MESOTHELIOMA

Not Just a Late Night Commercial

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Saturday Session

Thoracic Surgery Nurse Practitioner

Greater Los Angeles Veteran Affairs

Objectives

Course Objectives:

- Discuss risk factors for malignant pleural mesothelioma
- Discuss clinical and radiologic findings in mesothelioma
- Discuss current treatment/disease management options

At the end of the presentation, participant will be able to:

- State at least 3 mesothelioma risk factors
- Identify at least 3 clinical and radiologic finding in patients with mesothelioma
- Describe current lung-sparing treatment modalities for mesothelioma

Mesothelioma

- Tumor arising from the mesothelium
  - Pleural
  - Pericardium
  - Peritoneum
- 80% are Pleural Mesotheliomas (MPM)
  - 60% right-sided
- Usually spreads locally along ipsilateral pleura
- Linked to asbestos exposure in 1960[1]

[2]Wagner JC, et. al. Meso and asbestos in NW Cape Prov. Br J Ind Med 1960;17:260-71

MPM Epidemiology

Incidence

- US 2000-3000/yr[2]
  - Overall: 1.2/100,000
  - High risk males: 63.6/100,000
  - High risk females: 9.6/100,000
- Global[3]
  - Overall mortality 1994 – 2008: 4.9/million

MPM Epidemiology

- Latency period of 20-40+ years
- Median age = 60 yrs (5^{th}-7^{th} decades)
- Age range 28-90+
- Male:female = 3:1
- Etiology: Asbestos

Asbestos


THE GREAT SEAL OF THE STATE OF CALIFORNIA
EUREKA


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Asbestos

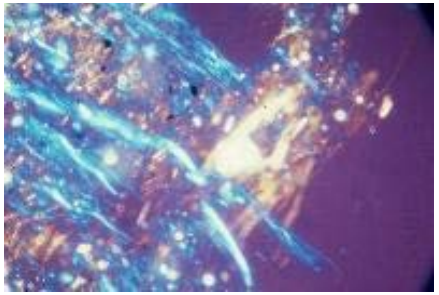
- Group of hydrated magnesium silicate fibrous minerals
- 2 Major types
  - Serpentine
  - Amphibole
- Resistant to heat and combustion
- Used in production of
  - Cement
  - Ceiling
  - Tiles
  - Brake linings
  - Ship buildings

Sterman, D. H., & Albelda, S. M. (2005). Advances in the diagnosis, evaluation, and management of malignant pleural mesothelioma. *Respirology*, *10*(3), 266-283.

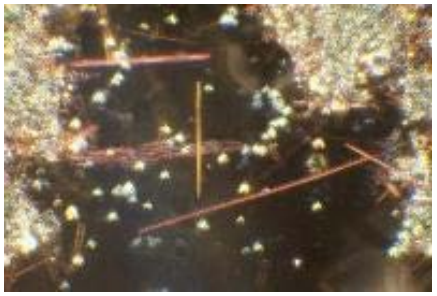
Asbestos

Fiber Types

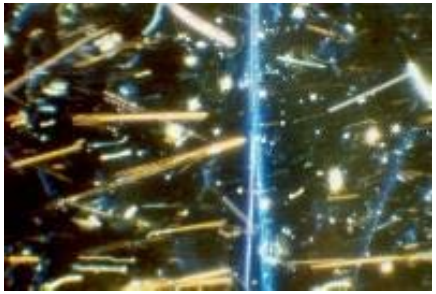
- Serpentine (large curly pliable fibers)
  - Chrysotile



- Amphibole (long narrow rod-like fibers)
  - Crocidolite
  - Amosite
  - Tremolite
  - Anthophyllite
  - Actinolite

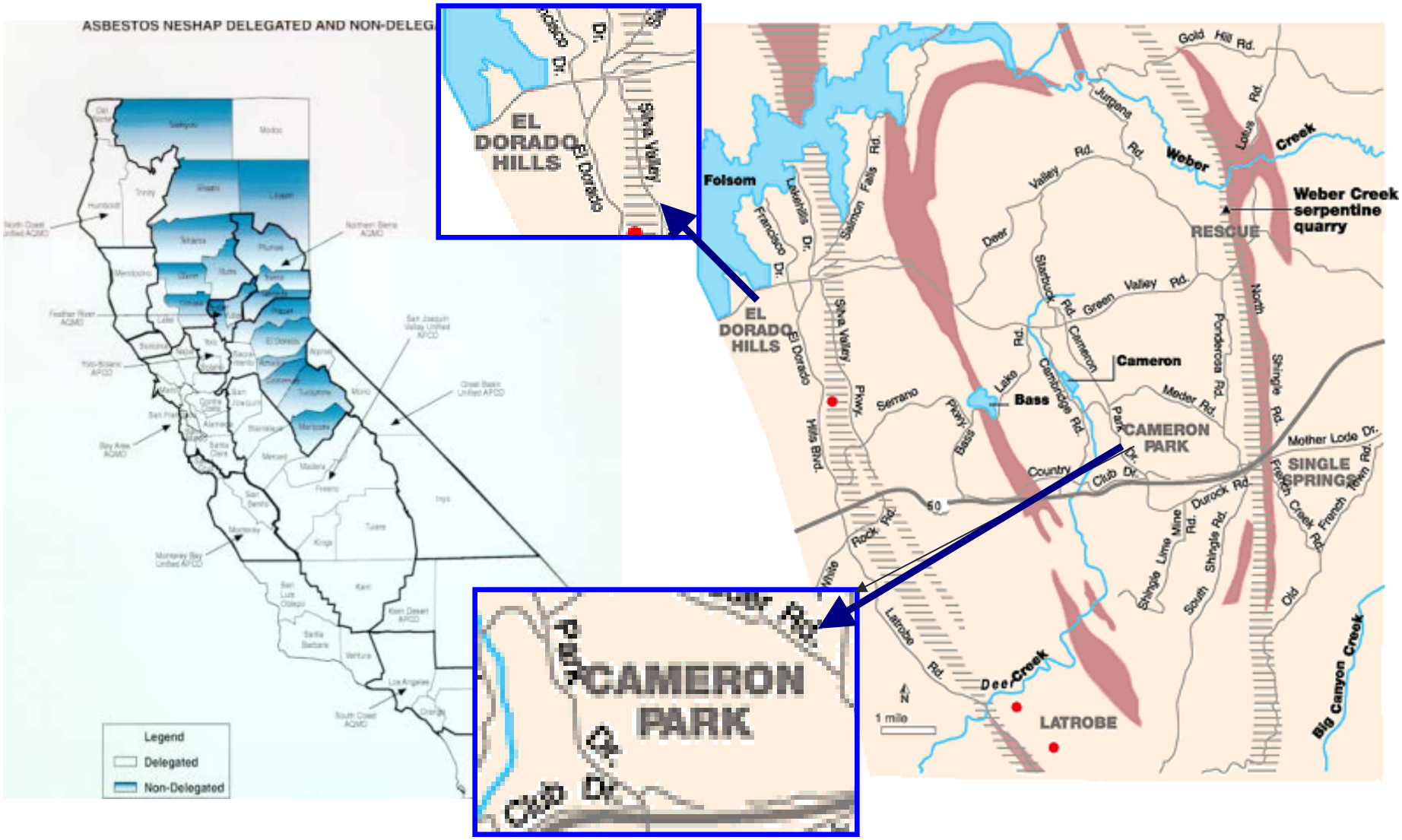


- Silicates (contaminated with tremolite)
  - Zeolite (Turkey)
  - Vermiculite (Libby, Montana)



Asbestos Geological Hot Spots

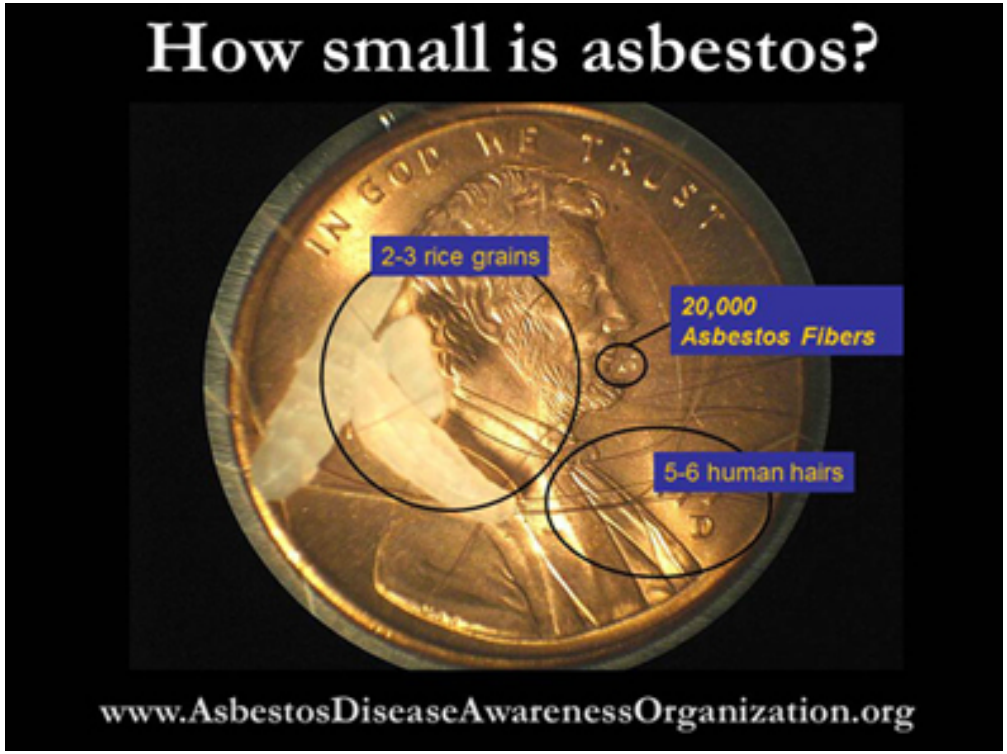
California



Asbestos Regulation

OSHA Regulation[4]

- 1970: 5 fibres/mL[3] of air
- Now: 0.2 fibres/mL[3] of air



Asbestos

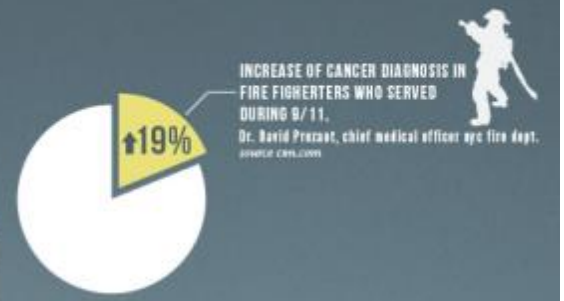
911

9/11 AIR TOXINS
RELATED TO CANCER

10 YEARS LATER

presented by Asbestos.com

The four terrorist attacks on Sept. 11, 2001, two of them on the Twin Towers at the World Trade Center in New York City, changed America forever. In the decade since, researchers and doctors have discovered just how toxic dust can be. One recent study found that every first responder to the fallen Twin Towers has suffered some degree of lung impairment.



INCREASE OF CANCER DIAGNOSIS IN FIRE FIGHERTERS WHO SERVED DURING 9/11.

Dr. David Prezant, chief medical officer nyc fire dept.

source cnn.com

410,000 PEOPLE EXPOSED

Nearly half a million people were impacted by contaminated air in the wake of the Twin Towers' collapse, including first responders, nearby residents and workers charged with cleaning up the massive amounts of debris at the site and nearby dust.

2,000 TONS The amount of asbestos fibers that were released into the air by the towers' collapse.

That is the equivalent of **182 SCHOOL BUSES**

1,506,124 The tons of debris that was removed from Ground Zero.

204 THE NUMBER OF FIRST RESPONDERS THAT HAVE DIED AFTER 9/11

55 THE NUMBER OF PEOPLE THAT HAVE DIED FROM LUNG OR OTHER CANCERS RELATED

112,000 x

The magnitude of the asbestos level above the legal limit of a building next to Ground Zero. Tests showed the building essentially had become toxic itself.

$2.775 BILLION

The amount of money in a 9/11 compensation fund now able to be accessed by families of victims and survivors. The fund was reopened in July 2011 as part of James Zadroga 9/11 Health and Compensation Act. The law was universally hailed until cancer victims learned they are not covered. However, the law ensures that some 25,000 survivors and 25,000 responders have access to specialized medical services and promotes and provides funding for medical research.

CREATED BY Asbestos.com

Risk Factors

- ASBESTOS EXPOSURE[4]
  - Lifetime risk 8 – 13%
  - Latency period 30 – 40 yrs from exposure

- Ship yard workers/ship builders
- Electricians
- Plumbers
- Carpenters
- Insulation installers
- Construction Workers
- Auto mechanics (brake removal and installation)

Clinical Presentation

Subjective

- Cough*
- Shortness of breath*
- Chest pain/discomfort*

- *History of asbestos exposure*

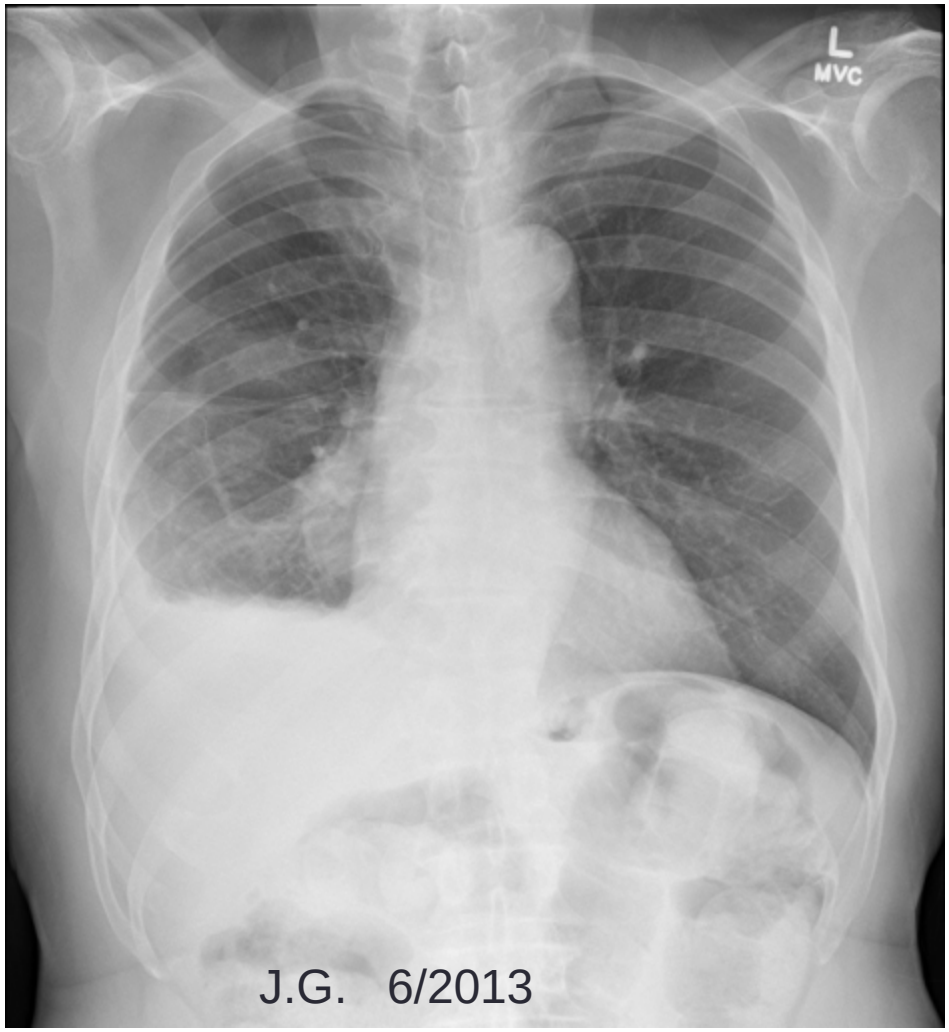
*(>90% of patients present with combinations of these symptoms)

Clinical Presentation

Objective

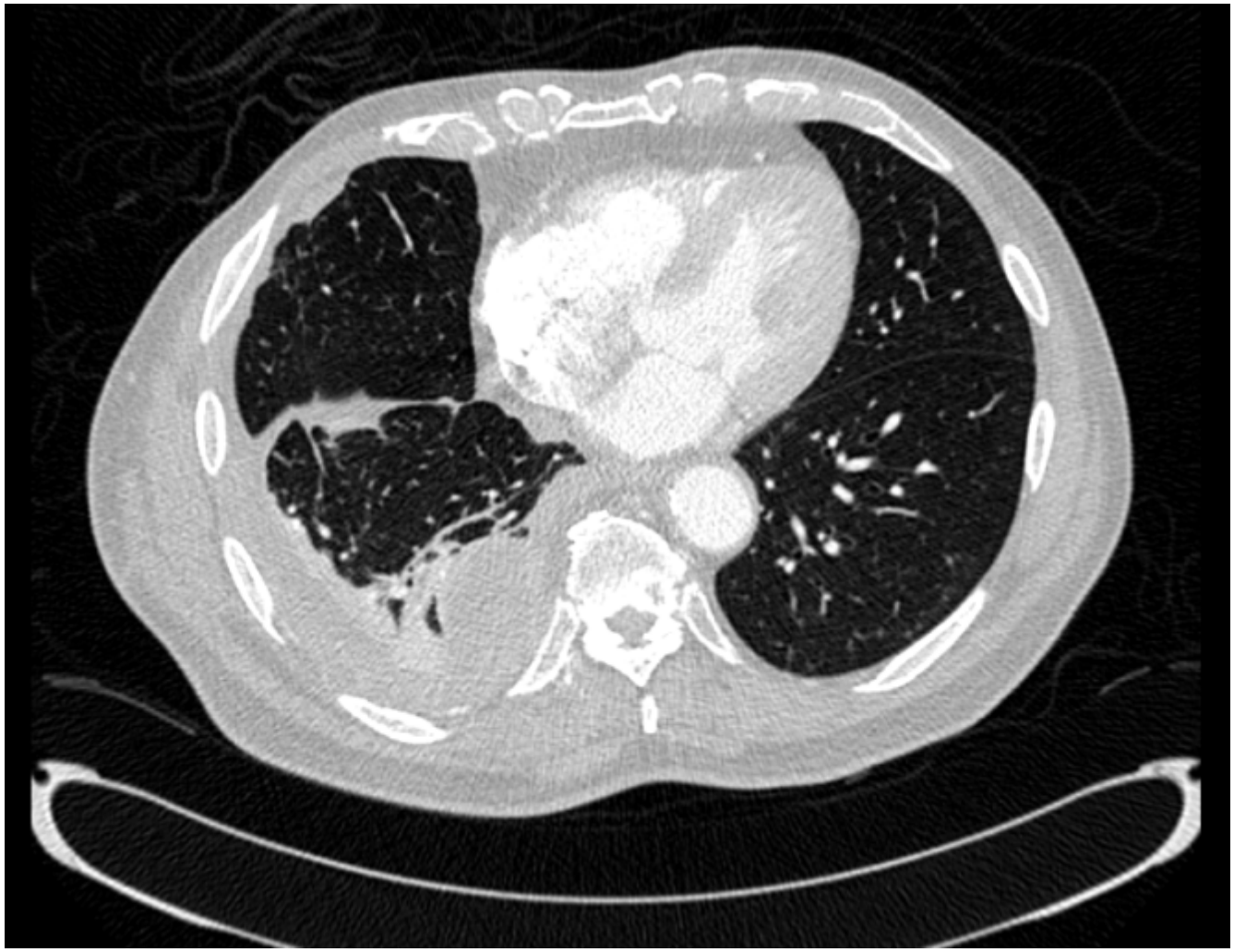
- Unilateral dullness to percussion
- Unilateral distant breath sounds
- Scoliosis towards side of malignancy
- Abnormal x-ray
  - Unilateral pleural thickening
  - Unilateral pleural effusion

MPM Presentation

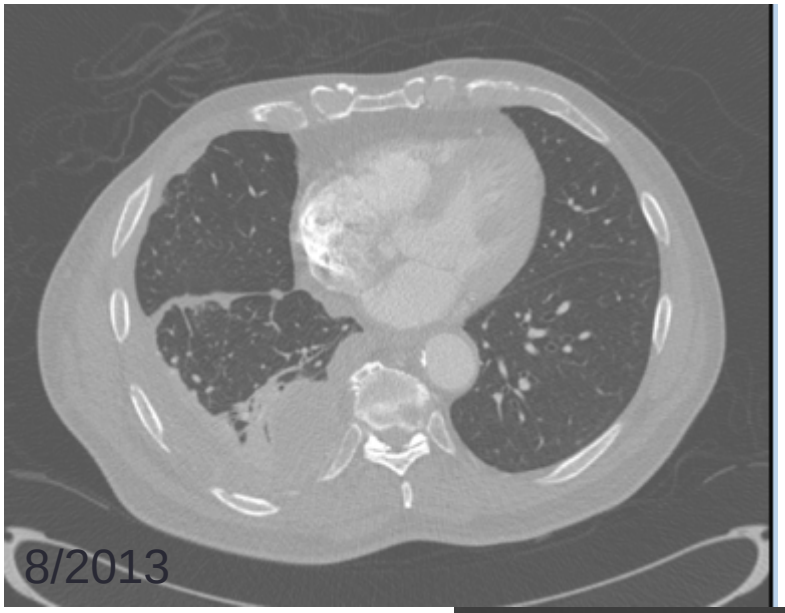


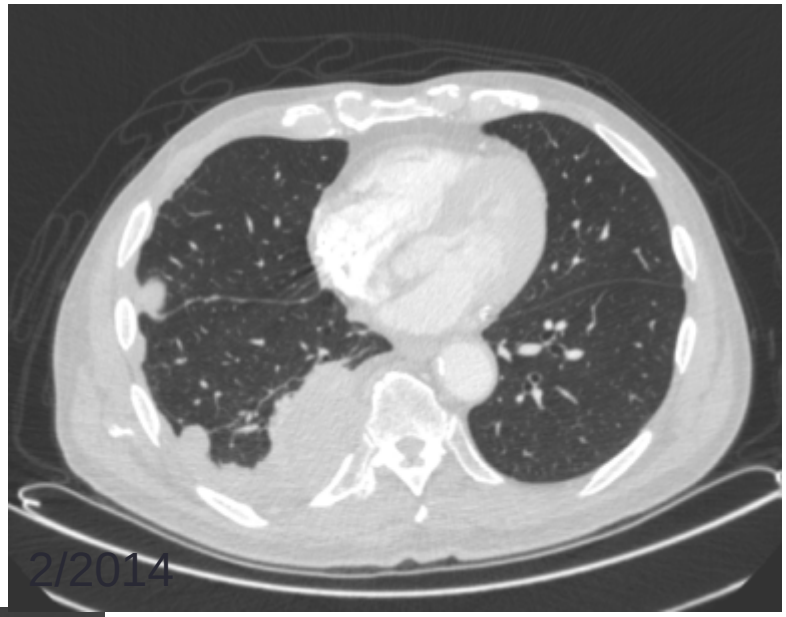
MPM Presentation (6/2013)

MPM (8/4/13)

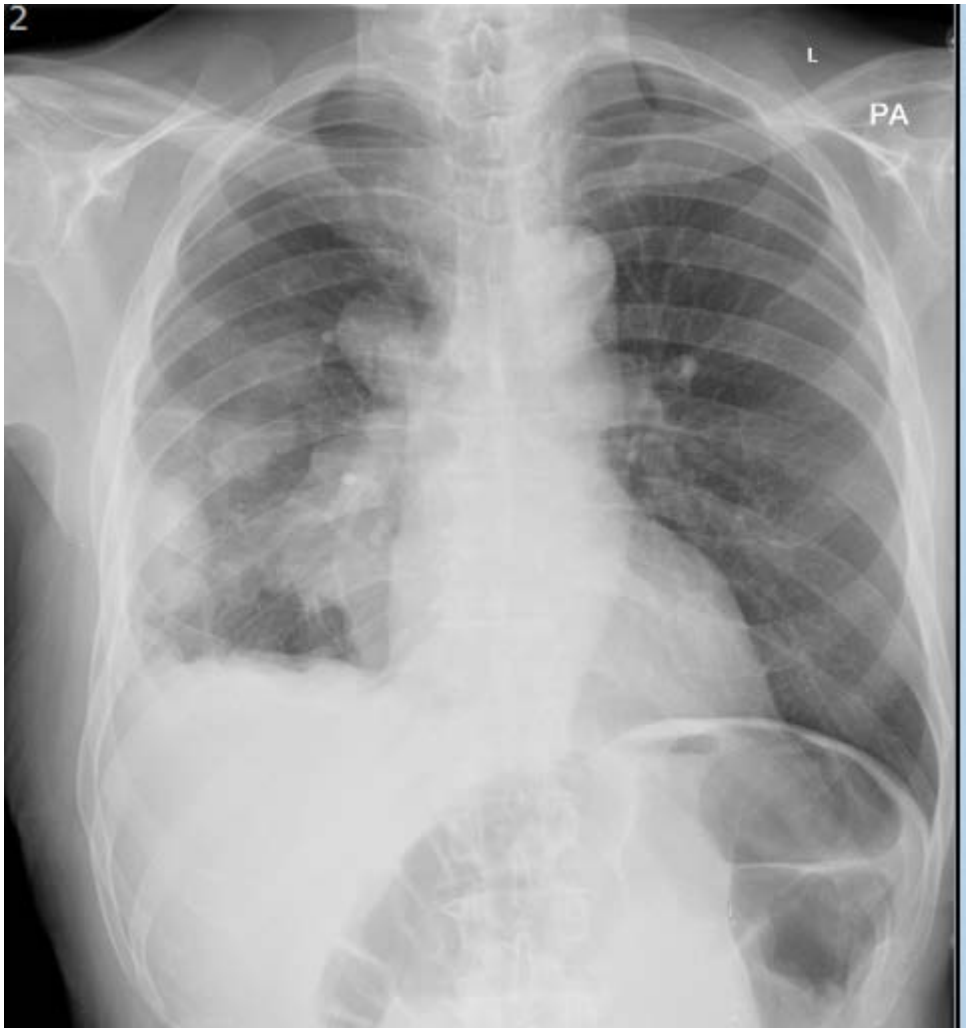


Patient J.G.



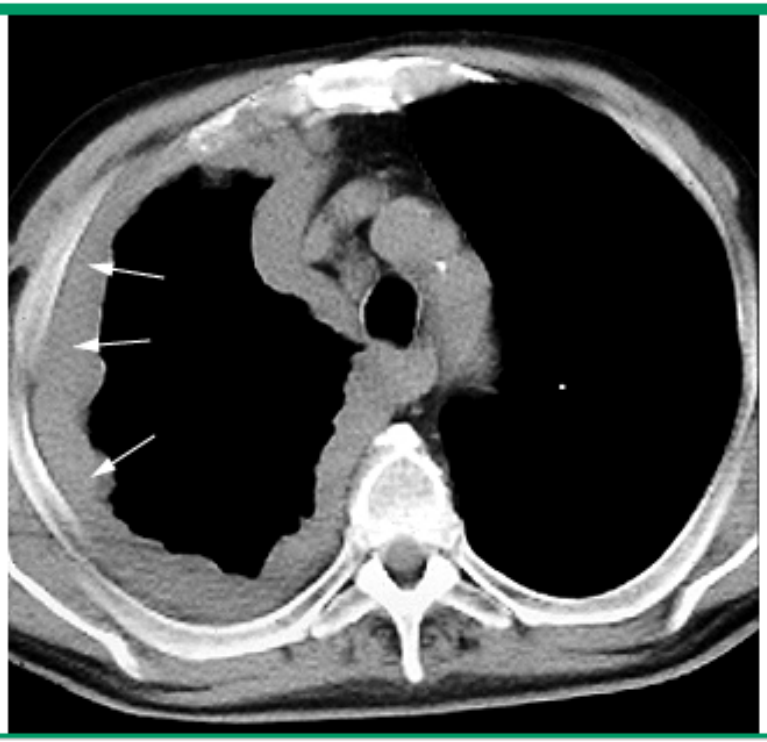


Patient J.G. 2/2014



MPM

Malignant mesothelioma



CT scan shows right sided nodular circumferential pleural thickening exceeding 1 cm in thickness, typical of a malignant process (arrows). No clear cut invasion of the chest wall is present. A slightly enlarged pretracheal lymph node proved to be reactive in nature.

MPM Diagnosis

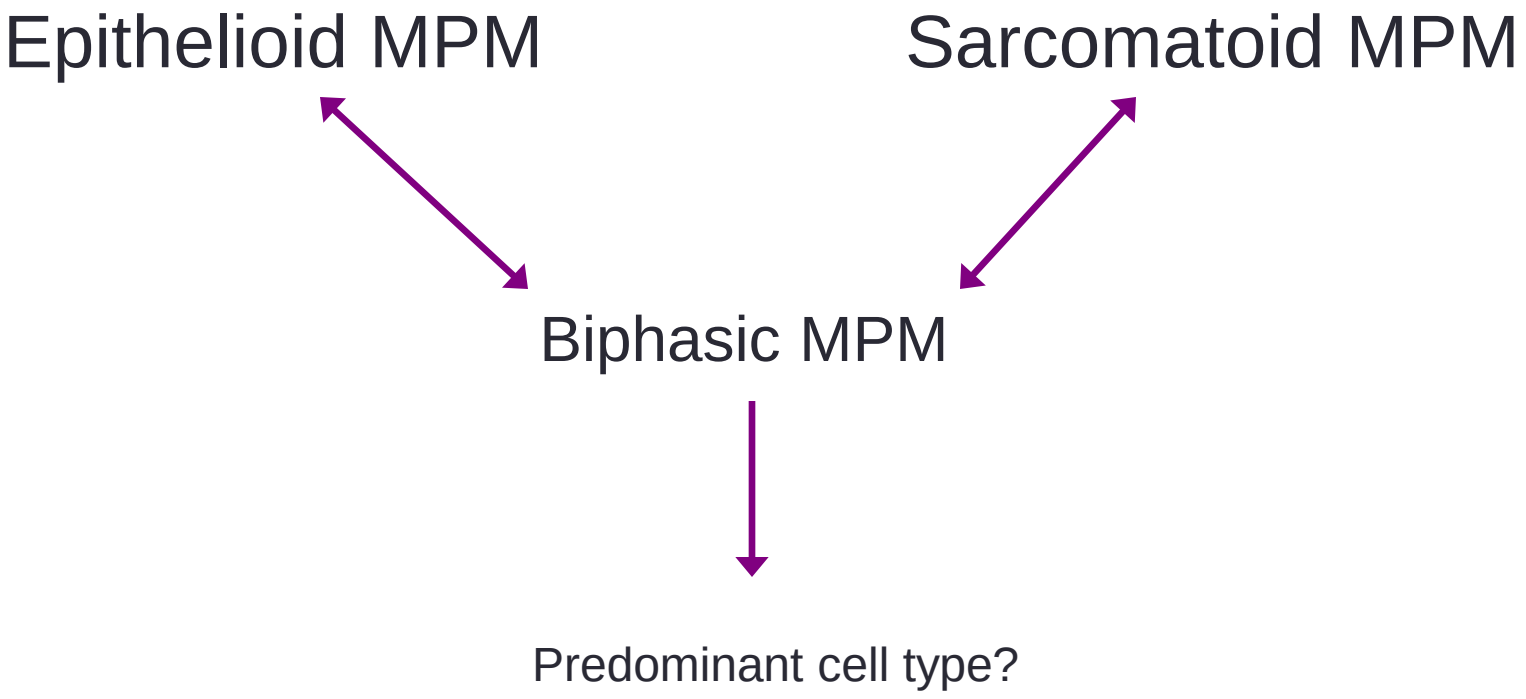
- *Often misdiagnosed*
- Thoracentesis or closed pleural biopsy
  - Cytology of effusion can be diagnostic of MPM, but negative results DOES NOT exclude the possibility of mesothelioma
  - Sample errors

- Thoracoscopic or open pleural biopsy
  - Gold standard
  - Highest diagnostic value

mesothelioma will seed biopsy site(s)

MPM Diagnosis

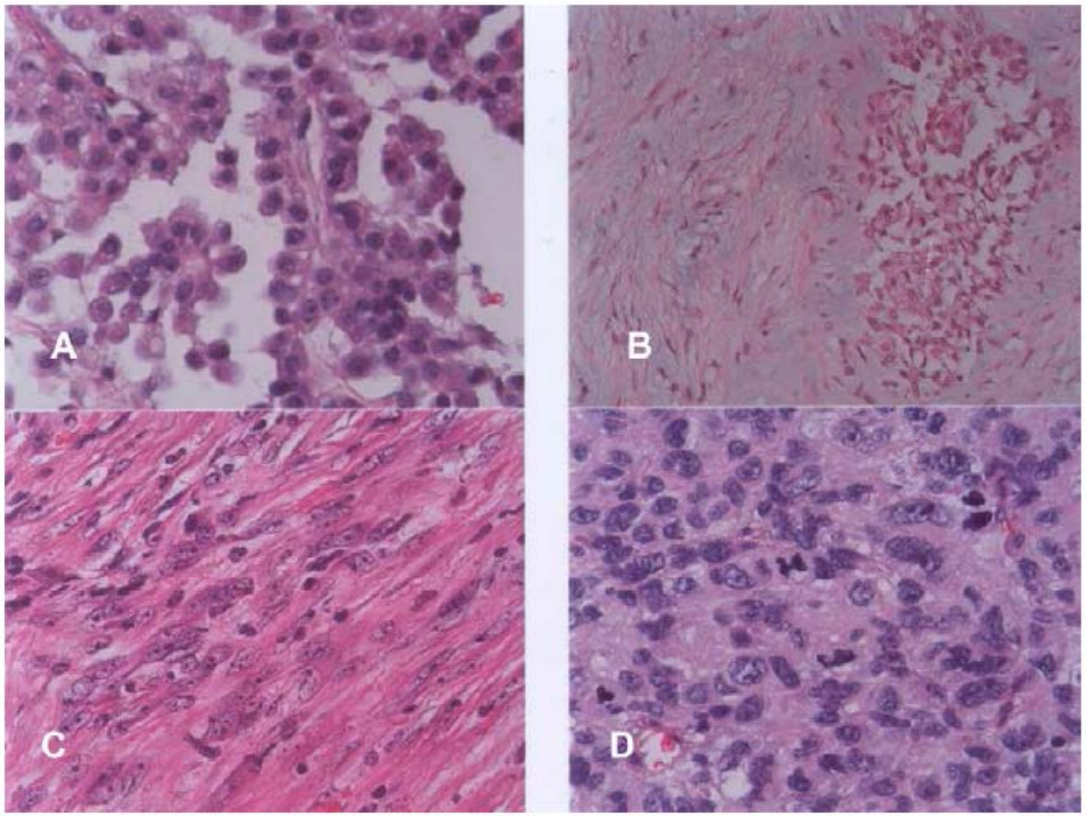
Two Diseases



MPM Diagnosis

Histology

Epithelioid **Biphasic**



Sarcomatoid **Undifferentiated**

MPM Diagnosis

Epithelioid

- Better prognosis
- 50 – 60% of cases
- Less invasive
- Fewer distant metastases
- Requires local control more than systemic control

Sarcomatoid

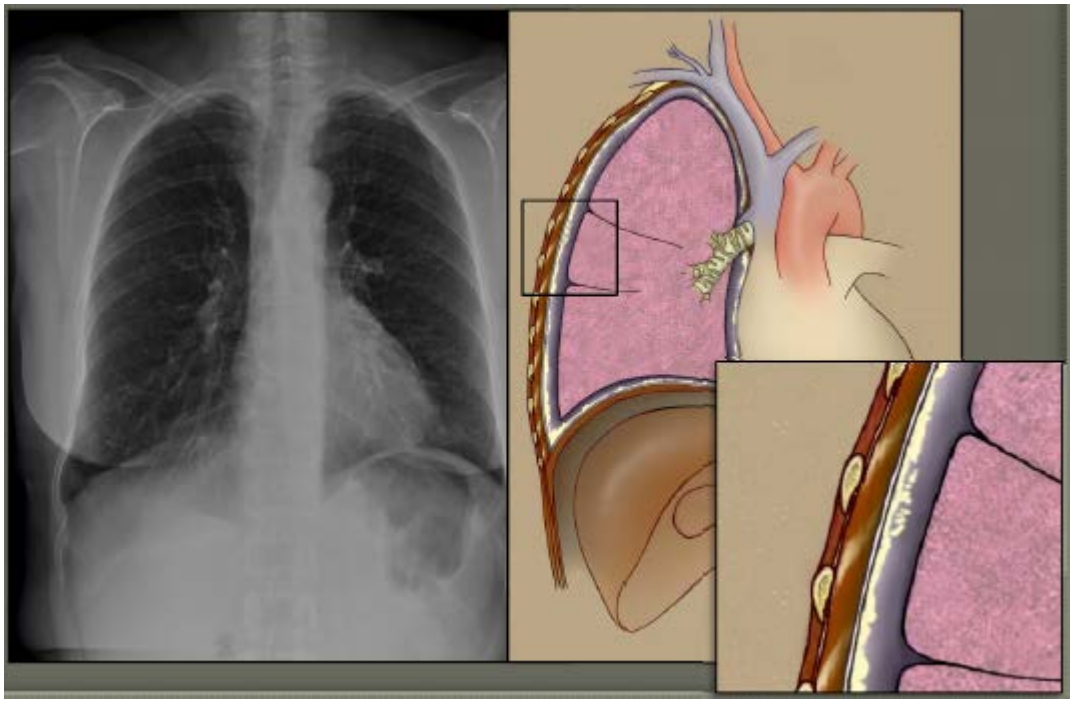
- Worse prognosis
- 10 – 15% of cases
- More invasive
- More likely to metastasis
- Requires more systemic control than local control

IMIG TNM Staging

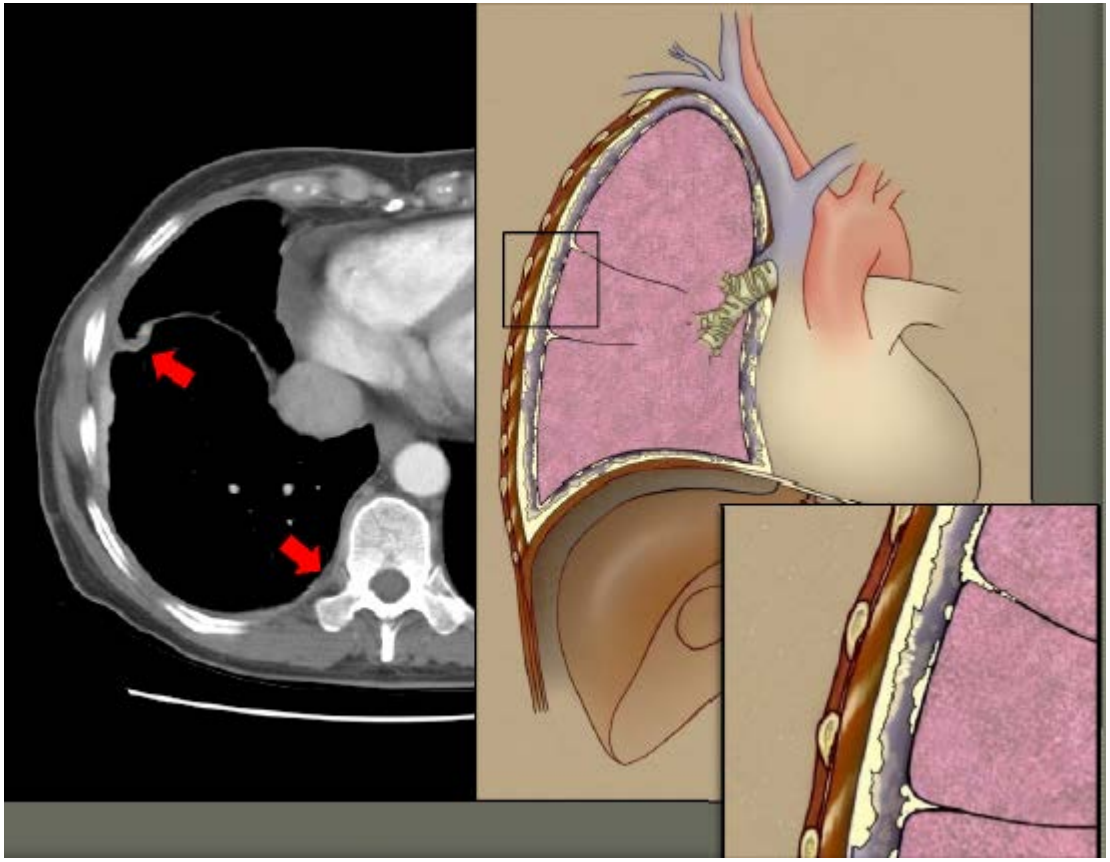
Table 1.
TNM staging system for MPM

Stage	TNM	Comments
Ia	T1a N0 M0	Primary tumour limited to ipsilateral parietal pleura
Ib	T1b N0 M0	As stage Ia plus focal involvement of visceral pleura
II	T2 N0 M0	As stage Ia or Ib plus confluent involvement of diaphragm or visceral pleura or involvement of the lung
III	Any T3 M0	Locally advanced tumour
	Any N1 M0	Ipsilateral, bronchopulmonary or hilar lymph node involvement
	Any N2 M0	Subcarinal or ipsilateral mediastinal lymph node involvement
IV	Any T4	Locally advanced technically unresectable tumour
	Any N3	Contralateral mediastinal, internal mammary, and ipsilateral or contralateral supraclavicular lymph node involvement
	Any M1	Distant metastases

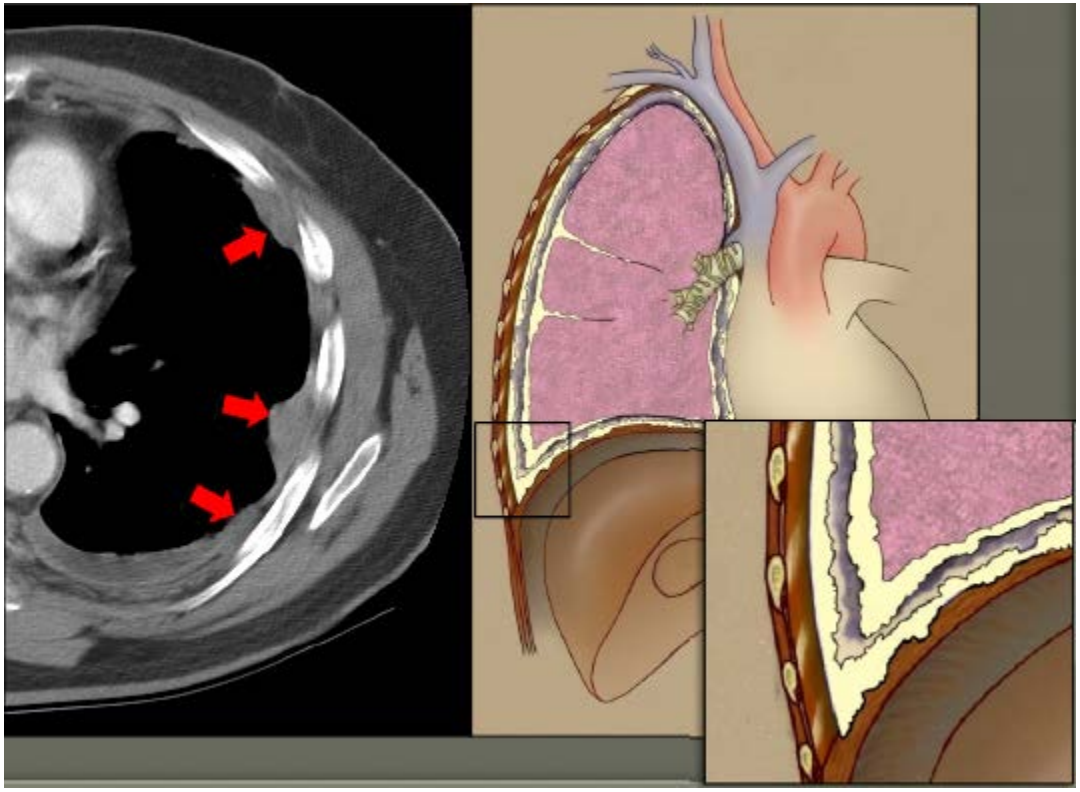
Stage Ia



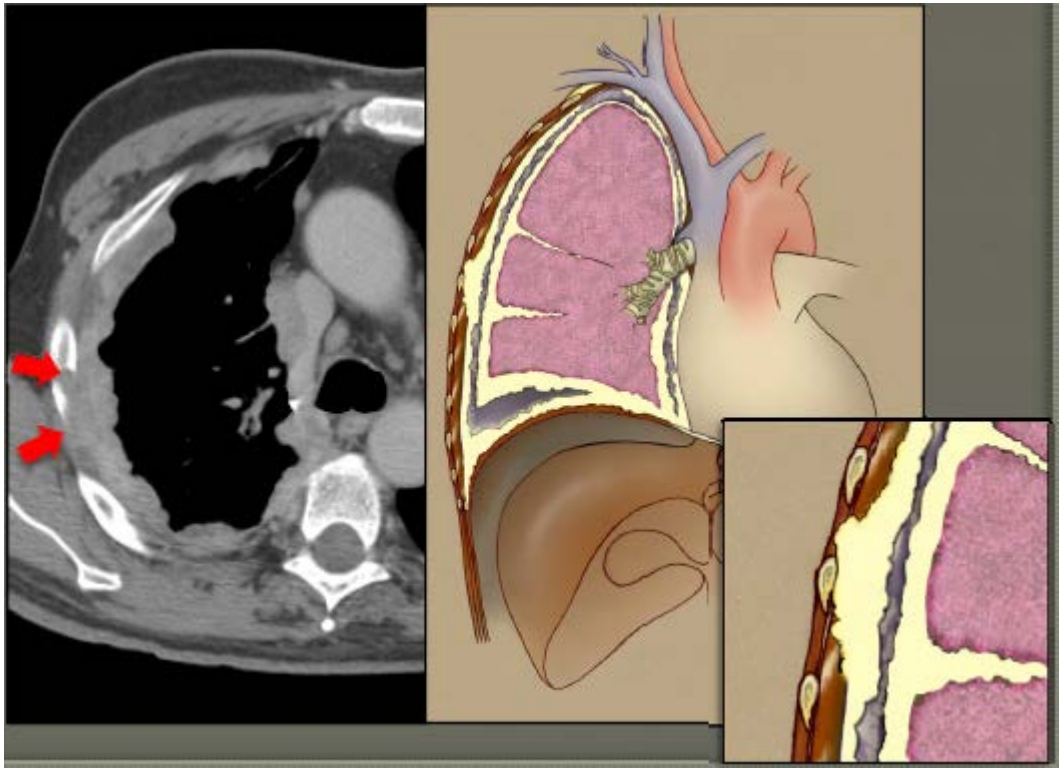
Stage Ib



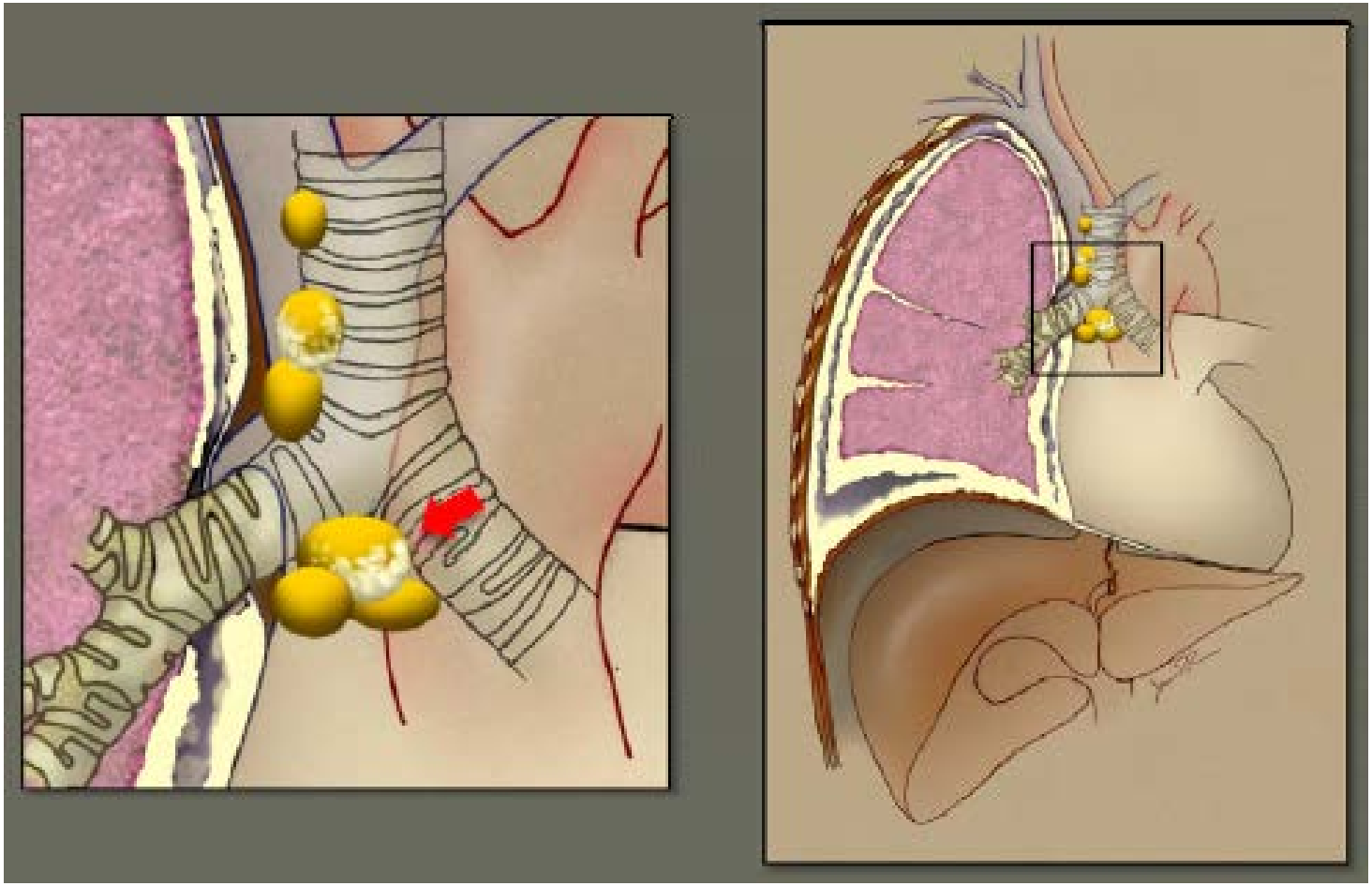
Stage II



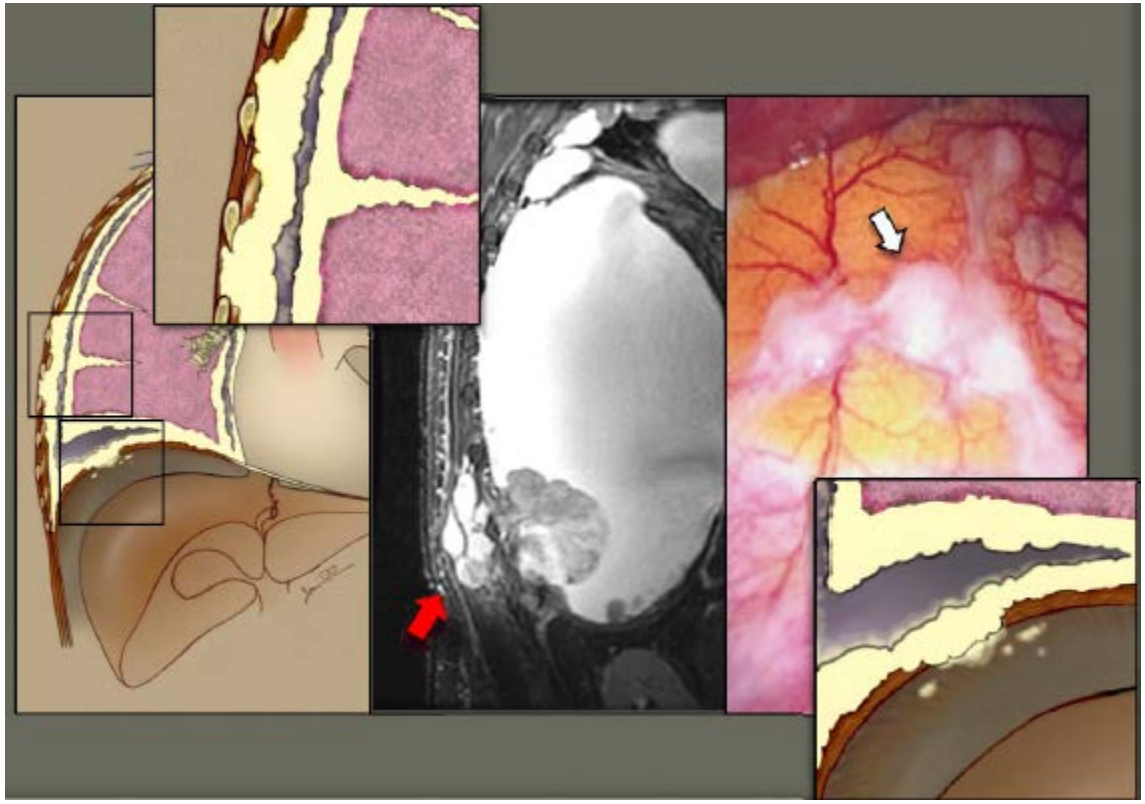
Stage III



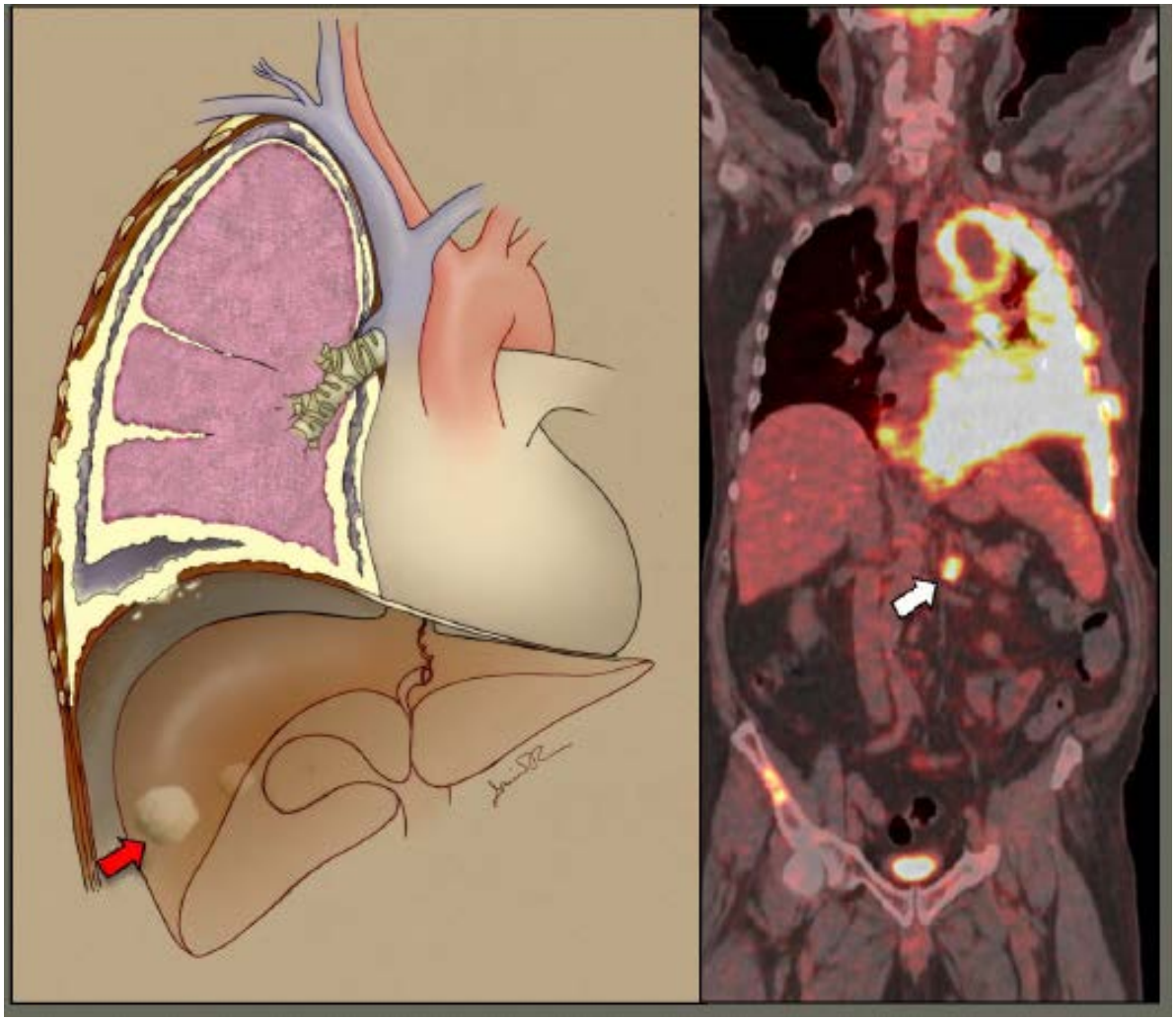
Stage III



Stage IV



Stage IV



MPM Treatment Options

"The only realistic treatment goal in advanced MPM is control of disease progression." [5]

[5]Nakas, Apostolos, et al. "Long-term survival after lung-sparing total pleurectomy for locally advanced (International Mesothelioma Interest Group Stage T3–T4) non-sarcomatoid malignant pleural mesothelioma." *European Journal of Cardio-Thoracic Surgery* 41.5 (2012): 1031-1036.

MPM Treatment Options

- Median survival is ~9 – 12 months[6]
- No known curative treatment[6]
- Chemotherapy
- Radiation Therapy
- Surgery
  - Radical Extrapleural pneumonectomy (EPP)
  - Radical pleurectomy/decortication (P/D)
  - Pleurodesis

[6]Lang-Lazdunski, Loïc, et al. "Pleurectomy/decortication is superior to extrapleural pneumonectomy in the multimodality management of patients with malignant pleural mesothelioma." *Journal of Thoracic Oncology* 7.4 (2012): 737-743.

MPM Treatment Options

Chemotherapy

- Cisplatin and pemetrexed
- ~ 3-month survival benefit[7]

[7]Vogelzang, Nicholas J., et al. "Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma." *Journal of Clinical Oncology* 21.14 (2003): 2636-2644.

MPM Treatment Options

FDA Pemetrexed Approval

On February 4, 2004, the FDA approved pemetrexed disodium for injection (Alimta®, made by Eli Lilly and Company) in combination with cisplatin for the treatment of patients with malignant pleural mesothelioma whose disease is either unresectable or who are not otherwise candidates for curative surgery.

MPM Treatment: Surgery

EPP

En bloc resection of lung, pleura, pericardium, and diaphragm

P/D

Resection of the parietal and visceral pleurae, pericardium, and diaphram when necessary, but sparing lung

--

Keep existing tissue planes intact (pericardium, diaphragm, etc.) to prevent seeding of additional areas

[8]Flores, Raja M., et al. "Extrapleural pneumonectomy versus pleurectomy/decortication in the surgical management of malignant pleural mesothelioma: results in 663 patients." *The Journal of thoracic and cardiovascular surgery* 135.3 (2008): 620-626.

MPM Treatment: Surgery

EPP

- Radical surgery
- Allows higher radiation doses
- Longer disease free period
- Less local recurrence
- Higher mortality and morbidity
- Patient selection: less comorbidities
- At best: R1 resection

P/D

- Radical surgery
- Lower radiation doses & more specialized technique
- Disease free period shorter
- Local recurrence
- Lower mortality and morbidity
- Patient selection: more comorbidities
- At best: R1 resection

Table 2.

Site of first recurrence after extrapleural pneumonectomy versus pleurectomy/decortication

	EPP (n = 219) n (%)	P/D (n = 133) n (%)
Local recurrences	73 (33%)	86 (65%)
Ipsilateral chest	68 (31%)	84 (63%)
Pericardium	5 (2%)	2 (2%)
Distant recurrences	146 (66%)	47 (35%)
Contralateral lung/pleura	49 (22%)	14 (11%)
Peritoneum	57 (26%)	24 (18%)
Peritoneum + chest	17 (8%)	1
Abdominal viscera	12 (5%)	4 (3%)
Bone	7 (3%)	–
Brain	1	1
Cutaneous (distant)	1	1
Other	2	2 (2%)

EPP, Extrapleural pneumonectomy; *P/D,* pleurectomy/decortication.

Flores, Raja M., et al. "Extrapleural pneumonectomy versus pleurectomy/decortication in the surgical management of malignant pleural mesothelioma: results in 663 patients." *The Journal of thoracic and cardiovascular surgery* 135.3 (2008): 620-626.

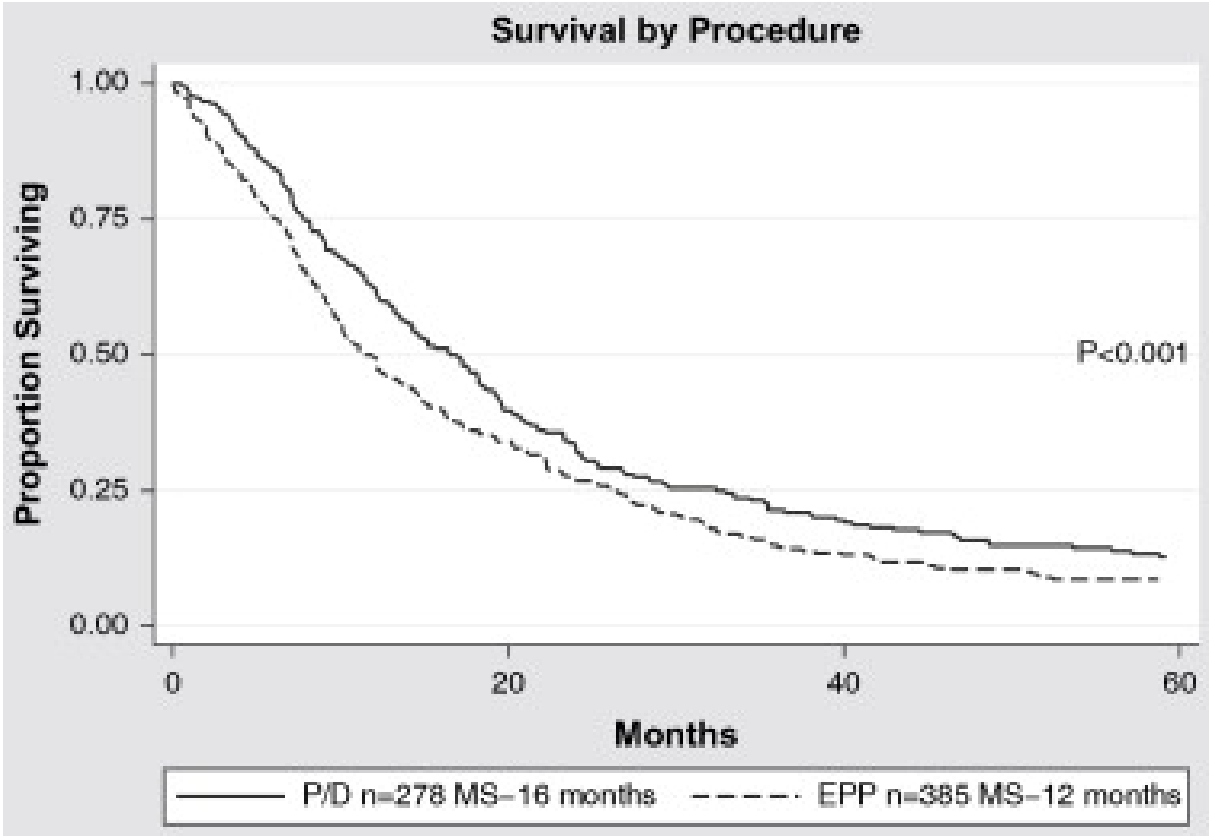


Figure 3 Overall survival of EPP versus P/D, by univariate analysis. EPP, Extrapleural pneumonectomy; P/D, pleurectomy/decortication.

Raja M. Flores , Harvey I. Pass , Venkatraman E. Seshan , Joseph Dycoco , Maureen Zakowski , Michele Carbone , Man...

Extrapleural pneumonectomy versus pleurectomy/decortication in the surgical management of malignant pleural mesothelioma: Results in 663 patients

The Journal of Thoracic and Cardiovascular Surgery, Volume 135, Issue 3, 2008, 620 - 626.e3

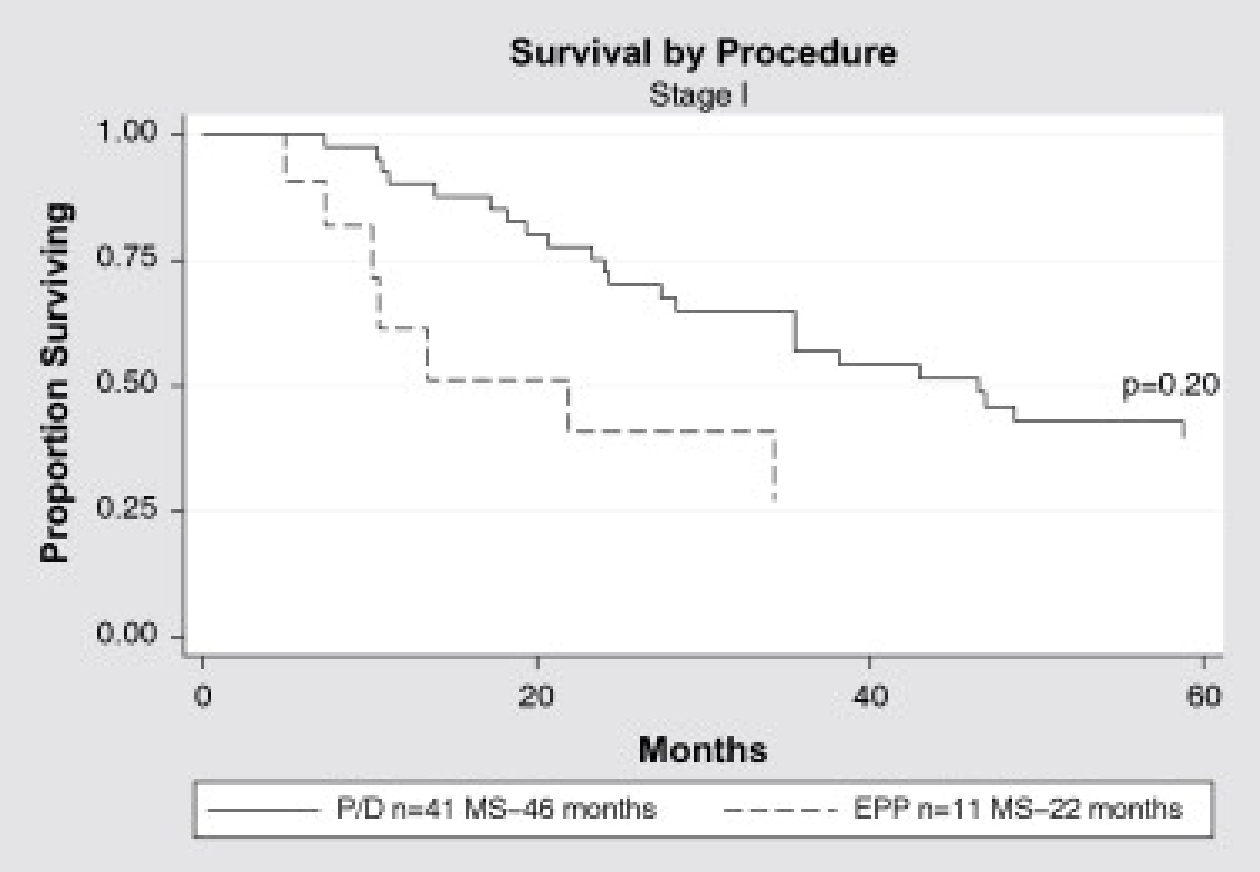


Figure 4 Overall survival of EPP versus P/D for patients with stage I. EPP, Extrapleural pneumonectomy; P/D, pleurectomy/decortication.

Raja M. Flores , Harvey I. Pass , Venkatraman E. Seshan , Joseph Dycoco , Maureen Zakowski , Michele Carbone , Man...

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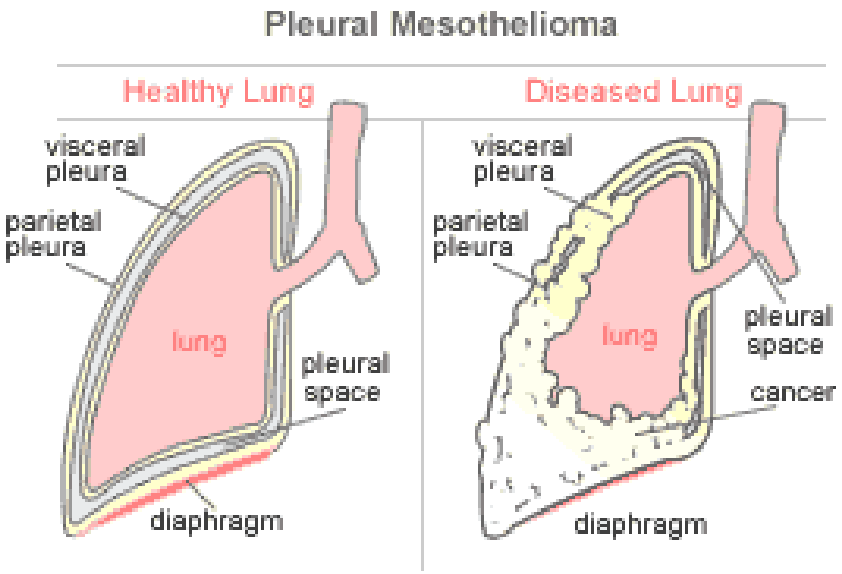
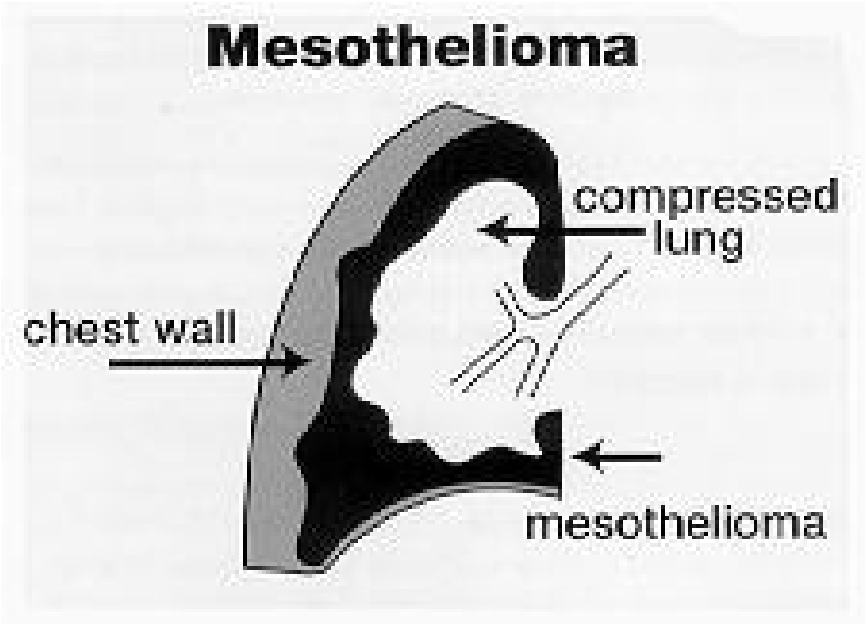
Mesothelioma: The Problem



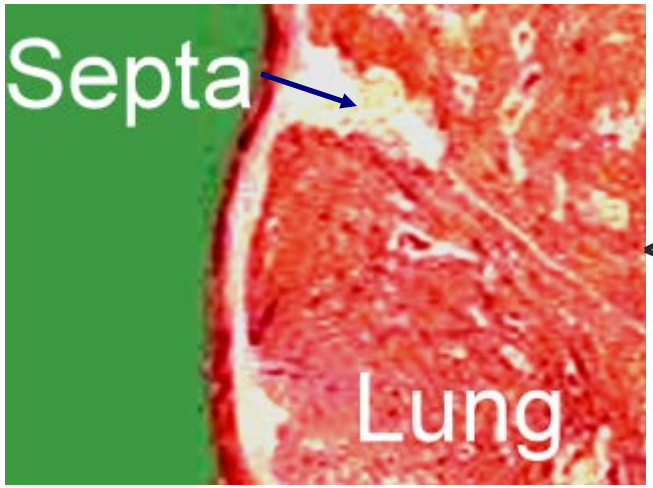


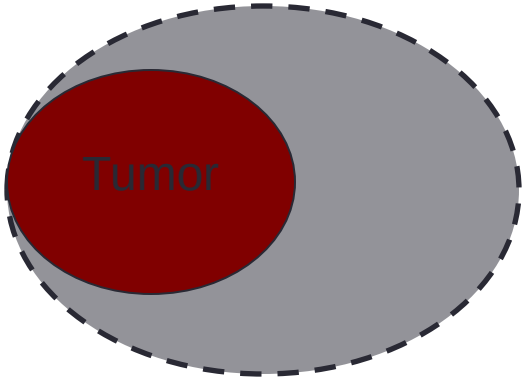
MPM Treatment: Surgery

Classification of Surgical Oncology Resections

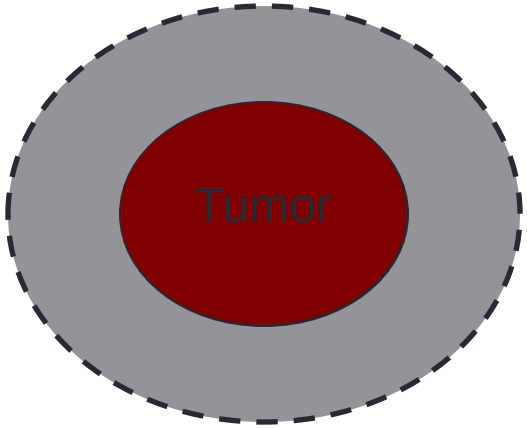
- R0: Radical resection (amputation, muscle groups, wide local resection with 2-3 cm margins)
- R1: Marginal resection (within tumor “capsule”)
- R2: Incomplete resection of gross tumor

Mesothelioma: The Problem





Marginal Resection



Radical Resection

MPM Treatment: The Problem

"You are only as good as your **CLOSEST** surgical margin"

Mesothelioma: EPP versus P/D

	EPP	**P/D**
Margins	Minimal	Minimal
△PFT's	---	+/-
Mortality	3-6%	<1%
Operative time	Intermediate	Long
Surgeon's Fee	$1348.46-$2676.83	$1249.68-$2444.26
Ages	Younger	Almost any
Lung Status	Good PFT's	Almost any
Radiation	Easy	Hard
Recurrence	Hard to detect	Easy to detect

Mesothelioma: “Rational” Therapy

- Surgery may provide benefit from “debulking” tumor mass (ovarian cancer as prototype)
- Radical procedures do not provide safer “margin” than more conservative procedures
- Radiation may provide benefit with microscopic disease
- Chemotherapy provides minimal benefit

Mesothelioma: GLA VA Approach

- Radical parietal pleurectomy
- Complete pulmonary decortication (radical visceral pleurectomy)
- Removal of all pleural tumor off diaphragm, pericardium, mediastinum, and hilum
- Lymph node dissection
- Preservation of all tissue planes possible
- Postoperative radiation therapy
- Novel biologic therapies when available

Mesothelioma: GLA VA Surgical Goals

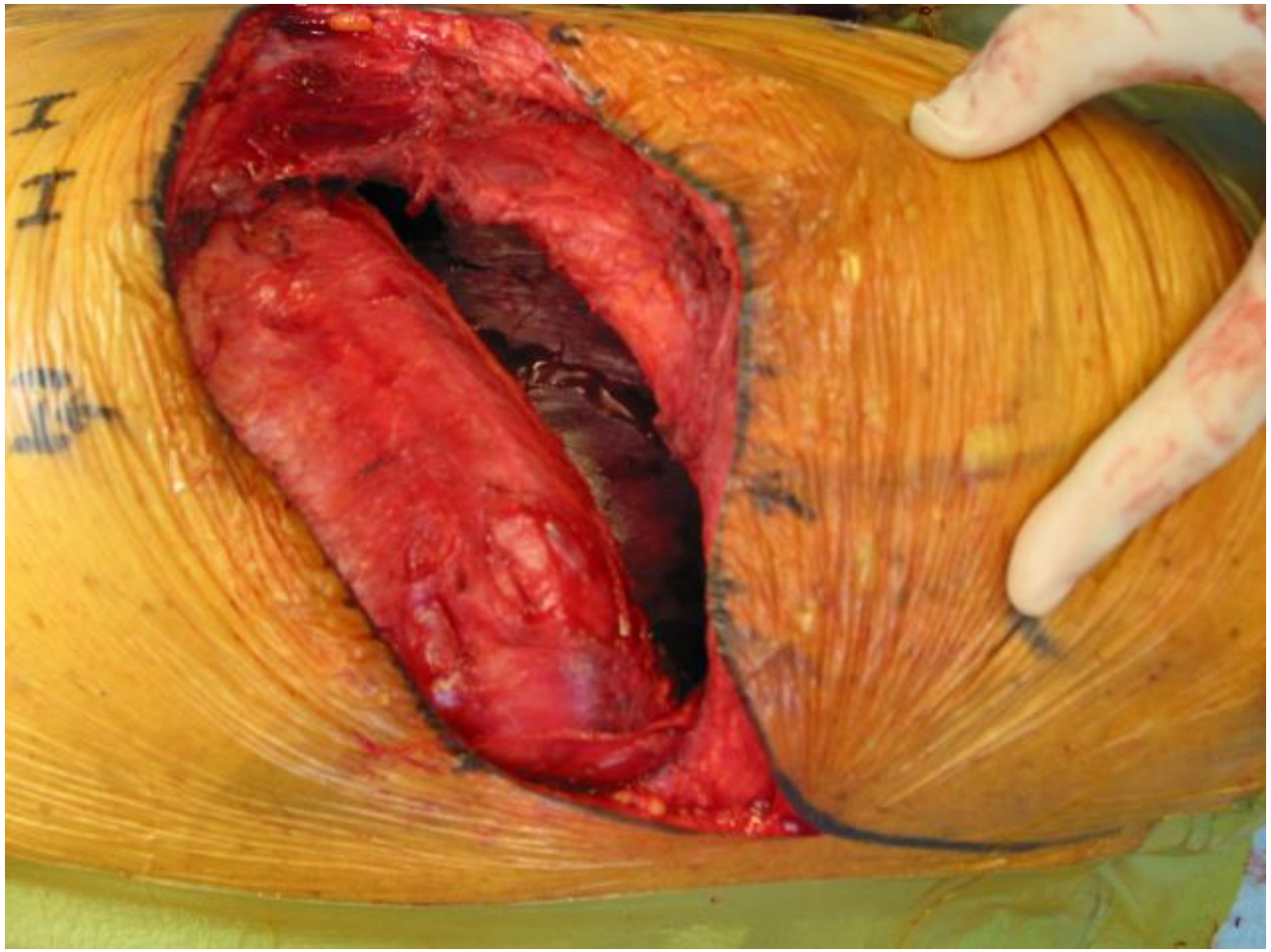
- Remove/destroy all tumor (gross)
- Preserve tissue boundaries
- Preserve vital organ function
- Use effective adjuvant therapies
- Use maintenance therapies
- Develop screening/detection tests
- Develop prevention stratagies

Mesothelioma: GLA VA P/D

The Incision

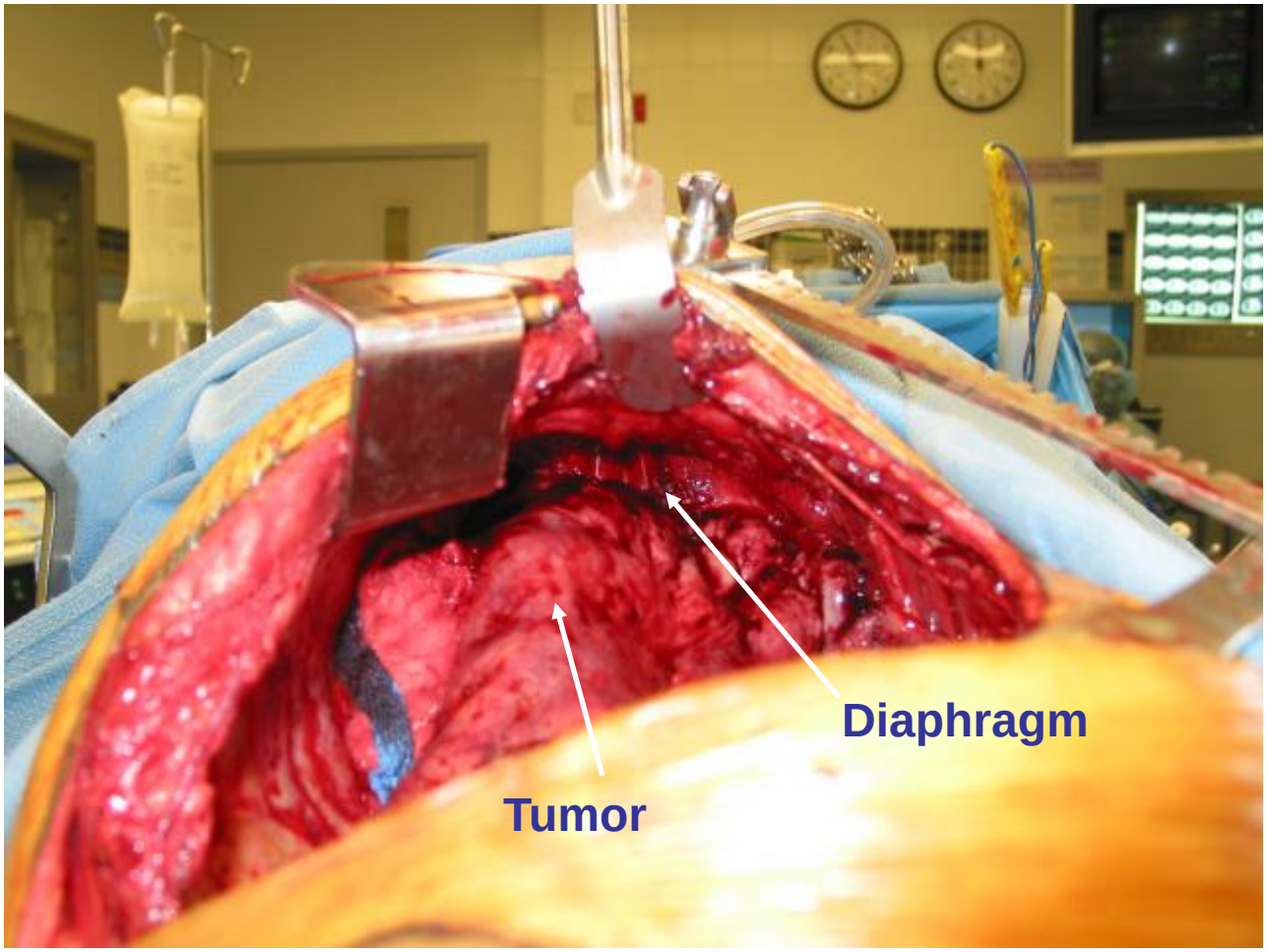
Mesothelioma: GLA VA P/D

Initial View



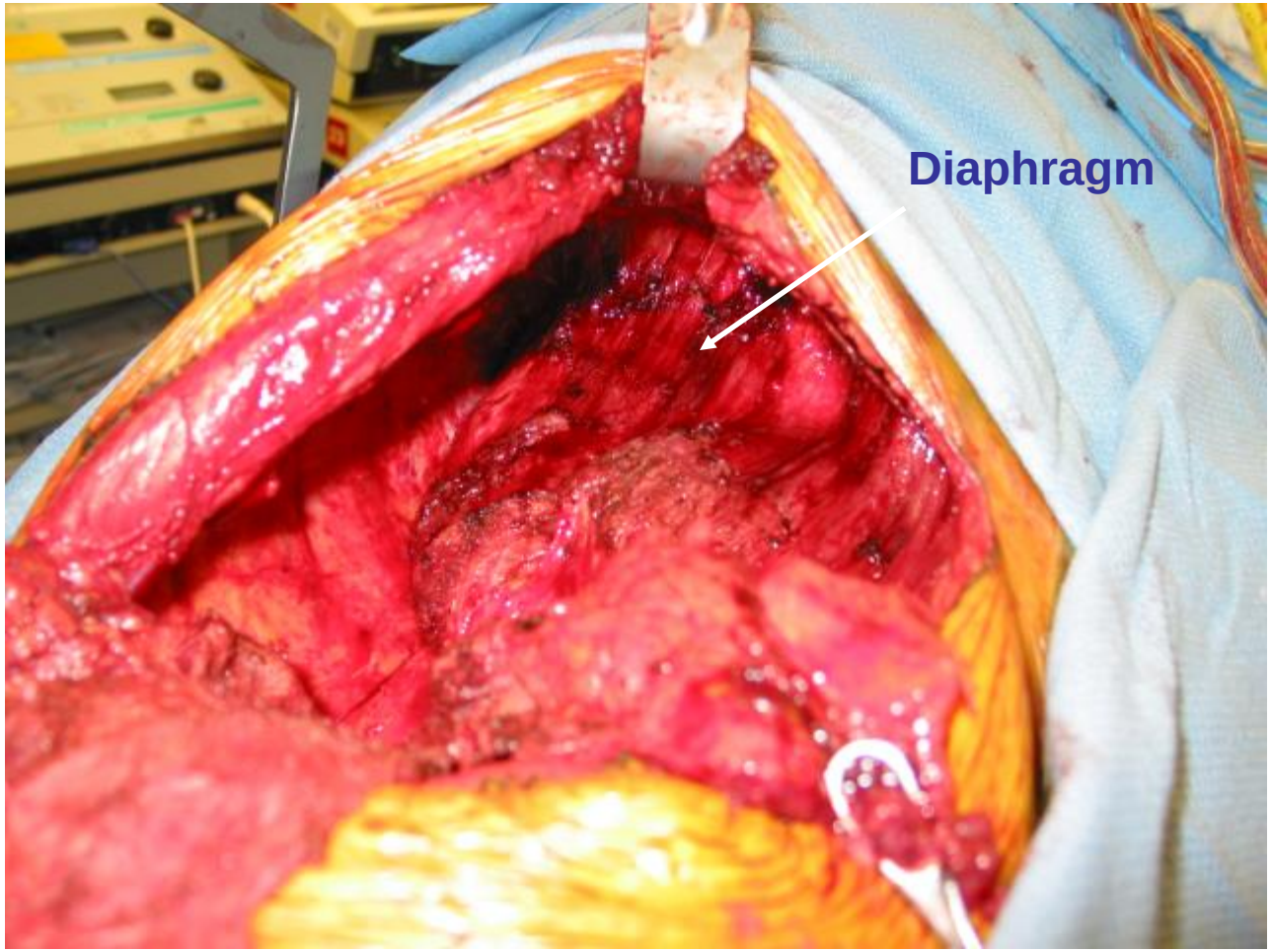
Mesothelioma: The UCLA P/D

Chest Wall Retractor



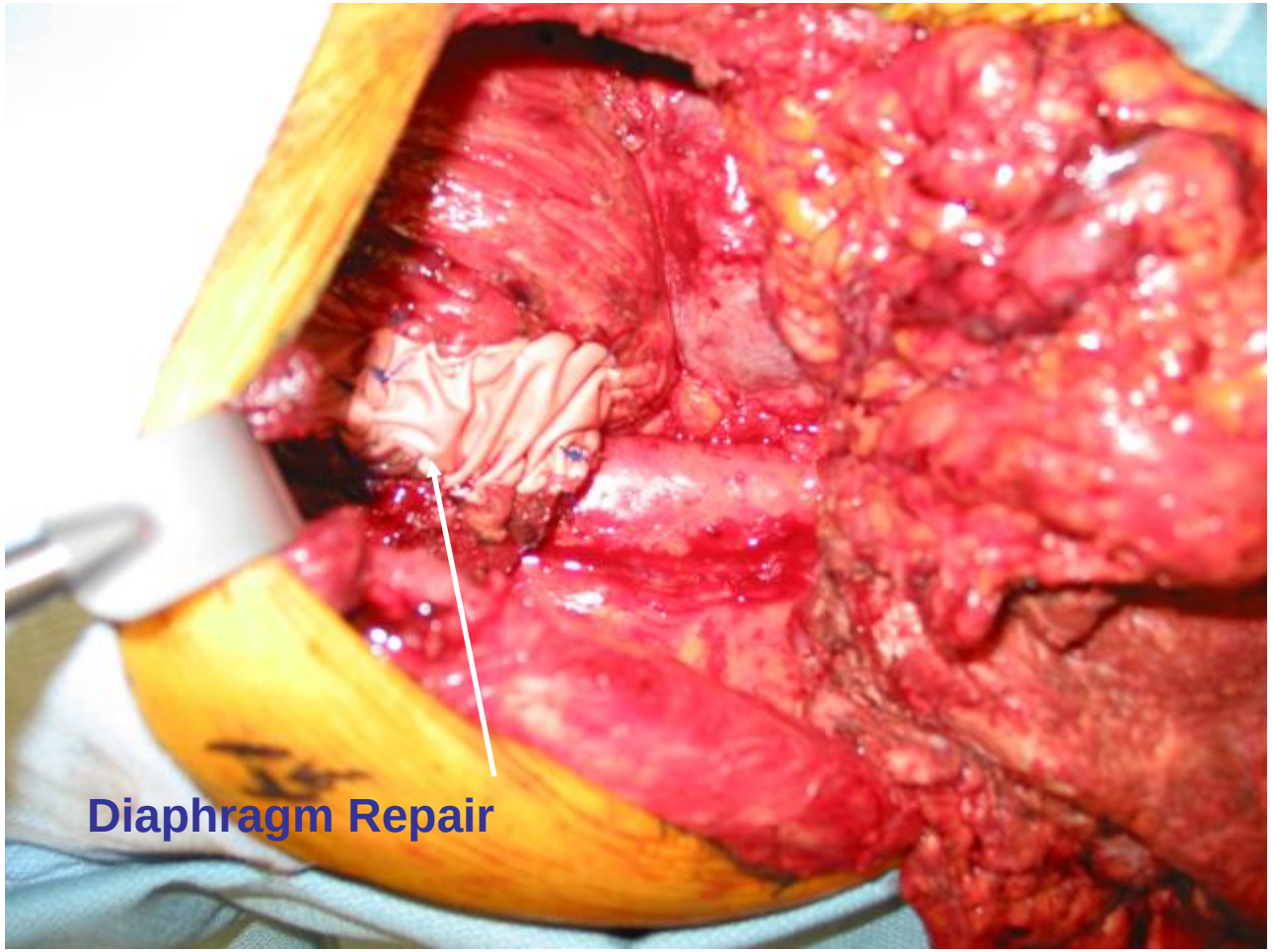
Mesothelioma: GLA VA P/D

Diaphragm



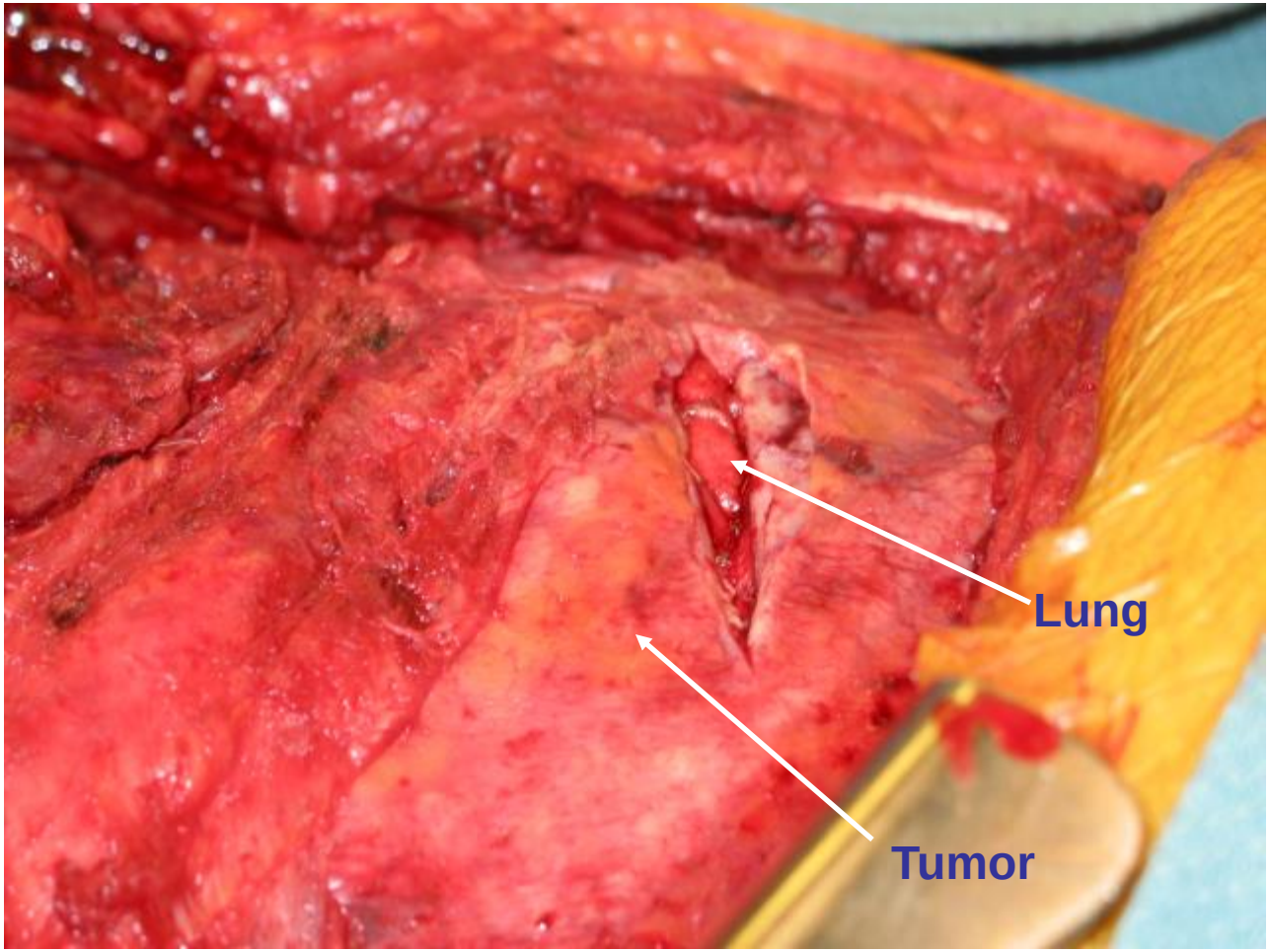
Mesothelioma:GLA VA P/D

Diaphragm Repair



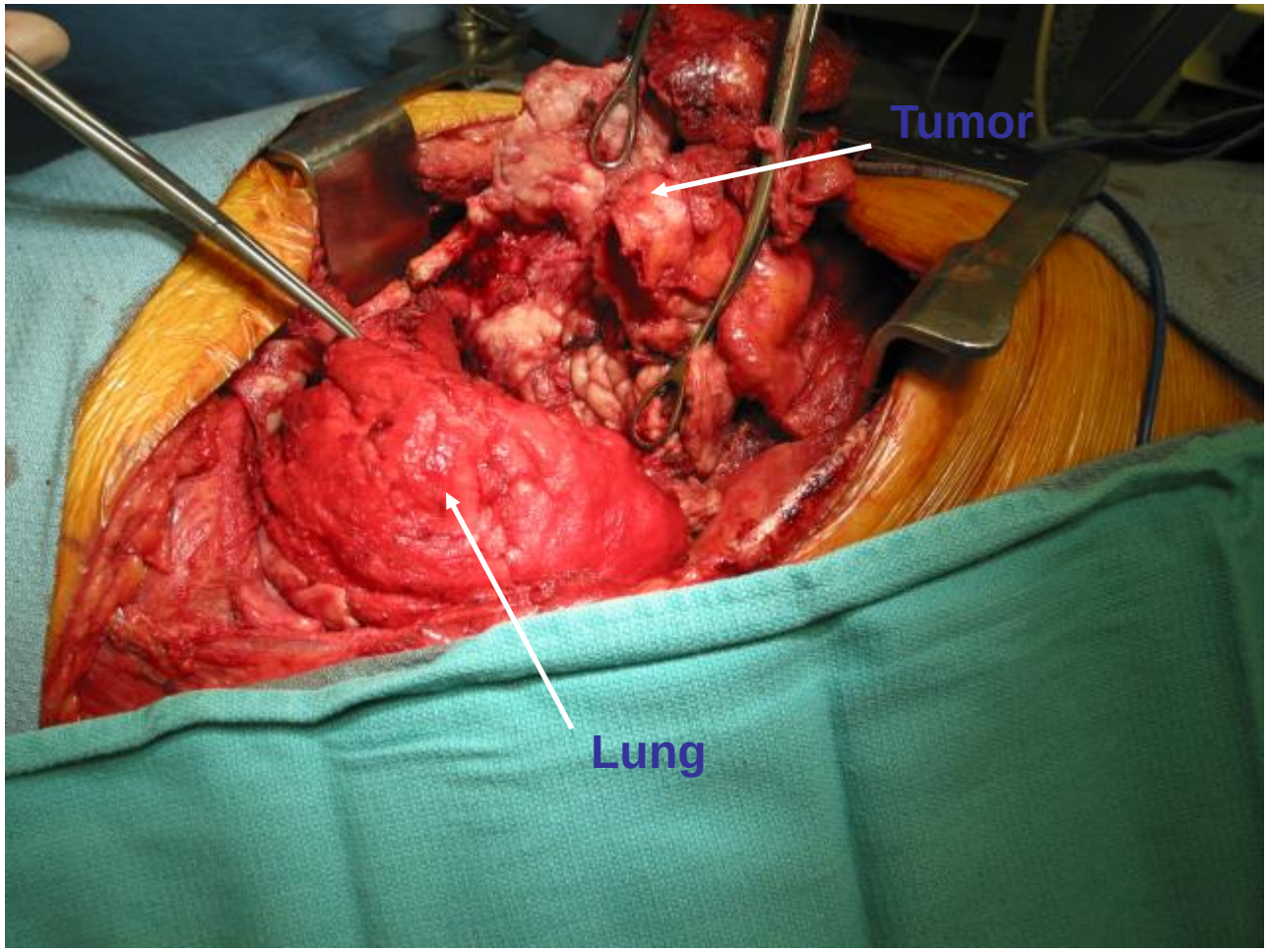
Mesothelioma:GLA VA P/D

Visceral Pleurectomy



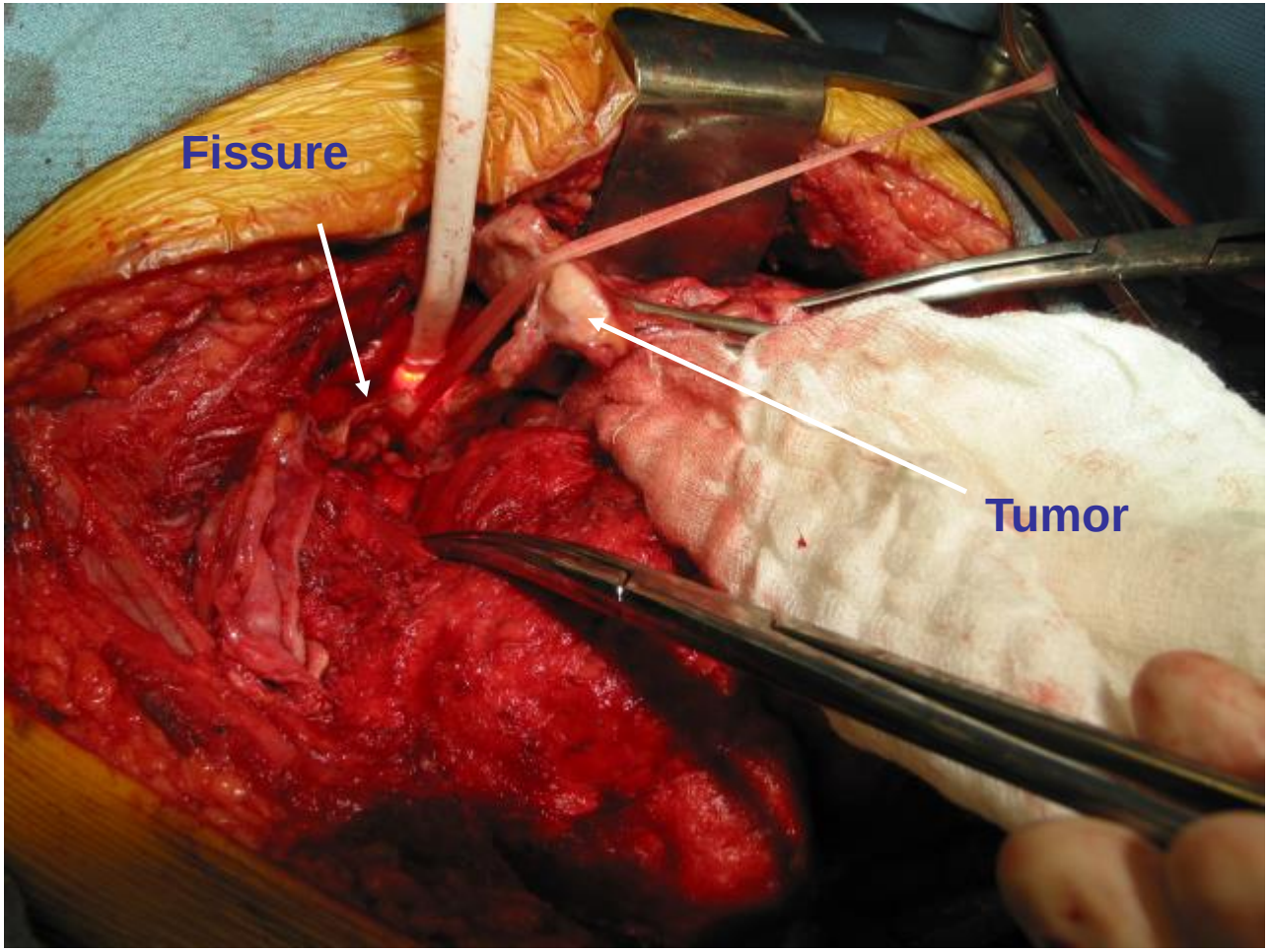
Mesothelioma:GLA VA P/D

Decortication



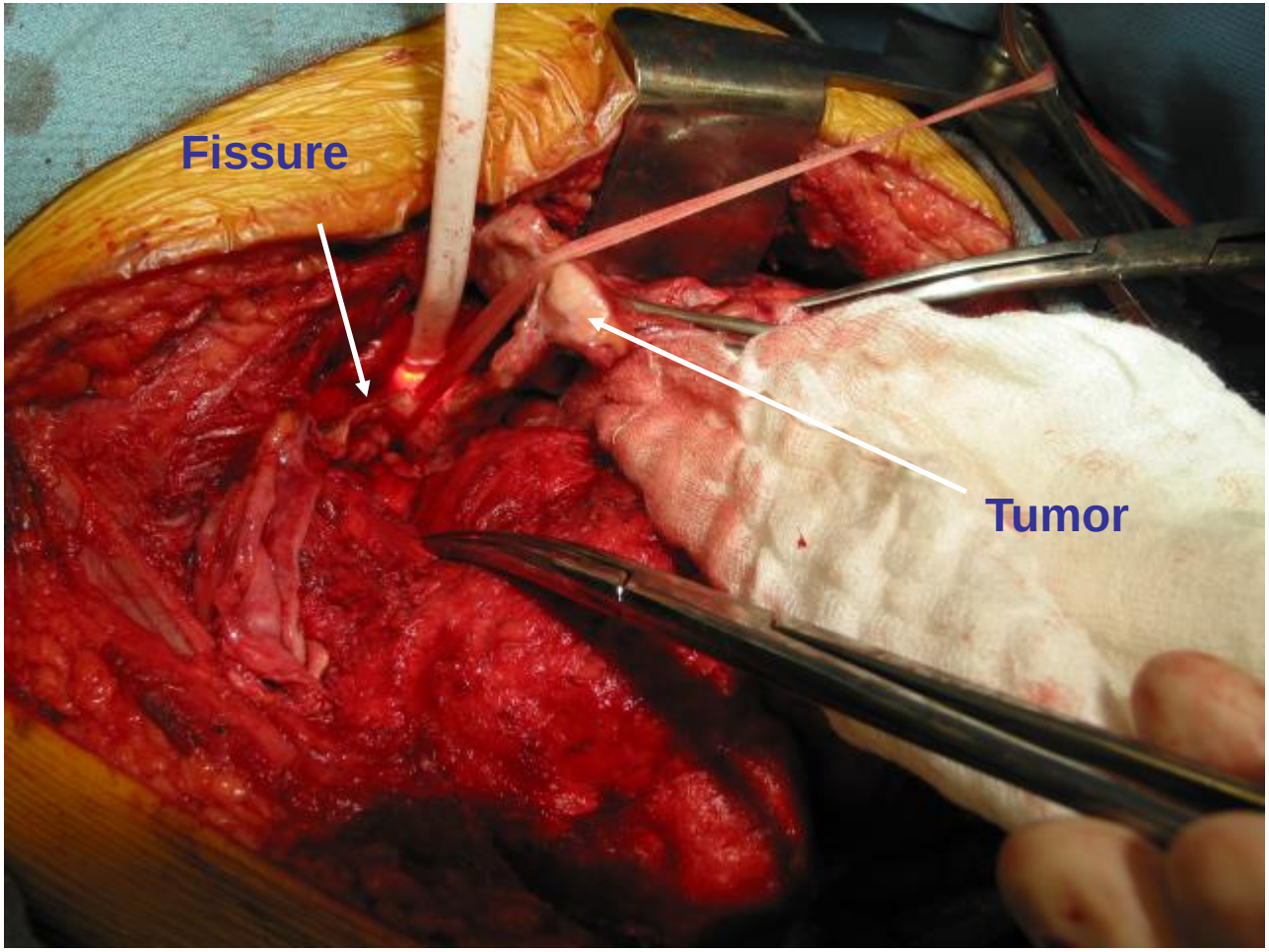
Mesothelioma:GLA VA P/D

Tumor in the Fissure



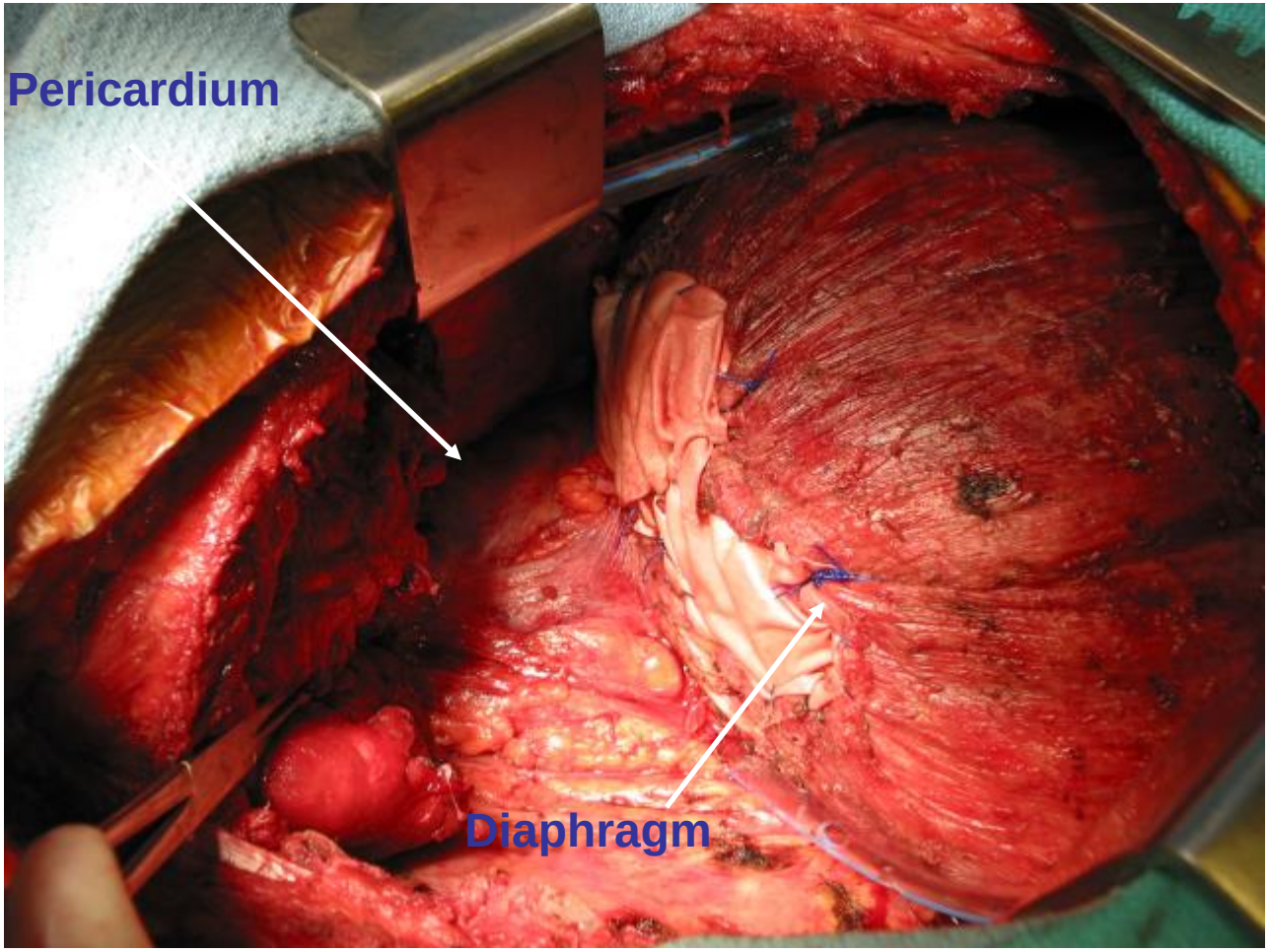
Mesothelioma: GLA VA P/D

Tumor in the Fissure



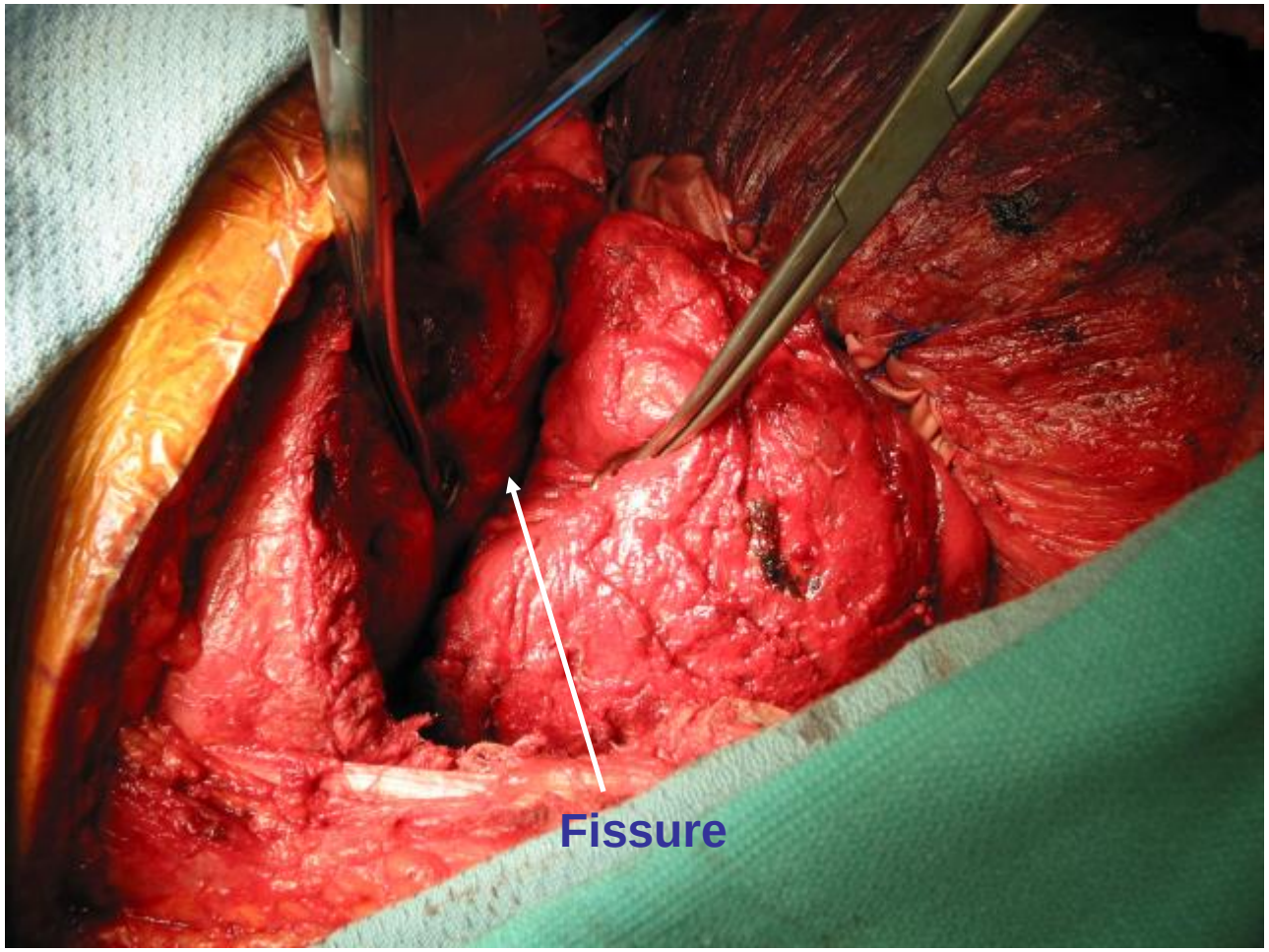
Mesothelioma: GLA VA P/D

Pericardium



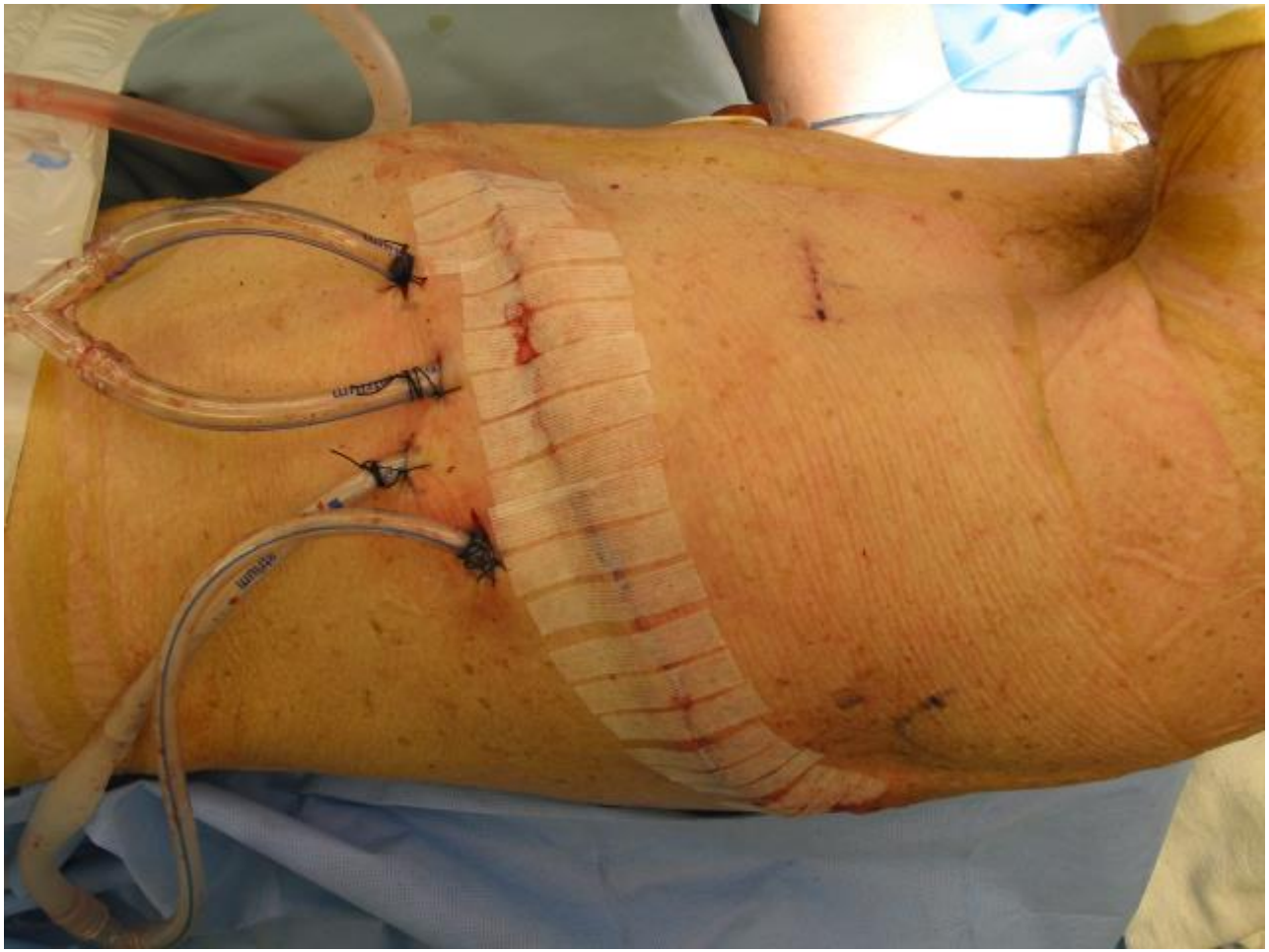
Mesothelioma:GLA VA P/D

Complete Decortication



Mesothelioma: GLA VA P/D

Final Appearance



Mesothelioma: GLA VA P/D

Pathology Specimen

P/D Post-op Management

- ICU care (at UCLA: PCU care)
- Average LOS 10 days
- Extubate in OR
- CT x4 to -20 cm H20 continuous wall suction
- Begin ambulation POD1
- Epidural x 7-8 days
- Replace pleural fluid drainage
- DC f/c POD2

MPM: GLA VA Protocol

Epithelioid Histology

↓

P/D

↓

IMRT

↓

+/- chemotherapy

↓

Immunotherapy

↓

Surviellance PET q3m

Sarcomatoid Histology

↓

Neoadjuvant Chemo

↓

+/- P/D

↓

IMRT

↓

Immunotherapy vs chemo

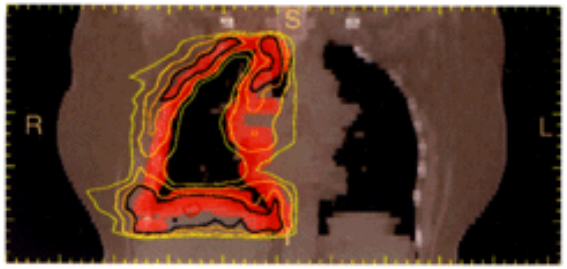
↓

Surviellance PET q3m

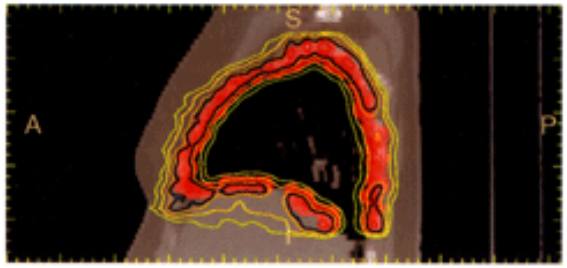
Neoadjuvant IMRT

Goal is to radiate edges and surgical incision while sparing the lung

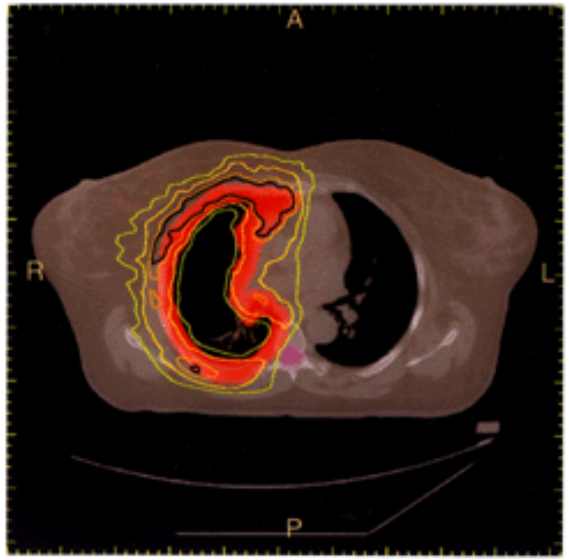
Mesothelioma: IMRT



Coronal Image 270



Sagittal Image 319



60.0%
39.0 Gy

70.0%
45.4 Gy

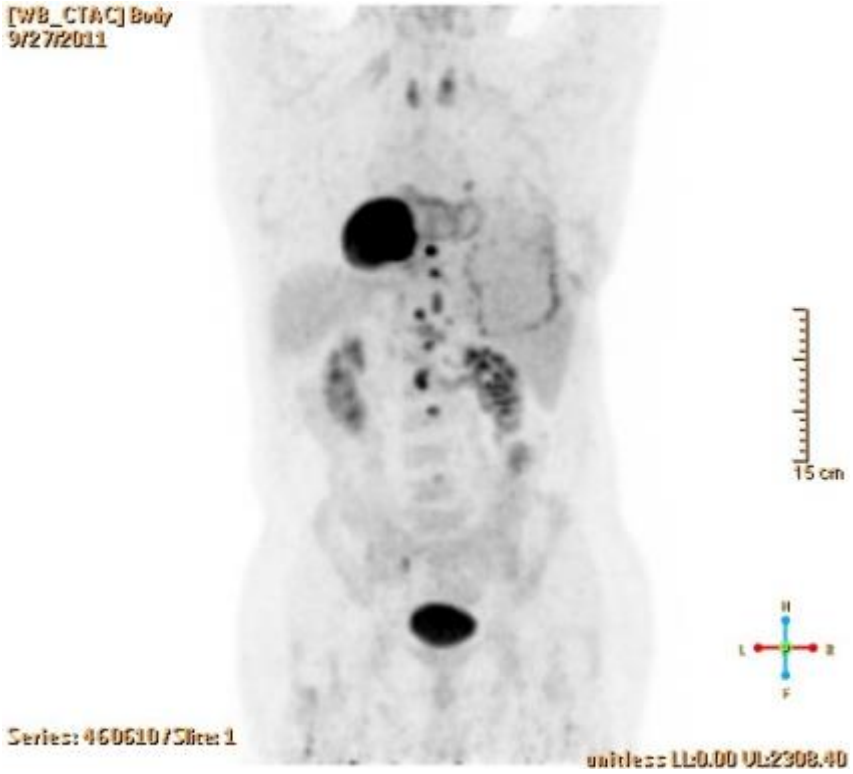
80.0%
51.9 Gy

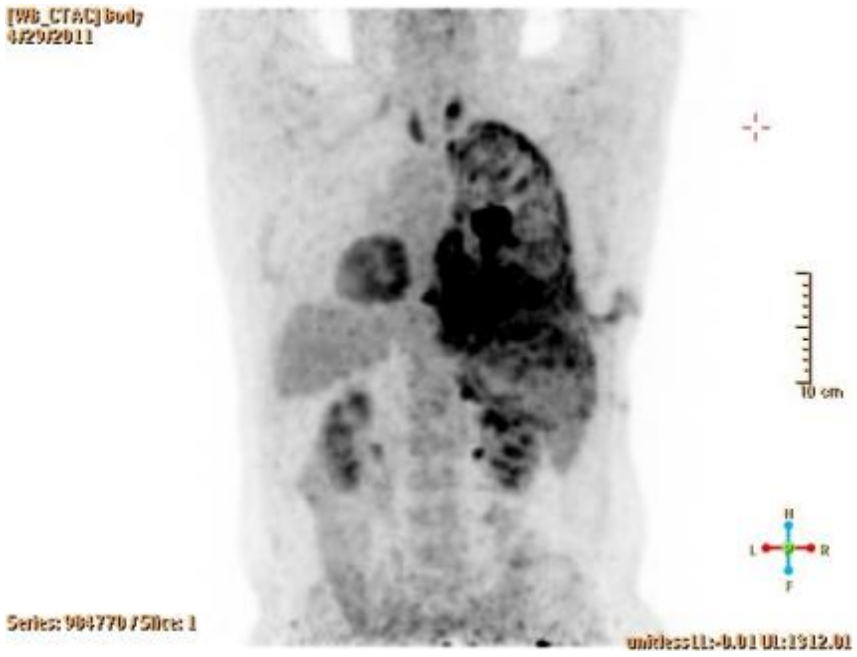
90.0%
58.4 Gy

83.0%
53.9 Gy

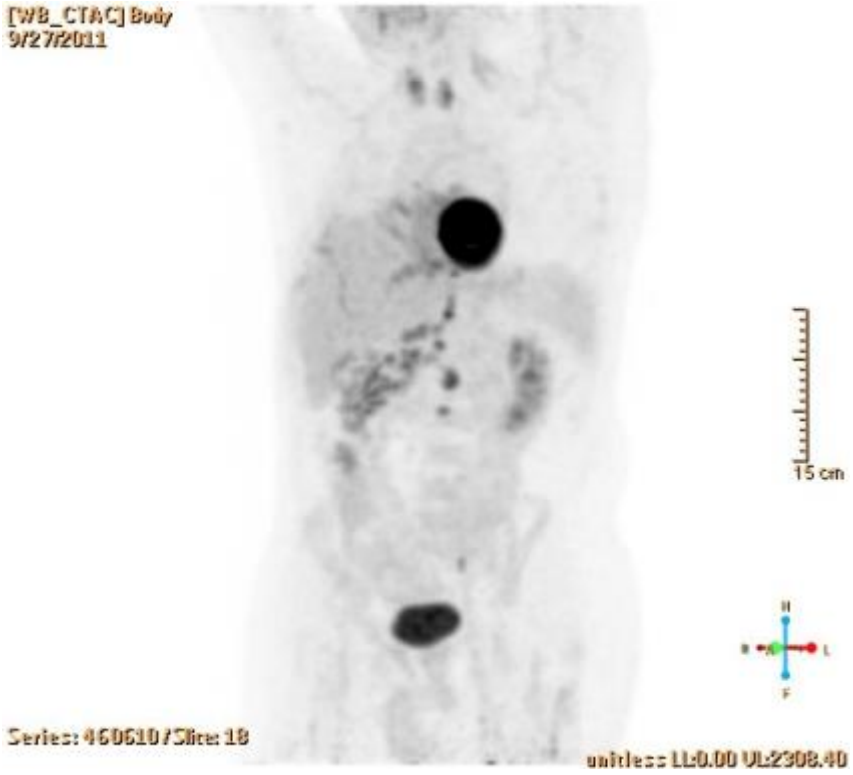
Axial Image 121

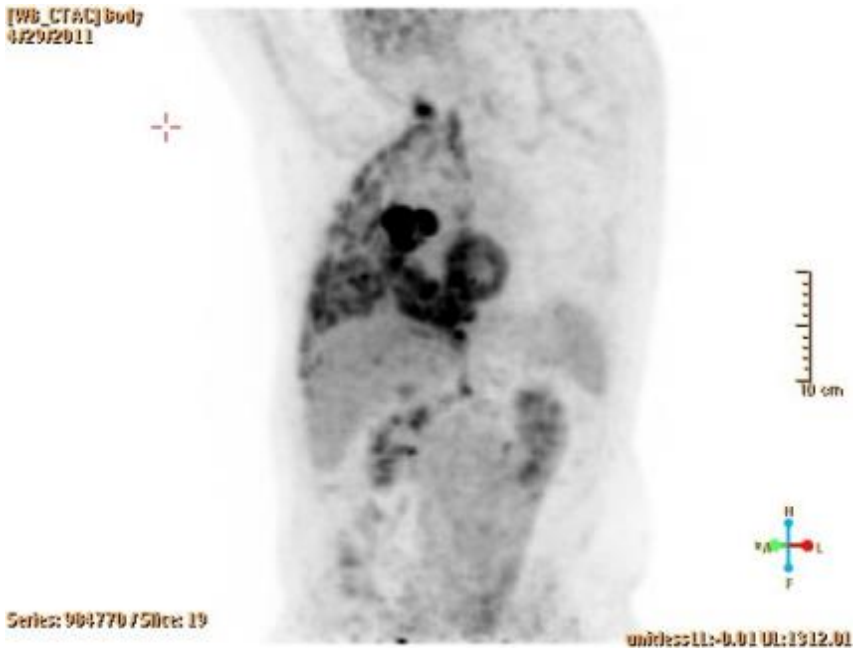
Mr. S Before and After



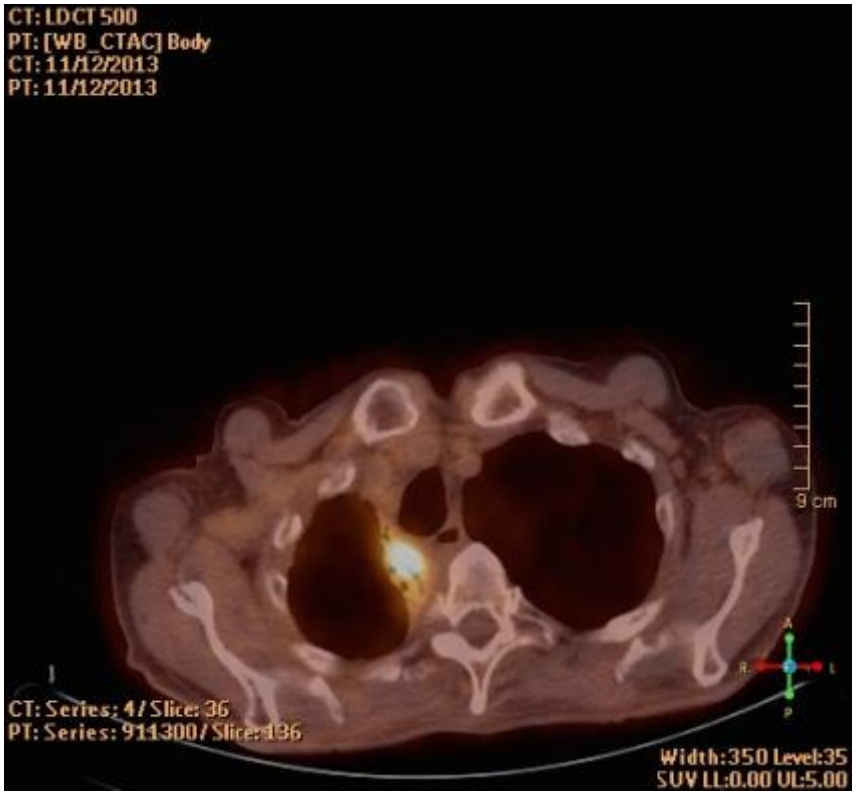


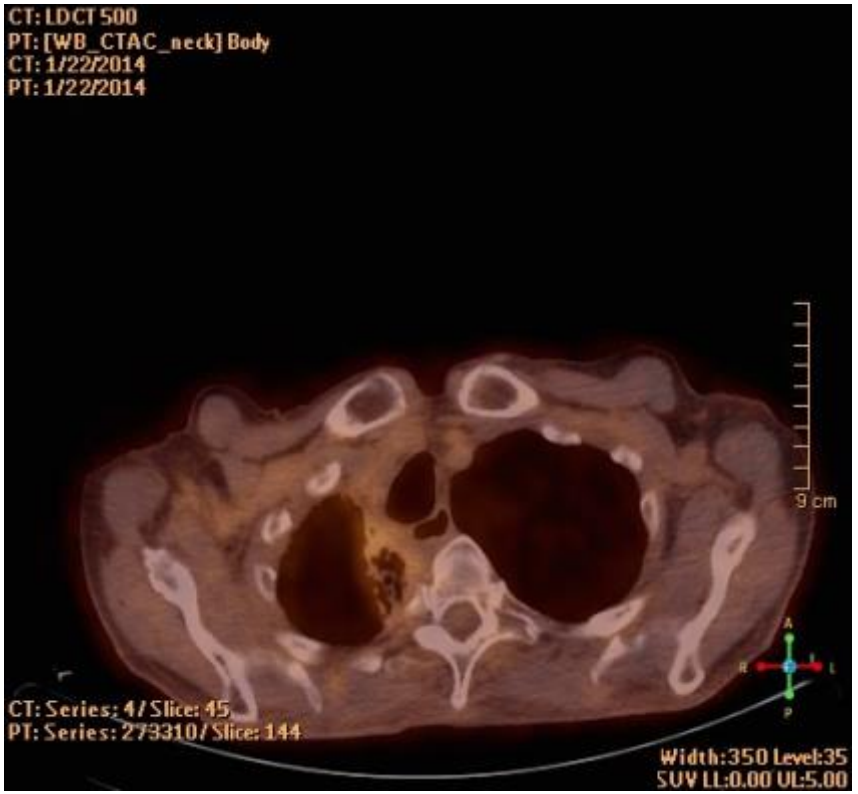
Mr. S Before and After





Cryoablation





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