

Mediastinale (her)stadiering dmv beeldvorming

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Imaging for mediastinal staging

- **Computer tomography**
 - Based on size criteria (> 10 mm short axis)
- **FDG-PET**
 - Based on increased glycolysis of cancer cells
- **Magnetic Resonance Imaging**
 - Size (T1)
 - Morphology (T2)(cortical thickening, obliteration of fatty hilum)
 - USPIO
 - Diffusion

PET for N-staging

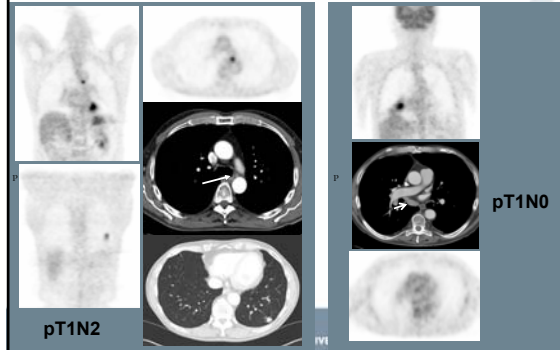
Meta analysis Gould et al. Annals of Internal Medicine 2003

Table. Summary of Meta-Analysis Results*

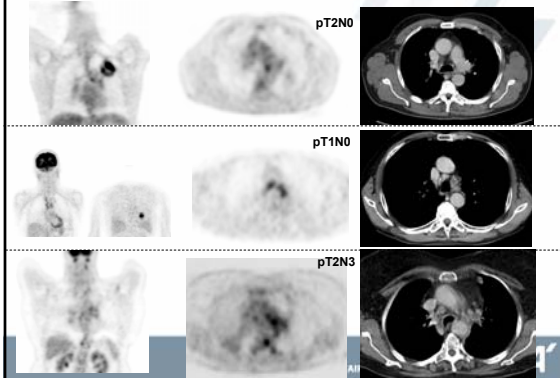
Variable	Median Sensitivity (95% CI)	Median Specificity (95% CI)	Maximum Joint Sensitivity and Specificity (95% CI)†	Sensitivity at Point on Summary ROC Curve Corresponding to Median Specificity (95% CI)	Specificity at Point on Summary ROC Curve Corresponding to Median Sensitivity (95% CI)	Likelihood Ratio for Positive Tests	Likelihood Ratio for Negative Tests
CT							
All studies (1119 patients in 23 studies)	61 (50-71)	79 (66-89)	70 (67-73)	59 (52-66)	79 (72-83)	2.8	0.5
PET							
All studies (1369 patients in 32 studies)	85 (82-91)	90 (82-96)	86 (84-88)	81 (74-86)	86 (81-90)	8.1	0.2
Patients with enlarged lymph nodes on CT (214 patients in 12 studies)	100 (90-100)	78 (68-100)	85 (79-90)	91 (79-96)	NC	4.1	0.1
Patients without enlarged lymph nodes on CT (1479 patients in 14 studies)	82 (65-100)	93 (92-100)	87 (84-89)	75 (59-87)	90 (82-95)	10.7	0.3

* CT = computed tomography; IQR = interquartile range; NC = not able to calculate; PET = positron emission tomography; ROC = receiver operating characteristic.
† The maximum joint sensitivity and specificity is the point on the summary ROC curve at which sensitivity and specificity are equal; it is a global measure of test performance, similar to the size under the curve, and does not necessarily represent the optimal operating point or the one applied to everyday clinical practice.
‡ To calculate likelihood ratios, we used the point on the summary ROC curve that corresponded to the median specificity.

PET for N-staging



DD malignant vs benign LN



PET for N-staging

- **Pitfalls**
 - Minimal disease → false negative
 - Inflammatory disease → false positives
 - Limited spatial resolution → N1 vs N2, central T

Impact of size of metastatic foci

Nomori et al, J. Thorac cardiovasc Surg 2004

TABLE 5. Diagnostic results of PET and CT scanning

Variable	PET	CT	Difference
Sensitivity	0.78	0.53	$P = .026$
Specificity	0.98	0.98	0.63
Accuracy	0.97	0.96	0.28
Positive predictive value	0.74	0.76	0.77
Negative predictive value	0.98	0.97	0.06

PET, Positron emission tomography; CT, computed tomography.

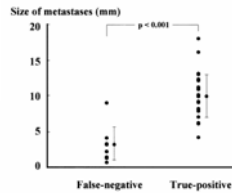
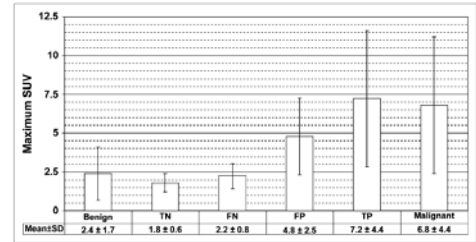


Figure 2. The distribution of sizes of metastatic foci in false-negative and true-positive lymph nodes with PET scan.

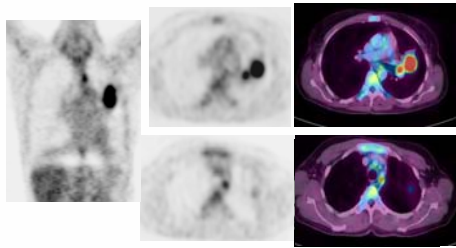
Definition of PET+LN

Hellwig et al, JNM 2007

Retrospective analysis of 95 patients with suspected NSCLC and underwent mediastinoscopy and had PET prior to surgery
Comparison of visual analysis (> mediastinal BG) and SUV max LN



PET for N-staging Impact of integrated PET-CT



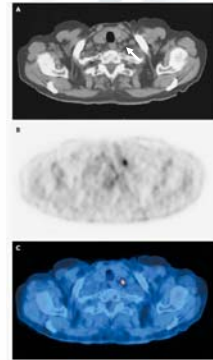
pT2N1

Staging of Non-Small-Cell Lung Cancer with Integrated Positron-Emission Tomography and Computed Tomography

Diller Ludovini, M.D., Walter Weber, M.D., Thomas F. Hany, M.D., Erik M. Karner, M.D., Stephan Koenig, M.D., Burkhard Seifert, Ph.D., Gosta K. von Schulthess, M.D., Ph.D., and Hans C. Simon, M.D.

Table 3. Diagnostic Accuracy of the Imaging Methods with Respect to Node Stages in 17 Patients.

Imaging Method	Classification		
	Correct (Score of 3)	Correct but Equivocal (Score of 2)	Incorrect (Score of 1 or 0)
CT alone	22 (59)	2 (5)	13 (35)
PET alone	18 (49)	14 (38)	3 (14)
Visual comparison of PET and CT	22 (59)	4 (11)	11 (30)
Integrated PET-CT	30 (81)	1 (3)	6 (16)



Preoperative Staging of Lung Cancer with Combined PET-CT

Barbara Fischer, Ph.D., Ulrik Lassen, Ph.D., Jann Morten

1. Reduction number of thoracotomies
20/91 (22%) → 38/98 (39%)

2. Reduction number of futile thoracotomies
21/60 (35%) → 38/73 (52%)

Table 3. Distribution of Futile Thoracotomies.*

Characteristic	PET-CT	Conventional Staging	Total
Futile thoracotomy			
No	39 (85)	35 (48)	74 (56)
Yes	21 (35)	38 (52)	59 (44)
Total	60 (100)	73 (100)	133 (100)
Reason that thoracotomy was considered futile			
Exploratory thoracotomy	5 (24)	4 (11)	9 (15)
Benign lung lesion	0	3 (8)	3 (5)
Stage IV disease	3 (14)	0	3 (5)
Stage IIIb disease	4 (19)	8 (21)	12 (20)
Stage IIIa (N2) disease	5 (24)	6 (16)	11 (19)
Recurrence within 12 mo	3 (14)	13 (34)	16 (27)
Death within 12 mo	1 (5)	4 (11)	5 (8)
Total	21 (100)	38 (100)	59 (100)

PET for N-staging Impact of integrated PET-CT

Lee et al. (Journal of Thoracic and cardiovascular surgery 2007)

Comparison of PET (n=210) and integrated PET-CT (n=126) with ISS
Definition of PET+ = visual (> mediastinal BG)

TABLE 4. Efficacy of mediastinal staging by PET versus PET/CT

	Standard PET (n = 210)	Integrated PET/CT (n = 126)	P value*
Sensitivity (%; 95% CI)	61.1 (43.5-76.3)	85.7 (87.3-96.0)	.0299
Specificity (%; 95% CI)	94.3 (89.3-97.2)	80.6 (71.4-87.9)	.0005
Positive predictive value (%; 95% CI)	68.8 (50.0-83.3)	55.8 (38.9-70.9)	.2552
Negative predictive value (%; 95% CI)	92.1 (87.2-95.6)	95.2 (88.1-98.7)	.3658
Accuracy (%; 95% CI)	88.6 (87.2-95.6)	81.7 (88.1-98.7)	.0808

TABLE 5. Analysis of operations performed

	Standard PET (n = 210)	Integrated PET/CT (n = 126)
Mediastinoscopy or mediastinotomy (No., %)	33 (16)	25 (20)
Mediastinoscopy followed by thoracotomy (No., %)	51 (24)	44 (35)
Thoracotomy (No., %)	126 (60)	57 (45)

PET, Positron emission tomography; CT, computed tomography; P value for χ^2 test = .028.

PET, Positron emission tomography; CT, computed tomography; CI, confidence interval. *P value for χ^2 test.

PET for N-Staging

Langen et al, Eur J Cardio Thor Surgery 2006

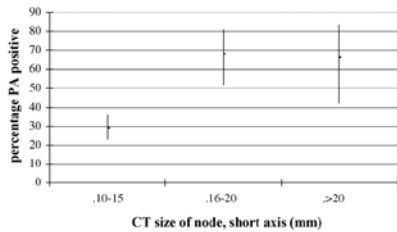


Fig. 2. Pooled values of metastatic involvement of CT-based lymph node size categories (error bars represent 95% CIs).

PET for N-staging

Langen et al, Eur J Cardio Thor Surgery 2006

Table 2
Predicted positive and negative values of FDG-PET in patients with enlarged lymph nodes of different size categories, assuming FDG-PET sensitivity of 91% and specificity of 78% for enlarged nodes [4]

Lymph node size category	NPV (%)	PPV (%)
CT 10–15 mm	95	62
CT 16–20 mm	81	90
CT >20 mm, with outlier	82	90
CT >20 mm, without outlier	80	90

NPV: negative predictive value; PPV: positive predictive value.

PET for N-staging Predictors of false negative PET

Al-Sarraf et al. (Eur J of cardiothoracic Surgery, 2008)

Retrospective analysis in patients who underwent direct thoracotomy after a negative mediastinal PET-CT and were found to have occult N2 disease PET+ if SUV max >2.5

N= 153; occult N2 in 25 (16%) especially ATS 7 and 4R

Univariate analyse

Central tumour p=0.049
RUL p=0.040
Enlarged LN on CT p=0.048
PET N1 p=0.006

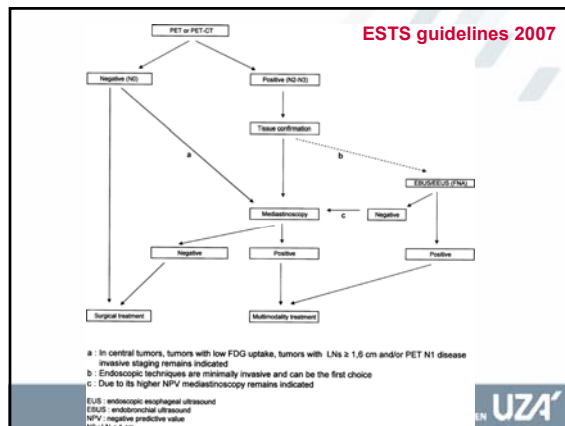
Histology, T stage, differentiation, SUV max primary p=NS

Multivariate analysis

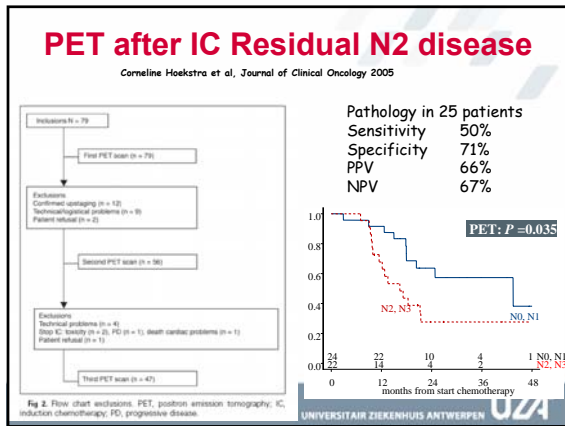
Central T, RUL and PET N1

PET for N- staging Conclusions

- High NPV of PET-CT in LN staging
-> omit invasive tests
- BUT "side conditions"
 - adequate FDG-uptake of primary tumour
 - caution with central tumours and hilar N1 disease
 - Large nodes on CT
- Always confirm PET+ nodes histologically
 - PET and EBUS/EUS are complementary



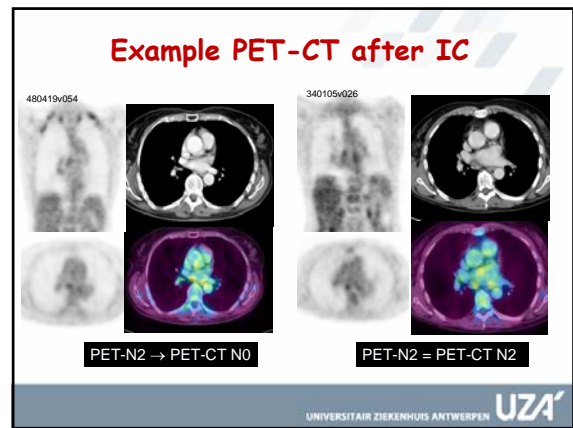
PET for mediastinal restaging



PET for N-restaging

Study	Year	N	Stage	CRTR	Imaging	Sensitivity	Specificity
Vansteenkiste et al.	2001	31	IIIA-N2	0%	PET + CT (visual corr.)	71%	88%
Akhurst et al.	2002	56	I-III	29%	PET + CT (visual corr.)	67%	61%
Ryu et al.	2002	26	III	100%	PET + CT (visual corr.)	58%	93%
Cerfolio et al.	2003	34	IB-IIIA	21%	PET + CT (visual corr.)	50%	99%
Hellwig et al.	2004	37	III	70%	PET + CT (visual corr.)	50%	88%
Port et al.	2004	25	I-IIIA	0%	PET + CT (visual corr.)	20%	71%
Hoekstra et al.	2005	25	IIIA-N2	0%	PET + CT (visual corr.)	50%	71%
Cerfolio et al.	2006	93	IIIA-N2	100%	Integrated PET-CT	62%	88%
Pottgen et al.	2006	37	IIIA/B	100%	Integrated PET-CT	73%	89%
De Leyn et al.	2006	30	IIIA-N2	0%	Integrated PET-CT	77%	92%

- ### Mediastinal downstaging after IC
- De Leyn et al, JCO 2006
 - Prospective study
 - 30 patients stage IIIA-N2 NSCLC
 - Cisplatin based IC
 - PET-CT after IC prior to surgery
 - Re - mediastinoscopy
 - Lymphadenectomy at surgery



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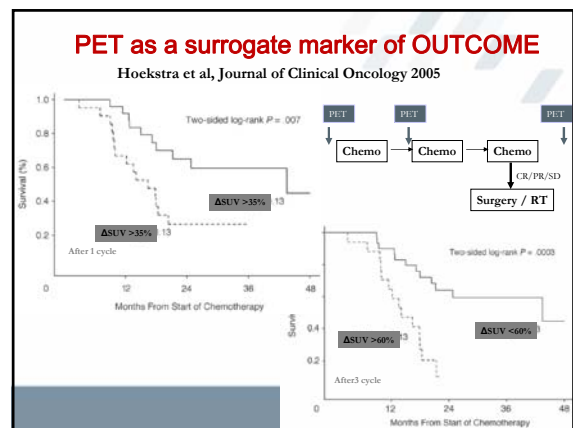
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

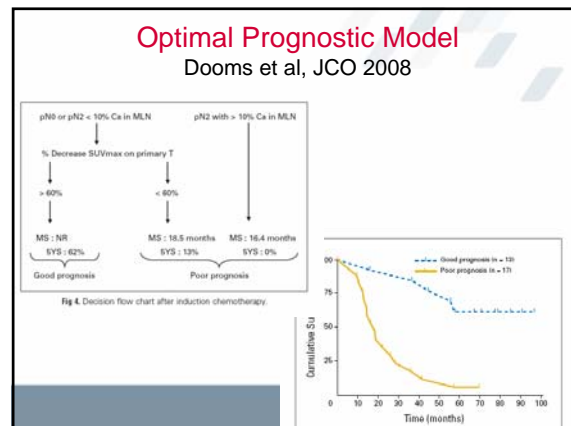
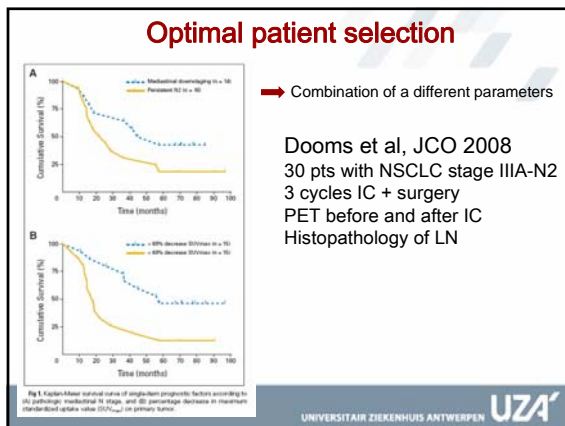
Prospective Comparative Study of Integrated Positron Emission Tomography-Computed Tomography Scan Compared With Remediastinoscopy in the Assessment of Residual Mediastinal Lymph Node Disease After Induction Chemotherapy for Mediastinoscopy-Proven Stage IIIA-N2 Non-Small-Cell Lung Cancer: A Leuven Lung Cancer Group Study

Roel De Leyn, Sigrid Stroobants, Walter De Weert, Tom Leyn, Willy Coenenmans, Georges Decker, Philippe Noffels, Dirk Van Raemdonck, Luc Mortelmans, Kristiaan Nackaerts, and Johan Vansteenkiste

Test	CT Alone (%)	PET Alone (%)	PET-CT (%)
Sensitivity	59	71	77
Specificity	62	69	92
Accuracy	60	70	83
PPV	66	75	93
NPV	53	64	75

Abbreviations: CT, computed tomography; PET, positron emission tomography; PPV, positive predictive value; NPV, negative predictive value.





PET for Restaging in NSCLC

- Lower accuracy for detection of mediastinal involvement compared to chemo-naïve patients
 - Use of other modalities
 - eg. PET-CT + EBUS/EUS upfront, re-mediastino after
- Promising results as prognostic marker
 - Validation in a multicenter setting

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