XXXII CONGRESSO NAZIONALE AIRO
XXXIII CONGRESSO NAZIONALE AIRB
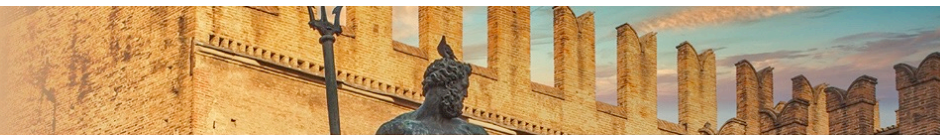XII CONGRESSO NAZIONALE AIRO GIOVANI

# AIRO2022

Radioterapia di precisione per un'oncologia innovativa e sostenibile

BOLOGNA, 25-27 NOVEMBRE
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e Oncologia
clinica

# DICHIARAZIONE

## PIERO CANDOLI

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario  Nessuna

- Consulenza ad aziende con interessi commerciali in campo sanitario **Niente da dichiarare**

- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **Niente da dichiarare**

- Partecipazione ad Advisory Board **AZ, COOK, PENTAX**

- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **Niente da dichiarare**

- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **Niente da dichiarare**

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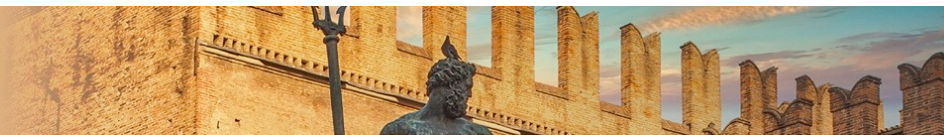# La stadiazione mediastinica nel NSCLC III° stadio inoperabile

*PIERO CANDOLI, MD*

*Dipartimento Cardio Toraco Vascolare*
*UOC Pneumologia Interventistica*
*IRCCS - Azienda Ospedaliero-Universitaria Bologna*

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# NSCLC or not NSCLC??
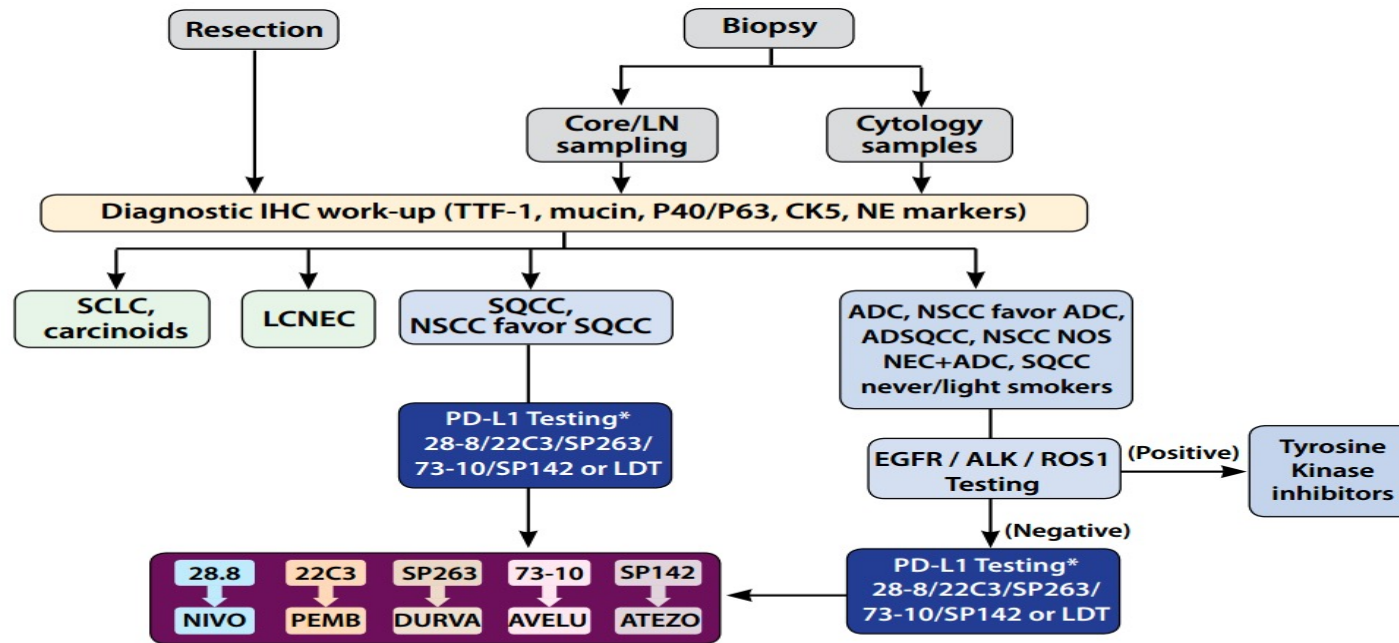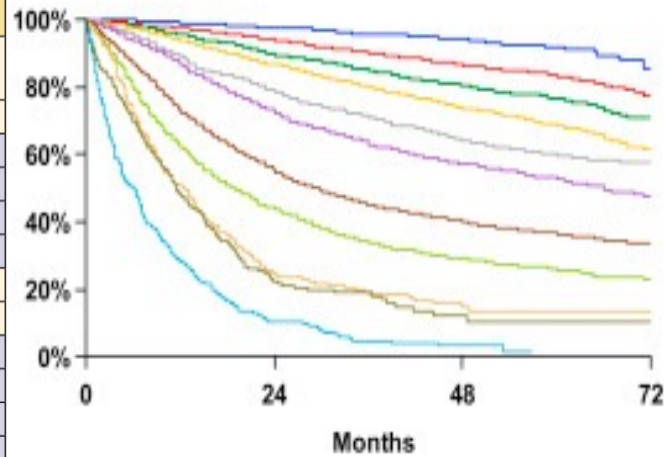
THAT WAS THE QUESTION....

**Figure 1.** Immunohistochemistry (IHC) tests that are integral to diagnostic considerations in the treatment of patients with of lung cancer. LN = lymph node, TTF-1 = thyroid transcription factor-1, CK5 = cytokeratin 5, NE = neuroendocrine, SCLC = small cell lung cancer, LCNEC = large cell neuroendocrine carcinoma, SQCC = squamous cell carcinoma, NSCC = non-small cell carcinoma, ADC = adenocarcinoma, ADSQCC = adenosquamous cell carcinoma, NEC = neuroendocrine cancer, PD-L1 = programmed cell death ligand-1, TKI = tyrosine kinase inhibitor, EGFR = epidermal growth factor receptor, ALK = anaplastic lymphoma kinase, NIVO = nivolumab, PEMB = pembrolizumab, DURVA = durvalumab, AVELU = avelumumab, ATEZO = atezolizumab, LDT = laboratory developed test. *Only the 22C3 assay is required as a companion diagnostic for first-line and second/third- line pembrolizumab therapy. The other assays are for clinical trials or complementary diagnostics.

| STAGE | T | N | M |
|---|---|---|---|
| Occult carcinoma | TX | N0 | M0 |
| 0 | Tis | N0 | M0 |
| IA1 | T1mi | N0 | M0 |
| | T1a | N0 | M0 |
| IA2 | T1b | N0 | M0 |
| IA3 | T1c | N0 | M0 |
| IB | T2a | N0 | M0 |
| IIA | T2b | N0 | M0 |
| IIB | T1a | N1 | M0 |
| | T1b | N1 | M0 |
| | T1c | N1 | M0 |
| | T2a | N1 | M0 |
| | T2b | N1 | M0 |
| | T3 | N0 | M0 |
| IIIA | T1a | N2 | M0 |
| | T1b | N2 | M0 |
| | T1c | N2 | M0 |
| | T2a | N2 | M0 |
| | T2b | N2 | M0 |
| | T3 | N1 | M0 |
| | T4 | N0 | M0 |
| | T4 | N1 | M0 |
| IIIB | T1a | N3 | M0 |
| | T1b | N3 | M0 |
| | T1c | N3 | M0 |
| | T2a | N3 | M0 |
| | T2b | N3 | M0 |
| | T3 | N2 | M0 |
| | T4 | N2 | M0 |
| IIIC | T3 | N3 | M0 |
| | T4 | N3 | M0 |
| IVA | Any T | Any N | M1a |
| | Any T | Any N | M1b |
| IVB | Any T | Any N | M1c |



| Proposed | Events / N | MST | 24 Month | 60 Month |
|---|---|---|---|---|
| IA1 | 68 / 781 | NR | 97% | 92% |
| IA2 | 505 / 3105 | NR | 94% | 83% |
| IA3 | 546 / 2417 | NR | 90% | 77% |
| IB | 560 / 1928 | NR | 87% | 68% |
| IIA | 215 / 585 | NR | 79% | 60% |
| IIB | 605 / 1453 | 66.0 | 72% | 53% |
| IIIA | 2052 / 3200 | 29.3 | 55% | 36% |
| IIIB | 1551 / 2140 | 19.0 | 44% | 26% |
| IIIC | 631 / 996 | 12.6 | 24% | 13% |
| IVA | 336 / 484 | 11.5 | 23% | 10% |
| IVB | 328 / 398 | 6.0 | 10% | 0% |



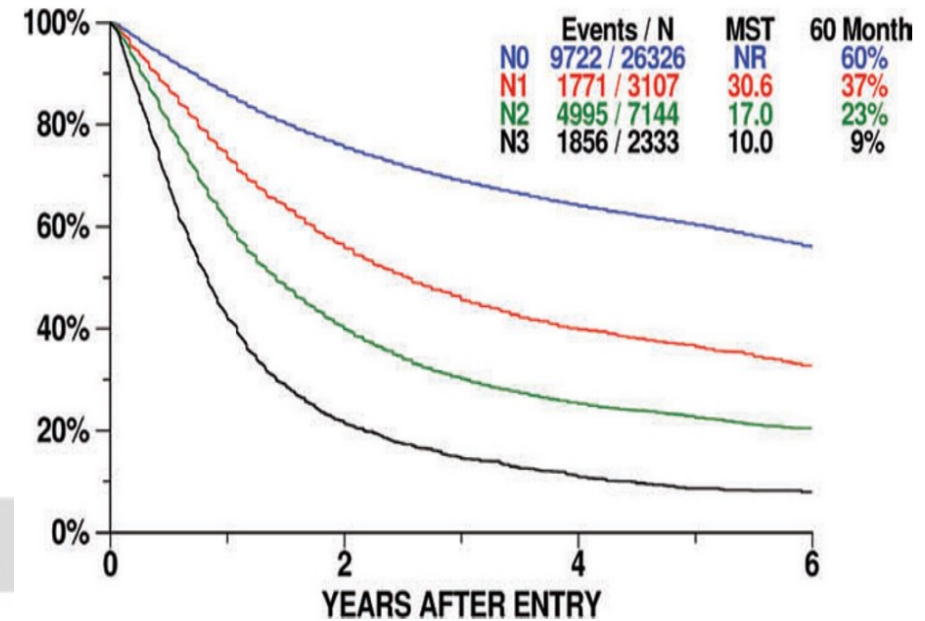| | Events / N | MST | 60 Month |
|---|---|---|---|
| N0 | 9722 / 26326 | NR | 60% |
| N1 | 1771 / 3107 | 30.6 | 37% |
| N2 | 4995 / 7144 | 17.0 | 23% |
| N3 | 1856 / 2333 | 10.0 | 9% |

FIGURE 1. Survival curves for cN0, cN1, cN2, and cN3, T-any M0 tumors. The differences of survival between neighboring categories are all statistically significant (p values: between cN0 and cN1, p < 0.0001; between cN1 and cN2, p < 0.0001; between cN2 and cN3, p < 0.0001).
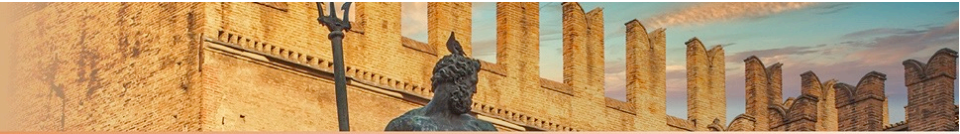
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# APPROCCIO DIAGNOSTICO AI LINFONODI MEDIASTINICI

## TECNICHE NON INVASIVE:

- **CT**
- **PET**

## TECNICHE INVASIVE:

- **ENDOSCOPIC (TBNA, EBUS-TBNA, EUS-NA)**
- **SURGICAL (MEDIASTINOSCOPY/TOMY, VATS)**
- **TRANSTHORACIC (TTNA)**

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# Thoroughness of Mediastinal Staging in Stage IIIA Non-small Cell Lung Cancer

Michael T. Vest, DO,* Lynn Tanoue, MD,* Pamela R. Soulos, MPH,† Anthony W. Kim, MD,‡
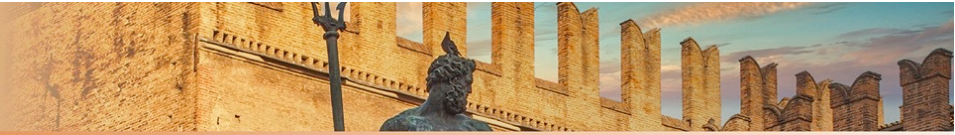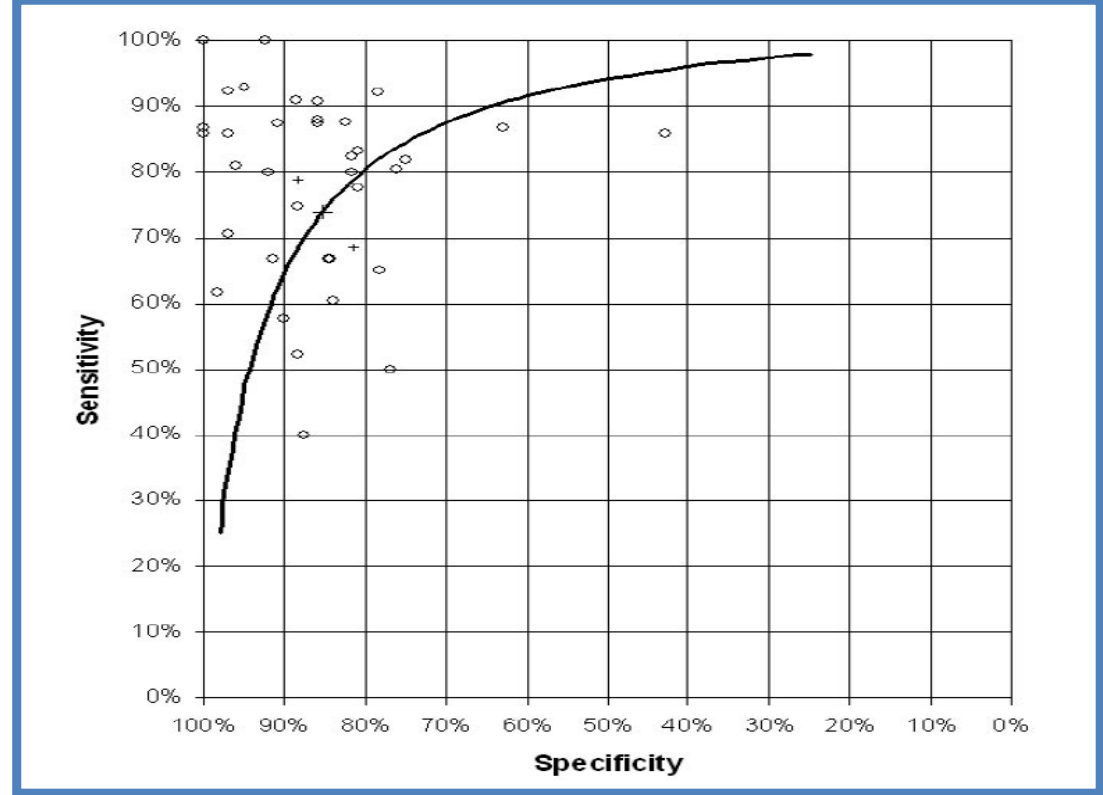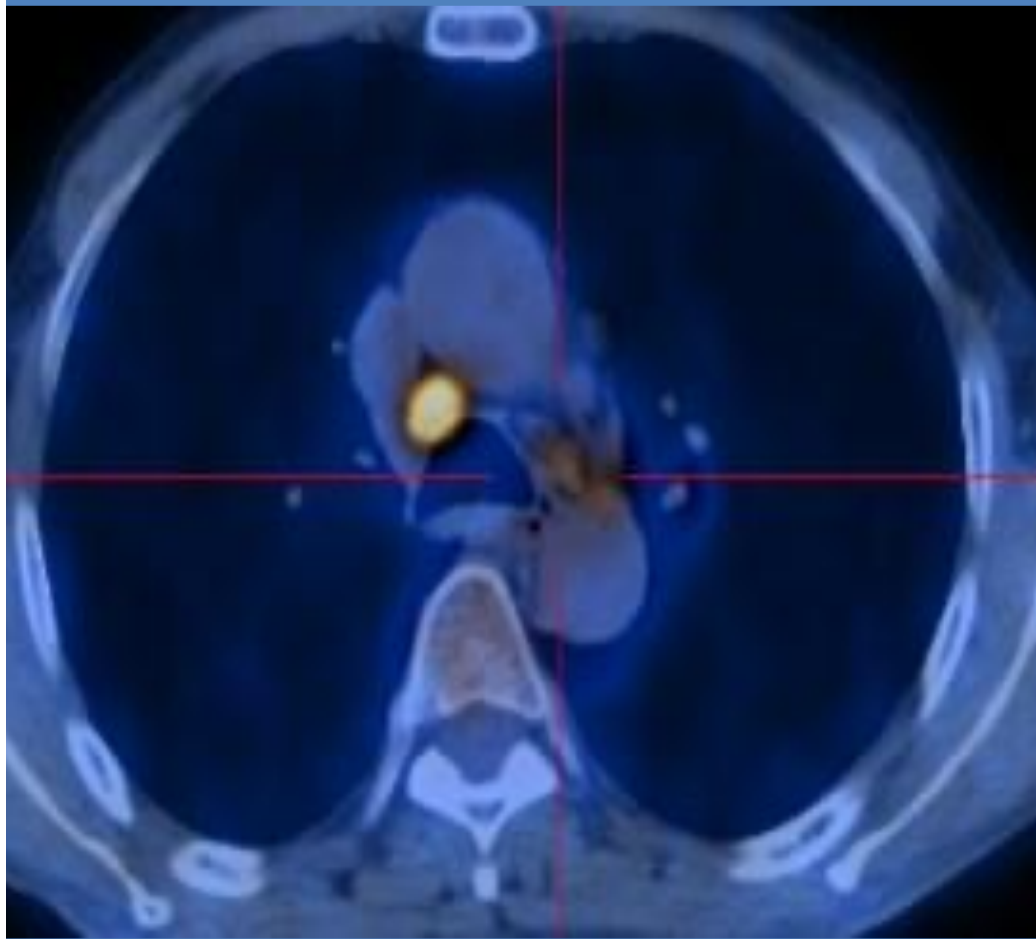Frank Detterbeck, MD,‡ Daniel Morgensztern, MD,§ and Cary P. Gross, MD†
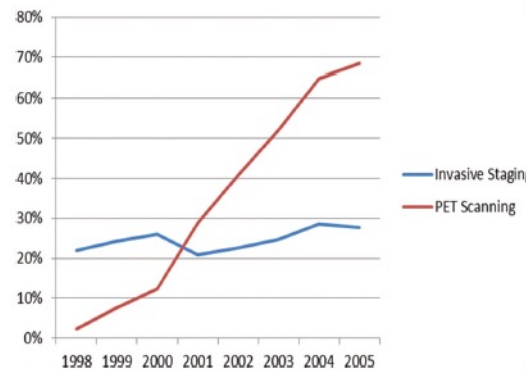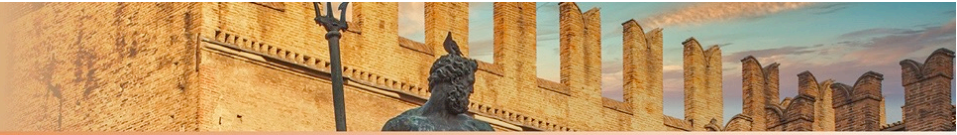
**FIGURE 2.** Use of PET (positron emission tomography) scanning and invasive staging, 1998 to 2005, in preexpansion registries.

**Conclusion:** Nearly 80% of Medicare beneficiaries with stage IIIA NSCLC do not receive guideline adherent mediastinal staging; this failure cannot be entirely explained by patient factors or a reliance on PET imaging. Incentives to encourage use of invasive staging may improve care.

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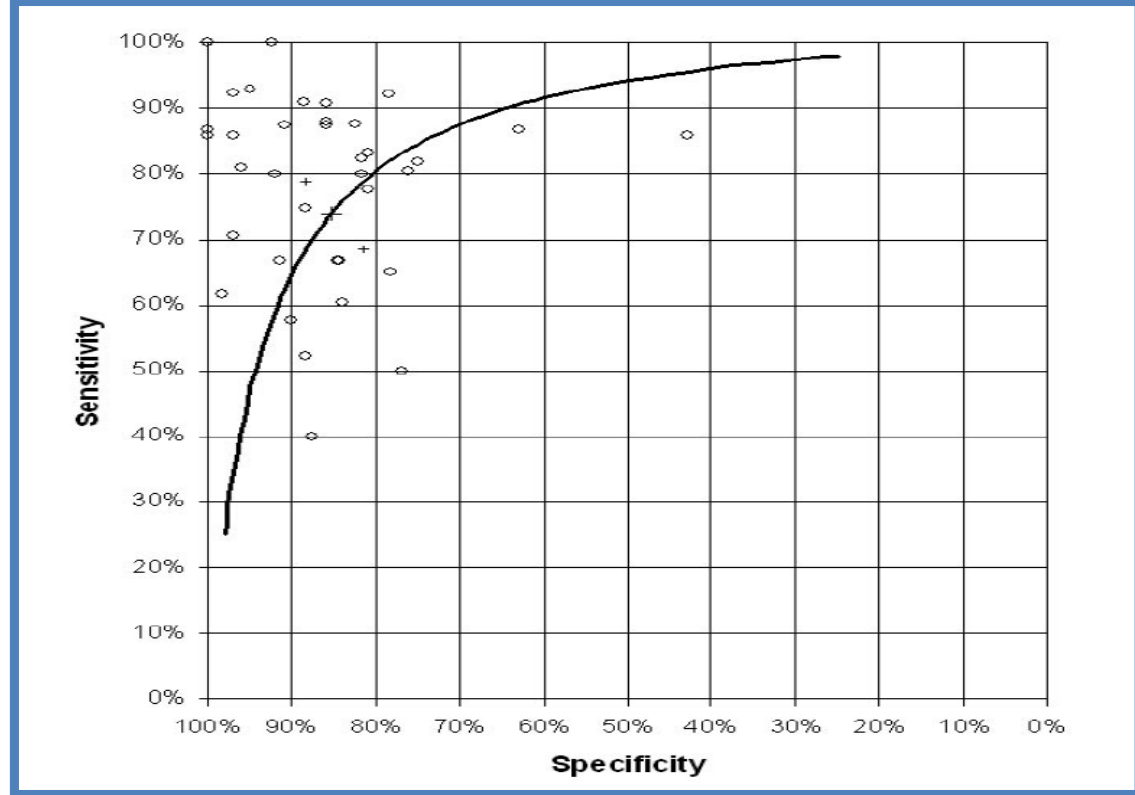
SENSITIVITY OF PET SCAN FOR MEDIASTINAL LNs:
SENSITIVITY: 74% (95% CI 69-79%)

SPECIFICITY OF PET SCAN FOR MEDIASTINAL LNs:
85% (95% CI 82-88%)

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

# Nodal Chart–8th Edition
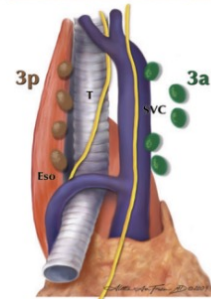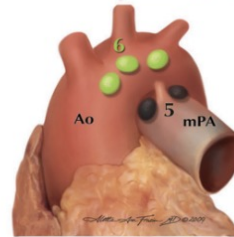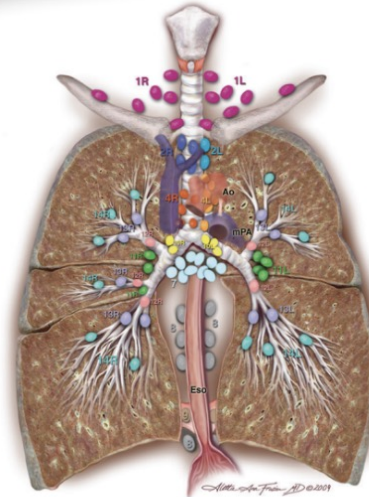
*Supraclavicular zone*
1 Low cervical, supraclavicular, and sternal notch nodes

## SUPERIOR MEDIASTINAL NODES

*Upper zone*
2R Upper Paratracheal (right)
2L Upper Paratracheal (left)
3a Prevascular
3p Retrotracheal
4R Lower Paratracheal (right)
4L Lower Paratracheal (left)

## AORTIC NODES

*AP zone*
5 Subaortic
6 Para-aortic (ascending aorta or phrenic)

## INFERIOR MEDIASTINAL NODES

*Subcarinal zone*
7 Subcarinal

*Lower zone*
8 Paraesophageal (below carina)
9 Pulmonary ligament

## N1 NODES

*Hilar/Interlobar zone*
10 Hilar
11 Interlobar

*Peripheral zone*
12 Lobar
13 Segmental
14 Subsegmental

241 patients randomized to endosonography (n=123) OR mediastinoscopy (n=118)

Prevalence of N2/3 metastases: **49%**

Sensitivity for N2 (primary outcome):

 endosonography: **85%**

 mediastinoscopy: **79%**

 endosonography followed by mediastinoscopy: **94%**

Unnecessary thoracotomies (secondary outcome):

 endosonography: **7%**

 mediastinoscopy: **21%**

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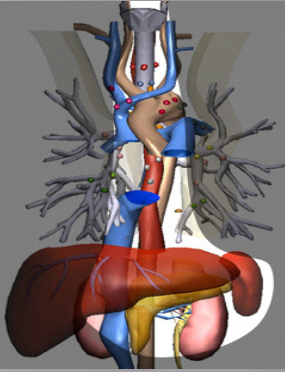PALAZZO DEI CONGRESSI

# Methods for Staging Non-small Cell Lung Cancer

## Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

*Gerard A. Silvestri, MD, FCCP; Anne V. Gonzalez, MD; Michael A. Jantz, MD, FCCP; Mitchell L. Margolis, MD, FCCP; Michael K. Gould, MD, FCCP; Lynn T. Tanoue, MD, FCCP; Loren J. Harris, MD, FCCP; and Frank C. Detterbeck, MD, FCCP*
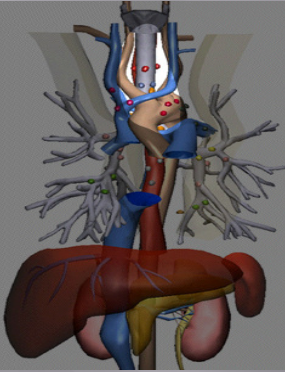
FIGURE 16. [Section 4.3.2.5] Real-time EBUS-TBNA and EUS-NA of the mediastinum in patients with lung cancer.

| First Author | Year | No. | Stage | Thoro | Prev | Sens | Spec[a] | PPV[a] | NPV |
|---|---|---|---|---|---|---|---|---|---|
| Vilmann[353] | 2005 | 31 | cN0-3 | sys | 65 | 100 | (100)[a] | (100)[a] | 100 |
| Annema[228] | 2010 | 123 | cN1-3 | sys | 54 | 82 | (100)[a] | (100)[a] | 80 |
| Herth[307] | 2010 | 139 | cN1-3 | sel | 52 | 96 | (100)[a] | (100)[a] | 96 |
| Ohnishi[352] | 2011 | 110 | cN0-3 | sys | 35 | 72 | (100)[a] | (100)[a] | 87 |
| Hwangbo[335] | 2010 | 150 | cN2-3 | sys | 31 | 91 | (100)[a] | (100)[a] | 96 |
| Wallace[296] | 2008 | 138 | cN2-3 | sys | 30 | 93 | (100)[a] | (100)[a] | 97 |
| Szlubowski[308] | 2010 | 120 | cN0 | sel | 22 | 68 | 98 | 91 | 91 |
| Median: prevalence 40-65 | | | | | | 96 | | | 96 |
| Median: prevalence 20-39 | | | | | | 82 | | | 94 |
| **Summary: median** | | **811** | | | **33** | **91** | **(100)[a]** | **(100)[a]** | **96** |

**EUS – FNA**
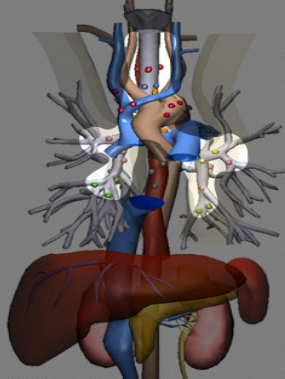
Chest X-Ray
Computer Tomography (CT)
Positron Emission Tomography (PET)
Bronchoscopy
Transthoracic Needle Aspiration (TTNA)
Transbronchial Needle Aspiration (TBNA)
Transoesophageal Endosonography with Fine Needle Aspiration (EUS-FNA)
EBUS guided TBNA (EBUS Miniature Probes)
EBUS-Transbronchial Needle Aspiration under direct ultrasonic vision (EBUS-TBNA)
Mediastinoscopy
Thoracoscopy (VATS)
Thoracotomy

**MEDIASTINOSCOPIA**

Chest X-Ray
Computer Tomography (CT)
Positron Emission Tomography (PET)
Bronchoscopy
Transthoracic Needle Aspiration (TTNA)
Transbronchial Needle Aspiration (TBNA)
Transoesophageal Endosonography with Fine Needle Aspiration (EUS-FNA)
EBUS guided TBNA (EBUS Miniature Probes)
EBUS-Transbronchial Needle Aspiration under direct ultrasonic vision (EBUS-TBNA)
Mediastinoscopy
Thoracoscopy (VATS)
Thoracotomy

**EBUS-TBNA**

Chest X-Ray
Computer Tomography (CT)
Positron Emission Tomography (PET)
Bronchoscopy
Transthoracic Needle Aspiration (TTNA)
Transbronchial Needle Aspiration (TBNA)
Transoesophageal Endosonography with Fine Needle Aspiration (EUS-FNA)
EBUS guided TBNA (EBUS Miniature Probes)
EBUS-Transbronchial Needle Aspiration under direct ultrasonic vision (EBUS-TBNA)
Mediastinoscopy
Thoracoscopy (VATS)
Thoracotomy

# Staging Strategies' skills

- **Competence** is referred to the **strategies in planning every single case**, too.

- To make an accurate staging with EBUS/EUS, it is necessary to follow **a precise order of sampling** and depends on the **side** and **the localization of tumor** determined by CT scan.

- Distant metastases (M1) should be excluded first, followed by lymph node staging in the order N3 (controlateral lymph nodes) → N2 (ipsilateral mediastinal and subcarinal lymph nodes) → N1 (ipsilateral hilar lymph nodes)
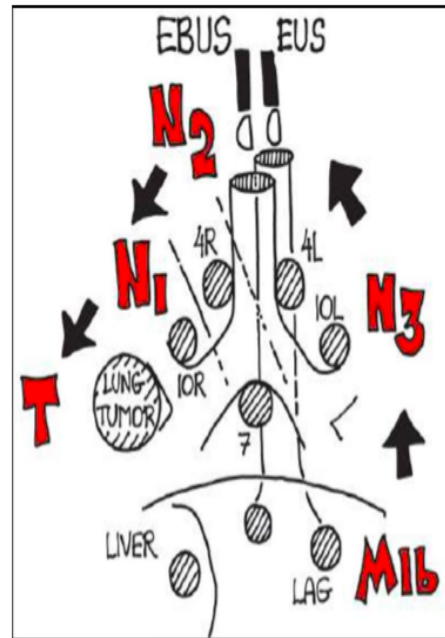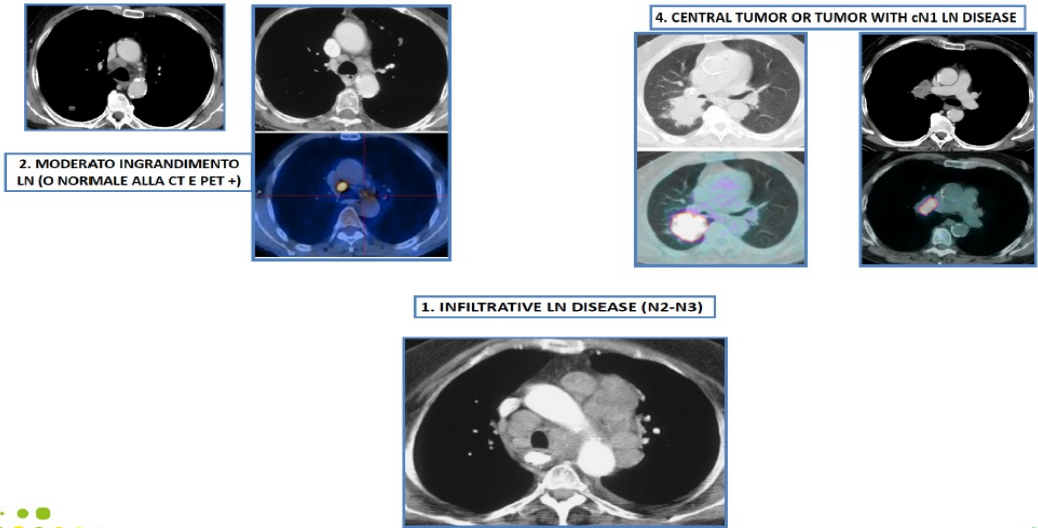


Figure 4 –Order of sampling

Candoli P. et al. Panminerva Medica 2018

*Remark*: This recommendation is based on the availability of these technologies (EBUS-NA, EUS-NA or combined EBUS/EUS-NA) and the appropriate experience and skill of the operator.
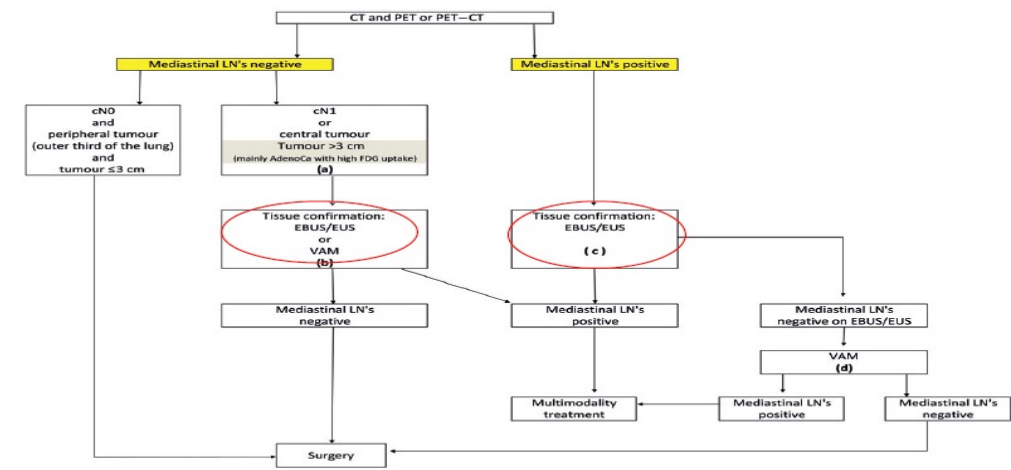


*Remark*: The reliability of mediastinal staging may be more dependent on the thoroughness with which the procedure is performed than by which test is used.

## ACCP SCENARIOS

**2. MODERATO INGRANDIMENTO LN (O NORMALE ALLA CT E PET +)**

**4. CENTRAL TUMOR OR TUMOR WITH cN1 LN DISEASE**

**1. INFILTRATIVE LN DISEASE (N2-N3)**

## STAGING DEL MEDIASTINO

**Combined endobronchial and oesophageal endosonography for the diagnosis and staging of lung cancer**

European Society of Gastrointestinal Endoscopy (ESGE) Guideline, in cooperation with the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS)

Peter Vilmann[1], Paul Frost Clementsen[2,3], Sara Colella[2], Mette Siemsen[4], Paul De Leyn[5], Jean-Marc Dumonceau[6], Felix J. Herth[7], Alberto Larghi[8], Enrique Vazquez-Sequeiros[9], Cesare Hassan[8], Laurence Crombag[10], Daniël A. Korevaar[11], Lars Konge[3] and Jouke T. Annema[10]

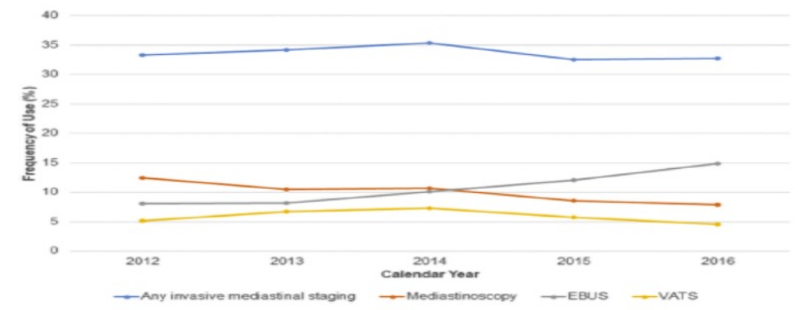| PERIPHERAL CONFIRMED OR SUSPECTED LUNG CANCER (without distant metastasis) | CENTRAL CONFIRMED OR SUSPECTED LUNG CANCER (without distant metastasis) |
|---|---|
| Enlarged and/or PET + Mediastinal Nodes | Centrally Located cancer with normal or discrete enlarged nodes regardless PET activity |
| Enlarged and/or PET + Hilar Nodes | |
| Small (<1 cm Short axis) and PET – med. and hilar nodes with PET + primary Tumor 3 cm or above | *Pts with centrally located cancer with invasion of mediastinum might require EBUS to obtain diagnosis* |

### Revised ESTS guidelines for preoperative mediastinal lymph node staging for non-small-cell lung cancer[†]

Paul De Leyn[a,*], Christophe Dooms[b], Jaroslaw Kuzdzal[c], Didier Lardinois[d], Bernward Passlick[e], Ramon Rami-Porta[f], Akif Turna[g], Paul Van Schil[h], Frederico Venuta[i], David Waller[j], Walter Weder[k] and Marcin Zielinski[l]

CT and PET or PET—CT

Mediastinal LN's negative | Mediastinal LN's positive

cN0 and peripheral tumour (outer third of the lung) and tumour ≤3 cm

cN1 or central tumour Tumour >3 cm (mainly AdenoCa with high FDG uptake) (a)

Tissue confirmation: EBUS/EUS or VAM (b)

Tissue confirmation: EBUS/EUS (c)

Mediastinal LN's negative

Mediastinal LN's positive

Mediastinal LN's negative on EBUS/EUS

VAM (d)

Multimodality treatment

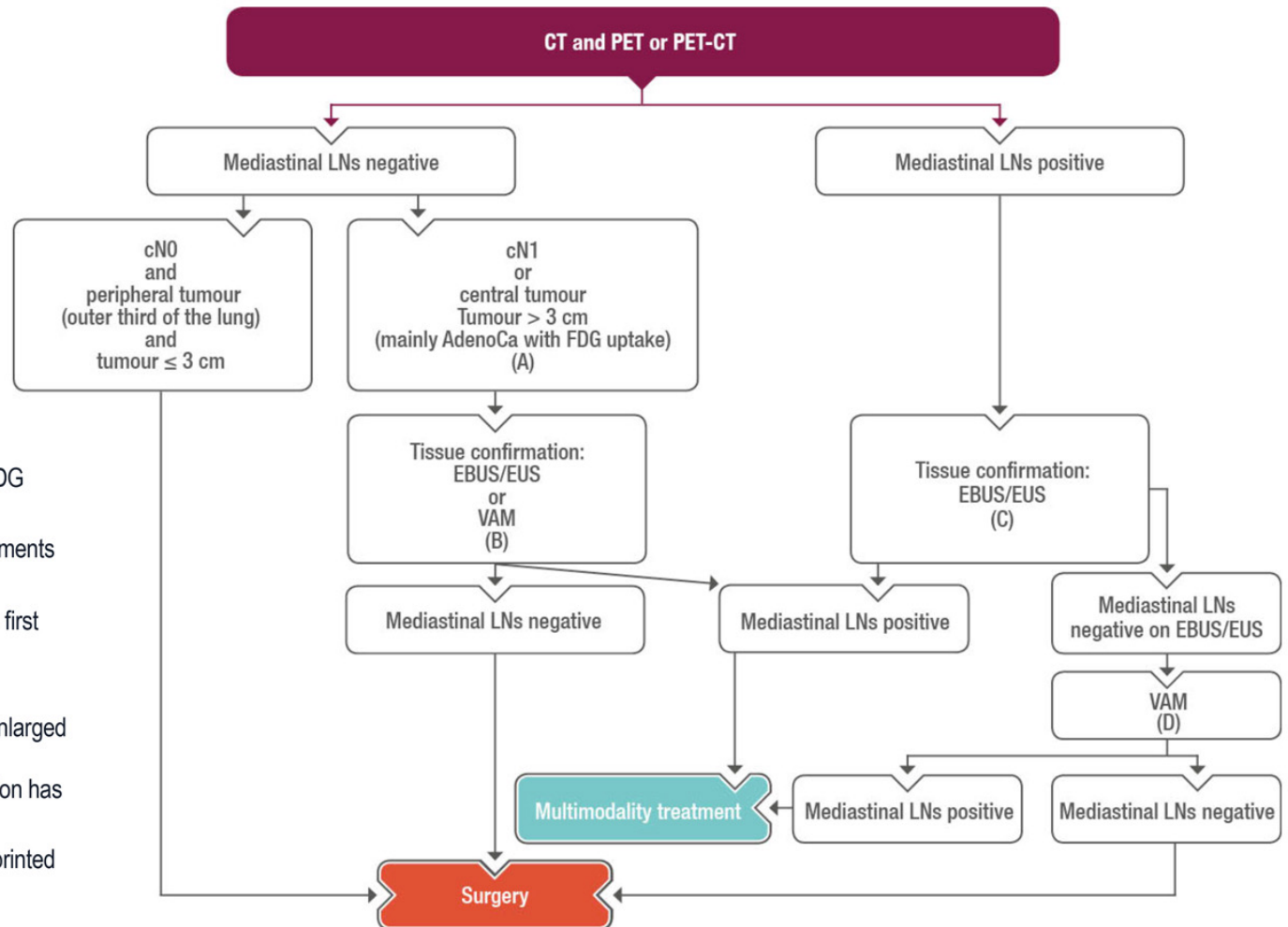Mediastinal LN's positive

Mediastinal LN's negative

Surgery

(a) : In tumours > 3 cm (mainly in adenocarcinoma with high FDG uptake) invasive staging should be considered
(b) : Depending on local expertise to adhere to minimal requirements for staging
(c) : Endoscopic techniques are minimally invasive and are the first choice if local expertise with EBUS/EUS needle aspiration is available
(d) : Due to its higher NPV, in case of PET positive or CT enlarged mediastinal LN's, videoassisted mediastinoscopy (VAM) with nodal dissection or biopsy remain indicated when endoscopic staging is negative. Nodal dissection has an increased accuracy over biopsy

### Invasive Mediastinal Staging for Lung Cancer by The Society of Thoracic Surgeons Database Participants

Check for updates

(Ann Thorac Surg 2018;106:1055–62)
© 2018 by The Society of Thoracic Surgeons

Seth B. Krantz, MD, John A. Howington, MD, Douglas E. Wood, MD, Ki Wan Kim, MD, Andrzej S. Kosinski, PhD, Morgan L. Cox, MD, Sunghee Kim, PhD, Michael S. Mulligan, MD, and Farhood Farjah, MD, MPH

Division of Thoracic Surgery, NorthShore University Health System, Evanston, Illinois; Department of Thoracic Surgery, Saint Thomas Healthcare, Nashville, Tennessee; Division of Cardiothoracic Surgery, University of Washington, Seattle, Washington; and Department of Biostatistics and Bioinformatics and Duke Clinical Research Institute, Duke University, Durham, North Carolina

# Staging and risk assessment

Locoregional LN staging in patients with non-metastatic NSCLC

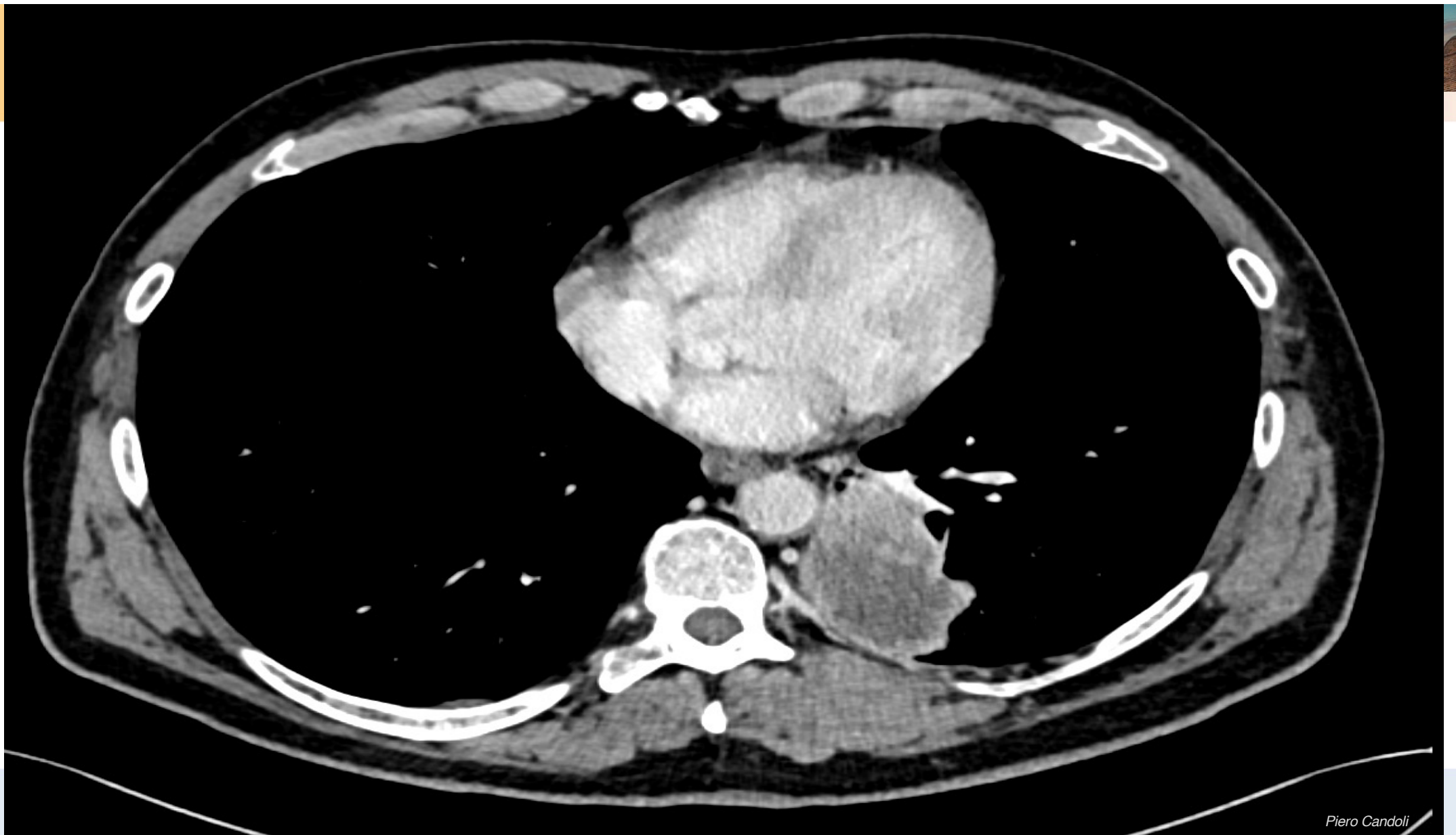(A) In tumours > 3 cm (mainly in adenocarcinoma with high FDG uptake) invasive staging should be considered

(B) Depending on local expertise to adhere to minimal requirements for staging

(C) Endoscopic techniques are minimally invasive and are the first choice if local expertise with EBUS/EUS needle aspiration is available

(D) Due to its higher NPV, in the case of PET-positive or CT-enlarged mediastinal LNs, VAM with nodal dissection or biopsy remain indicated when endoscopic staging is negative. Nodal dissection has an increased accuracy over biopsy

De Leyn P et al. Eur J Cardiothorac Surg 2014;3:787–98. Reprinted with permission.

**ESMO**

CT and PET or PET-CT

Mediastinal LNs negative

Mediastinal LNs positive

cN0
and
peripheral tumour
(outer third of the lung)
and
tumour ≤ 3 cm

cN1
or
central tumour
Tumour > 3 cm
(mainly AdenoCa with FDG uptake)
(A)

Tissue confirmation:
EBUS/EUS
or
VAM
(B)

Tissue confirmation:
EBUS/EUS
(C)

Mediastinal LNs negative

Mediastinal LNs positive

Mediastinal LNs
negative on EBUS/EUS

VAM
(D)

Multimodality treatment

Mediastinal LNs positive

Mediastinal LNs negative

Surgery

I: 244.3
Im: 79

DFOV 43.9 cm
10.00

0.00
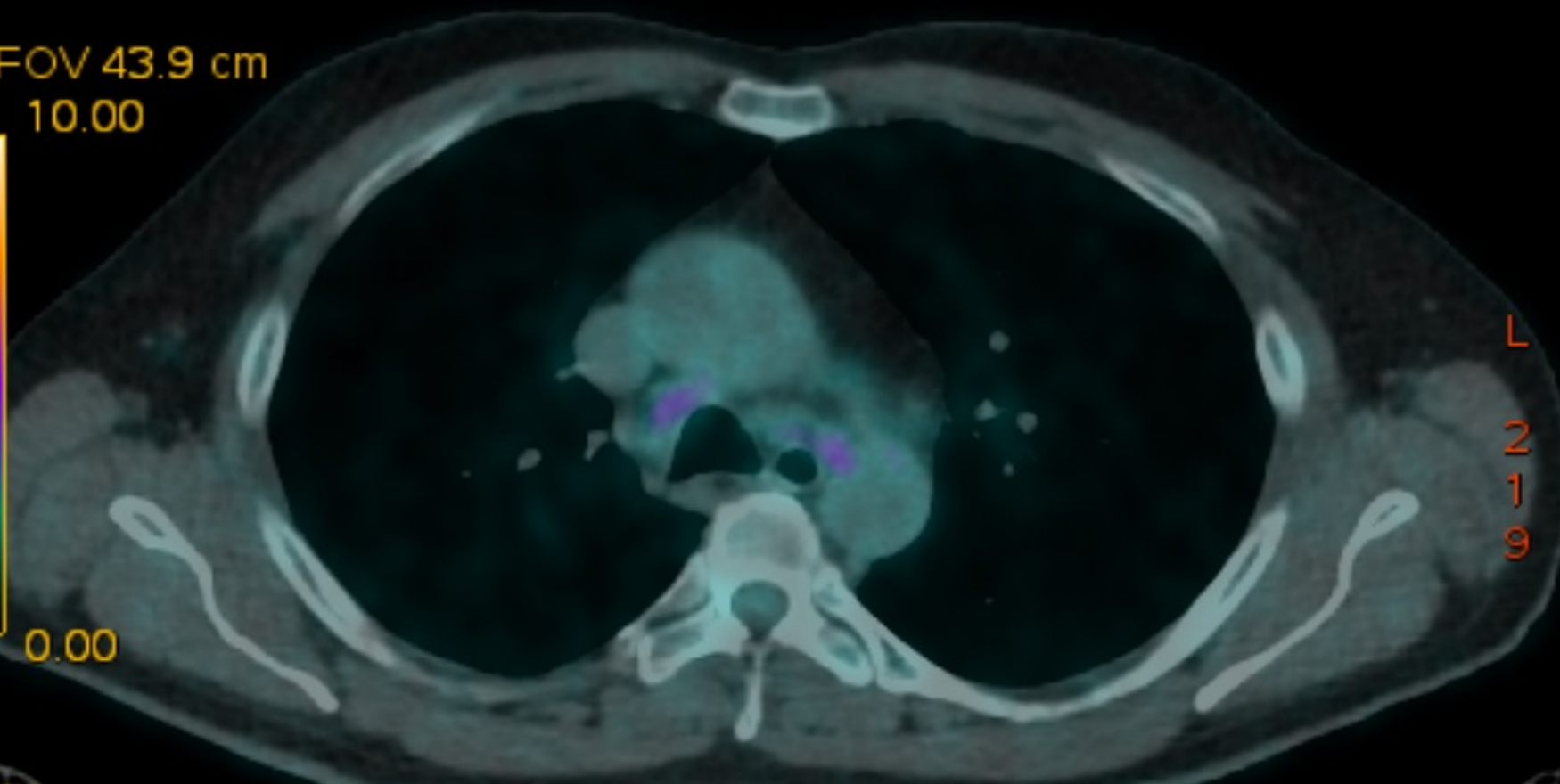
L 2 1 9

I: 270.5
Im: 87

Ex:Apr 18 2019

DFOV 43.9 cm
10.00

0.00

L

L
2
1
9

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RAO G.

BOLOGNA, 25-27 NOVEMBRE
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# The International Association for the Study of Lung Cancer Lung Cancer Staging Project

## Proposals for the Revision of the N Descriptors in the Forthcoming 8th Edition of the TNM Classification for Lung Cancer

Hisao Asamura, MD,* Kari Chansky, MS,† John Crowley, PhD,† Peter Goldstraw, MBChB, FRCS,‡ Valerie W. Rusch, MD,§ Johan F. Vansteenkiste, MD,‖ Hirokazu Watanabe, MD,¶ Yi-Long Wu, MD,# Marcin Zielinski, MD,** David Ball, MD,†† and Ramon Rami-Porta, MD,‡‡§§ On behalf of the International Association for the Study of Lung Cancer Staging and Prognostic Factors Committee, Advisory Board Members, and Participating Institutions‖‖

N1a , single-station N1 involvement

N1b , multiple-station N1 involvement

N2a1 , single-station N2 involvement without N1 ( skip metastases)

N2a2 , single-station N2 with N1 disease

N2b , multiple-station N2 involvement

N3

# Lung cancer - major changes in the American Joint Committee on Cancer eighth edition cancer staging manual.

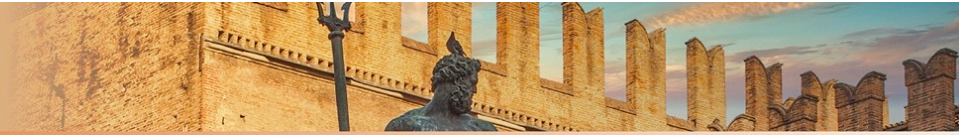Rami-Porta R, Asamura H, Travis WD, Rusch VW

- N1a: involvement of a single N1 nodal station;
- N1b: involvement of multiple N1 nodal stations;
- N2a1: involvement of a single N2 nodal station without N1 involvement (skip metastasis);
- N2a2: involvement of a single N2 nodal station with N1 involvement; and
- N2b: involvement of multiple N2 nodal stations.

- Prognosis worsens as the number of involved nodal stations increases, but N1b and N2a1 have the same prognosis.

- This new analysis shows that discreet (one-station) mediastinal nodal disease without N1 disease has the same prognosis as multiple N1 stations.

- Five-year survival rates in the population of patients who underwent complete resection for the different N subcategories are: N1a, 59%; N1b, 50%; N2a1, 54%; N2a2, 43%; and N2b, 38%.
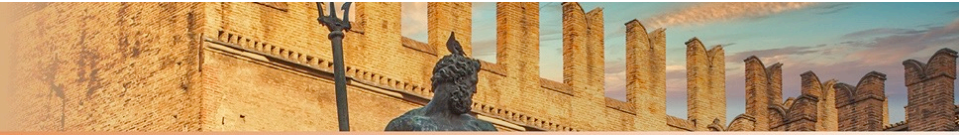
# UNFORESEEN N2

**Unforeseen N2 disease**. Pathologically proven N2 disease at final lung tumor resection and lymph node dissection when previous mediastinal staging showed N0 or N1 disease.

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# Why endosonography often fails to identify occult N2 disease in cN0/1 NSCLC?

- Left sided tumors (Mets to LNs. #5 and #6)

- Minimal metastatic involvement in small nodes

- Multiple small LNs in the same station/area

- Thoroughness of the staging

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# Thoroughness of staging
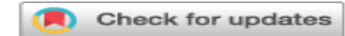
Wich kind size cut-off could be used to prompt aspiration?

Wich lymph node stations need to be explored?

EBUS versus combined EBUS/EUS-B

B-mode findings likely unreliable for lymph nodes < 1 cm

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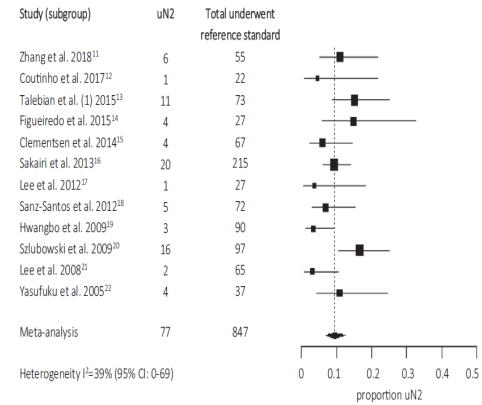BOLOGNA, 25-27 NOVEMBRE
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# Unforeseen N2 Disease after Negative Endosonography Findings with or without Confirmatory Mediastinoscopy in Resectable Non-Small Cell Lung Cancer: A Systematic Review and Meta-Analysis
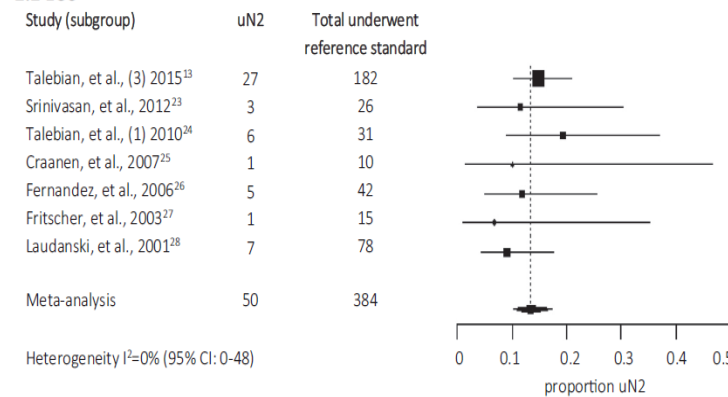
Jelle E. Bousema, MD,[a] Martijn van Dorp, MD,[b] Valentin J. J. M. Noyez, MD,[c] Marcel G. W. Dijkgraaf, PhD,[d] Jouke T. Annema, MD, PhD,[e] Frank J. C. van den Broek, MD, PhD[a,*]

**2.1 EBUS**

| Study (subgroup) | uN2 | Total underwent reference standard |
|---|---|---|
| Zhang et al. 2018[31] | 6 | 55 |
| Coutinho et al. 2017[12] | 1 | 22 |
| Talebian et al. (1) 2015[13] | 11 | 73 |
| Figueiredo et al. 2015[14] | 4 | 27 |
| Clementsen et al. 2014[15] | 4 | 67 |
| Sakairi et al. 2013[16] | 20 | 215 |
| Lee et al. 2012[17] | 1 | 27 |
| Sanz-Santos et al. 2012[18] | 5 | 72 |
| Hwangbo et al. 2009[19] | 3 | 90 |
| Szlubowski et al. 2009[20] | 16 | 97 |
| Lee et al. 2008[21] | 2 | 65 |
| Yasufuku et al. 2005[22] | 4 | 37 |
| Meta-analysis | 77 | 847 |

Heterogeneity I²=39% (95% CI: 0-69)

**2.2 EUS**

| Study (subgroup) | uN2 | Total underwent reference standard |
|---|---|---|
| Talebian, et al., (3) 2015[13] | 27 | 182 |
| Srinivasan, et al., 2012[23] | 3 | 26 |
| Talebian, et al., (1) 2010[24] | 6 | 31 |
| Craanen, et al., 2007[25] | 1 | 10 |
| Fernandez, et al., 2006[26] | 5 | 42 |
| Fritscher, et al., 2003[27] | 1 | 15 |
| Laudanski, et al., 2001[28] | 7 | 78 |
| Meta-analysis | 50 | 384 |

Heterogeneity I²=0% (95% CI: 0-48)

**2.3 EBUS plus EUS**

| Study (subgroup) | uN2 | Total underwent reference standard |
|---|---|---|
| Talebian, et al., (5) 2015[13] | 2 | 38 |
| Dooms, et al., (1) 2015[29] | 1 | 10 |
| Oki, et al., 2014[30] | 7 | 107 |
| Kang, et al., (1) 2014[31] | 5 | 45 |
| Kang, et al., (2) 2014[31] | 2 | 51 |
| Verhagen, et al., (1) 2013[32] | 4 | 23 |
| Szlubowski, et al.,(1)2012[33] | 5 | 55 |
| Szlubowski, et al.,(2)2012[33] | 9 | 53 |
| Ohnishi, et al., 2011[34] | 12 | 79 |
| Hwangbo, et al., 2010[35] | 4 | 102 |
| Szlubowski, et al., 2010[36] | 9 | 101 |
| Vilmann, et al., 2005[37] | 0 | 7 |
| Meta-analysis | 60 | 671 |

Heterogeneity I²=26% (95% CI: 0-63)
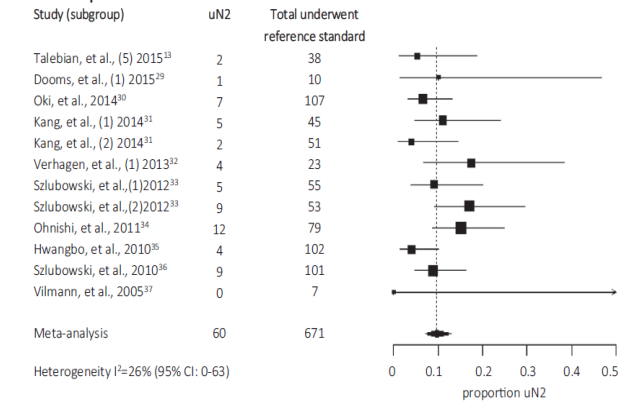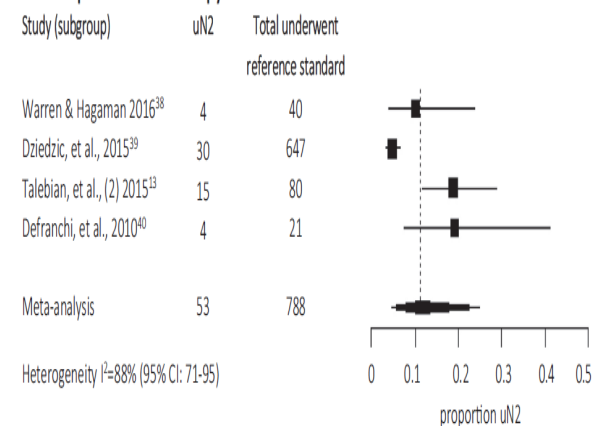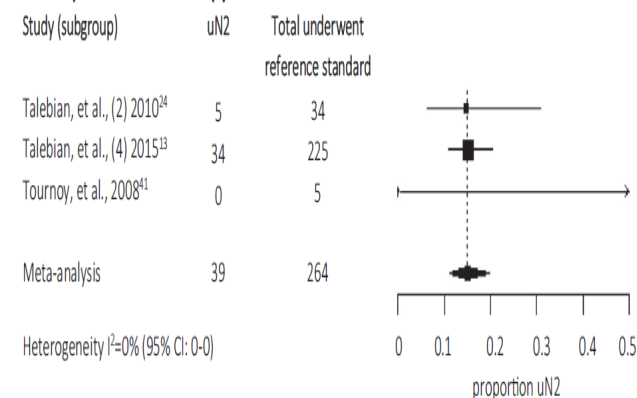
32% Paratracheali > 4R
30% Sottocarenali
22%  Paraaortici

**9.3 – 9.7 % uN2**

# Unforeseen N2 Disease after Negative Endosonography Findings with or without Confirmatory Mediastinoscopy in Resectable Non-Small Cell Lung Cancer: A Systematic Review and Meta-Analysis

Jelle E. Bousema, MD,[a] Martijn van Dorp, MD,[b] Valentin J. J. M. Noyez, MD,[c] Marcel G. W. Dijkgraaf, PhD,[d] Jouke T. Annema, MD, PhD,[e] Frank J. C. van den Broek, MD, PhD[a,*]
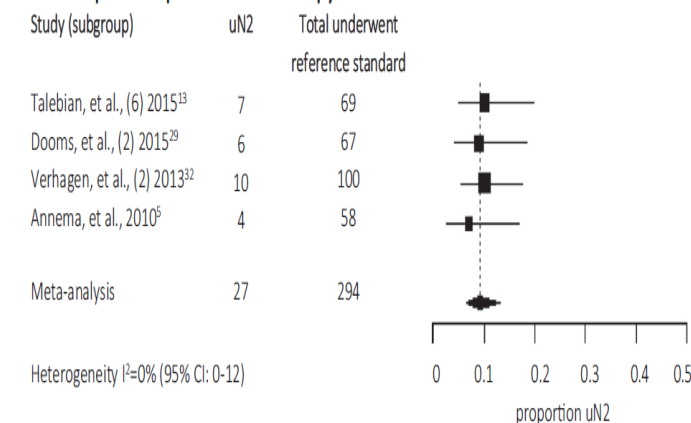
26% Paratracheali > 4R
35% Sottocarenali
28% Paraaortici

**9.9 % uN2**

# Unforeseen N2 Disease after Negative Endosonography Findings with or without Confirmatory Mediastinoscopy in Resectable Non–Small Cell Lung Cancer: A Systematic Review and Meta-Analysis

Jelle E. Bousema, MD,[a] Martijn van Dorp, MD,[b] Valentin J. J. M. Noyez, MD,[c] Marcel G. W. Dijkgraaf, PhD,[d] Jouke T. Annema, MD, PhD,[e] Frank J. C. van den Broek, MD, PhD[a,*]

**Table 1.** Random Effects Meta-Analysis of Complications of Cervical Video-Assisted Mediastinoscopy

| Study | Lymph Node Stations Targeted for Assessment | Mean No. of Stations Subjected to Biopsy | Mean No. of Lymph Nodes Subjected to Biopsy | n | Complications | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Overall | Laryngeal Recurrent Nerve Palsy | Clavien-Dindo Grade III-IV | Mortality |
| Decaluwé et al., 2017[42] | 4R, 7, 4L | 3.9 (SD 1.2) | N/S | 82 | 4.9% | 2.4% | 1.2% | 0.0% |
| Sayar et al., 2016[43] | 2R, 4R, 7, 4L, 2L | 4.3 (SD 0.8) | 7.9 (SD 2.0) | 261 | 7.7% | 1.2% | 0.8% | 0.0% |
| Steunenberg et al., 2016[44] | 2R, 4R, 7, 4L, 2L | 2.8 (SD 1.1) | 12.0 (SD 7.0) | 102 | 6.9% | 2.9% | 3.9% | 1.0% |
| Citak et al., 2014[45] | 2R, 4R, 7, 4L, 2L | 4.2 (SD 0.8) | 7.7 (SD 1.7) | 260 | 5.4% | 4.2% | 1.2% | 0.0% |
| Annema et al., 2010[5] | 2R, 4R, 7, 4L, 2L | 4.0 (range 0-5) | N/S | 182 | 6.6% | 3.3% | 3.3% | 0.0% |
| Anraku et al., 2010[46] | 2R, 4R, 7, 4L, 2L | 3.6 (SD 1.1) | 7.0 (SD 3.2) | 104 | 3.9% | 1.0% | 1.9% | 0.0% |
| Leschber et al., 2008[47,a] | 2R, 4R, 7, 4L, 2L | N/S | 7.6 (range 3-25) | 234 | 4.3% | 2.1% | 1.3% | 0.0% |
| Kuzdzal et al., 2007[48] | 2R, 4R, 7, 4L, 2L | 4.3 (SD N/S) | N/S | 20 | 10.0% | 0.0% | 0.0% | 0.0% |
| Meta-analysis 95% CI Heterogeneity | | | | | 6.0% (4.8-7.5) $I^2 = 0\%$ | 2.8% (2.0-4.0) $I^2 = 0\%$ | 1.9% (1.1-3.2) $I^2 = 21\%$ | 0.5% (0.2-1.2) $I^2 = 0\%$ |

# What's new in endobronchial ultrasound for mediastinal staging?

*Mathieu Marcoux and David E. Ost*

KEY POINTS

- Since the publication of the 2016 ACCP guideline, evidence has grown and significant advances have been made in EBUS-TBNA for lung cancer staging

- New findings have been identified in regards to:
  - ROSE
  - needle size
  - ultrasound lymph node characteristics,
  - molecular testing
  - practice patterns and gaps in quality of care

- Current gaps in knowledge highlight promising areas for future research.

# What's new in endobronchial ultrasound for mediastinal staging?

*Mathieu Marcoux and David E. Ost*

Neoplasms of the lung
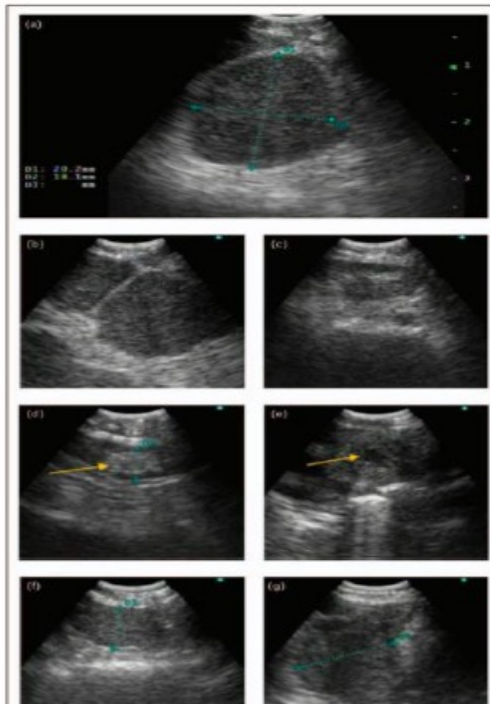


Sum score prediction model for malignancy based on the following prespecified ultrasound characteristics:
1. Short axis >1 cm
2. Heterogeneous pattern
3. Round shape
4. Distinct margin
5. Absence of central hilar structure
6. High blood flow within a lymph node (measured by the color power Doppler Index)

Final score obtained corresponded to the number of positive criteria. A score of 0–2 was classified 'low-risk' of malignancy, whereas a score of 3 to 6 was considered 'high-risk'. Presence of 3 or more ultrasound characteristics resulted in an odds ratio of 15.5 (95% CI: 3.63–66.17) for malignant lymph node involvement.

# Vascular Image Patterns of Lymph Nodes for the Prediction of Metastatic Disease During EBUS–TBNA for Mediastinal Staging of Lung Cancer

*Takahiro Nakajima, MD, PhD,* \*†‡ *Takashi Anayama, MD, PhD,* \* *Masato Shingyoji, MD, PhD,* † *Hideki Kimura, MD, PhD,* † *Ichiro Yoshino, MD, PhD,* ‡ *and Kazuhiro Yasufuku, MD, PhD* \*
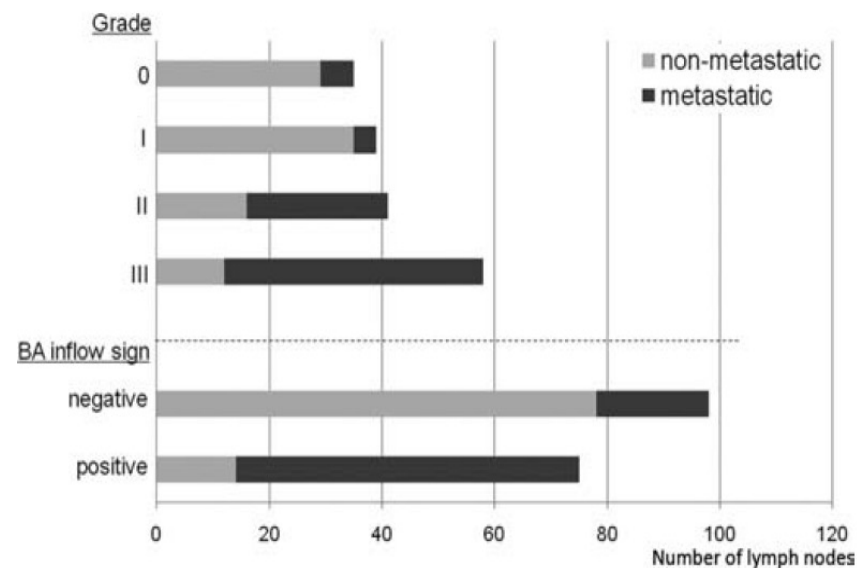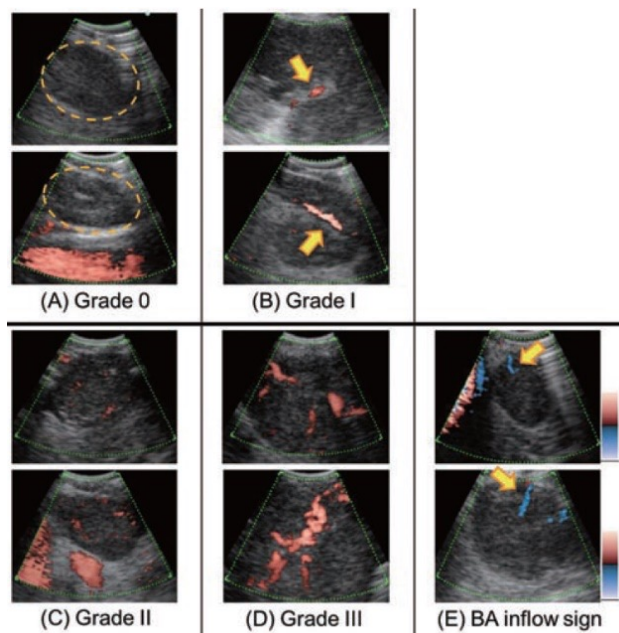
(A) Grade 0 (B) Grade I (C) Grade II (D) Grade III (E) BA inflow sign
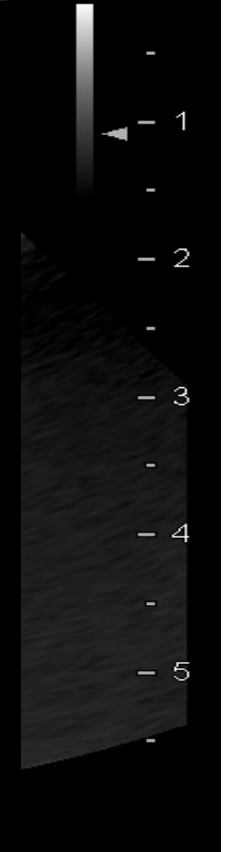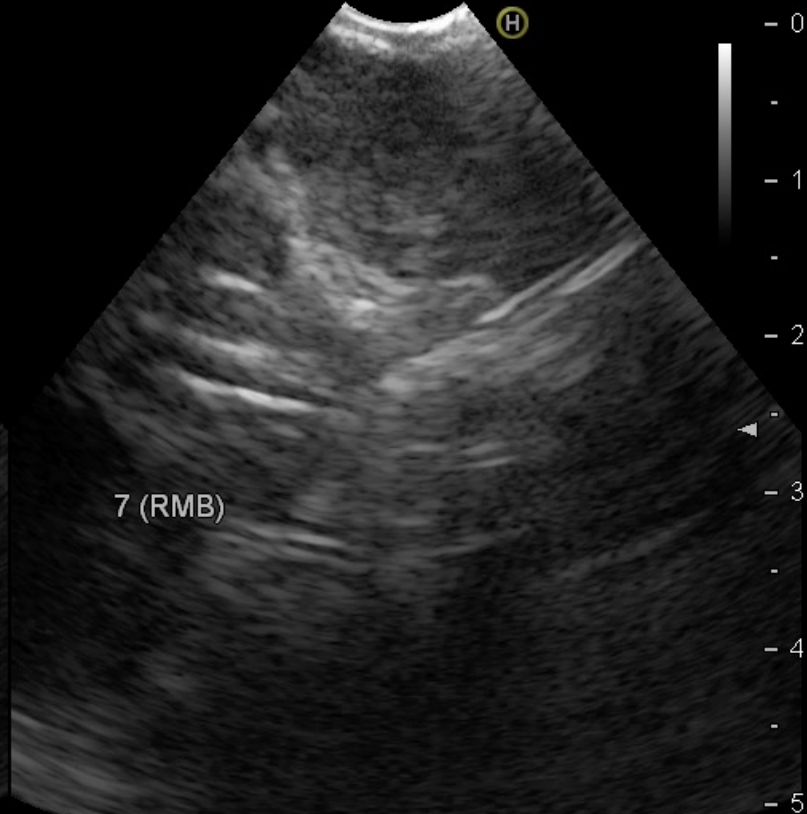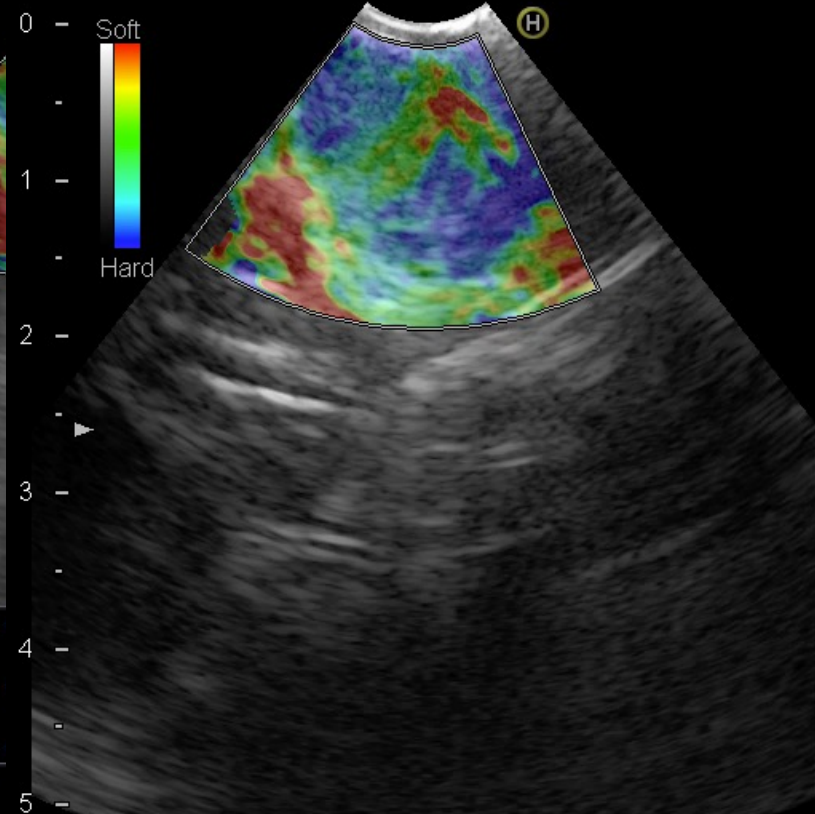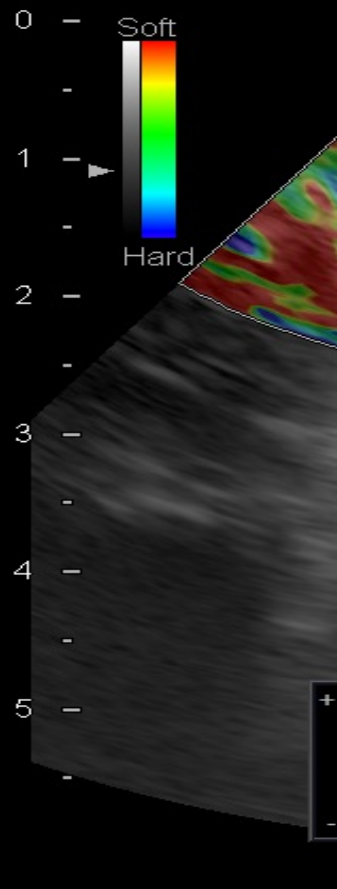
# EBUS elastography imaging
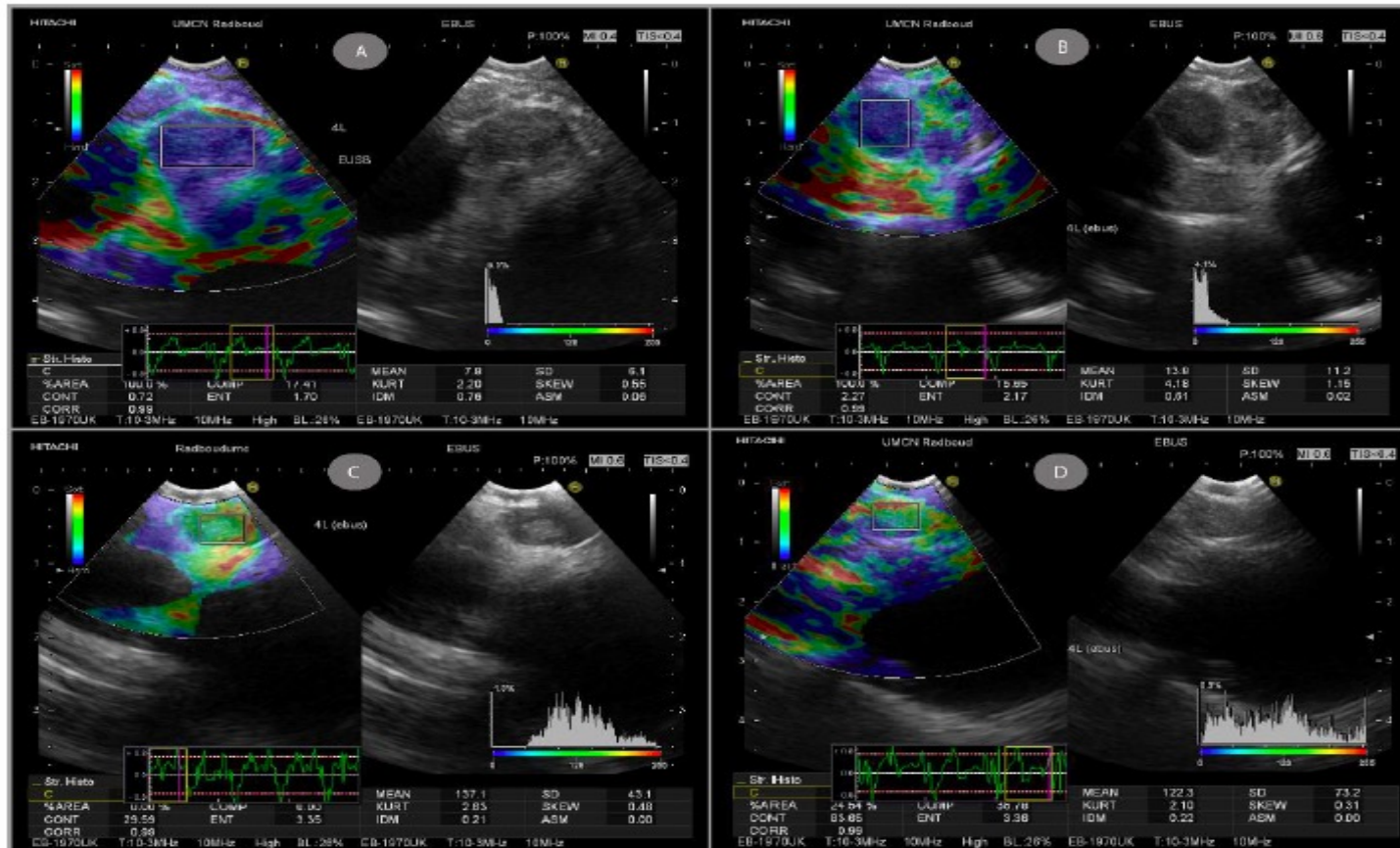


a. 4L – EUSb – malignant

b. 4L – EBUS – malignant

c. 4L – EBUS – benign

d. 4L – EBUS - benign

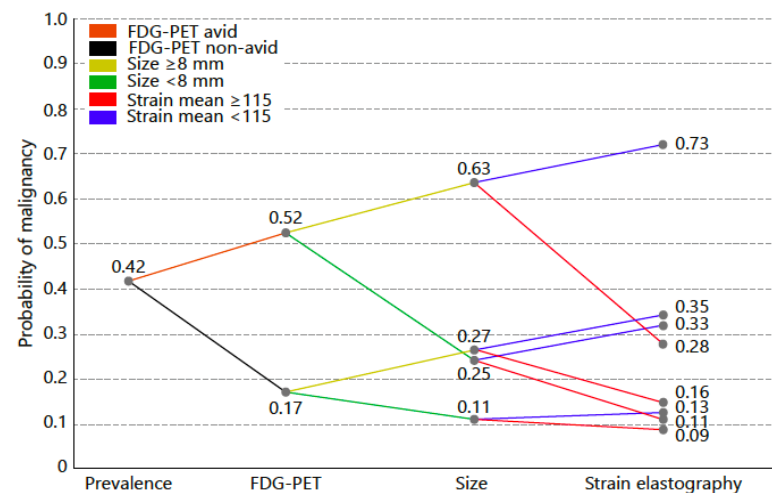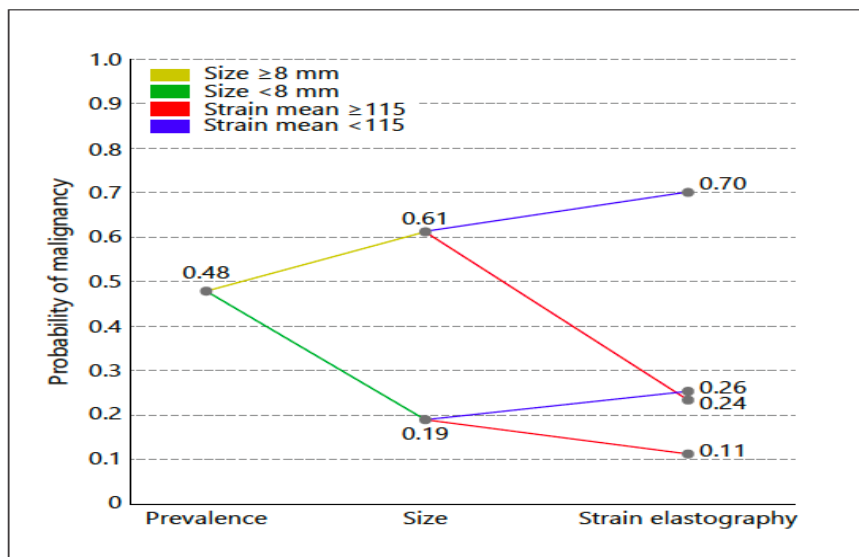Verhoeven RLJ etal, Respiration 2019 - DOI: 10.1159/000494143

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# Predictive Value of Endobronchial Ultrasound Strain Elastography in Mediastinal Lymph Node Staging: The E-Predict Multicenter Study Results

Roel Lambertus Johannes Verhoeven[a, b]    Rocco Trisolini[c, d]    Fausto Leoncini[d, e]
Piero Candoli[f]    Michela Bezzi[e]    Alessandro Messi[g]    Mark Krasnik[h]
Chris L. de Korte[b]    Jouke T. Annema[i]    Erik H.F.M. van der Heijden[a]

È stato rilevato che una dimensione linfonodale di 8 mm in combinazione con un valore medio di cut-off di 115 stratificherebbero meglio il rischio di malignità. In tutti gli scenari in cui la PET-FDG e le dimensioni linfonodali sono state combinate, l'EBUS-SE ha aumentato o diminuito la probabilità di malignità rispettivamente nei casi di bassa ed elevata deformabilità

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Respiration

# Predictive Value of Endobronchial Ultrasound Strain Elastography in Mediastinal Lymph Node Staging: The E-Predict Multicenter Study Results

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# Respirology Case Reports

# Endobronchial ultrasound-guided transbronchial cryo-nodal biopsy: a novel approach for mediastinal lymph node sampling

Hari Kishan Gonuguntla[1] [ID], Milap Shah[2], Nitesh Gupta[3] [ID], Sumita Agrawal[4], Venerino Poletti[5] & Gustavo Cumbo Nacheli[6]

[1]Department of Interventional Pulmonology, Yashoda Hospital, Hyderabad, India.
[2]Department of Laboratory Medicine, Yashoda Hospital, Hyderabad, India.
[3]Department of Pulmonary, Critical Care and Sleep Medicine, VMMC and Safdarjung Hospital, New Delhi, India.
[4]Department of Pulmonary, Critical Care and Sleep Medicine, Medipulse Hospital, Jodhpur, India.
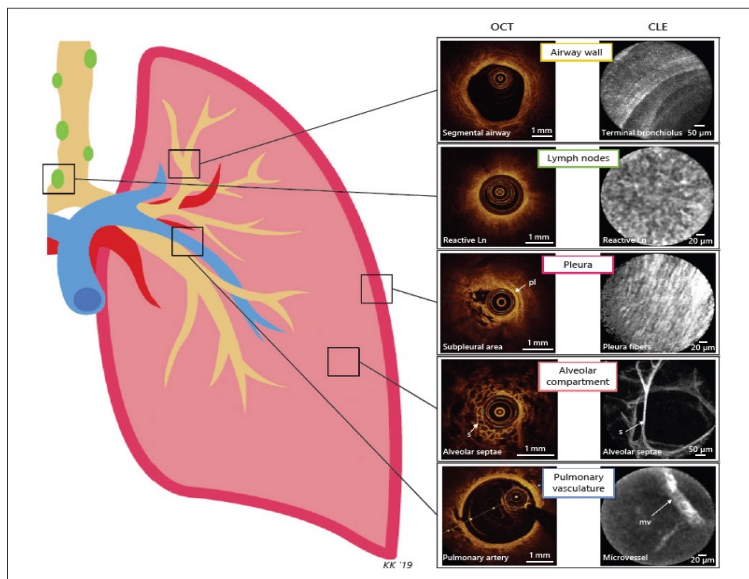[5]Department of Diseases of the Thorax, Ospedale GB Morgagni, Forlì, Italy.
[6]Division of Bronchoscopy and Interventional Pulmonology, Pulmonary and Critical Care Division, Spectrum Health Medical Group, Grand Rapids, MI, USA.
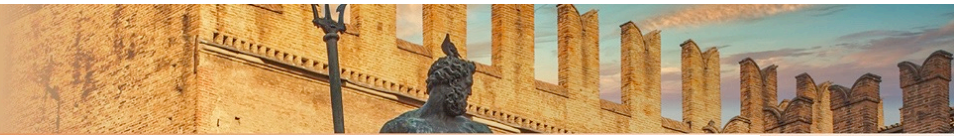
# Respiration
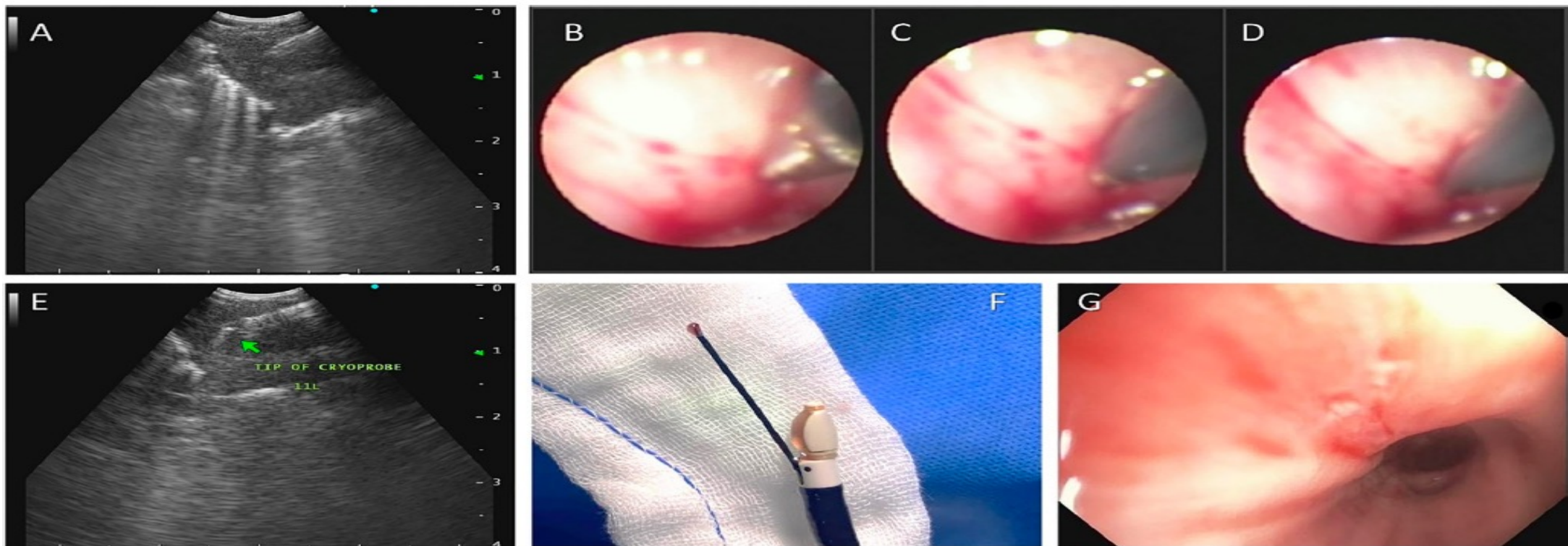
# Advances in Optical Coherence Tomography and Confocal Laser Endomicroscopy in Pulmonary Diseases

Annika Goorsenberg    Kirsten A. Kalverda    Jouke Annema    Peter Bonta

Department of Pulmonology, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, The Netherlands

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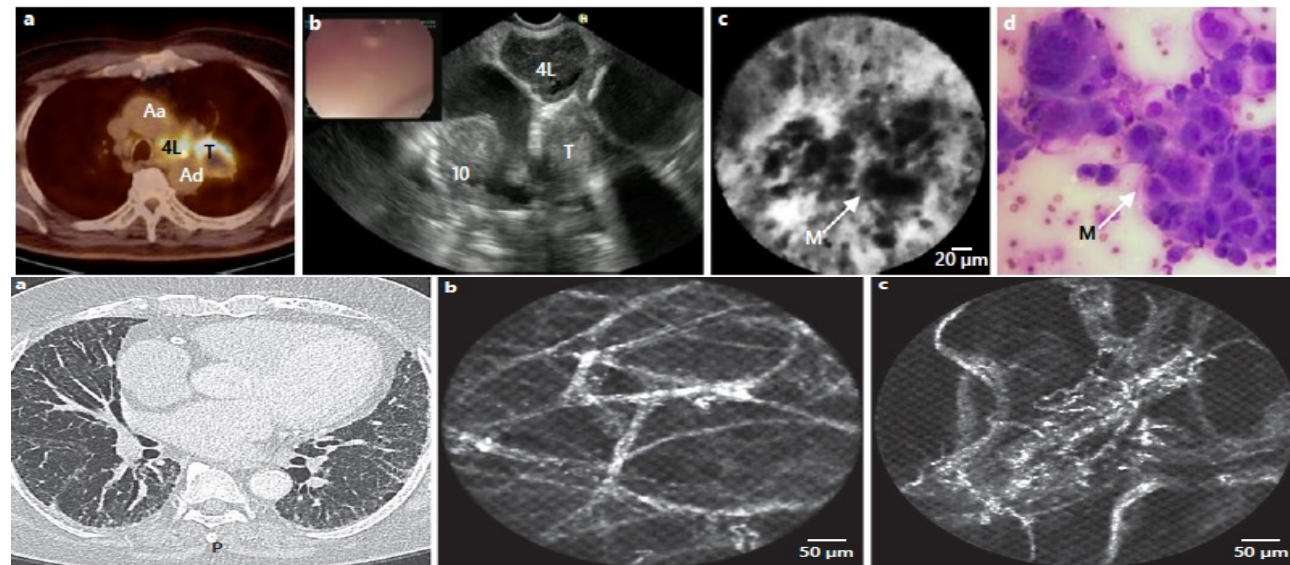
## Lymph node structures

## Metastatic lymph node

### Capsule

### Cortex

### Adipocytes
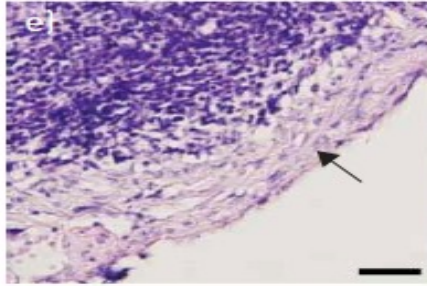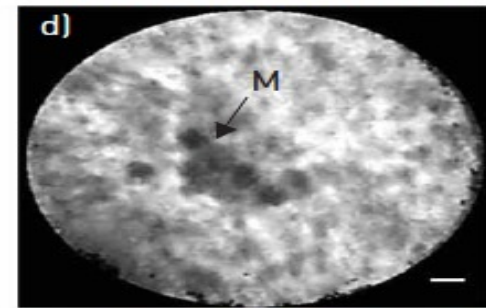
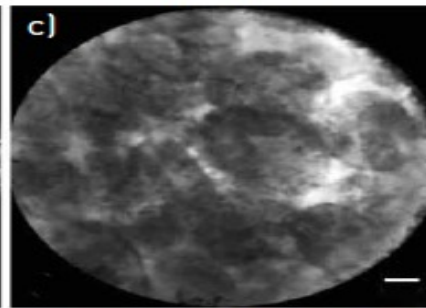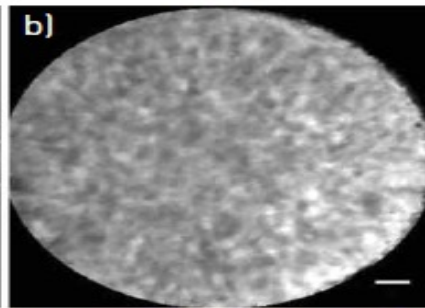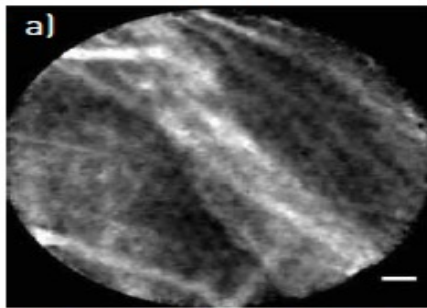### Clump with enlarged cells in cortex of lymph node
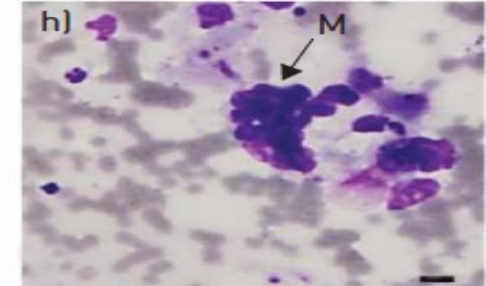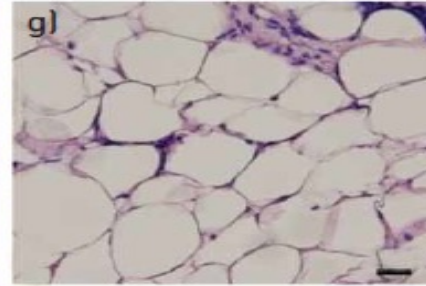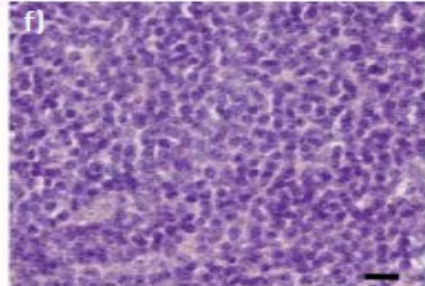


FIGURE 5 a–c) *In vivo* needle-based confocal laser endomicroscopy (nCLE) imaging of reactive lymph node structures with the e–g) corresponding histology image after surgical excision of the node. a) The dark background with bright fibre structure represents the capsular structures of a lymph node (indicated in e by the arrow). b) Homogenously distributed grey dots visualised in the cortex of a lymph node with homogenously shaped and sized lymphocytes (f). c) Large dark bubbles represent adipocytes (g). d) *In vivo* nCLE imaging of a metastatic lymph node with a background of cortex-appearance and a cluster of enlarged cells with h) corresponding cytology of the fine-needle aspirate revealing a cluster of malignant cells (M) of a squamous cell carcinoma on a background of normal lymphocytes and erythrocytes. Scale bars: a–d, f–h) 20 μm; e) 100 μm.

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