

Case # 7

NSCLC in the Elderly: Meeting the Challenges

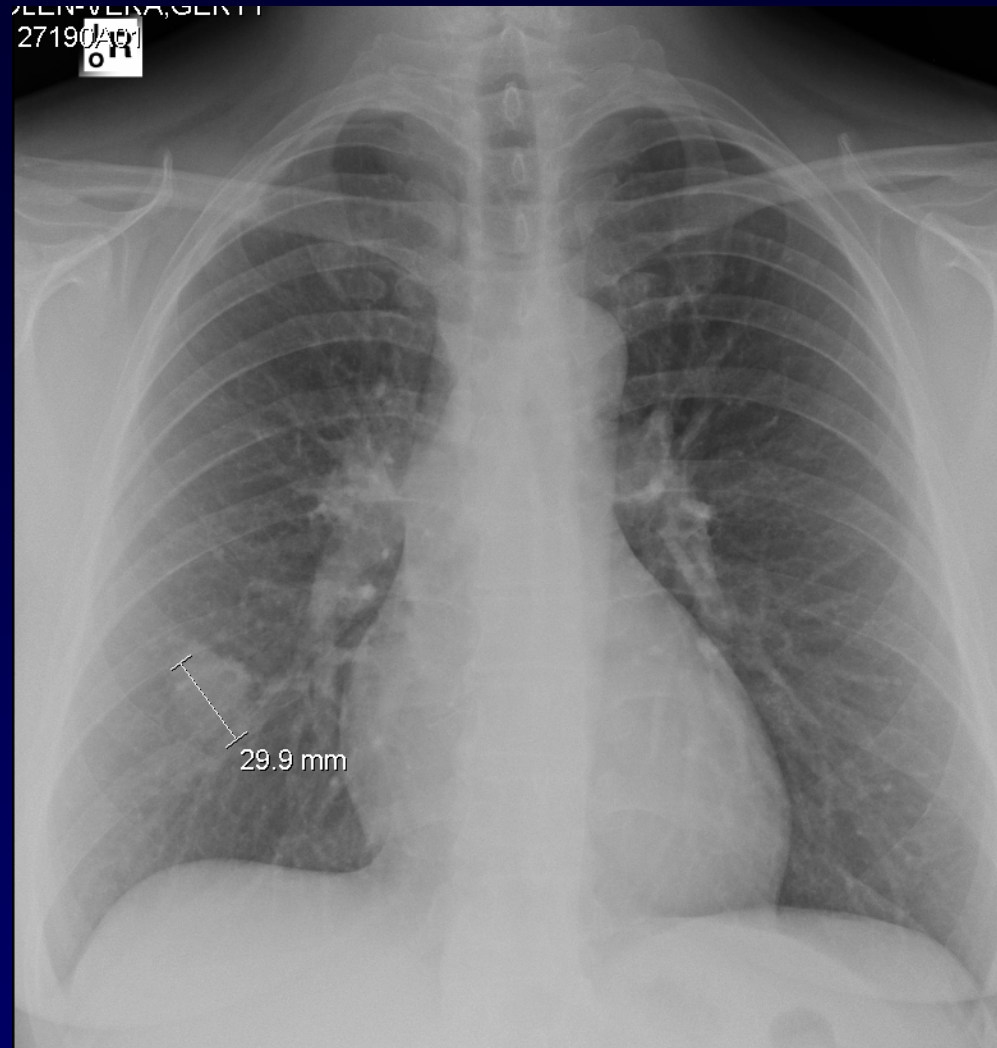
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75-year-old female
smoker presents with
cough.

Bronchoscopy :
submucosal tumor in
apex of right lower lobe.

Biopsy: squamous cell
cancer

No previous medical
history of significance



Case Stage III NSCLC

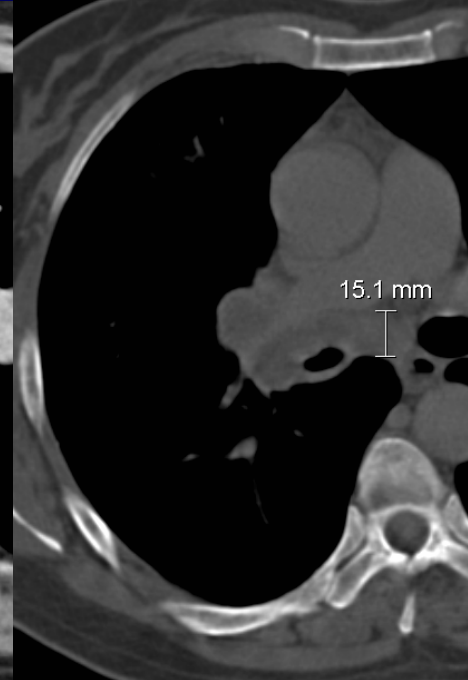
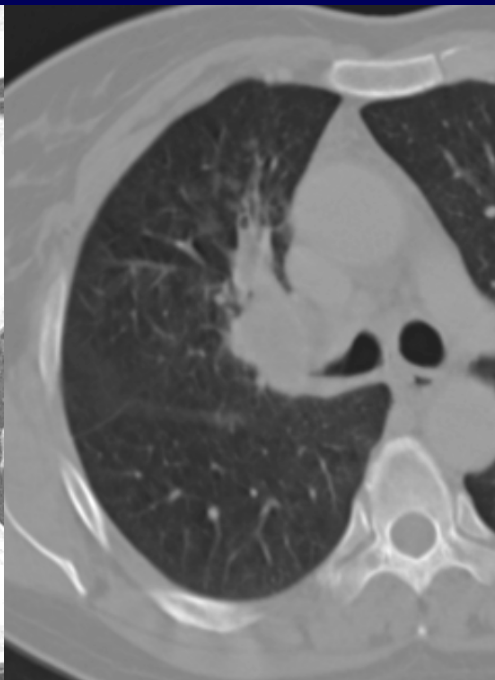
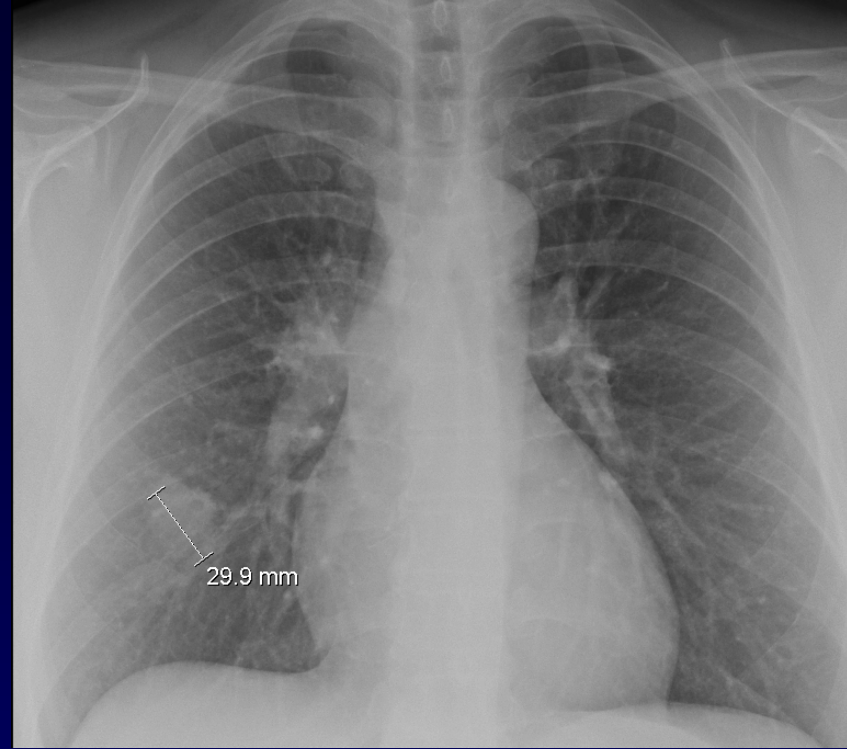
Lung function tests:

FVC = 91%

FEV1 = 71%

DLCO = 61% of predicted

Normal renal and hepatic function tests



75-year-old Female Smoker

- FDG-PET scan: uptake in intrapulmonary lesion and hilar mass, extending to the mediastinum (4 right) and subcarinal regions.
- Pathology: squamous cell cancer
- Normal hematological, renal and hepatic function tests

What is the Clinical TMN Stage?

Which additional investigations would you perform?

- None - assume that it is bulky stage III NSCLC
- Endoscopic biopsy of the mediastinal nodes
- Cervical mediastinoscopy
- MRI scan of the brain
- Endoscopic biopsy of nodes & MRI scan of the brain
- Cervical mediastinoscopy & MRI scan of the brain

Case 7: Part III

Which chemotherapy regimens would you select for the patient?

- Etoposide + cisplatin (SWOG scheme – every 28 days)
- Etoposide + cisplatin (3 weekly scheme with cisplatin 80 mg/m²)
- Carboplatin + paclitaxel
- Navelbine + cisplatin
- Gemcitabine + cisplatin
- Combinations of the above

SEER analysis: Age distribution

≥80 years = 14%

70-79 years = 33%

<70 years = 53%

30% increase in patients aged ≥ 80 years observed from 1988-97 to 1998-03.

Reluctance to treat even in the fit elderly patients due to fears of toxicity and operative morbidity-mortality

Stage III-N2: Treatment Subgroups

- Based on tumor extent and performance score, 3 subgroups can be identified:
 - Patients eligible to receive concurrent CT-RT
 - Patients fit for sequential CT-RT
 - Patients who require a tailored approach, including palliative care only

Eligibility for Concurrent CT-RT

>50% of stage III lung cancer patients are theoretically ineligible for concurrent CT-RT; less toxic alternatives are required

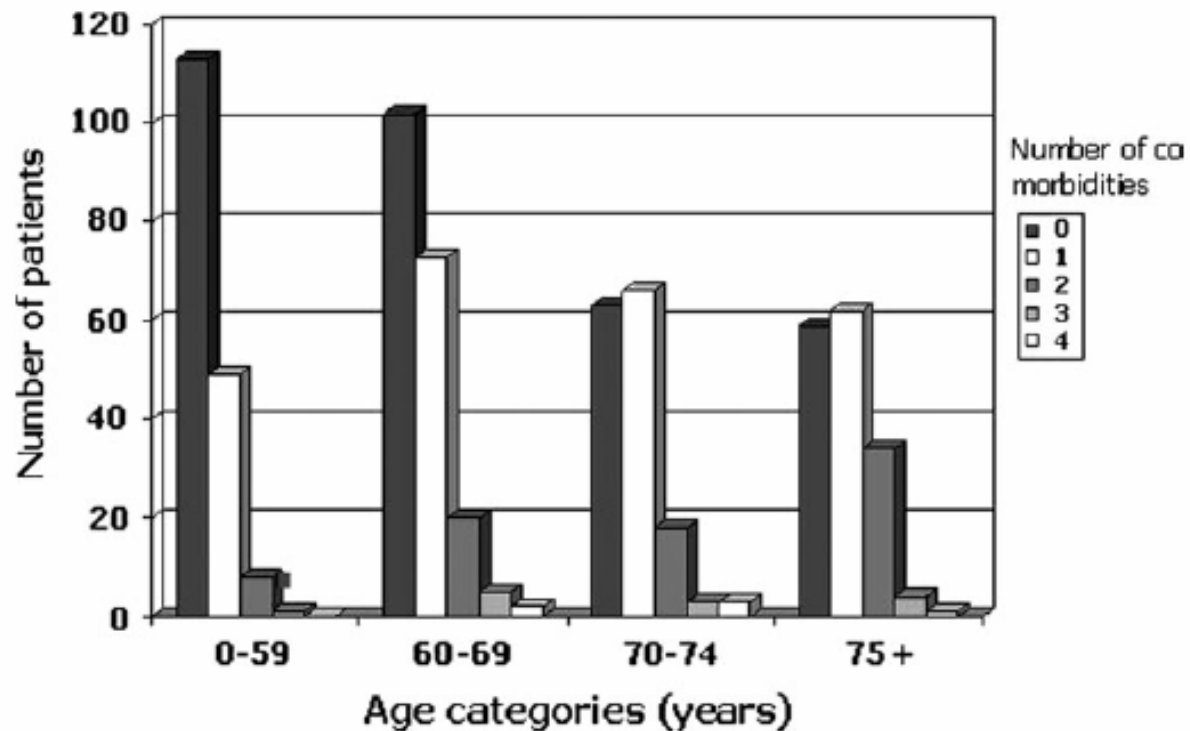


Figure 1. Number of comorbidities per age category, stage III non-small-cell lung cancer and limited disease small-cell lung cancer.

Toxicity of Thoracic CT-RT in Elderly

Elderly defined as >70 years

Author	Trial	Toxicity
Langer '02	RTOG 94-10	Gr 3 esophagitis more common in patient older than 70 yrs
Schild '03	NCCTG 94-24-52	More Gr 4 myelosuppression (81% vs 62%) and pneumonitis (6% vs 1%)
Rocha Lima '02	CALGB 9130	More Gr 3+ neutropenia and renal toxicity
Yuen '00	INT 0096 (LD-SCLC)	More Gr 3-4 hematological toxicity (84% vs 61%) and more fatal toxicities (10% vs 1%)

Stage III-N2: Subgroups and Survival

Subset	Description
IIIA ₁	Nodal metastases found incidentally on the final pathological examination of resected surgical specimen
IIIA ₂	Nodal metastases (single station) found intraoperatively
IIIA ₃	Nodal metastases identified during pre-thoracotomy staging (mediastinoscopy; endoscopy, PET scan)
IIIA ₄	Bulky or fixed multi-station N2 disease
IIIB	T4 – N3

Median survival reported in phase III trials of CT-RT

22.2 months
Albain '05

17.9- 23.2 months
Movsas '05; Hanna '08

Risks and Benefits of CT-RT

	$V_{20} \leq 35\%$	$V_{20} > 35\%$
Radiation pneumonitis \geq Grade 3	4 %	10 %
Median survival	24 mo	12 mo

Toxicity of CT-RT: CTC AE v3.0

	Grade 3	Grade 4
Pneumonitis	Symptomatic and interfering with ADL; Oxygen indicated	Life-threatening; ventilatory support needed
Esophagitis	Symptomatic and severely altered eating/swallowing; IV fluids, tube feedings, or TPN indicated >24 hrs	Life-threatening consequences (e.g. obstruction, perforation)

Post-surgical 30-day Mortality

	Age								
	20–59 Years			60–69 Years			70 Years and older		
	<i>N</i>	%	POM (%)	<i>N</i>	%	POM (%)	<i>N</i>	%	POM (%)
(Bi)lobectomy	1049	68	0.8	1725	71	2.4	1642	77	4.9
Pneumonectomy	496	32	3.8	702	29	7.3	496	23	11.5

POM – post-operative mortality

Which Cisplatin-Etoposide Scheme?

Cisplatin 80 mg/m² on days 1, 21, 42 and **etoposide** 100 mg/m² days 1-3, 21-23 and 42-45 (commonly used in European centers)

Cisplatin 50 mg/m² on days 1, 8, 29, and 36, and **etoposide** 50 mg/m² on days 1-5 and 29-33
[Albain 2005; Rusch 2007; Hanna 2008]

Treatment Scheme Used

1 cycle cis-gemcitabine, followed by:

Radiotherapy planned using a 4DCT to **60 Gy** (30 fractions of 2 Gy) concurrent with 2 cycles cisplatin-etoposide administered 3 weekly

Esophagitis with Involved-field CT-RT

Incidence related to **volume** of irradiated and **radiation dose**. In 3 randomised phase II studies, G3 \geq esophagitis seen in **17-24%**

Minimize impact of high-grade esophagitis by:

- Referral to a dietician,
- Monitoring body weight twice-weekly,
- Aggressive treatment with analgesics,
- Anti-fungal therapy,
- Early placement of feeding tubes when indicated.

Hematopoietic CSF's During CT-RT

White blood cell growth factors should be avoided in patients receiving concomitant chemotherapy and RT, particularly involving the mediastinum.

Erythropoiesis-stimulating Agents?

8 controlled trials of ESA's show a **worse outcome**, either **increased mortality** or **increased tumor progression**:

Significantly worse survival in 6 trials

BEST — chemotherapy in metastatic breast cancer (n=939);
2001-0161 — chemotherapy in lymphoid malignancy (n=344);
ENHANCE — radiotherapy alone in head and neck cancer (n=351);
DAHANCA — radiotherapy alone in head and neck cancer (n=522);
EPO-CAN-20 — no chemotherapy or radiotherapy in NSCLC (n=70);
2001-0130 — no chemotherapy or radiotherapy in non-myeloid malignancy (n=989).

2 trials show trend toward shorter survival

PREPARE — chemotherapy in neoadjuvant breast cancer (n=733);
GOG 0191 — chemotherapy in cervical cancer (n=114).