Norwegian Society of Thoracic Imaging

Oslo, October 2011

Lung Cancer Staging: **The Revised TNM Classification**

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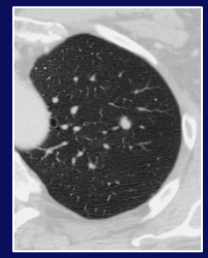
Lung Cancer

The Scale of the Problem

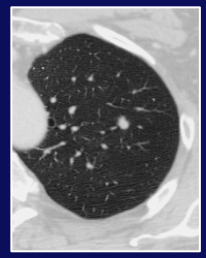


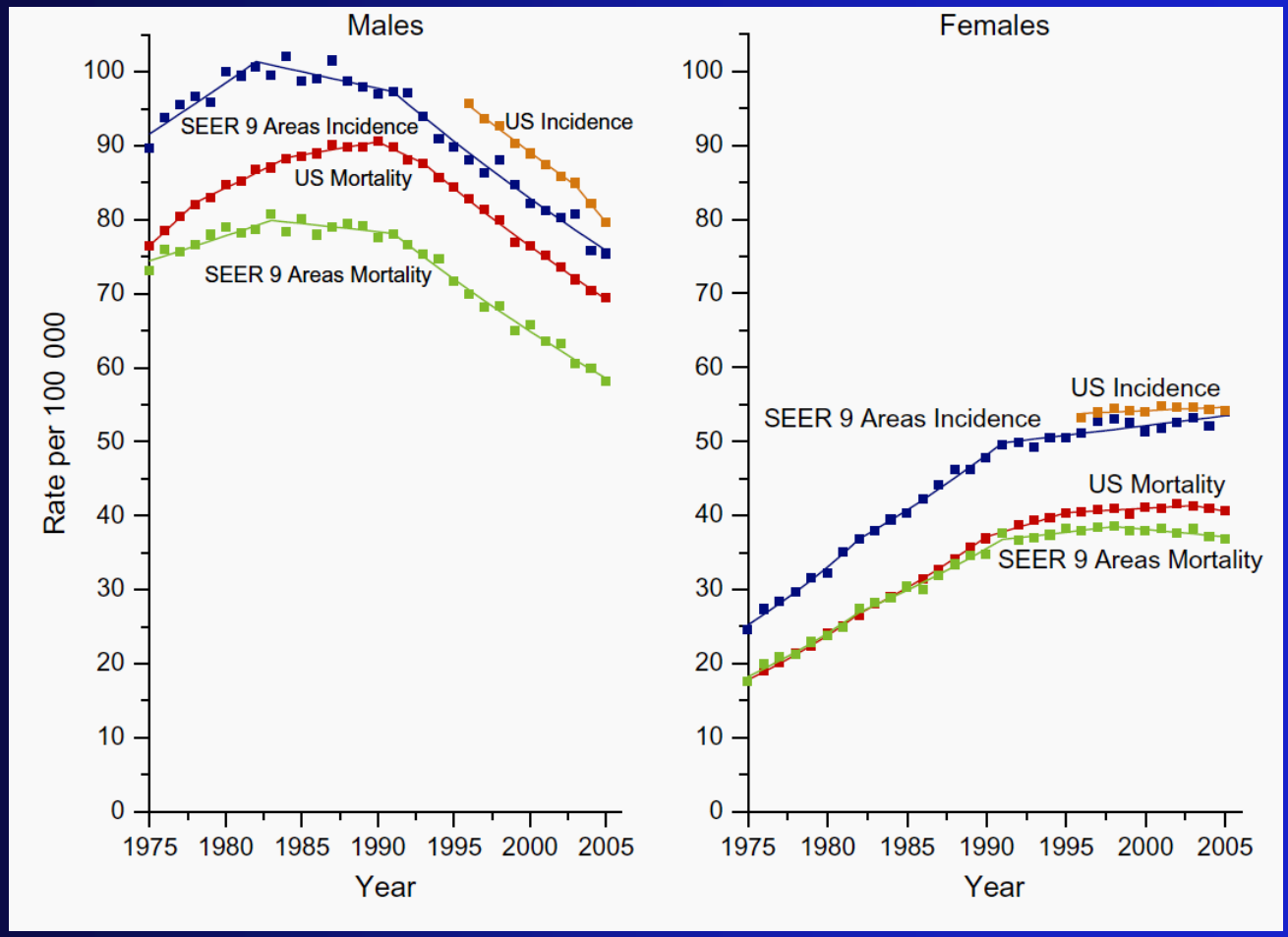
- Leading cause of cancer-related death in West. UK: ~40000 new diagnoses/deaths. US: ~ 170000 new cases and 155000 deaths
- <15% (overall) vs 70% 5ys (Stage I disease) >70% stage IIIB or greater at presentation
- Smoking rates declining: >90 $x10^6$ US population with smoking history/ 50% current smokers (2007)

National Lung Screening Trial Research Team. The national lung screening trial: overview and study design *Radiology* 2011;258:243-253

Lung Cancer

The Scale of the Problem

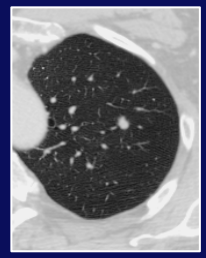




Ahmedin J et al. Annual report to the nation on the status of cancer, 1975-2005, featuring trends in lung cancer, tobacco use, and tobacco control *J Natl Cancer Inst* 2008;100:1672-1694

Lung Cancer

The Scale of the Problem



5-year cumulative relative survival

	Age 0–49	
	Men	**Women**
England	14.0 (12.6 to 15.4)	17.8 (16.2 to 19.4)
Norway	17.6 (13.5 to 22.0)	29.3 (23.5 to 35.3)
Sweden	20.3 (15.8 to 25.3)	27.4 (22.8 to 32.3)
	Age 70–79	
	Men	**Women**
England	5.4 (5.2 to 5.7)	6.1 (5.8 to 6.5)
Norway	7.5 (6.4 to 8.9)	9.5 (7.8 to 11.4)
Sweden	9.9 (8.8 to 11.2)	13.0 (11.4 to 14.7)

Holmberg L et al. National comparisons of lung cancer survival in England, Norway and Sweden 2001-2004: differences occur early in follow-up *Thorax* 2011;65:436-441

Lung Cancer

Major Paradigm Shifts...

- **IASLC/ATS/ERS reclassification of adenocarcinoma**
- **Lung cancer screening - NLST aborted; 20% reduction in lung-cancer specific mortality**
- **Revision to the TNM classification (version 7)**

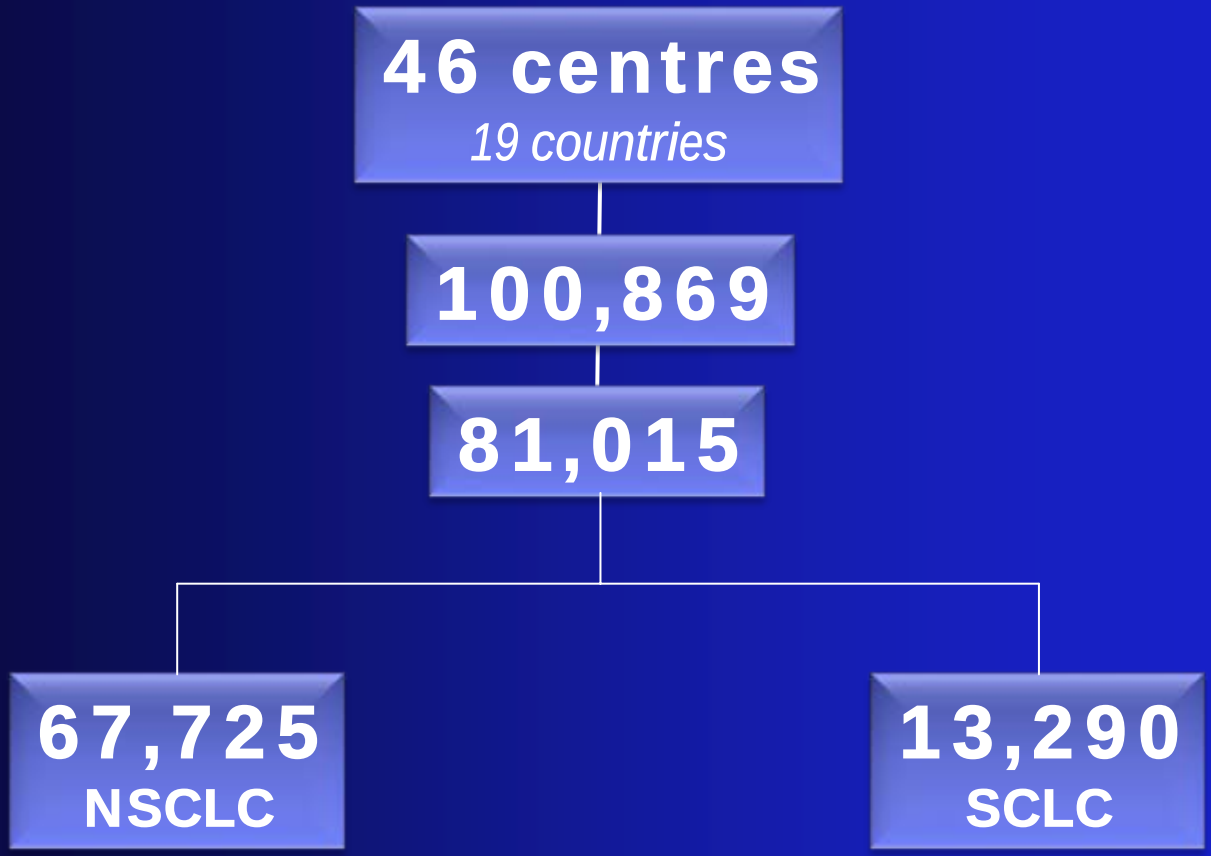
Lung Cancer Staging
Issues with TNM-6 (& earlier)

- TNM-6 based on earlier versions and unchanged
- Small numbers (~5300); predominant surgically treated
- Single centre data; limited internal, no external validation
- No account of developing technologies (MDCT)

Goldstraw P et al. The IASCLC lung cancer staging project: proposals for the revision of the TNM group stagings in the forthcoming (seventh) editon of the TNM classification of malignant tumours *J Thorac Oncol* 2007;2:706-714

Lung Cancer Staging

The Revised (TNM-7) Criteria



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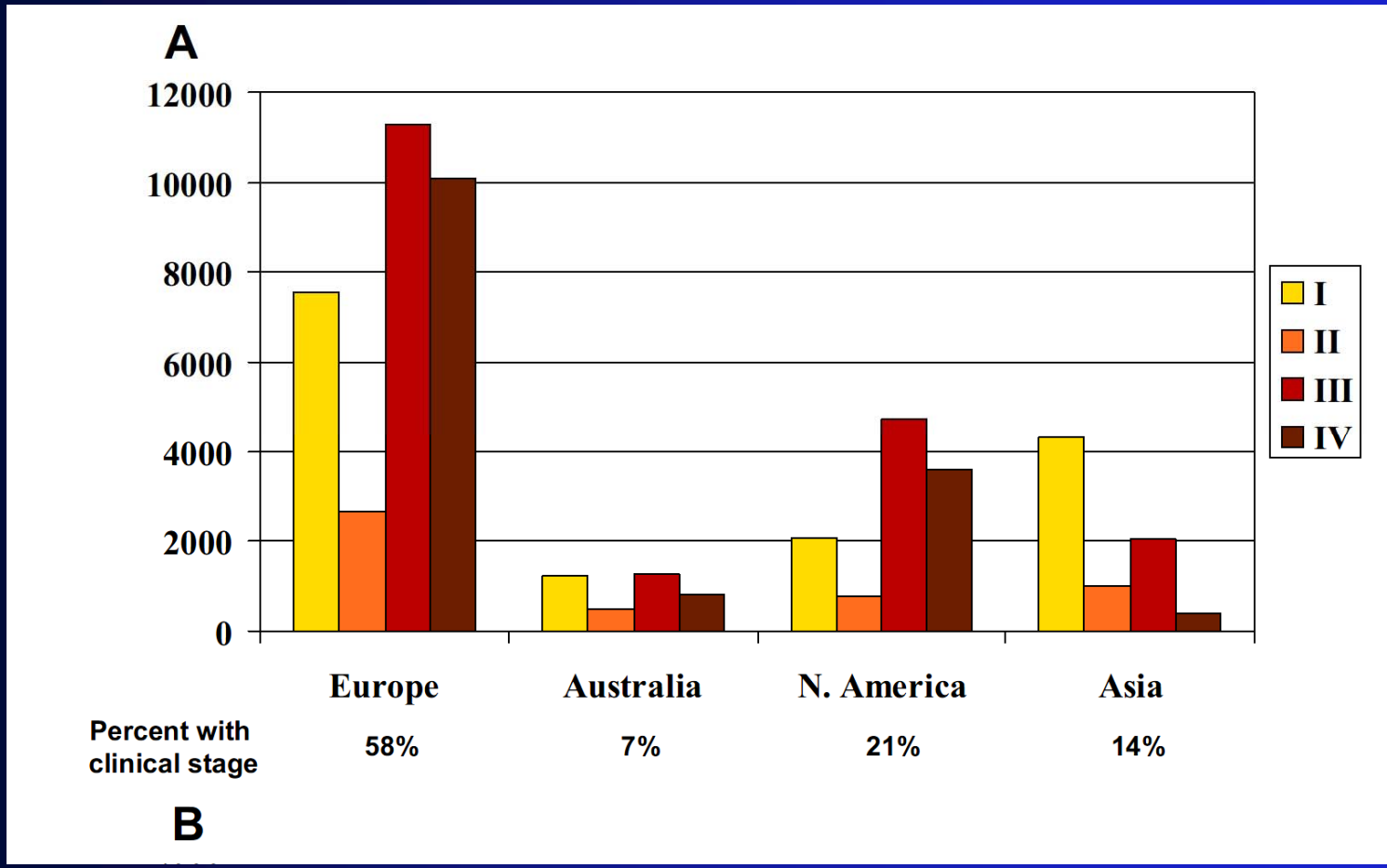
Lung Cancer Staging

The Revised (TNM-7) Criteria



Groome PA et al. The IASCLC lung cancer staging project: validation of the proposals for revision of the T, N, and M descriptors and consequent stage groupings in the forthcoming (seventh) edition of TNM classification of malignant tumours *J Thorac Oncol* 2007;2:694-705

Lung Cancer Staging

Aims

- To summarise differences between the revised (TNM-7) descriptors and earlier versions
- To present the radiological (CT) features of lung cancer relevant to the revised staging system
- To discuss the limitations and (continuing) uncertainties in the radiological staging of lung cancer

Lung Cancer Staging

Key Changes to TNM-6

Subdivision of T1 stage:

	1 Yr	5 Yrs	Comparison	HR	P
T1a	88%	51%			
T1b	85%	47%	vs T1a:	1.27	<.0001

T1a
≤2cm

T1b
>2, ≤3cm

TNM-7

Groome PA et al. The IASCLC lung cancer staging project: validation of the proposals for revision of the T, N, and M descriptors and consequent stage groupings in the forthcoming (seventh) edition of TNM classification of malignant tumours *J Thorac Oncol* 2007;2:694-705

Lung Cancer Staging

Key Changes to TNM-6

Subdivision of T2 stage:

	1 Yr	5 Yrs	Comparison	HR	P
T2a	81%	45%	vs T1b:	1.14	0.0039
T2b	68%	31%	vs T2a:	1.51	<.0001

T2a
>3, ≤5cms

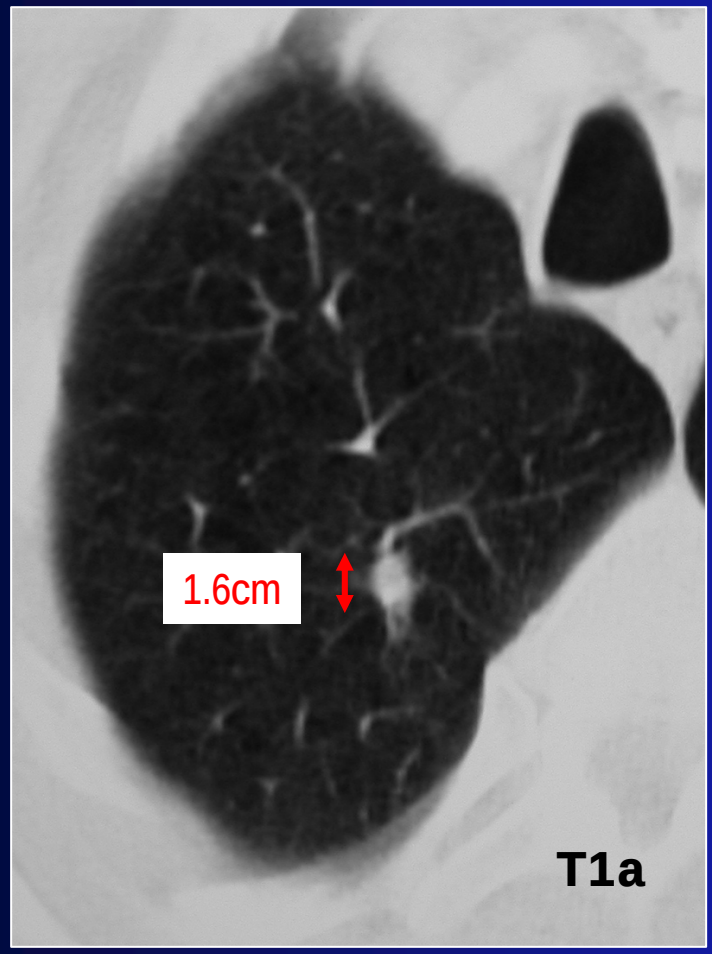
T2b
>5, ≤7

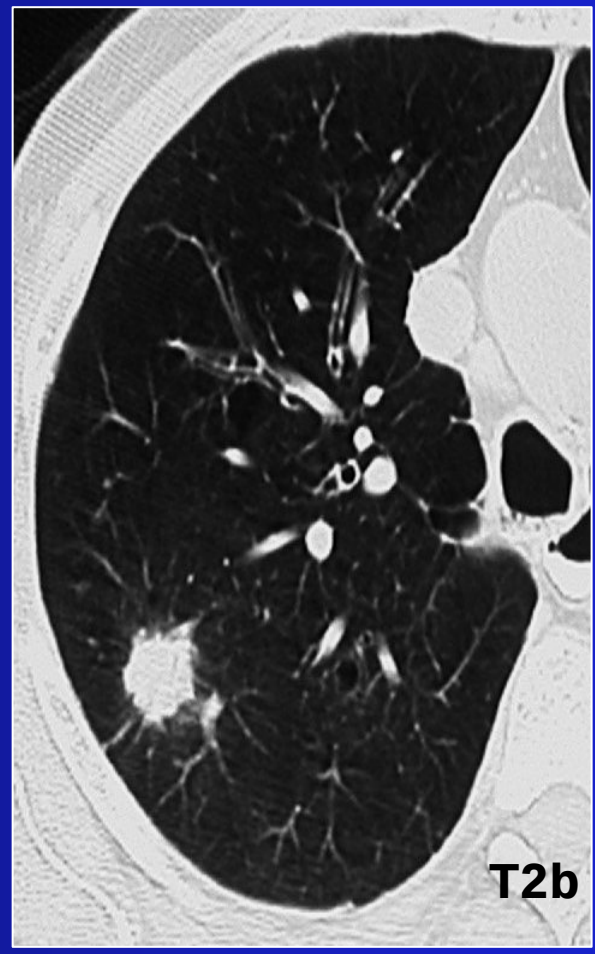
TNM-7

Groome PA et al. The IASCLC lung cancer staging project: validation of the proposals for revision of the T, N, and M descriptors and consequent stage groupings in the forthcoming (seventh) edition of TNM classification of malignant tumours *J Thorac Oncol* 2007;2:694-705

Lung Cancer Staging

T1 and T2 Tumours

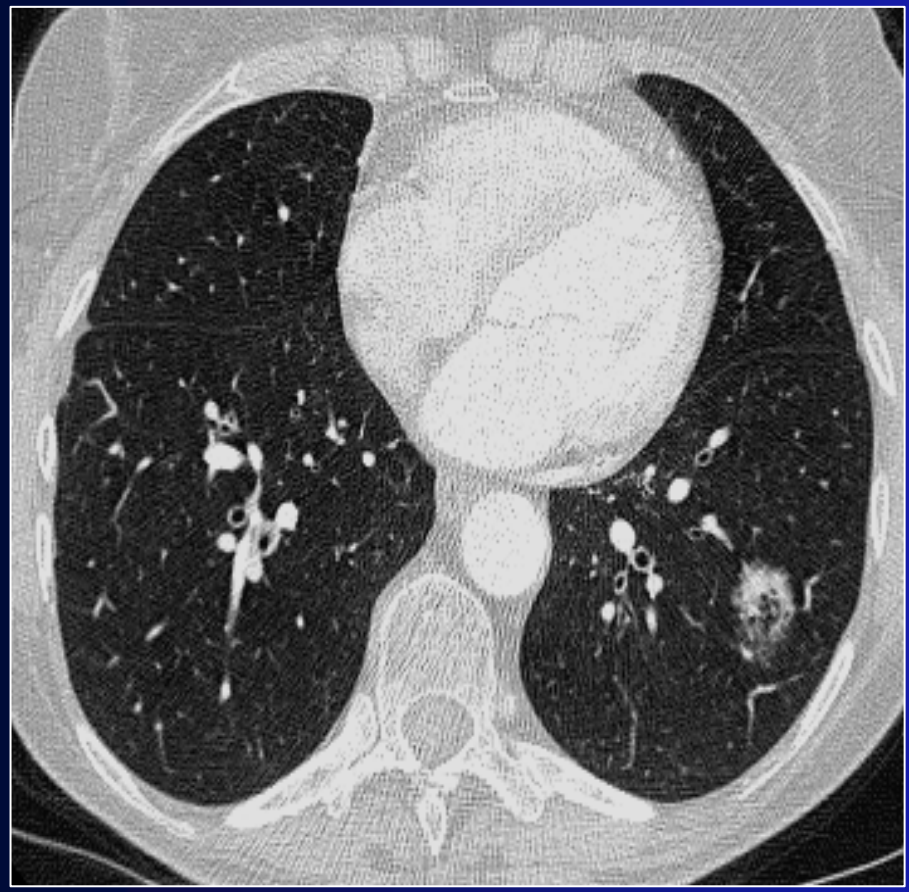




Lung Cancer Staging

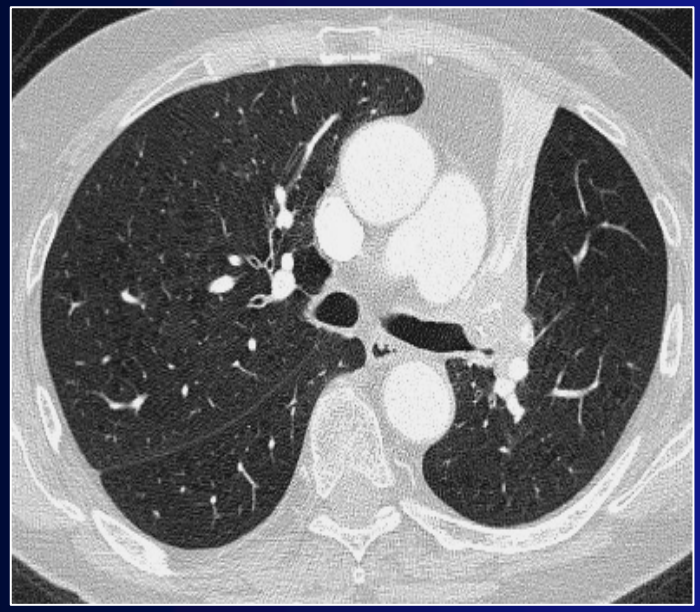
T1 and T2 Tumours…difficulties

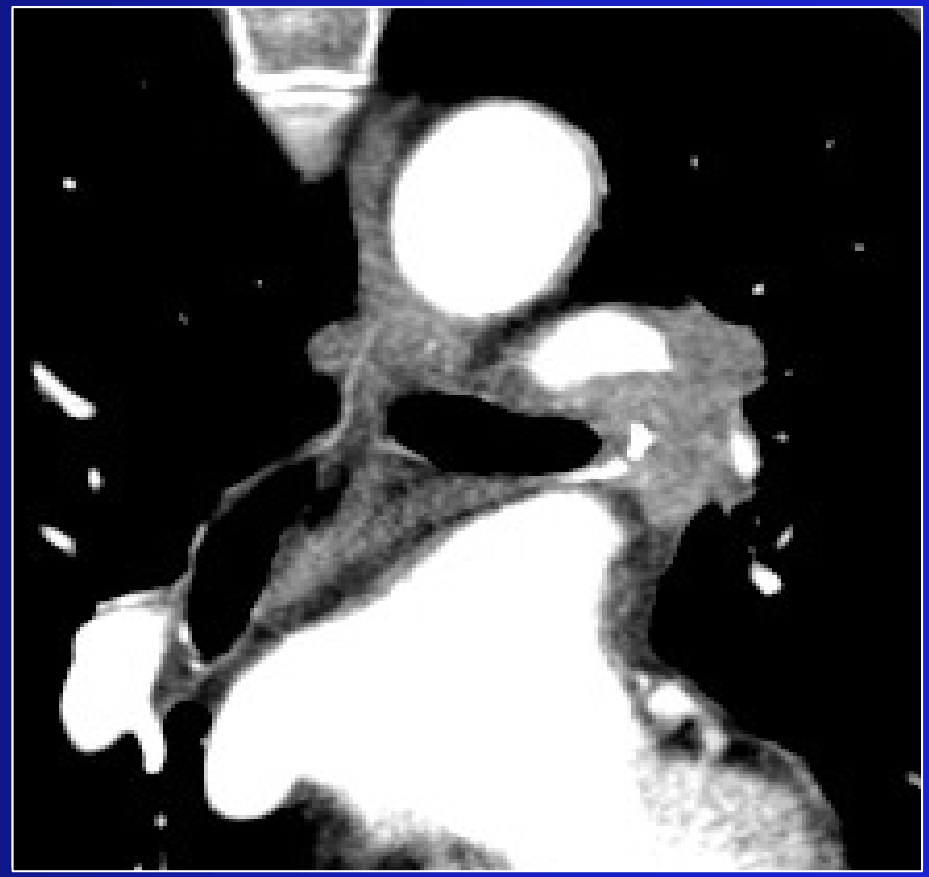
T1 or T2?



Lung Cancer Staging

T1 and T2 Tumours…difficulties

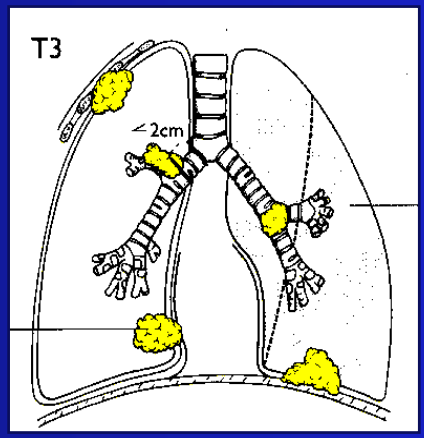




Lung Cancer Staging

Key Changes to TNM-6

Tumour of *any* size but with invasion of chest wall,diaphragm, mediastinal pleura, parietal pleura, parietal pericardium, or tumour in main bronchus <2cm from carina but not involving carina; or atelectasis / obstructive pneumonitis of entire lung



T3

T3 Tumor >7 cm

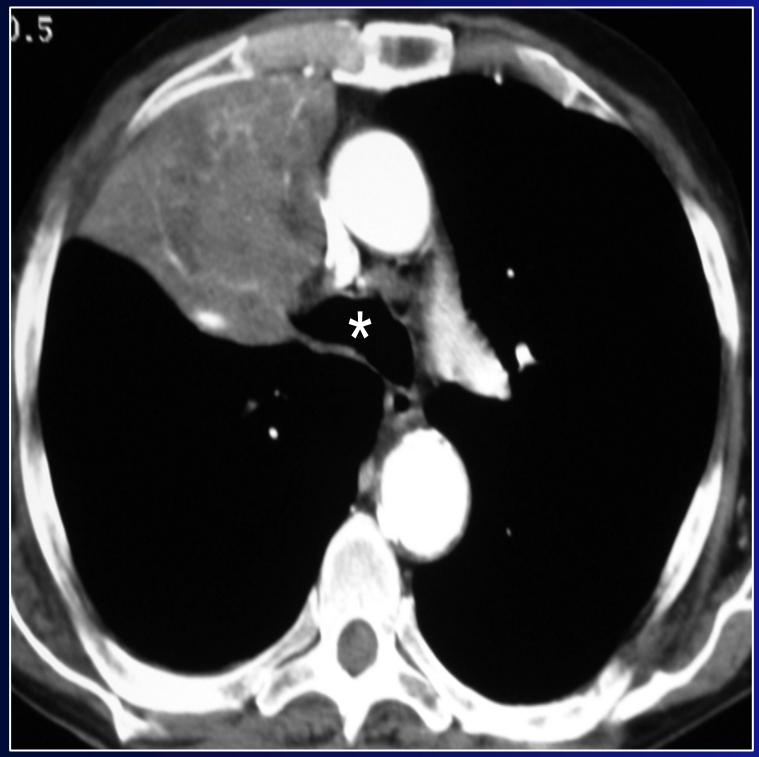
or separate tumor

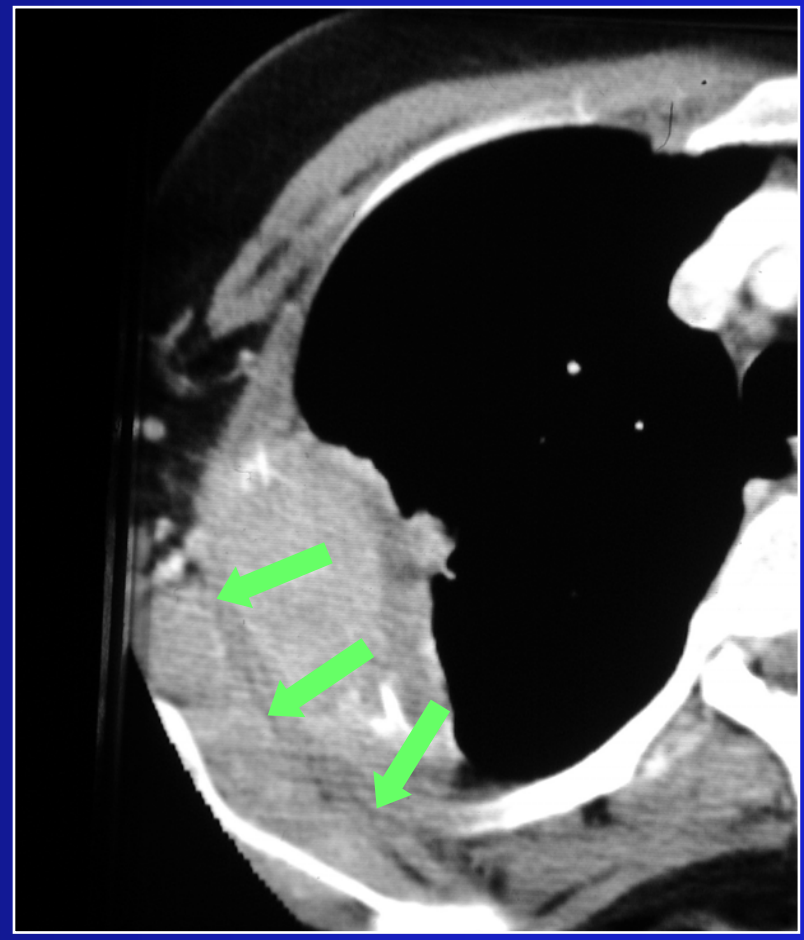
nodule(s) in the same lobe

Goldstraw P et al. The IASCLC lung cancer staging project: proposals for the revision of the TNM group stagings in the forthcoming (seventh) editon of the TNM classification of malignant tumours *J Thorac Oncol* 2007;2:706-714

Lung Cancer Staging

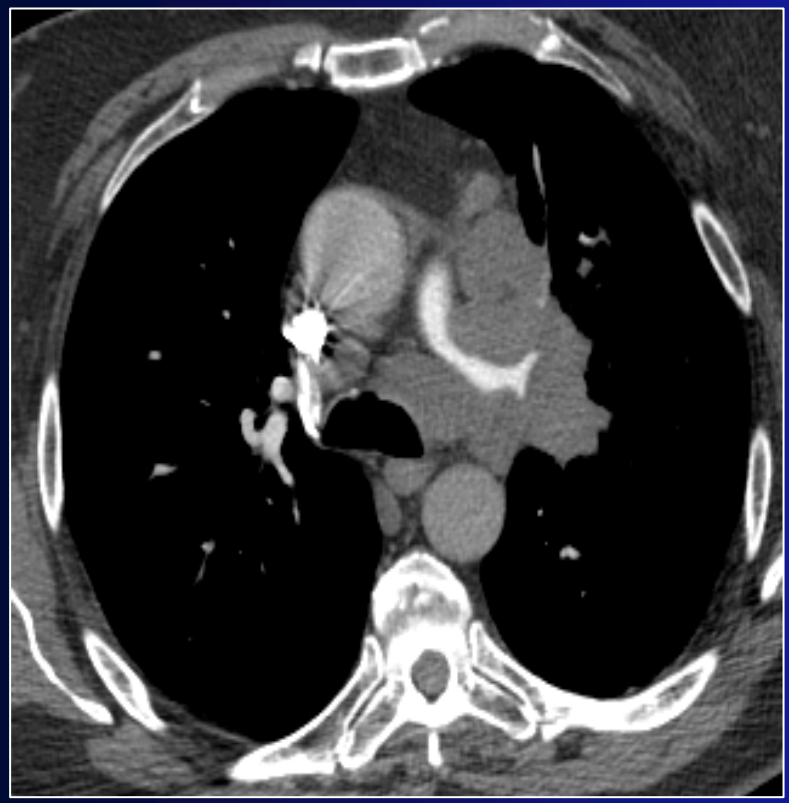
Unequivocal T3 Tumours

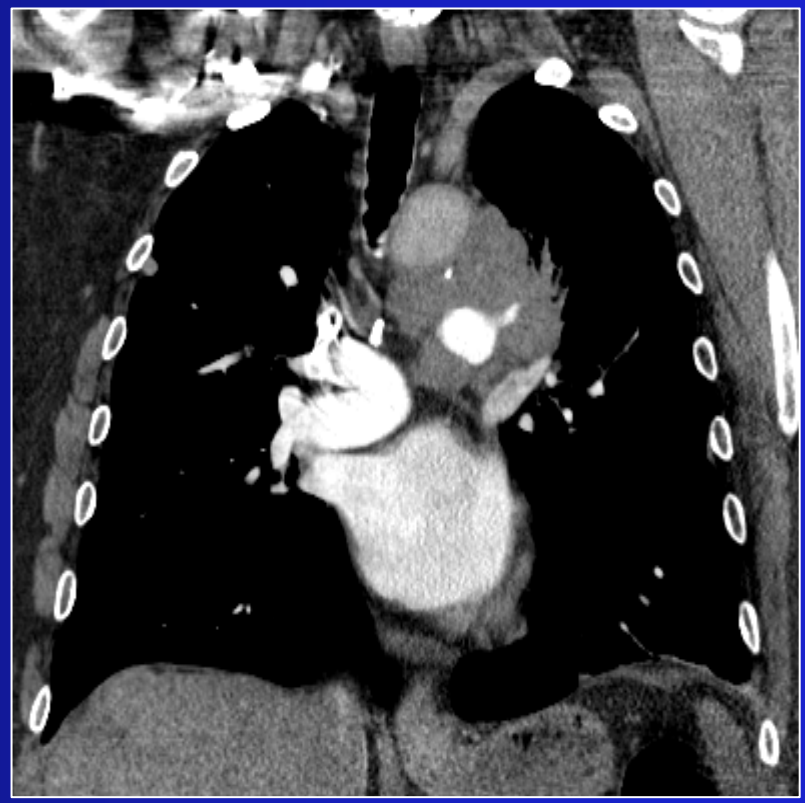




Lung Cancer Staging

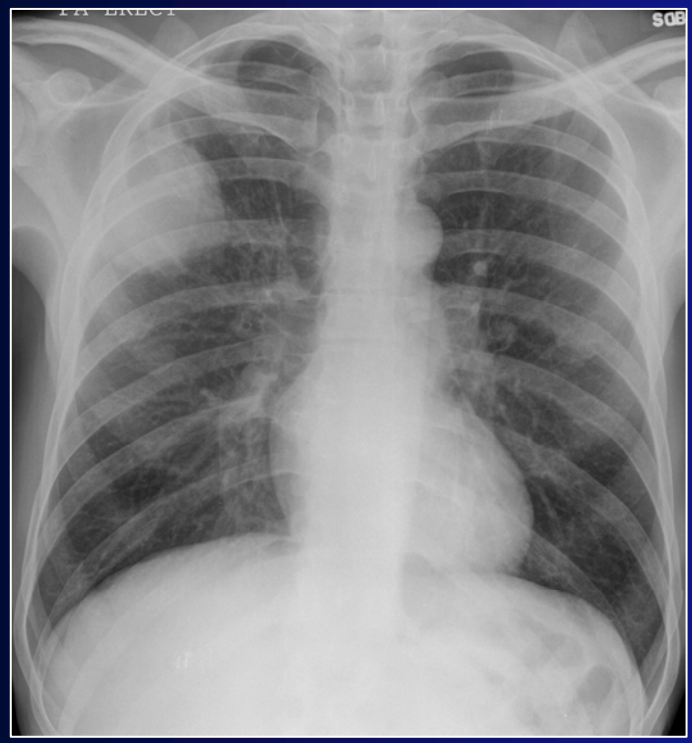
Unequivocal T3 Tumours



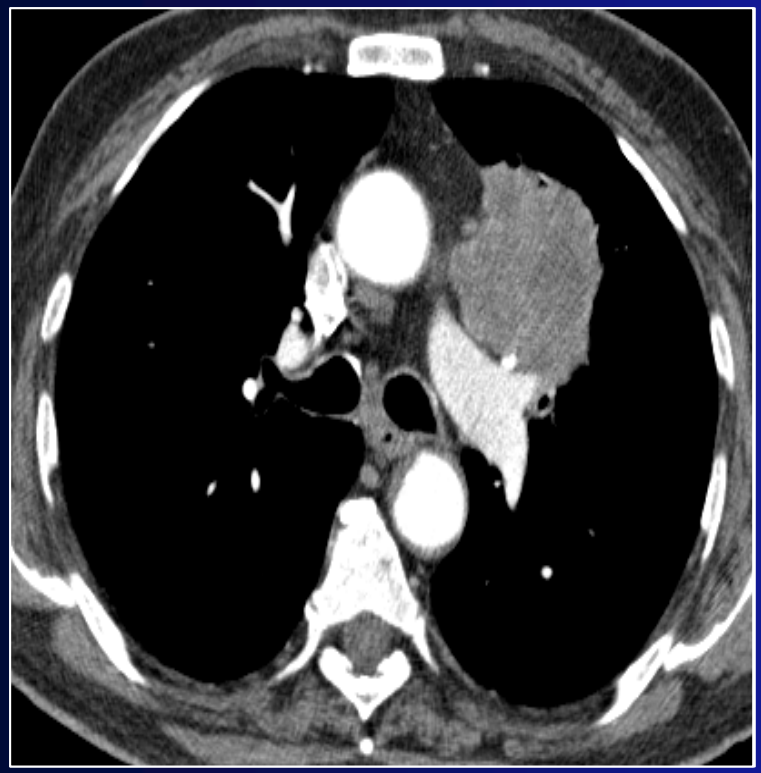


Lung Cancer Staging

Contentious T3 Tumours



Lung Cancer Staging
Contentious T3 Tumours



- *< 3cm mediastinal contact*
- *Preserved fat planes*
- *<90º circumferential contact*

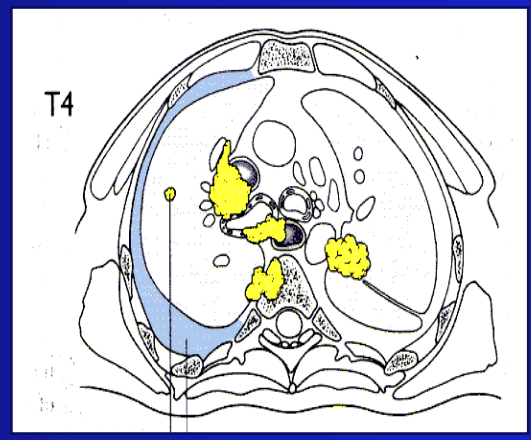
*Presence of at least one of these features predicts resectability (97%) **

[1] Glazer HS Indeterminate mediastinal invasion by bronchogenic carcinoma: CT evaluation *Radiology* 1989;173:37

Lung Cancer Staging

Key Changes to TNM-6

Tumour of any size but with invasion of: heart, great vessels, trachea, oesophagus, vertebral body, carina; tumour with malignant pleural / pericardial effusion; or with satellite tumour nodule(s) in ipsilateral primary-tumour lobe



T4

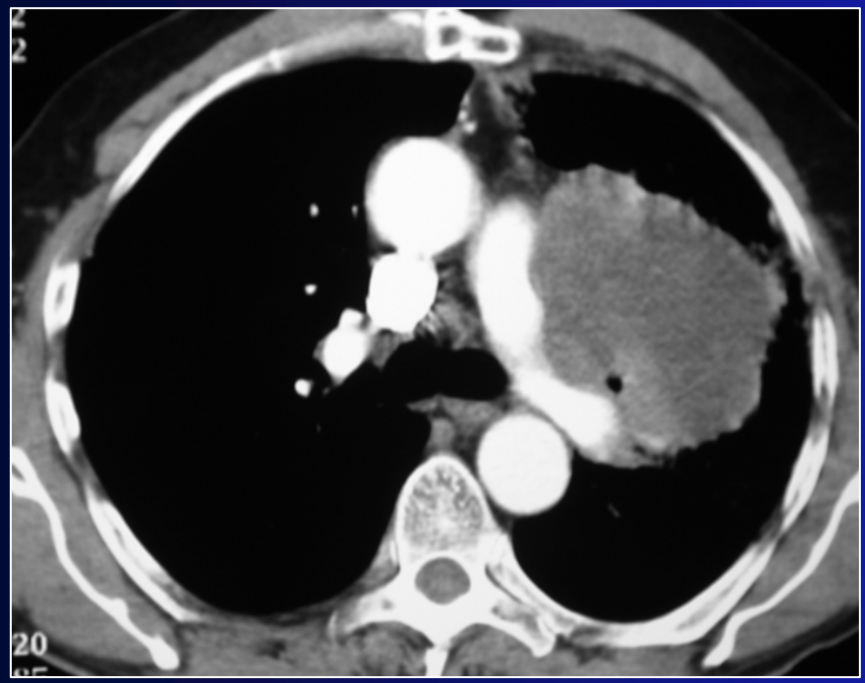
T4

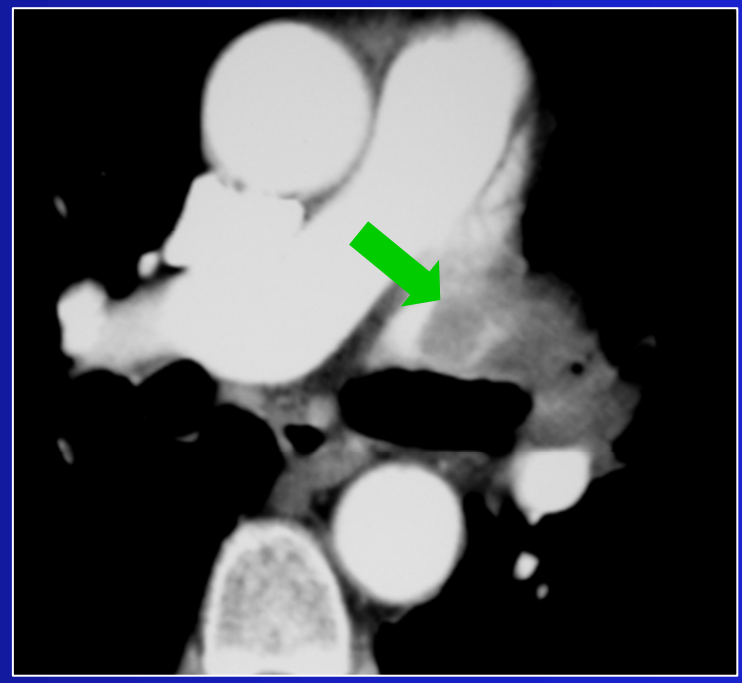
separate tumor nodule(s) in a different ipsilateral lobe

Groome PA et al. The IASCLC lung cancer staging project: validation of the proposals for revision of the T, N, and M descriptors and consequent stage groupings in the forthcoming (seventh) edition of TNM classification of malignant tumours *J Thorac Oncol* 2007;2:694-705

Lung Cancer Staging

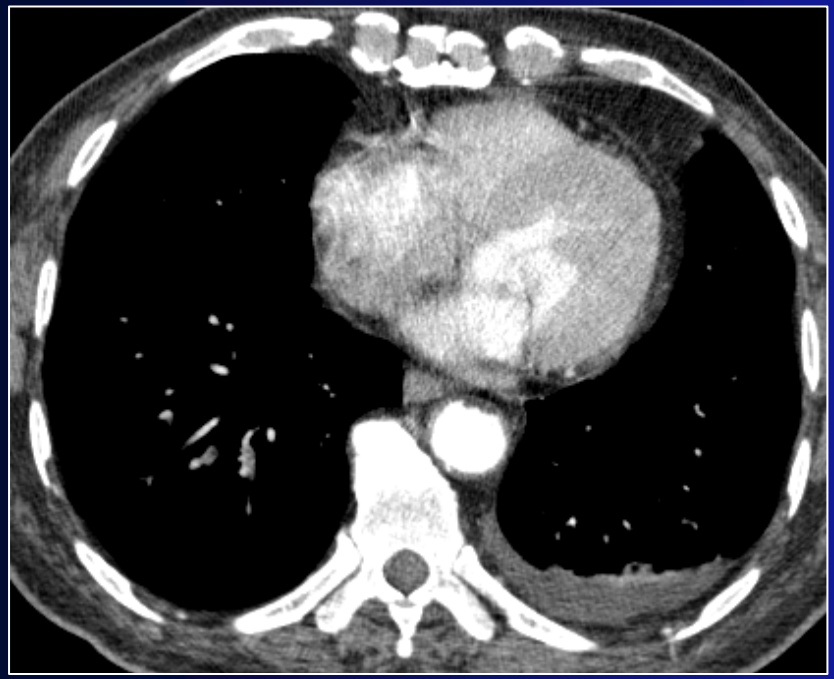
Unequivocal T4 Tumours





Lung Cancer Staging

Unequivocal T4 Tumours



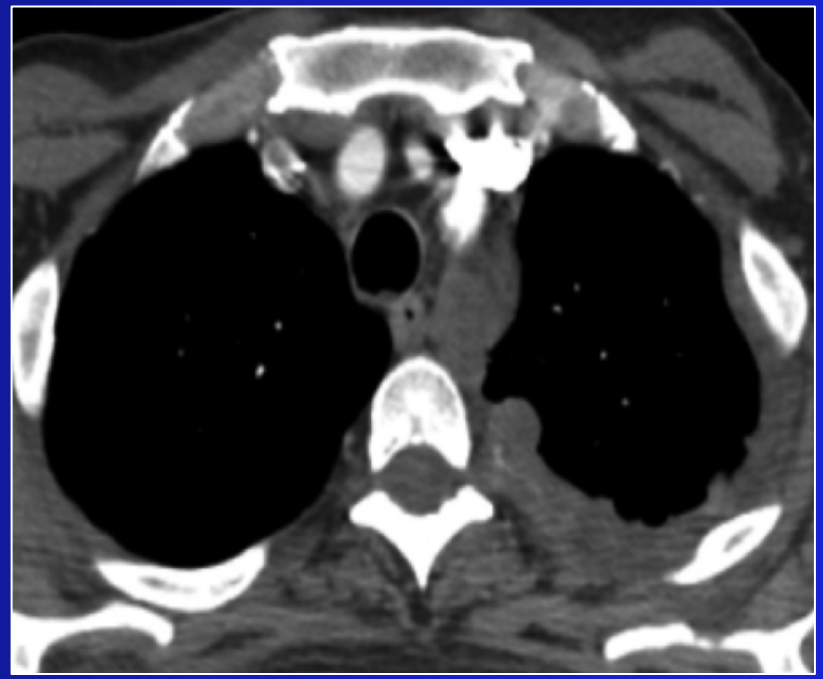


IMAGE FROM: Nair A et al. Revisions to the TNM staging of non-small cell lung cancer: rationale, clinicoradiologic implications, and persistent limitations *Radiographics* 2011;31:215-238

Lung Cancer Staging

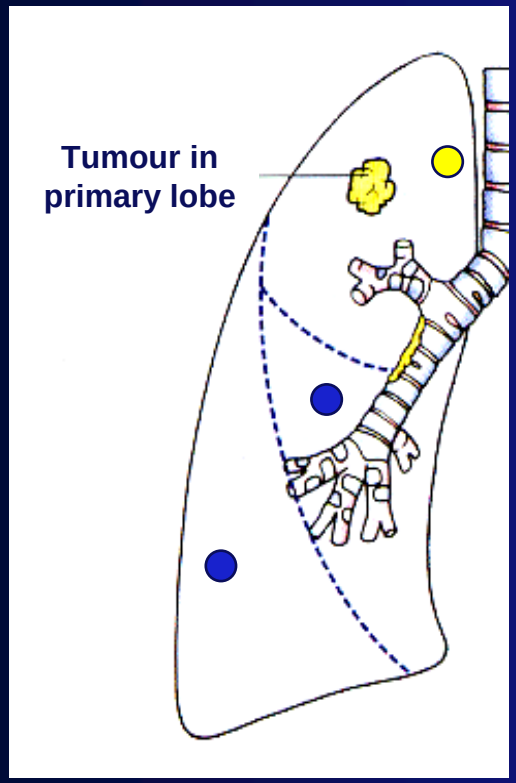
Key Changes to TNM-6

T4 Add Nodules, Same Lobe	59%	25%	vs T3:	0.70	<.0001
T4 by Other Factor	39%	7%	vs T4 Same Lobe:	1.88	<.0001

Groome PA et al. The IASCLC lung cancer staging project: validation of the proposals for revision of the T, N, and M descriptors and consequent stage groupings in the forthcoming (seventh) edition of TNM classification of malignant tumours *J Thorac Oncol* 2007;2:694-705

Lung Cancer Staging

Key Changes to TNM-6

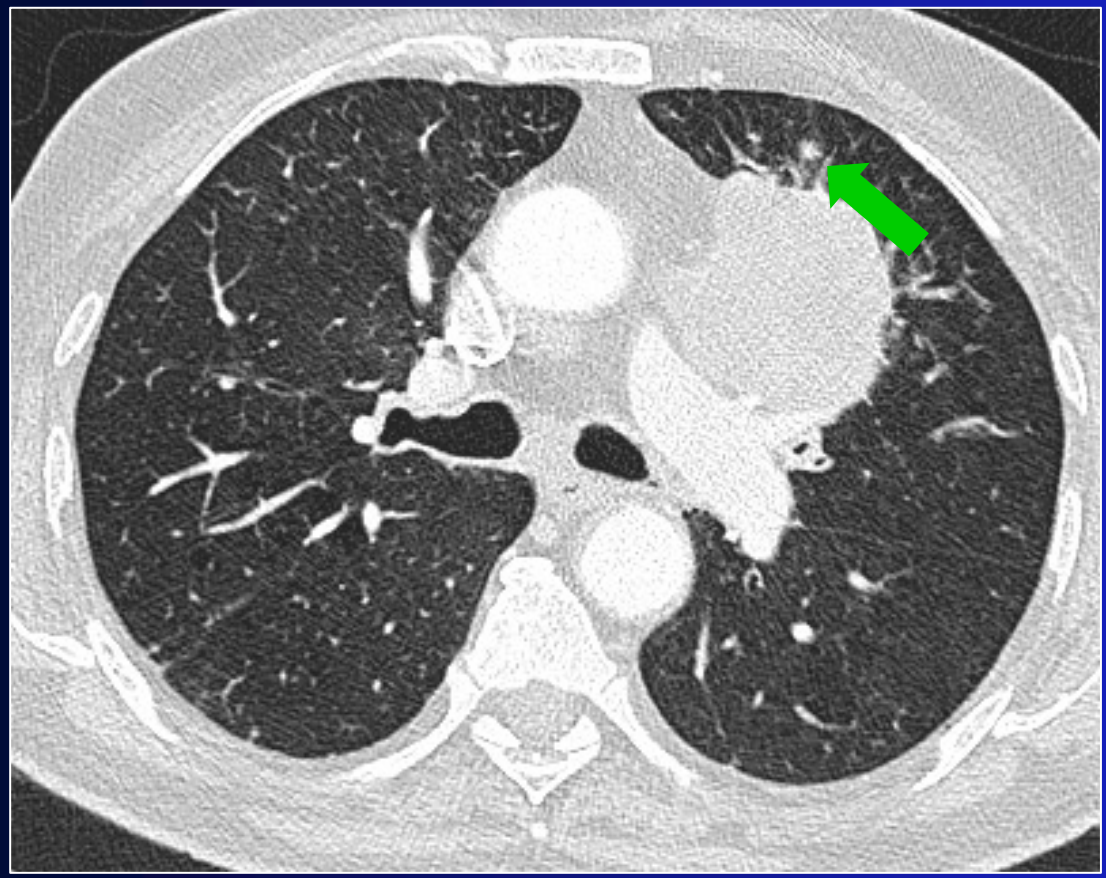


	TNM-6	TNM-7
	T4	T3
	M1	T4
OTHER LUNG	(M1	M1a)

Groome PA et al. The IASCLC lung cancer staging project: validation of the proposals for revision of the T, N, and M descriptors and consequent stage groupings in the forthcoming (seventh) edition of TNM classification of malignant tumours *J Thorac Oncol* 2007;2:694-705

Lung Cancer Staging

Key Changes to TNM-6



T3

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Lung Cancer Staging

Key Changes to TNM-6

Table 3
Survival Rates Associated with Various Pathologically Staged T Descriptors in TNM-6 and Their Corresponding TNM-7 Designations

TNM-6	5-year Survival Rate (%)	TNM-7
T1 (≤2 cm)	71	T1a*
T1 (>2 cm and ≤3 cm)	62	T1b*
T2 (>3 cm and ≤5 cm)	49	T2a*
T2 (>5 cm and ≤7 cm)	40	T2b*
T2 (>7 cm)	28	T3*
T3	31	T3
T4 (with a same-lobe nodule)	28	T3*
T4 (with factors other than a same-lobe nodule)	22	T4
M1 (with a nodule in a different lobe or the ipsilateral lung)	22	T4*
T4 (with pleural dissemination)	11	M1a*

FROM: Nair A et al. Revisions to the TNM staging of non-small cell lung cancer: rationale, clinicoradiologic implications, and persistent limitations *Radiographics* 2011;31:215-238

Lung Cancer Staging

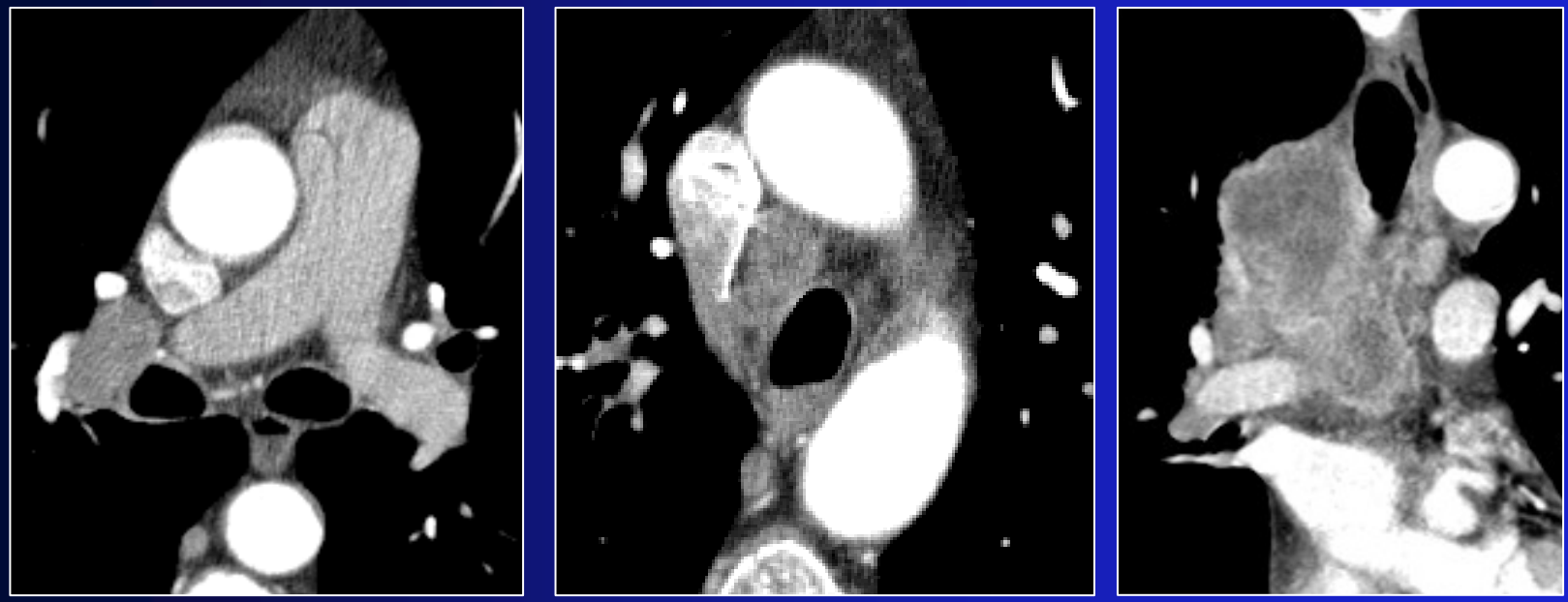
Nodal Staging

N (Regional Lymph Nodes)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

Goldstraw P et al. The IASCLC lung cancer staging project: proposals for the revision of the TNM group stagings in the forthcoming (seventh) editon of the TNM classification of malignant tumours *J Thorac Oncol* 2007;2:706-714

Lung Cancer Staging

Nodal Staging



N1

N2

Lung Cancer Staging

Nodal Staging Issues

- The reliance on size criteria (1cm CT cut-off)
- Variable dimensions of normal nodes (0.7-1.5 cm)
- “Small” nodes (<1cm) may harbour metastases
- Large nodes may be reactive

Lung Cancer Staging
Nodal Staging Issues: Value of PET

- 102 patients NSCLC
- "Standard" Staging -versus- Staging + PET
- Mediastinal LN and distant metastases

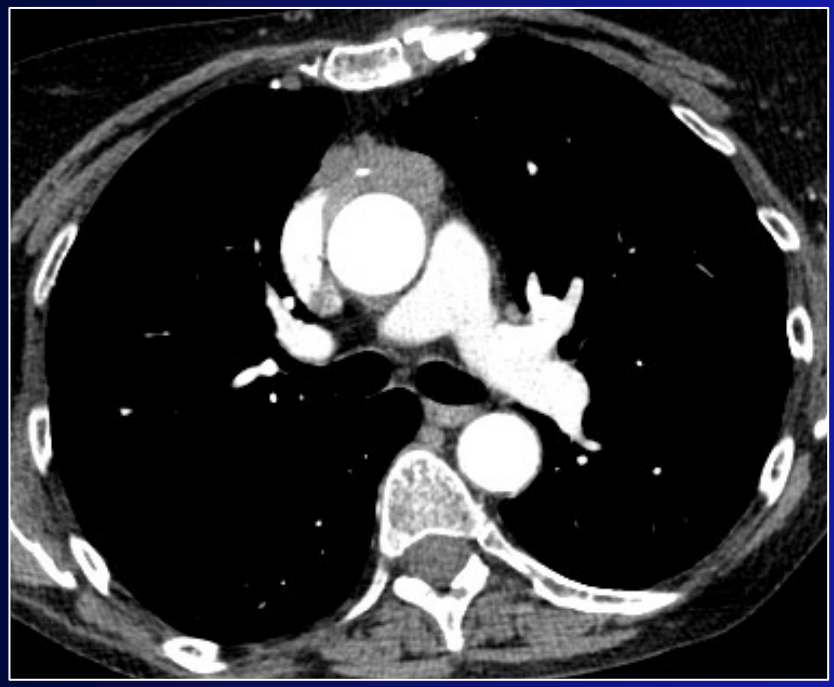
	PET	CT
Sensitivity	91	75
Specificity	86	66

PET → Different staging (cpd standard) in 62/102 patients;
Downstaging in 20 / Upstaging in 42

Pieterman RM et al. Pre-operative staging of non-small-cell lung cancer with positron-emission tomography *N Engl J Med* 2000;343:254

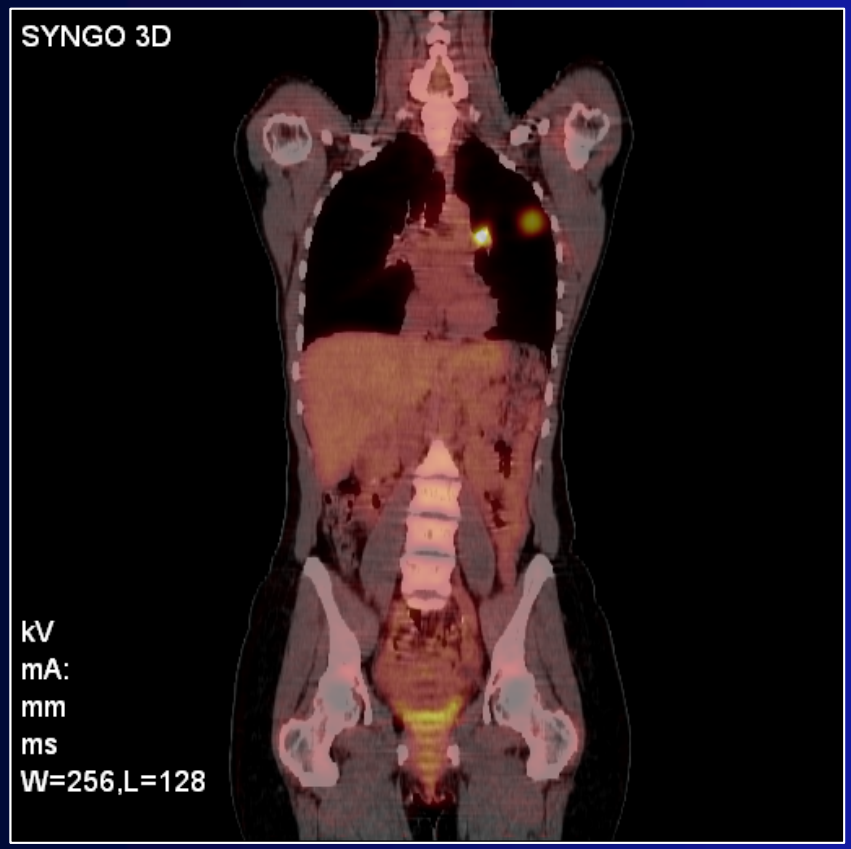
Lung Cancer Staging

Nodal Staging Issues: Value of PET, PET/CT



Lung Cancer Staging

Nodal Staging Issues: Value of PET, PET/CT



- **50 patients**
- **NSCLC**
- **Nodal staging**

- *PET/CT vs PET*
- *PET/CT vs CT*

PET / CT > PET
PET / CT = CT

Lardinois D et al. Staging of non-small-cell lung cancer with intergrated positron-emission tomography and computed tomography ***N Engl J Med*** 2003;348:2500-2507

Lung Cancer Staging

Nodal Staging: PET/CT vs CT vs "invasive" staging

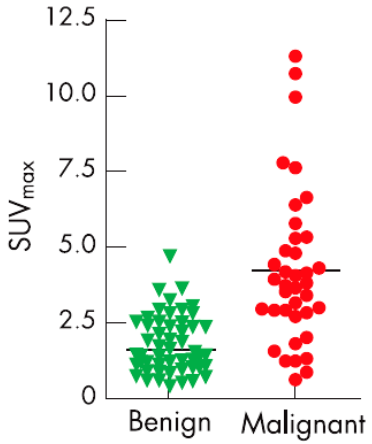
Table 1 Characteristics of patients and investigations

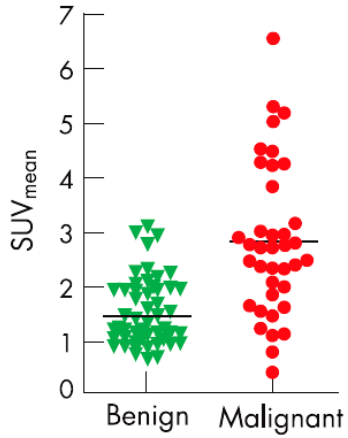
	n
Number of patients	52
Lymph nodes with pathology	105
Sex	
Male	39 (75%)
Female	13 (25%)
Median (range) age (years)	68 (48–80)

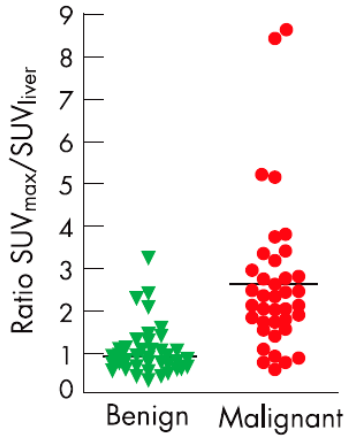
Tournoy KG et al. Integrated FDG-PET/CT does not make invasive staging of the intrathoracic lymph nodes in non-small cell lung cancer redundant: a prospective study ***Thorax*** 2007;62:696-701

Lung Cancer Staging

Nodal Staging: PET/CT vs CT vs "invasive" staging







Mean (SD)	SUV_{max}	SUV_{mean}	SUV_{max}/SUV_{liver}
Benign LNs N = 67 (64%)	1.69 (0.88)	1.39 (0.64)	0.94 (0.49)
Malignant LNs N = 38 (36%)	4.28 (2.59)*	2.84 (1.40)*	2.63 (1.79)*
Mann-Whitney U-test	$p < 0.001$	$p < 0.001$	$p < 0.001$

Tournoy KG et al. Integrated FDG-PET/CT does not make invasive staging of the intrathoracic lymph nodes in non-small cell lung cancer redundant: a prospective study ***Thorax*** 2007;62:696-701

Lung Cancer Staging

Nodal Staging: PET/CT vs CT vs "invasive" staging

	All lymph nodes n = 105
CT read-out	
CT positive (short axis range 10–40 mm)	58 (55%)
CT negative (short axis range 1–9 mm)	47 (45%)
CT sensitivity	84 (68–93)
CT specificity	61 (48–73)
CT LR+	2.17 (1.56–3.02)
CT LR–	0.26 (0.12–0.55)
PET/CT read-out	
PET/CT positive (fusion images)	42 (40%)
PET/CT negative (fusion images)	63 (60%)
PET/CT sensitivity	84 (68–93)
PET/CT specificity	85 (74–92)
PET/CT LR+	5.64 (3.13–10.16)
PET/CT LR–	0.19 (0.09–0.39)

SENSITIVITY

SPECIFICITY

Tournoy KG et al. Integrated FDG-PET/CT does not make invasive staging of the intrathoracic lymph nodes in non-small cell lung cancer redundant: a prospective study ***Thorax*** 2007;62:696-701

Lung Cancer Staging

Nodal Staging: PET/CT vs CT vs "invasive" staging

Negative Predictive Values:

- Small LN without FDG uptake 91%
- Large LN without FDG uptake 90%

Positive Predictive Values:

- Small LN with FDG uptake 50%
- Large LN with FDG uptake 79%

Tournoy KG et al. Integrated FDG-PET/CT does not make invasive staging of the intrathoracic lymph nodes in non-small cell lung cancer redundant: a prospective study ***Thorax*** 2007;62:696-701

Lung Cancer Staging

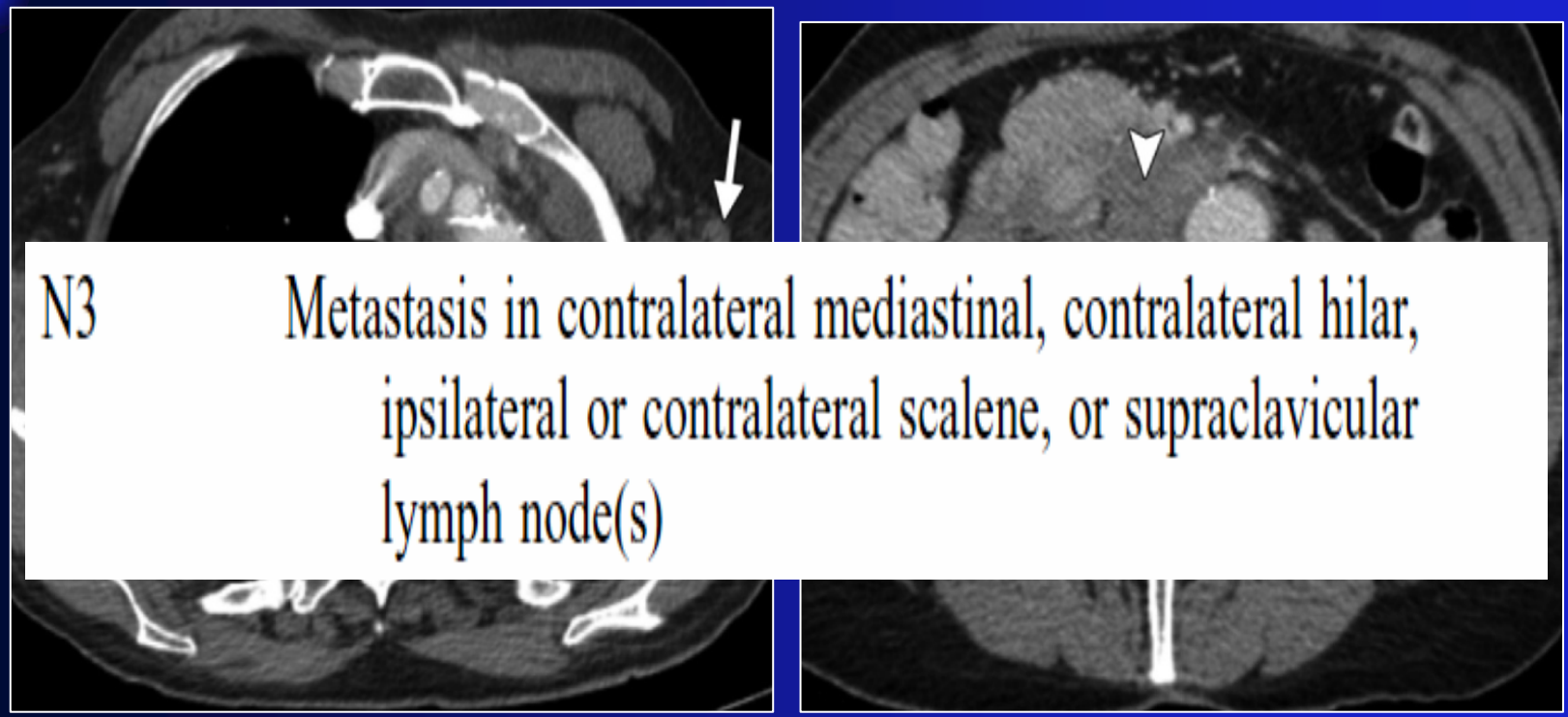
Nodal Staging: PET/CT vs CT vs "invasive" staging

In conclusion, integrated FDG-PET/CT scanning has an overall accuracy which is too low to replace invasive intrathoracic lymph node staging in patients with NSCLC.

Tournoy KG et al. Integrated FDG-PET/CT does not make invasive staging of the intrathoracic lymph nodes in non-small cell lung cancer redundant: a prospective study ***Thorax*** 2007;62:696-701

Lung Cancer Staging

Nodal Staging Issues



N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

N3 or M1?

IMAGE FROM: Nair A et al. Revisions to the TNM staging of non-small cell lung cancer: rationale, clinicoradiologic implications, and persistent limitations *Radiographics* 2011;31:215-238

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Metastatic Disease

M (Distant Metastasis)	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant pleural (or pericardial) effusion[b]
M1b	Distant metastasis

Goldstraw P et al. The IASCLC lung cancer staging project: proposals for the revision of the TNM group stagings in the forthcoming (seventh) editon of the TNM classification of malignant tumours *J Thorac Oncol* 2007;2:706-714

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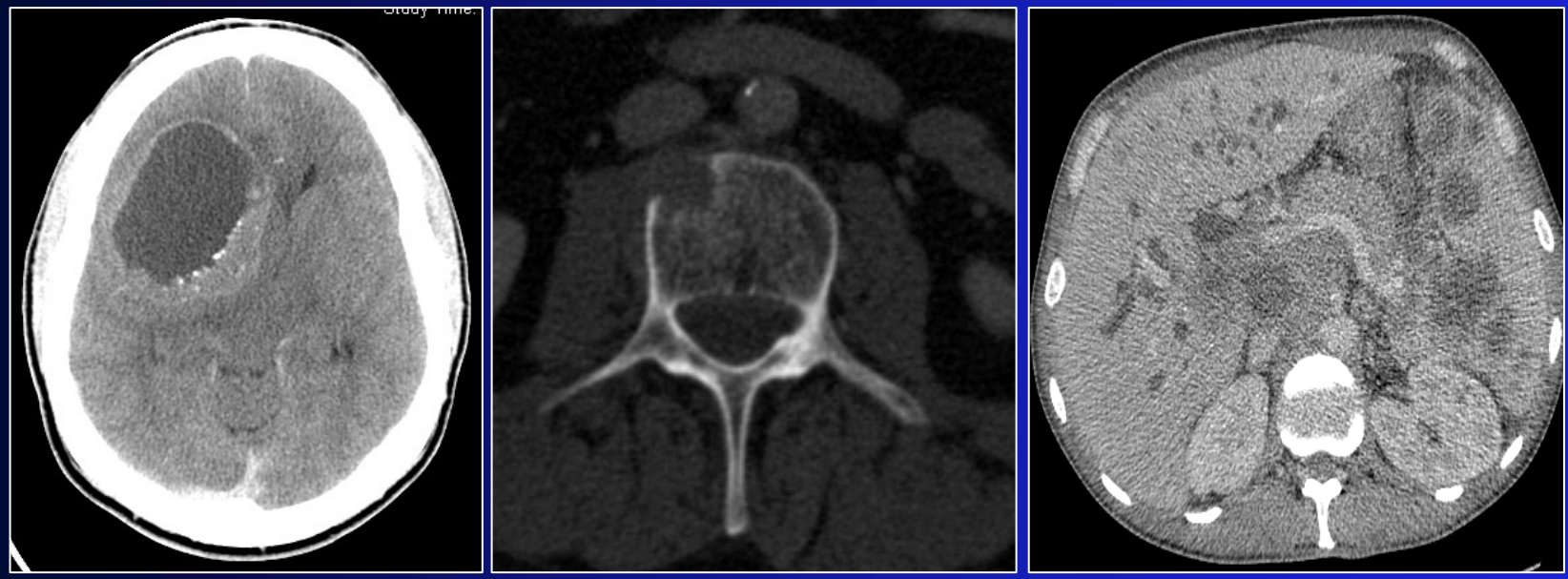
Metastatic Disease



- **Liver** 33-39%
- **Adrenals** 20-33%
- **Brain** 16-26%
- **Bone** 15-21%

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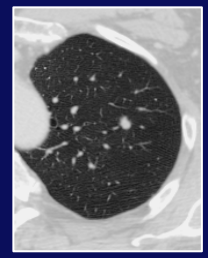
Summary



- Lung cancer staging is an important component of management
- New revisions to the existing TNM-6 descriptors are an improvement: based on larger numbers, multiple centre and “validated”
- Limitations and uncertainties exist in the radiological staging of disease

An Invitation in 2012