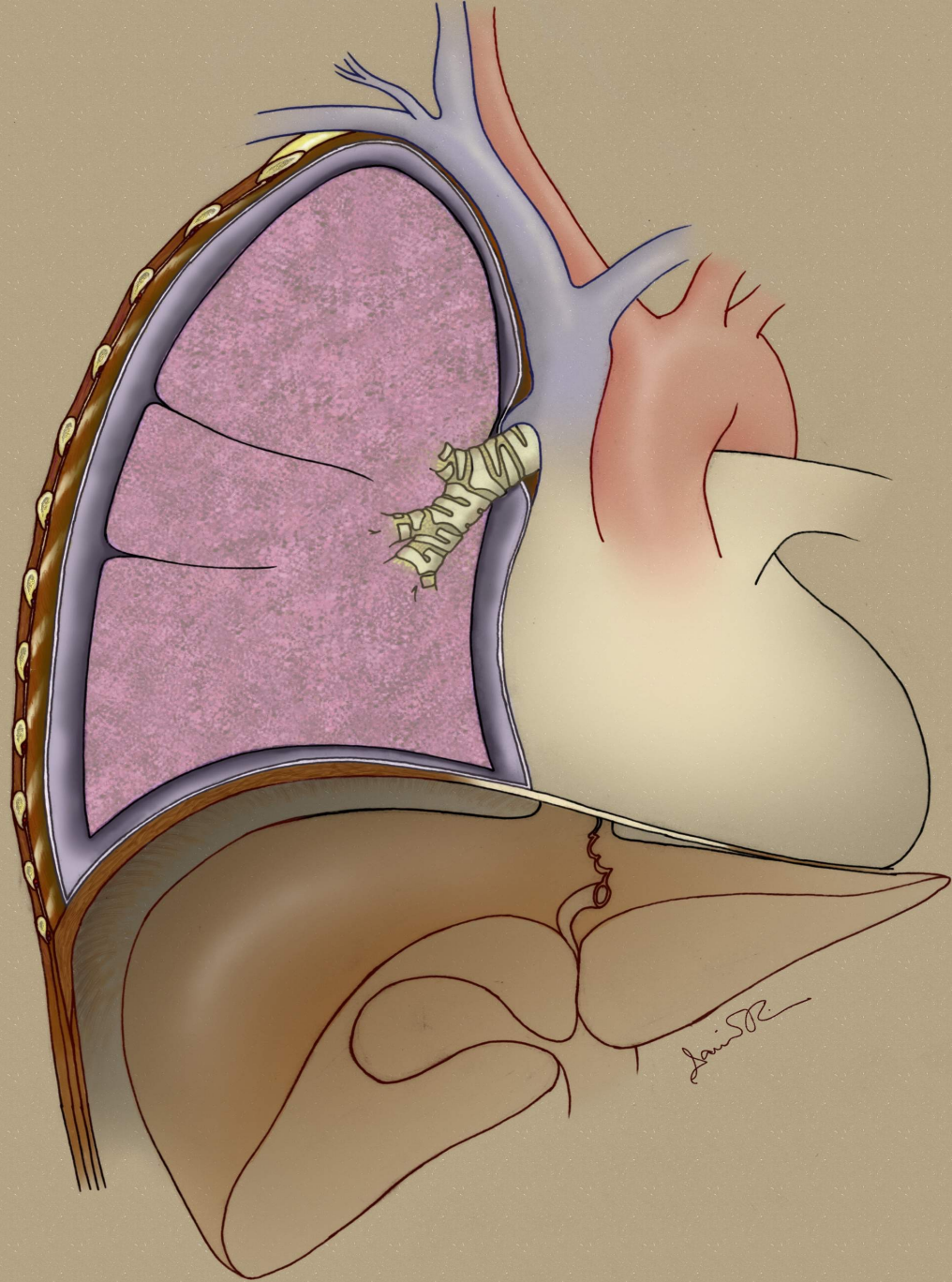
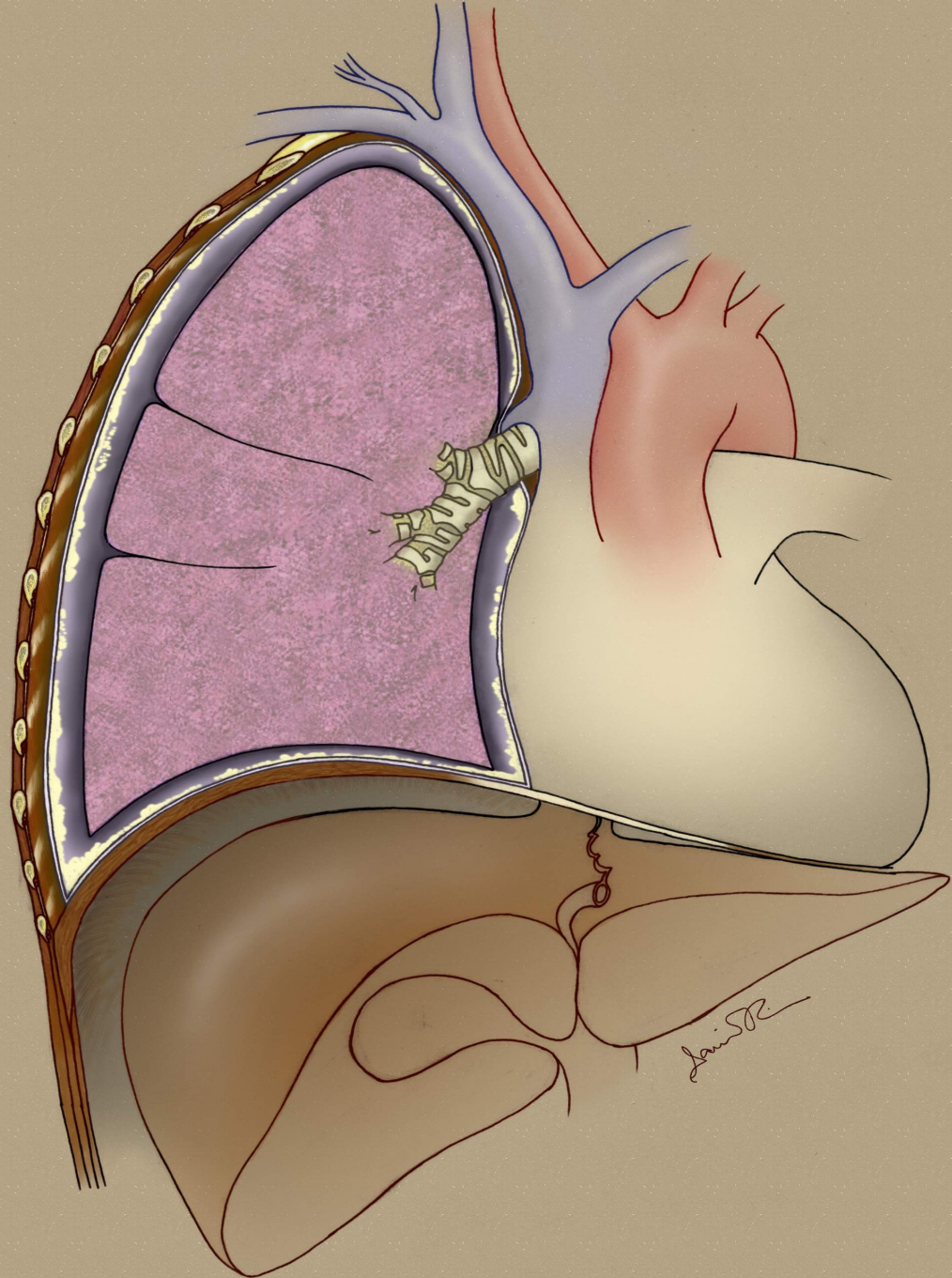


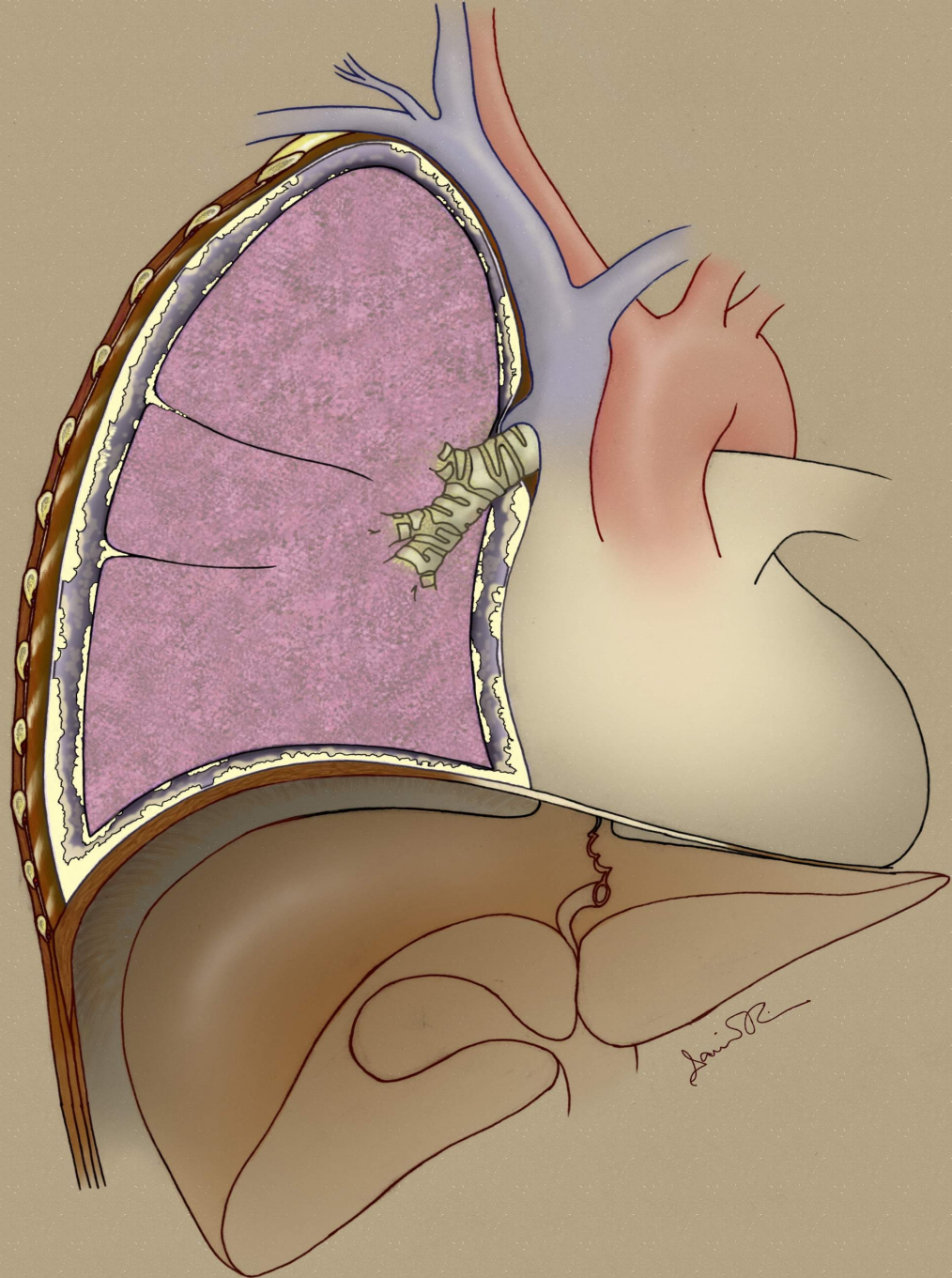
Surgery for Malignant Pleural Mesothelioma

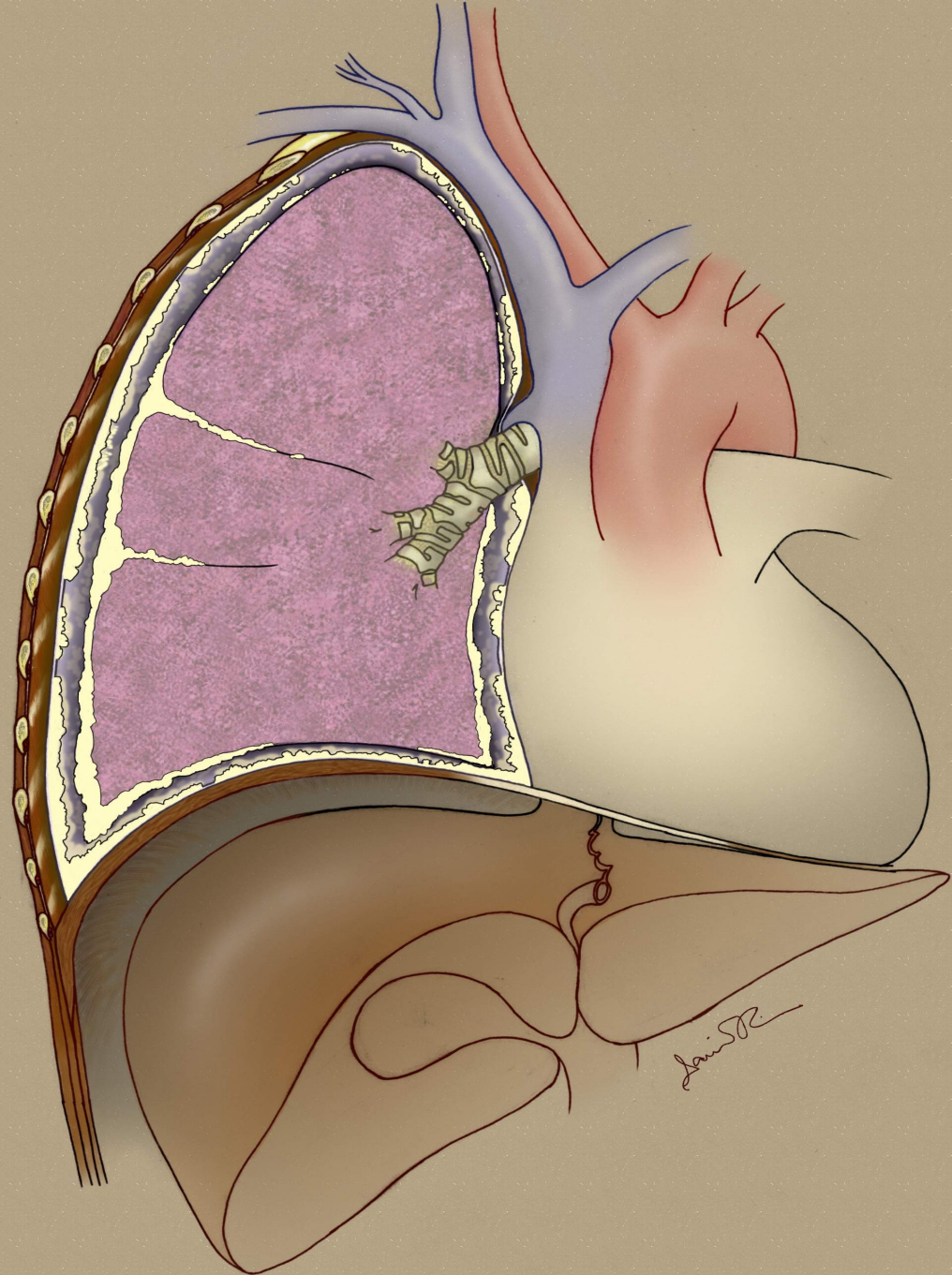
**Raja M Flores MD
Professor and Chief
Thoracic Surgery
Mount Sinai School of Medicine
New York, New York, USA**

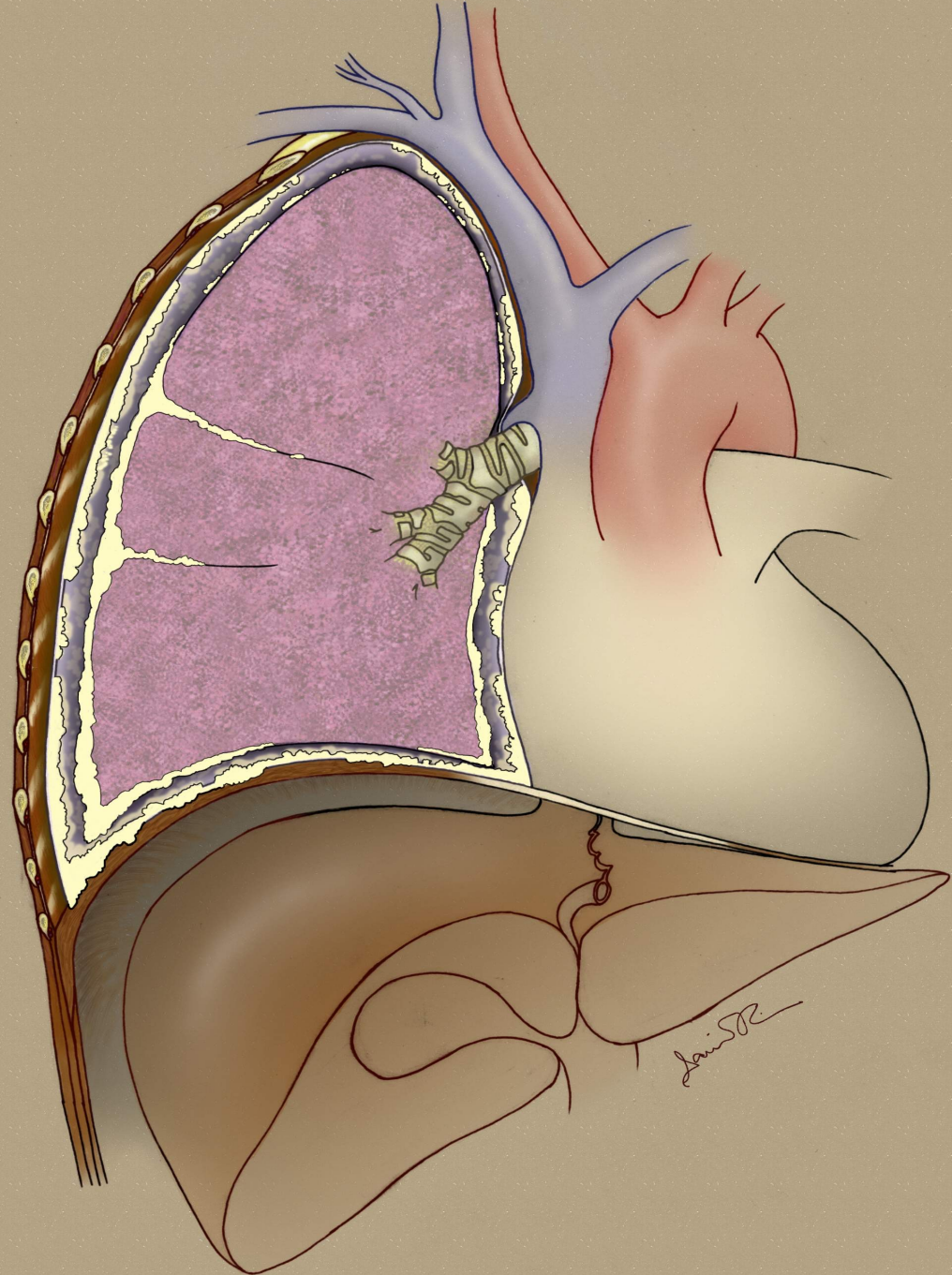


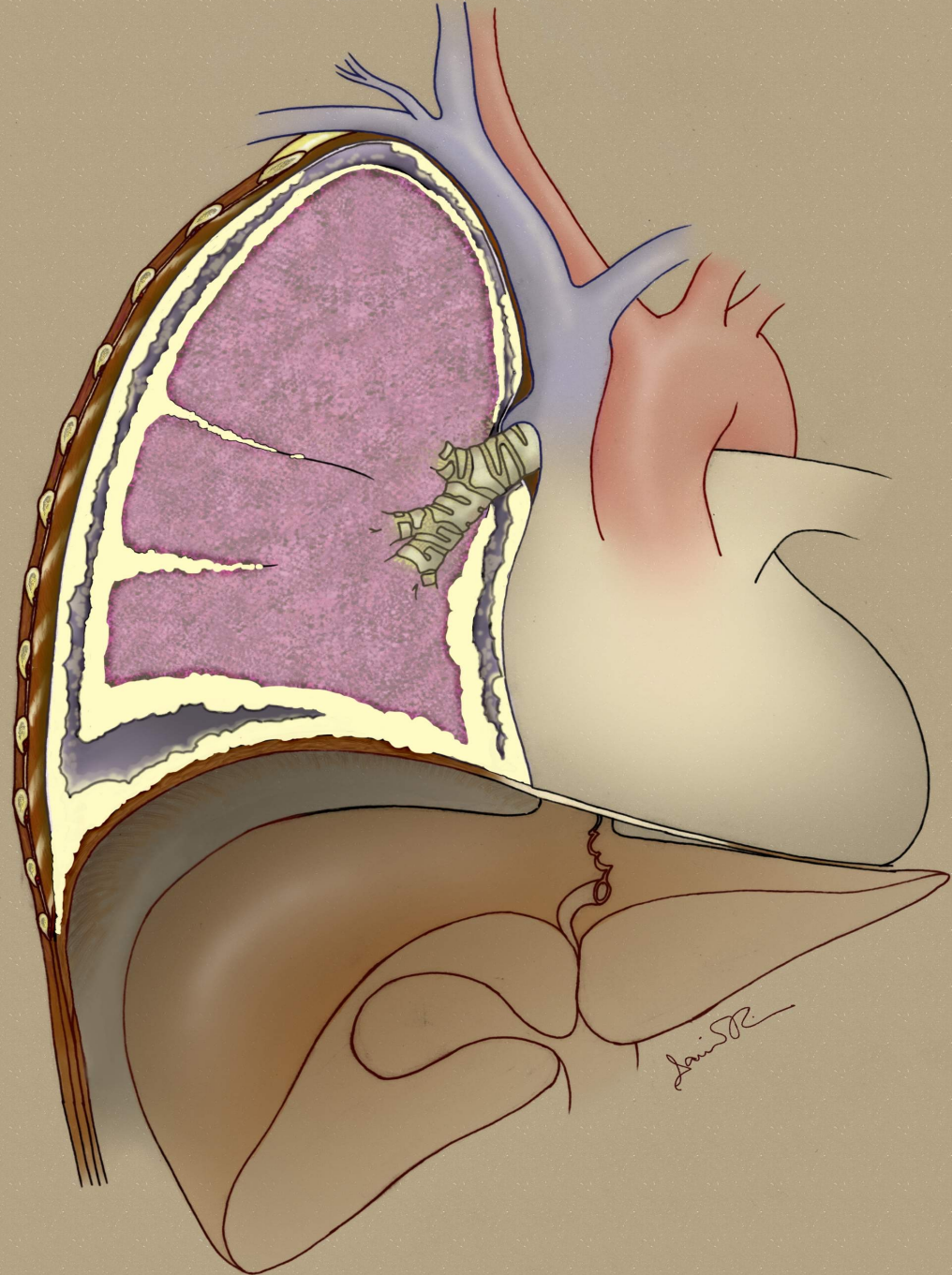
Jan 5/02

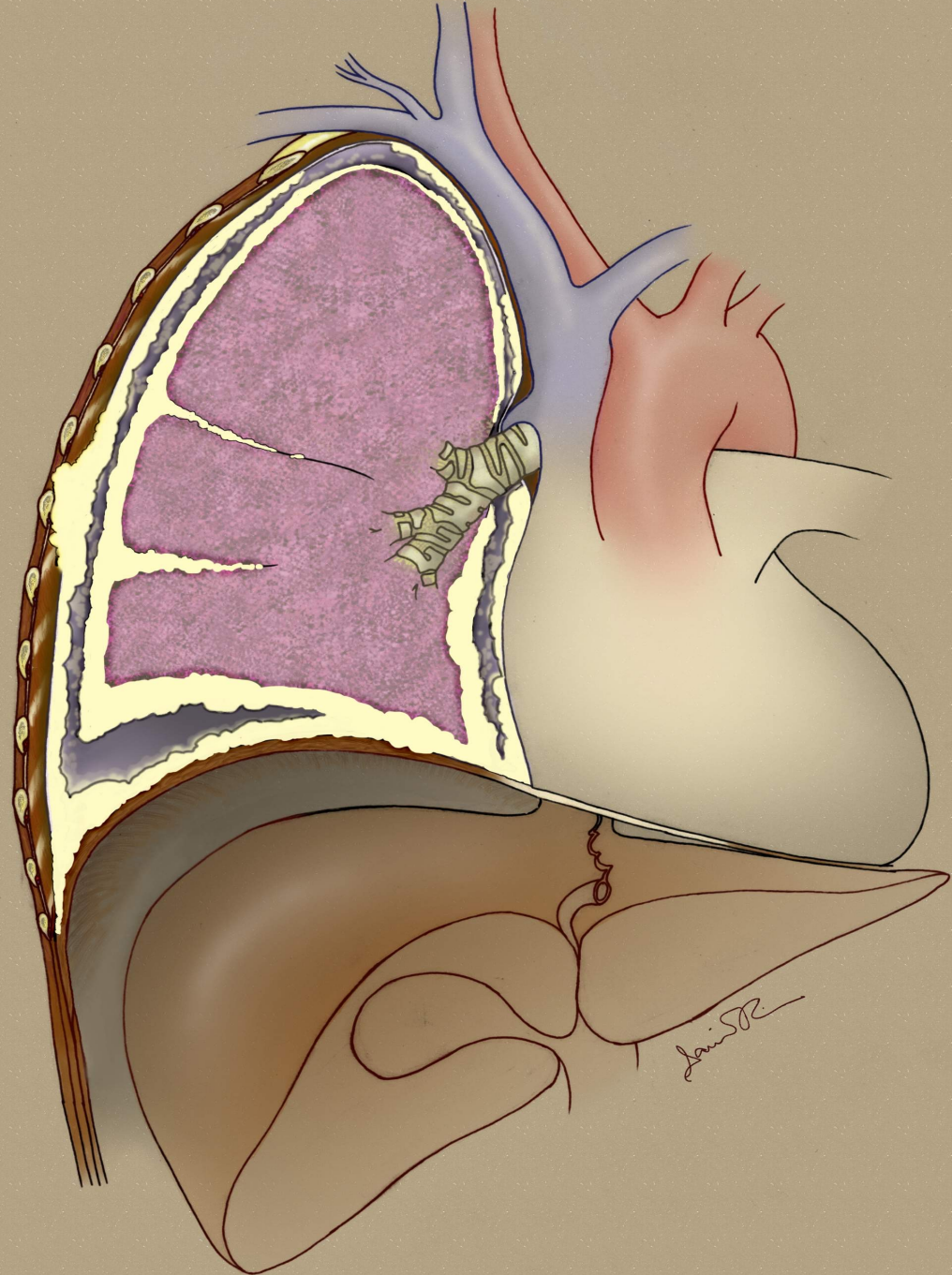


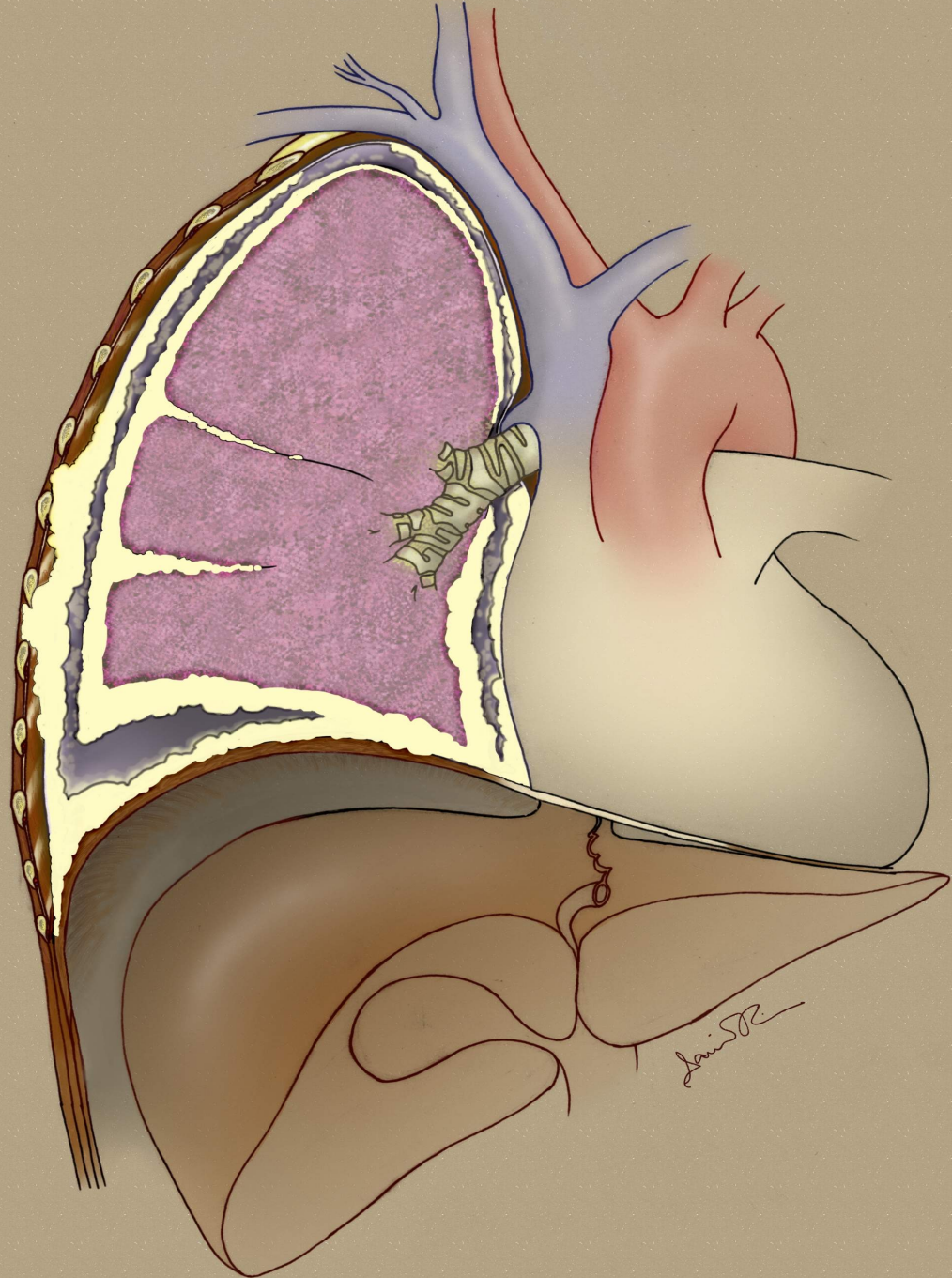


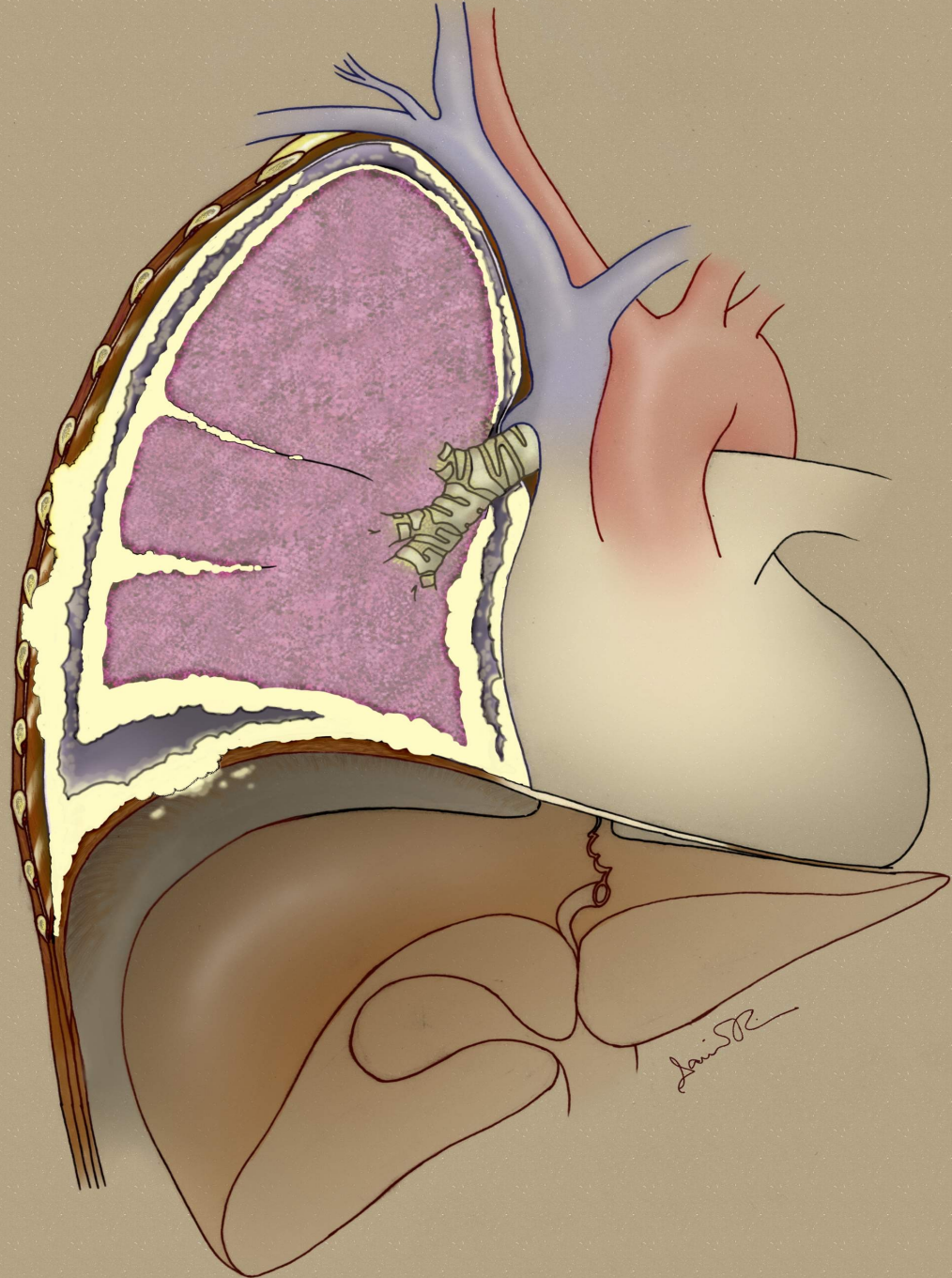


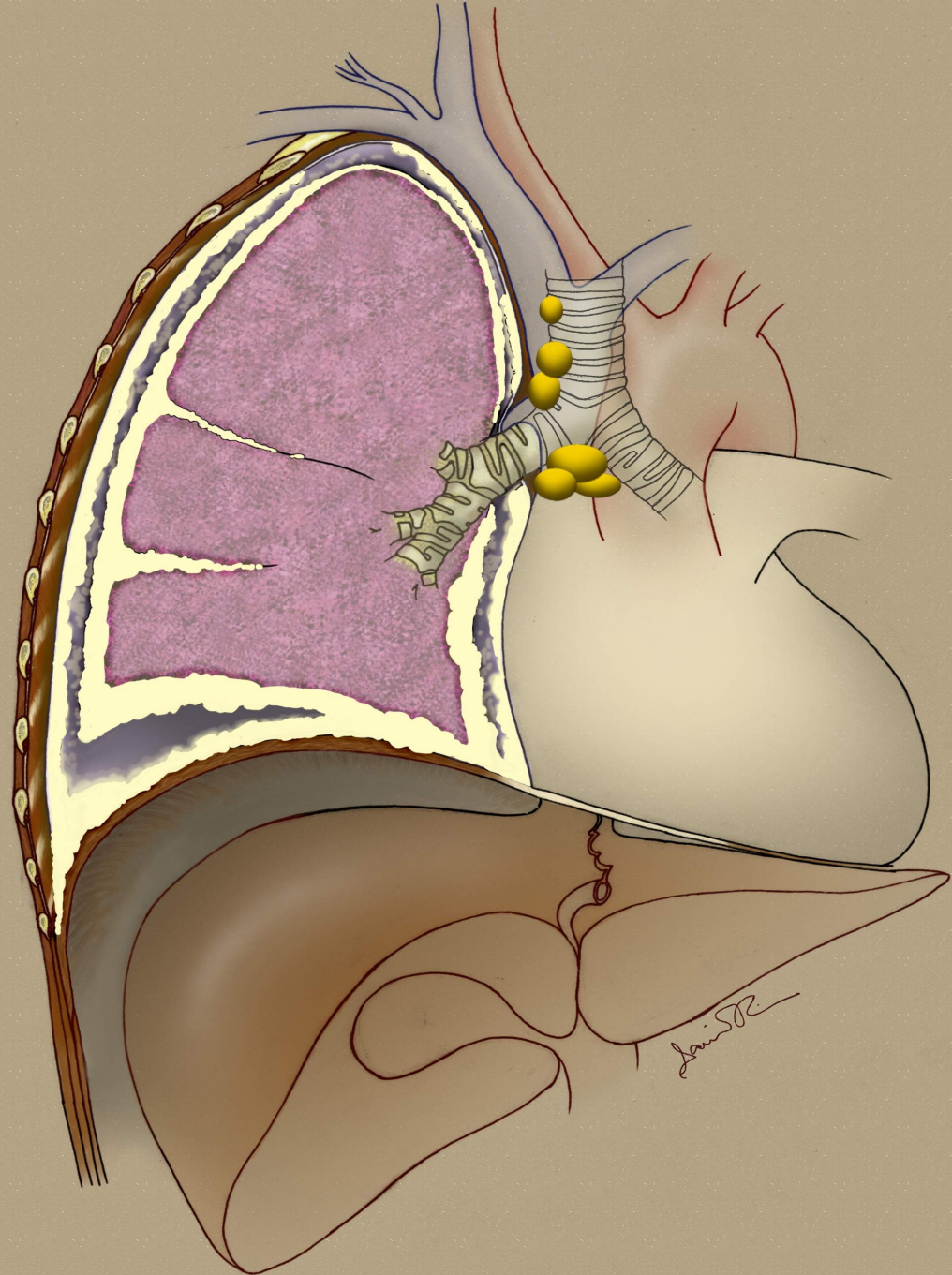


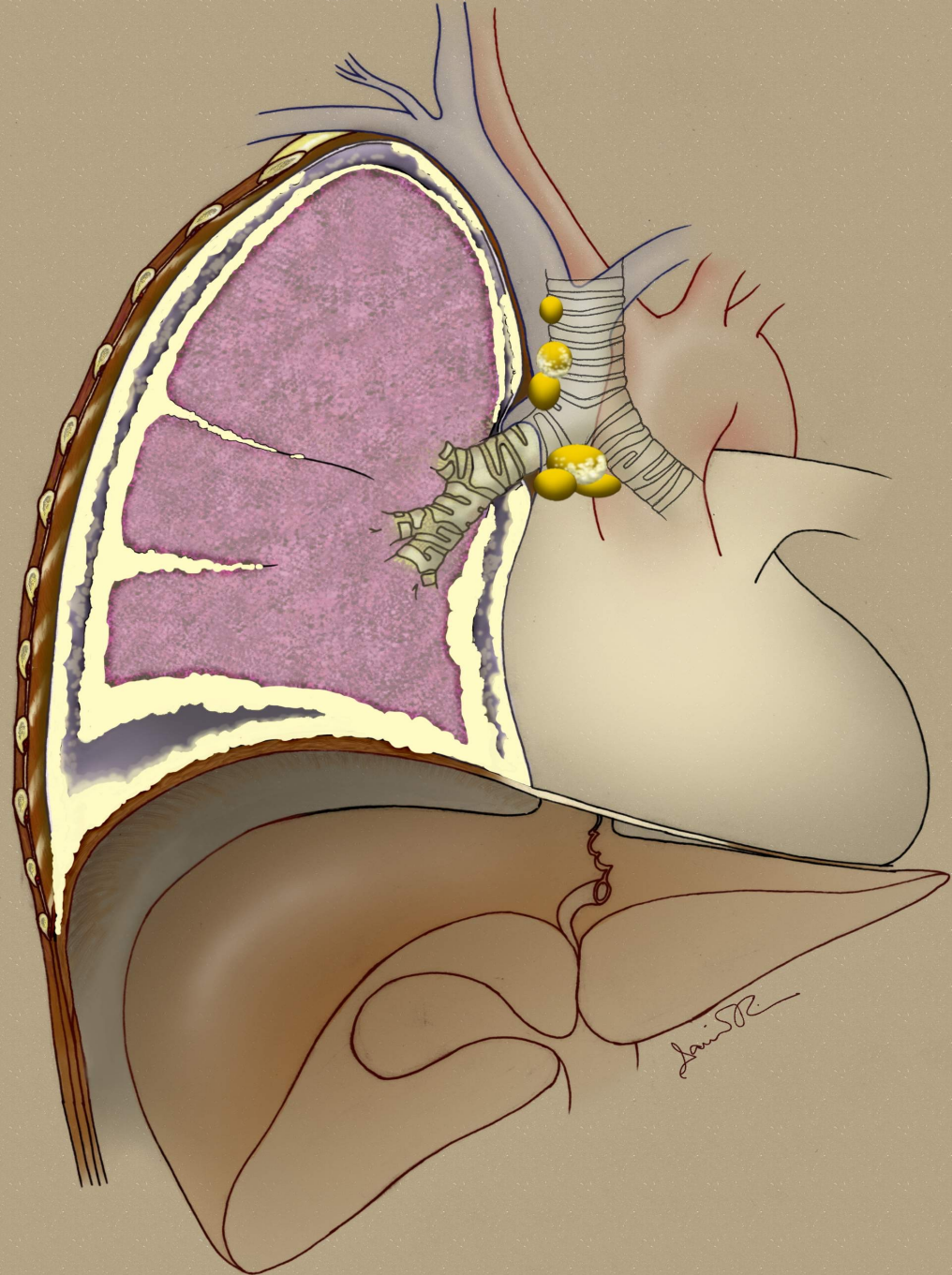


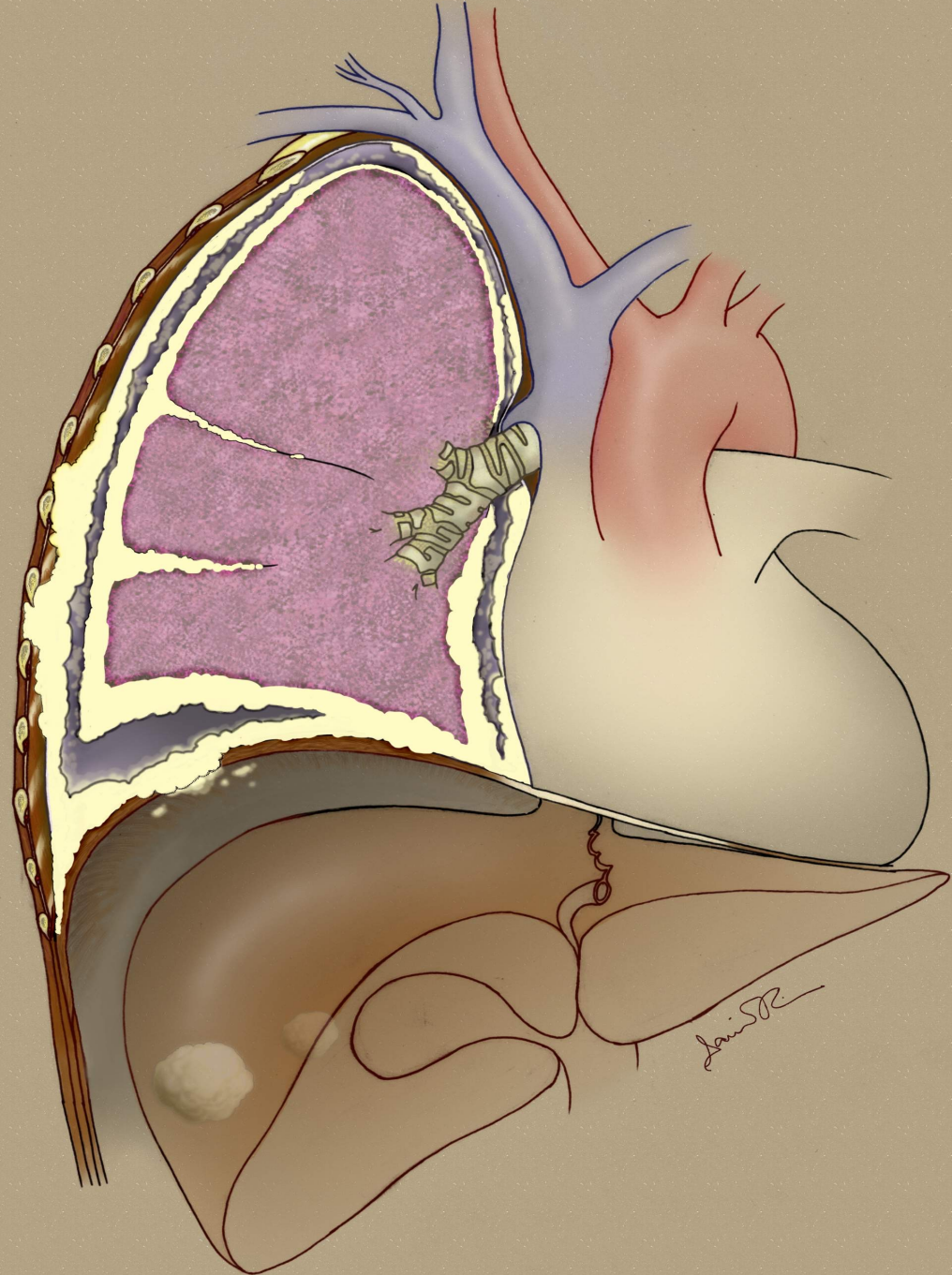




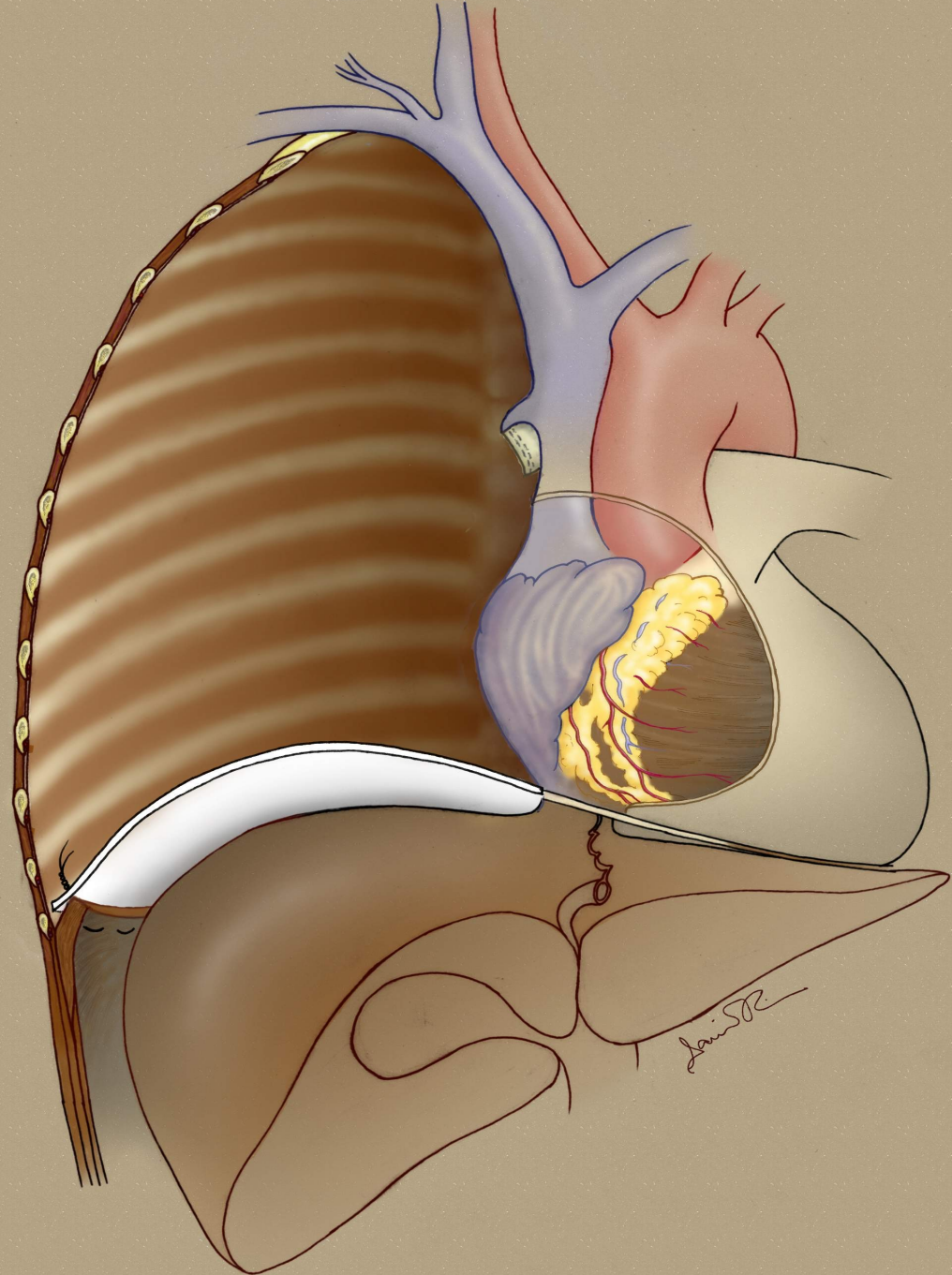


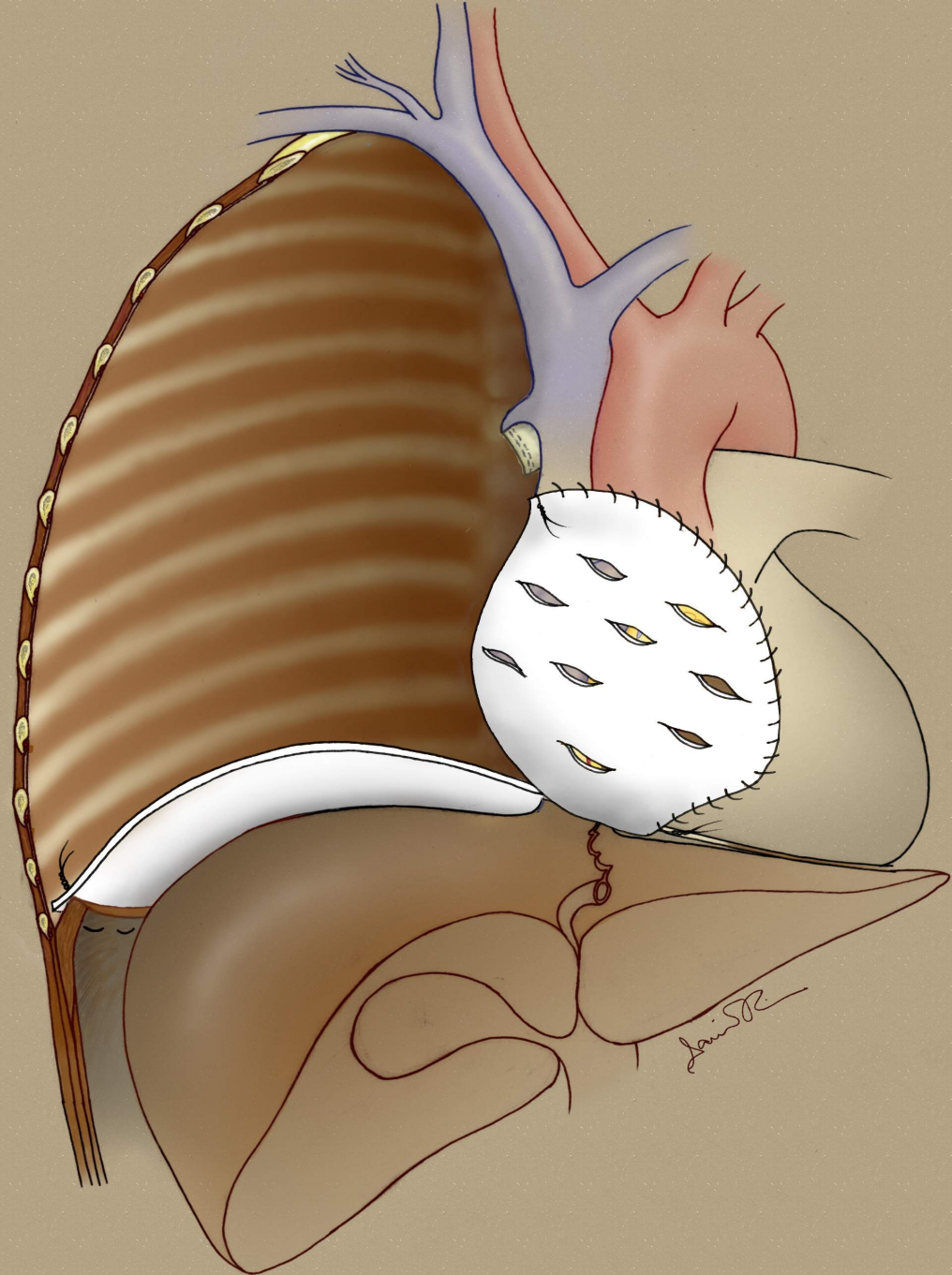












Extrapleural Pneumonectomy
versus
Pleurectomy Decortication

EPP versus P/D in MPM

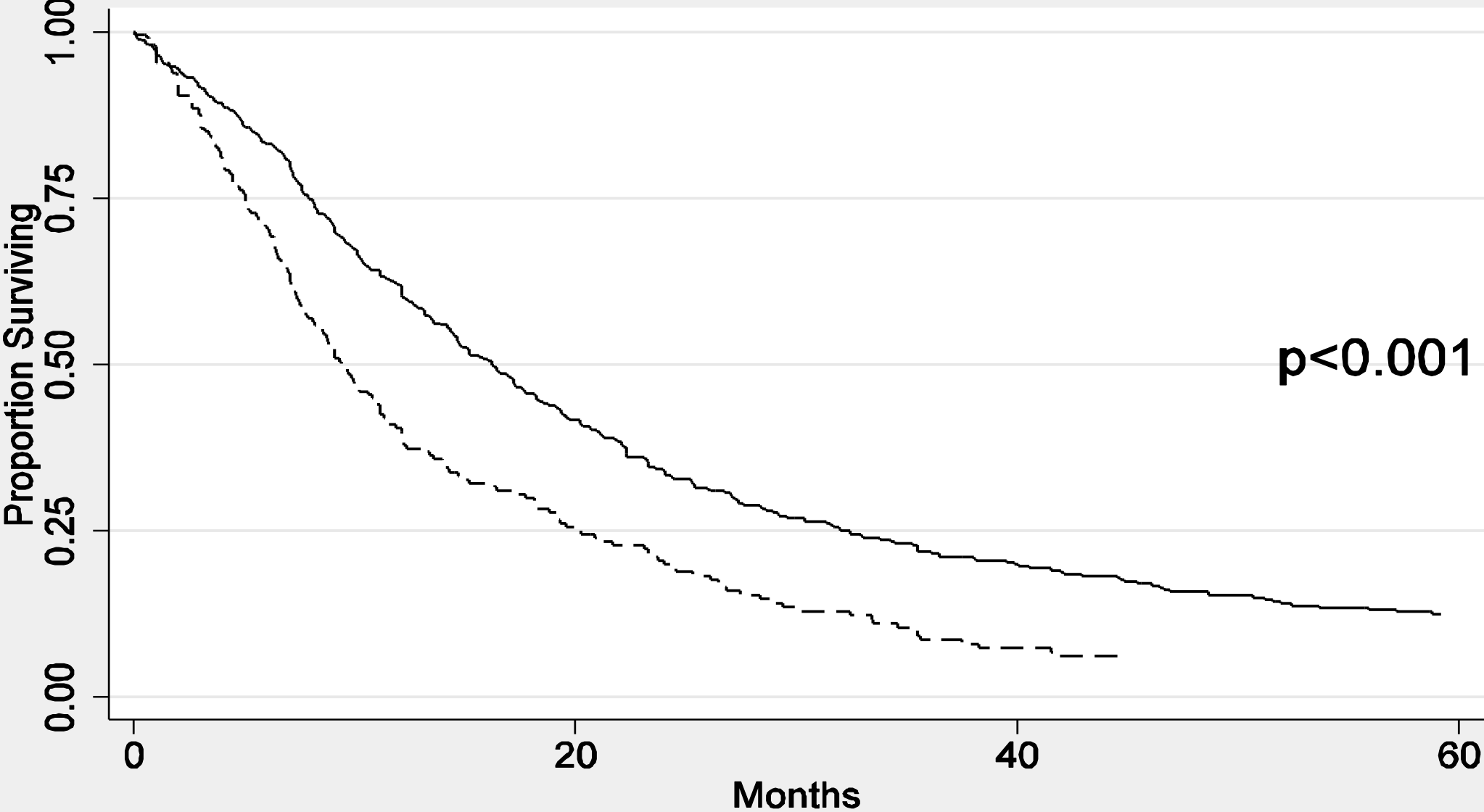
- **From 1990-2006, 663 consecutive patients**
- **Memorial Sloan-Kettering – n=448**
- **National Cancer Institute – n=96**
- **Karmanos Cancer Institute – n=119**
- **Median Follow up – 17 months**

EPP versus P/D in MPM

	EPP (n=385)	P/D (n=278)	p-value
Age (mean)	60	63	<0.001
Male Gender	316 (82%)	220 (79%)	0.267
Epithelioid Histology	269 (69%)	178 (64%)	0.090
Early Stage (I + II)	96 (25%)	98 (35%)	<0.001

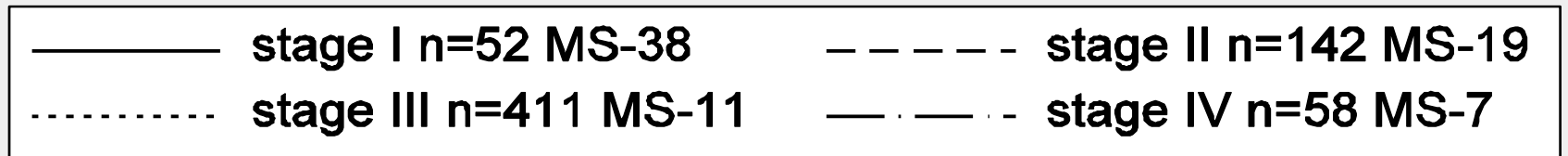
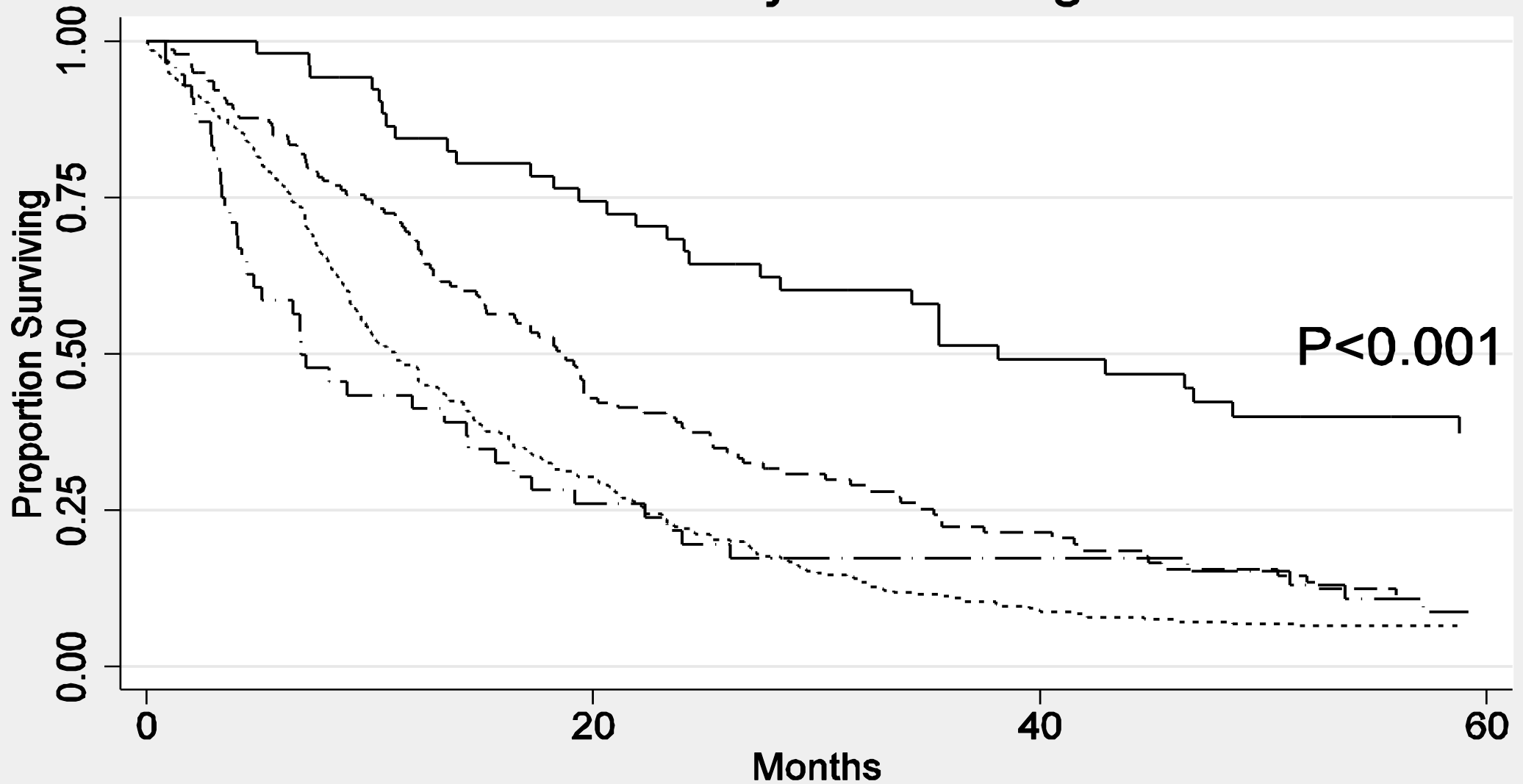
Flores et al JTCVS, 2008 135: 620-6

Survival by Histology

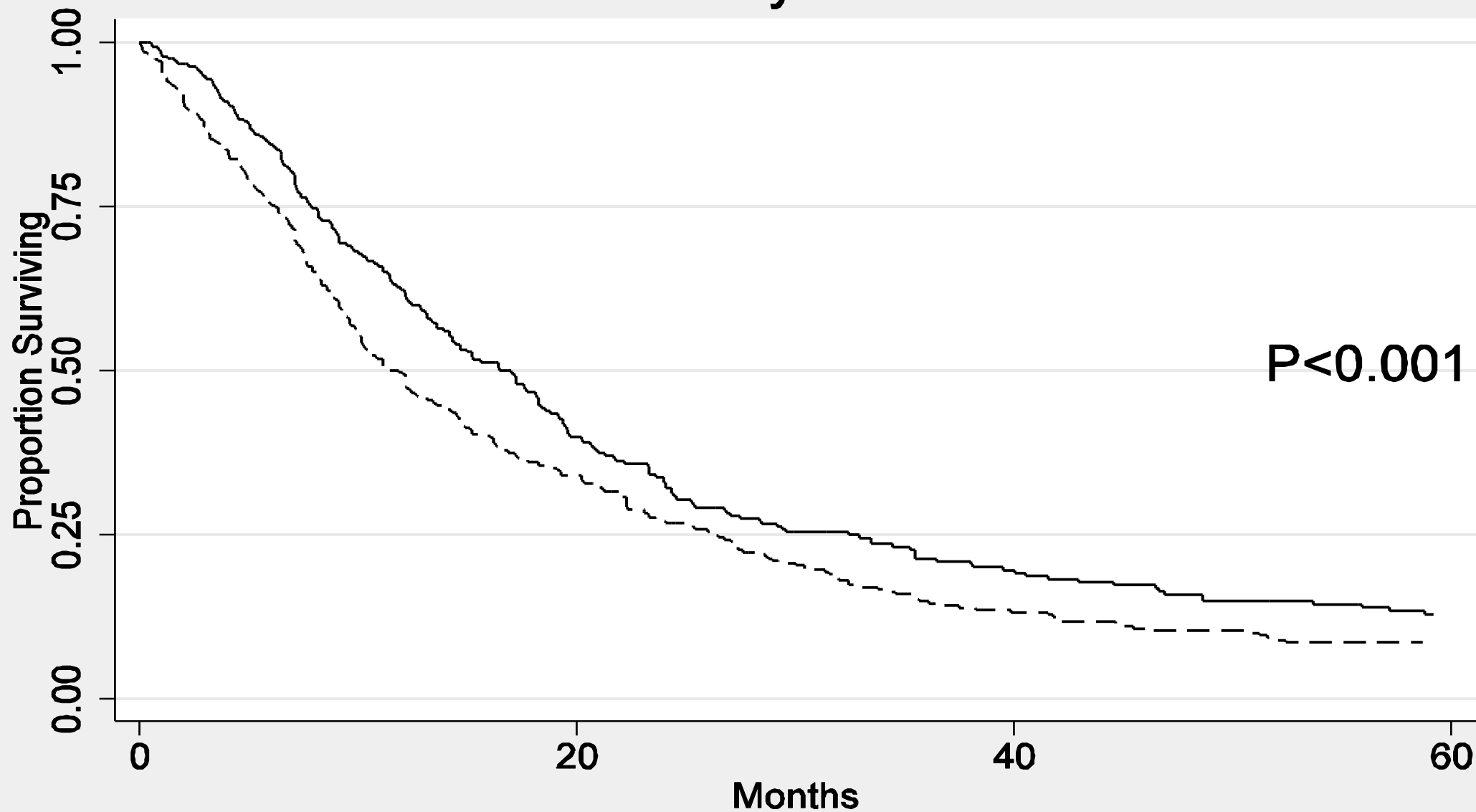


— Epithelioid n=447 MS-16 - - - - Non-epithelioid n=216 MS-9

Survival by AJCC Stage



Survival by Procedure



— P/D n=278 MS-16 months - - - - EPP n=385 MS-12 months

EPP versus P/D in MPM

Multivariate Model

	Hazard Ratio	Confidence Interval	p value
EPP	1.2	(1.0, 1.4)	p=0.04
Non-epithelioid	1.5	(1.3, 1.8)	p<0.001
Stage III/IV	1.9	(1.6, 2.3)	p<0.001

Flores et al JTCVS, 2008 135: 620-6

Positron Emission Tomography (PET)

- 63 patients, retrospective study, 10% of patients identified with metastatic disease undetected by CT scan ¹
- 137 patients, SUV directly proportional to survival. SUV < 10 correlated with improved survival ²

1.Flores RM et al. JTCVS 2003, 126;11-6

2.Flores RM et al. JTCVS 2006, 132;763-8

Modern day Mortality

Meta-Analysis of Survival After Pleurectomy Decortication Versus Extrapleural Pneumonectomy in Mesothelioma

Emanuela Taioli, MD, PhD, Andrea S. Wolf, MD, and Raja M. Flores, MD

Department of Population Health, Hofstra North Shore-LIJ School of Medicine, Hempstead; and Department of Thoracic Surgery, Icahn School of Medicine, Mount Sinai Health System, New York, New York

(Ann Thorac Surg 2015;99:472–81)

24 distinct datasets

EPP – n= 1,391 Mortality 4.5%

P/D – n= 1,512 Mortality 1.7%



**2023 World Conference
on Lung Cancer**

SEPTEMBER 9-12, 2023 | SINGAPORE



MARS2: A multicentre randomised trial comparing (extended) pleurectomy decortication versus no radical surgery for mesothelioma





Extra-pleural pneumonectomy versus no extra-pleural pneumonectomy for patients with malignant pleural mesothelioma: clinical outcomes of the Mesothelioma and Radical Surgery (MARS) randomised feasibility study

Tom Treasure, Loic Lang-Lazdunski, David Waller, Judith M Bliss, Carol Tan, James Entwisle, Michael Snee, Mary O'Brien, Gill Thomas, Suresh Senan, Ken O'Byrne, Lucy S Kilburn, James Spicer, David Landau, John Edwards, Gill Coombes, Liz Darlison, Julian Peto, for the MARS trialists*

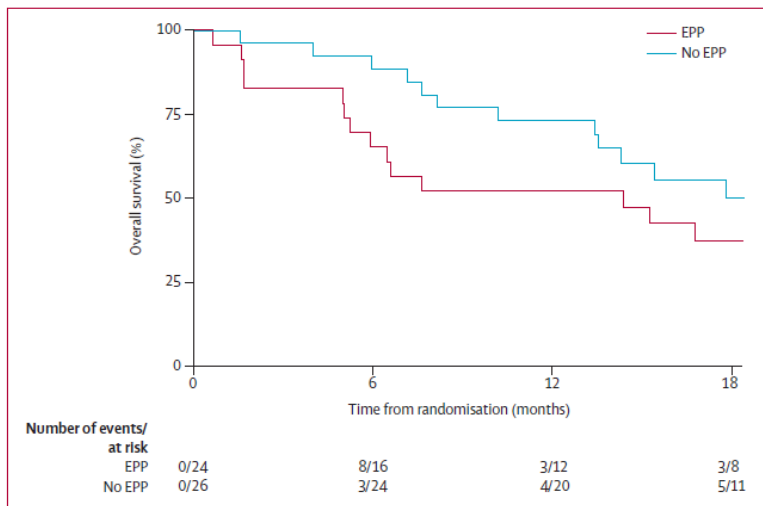


Figure 4: Overall survival
EPP=extra-pleural pneumonectomy.

Lancet Oncol 2011; 12: 763-72

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

Raja M. Flores, MD,^a Harvey I. Pass, MD,^d Venkatraman E. Seshan, PhD,^b Joseph Dycoco, BA,^a Maureen Zakowski, MD,^c Michele Carbone, MD,^a Manjit S. Bains, MD,^a and Valerie W. Rusch, MD^a

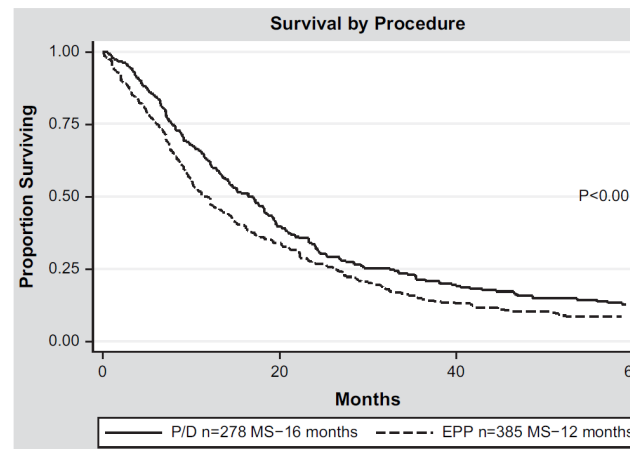


Figure 3. Overall survival of EPP versus P/D, by univariate analysis. *EPP*, Extraleural pneumonectomy; *P/D*, pleurectomy/decortication.

J Thorac Cardiovasc Surg 2008; 135:620-6





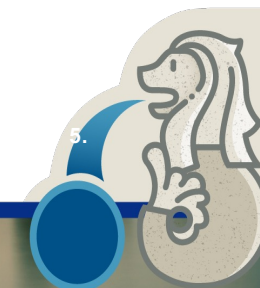
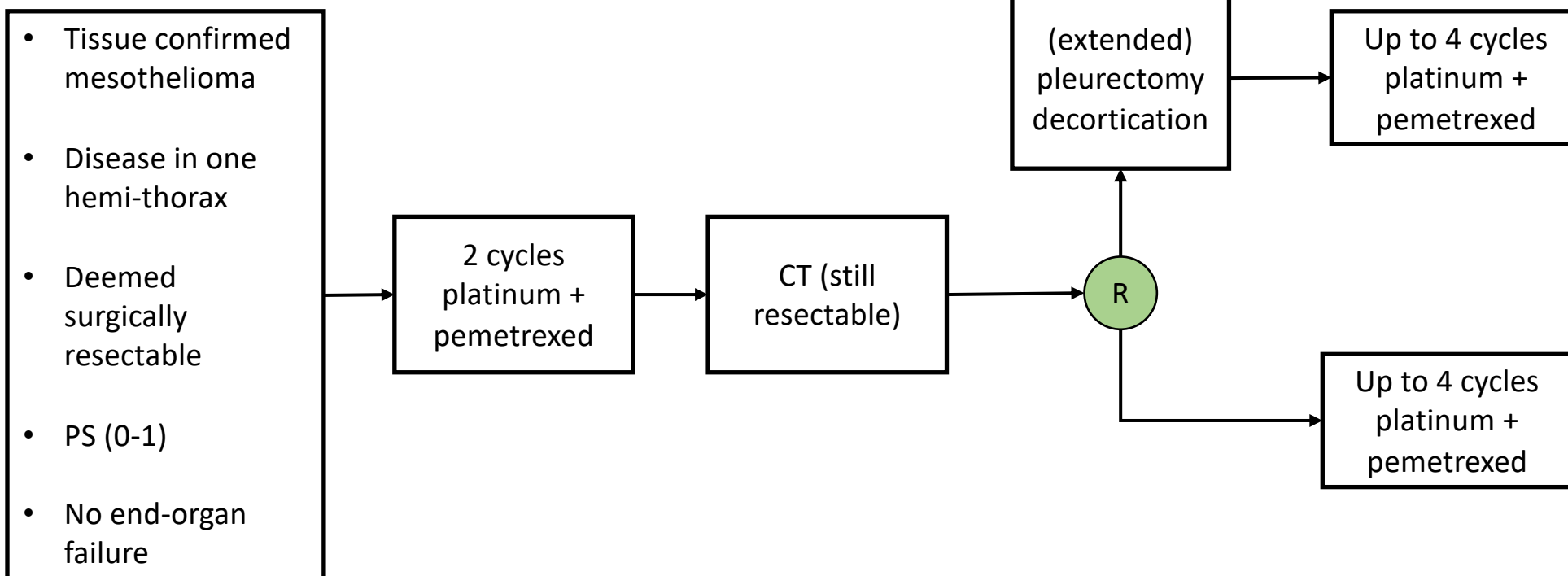
MARS 2: Trial design

- Primary outcome - overall survival
 - test the hypothesis that (extended) pleurectomy decortication and chemotherapy is superior (**30% relative improvement**) to chemotherapy alone
- Secondary outcomes:
 - PFS, safety, health related quality of life (EORTC, EQ5D), cost effectiveness



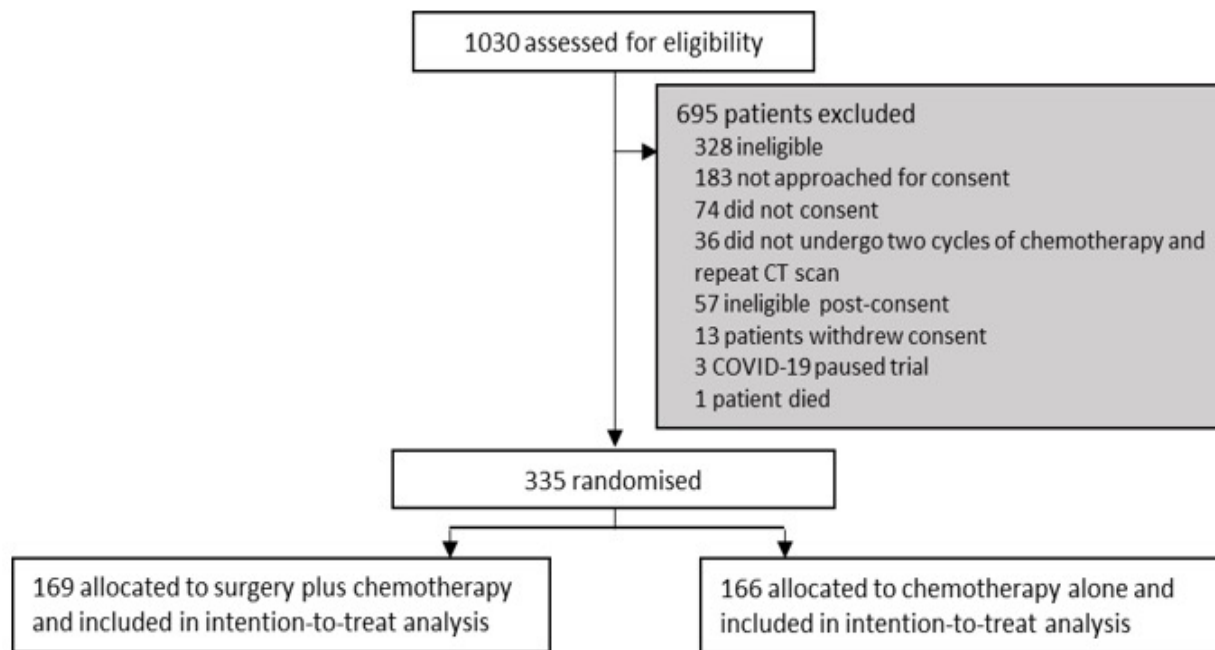


MARS 2 trial schema





Participant flow





Surgery

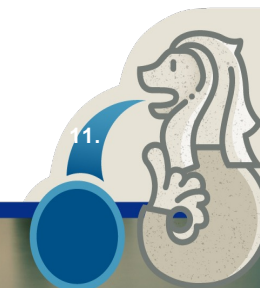
	Received surgery (n=158*)
Surgical procedure	
Extended pleurectomy/decortication	139/157 (88.5%)
Pleurectomy decortication	13/157 (8.3%)
Partial pleurectomy	3/157 (1.9%)
Exploration, no pleurodesis	1/157 (0.6%)
Other	1/157 (0.6%)
Resection and reconstruction	
Diaphragm resection	130/157 (82.8%)
Diaphragm reconstructed	128/157 (81.5%)
Pericardium resection	105/157 (66.9%)
Pericardium reconstructed	84/157 (53.5%)
Chest wall resection	19/157 (12.1%)
Chest wall reconstructed	9/157 (5.7%)
Other ipsilateral lung resection	67/157 (42.7%)
Wedge resection	64/67 (95.5%)
Bilobectomy	1/67 (1.5%)
Lobectomy	2/67 (3.0%)

Completeness of resection	
R0 (no residual tumour)	5/157 (3.2%)
R1 (microscopic residual tumour)	127/157 (80.9%)
R2 (macroscopic residual tumour)	25/157 (15.9%)
Length of hospital stay (days) §	
In-hospital mortality	6/157 (3.8%)
30 day mortality	6/157 (3.8%)
90 day mortality	14/157 (8.9%)

Data are n/N (%)

* 1 patient withdrew to receive surgery privately and operative details were unable to be obtained. § in-hospital deaths censored at maximum length of stay

Lim E, Darlison L, Edwards J *et al.* on behalf of MARS 2 Trialists. Mesothelioma and Radical Surgery 2 (MARS 2): protocol for a multicentre randomised trial comparing (extended) pleurectomy decortication versus no (extended) pleurectomy decortication for patients with malignant pleural mesothelioma *BMJ Open* 2020;**10**:e038892. doi: 10.1136/bmjopen-2020-038892



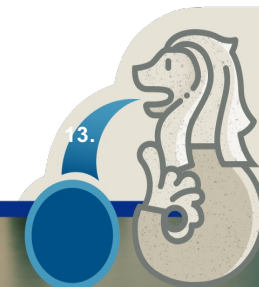
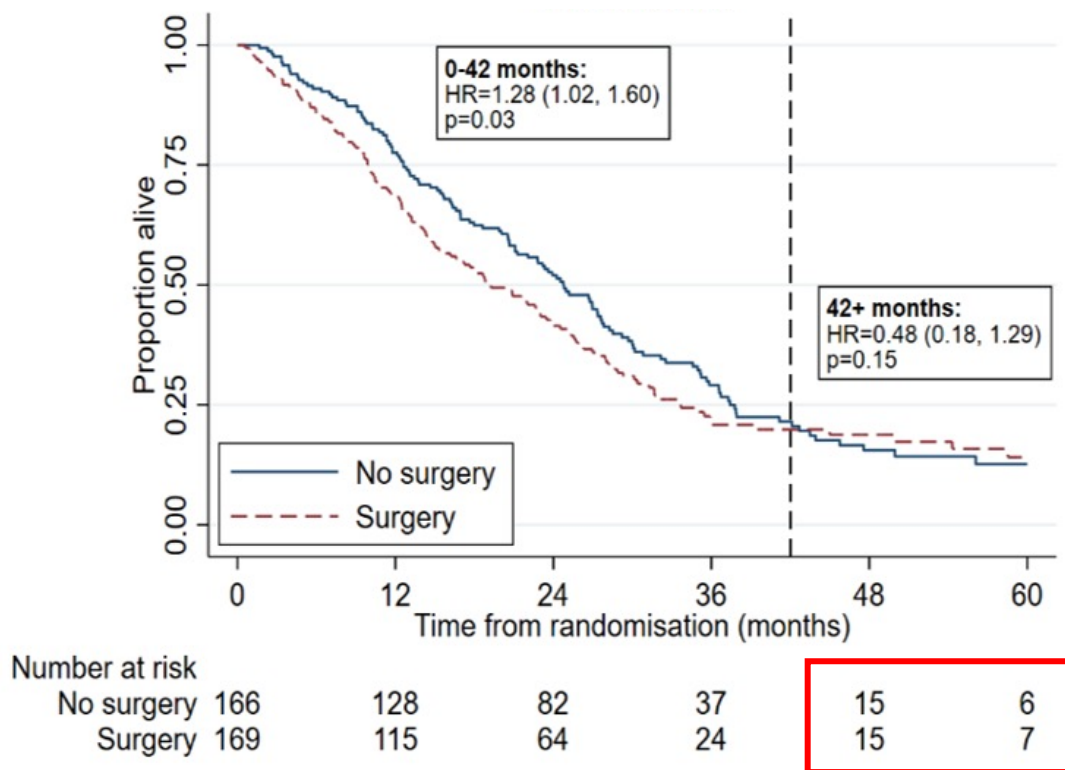


<u>P-VALUE</u>	<u>INTERPRETATION</u>
0.001	HIGHLY SIGNIFICANT
0.01	
0.02	
0.03	
0.04	SIGNIFICANT
0.049	
0.050	OH CRAP. REDO CALCULATIONS.
0.051	ON THE EDGE OF SIGNIFICANCE
0.06	
0.07	HIGHLY SUGGESTIVE, SIGNIFICANT AT THE P<0.10 LEVEL
0.08	
0.09	
0.099	HEY, LOOK AT THIS INTERESTING SUBGROUP ANALYSIS
≥ 0.1	



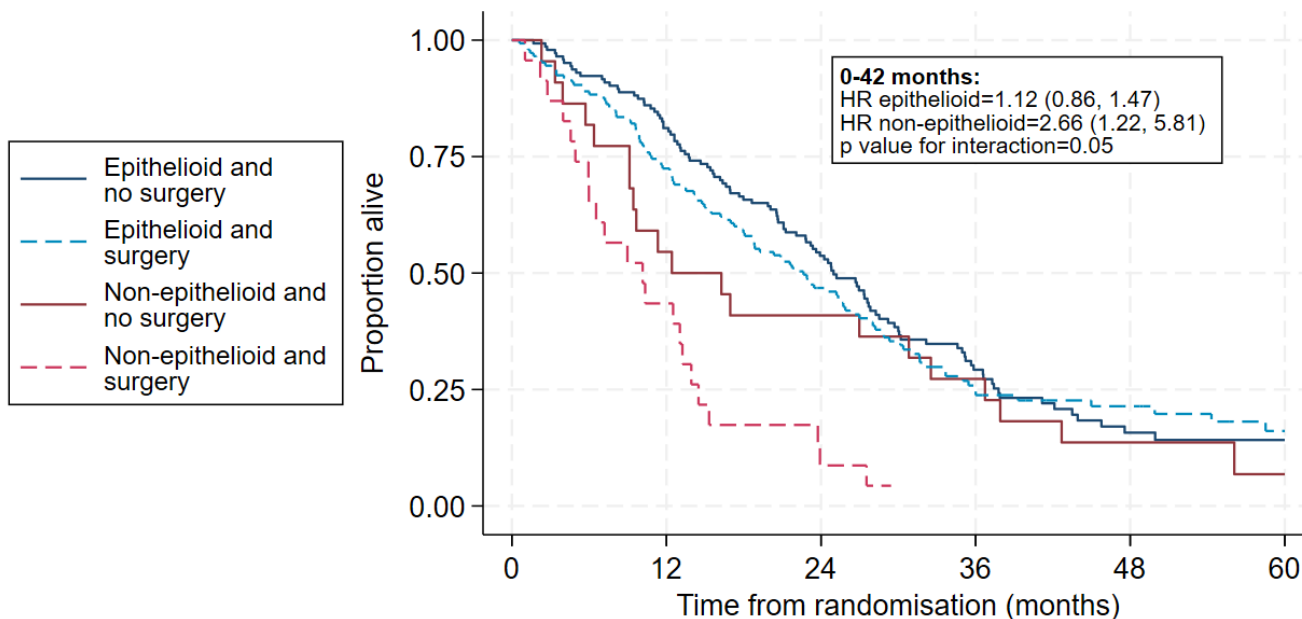


Primary outcome - overall survival





Survival by histology

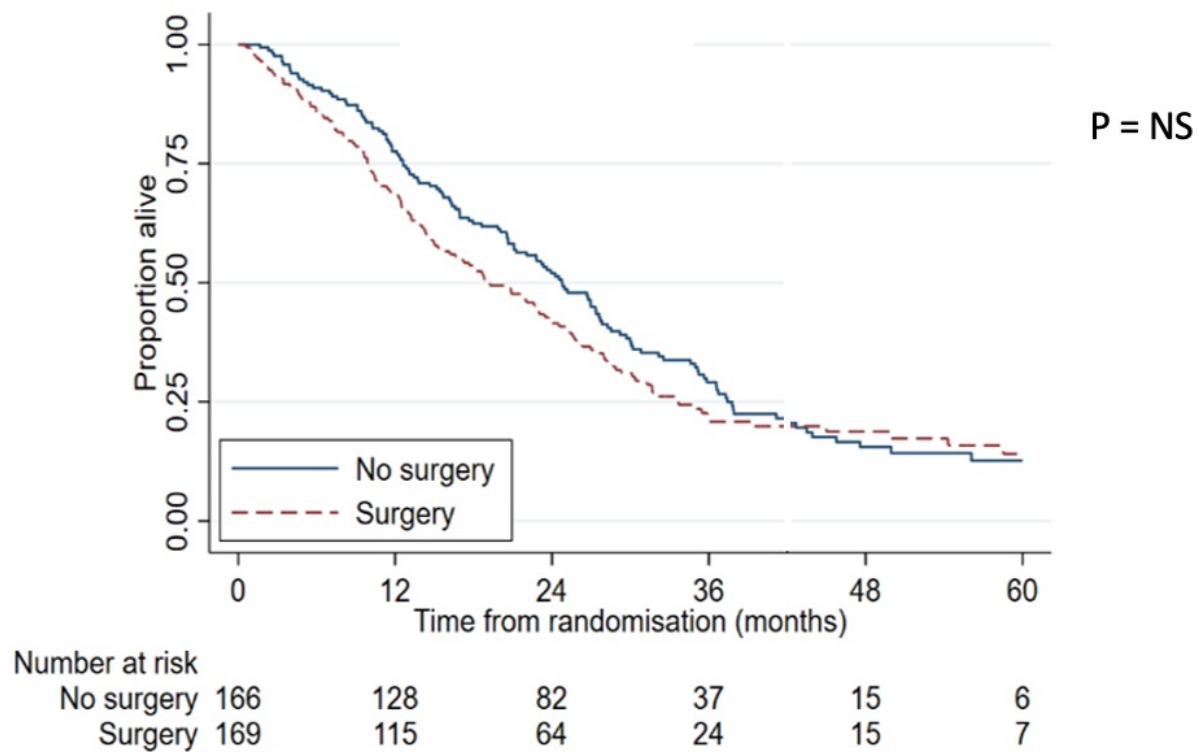


	0	12	24	36	48	60
Number at risk						
Epithelioid and no surgery	144	116	73	31	12	5
Epithelioid and surgery	146	105	62	24	15	7
Non-epithelioid and no surgery	22	12	9	6	3	1
Non-epithelioid and surgery	23	10	2	0	0	0





Primary outcome - overall survival





Weaknesses of MARS 2

- **Preoperative effusion mgmt ???**
- **Induction is not standard**
- **No PET scan – PET IS STANDARD**
- **Surgery for M1 dz included- 4%**
- **Sarcomatoid and biphasic included**
- **Surgical Mortality 9% despite no difference in overall survival**



Malignant Pleural Mesothelioma

Conclusions

- **Surgical mortality for EPP acceptable**
- **EPP and P/D similar survival – type of surgery dictated by intra-operative findings**
- **P/D is preferred**
- **Decision about procedure type should consider multimodality therapy options**
- **MARS 2 results has not changed management at this time**