Crossroads Congress in Cardiothoracic Surgery Athens 2018
Malignant Pleural Mesothelioma in the UK: Current Research and Experience

Mr Apostolos Nakas

Consultant Thoracic Surgeon

Head of Department of Thoracic Surgery Glenfield Hospital

University Hospitals of Leicester NHS Trust

United Kingdom

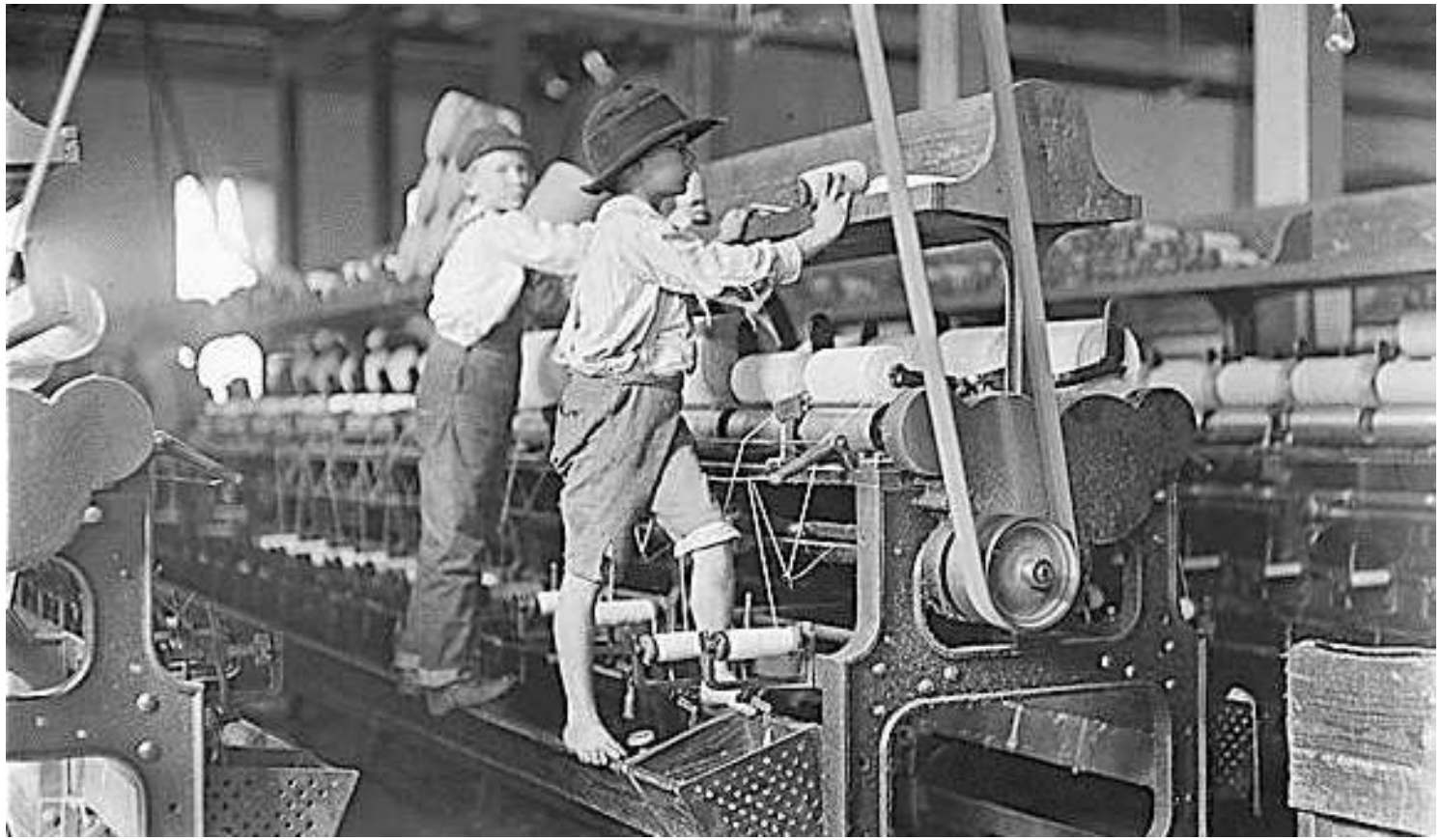
Declarations of Interest

- Investigator in MARS 2, MesoTRAP, MiST, MEDUSA studies
- Member of BTS Mesothelioma Guidelines Development Group
- Lead Clinician for East Midlands Cancer Network Mesothelioma Expert Clinical Advisory Group and Regional Mesothelioma MDT
- Received training related sponsorship from Medtronics, Ethicon, Synthes
- Received Honoraria related to educational and proctorship activities from Johnson and Johnson, KLS Martin Gmbh and Lynton Lasers Ltd
- I am a Surgeon and openly support Surgery for MPM

Sir William Osler, 1849-1919

- Medicine is a science of uncertainty and an art of probability
- The greater the ignorance, the greater the dogmatism

Epidemiology and pathogenesis



Epidemiology and Incidence

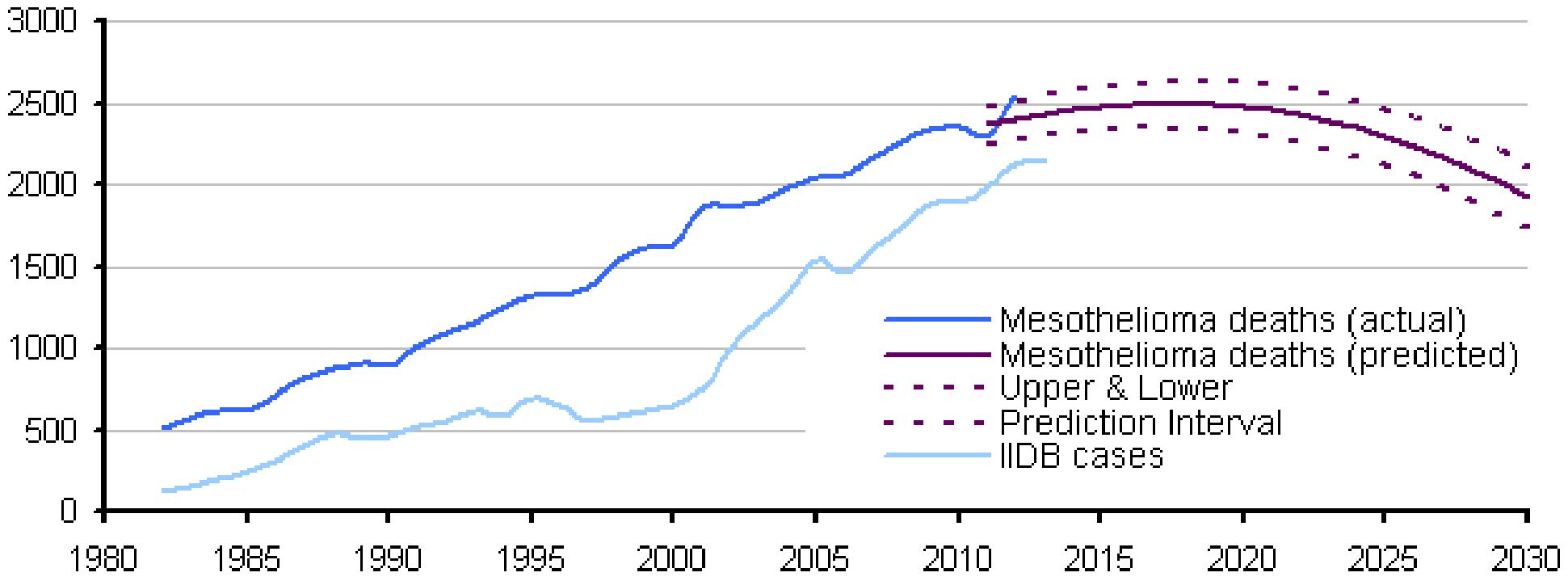
- Relationship of pleural malignancy with **Asbestos Exposure** was first recognized in 1906 (textile workers)
- **1920: DuBray**, first use of term “Mesothelioma” to describe pleural malignancy
- In **1986 Wagner** et al demonstrated the **epidemiologic relationship** between exposure and MPM
- **Klerk and Armstrong in 1992** reported the significance of the **type of asbestos fibre** in the development of the disease.

Shipyard workers pause for the camera in 1948

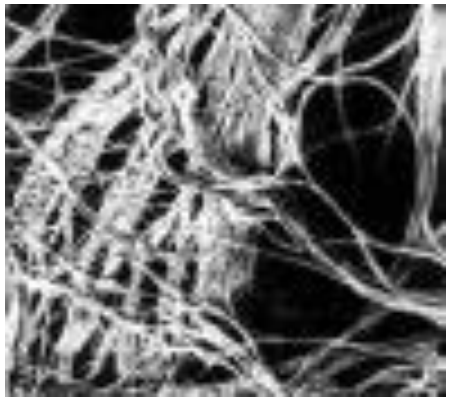
Epidemiology and Incidence

- 563 new cases in the UK in 2002
- The annual number of mesothelioma deaths has increased from 153 in 1968 to 1874 in 2003 and to 2,500 in 2014
- The latest projections suggest that the annual total number of mesothelioma deaths in Great Britain is estimated to peak at around 2,500 deaths some time after 2020
- 2500 new cases per year in US
- Estimated 250.000 DEATHS in Western Europe over the next 30 years

MPM IN GB 2014: HSE



Epidemiology and Incidence



- Amphibole Fibres:
- Small Fibres→MPM
  - Crocidolite (Blue Asbestos)
  - Amosite
  - Tremolite
  - Anthophyllite
  - Actinolite

- Serpentine Fibres
- Large fibres→ Lung Cancer
  - Chrysotile

Epidemiology and Incidence

Less common causes of MPM

- Radiation exposure 10-31 years before MPM occurs
- Beryllium
- Liquid Paraffin
- TB Pleuritis
- Recurrent Lung Infections
- Shoe Industry, Petrochemical workers, Stone Cutters
- Genetic Predisposition

Epidemiology and Incidence

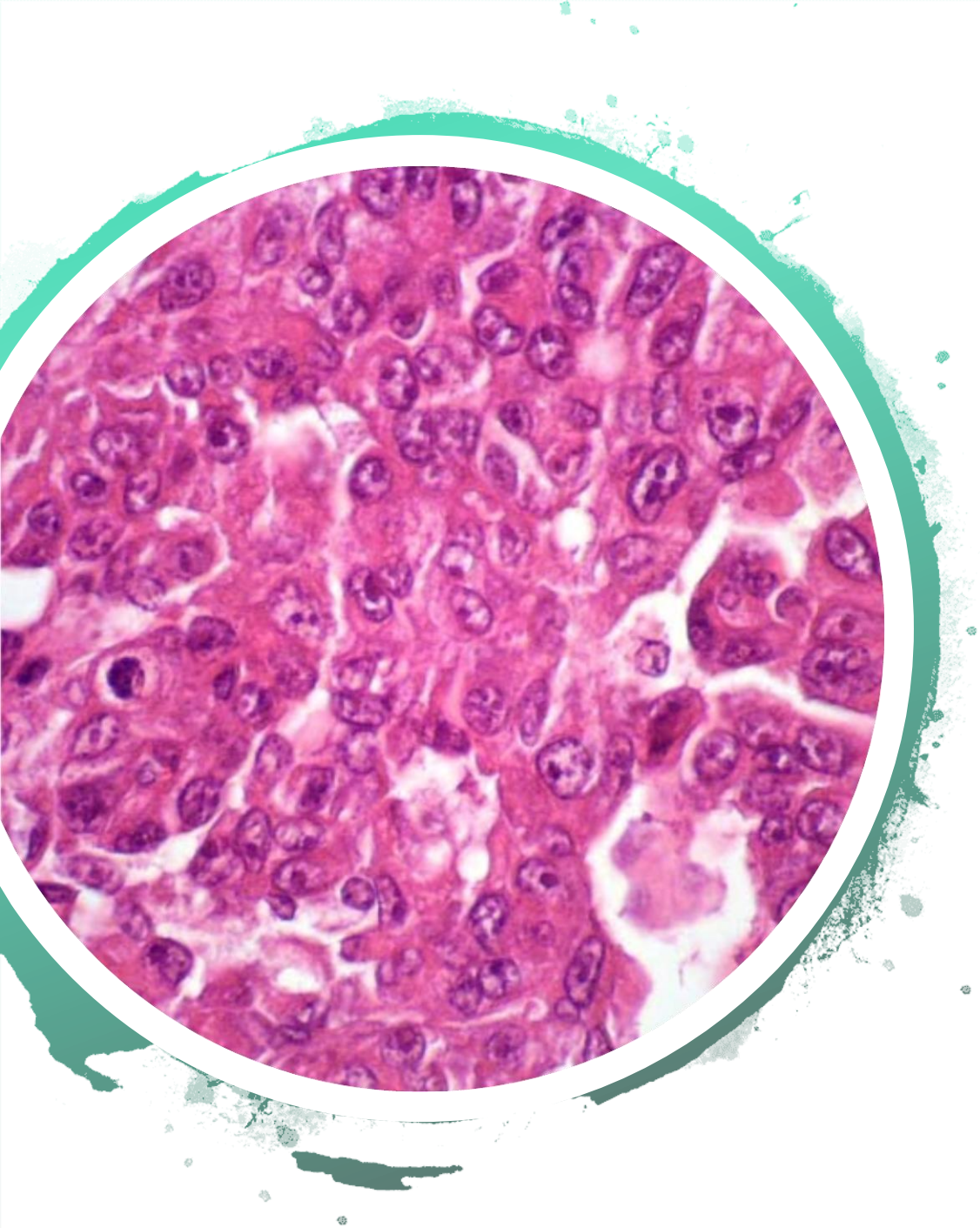
Peak Age 7th Decade of Life

Male:Female ratio 5:1

20-60 years latency period

It can occur in childhood

Histopathology



Pathology

- Epithelioid (50%)
- Sarcomatoid (16%)
- Biphasic (34%)

- The histologic appearance of MPM is easily confused with that of other neoplasms.
- Immunohistochemistry is very often essential for diagnosis.

Molecular Biology

Relatively little is understood

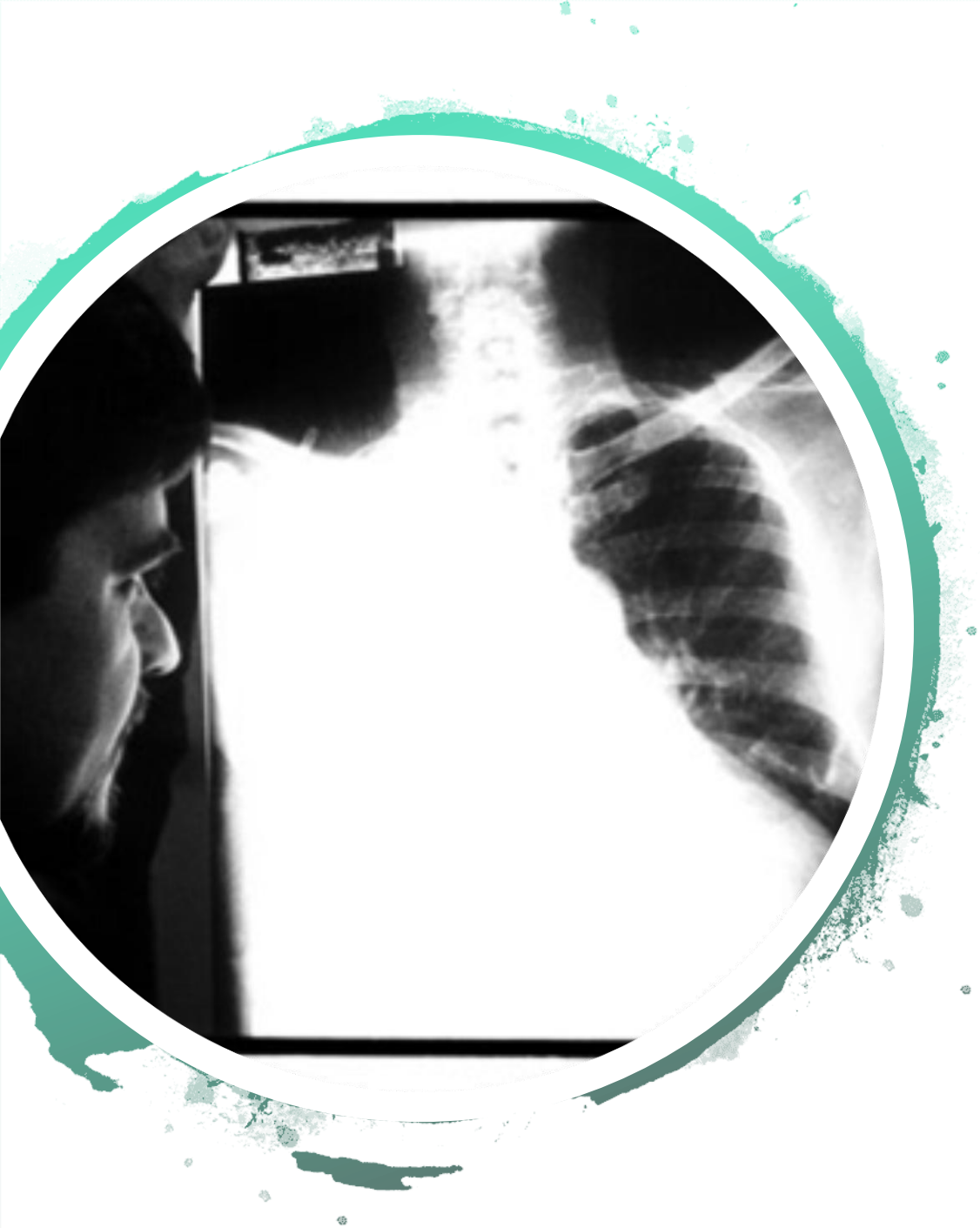
Asbestos is thought to cause DNA damage partly through the production of free radicals from the iron contained in asbestos fibres.

Multiple chromosomal changes can occur in combination suggesting a genetic cascade involvement

Overexpression of PDGF

? SV 40 virus synergistic role (contaminated polio vaccines 1950s)

Diagnosis and staging

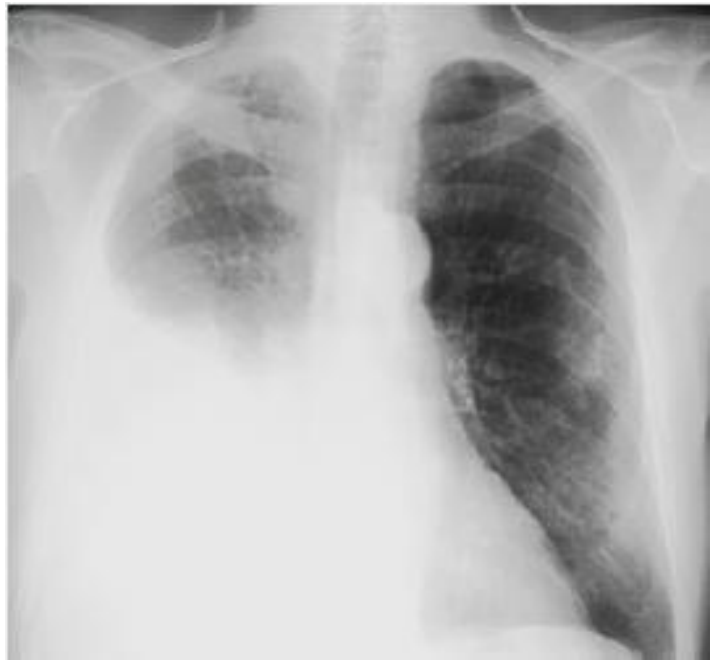


Clinical Presentation

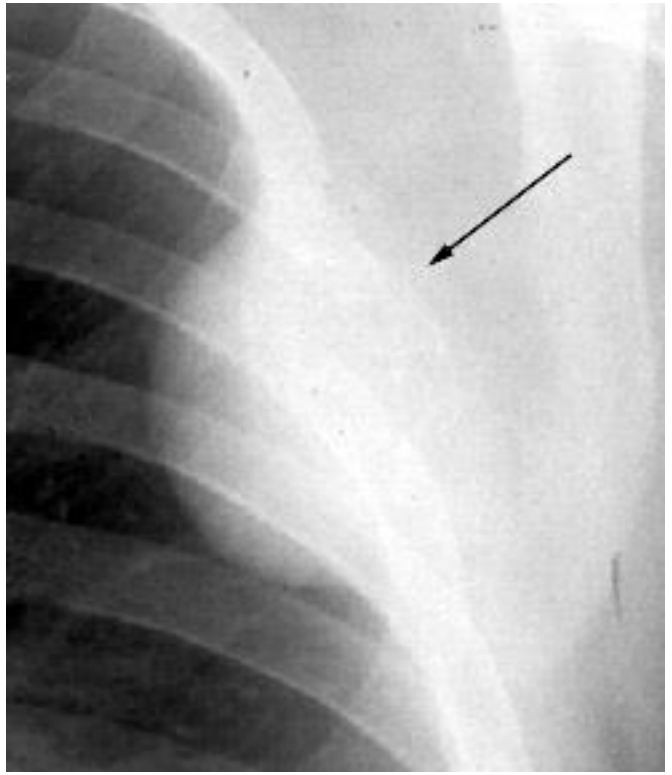
- Insidious Onset
- Pleural effusion and dyspnea
- Chest Discomfort
- Severe Chest Pain
- Mediastinal Shift and compression of contralateral lung
- Weight Loss
- Cough
- Weakness
- Dysphagia
- Haemoptysis
- Hoarseness

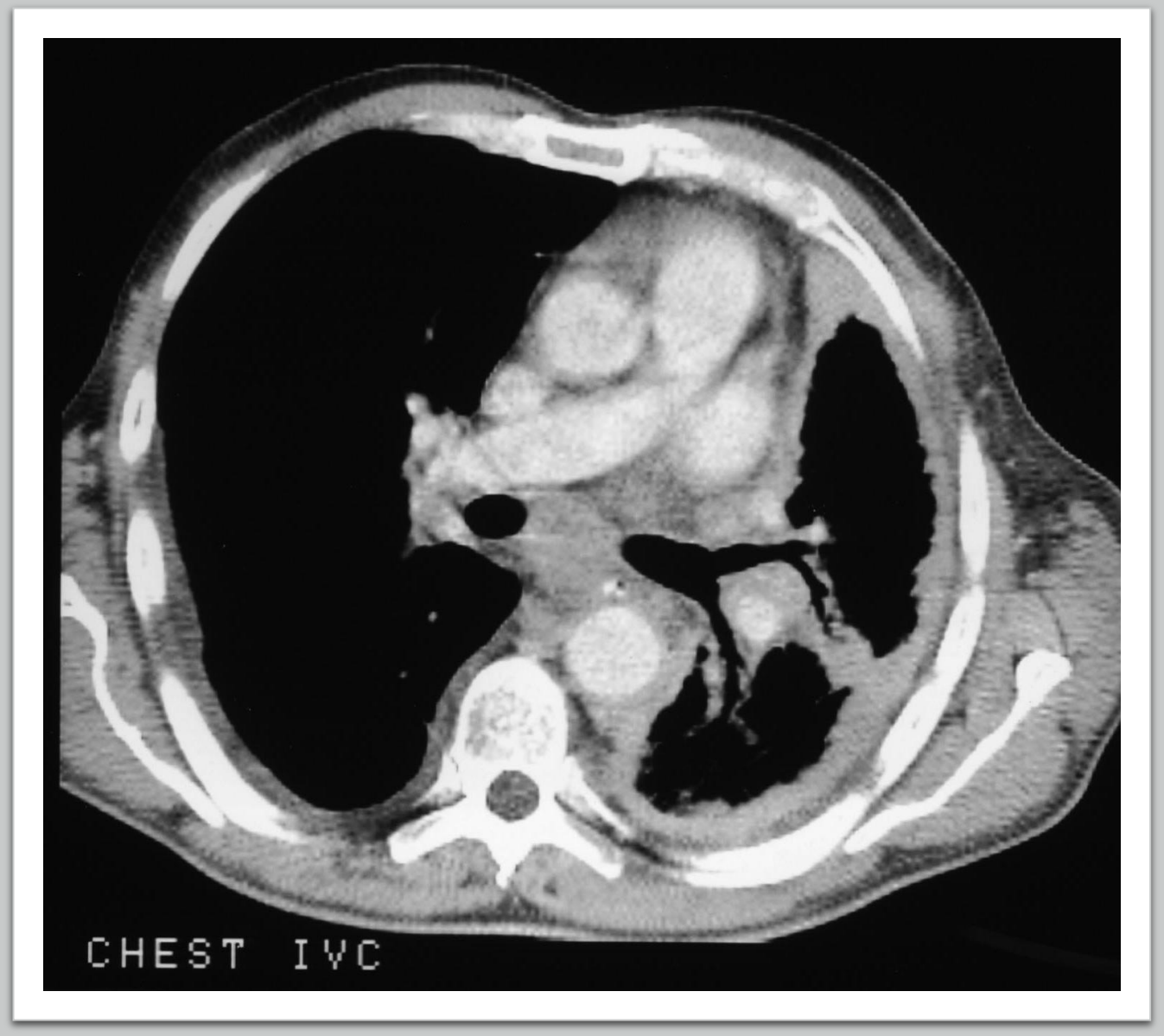
Radiological Features

Pleural Effusion



Localised Tumour



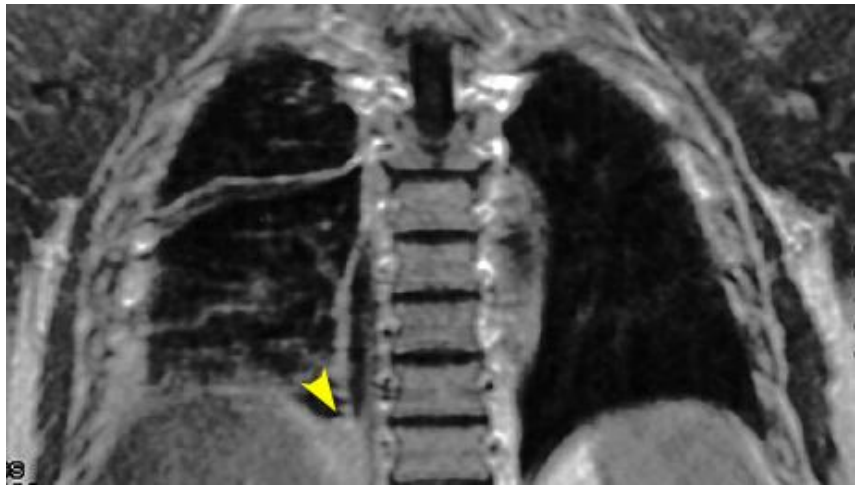


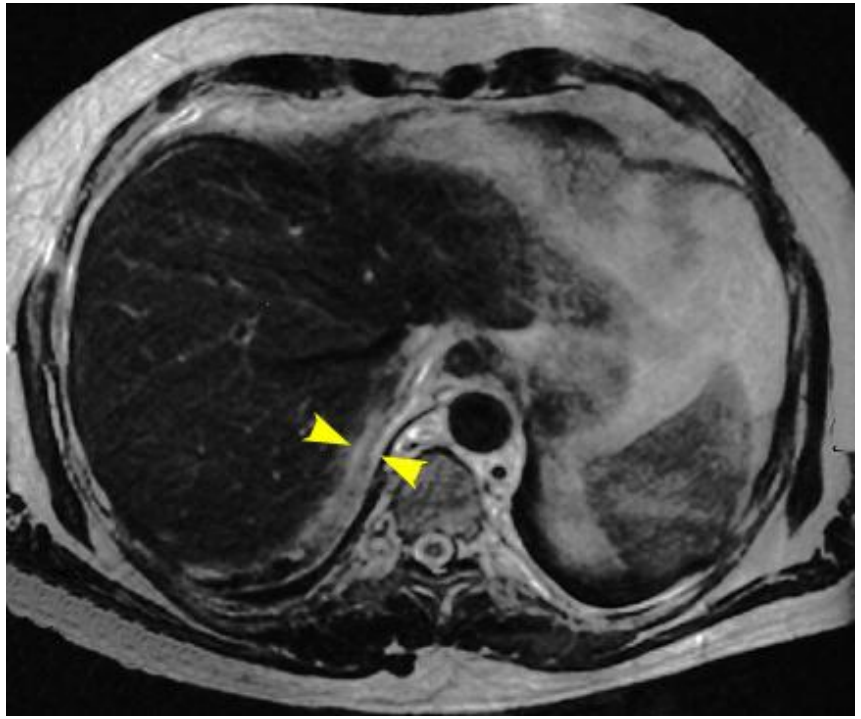
Radiological Features

Mediastinal Pleural Thickening

Radiological Features

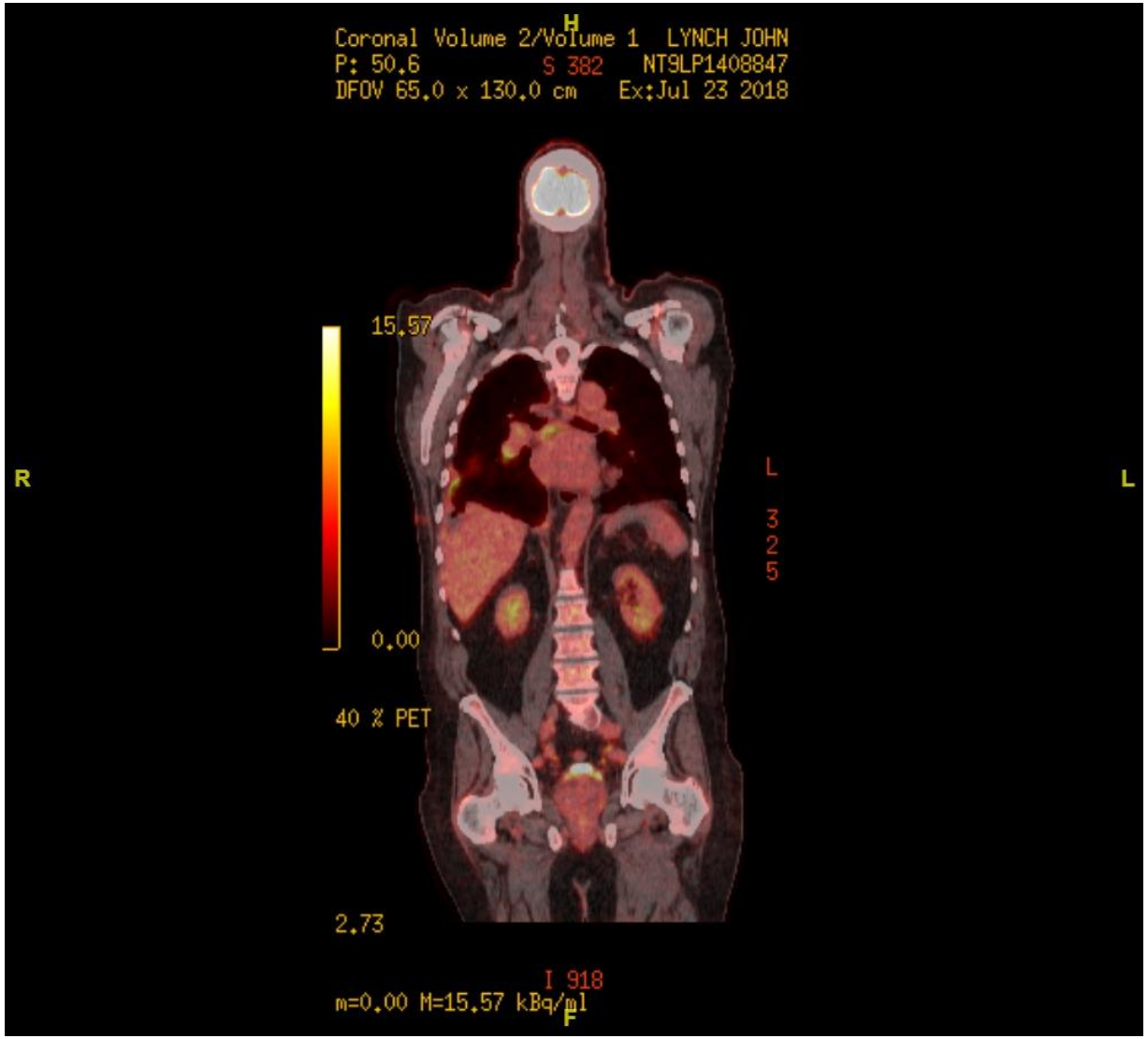
- Pleural Effusion
- Pleural Thickening
- Pleural based mass
- Mediastinal Thickening/ Infiltration
- Mediastinal Adenopathy
- Pericardial Effusion
- Diaphragmatic Infiltration



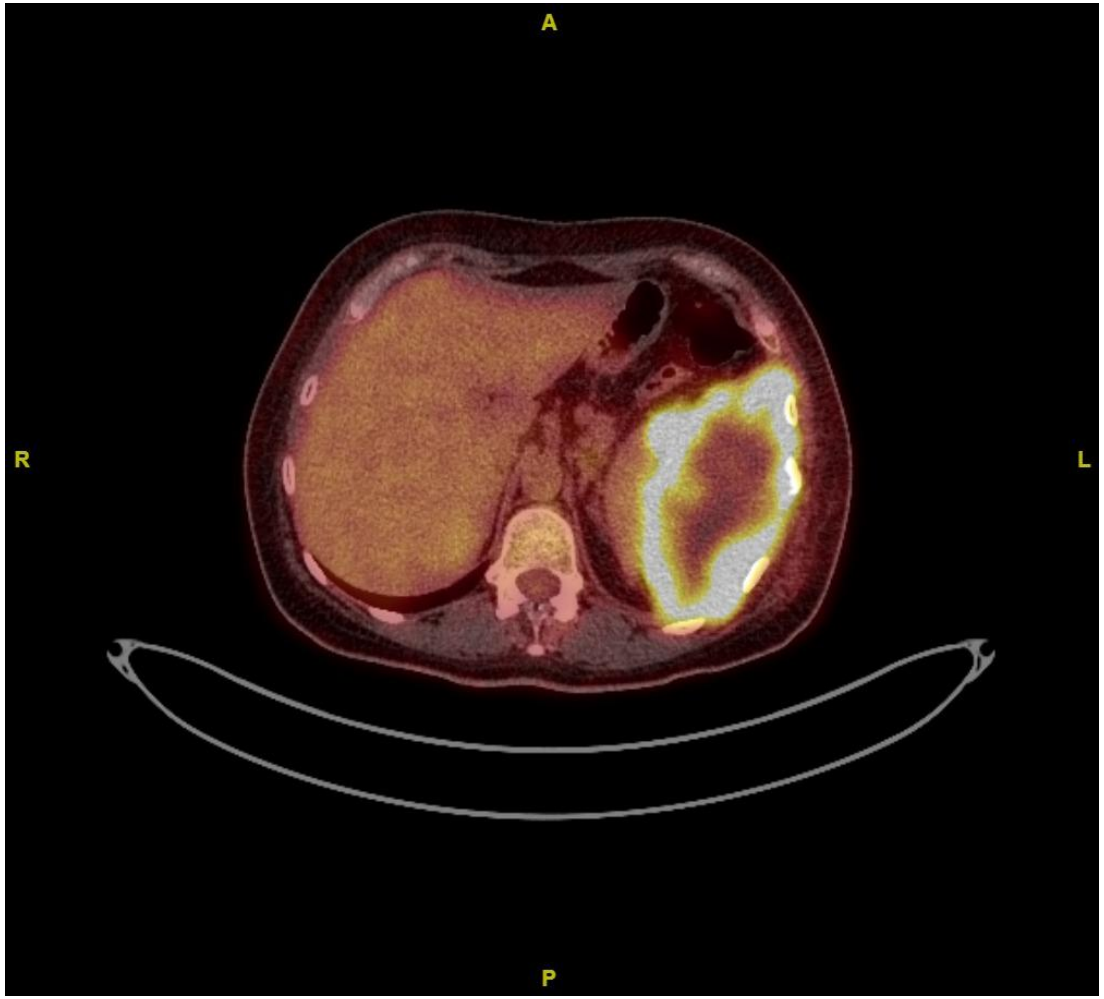


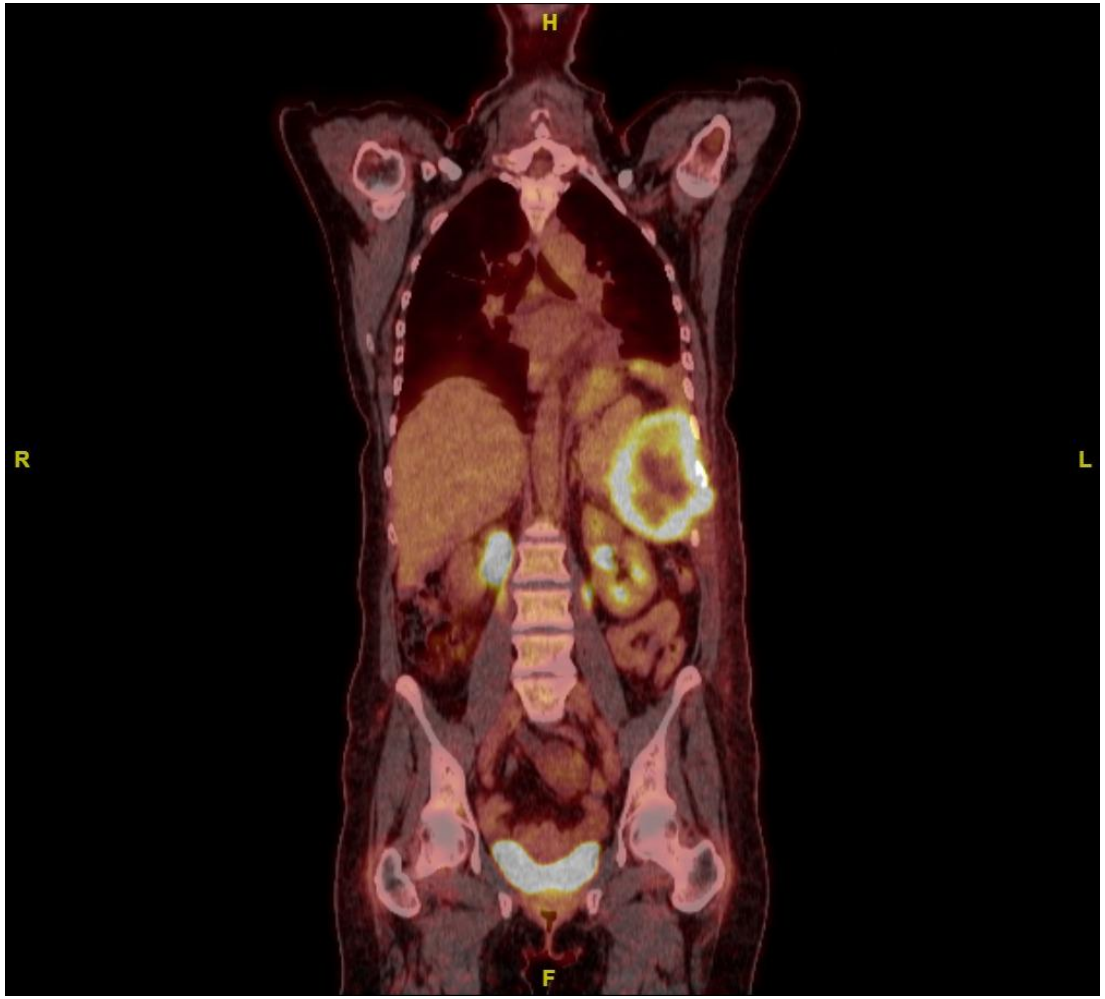
CT PET Scanning for MPM

- Useful in detecting distant disease (10% undetected on CT)
- Not useful in assessing locoregional disease (local tumor extension and mediastinal nodal involvement)
- Total Glycolytic Volume might be useful for prognosis

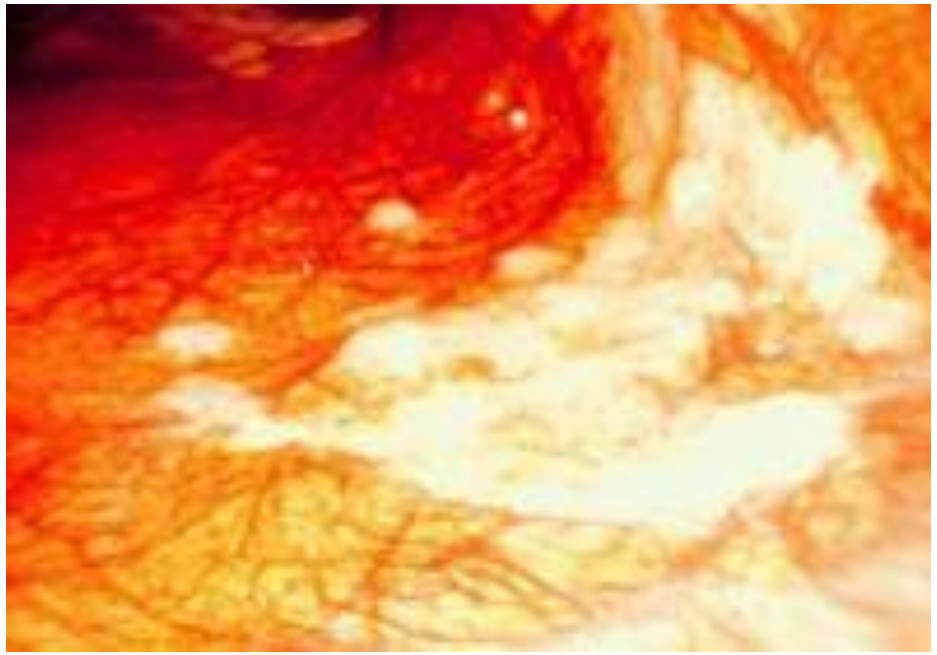


PET in Localized MPM

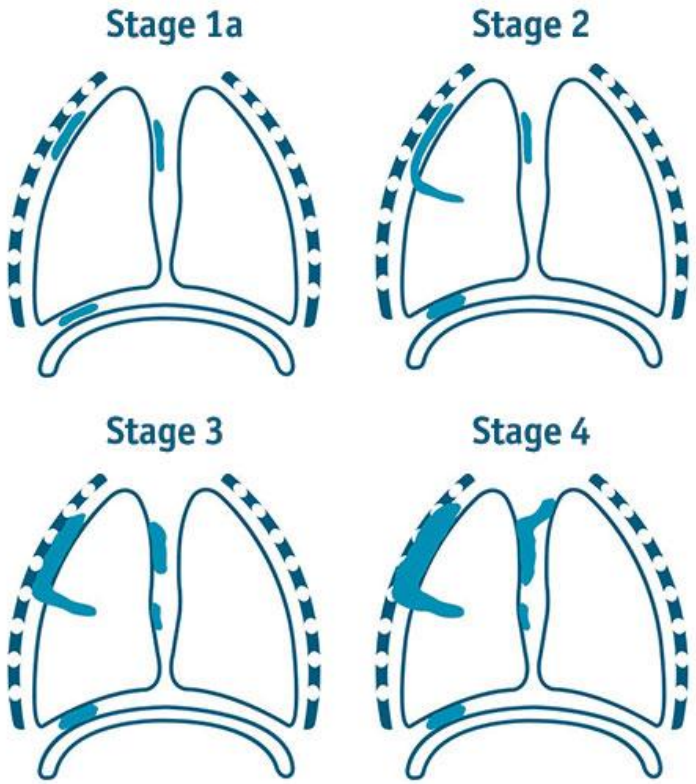




Diagnosis



- **Thoracentesis** is usually the first diagnostic attempt
- 30-50% **cytology** is positive for malignancy though rarely diagnostic for MPM and cannot diagnose subtype
- **Thoracoscopy** is diagnostic in 80% of cases
- **Open biopsy** when pleural space is obliterated
- **Tissue subtyping** (Epithelioid/ Biphasic/ Sarcomatoid) essential for:
  - Treatment
  - Prognosis
  - Survival



- **T: Tx**
  - **T0**
  - **T1** ipsilateral parietal pleura +/- visceral (a,b)
  - **T2** T1 + at least 1 of: fissure, diaphragm, lung parenchyma
  - **T3** T1 + at least 1 of: endothoracic fascia, mediastinal fat, chest wall, non trans pericardium
  - **T4** chest wall, rib, peritoneum, mediastinum, contralateral pleura, positive pericardial effusion, brachial plexus
- **N:Nx**
  - **N1** Ipsilateral bronchopulmonary and/ or hilar
  - **N2** Subcarinal and or IMA LN
  - **N3** contralateralmediastinal, ipsilateral SC
- **M:Mx**
  - **M0**
  - **M1**

Staging AJCC / UICC/ IMIG (1995)

AJCC-UICC MPM Staging System 8th Revision

Primary tumor	
T0	No evidence of primary tumor
T1	Tumor involves ipsilateral parietal pleura
T1a	Tumor involves ipsilateral parietal (mediastinal, diaphragmatic) pleura with no involvement of the visceral pleura
T1b	Tumor involves ipsilateral parietal (mediastinal, diaphragmatic) pleura with focal involvement of visceral pleura
T2	Tumor involves any of the ipsilateral pleural surfaces with at least one of the following: •invasion of diaphragmatic muscle •extension into the lung parenchyma
T3	Describes locally advanced but potentially resectable tumor (i.e., it might be possible to remove it) Tumor involves any of the ipsilateral pleural surfaces with at least one of the following: •invasion of the endothoracic fascia •invasion into mediastinal fat •solitary, completely resectable focus of tumor invading the soft tissues of the chest wall •non-transmural involvement of the pericardium
T4	Describes locally advanced technically unresectable tumor (i.e., it cannot be removed) Tumor involves any of the ipsilateral pleural surfaces with at least one of the following: •diffuse or multifocal masses in the chest wall (with or without rib destruction) •invasion through the diaphragm to the peritoneum •direct extension to the contralateral pleura •extension to mediastinal organs •invasion into the spine •extension through the internal surface of the pericardium (with or without a pericardial effusion or involvement of the myocardium)

Regional lymph nodes (N)	
N0	No regional lymph node metastasis
N1	Metastasis in the ipsilateral bronchopulmonary and/or hilar lymph nodes
N1	Metastasis in the subcarinal lymph nodes, ipsilateral internal mammary, mediastinal lymph nodes, or the peridiaphragmatic lymph nodes
N2	Metastases in the contralateral mediastinal, contralateral internal mammary, or hilar lymph nodes and/or the ipsilateral supraclavicular or scalene lymph nodes

AJCC-UICC MPM Staging System 8th Revision

AJCC-UICC MPM Staging System 8th Revision

Distant metastases (M)	
M0	No distant metastases
M1	Distant metastases present

AJCC-UICC MPM Staging System 8th Revision

Group Stage	
IA	T1, N0
IB	T2,T3, N0
II	T1, T2, N1
IIIA IIIB	T3, N1 T1, T2, T3, N2
IV	Any T, Any N, M1

National Lung Cancer audit Mesothelioma Report 2018

2018 NLCA Mesothelioma Audit (01.01.14-31.12.16 data)

No of UK cases:7,192 (3 years)

- Pleural: 6,932 (96%)
- Peritoneal: 260 (4%)
- 84% male
- 46 % Disease Stage not recorded
- 31% PS not recorded
- 51% PS 0-1
- 14% PS2
- 11% PS3-4
- 46% of cases NOT subtyped

MDT :81%

LCNS input: 28-93% (Avg for England 54%)

Chemo: 40%

Anticancer Treatment:51%

Radical Surgery: 4%

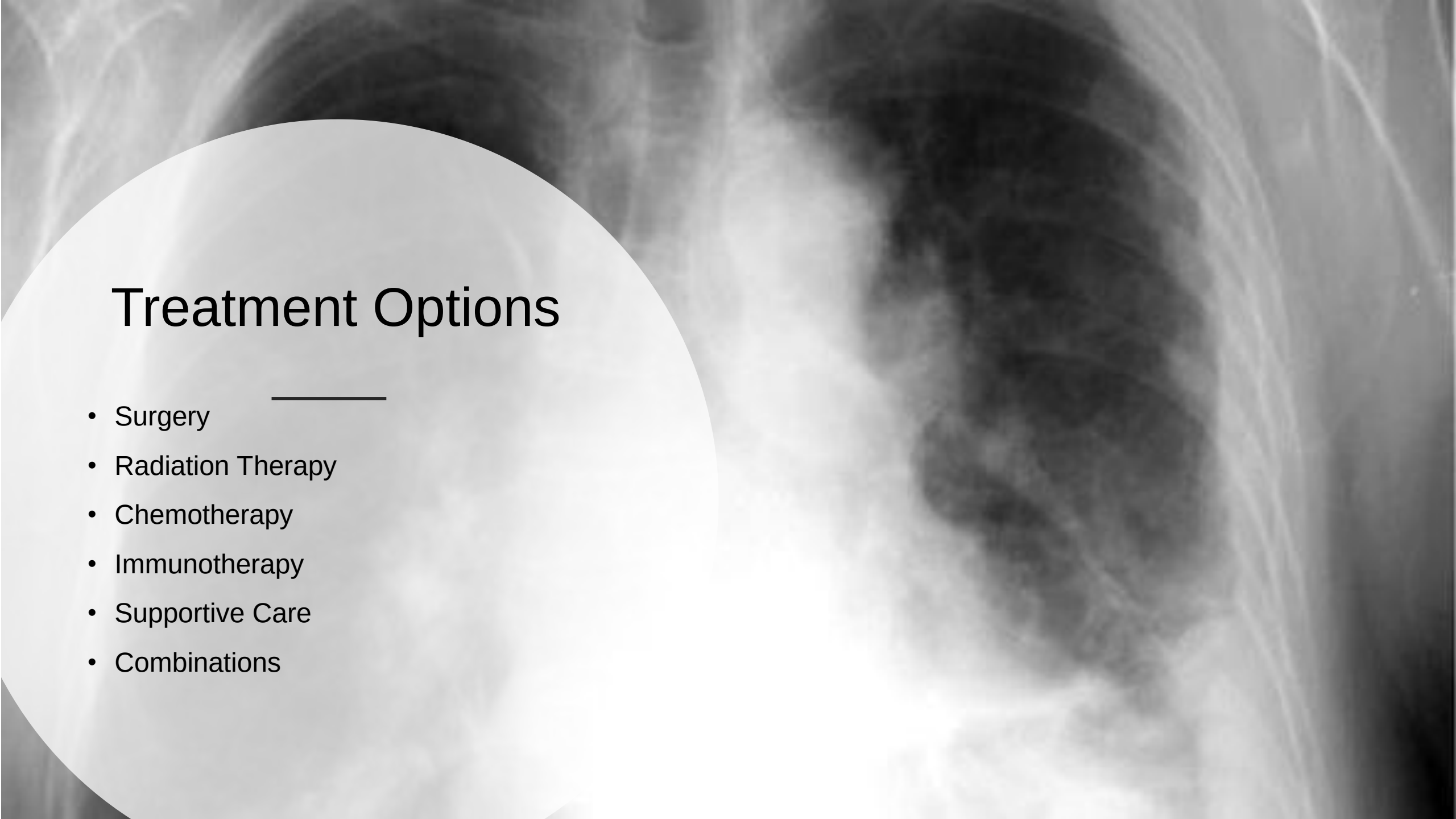
1 year Survival: 38%

3 year Survival: 7%

2018 NLCA Mesothelioma Audit (01.01.14 - 31.12.16 data)

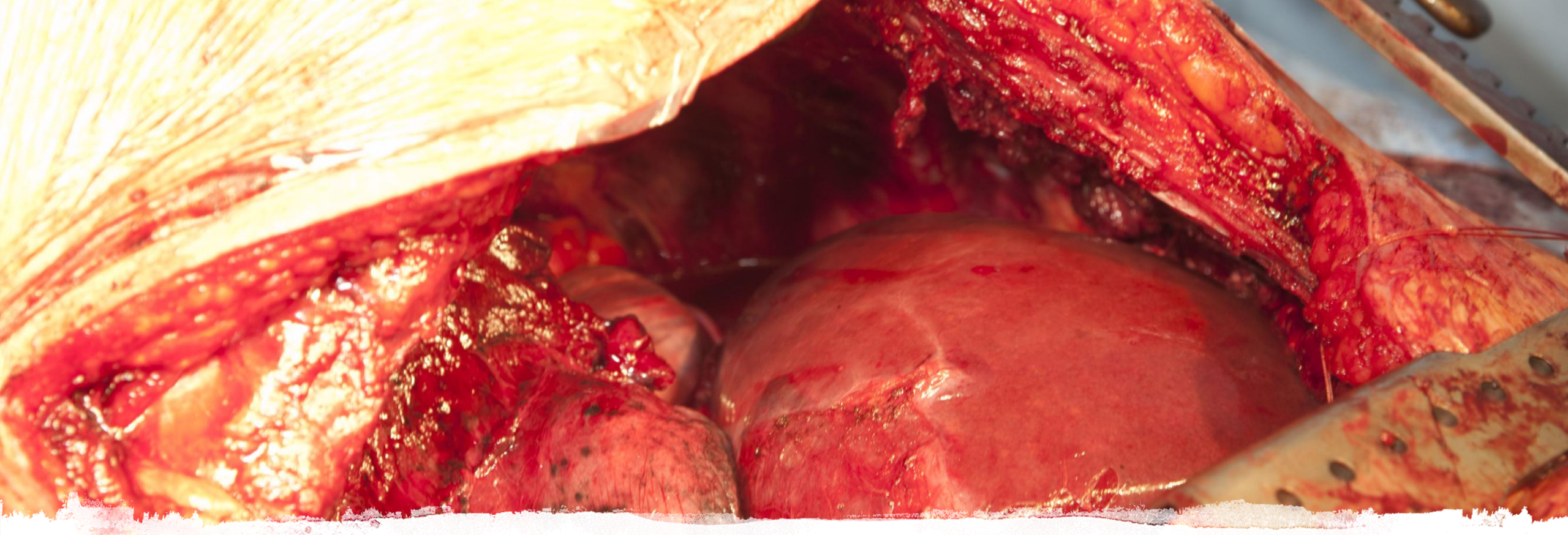
Pathology	1 year survival	3 year survival	Median survival (days)
Epithelioid	51%	3%	400(198-710)
Biphasic	28%	1%	243(122-420)
Sarcomatoid	14%	1%	133(69-249)
Unspecified	29%	2%	195(69-447)

Treatment options



Treatment Options

- Surgery
- Radiation Therapy
- Chemotherapy
- Immunotherapy
- Supportive Care
- Combinations



Surgery Part 1: Radical

- Aims to extend survival
- Aims to remove all disease achieving Macroscopic Complete Resection (R1)

Surgery Part 2: Non Radical

Diagnosis

Staging

Effusion control

Dyspnoea Control

Pain Control

Procedures on offer

- VATS Biopsy and Pleurodesis
- VATS Decortication
- Open Decortication
- Extended Pleurectomy Decortication
- Extrapleural Pneumonectomy

  +

  - Cervical Mediastinoscopy
  - Staging Thoracoscopy
  - Staging Laparoscopy
  - Airway Stenting
  - Oesophageal Stenting
  - IC Chemotherapy
  - PDT

1. Vats Biopsy and talc

1. VATS Pleural Biopsy +/- Talc Pleurodesis

- Single 2 cm port access (in line of thoracotomy)
- Drainage of Effusion
- Targeted Biopsies (4-5, deep layer)
- <5 grs talc

1. VATS Bx + Talc

Advantages

1. Minimal Surgical Insult, Can be tolerated by most of the patients
2. Targeted biopsies, high diagnostic yield
3. Biopsy and effusion control achieved in one procedure
4. Radical surgery can still be performed at a latter stage

Disadvantages

1. Palliative procedure, median survival similar to natural progress of disease
2. General Anaesthetic
3. If lung is trapped pleurodesis will fail:
    1. IPC
    2. VATS PD

1. VATS Bx + Talc

Evidence

1. **Phase III intergroup study of talc poudrage vs talc slurry sclerosis for malignant pleural effusion. Dresler et al, Chest 2005**
    1. RCT, Insufflation vs slurry, 480 pts
    2. Similar efficacy, insufflation might be better in lung cancer or breast

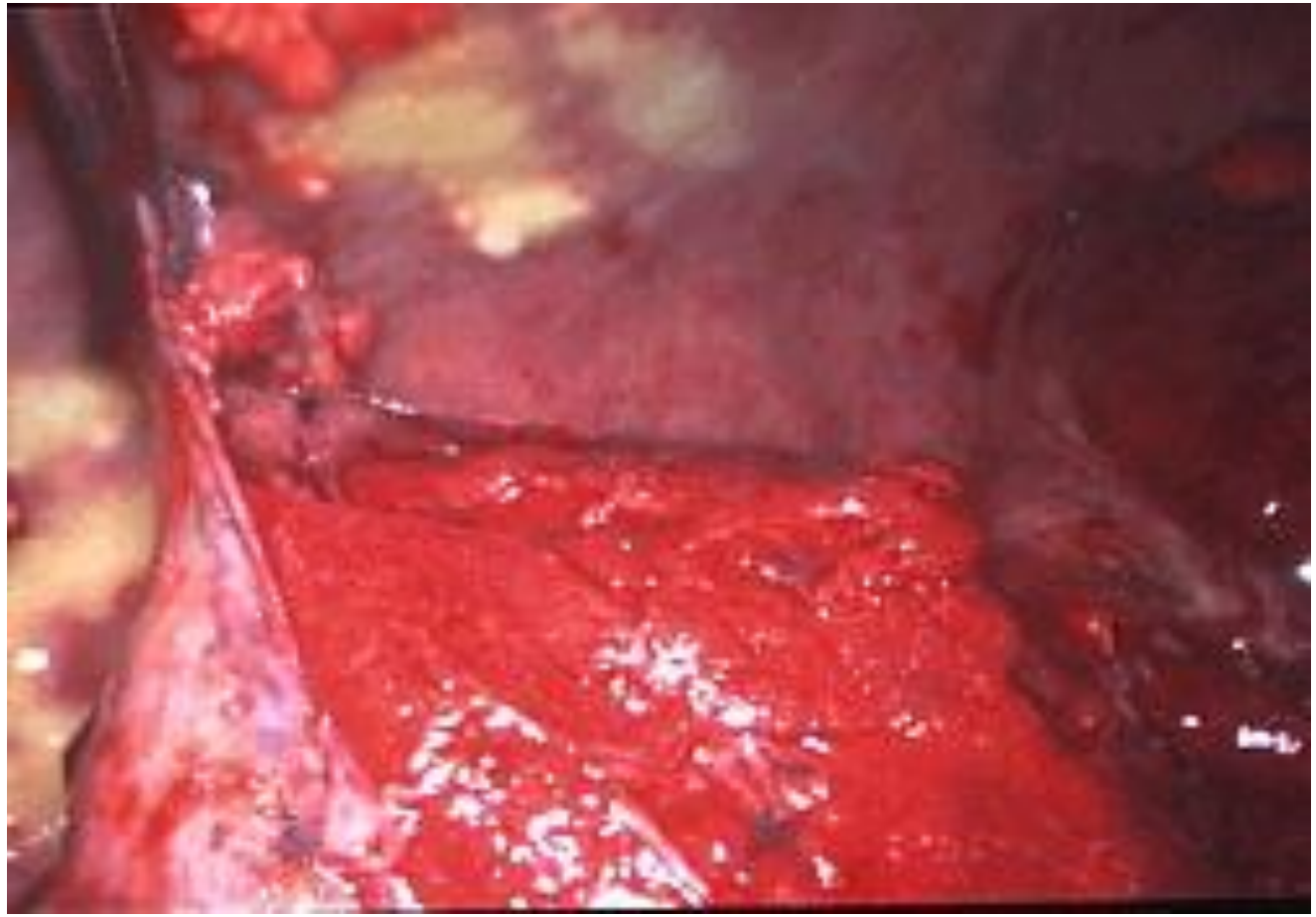
Not much Evidence

1. We need the biopsies
    1. Guide Treatment
    2. Inform prognosis
2. We might need to have a look (+/- feel)
3. Collapsed Lung makes assessment easier
4. We choose where to do the incision

2. Vats Pleurectomy Decortication

2. VATS Pleurectomy Decortication

- Three 2 cm ports
- Parietal Pleurectomy
- Visceral Decortication
- Debulking
- Lung re expansion



2. VATS P/D

Advantages

1. Elderly patients
2. Lung re expansion might (?) achieve better effusion control
3. Could (?) be superior to VATS talc pleurodesis in effusion/ pain/ dyspnoea control

Disadvantages

1. Significant mortality
2. Prolonged Air Leak
3. Difficulty in debulking mediastinum/ diaphragm
4. Not suitable for bulky disease
5. Unlikely to prolong survival

If lung does not expand conversion to **Open P/D** might be necessary

2. VATS P/D

Evidence

1. **Efficacy and cost of video-assisted thoracoscopic partial pleurectomy versus talc pleurodesis in patients with malignant pleural mesothelioma (MesoVATS): an open-label, randomised, controlled trial, RC Rintoul et al, Lancet 2014:** RCT, 175 pts, no benefit in survival and worse complications and LOS in VATS PD group

Not much Evidence

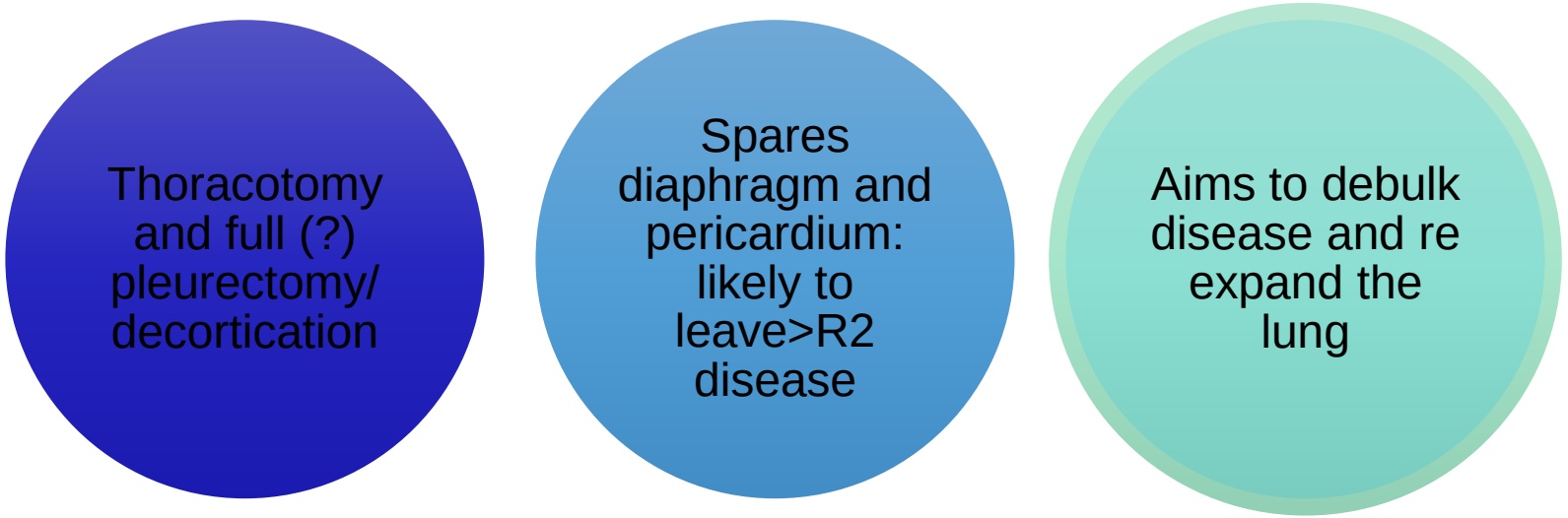
1. Operation Relevant in the EPP era, not relevant now
2. ? Group of patients? Radical Surgery offered to octogenarians

MesoVATS: Results

- 196 patients recruited as planned, 98 each arm, 9 years
- 11% in VATS PP and 10% in Pleurodesis arm did not have MPM leaving 87 and 88 pts respectively.
- 12/12/ deaths: 48% VATS PP, 43% Talc,
- 12/12 survival: 52% vs 57%, median 13.1 vs 13.5, HR 1.04, 95% CI 0.76-1.42, p=0.81.
- 16% and 17% respectively withdrew from study or did not attend final appointment
- Secondary outcomes at 12 months were available for 34 (39%) of patients in VATS PP and 37 (42%) in Talc group.
  - VAT PP group had better effusion control at 1 and 6 months but not at 3 and 12!
  - QoL similar
  - Higher FEV1 and greater distance on SWT but only 36 patients had SWT.
  - Longer Hospital stay (7 vs 3 days) and more complications on VAT PP
  - Mean cost of VAT PP was £3,800 higher per case on average.
  - VAT PP offered the equivalent of 12.5 days of full health (0.035 QALYs)

3. Simple Pleurectomy Decortication

3. Simple Pleurectomy Decortication



3. Simple P/D

Advantages

1. Easier to achieve lung expansion than VATS P/D
2. Avoids complications associated with diaphragmatic/ pericardial resection
3. Spares the lung compared to EPP
4. Might (?) achieve macroscopic clearance in very few early cases

Disadvantages

1. Adds thoracotomy to surgical insult
2. Pericardium and diaphragm are usually heavily involved in MPM
3. If we accept that macroscopic clearance is important we need to consider **Extended Pleurectomy Decortication**

3. Simple P/D

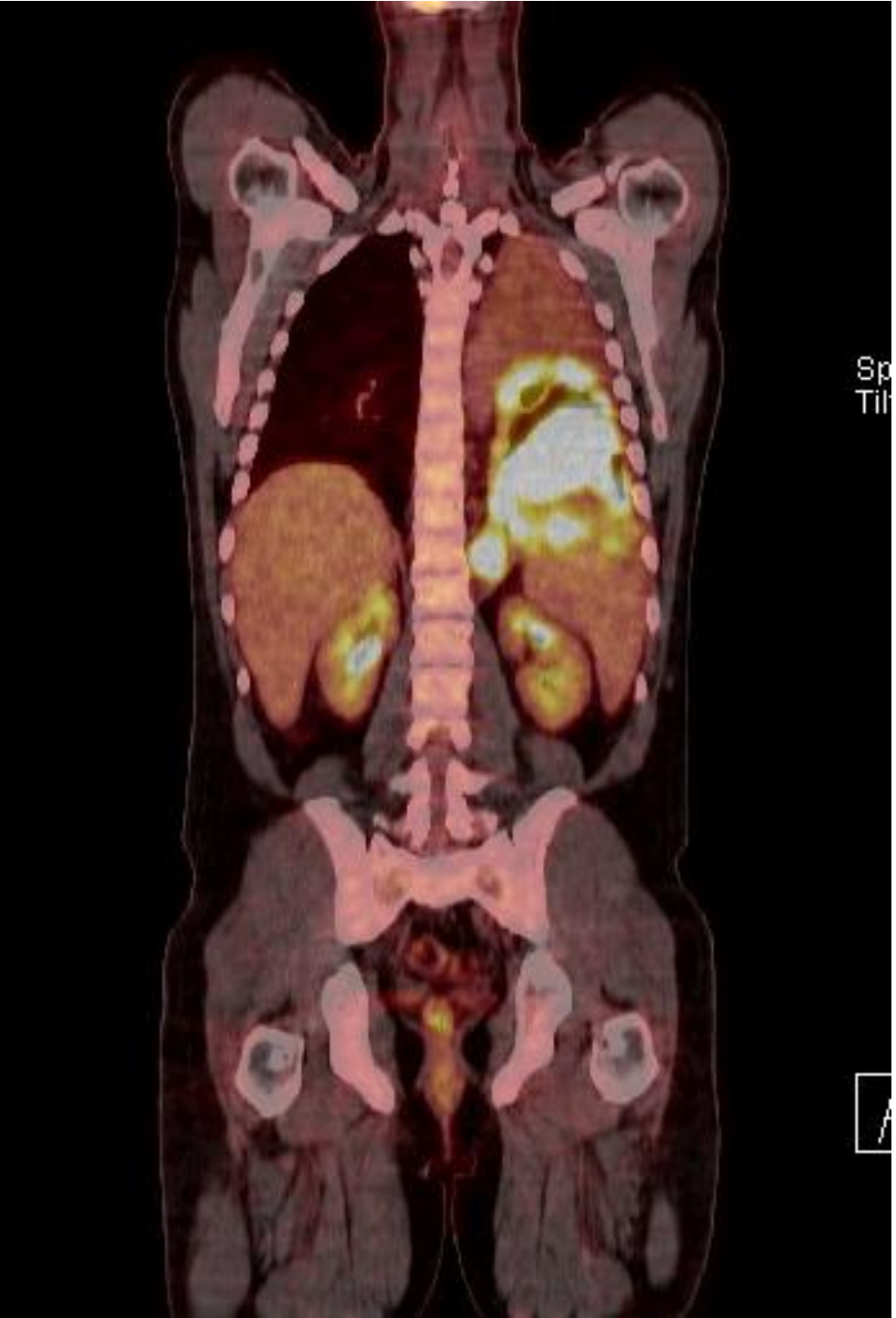
Evidence

1. **Systematic review of pleurectomy in the treatment of malignant pleural mesothelioma, Cao et al, Lung Cancer 2013: “**Evidence from the existing literature suggests that selected patients who undergo extended P/D may achieve a longer overall and disease-free survival compared to patients who undergo less aggressive procedures such as P/D or partial pleurectomy. However, this may be associated with higher morbidity and longer hospitalization.”

Not much Evidence

1. Acceptable (?) Compromise if EPD not feasible intraoperatively
2. Patients suitable for Simple PD will be suitable for EPD
3. Macroscopic Complete Resection makes more sense than leaving disease behind

4. Extended Pleurectomy Decortication



4. Extended PD (EPD)

- P/D that removes ALL macroscopic disease
- Full parietal pleurectomy
- Visceral decortication extending into fissures
- Removal of pericardium and diaphragm and reconstruction with synthetic/ biological patches

4. EPD

Advantages

1. Spares the lung
2. Achieves macroscopic clearance
3. Suitable for patients who would not tolerate pneumonectomy
4. Probably more suitable for elderly patients
5. Significantly less morbidity, complications and impact on QoL than EPP

Disadvantages

1. Prolonged air leak and pleural sepsis secondary to prolonged drainage
2. Significant blood loss and perioperative mortality (2-7%)
3. Patients need to be fit for surgery
4. Technically demanding, better results in high volume centres
5. Presence of lung does not allow hemithorax radiotherapy
6. If disease involves the lung parenchyma extensively **EPP** might be necessary (?).

4. EPD

Evidence

1. **A systematic review and meta-analysis of surgical treatments for malignant pleural mesothelioma, Cao et al, Lung Cancer 2014: "…**results of the present meta-analysis suggested that extended P/D can be performed with lower morbidity and mortality outcomes, as well as comparable long-term survival outcomes to EPP. However, it is important to emphasize that EPP and extended P/D are not interchangeable procedures for all patients, and that individualized treatment plans should be based on the extent of disease, patient comorbidities and surgeon's experience."

Not much Evidence

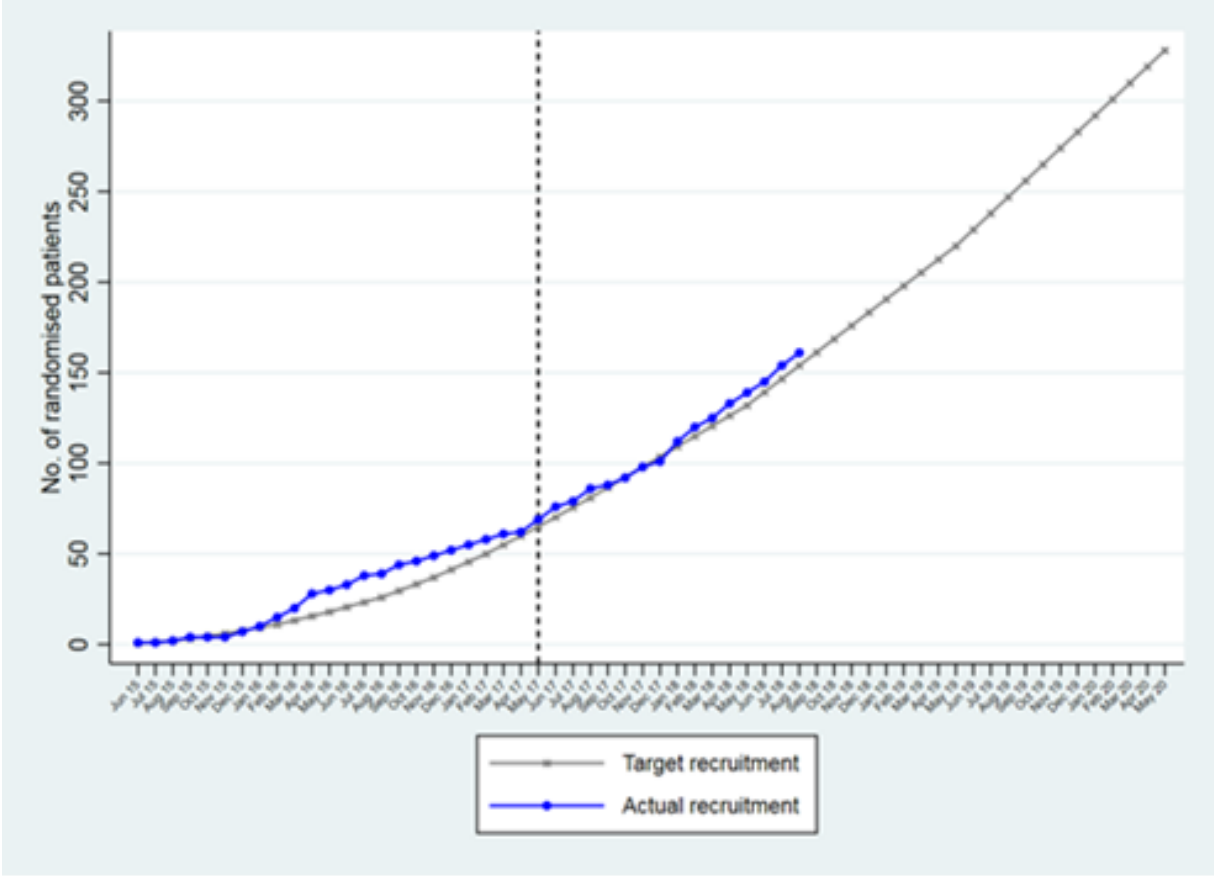
1. MPM is not Lung Cancer: the lung can be spared
2. Pneumonectomy is (?) a disease in itself
3. If volume of disease is associated with outcome (TGV, response to chemo, RECIST criteria), surely removing all disease makes sense(?)
4. Cytoreduction works in other diffuse malignancies (ovarian, pseudomyxoma)

MARS 2 Trial

- 2 stage (registration followed by randomization) unblinded two-arm parallel design randomized trial
- EPD+ Chemotherapy versus Chemotherapy (2+4 Cisplatin Pemetrexed)
- Feasibility: 50 patients in 2 years or recruit 25 patients in any 6 month period: Completed
- Full Study 285 within 5 years (Total 335 including the 50 from pilot study)
- 4 Surgical Centres:
  - Leicester
  - Sheffield
  - London
  - Glasgow
- Methodology:
  - Assessment, consent,
  - Chemotherapy 2 cycles
  - CT week 5, MDT week 6,if patient randomized to non surgical arm 4 more cycles of chemo starting week7-8

MARS2 Recruitment Aug 2018

Centre	Jun 18	Jul 18	Aug 18	Number randomised
Clatterbridge	0	2	0	22
Leicester	0	1	0	18
Derby	2	1	1	16
Barts	1	0	0	13
Wythenshawe	0	0	1	13
Papworth	0	0	1	11
Royal Marsden	0	2	0	11
Colchester	0	0	0	9
Sheffield	0	0	1	9
Glasgow Beatson	0	0	0	7
South Tees	2	2	0	7
South Tyneside	0	0	1	5
Wolverhampton	0	0	0	5
Royal Gwent	1	0	0	4
Leeds	0	0	1	4
Peterborough	0	0	0	4
Bristol	0	1	1	3
Cardiff	0	0	0	0
Norwich	0	0	0	0
Barking	-	0	0	0
Plymouth	-	0	0	0
Overall	**6**	**9**	**7**	**161**



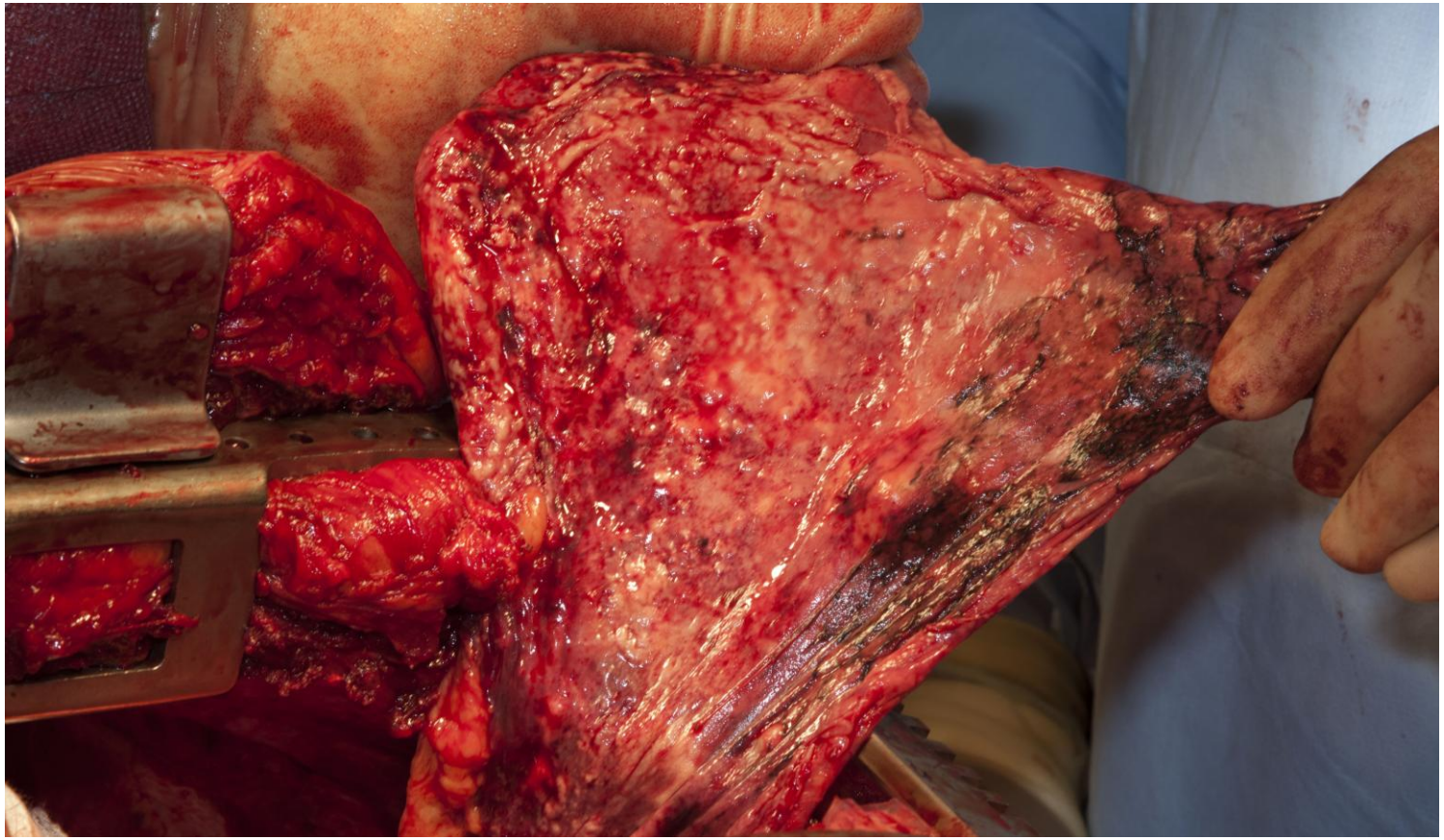
MARS 2 Inclusion / Exclusion Criteria

Inclusion

1. Histological confirmation of Mesothelioma
2. Disease confined to one hemithorax

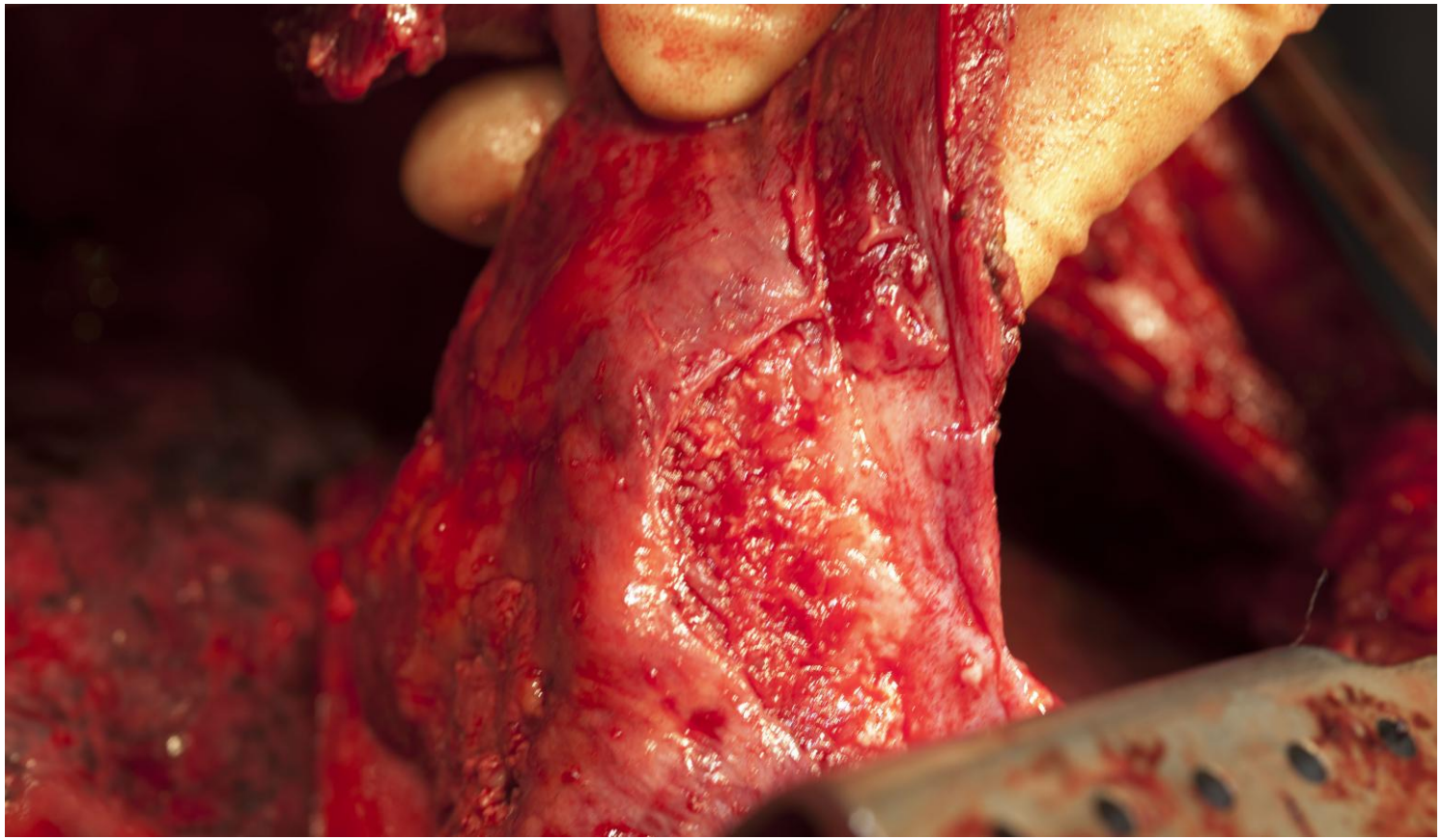
Exclusion

1. Unable to give informed consent
2. Unwillingness to randomization
3. Unresectable disease
4. ECOG>=2
5. ppoFEV1/ TLCO<20%
6. Severe Heart Failure (EF<30%)
7. End Stage CKD requiring dialysis
8. Liver Failure
9. Participants in other interventional clinical trial



EPD Selection Criteria

- T3N2M0
- T3/4 not clearly defined
- PS<=1
- Normal Cardiac Function
- Sterile Pleural Space
- Relative Contraindications:
  - Sarcomatoid (include in MARS 2)
  - Progression on chemotherapy
  - Age>80
- Absolute Contraindications:
  - True T4/ N3/ M1
  - Infected Space

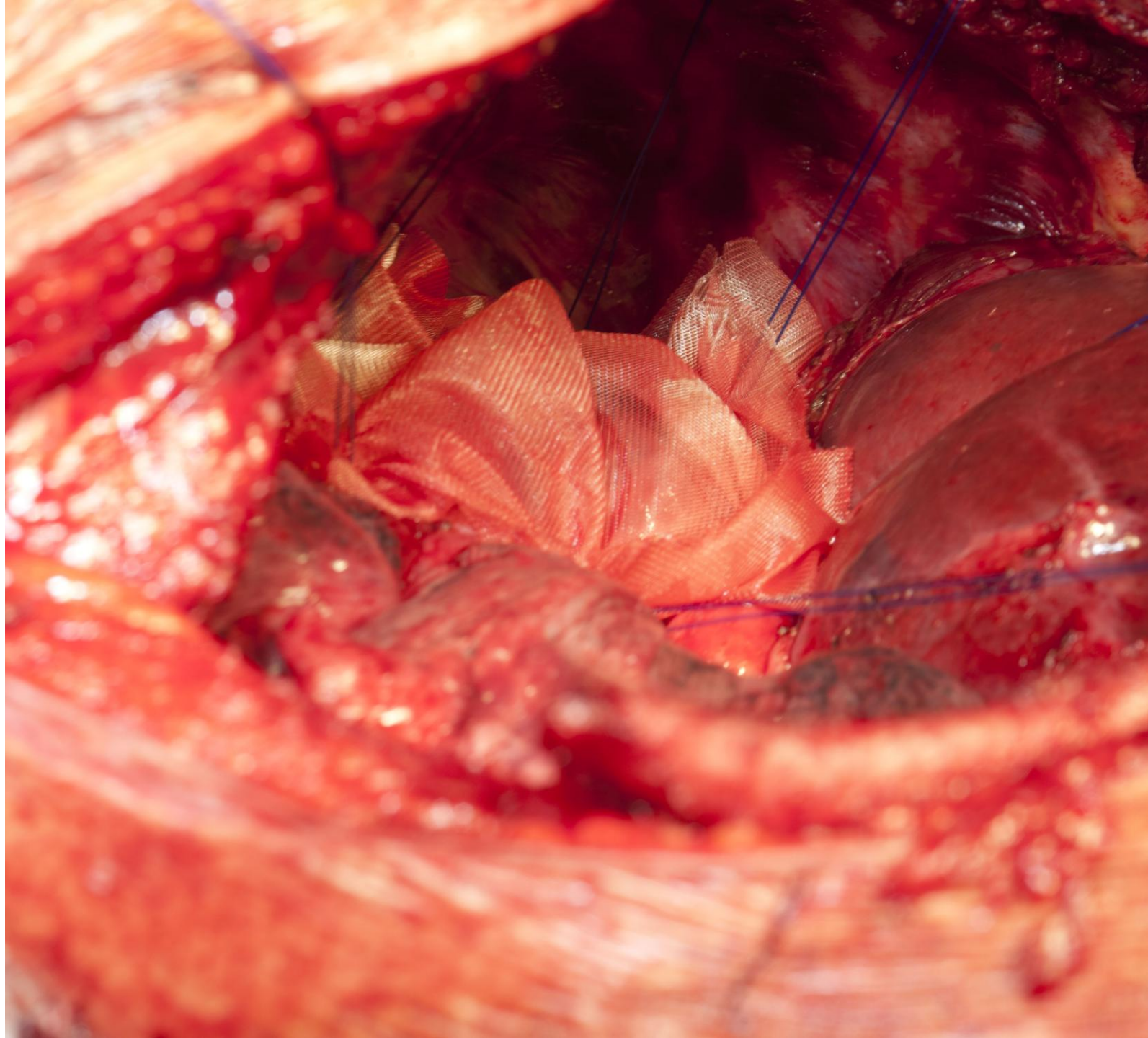


Resectability: Factors

- Thickness
- Hardness
- Subclavian Vessels
- SVC
- IVC
- Chest Wall
- Lung
- Pericardium
- Heart
- Spine

Operability: Factors

- PFTs
- Cardiac Reserve
- Previous Thoracic Operations
    - CABG
    - Pulmonary Procedures
- Presence of Infection
- Cell Type
- Time from Pleurodesis/ chemotherapy
- Progression on chemotherapy
- Age



	Median Survival months	SE	95% CI	1 year % (pts at risk)	2 years % (pts at risk)	3 years % (pts at risk)	4 years % (pts at risk)	5 years % (pts at risk)
EPP n=112	19.2	1.6	16.3-22.5	73% (82)	40% (45)	20% (23)	15% (15)	11% (10)
EPD n=140	16.2	1.7	12.8-19.5	60% (73)	31% (33)	21% (19)	12% (10)	5% (3)
Overall n=252	18.2	1.3	15.8-20.7					

- **Predictors of long-term survival following radical surgery for malignant pleural mesothelioma.**
- Nakas A. et al, Eur J Cardiothorac Surg. 2014 Sep;46(3):380-5

Survival following Radical Surgery: EPP no different to EPD, p=0.92

- **Predictors of long-term survival following radical surgery for malignant pleural mesothelioma.**
- Nakas A. et al, Eur J Cardiothorac Surg. 2014 Sep;46(3):380-5

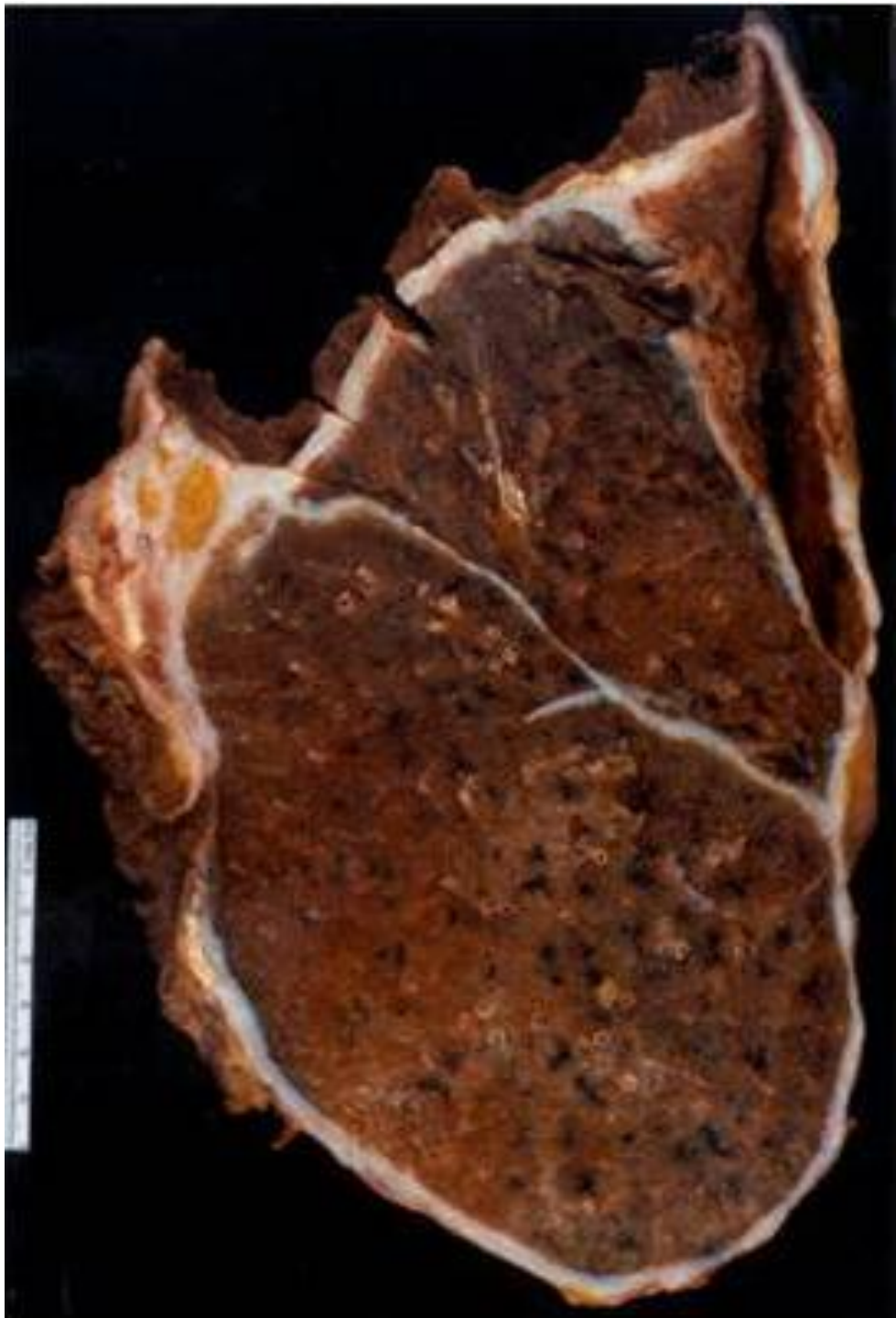
		Median survival	SE	95% CI	Significance, *P*	1 year survival (patients at risk)	2 years survival (patients at risk)	3 years survival (patients at risk)	4 years survival (patients at risk)	5 years survival (patients at risk)
Chemotherapy (n = 230)	**No chemo (n = 102)**	12.4	1.3	7.7–14.9		51% 47	26% 23	12% 10	7% 4	3% 2
	Chemo (n = 128)	22.1	1.5	19.1–25.1	0.000	81% 99	43% 47	28% 29	20% 19	12% 10
	Total	18.7	1.2	16.4–20.9						

Multimodality treatment?

5. Pleuropneumonectomy

5. Pleuropneumonectomy, *aka* Extra Pleural Pneumonectomy (EPP)

- En bloc removal of pleura, lung pericardium and diaphragm.
- Reconstruction of pericardium and diaphragm with synthetic patches



5. EPP

Advantages

1. Maximum cytoreduction (but not necessarily better than Extended P/D)
2. Empty Hemithorax can be treated with High Dose Radiotherapy (albeit with risk of complications)
3. Not complicated by air leak

Disadvantages

1. Not suitable for N2 disease (debatable)
2. Adds pneumonectomy to an already major operation
3. Space problems
4. High morbidity (40-60%) and mortality (6-7%) rates
5. Removal of lung compromises QoL
6. Patient should be able to tolerate pneumonectomy
7. High morbidity will result in less patients completing trimodality treatment.

5. EPP

Evidence

1. **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. T. Treasure et al, Lancet Oncol 2011:** "In view of the high morbidity associated with EPP in this trial and in other non-randomised studies a larger study is not feasible. These data, although limited, suggest that radical surgery in the form of EPP within trimodal therapy offers no benefit and possibly harms patients."

Not much Evidence

1. MPM is not Lung Cancer: the lung can be spared
2. Pneumonectomy is (?) a disease in itself
3. EPP is technically easier than EPD
4. EPP can be part of 3modality, EPD not.
5. EPP is dead?

MARS Feasibility Trial: Lancet Oncology 2011

Feasibility study: objective was to recruit 50 patients in one year to EPP or no EPP and to measure clinical outcomes

It was estimated that the power required for the main trial to show difference between EPP and no EPP would be 670 patients.

12 UK hospitals

3 cycles of platinum based chemotherapy after randomization followed by EPP and hemithorax irradiation or no EPP

MARS Trial: Results

- 112 patients registered Oct 2005-Nov 2008
- 50 randomized to EPP (n=24) or no EPP (n=26)
- 24 assigned to EPP:
  - 5 EPP not started
    - 3 patient refusal
    - 2 clinical decision
  - 3 EPP abandoned
    - 1 perioperative death
    - 2 unexpected disease progression
  - 16 had EPP
    - 11 postoperative complications
  - 8 received Radical Radiotherapy
  - 8 did not receive Radical Radiotherapy
    - 1 clinical decision
    - 2 toxicity
    - 2 disease progression
    - 3 died

MARS Trial: Results

- EPP median survival 14.4 months vs 19.5 months for no EPP
- HR for EPP 2.75 (1.21-6.26, p=0.016)
- 30 day mortality 10.5% (2/19 patients that EPP was started)
- 1 more patient died 6/52 post op from pneumonia
- Conclusion was that EPP within trimodality therapy offers no benefit and potentially harms patients

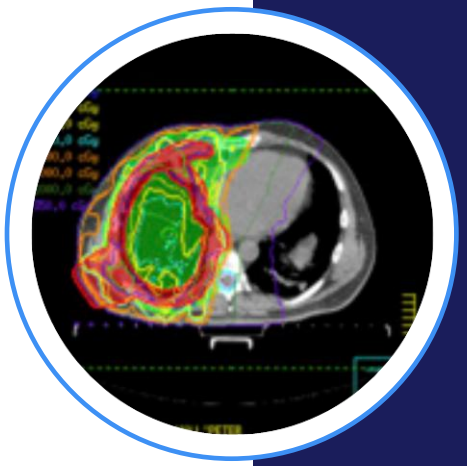
And the reaction was:

The MARS study did not show the feasibility of doing a trial comparing chemotherapy with EPP and radiotherapy. We believe the interpretation of the study—“These data, although limited, suggest that radical surgery in the form of EPP within trimodal therapy offers no benefit and possibly harms patients”—is inappropriate, could move clinical research for mesothelioma in the wrong direction, and might be harmful to patients seeking advice.

Walter Weder, Rolf A Stahel, Paul Baas, Urania Dafni, Marc de Perrot, Brian C McCaughan, Takashi Nakano, Harvey I Pass, Bruce W S Robinson, Valerie W Rusch, David J Sugarbaker, Nico van Zandwijk

Accelerated hemithoracic radiation followed by extrapleural pneumonectomy for malignant pleural mesothelioma,
dePerrot et al, JTCVS 2016

- 62/256 patients with MPM
- 25 Gy over 5 days+5 Gy to volumes at high risk
- EPP within 6+/-2 days
- Operative Mortality 1.6%
- 94% Stage III-IV, 52% ypN2
- Median survival 36 months (66% 3y with ypN0 Epithelioid disease)




Which
operation?

Therapeutic Procedures for MPM: From 5 to 2

1. VATS Pleural Biopsy +/- Talc Pleurodesis
2. ~~VATS Pleurectomy/ Decortication~~
3. ~~Open Non Radical Pleurectomy/ Decortication~~
4. Extended Pleurectomy Decortication
5. ~~Pleuropneumonectomy~~

Trials

MARS 2

Pilot (n=50) completed

N=161 Recruited Aug 2018

Target: 335

Should report in 3 years (2021)

MesoTRAP

A pilot clinical trial and feasibility study comparing video-assisted thoracoscopic partial pleurectomy/decortication with indwelling pleural catheter in patients with trapped lung due to malignant pleural mesothelioma designed to address recruitment and randomisation uncertainties and sample size requirements for a phase III trial. (n=38 pts)

i) What are the standard deviations of Visual Analogue Scale scores for dyspnoea in each treatment group following randomisation?

ii) Will patients accept randomisation to IPC or VAT-PD in a real life trial situation?

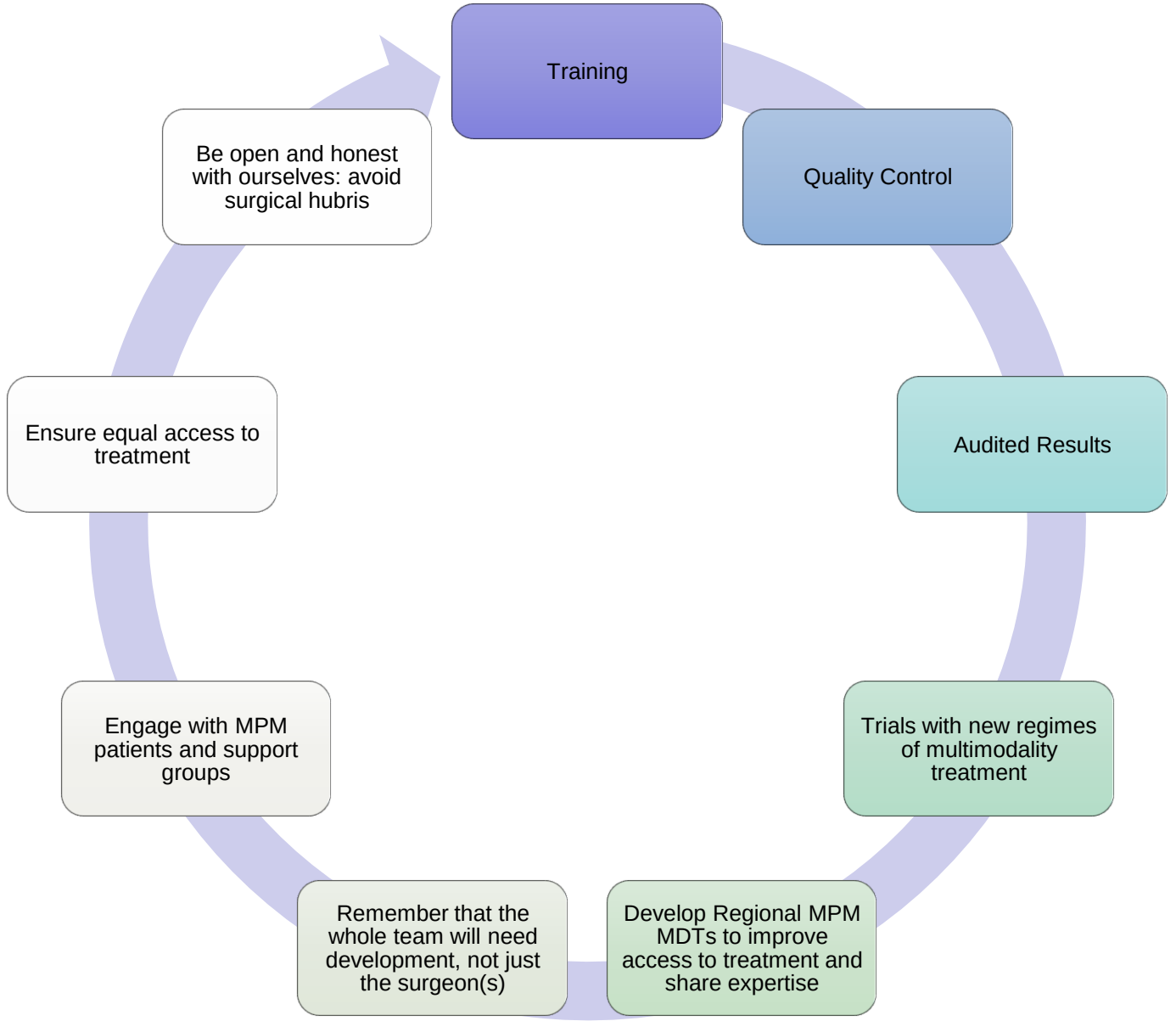
iii) How prevalent is trapped lung in MPM?

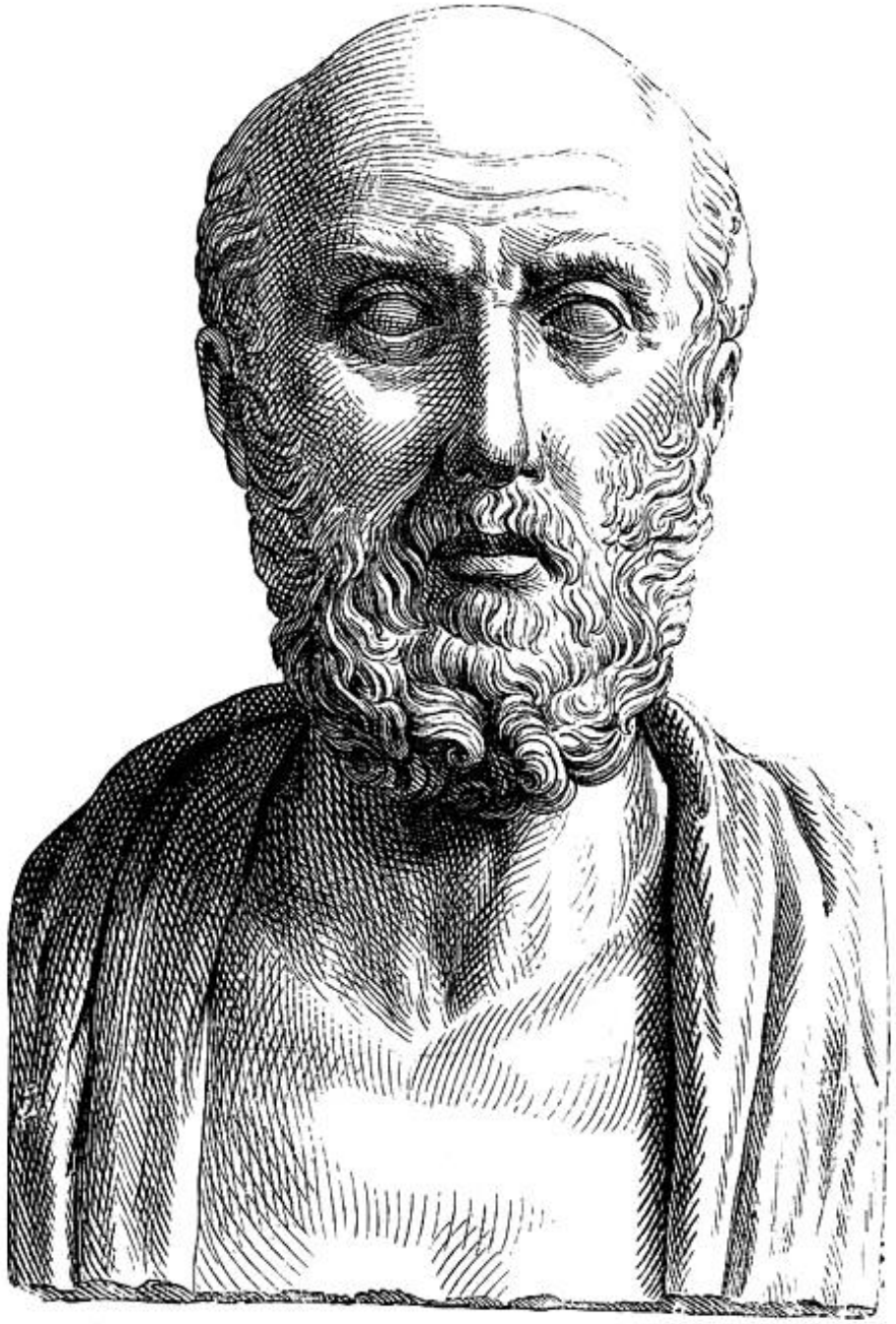
The future

Conclusions

1. VATS P/D has a very limited role to play in the elderly and unfit for radical surgery patients..
2. If we have to perform a thoracotomy Radical P/D (EPD) is preferable to Non Radical P/D
3. Radical P/D is not inferior to EPP in survival and is a sensible option even in the presence of pN2 disease
4. Radical P/D can be offered to an older age group than EPP
5. Macroscopic (R1) resection is the key target of Radical Surgery
6. Clinical Nodal Staging is not accurate therefore patients should not be denied radical surgery on the basis of this.
7. Pathological staging descriptors need modifications to improve accuracy
8. Surgical Centre experience is important: Surgical expertise and aggressive perioperative management of complications can drastically decrease mortality and increase percentage of patients undergoing radical surgery.
9. Beneficial effect of Radical Surgery will be tested in MARS 2 trial.

The (bright) future of Surgery for MPM





Hippocrates, 460-370 BC

Life is short,
and art long,
opportunity fleeting,
experimentations perilous,
and judgement difficult.

Thank You