same patient population
 - ▣ 5 evaluated small cell lung cancer
 - ▣ 1 other tumors
 - ▣ 1 only patients with stage I
 - ▣ 1 reported nodal stations not number of patients
 - ▣ ...
 - ▣ **17 eligible studies**

PET staging: N factor

■ Birim O *Ann Thorac Surg*

■ Total number: 833 pts (18 to 102)

■ No age data in 11, gender only in 3, only 6 described differentiation between N2 N3,.....

■ **All patients underwent PET imaging**

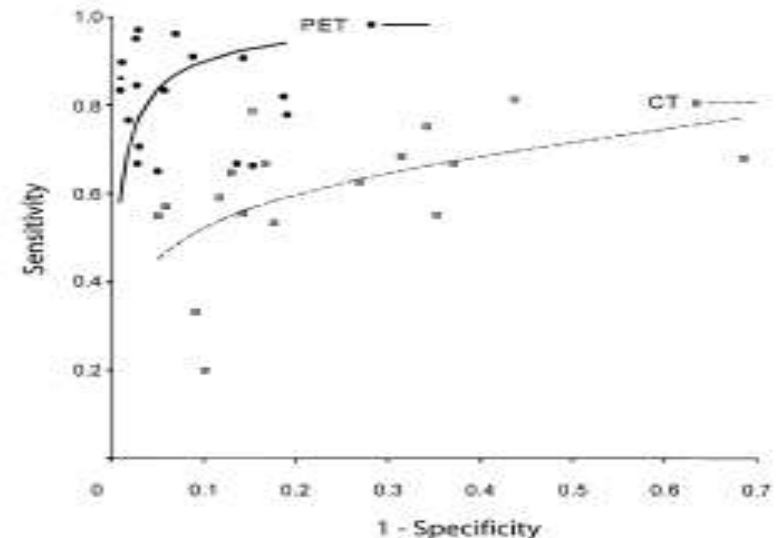
■ Diagnostic accuracy and meta-analysis

■ Sensitivity PET: 83% (95% CI, 77 to 89%)

■ Specificity PET: 81% (95% CI, 76 to 86%)

■ Sensitivity TAC: 59% (95% CI, 50 to 68%)

■ Specificity TAC: 78% (95% CI, 70 to 86%)



PET staging: N factor

- ▣ PET
 - ▣ High negative predictive value (94%)
 - ▣ Fails to identify microscopic N2 disease
 - ▣ Carcinoid, bronchioloalveolar

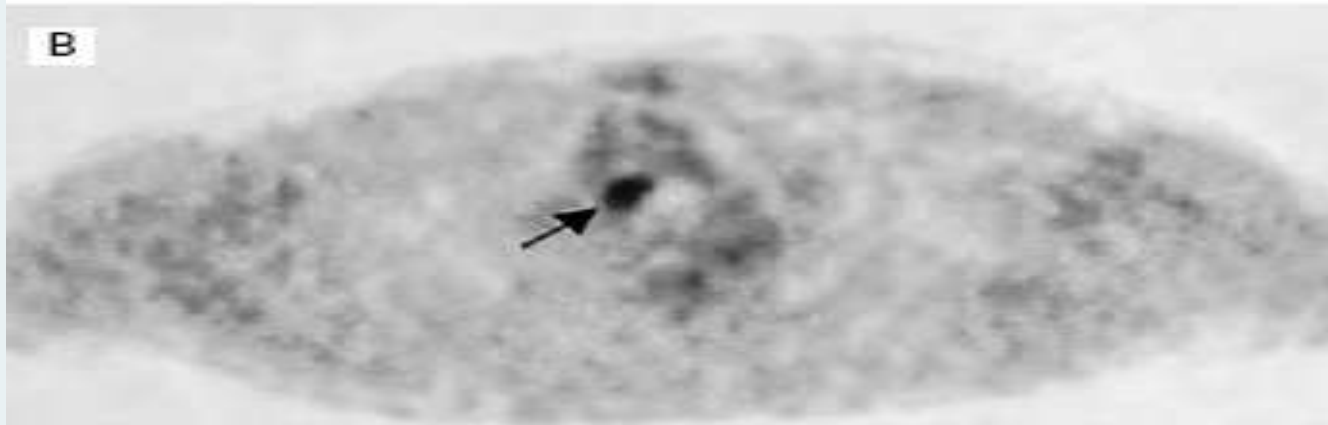
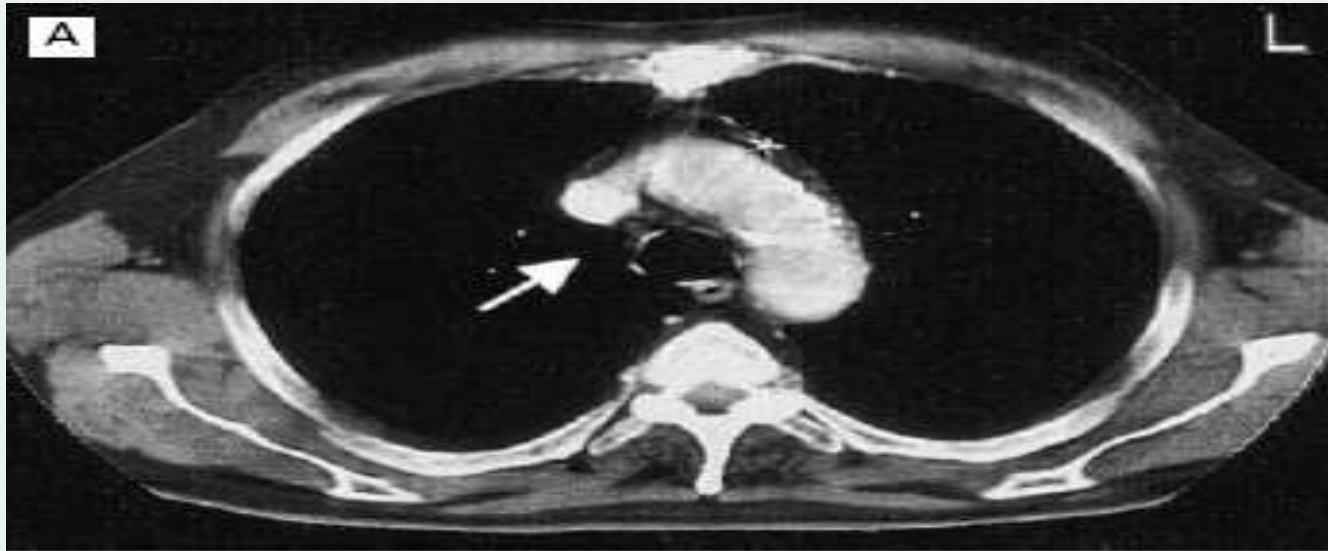
 - ▣ Lower positive predictive value (75%-79%), false-positive in:
 - ▣ Granulomas
 - ▣ Aspergillomas
 - ▣ Active tuberculosis
 - ▣ Abscesses
 - ▣ Sarcoidosis
 - ▣ Mediastinoscopy

The size of mediastinal lymph nodes a meta-analysis

Lymph node size	NPV (%)	PPV(%)
CT 10-15 mm	95	62
CT 16-20 mm	81	90
CT >20 mm	82	90

If < 15 mm, PET (-): 5% Tumor

If > 15 mm, PET (-): 20% Tumor



Pieterman NEJM 2000

Mariano Provencio

PET extrathoracic

- Forty percent of patients with NSCLC have distant metastases at presentation
 - most commonly in the adrenal glands, bones, liver, or brain.
- Organ-specific studies on the evaluation of distant metastases with PET often included only a small number of patients
 - PET was almost uniformly superior to conventional imaging techniques

PET extrathoracic staging: adrenal glands

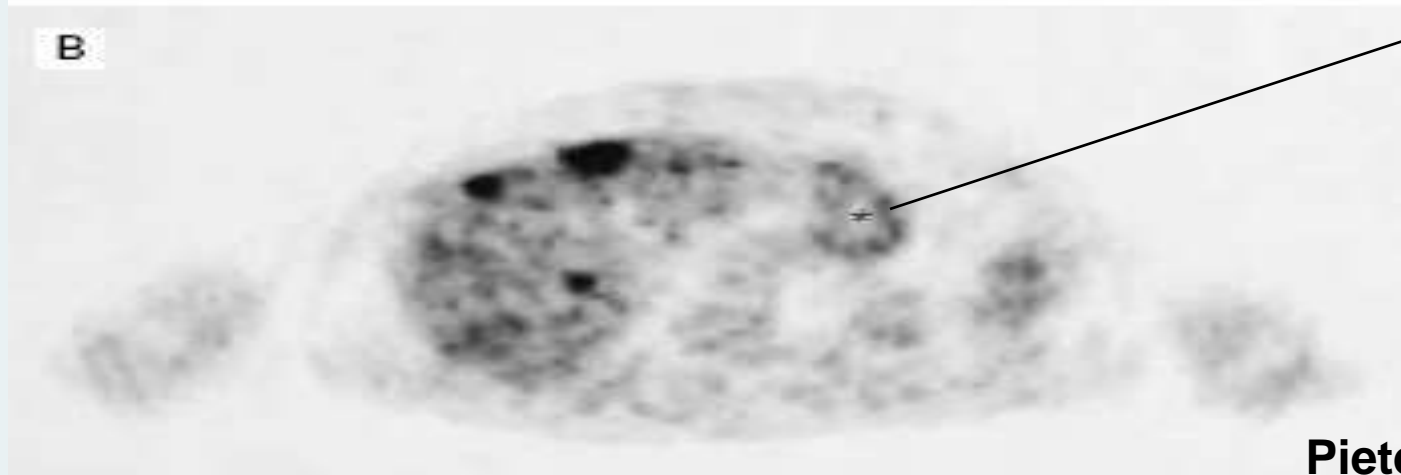
- In 10% of patients with NSCLC, CT reveals enlarged adrenal glands at initial presentation:
 - 2/3 are benign
 - PET: **95%- 100% sensitivity, 80-100% specificity**
 - Reduced unnecessary adrenal biopsies
 - However:
 - Vigilance required for small lesions (<1 cm)
 - False-positive have also been reported

PET extrathoracic staging: bone involvement

- ❑ ^{99m}Tc MDP: good sensitivity (90%) but low specificity (+/-60%), false-positive (degenerative or posttraumatic changes, inflammatory processes,..)
 - ❑ Additional imaging: bone x-ray, bone CT or MRI
- ❑ PET: **similar sensitivity** (90%), higher specificity >98% and accuracy >96%
- ❑ Replace bone scan? Bone scan: entire skeleton
 - ❑ PET scan standard :
 - ❑ Could miss metastases in lower extremities
 - ❑ False negatives in cases of osteoblastic lesions

PET and brain metastases

- ▣ **PET is not suitable for the detection of brain metastases**
 - ▣ Sensitivity is low (60%) due to the high glucose uptake of surrounding normal brain tissue
 - ▣ CT and/or MRI remain the method of choice to stage the brain



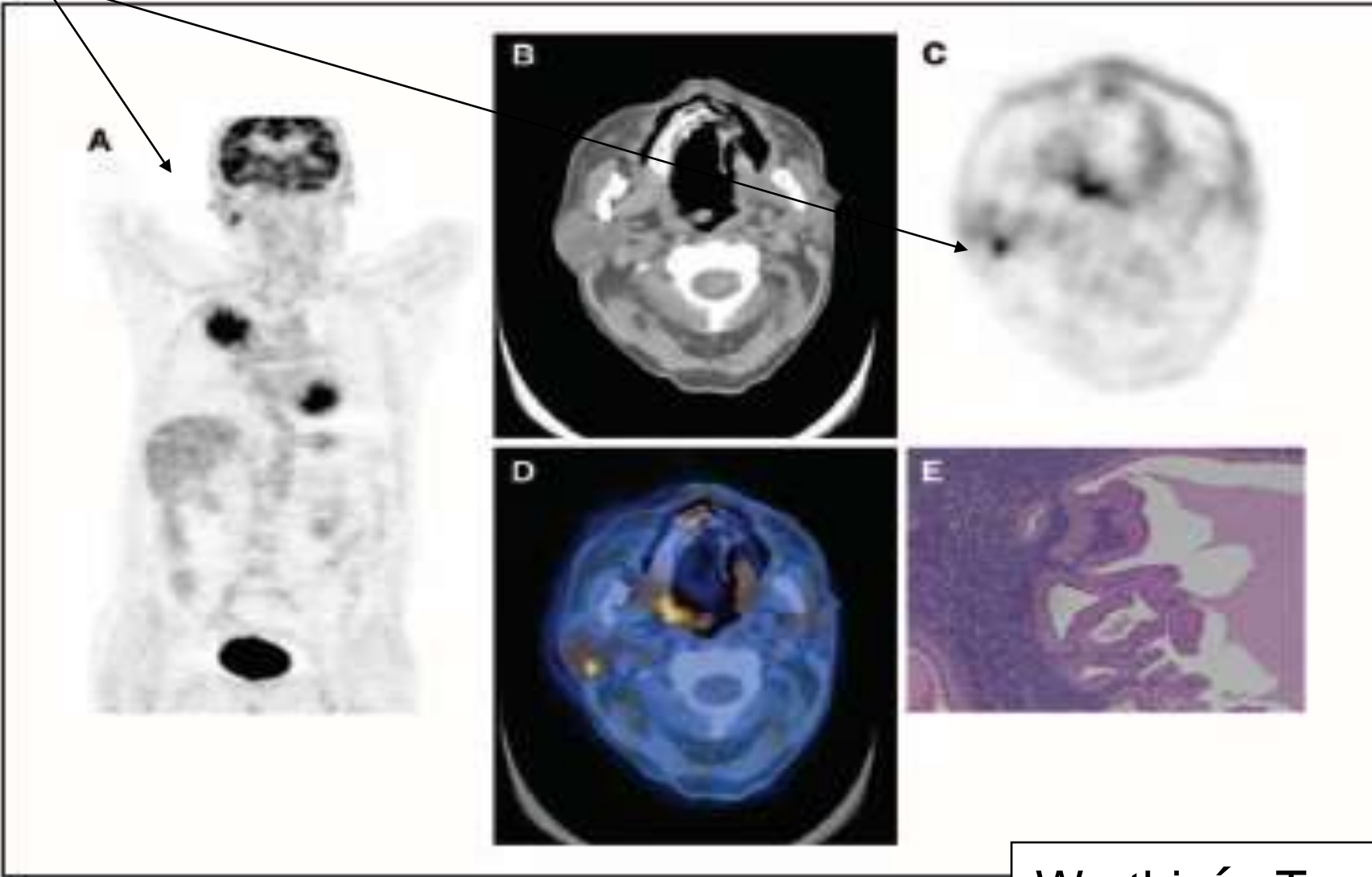
HP

Pieterman NEJM 2000

Value of PET in the detection of unexpected distant metastases

<i>Study</i>	<i>N° patients</i>	<i>Detection extra lesions %</i>
Bury	109	6
Lewis	34	29
MacManus	167	19
Marom	100	9
Pieterman	102	11
Saunders	97	17
Stroobants	144	5
Valk	99	11
Weder	100	15

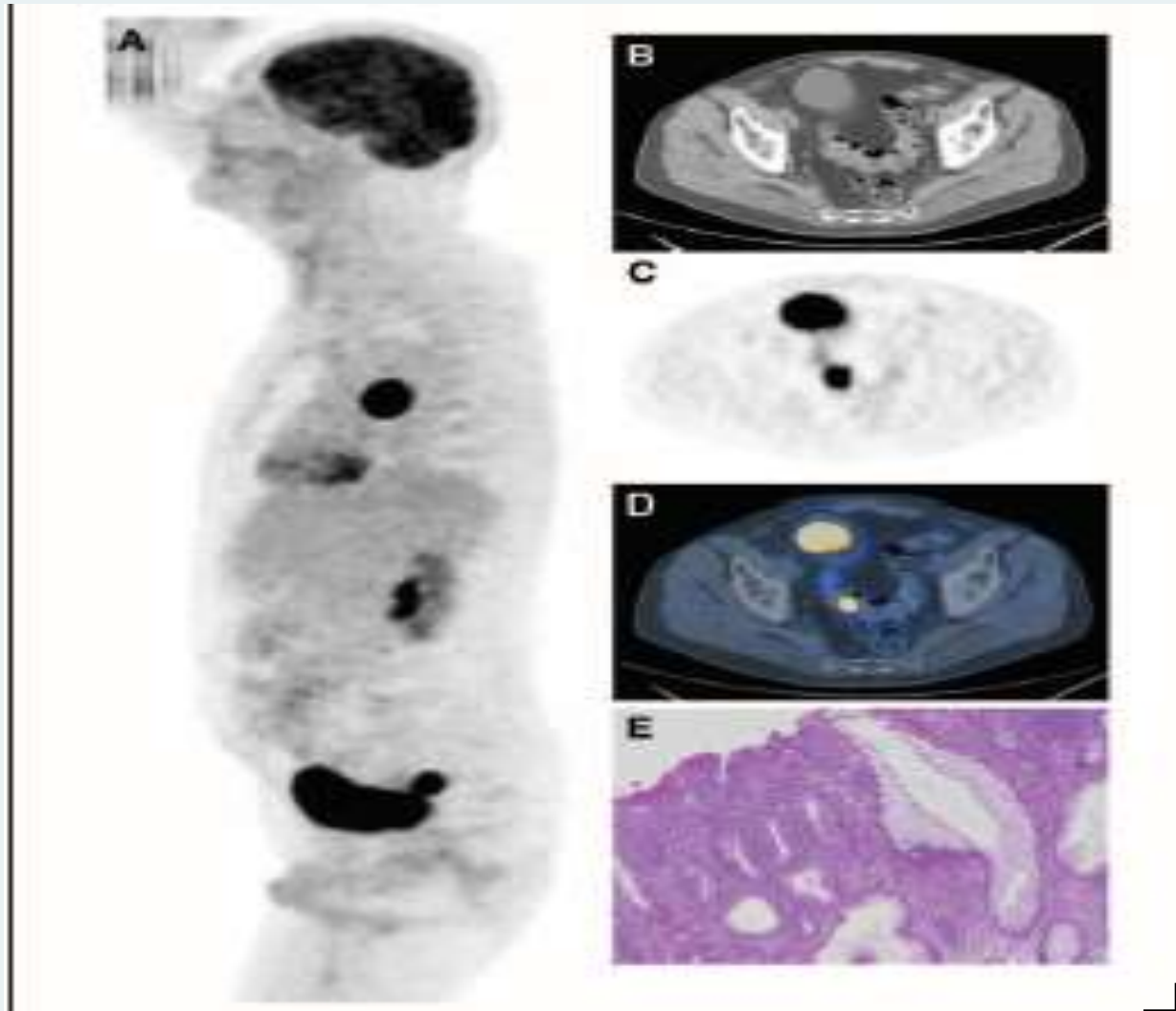
- Alteration of modality
 - chemotherapy vs radiotherapy: 9%
 - radical radiotherapy vs surgery in 9%



Lardinois D J Clin Oncol October 2005

Warthin's Tumor

72-year-old man Adenocarcinoma LSI

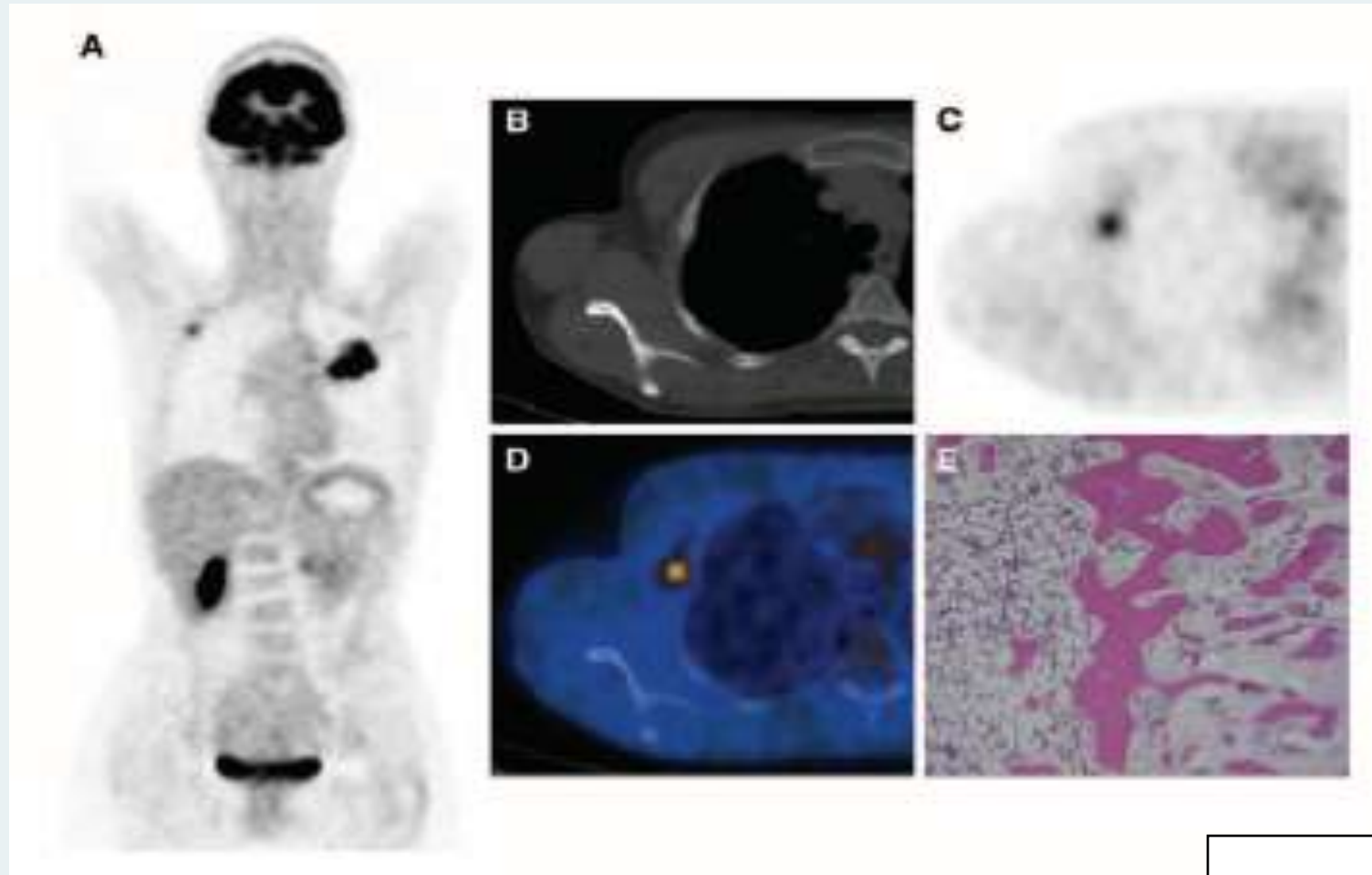


Lardinois D J Clin Oncol October 2005

Mariano Provencio

Tubular Adenoma

47-year-old woman Adenocarcinoma LSI



Lardinois D J Clin Oncol October 2005

Mariano Provencio

Callus formation

Focal Extrapulmonary abnormality and PET

▣ 350 NSCLC with PET/CT

▣ Additional evaluations were performed on all patients with single focal extrapulmonary abnormalities:

▣ 21% (72/350) (no IIB, or multifocal, ...IV)

▣ A diagnosis was obtained in 69 patients

▣ 37 (54%) with solitary metastases

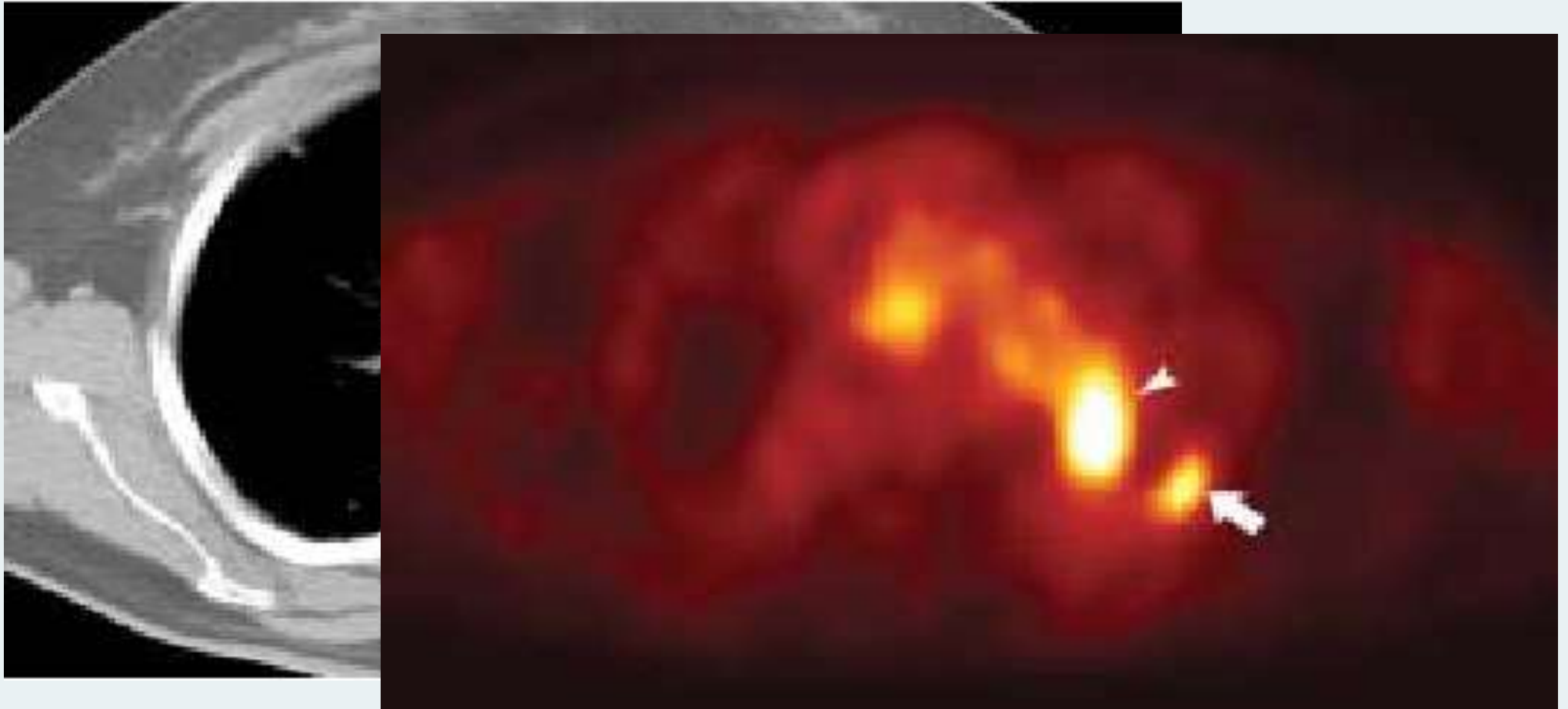
▣ 32 (46%) lesions unrelated to lung cancer

▣ 19% unsuspected malignancy

▣ 81% benign tumor or inflammatory

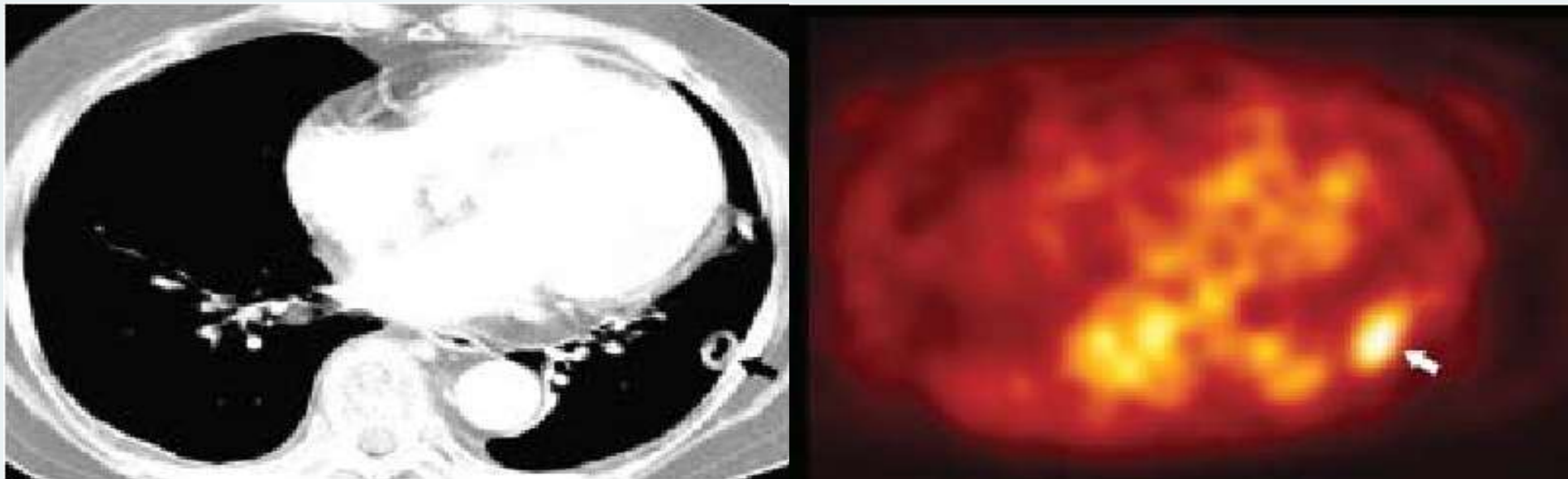
▣ ***Etiology of solitary PET positive should be determined (axillary, spleen, spinal, pancreas)***

Tuberculoma en mujer de 53 a



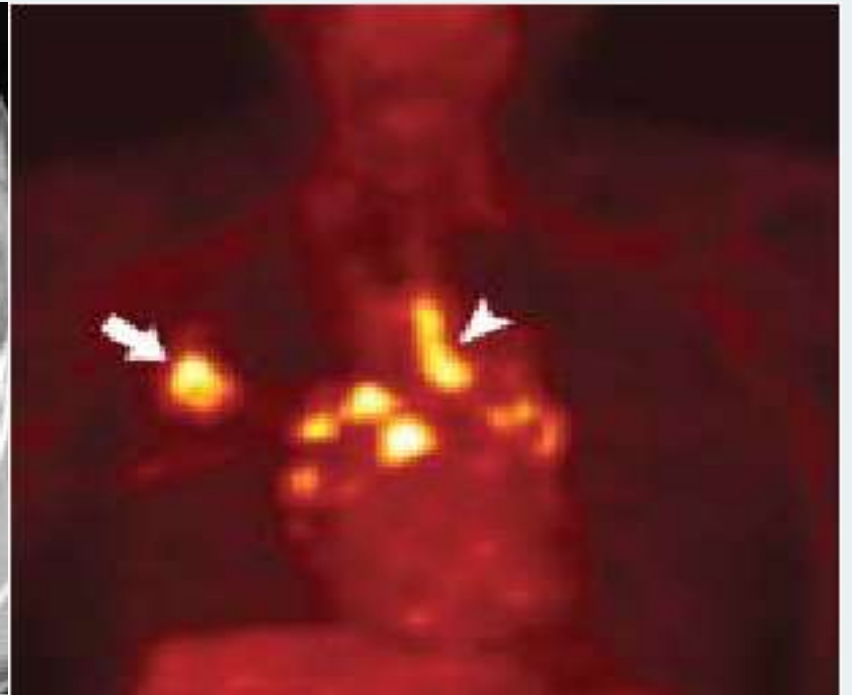
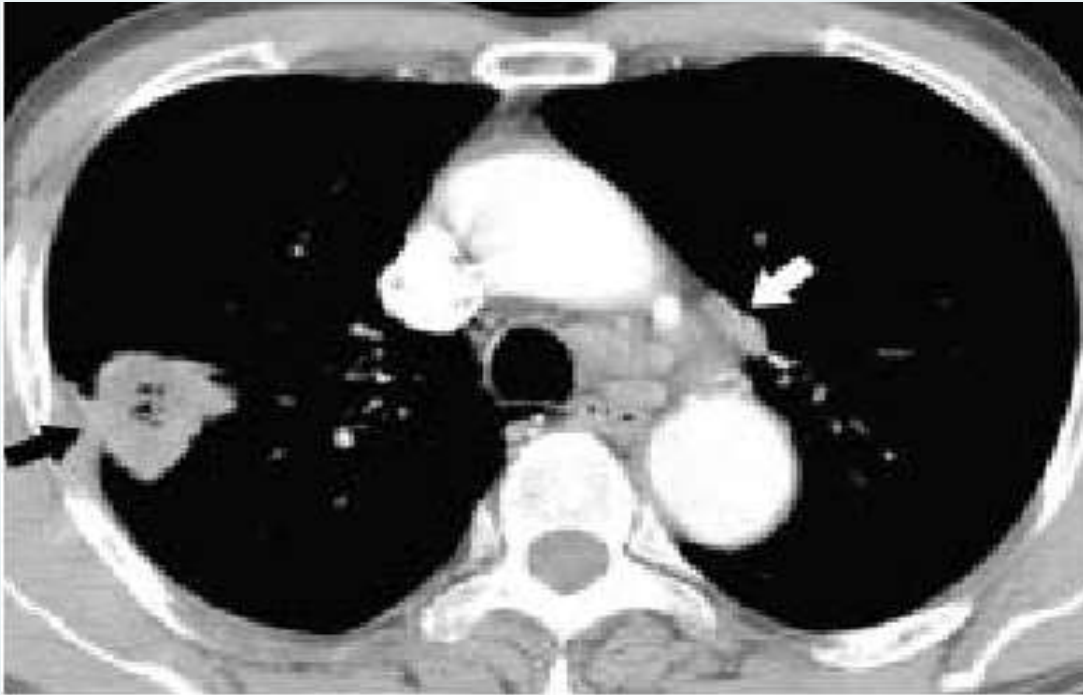
SUV 4.3

Criptococosis en mujer de 68 a

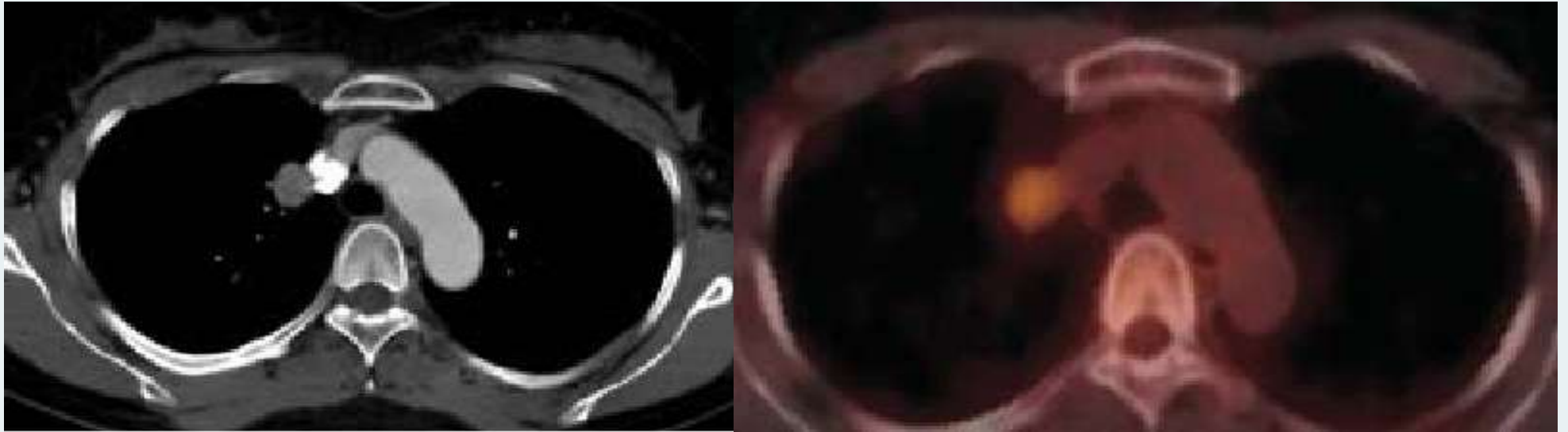


SUV 2.6

Absceso en varón de 72 a

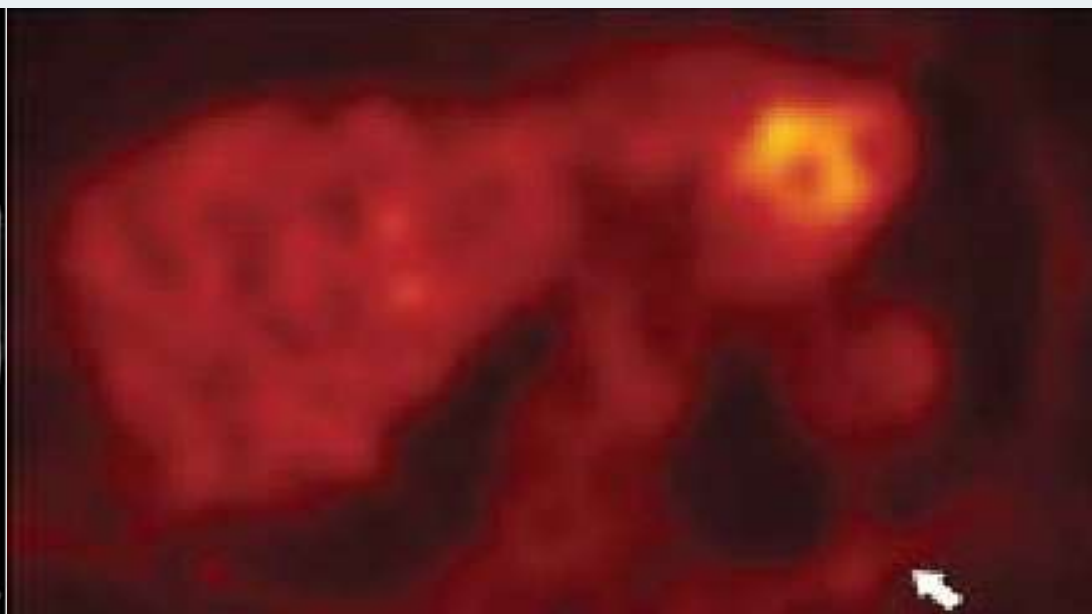


Hemangioma esclerosante en mujer de 43 a



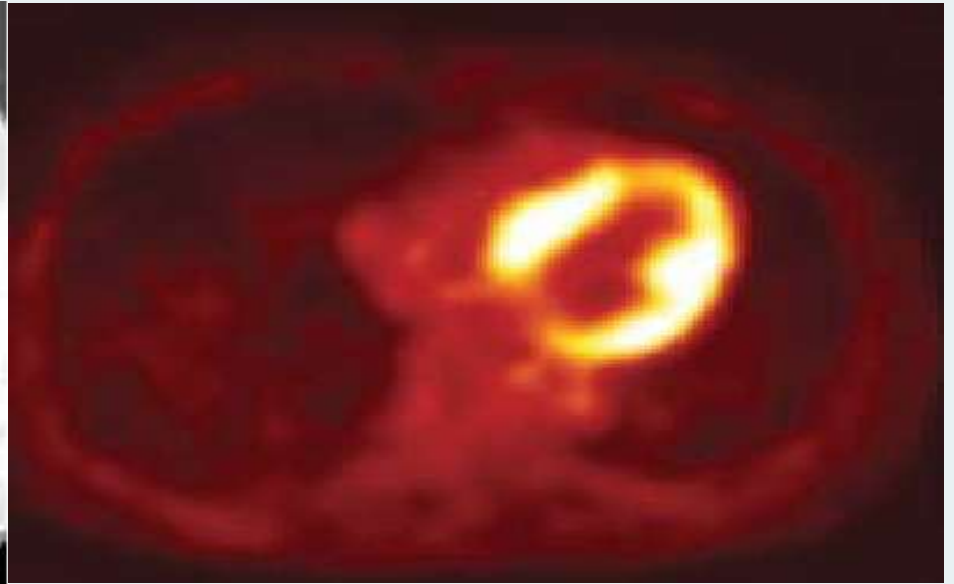
SUV 3.4

Carcinoma bronquioloalveolar en varón de 75a



SUV 1.7

Carcinoma bronquioloalveolar mucinoso en mujer de 61a



Metástasis de adenocarcinoma de mama

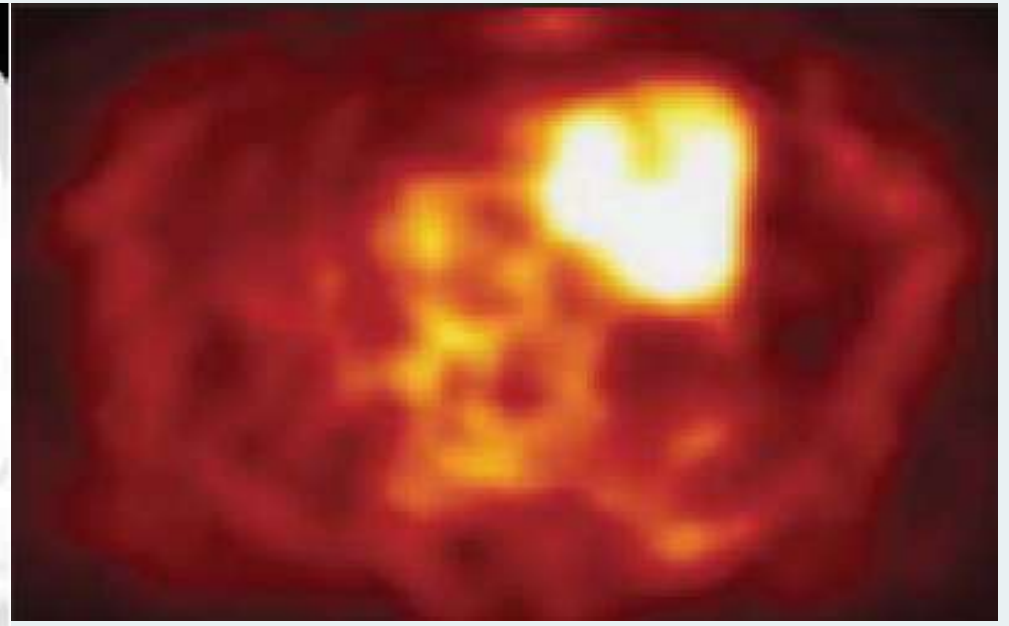


Breast-Feeding



HENDLER D , STEMMER S M JCO 2010;28:E659-E660

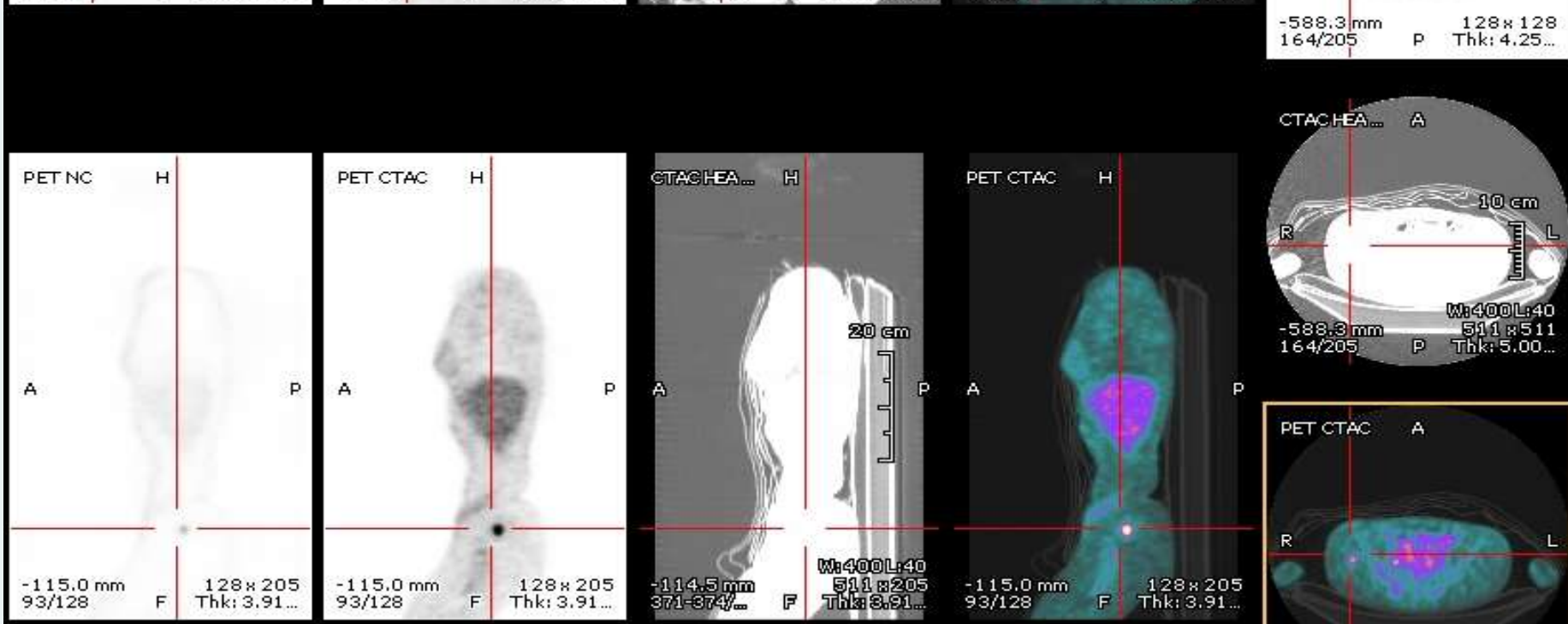
Metástasis de hipernefroma en varón de 83a

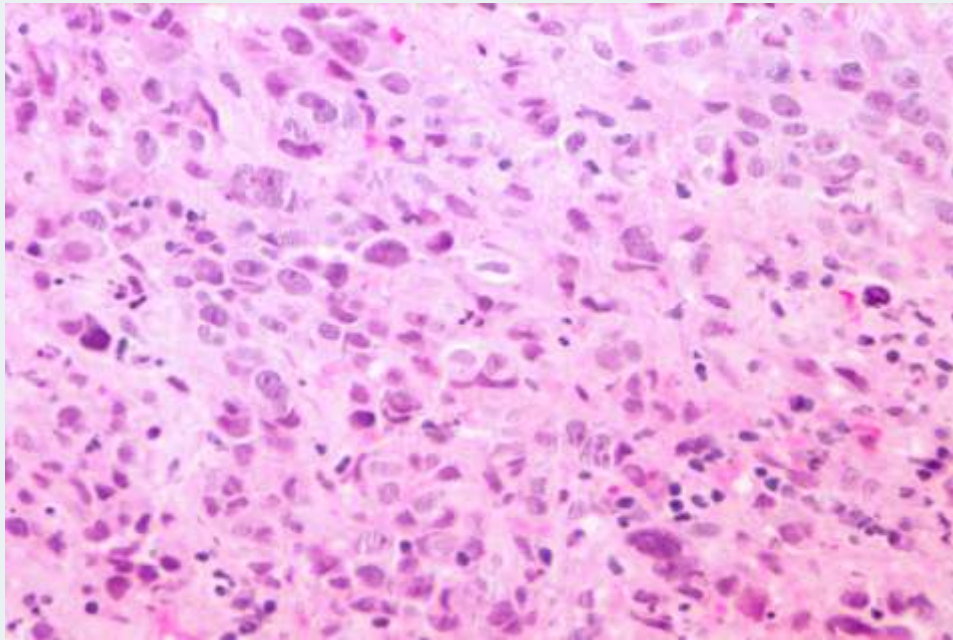


Otro, el último...

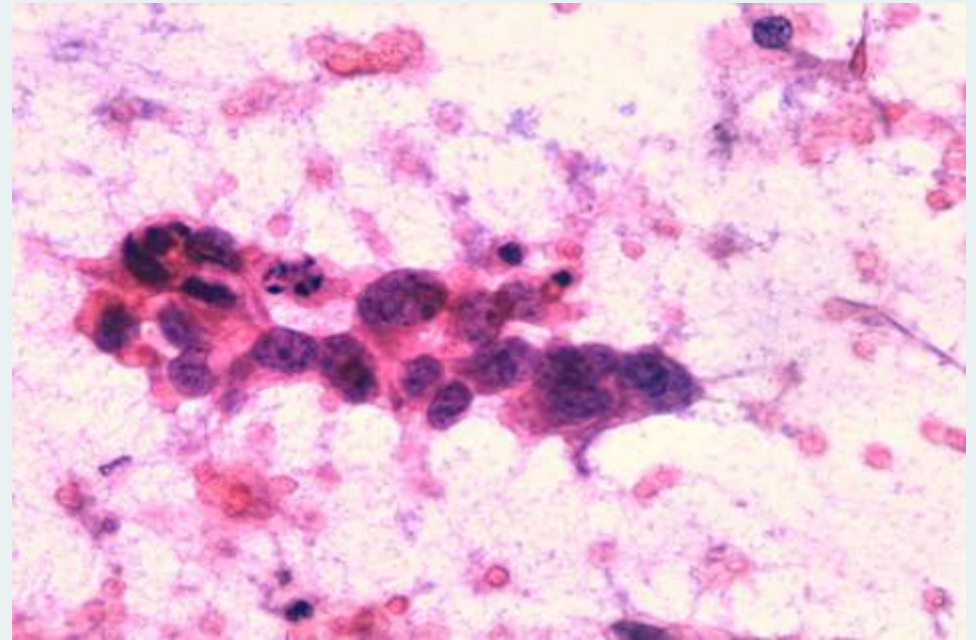
▣ Paciente de 47 años, T2 N2 M0







Biopsy of the mass by bronchoscopy



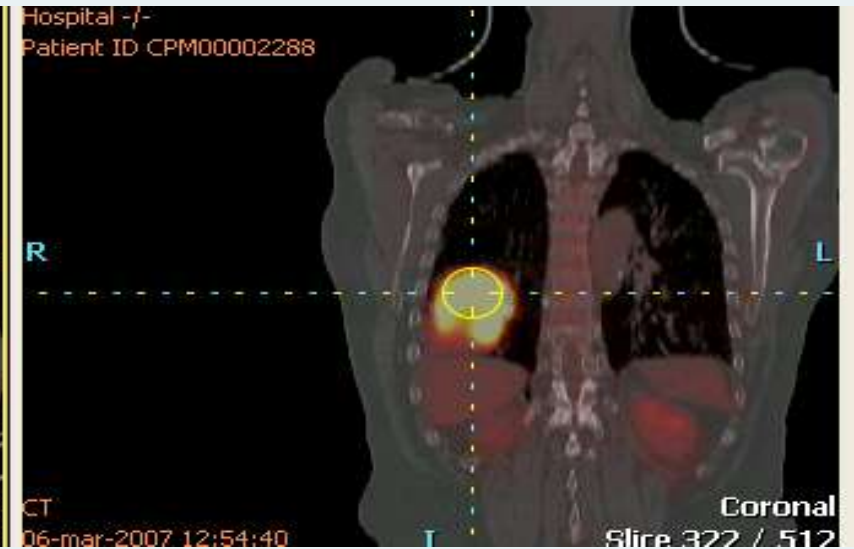
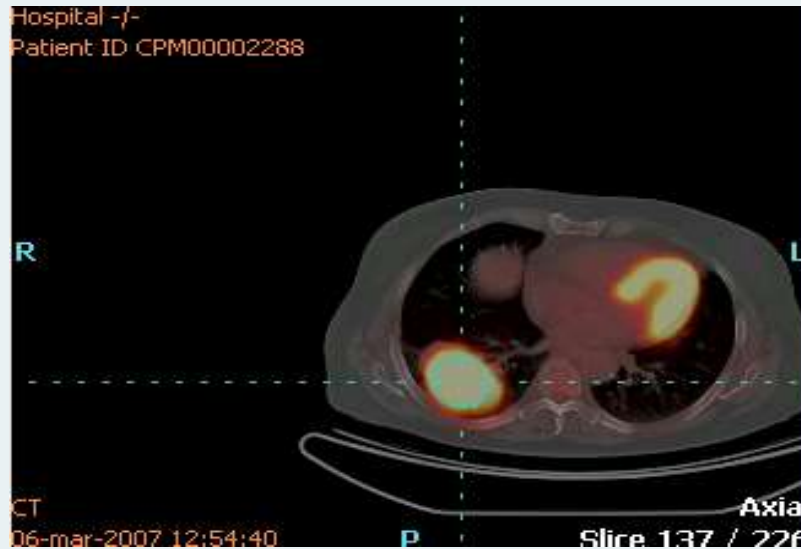
Fine-needle aspiration puncture
of the gluteus nodule

MARZO 2007;

Mujer 65 años,

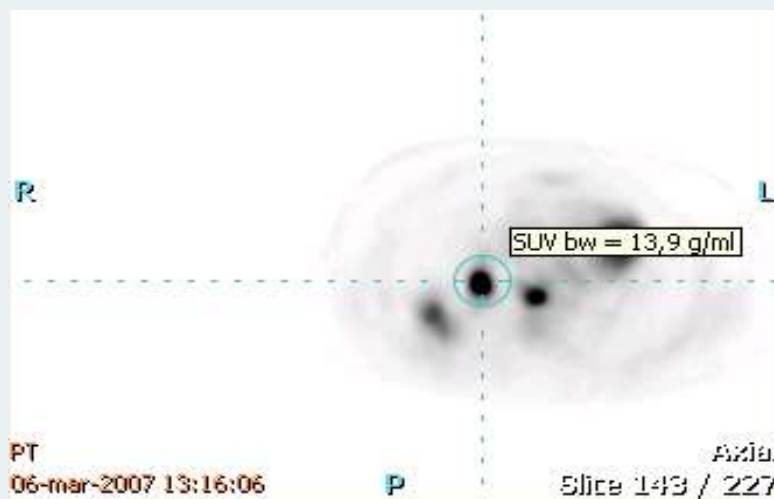
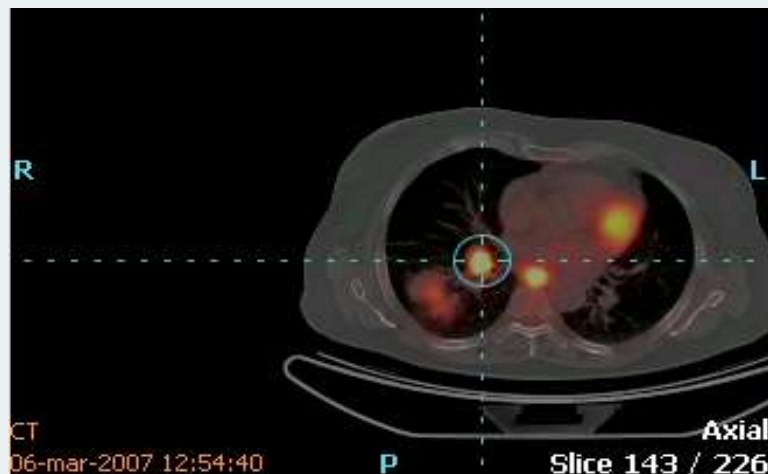
NSCLC

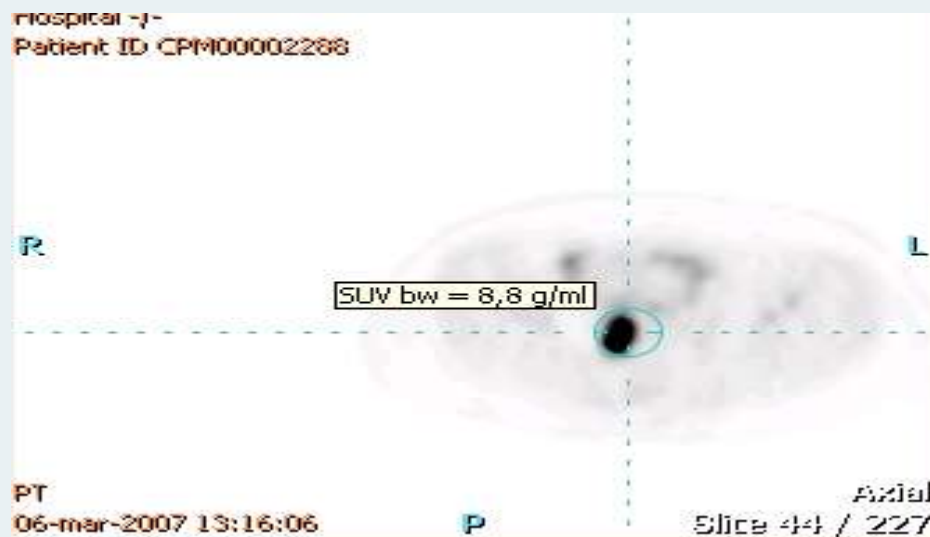
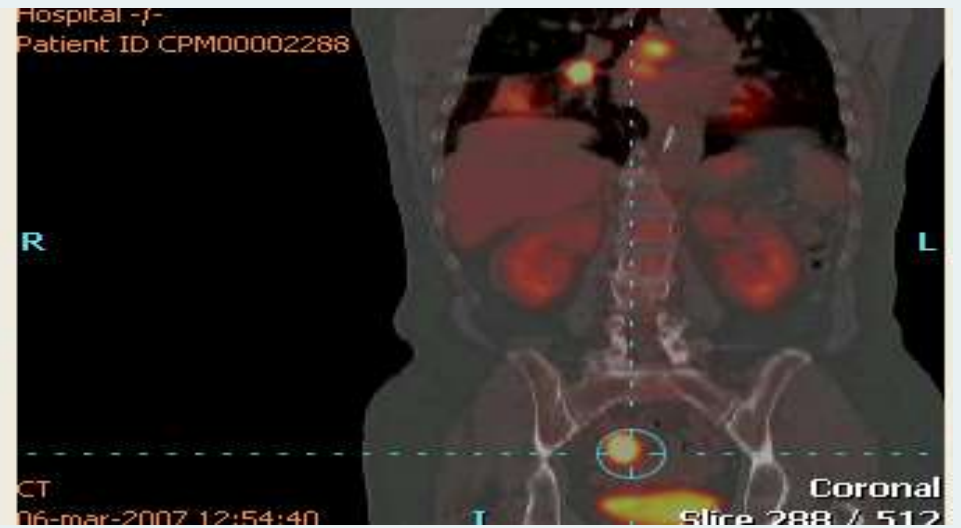
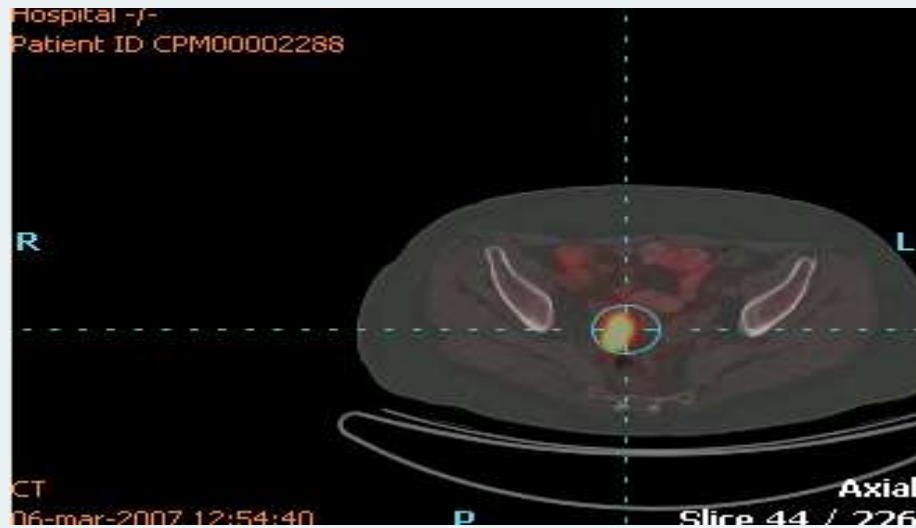
LID 6 cm



TAC T-Abdomen superior: N 2 Nada, salvo N2

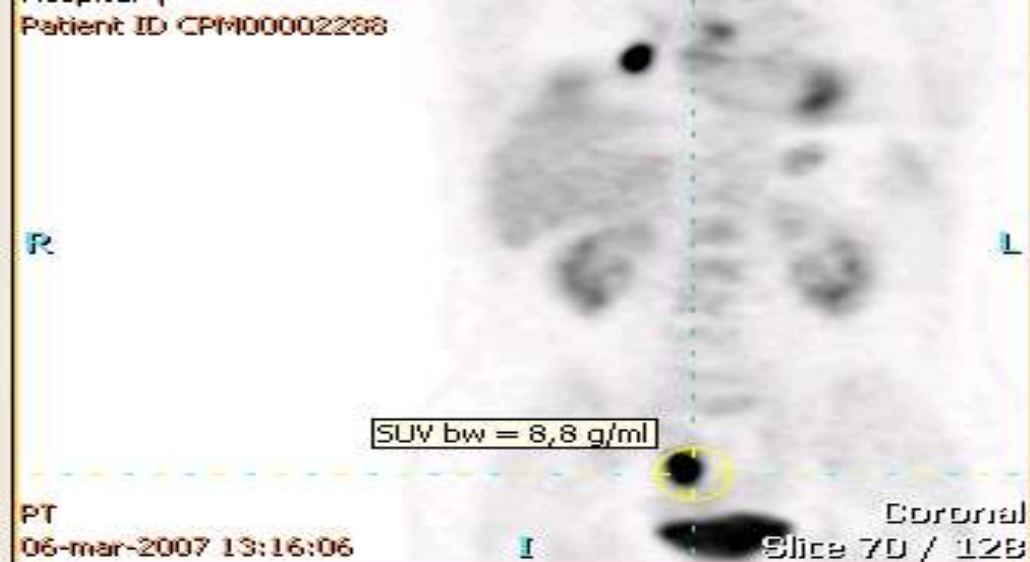
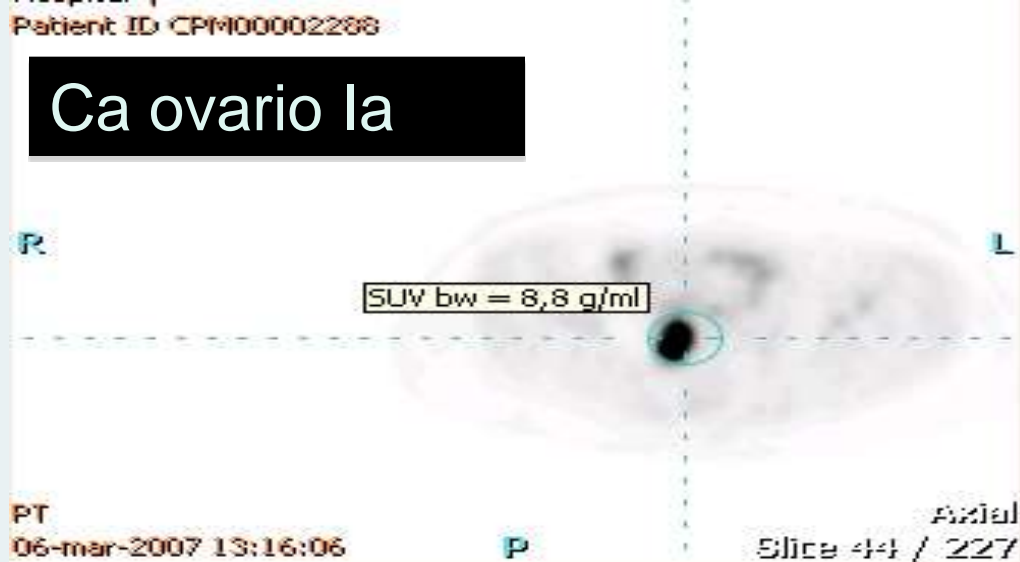
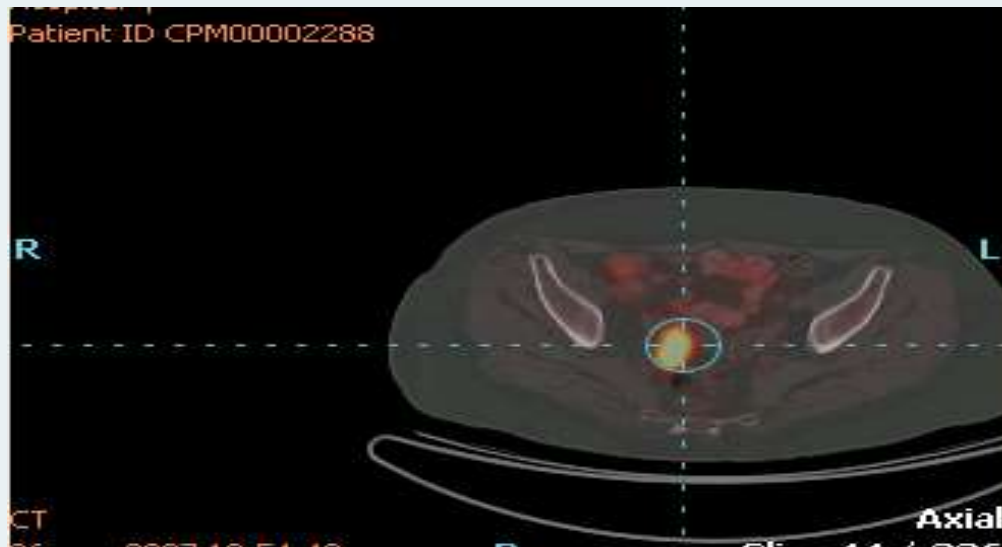
mediastinoscopia +





Mariana Provencio

TAC pélvico: características radiológicas claras de enf metastásica



Estadificación

- Parte más importante
- Piedra angular de todo lo que hagamos después
- Diagnóstico histológico imprescindible



Hospital Universitario
Puerta de Hierro
Majadahonda

mprovencio.hpth@madrid.salud.org

Mariano Provencio

Agrupación por estadios

Carcinoma oculto	Tx	N0	M0
Estadio 0	Tis	N0	M0
Estadio IA	T1a,b	N0	M0
Estadio IB	T2a	N0	M0
Estadio IIA	T1a,b	N1	M0
	T2a	N1	M0
	T2b	N0	M0
Estadio IIB	T2b	N1	M0
	T3	N0	M0
Estadio IIIA	T1, T2	N2	M0
	T3	N1, N2	M0
	T4	N0, N1	M0
Estadio IIIB	T4	N2	M0
	Cualquier T	N3	M0
Estadio IV	Cualquier T	Cualquier N	M1

Drenaje linfático

LSDch0

LSI

LM

LI Dcho

LII

