

## Do we need biopsy to treat early inoperable lung cancer?

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## Pathological verification of malignancy

<b>Patients</b>	402*
<b>Gender</b>	
Male	241 (60%)
Female	161 (40%)
<b>Median age</b>	74 Years
<b>Stage</b>	
T1 N0 M0	249 (62%)
T2 N0 M0	153 (38%)
<b>Pathological confirmation</b>	
Yes	139 (35%)
No	263 (65%)
<b>WHO class</b>	
0-1	251 (62%)
2-3	151 (38%)
<b>Charlson co-morbidity score (age-adjusted)</b>	
≤ 4	24 (6%)
5-6	131 (33%)
≥ 7	247 (61%)

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## How (un)acceptable is this policy to treat medically inoperable patients suspected to have early stage NSCLC without prior histological verification ?

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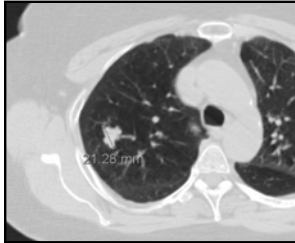
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### Case study



- 60 years old female
- Severe COPD  
*FEV<sub>1</sub> 0.92 (38%); DCO 45%*
- Diagnosed during routine fu
- Lesion 21 mm right upper lobe
- WHO 1; Charlson score 5
- Smoking history, never quit

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**How would you estimate the pre-test probability of malignancy in this patient (without FDG-PET)?**

- A. <40%
- B. 40-60%
- C. 60-80%
- D. >80%

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### Probability of malignancy of SPN

Swensen et al. 1997 (Mayo); clinical & radiological criteria

$$\text{Probability of malignancy} = e^{X/(1+e^X)}$$

X = -6.8272	+ 0.039 * age
	+ 0.792 * smoking
	+ 1.339 * prior cancer
	+ 0.127 * diameter
	+ 1.041 * spiculation
	+ 0.784 * upper lobe

For this patient, the pre-test probability of malignancy based on the Swensen calculation (X = 0.7968) is **69%**

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### Probability of malignancy of SPN

Gould et al. 2007 (Stanford): clinical & radiological criteria

Probability of malignancy =  $e^X / (1 + e^X)$

X = -8.404      + 0.779 \* age/10  
                   + 0.112 \* diameter  
                   + 2.061 \* smoking  
                   - 0.567 \* years quit

N=375  
Lesions 7-30 mm  
Prevalence of malignancy 54%

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### Probability of malignancy SPN (Gould 2007)

Diameter	5mm	10mm	15mm	20mm	25mm	30mm	35mm	40mm
<b>50 years</b>								
Current smoker	13	21	32	45	59	71	81	88
Never smoked	2	3	6	9	15	24	36	49
<b>60 years</b>								
Current smoker	25	37	50	64	76	84	90	94
Never smoked	4	7	11	18	28	41	55	68
<b>70 years</b>								
Current smoker	42	56	69	79	87	92	95	97
Never smoked	8	14	22	33	46	60	72	82
<b>80 years</b>								
Current smoker	61	73	83	89	94	96	98	99
Never smoked	17	26	38	52	65	77	85	91

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### Probability of malignancy of SPN

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X = -8.404      + 0.779 \* age/10  
                   + 0.112 \* diameter  
                   + 2.061 \* smoking  
                   - 0.567 \* years quit

N=375  
Lesions 7-30 mm  
Prevalence of malignancy 54%

For this patient, the pre-test probability of malignancy based on the Gould calculation (X = 0.683) is **66%**

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**How would you estimate the pre-test probability of malignancy in this patient (without FDG-PET)?**

- A. <40%
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- C. 60-80%**
- D. >80%

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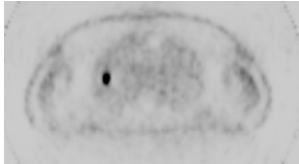
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**Case study**



<sup>18</sup>F-FDG-PET scan showed intense uptake in the lesion in the right upper lobe  
No pathological uptake in the mediastinum or elsewhere

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**Would you perform CT-guided biopsy in this patient with poor pulmonary function (FEV1 38%, DCO 45%)?**

- A. Yes
- B. No, not in regard of the pulmonary function
- C. No, the probability of malignancy is high enough to justify treatment

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### Transthoracic biopsy



Diagnostic transthoracic biopsy is a minimally invasive procedure, which is accurate and safe.....

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Transthoracic needle aspiration biopsy for the diagnosis of localised pulmonary lesions: a meta-analysis [Lacasse *et al.*]

- 48 studies included, with 9000 biopsies
- Sensitivity 88%; Specificity 98%
- Pneumothorax incidence 24.5% (range 3%-42%)
- Chest tube drainage 6.8% (range 0%-17%)

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### Transthoracic biopsy

Biopsy is accurate; the risk of significant toxicity is low, but not to be ignored (higher in COPD, advanced age)

TABLE 3 Rate of Pneumothorax for Each Range of Influencing Factors

Factor	Pneumothorax Rate (%)
% of predicted forced expiratory volume in 1 sec	
≤ 50	66.7*
51-60	45.7*
61-70	27.1*
71-80	2.9
≥ 81	0.0

Ohno *et al.*; 2003 (N=162 biopsies)

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### What does a positive <sup>18</sup>F-DG-PET indicate ?

False positive (and negative) findings are not uncommon; e.g. benign tumors, inflammatory disease; eg. lung infections, sarcoidosis, tuberculosis.

Sensitivity <sup>18</sup>F-DG-PET: 98%  
Specificity <sup>18</sup>F-DG-PET: 83% [meta-analysis Gould *et al.* 2001]

To answer the above question: assessment of the positive predictive value (PPV)

$$PPV = \frac{\text{True positive}}{\text{True positive} + \text{False positive}}$$

PPV is reported to be 50-100%, highly dependent on the prevalence of disease, i.e. larger in a high risk population. In meta analyses reported to be 88%-95%

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### Post-test probability of malignancy Integrating clinical, radiological and PET data

Herder *et al.* 2005; Swensen criteria + <sup>18</sup>F-DG-PET findings

$$\text{Probability of malignancy} = \frac{e^X}{1+e^X}$$

X = -4.739 + 3.691 \* (Swensen probability)

+2.322 (faint PET uptake) *or*  
+4.617 (moderate PET uptake) *or*  
+4.771 (intense PET uptake)

For this patient, the post-PET probability of malignancy based on the Herder calculation is **93%**

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### Would you perform CT-guided biopsy in this patient with poor pulmonary function (FEV1 38%, DCO 45%)?

- A. Yes
- B. No, not in regard of the pulmonary function
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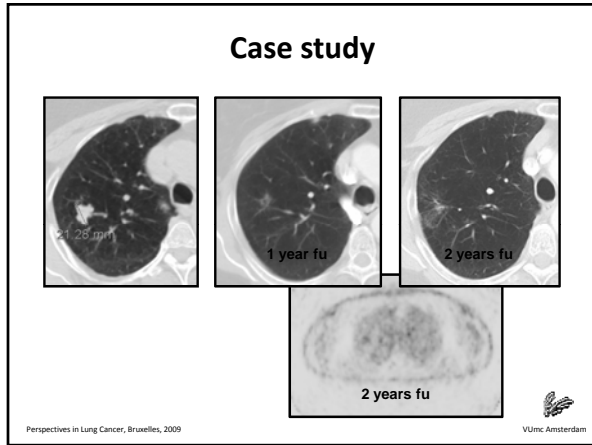
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Current smoker	61	73	83	89	94	96	98	99
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Age: mean 72 yrs, median 72 yrs, range 47-91 yrs  
 Smoking history: 98% (257/262); 65% current smokers  
 Lesion diameter: mean 26 mm, median 25 mm, range 6-79mm

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### Characteristics of SBRT pts without pathology

**Pre-test probability (Gould)**

**Post-test probability (Herder)**

In addition, only 2% of pts had no prior imaging (different from screening studies)  
 In addition, more than 35% of lesions had shown growth on sequential imaging

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### SBRT results in pts with/without pathology

Comparing 139 pts with and 263 pts without pathology treated with SBRT

Overall survival:	n.s. (p=0.23)
Local control:	n.s. (p=0.78)
Regional control:	n.s. (p=0.84)
Distant control:	n.s. (p=0.65)
Disease-free survival:	n.s. (p=0.82)

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### Management strategy for SPN pts ACCP guidelines; Chest 2007

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    graph TD
      A["New SPN (8-30mm) on CXR or CT scan without benign calcifications"] --> B["Surgical risk acceptable?"]
      B -- no --> C["Establish diagnosis by biopsy. Consider XRT or monitor for symptoms and palliation"]
      B -- YES --> D["Assess clinical probability of malignancy"]
      D --> E["Low probability (<5%)"]
      D --> F["Intermediate probability (5%-60%)"]
      D --> G["High probability (>60%)"]
      E --> H["Serial CT scans 3, 6, 12, 24 mos"]
      F --> I["Additional testing: FDG-PET, transthoracic biopsy, contrast-enhanced CT"]
      G --> J["VATS, frozen section, resection if malignant"]
      H -- "Negative tests ↑" --> I
      I -- "Positive tests ↓" --> J
    
```

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### Management strategy for SPN pts

Suspect SPN in a patient with a high pre-test probability for malignancy:  
surgery is recommended

Why wouldn't the same strategy apply to medically inoperable patients  
with a post-test (<sup>18</sup>F-DG-PET) probability of >80%

after all, the complication rate of 'invasive' diagnostic procedures (in this  
patient population) may be larger than that of curative SBRT

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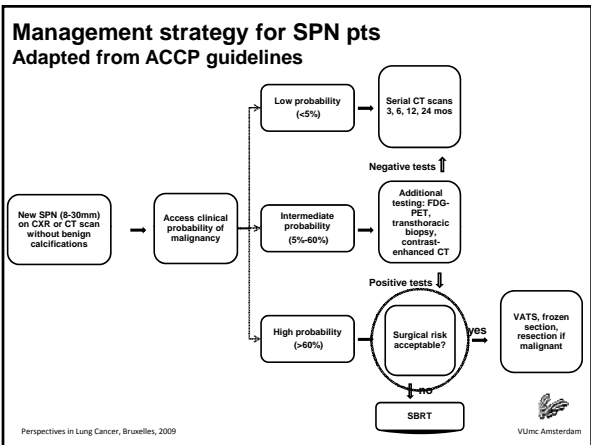
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## Thank you!



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