



Penn Medicine

Resident Report

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PGY3

Pennsylvania Hospital | UPHS

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Case



- ▶ 27 year old female with no past medical history who loves biking, skiing, and adventure racing

Adventure Racing

- ▶ Multidisciplinary team sport
 - Trekking
 - Mountain biking
 - Paddling
 - Other: climbing, rappelling, horse riding, skiing, and white-water rafting
- ▶ 2 hour to 5 days in length



- ▶ 27 year old female with no past medical history who loves biking, skiing, and adventure racing
- ▶ Over the summer she noted decreased race times and notes decreased exercise capacity
- ▶ Other symptoms
 - Exertional chest pain
 - Shortness of breath
 - Increased fatigue

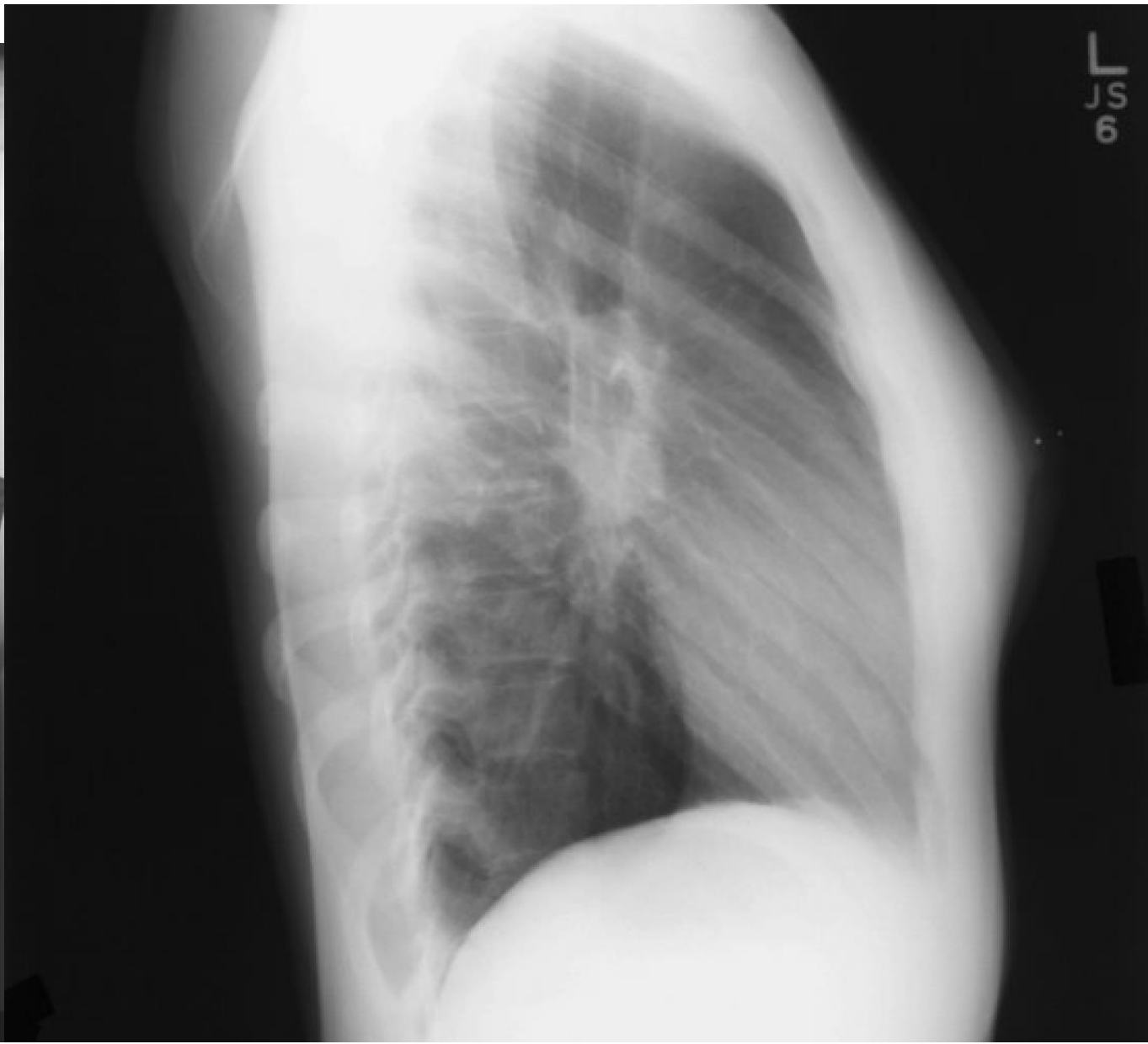
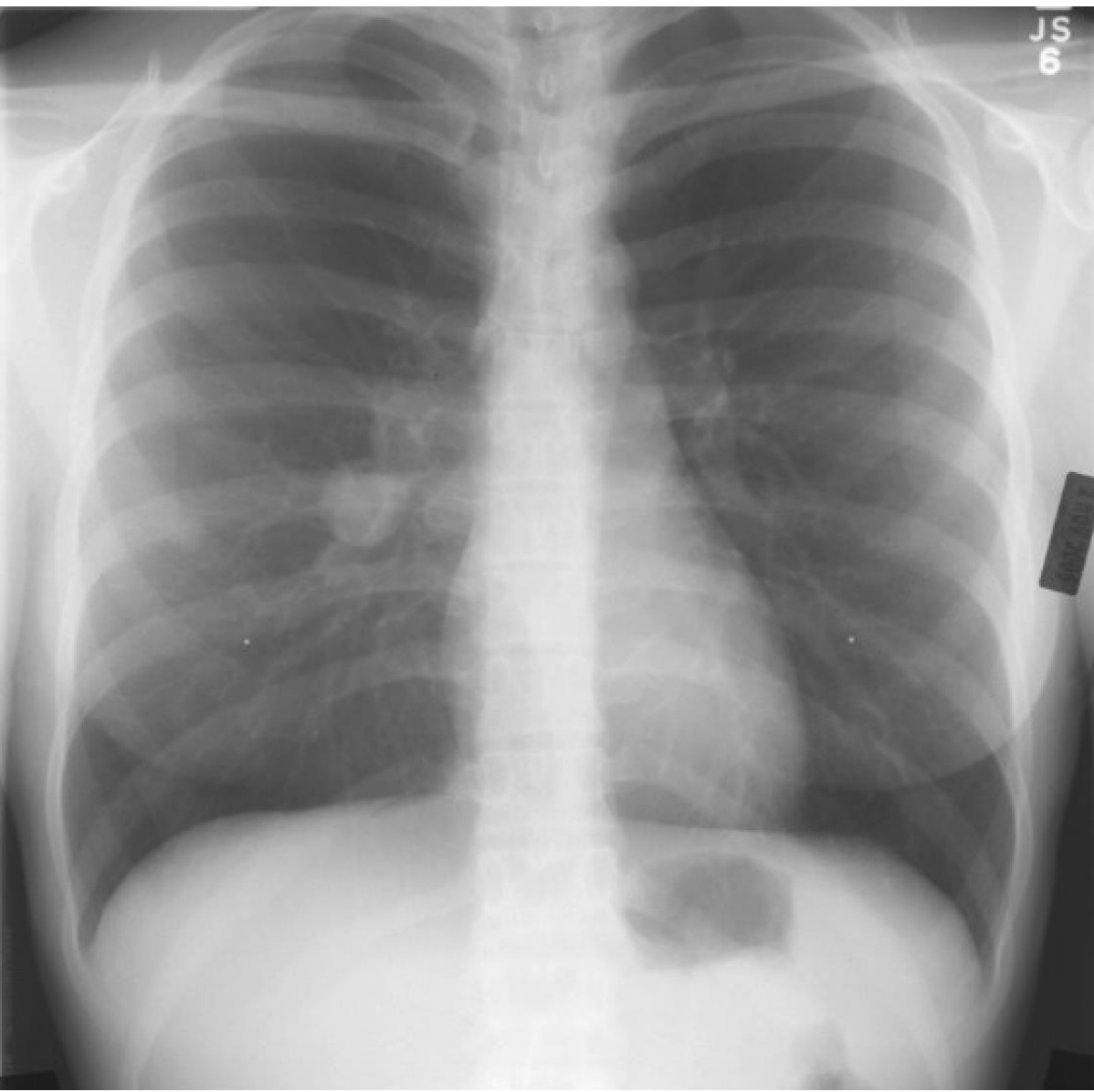
Reduced exercise capacity differential

- ▶ Pulmonary
 - Hypoventilation, shunt, decreased alveolar diffusion, dead space
- ▶ Hematologic
 - Anemia, hemoglobinopathy, CO toxicity
- ▶ Cardiovascular
 - Electrophysiological, decreased stroke volume
- ▶ Neuromuscular
 - Neuro: ALS, CIDP, GBS, MG. Muscular: myositis, myopathy
- ▶ Endocrine
 - Hypothyroidism, Cushing syndrome, DM
- ▶ Psychological
 - Phobia, social anxiety disorder, GAD, MDD

Labs

- ▶ Hb wnl
- ▶ TSH wnl
- ▶ Electrolytes wnl

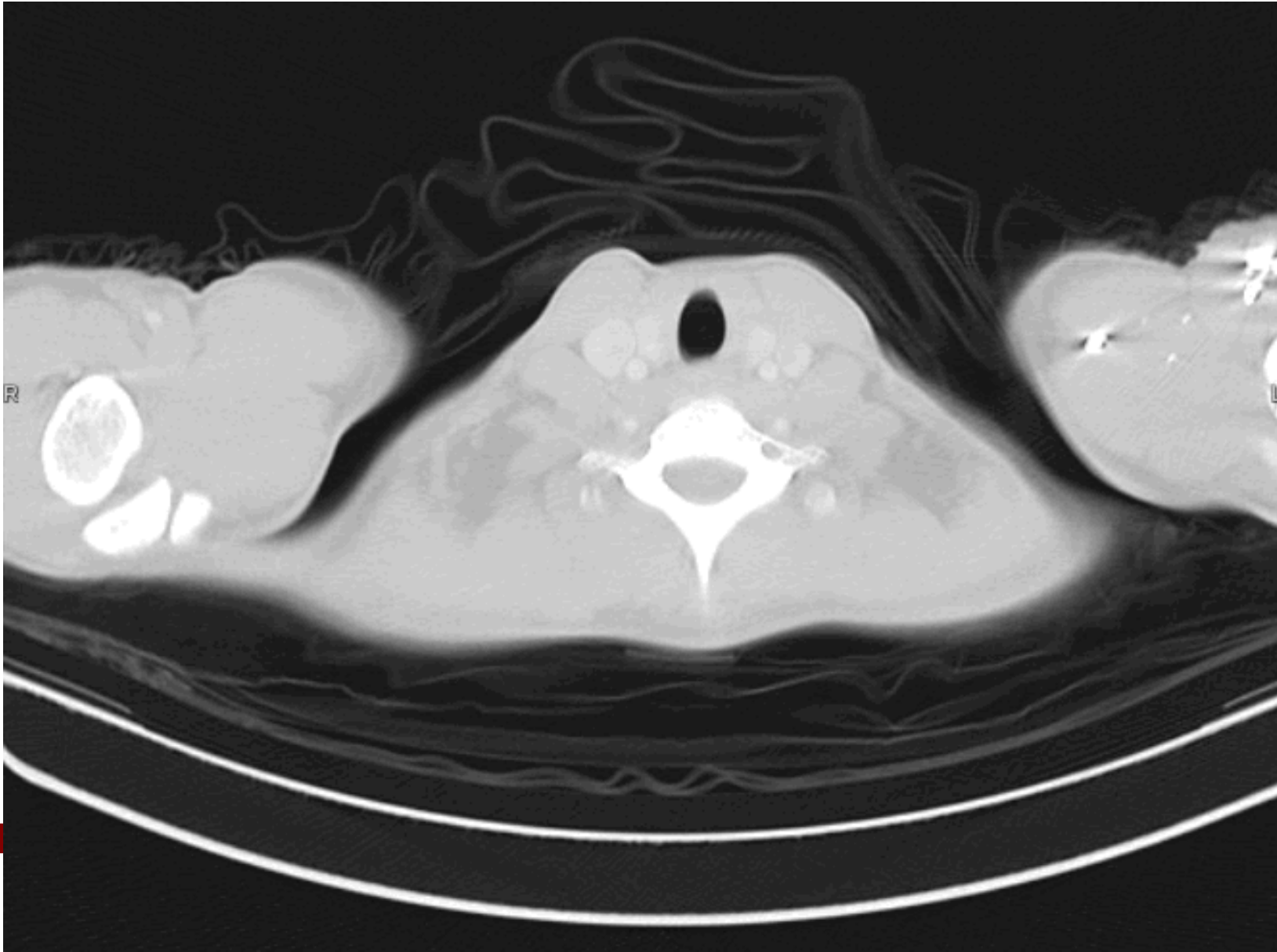
CXR



Coin Lesions

- ▶ Round or oval solitary pulmonary lesion
- ▶ Calcification +/-
- ▶ Typically asymptomatic
- ▶ Differential diagnosis
 - Malignancy
 - Infection
 - Benign disease process
- ▶ Mimics
 - Nipple shadow, costal cartilage calcification, rib fracture, pleural fluid cyst (pseudotumor), cutaneous lesion

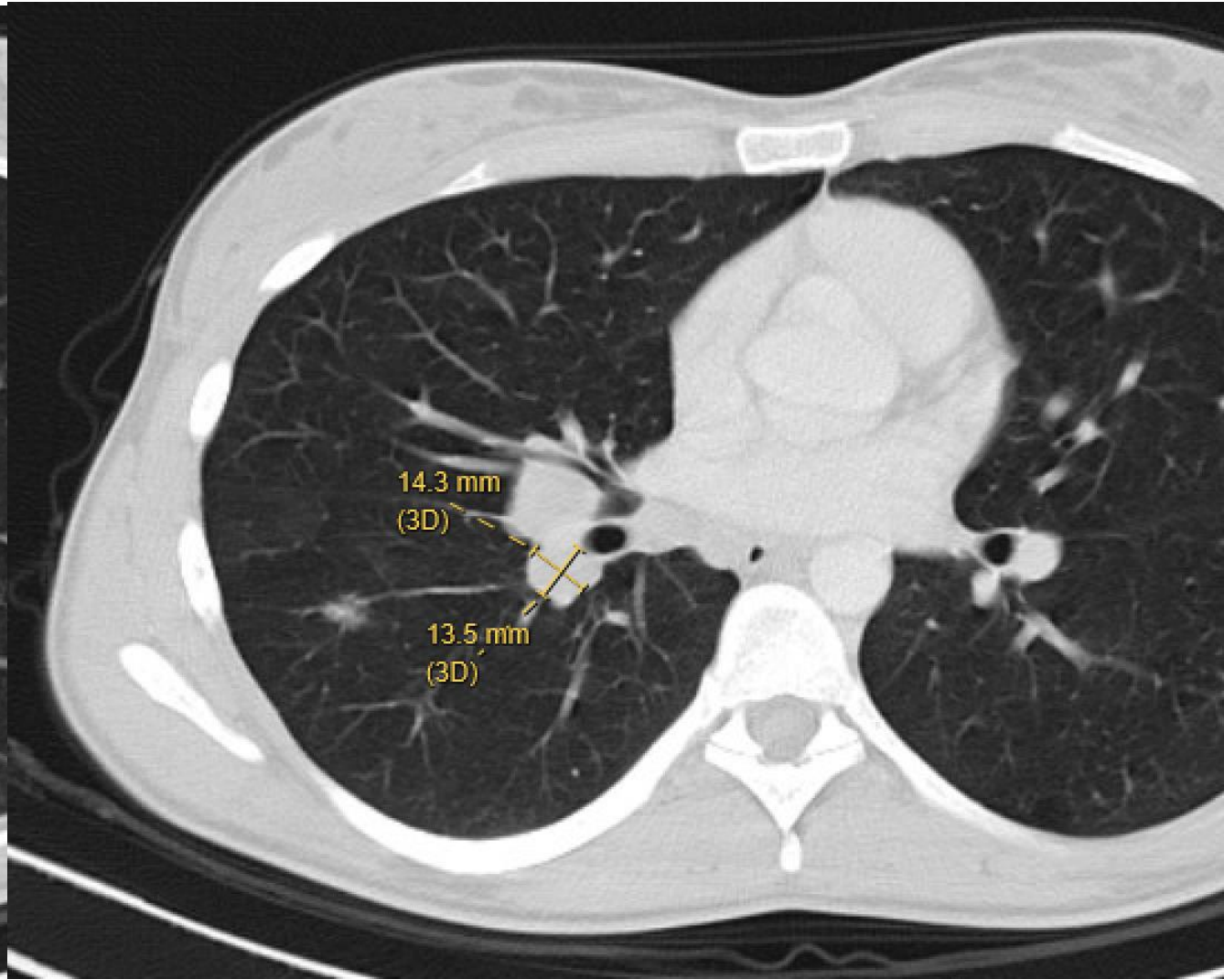
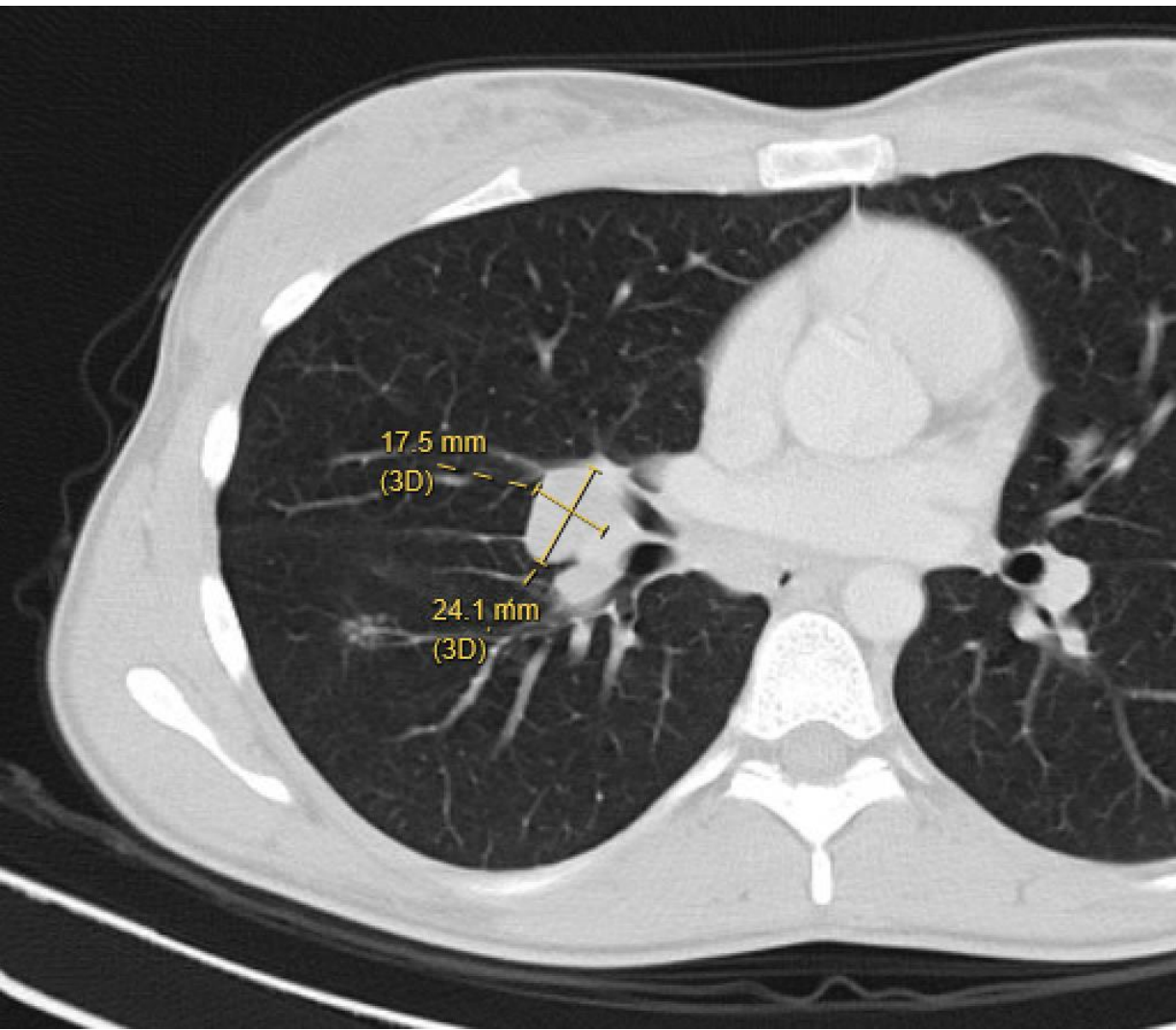
CT Chest w contrast



CT Chest w contrast



CT Chest w contrast



Staging of possible lung cancer

- ▶ Just do a CT chest, it's probably stage I



Staging of possible lung cancer

- ▶ CT Chest w contrast
- ▶ FDG PET/CT scan
- ▶ MRI brain

Staging of possible lung cancer

- ▶ PET/CT showing
 - R hilar mass
 - RUL nodule satellite metastasis
 - Hypermetabolic R hilar lymph nodes
 - R subcarinal lymph node

Staging



Tissue Biopsy

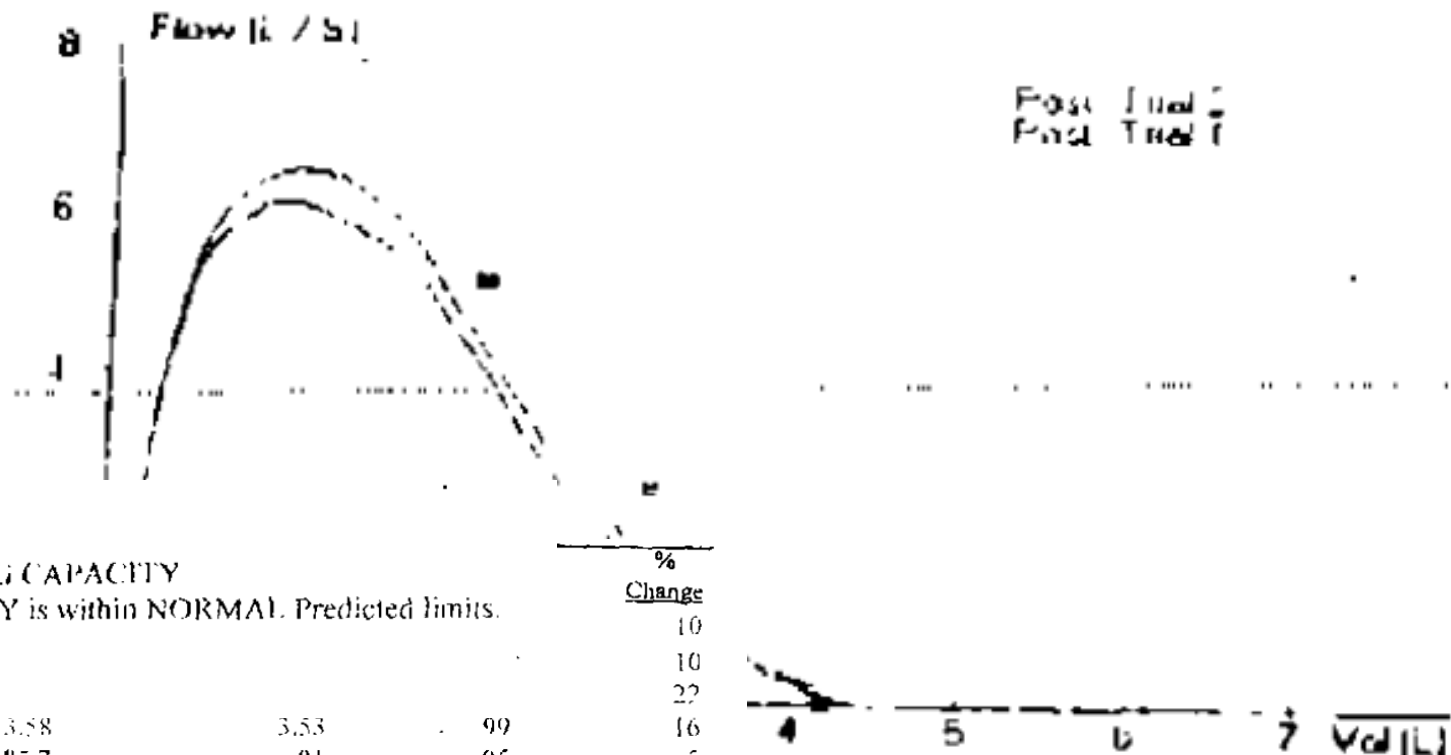
- ▶ How do we biopsy?



Tissue Biopsy

- ▶ Percutaneous transthoracic lung biopsy

Pulmonary function testing



Computer Impression:

LUNG VOLUMES are within NORMAL Predicted limits.

The Percent Predicted DLco is 99%, which suggests Normal range in DIFFUSING CAPACITY

Ratio FEV₁/FVC is 55%, suggesting POOR patient EFFORT. SPIROMETRY is within NORMAL Predicted limits.

Ratio of change in FEV₁ (16%) indicates that there is IMPROVEMENT.

FEV1	(L)	3.04	85	3.58	3.53	99	16
FVC	(L)	5.51	90	6.11	6.06	95	5
FEV3	(L)	3.81	93	4.11	4.28	104	12
FEV3/FVC	(%)	69	98	66.8	70.8	100	2
FEFmax	(L/S)	4.76	69	6.95	6.47	93	36
FEF25-75	(L/S)	2.73	67	4.11	3.49	85	27
FEF25	(L/S)	4.70	72	6.54	6.46	99	37
FEF50	(L/S)	3.12	66	5.17	4.53	82	24
FEF75	(L/S)	1.15	43	2.68	1.51	56	31
FEF100%	(Sec)	4.54		4.36			-4

(RTPS)

		Pre-BronchoDilator			Post-BronchoDilator		
# Lung Volumes #		Actual	% Predicted	Predicted	Actual	% Predicted	% Change
SVC	(L)	4.42	105	4.20	4.39	101	-1
IC	(L)	2.90	110	2.63	2.91	110	0
IRV	(L)	1.49	95	1.57	1.48	94	-1
RV	(L)	1.35	93	1.45			
TLC	(L)	5.62	102	5.50			
RV/TLC	(%)	24	91	26.42			
FRC	(L)	2.85	94	3.05			

Staging



Initial Imaging



Course

- ▶ 09/2006 CXR showing mass
- ▶ 10/2006 CT chest showing mass
- ▶ Unclear biopsy
 - Mediastinoscopy establishing carcinoma in R level 4 and level 7 lymph node involvement, no L sided lymph node involvement
- ▶ 11/2006 Neo-adjuvant cisplatin + docetaxel (Taxotere) with moderate response
- ▶ 02/2007 Surgical resection
 - Bronchoscopy, R thoracotomy, bilobectomy of R middle and lower lobes, mediastinal lymphadenectomy. Complicated by pneumothorax s/p chest tube.
 - Pathology:
 - Resection showed multiple positive N1 and N2 nodes but a resection with negative margins
 - Adenocarcinoma, 2.1cm with lymphovascular invasion and extensive necrosis
 - Metastatic carcinoma in 6/7 lobar lymph nodes
 - 2/2 level 9 lymph nodes
 - 6/6 level 7 lymph nodes
 - Level 10 lymph node negative 0/1
 - EGFR testing was negative
 - Stage IIIA NSCLC metastatic to mediastinal lymph nodes (N2)

- ▶ 27 year old female with no past medical history who loves biking, skiing, and adventure racing

Molecular and Biomarker-Directed Therapy for Advanced Disease

EGFR Exon 19 Deletion or Exon 21 L858R

- First-line therapy
 - Afatinib¹
 - Erlotinib²
 - Dacomitinib³
 - Gefitinib^{4,5}
 - Osimertinib⁶
 - Osimertinib + pemetrexed + (cisplatin or carboplatin) (nonsquamous)⁷
 - Erlotinib + ramucirumab⁸
 - Erlotinib + bevacizumab^c (nonsquamous)⁹
- Subsequent therapy
 - Osimertinib¹⁰
 - Amivantamab-vmjw + carboplatin + pemetrexed (nonsquamous)¹¹

EGFR S768I, L861Q, and/or G719X

- First-line therapy
 - Afatinib^{1,12}
 - Erlotinib²
 - Dacomitinib³
 - Gefitinib^{4,5}
 - Osimertinib^{6,13}
- Subsequent therapy
 - Osimertinib¹⁰
 - Amivantamab-vmjw + carboplatin + pemetrexed (nonsquamous)¹¹

EGFR Exon 20 Insertion Mutation

- First-line therapy
 - Amivantamab-vmjw + carboplatin + pemetrexed (nonsquamous)¹⁴
- Subsequent therapy
 - Amivantamab-vmjw¹⁵

KRAS G12C Mutation^d

- Subsequent therapy
 - Sotorasib¹⁶
 - Adagrasib¹⁷

ALK Rearrangement

- First-line therapy
 - Alectinib^{18,19}
 - Brigatinib²⁰
 - Ceritinib²¹
 - Crizotinib^{18,22}
 - Lorlatinib²³
- Subsequent therapy
 - Alectinib^{24,25}
 - Brigatinib²⁶
 - Ceritinib²⁷
 - Lorlatinib²⁸

ROS1 Rearrangement

- First-line therapy
 - Ceritinib²⁹
 - Crizotinib³⁰
 - Entrectinib³¹
 - Repotrectinib³²
- Subsequent therapy
 - Lorlatinib³³
 - Entrectinib³¹
 - Repotrectinib³²

BRAF V600E Mutation

- First-line therapy
 - Dabrafenib/trametinib³⁴
 - Encorafenib/binimetinib³⁵
 - Dabrafenib³⁶
 - Vemurafenib
- Subsequent therapy
 - Dabrafenib/trametinib^{36,37}
 - Encorafenib/binimetinib³⁵

NTRK1/2/3 Gene Fusion

- First-line/Subsequent therapy
 - Larotrectinib³⁸
 - Entrectinib³⁹

MET Exon 14 Skipping Mutation^d

- First-line therapy/Subsequent therapy
 - Capmatinib⁴⁰
 - Crizotinib⁴¹
 - Tepotinib⁴²

RET Rearrangement^d

- First-line therapy/Subsequent therapy
 - Selpercatinib⁴³
 - Pralsetinib⁴⁴
 - Cabozantinib^{45,46}

ERBB2 (HER2) Mutation^d

- Subsequent therapy
 - Fam-trastuzumab deruxtecan-nxki⁴⁷
 - Ado-trastuzumab emtansine⁴⁸

[PD-L1 ≥50% First-line Therapy](#)

[PD-L1 ≥1%–49% First-line Therapy](#)

Thank You!

