

# Radical radiotherapy in stage III non small cell lung cancer

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# Radiotherapy in lung cancer

- 1947 / 1948 : First publications in the literature
- Dr Jackson, USA, 1951: case reports:

*'...roentgen therapy has a definite place in the amelioration of symptoms and occasionally unexpected results occur'*

# Radiotherapy in lung cancer

- Systematic review 2001, Rowell:

*' ....radical radiotherapy appears to result in a better survival than might be expected had treatment not been given'*

- Up to 2000: stage III NSCLC 5-year survival 10 -15 %



# A lot has changed in the last 2 decades

- Modern linacs and software:
  - > higher precision
  - > higher doses possible, without more toxicity
- Increased use of combination with chemotherapy

# Radical radiotherapy NSCLC

- Stage I: operation or stereotactic radiotherapy
- Stage II: operation or conventional radiotherapy (+/- chemotherapy)
- Stage III: combined conventional radiotherapy and chemotherapy (chemoradiotherapy)

# Stage III NSCLC

- Heterogenous group!

From a large tumor without nodal metastases  
(T4 N0)

to a tiny tumor with profound nodal metastases  
(T1 N3)

# Stage III NSCLC

- Many chemoradiotherapy studies in the last 20 y
- Target group in these studies: inoperable  
younger patients  
in good condition  
without pathological weight loss and  
with small to moderate size tumors

# Stage III NSCLC

- These studies have shown:

Chemoradiotherapy better than radiotherapy

Concomitant chemotherapy better than sequential

Platinum based chemotherapy first choice

Minimum radiation dose 60Gy (2Gy\*30)

# Stage III NSCLC

- Guidelines radical radiotherapy:  
ECOG 0 - 1(2) and no pathological weight loss:

Radiation dose 60 – 66 Gy +

2 cycles of cisplatin / etoposide or  
cisplatin / vinorelbine, given concomitantly

At choice: + 1 cycle before start of radiotherapy

# Stage III NSCLC

- Believes that stopped and still stops several patients from getting radical treatment:
  - *Tumors over 7-8 cm are too big to be cured*
  - *N3 node disease cannot be cured*
  - *Patients above age 75 are too old for such treatment*
  - *Patients with pathological weight loss have no chance*
  - *Patients in poor performance status have no chance*

# Does size matter?

- J Thorac Oncol, 2013, IASLC, 868 pts

Tumor, cm	number	median survival
$\leq 3$ cm	233	1,8 y $p=0,02$
$> 3$ and $\leq 5$	297	1,3 y
$> 5$ and $\leq 7$	175	1,4 y
$> 7$ cm	163	1,1 y

# Does size matter? II

- Radioter Oncol, 2013, Trans-Tansman, 509 pts

> No significant prognostic effect of size

- So: Mostly, size does not matter

# Does advanced N stage matter?

- J Thorac Oncol, 2013, IASLC, 868 pts

	number	median surv	
N0	158	1,6 y	
N1	43	1,4 y	
N2	545	1,4 y	
N3	122	1,3 y	<i>ns</i>

# Does advanced N stage matter? II

- Radioter Oncol, 2013, Trans-Tasman, 509 pts
  - > No significant differences N1 vs N2 vs N3
- IJROBP, 2014, Rodrigues, 1274 pts
  - > No significant differences N1 vs N2 vs N3
- So: Advanced N-stage does not matter

# Does age matter?

- J Thorac Oncol, 2013, IASLC, 868 pts

> Age is prognostic as a continuous variable, but there is no cut-off value

- Radioter Oncol, 2013, Trans-Tasman, 509 pts

> No age differences

# Does weight loss matter?

- Patients with pathological weight loss have a worse outcome
- But there are studies in which this was not a significant factor



"Sudden weight loss, profuse sweating...  
I'm sorry, I'm afraid you're melting."

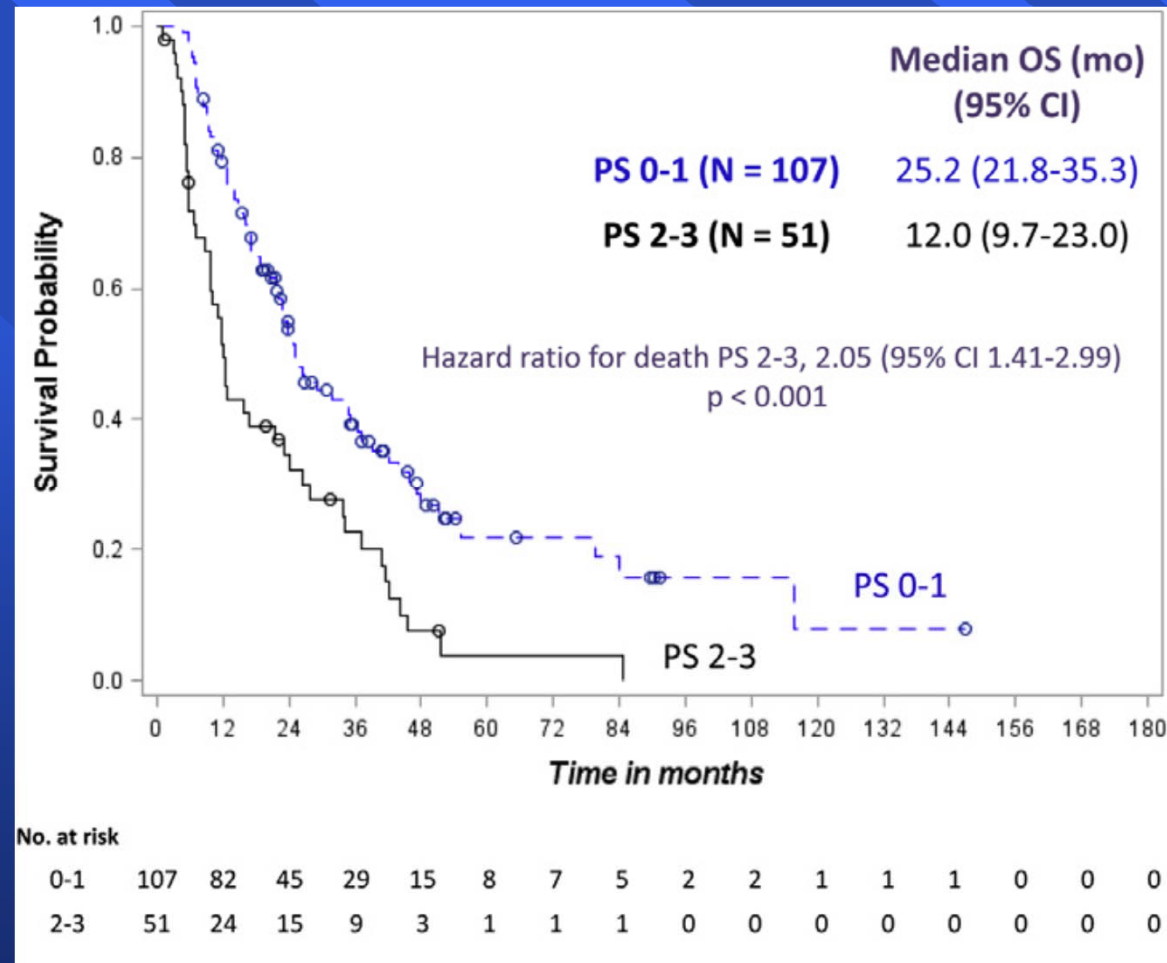
# Does Performance Status matter?

- Same conclusion in all studies with focus on performance status:

Bad outcome for patients with ECOG PS  $\geq 2$

- But mark the underlying cause:
  - Cancer related?
  - Comorbidity related?

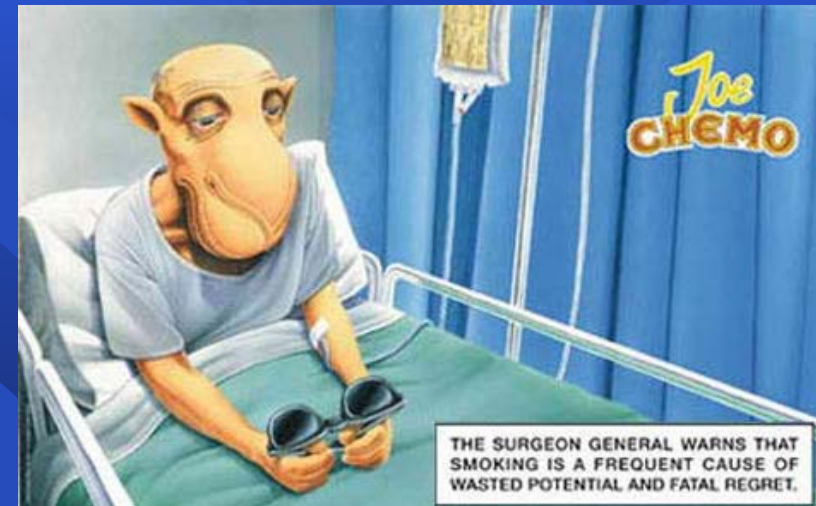
# Does Performance status matter? II



Dudani et al, Clin Lung Cancer, 2017

# Does continuing smoking matter?

- Continuous smokers have
  - Less effect of radiotherapy
  - Less effect of chemotherapy
  - More side-effects



# Stage III NSCLC today

- Radical chemoradiotherapy should be offered to inoperable patients in acceptable condition without too much weight loss, regardless of
  - Tumorsize
  - N-stage
  - Age

# Stage III NSCLC today II

- Population based 5-year survival:

Maastro Clinic, The Netherlands

Radical chemoradiotherapy      31 %

- So: more than a doubling in the last 2 decades

# Stage III NSCLC tomorrow?

- Chemoradiotherapy + .....



# PACIFIC-study: game changer?

- Median progression free survival:

– Durvalumab	16.8 mths
– Placebo	5.6 mths

- 1-year progression free survival:

– Durvalumab	55,9 %
– Placebo	35,3 %

