Neoadjuvant Hemithoracic Intensity Modulated RT: The "SMART" Approach for Malignant Pleural Mesothelioma

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29 Oct 2013

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Disclosures

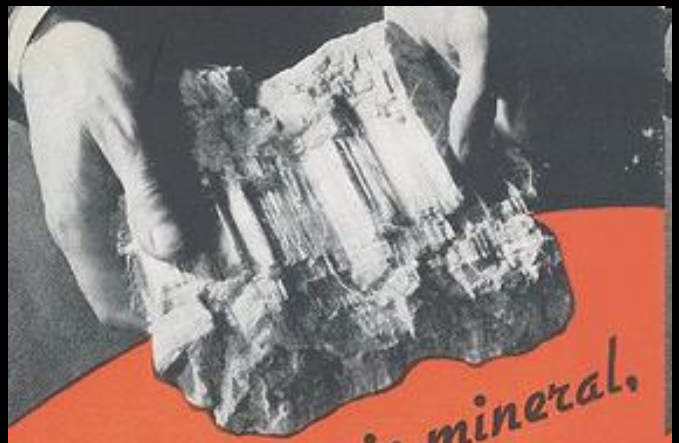
- None

Overview

- Asbestos
- Mesothelioma
- Evolution of Therapy
- SMART

Asbestos

- asbestos use dates back to 4500 years ago
  - Finnish pottery
- fabled fur of mythical salamander



Let this magic mineral, ASBESTOS, protect the buildings on your farm!

Asbestos! The magic mineral of the Middle Ages. Today, still a "magic" mineral; fireproof, rot-proof, and practically indestructible. When combined with portland cement it is manufactured into products which are especially important on the farm, because they provide permanent protection against fire, weather, and wear. Read this folder. Learn how to put this magic mineral to work on your farm.

AT THE RIGHT we see asbestos in its original form. This dense, rocklike substance, mined by Johns-Manville, is the raw material for some of the most useful products known to mankind.

BELOW is a handful of this same mineral, fluffed out into white, silklike fibers.

The magic mineral—ASBESTOS

Johns-Manville

Controls HEAT, COLD, SOUND, MOTION


AMAZING ASBESTOS!
by KEASBEY & MATTISON
STONE THAT TURNS TO FLOSS!
THOUGH ASBESTOS IS ROCK WHEN MINED ONCE BROKEN
IT CAN BE PULLED APART --- ACTUALLY MAKES A FLEECE
AS SOFT AND LIGHT AS A WISP OF WOOL!


WHITE CHRISTMAS
WHITE
CHRISTMAS

Sensitive Smokers:

Published medical reports show that about 1 out of 3 smokers is sensitive to the nicotine and tars in tobacco.

You can See the proof of Kent's health protection!

Exclusive "MICRONITE" FILTER removes 7 times more nicotine and tars than any other leading filter cigarette . . . and you can see and taste the difference!

Compare KENT smoke with the smoke of any other filter cigarette. KENT smoke is lighter, cleaner, almost white in color! Ordinary filter cigarette smoke is heavy, yellowish in color.

The difference is that KENTS' "MICRONITE" FILTER—used in its original form to purify the air in atomic energy plants—*removes 7 times more nicotine and tars!*

If you're a Sensitive Smoker—if you worry about the effects of smoking—try KENT with its extraordinary "MICRONITE" FILTER.

But expect a new smoking experience with KENT. After all, this is your first cigarette with a filter that really works (unlike ordinary cotton or crepe-paper filters)!

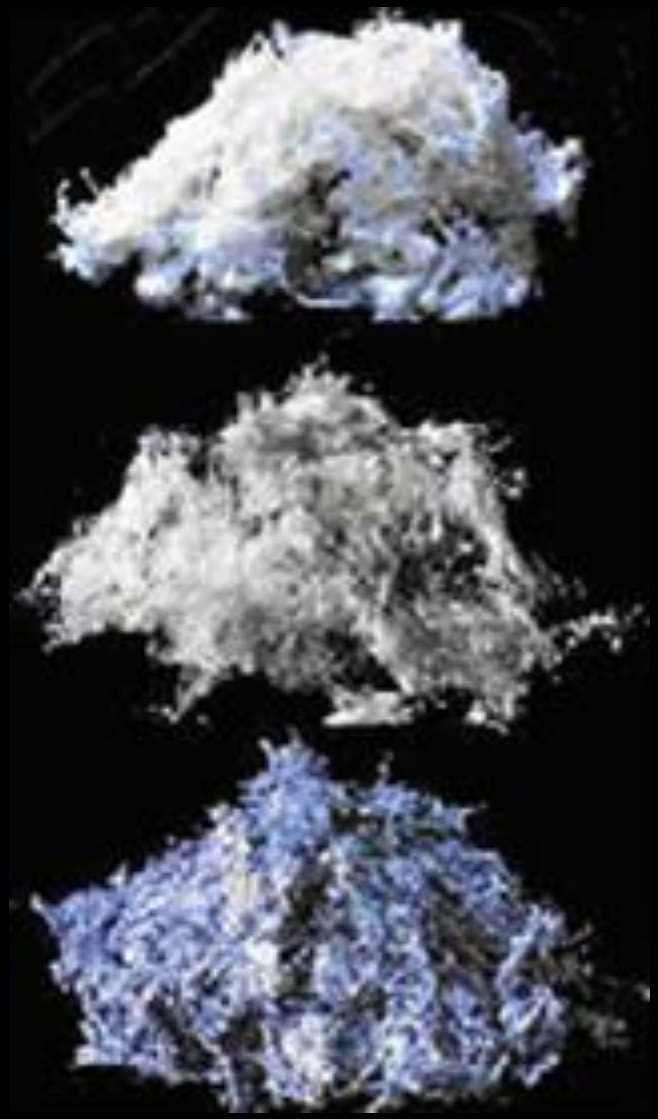
And if you'll give KENT a fair trial—not just one day of smoking, but a week or even two, time enough to allow your taste to adjust to so much less irritants in the smoke—we promise that KENTS' fine tobaccos will give you more smoking satisfaction that you've ever known.

And at the same time, you'll be enjoying the greatest health protection in cigarette history!

Stop to think . . . and you'll start to smoke KENT

Ad No. 19-A
N. Y. Daily News—May 18, 1952

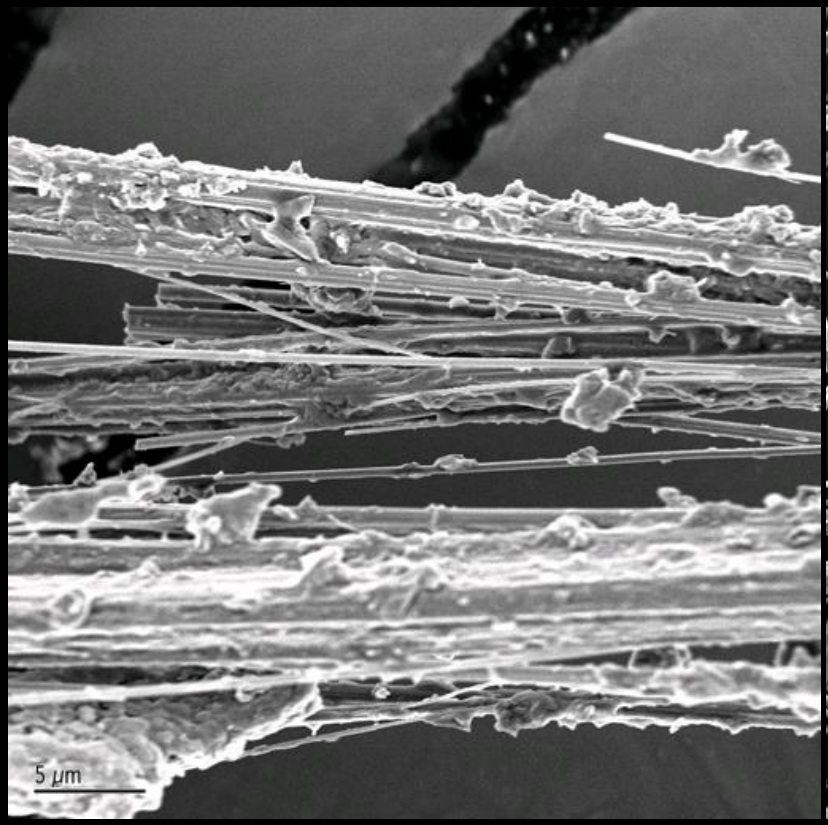
Asbestos



Chrysotile (white)

Amosite (brown)

Crocidolite (blue)


5 µm

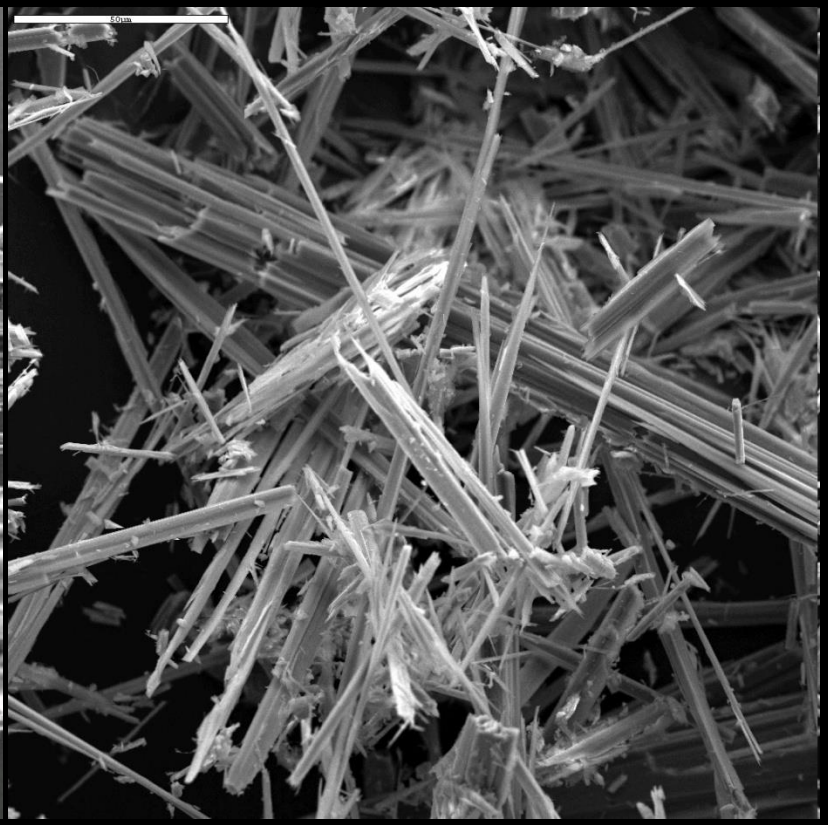
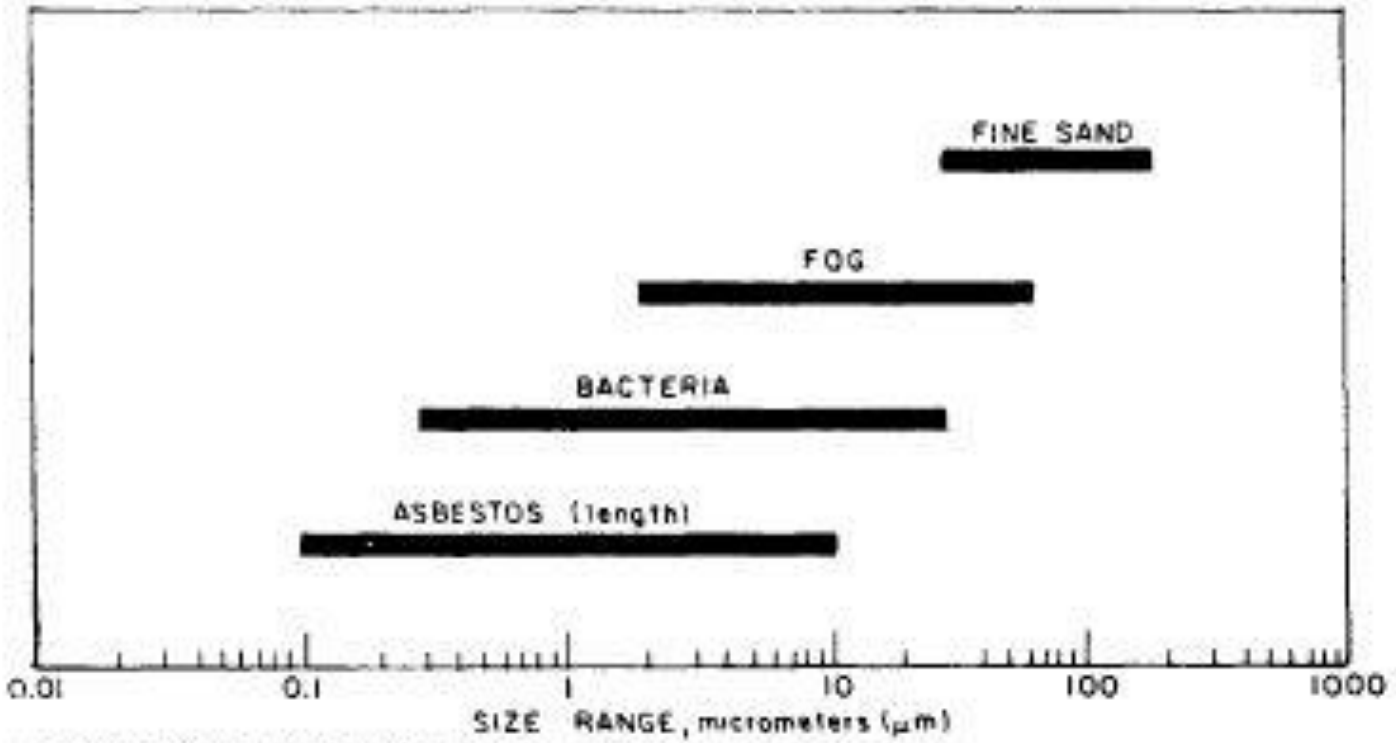


Figure 1. Asbestos size comparison with other particles.



Source: EPA 450/2-78-014, March 1978.

Brit. J. industr. Med., 1960, **17**, 260.

DIFFUSE PLEURAL MESOTHELIOMA AND ASBESTOS EXPOSURE IN THE NORTH WESTERN CAPE PROVINCE

BY

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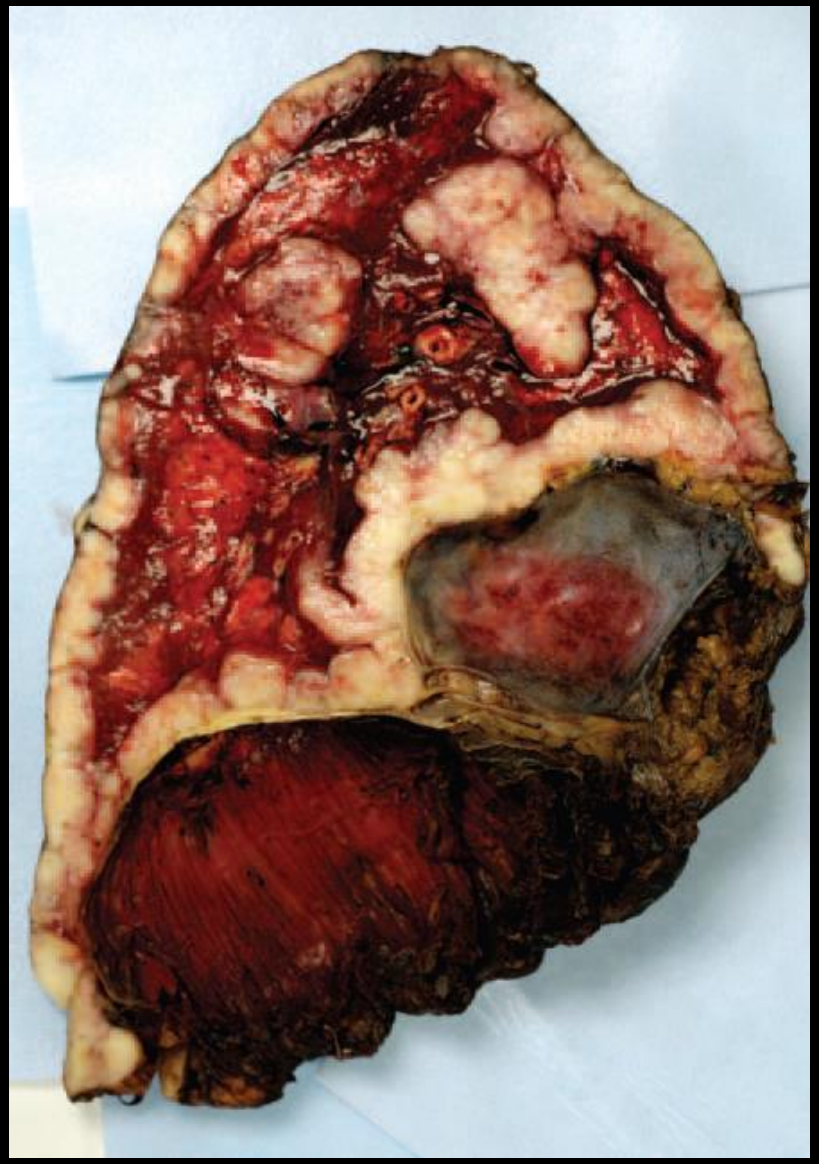
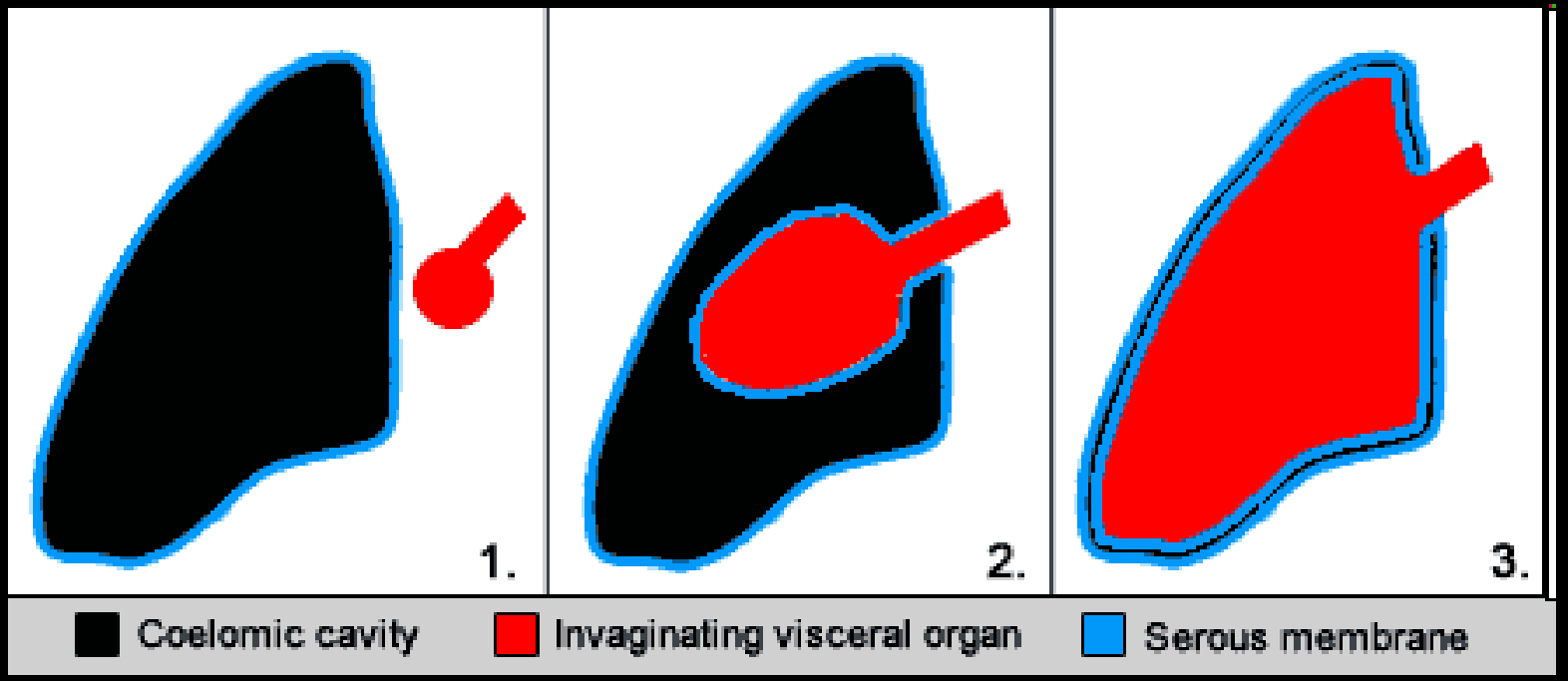
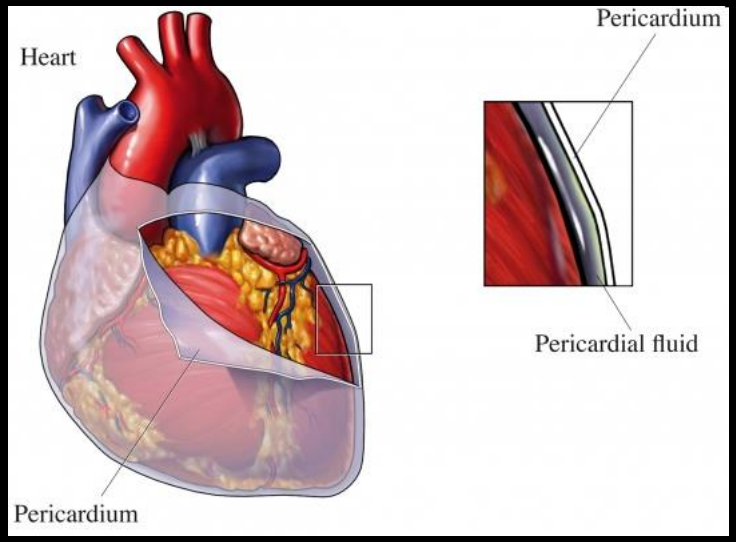
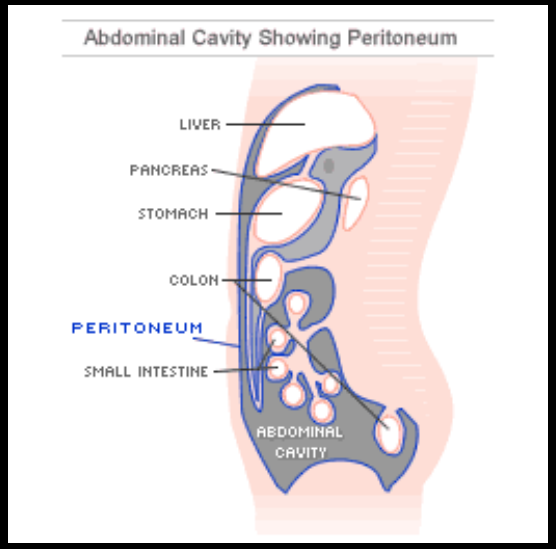
From the Pathology Division, Pneumoconiosis Research Unit of the Council for Scientific and Industrial Research, Johannesburg, West End Hospital, Kimberley, and the Department of Thoracic Surgery, University of the Witwatersrand and Johannesburg General Hospital

(RECEIVED FOR PUBLICATION APRIL 24, 1960)




1.
2.
3.
Coelomic cavity
Invaginating visceral organ
Serous membrane


Heart
Pericardium
Pericardial fluid
Pericardium


Abdominal Cavity Showing Peritoneum
LIVER
PANCREAS
STOMACH
COLON
PERITONEUM
SMALL INTESTINE
ABDOMINAL CAVITY

Resection

- early attempts at radical resection (pleurectomy/decortication, extrapleural pneumonectomy) universally disappointing
  - up to 30% perioperative mortality rate
  - up to 80% local recurrence rate

General
Thoracic Surgery

A phase II trial of surgical resection and adjuvant high-dose hemithoracic radiation for malignant pleural mesothelioma

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Kenneth Rosenzweig, MD[b]
Ennapadam Venkatraman, PhD[c]
Larry Leon, MS[c]
Adam Raben, MD[b]
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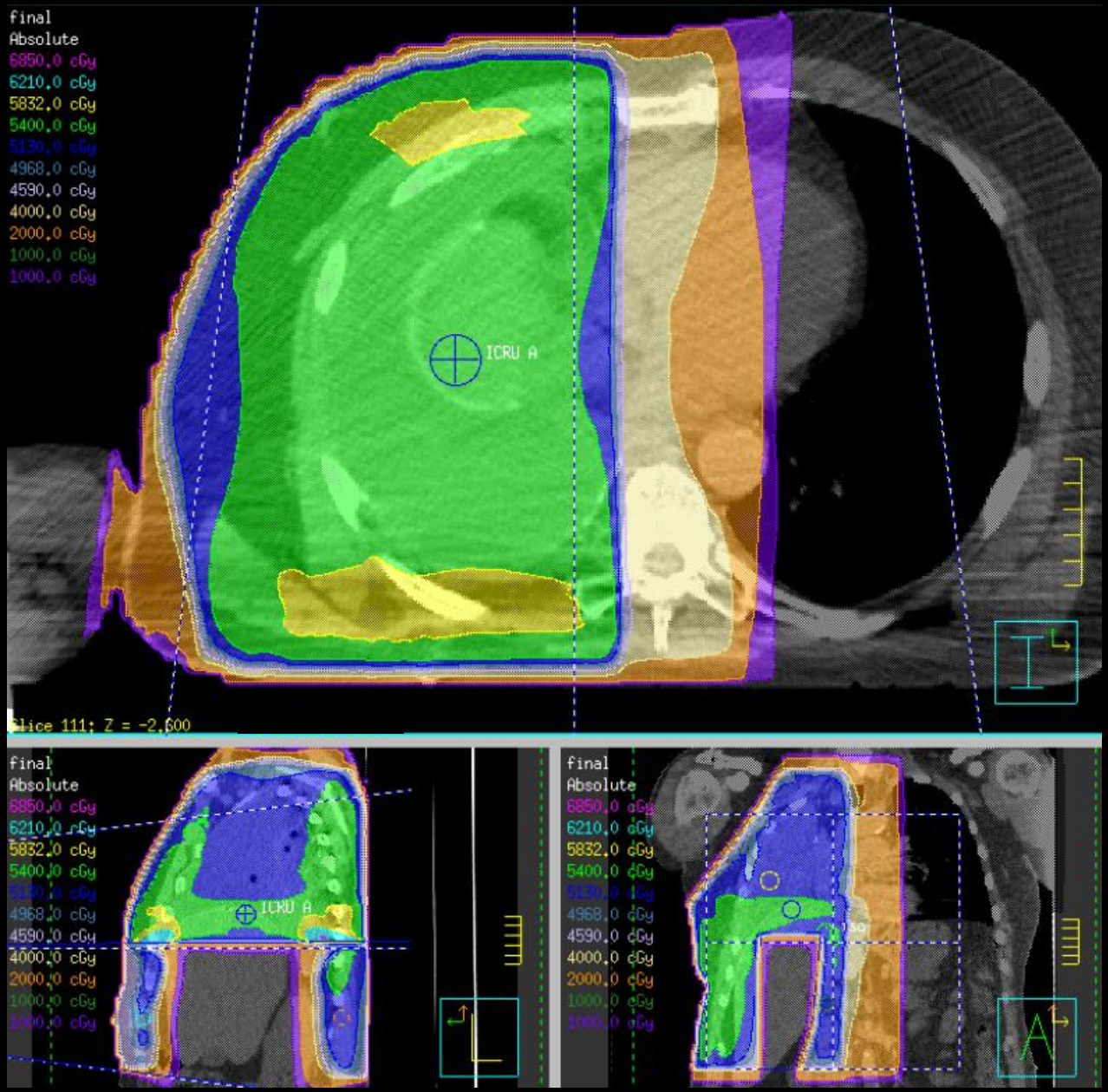
Robert J. Downey, MD[a]
Robert J. Ginsberg, MD[a]

Background: Surgical resection of malignant pleural mesothelioma is reported to have up to an 80% rate of local recurrence. We performed a phase II trial of high-dose hemithoracic radiation after complete resection to determine feasibility and to estimate rates of local recurrence and survival.

Methods: Patients were eligible if they had a resectable tumor, as determined by


final
Absolute
6850.0 cGy
6210.0 cGy
5832.0 cGy
5400.0 cGy
5130.0 cGy
4968.0 cGy
4590.0 cGy
4000.0 cGy
2000.0 cGy
1000.0 cGy
1000.0 cGy
ICRU A
Slice 111; Z = -2.600
final
Absolute
6850.0 cGy
6210.0 cGy
5832.0 cGy
5400.0 cGy
5130.0 cGy
4968.0 cGy
4590.0 cGy
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1000.0 cGy
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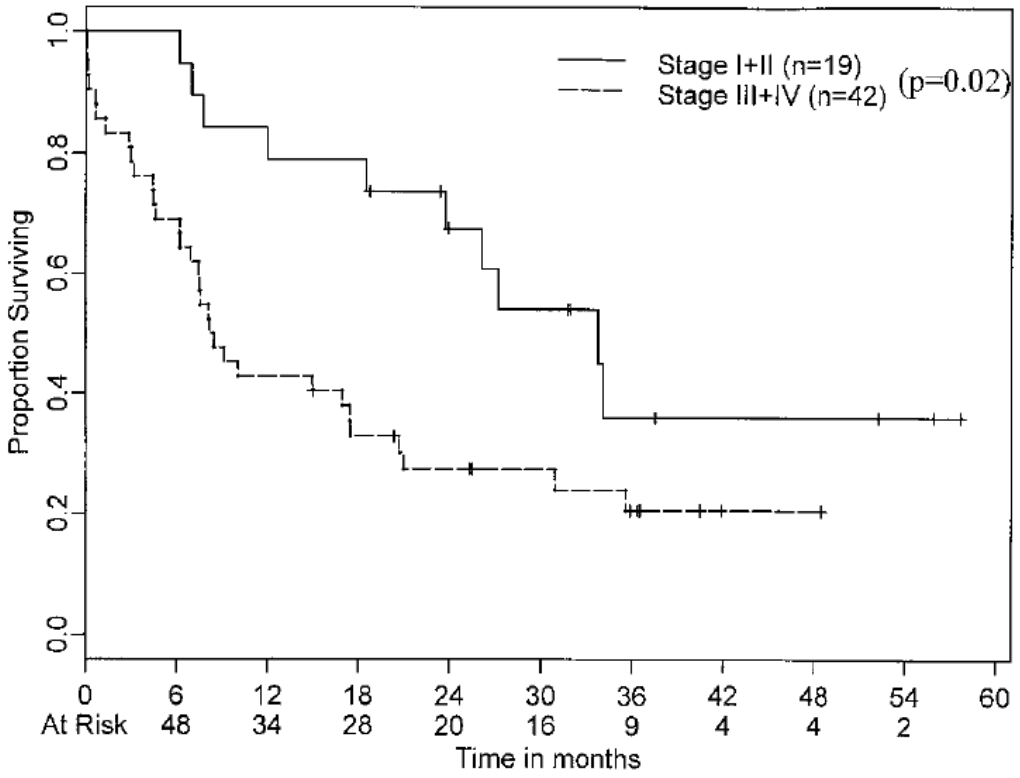

Figure 6. Overall survival of extrapleural pneumonectomy patients by stage.

Rusch. J Thorac Cardiovasc Surg 2001

VOLUME 27 · NUMBER 9 · MARCH 20 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Trimodality Therapy With Induction Chemotherapy Followed by Extrapleural Pneumonectomy and Adjuvant High-Dose Hemithoracic Radiation for Malignant Pleural Mesothelioma

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Submitted April 21, 2008; accepted October 20, 2008; published online ahead of print at www.jco.org on

ABSTRACT

Purpose

Malignant pleural mesothelioma (MPM) remains associated with poor outcome. We examined the results of trimodality therapy with cisplatin-based chemotherapy followed by extrapleural pneumonectomy (EPP) and adjuvant high-dose (50 to 60 Gy) hemithoracic radiation therapy for MPM.

Overall Survival

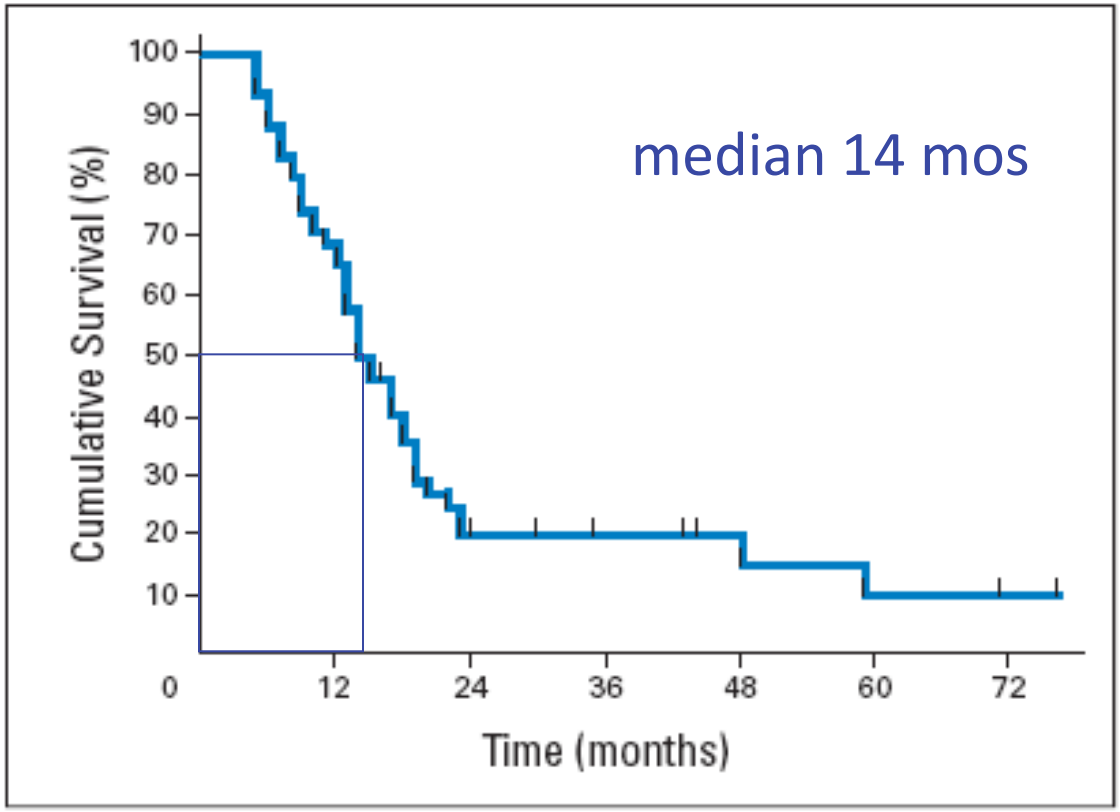


Fig 1. Cumulative survival of all 60 patients by intent-to-treat analysis.

Survival by Nodal Status and Therapy

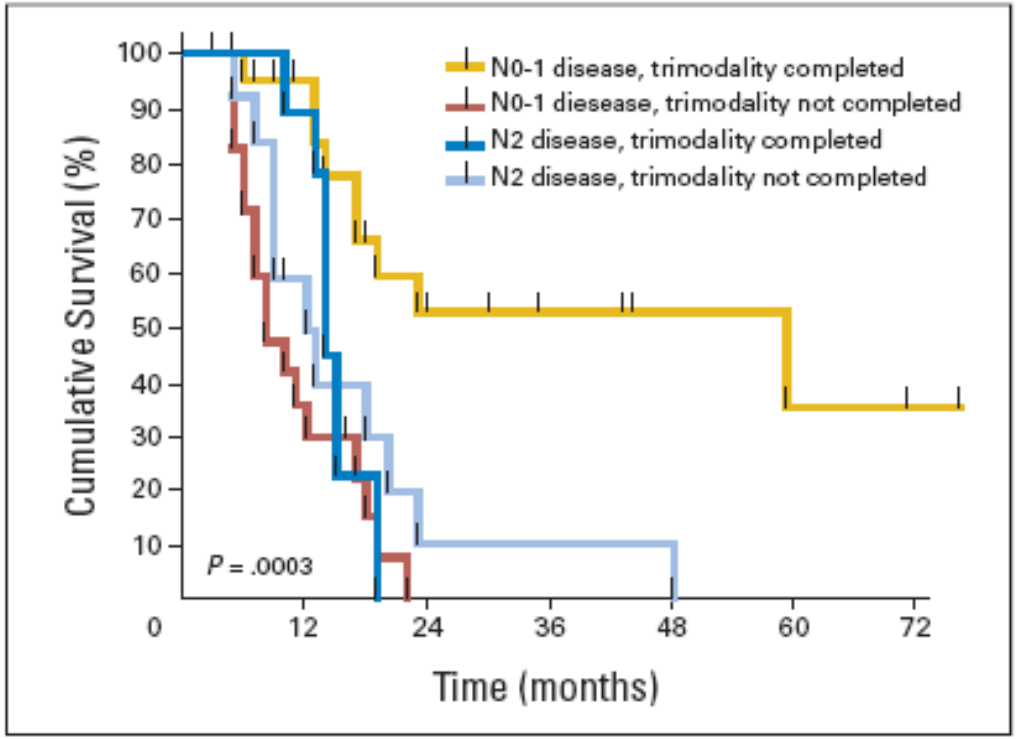


Fig 2. Survival according to mediastinal nodal status (N2 disease) and completion of the entire trimodality regimen. The median survival of patients who had no mediastinal node involvement (N0 or N1 disease) and completed the entire trimodality therapy regimen was 59 months (n = 21). The median survival of patients who had no mediastinal node involvement (N0 or N1 disease) but did not complete the entire trimodality therapy regimen was 8 months (n = 18). The median survival of patients with histologically proven N2 disease who completed the entire trimodality therapy regimen was 12 months (n = 9). The median survival of patients with histologically proven N2 disease who did not complete the entire trimodality therapy regimen was 14 months (n = 12).

Recurrences after Trimodality Therapy

- Recurrences
  - 16/30 patients
    - Ipsilateral chest: 4
    - Pericardium: 1
    - Peritoneum: 5
    - Contralateral chest: 4
    - Chest and peritoneum: 2

Recurrences after Trimodality Therapy

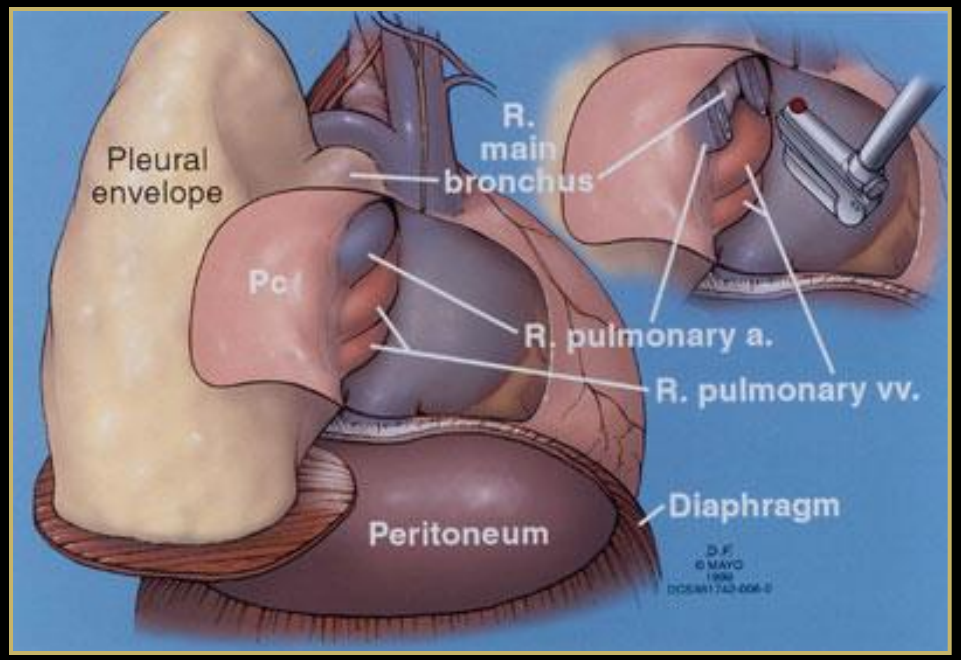
- Recurrences

  16/30 patients

Ipsilateral chest:	4	local
Pericardium:	1	distant mets
Peritoneum:	5	
Contralateral chest:	4	
Chest and peritoneum:	2	

Rationale for Neoadjuvant Therapy

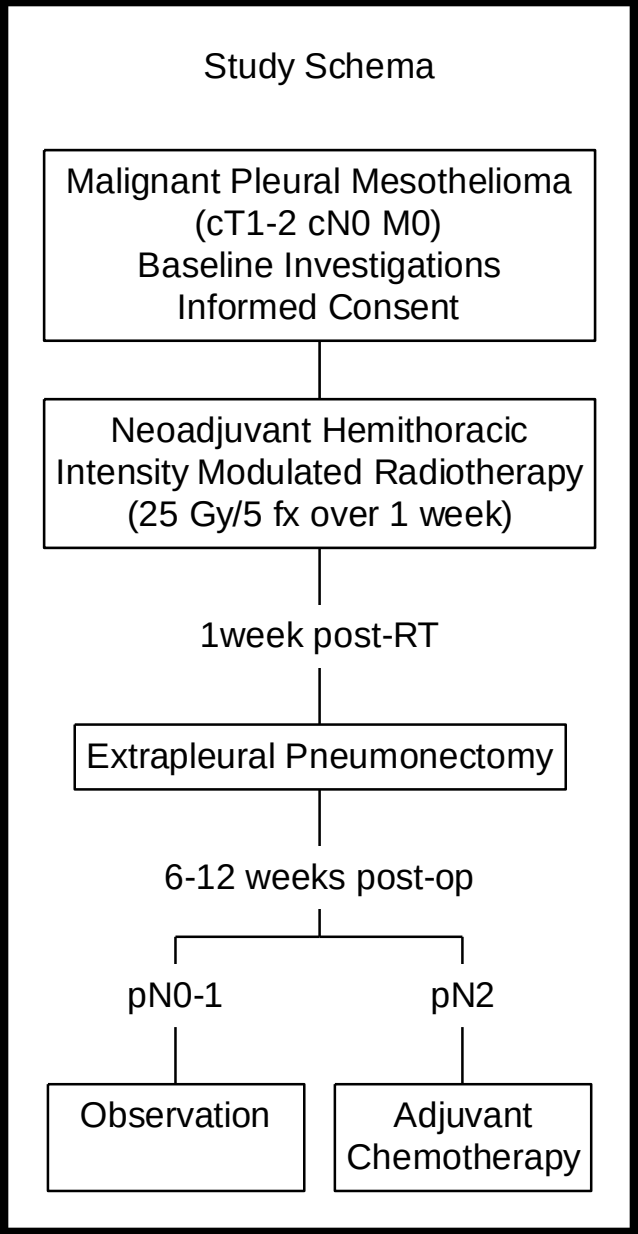
- to down stage tumour
  to improve resectability
  - R+ → R0
- to reduce local failure
  - sterilize “high risk” margins
- to reduce distant failure?

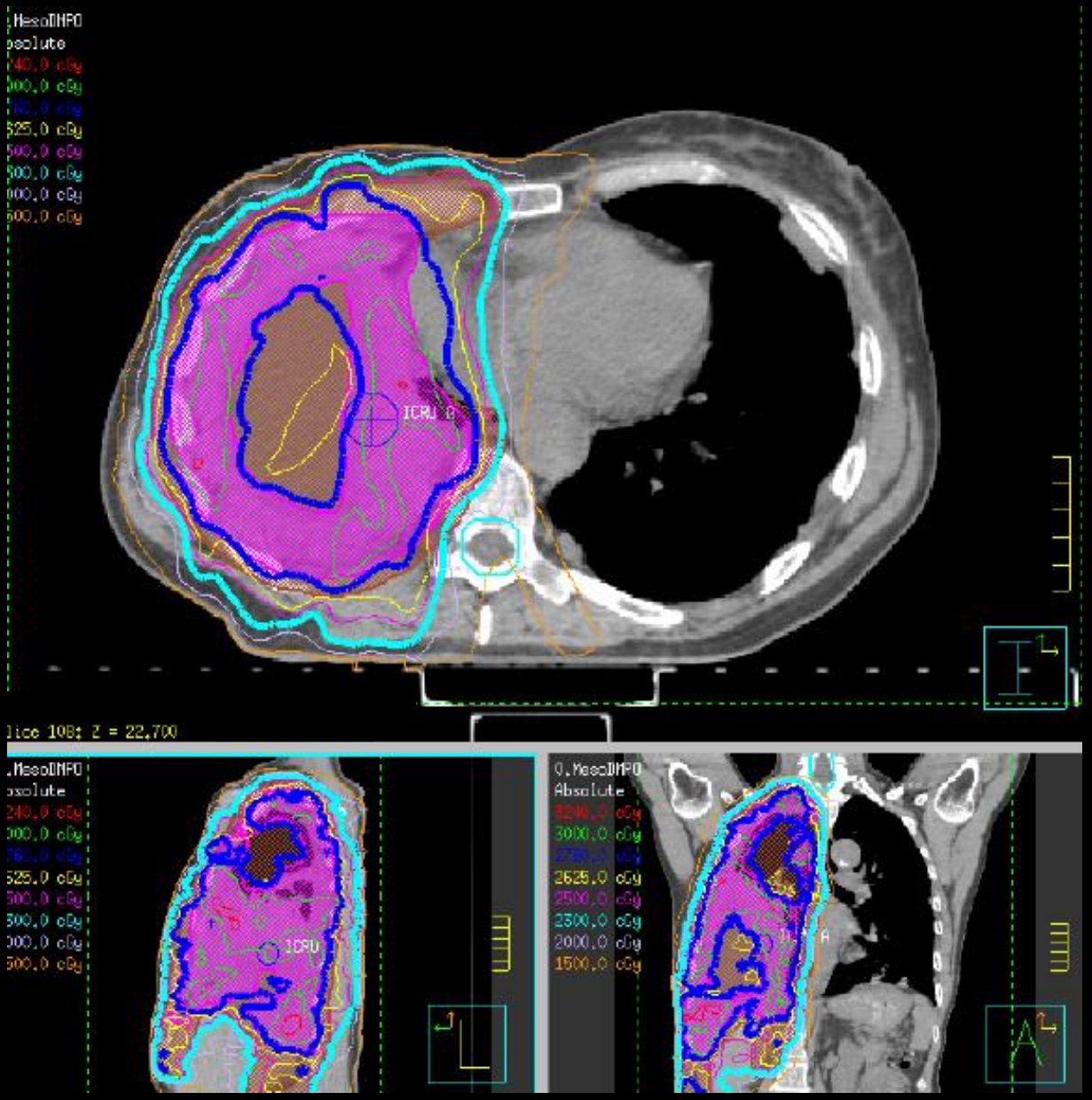


Neoadjuvant Hemithoracic RT

- large, complex volumes
- optimal fractionation and scheduling unknown
  - 45 Gy/25 fx x 5 w then EPP at 4 weeks?
  - risk of radiation pneumonitis?

Surgery for Mesothelioma After RT




MesoDMPO
Absolute
3000.0 cGy
2625.0 cGy
2500.0 cGy
2300.0 cGy
2000.0 cGy
1500.0 cGy
ICRU
Slice 108: Z = 22.700

Results

- accrual completed 10/2012
- 25 patients (19 males, 63±8 years old, 21 right sided tumors)
- all patients completed IMRT and EPP
- IMRT well tolerated with no grade 3-5 toxicity
  - limited to nausea, fatigue

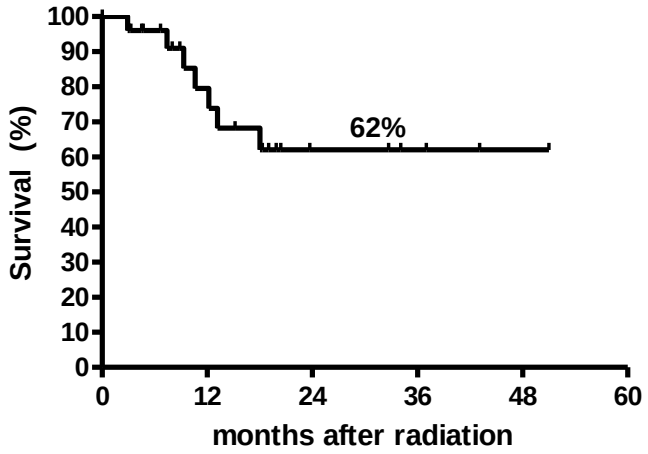
Results

- EPP performed 6±2 days after completion of IMRT
- no deaths within 30 days of surgery or in-hospital
- at least 1 complication occurred in 18 patients during follow-up after surgery

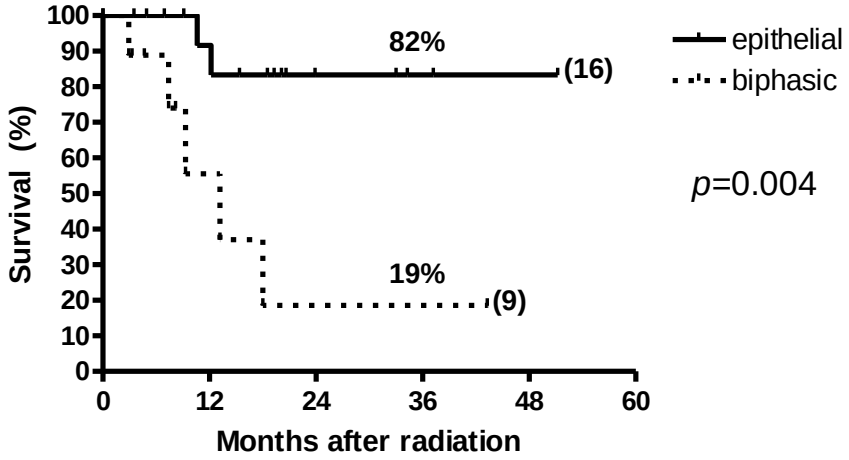
Table. Complications occurring after induction IMRT and EPP

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Thromboembolic event	22	0	1	1	1	0
Atrial fibrillation	15	0	5	5	0	0
Wound infections	22	0	2	1	0	0
Chylothorax	23	0	0	2	0	0
Hemothorax	24	0	0	0	1	0
Wound dehiscence	21	1	2	1	0	0
Renal dysfunction	24	0	0	1	0	0
Pneumonia	24	0	0	0	1	0
Empyema	23	0	0	1	0	1
Bronchopleural fistula	25	0	0	0	0	0

Overall survival

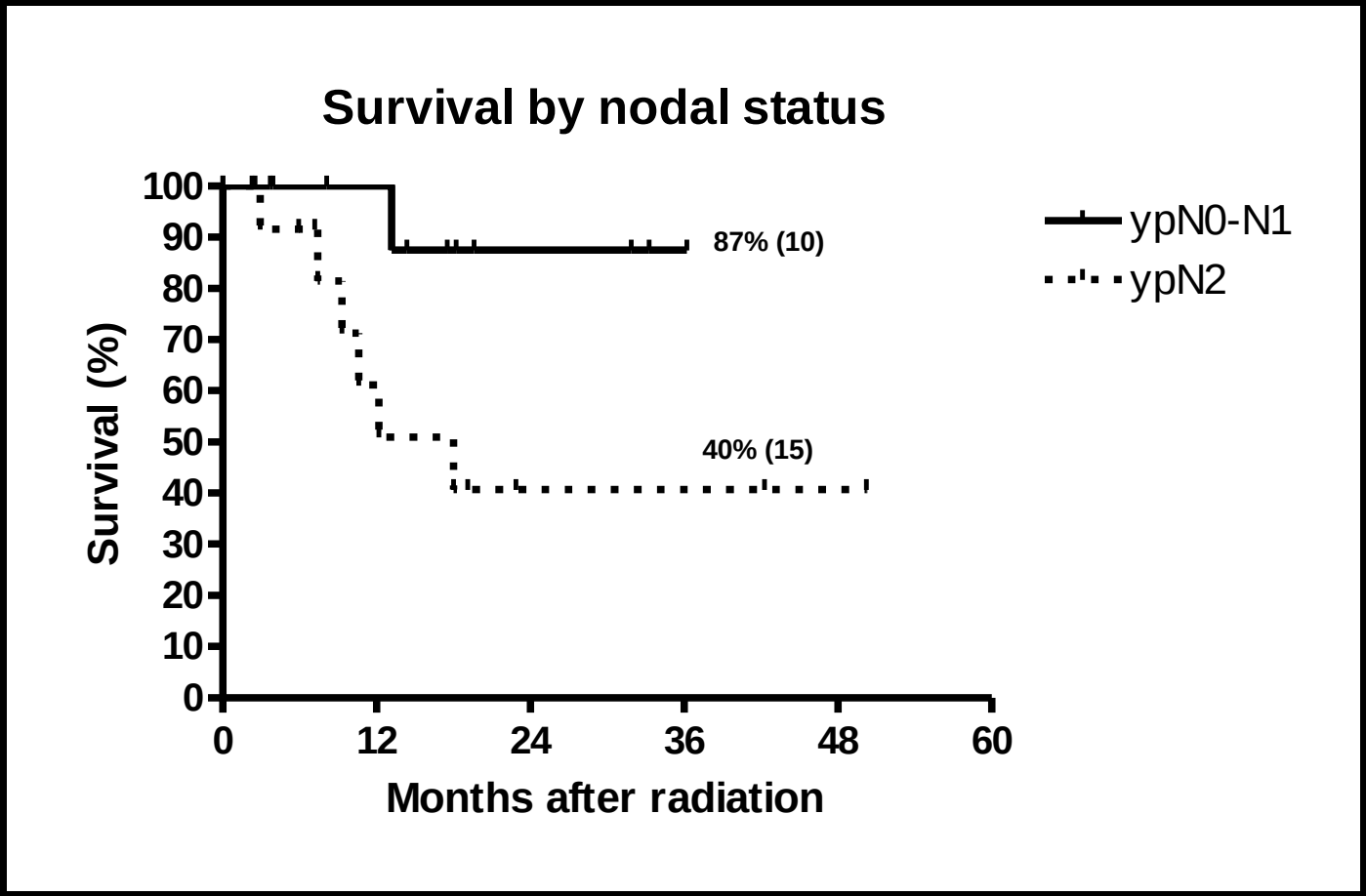


Survival by histology



Results

- median survival: 13 months
- median FU: 18 months
- overall 3-year survival: 62%
- significantly better OS for epithelial compared to biphasic MPM subtype (p=0.004)
  - OS at 3 yrs, 83% for epithelial (16) and 19% for biphasics (9)


Survival by nodal status
100
90
80
70
60
50
40
30
20
10
0
Survival (%)
0
12
24
36
48
60
Months after radiation
87% (10)
40% (15)
ypN0-N1
ypN2

Results

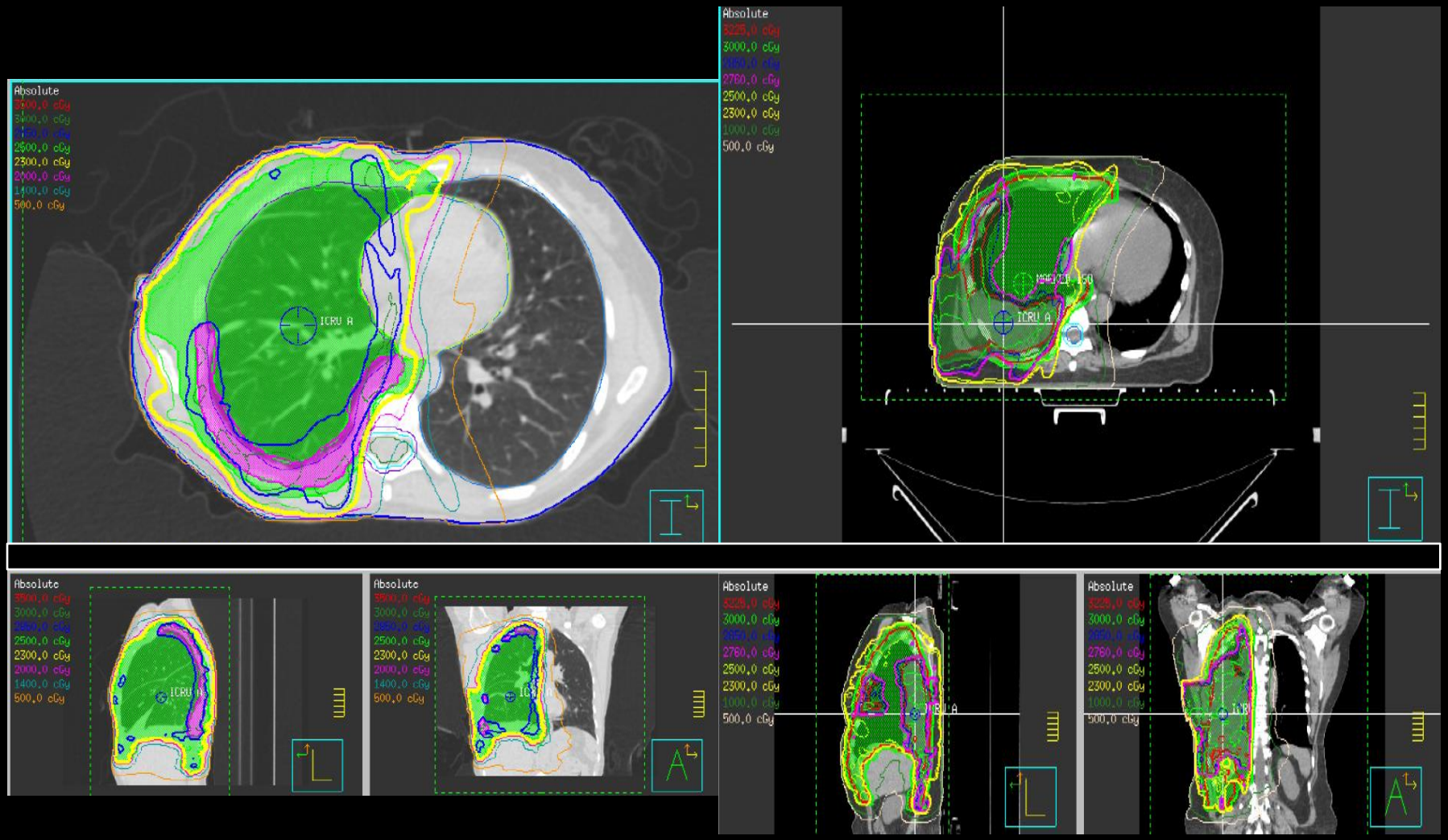
- 10 patients developed recurrence
  - ipsilateral chest only (n=2)
  - ipsilateral chest and distant sites (n=2)
  - distant sites only (n=6)

What we've learned

- short neoadjuvant hemithoracic RT followed by EPP for resectable MPM is feasible and safe
  - requires high degree of cooperation and coordination between surgical and radiotherapy teams
  - high rates of patient compliance

What we've learned

- radiotherapy continue to evolve and adapt as we optimize technique
  - well tolerated → extending target volume to thoracic outlet and diaphragmatic attachments
  - include high risk areas such as chest tube sites, retroperitoneal nodes → avoid geographical misses


Absolute
3000,0 cGy
2500,0 cGy
2300,0 cGy
2000,0 cGy
1400,0 cGy
500,0 cGy
ICRU A
Absolute
3000,0 cGy
2760,0 cGy
2500,0 cGy
2300,0 cGy
1000,0 cGy
500,0 cGy
ICRU A
Absolute
3000,0 cGy
2500,0 cGy
2300,0 cGy
2000,0 cGy
1400,0 cGy
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Absolute
3000,0 cGy
2500,0 cGy
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Absolute
3000,0 cGy
2760,0 cGy
2500,0 cGy
2300,0 cGy
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500,0 cGy
Absolute
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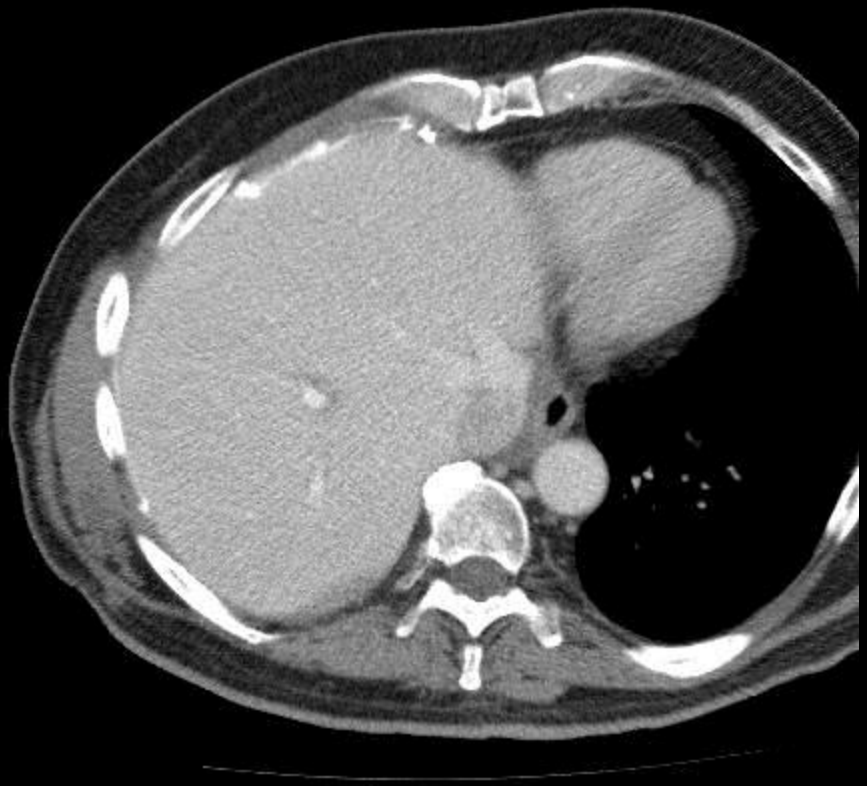
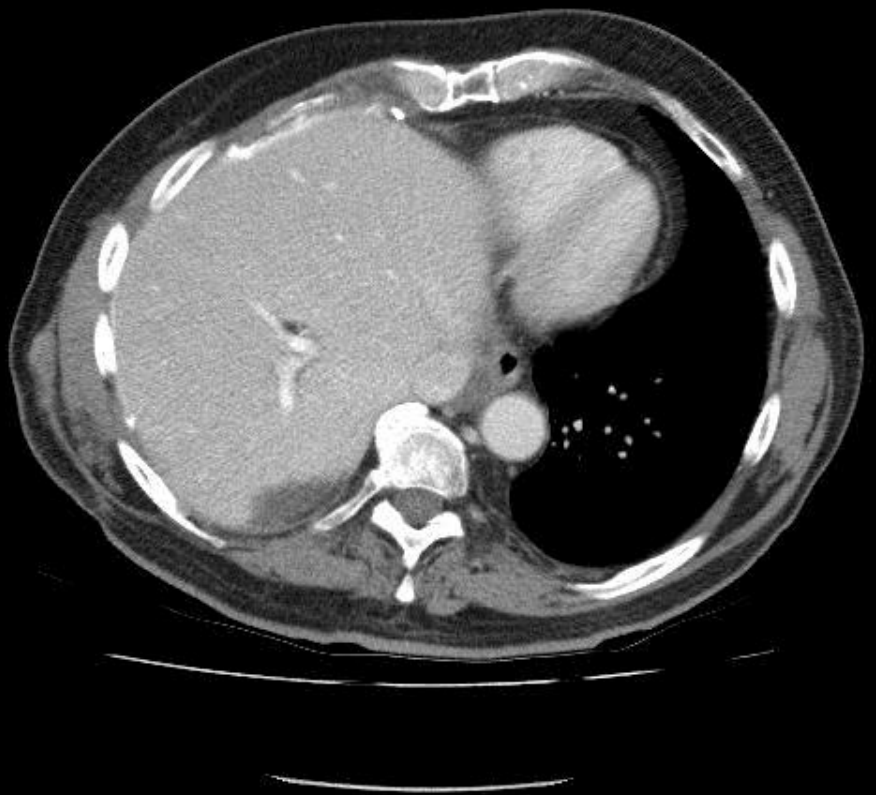
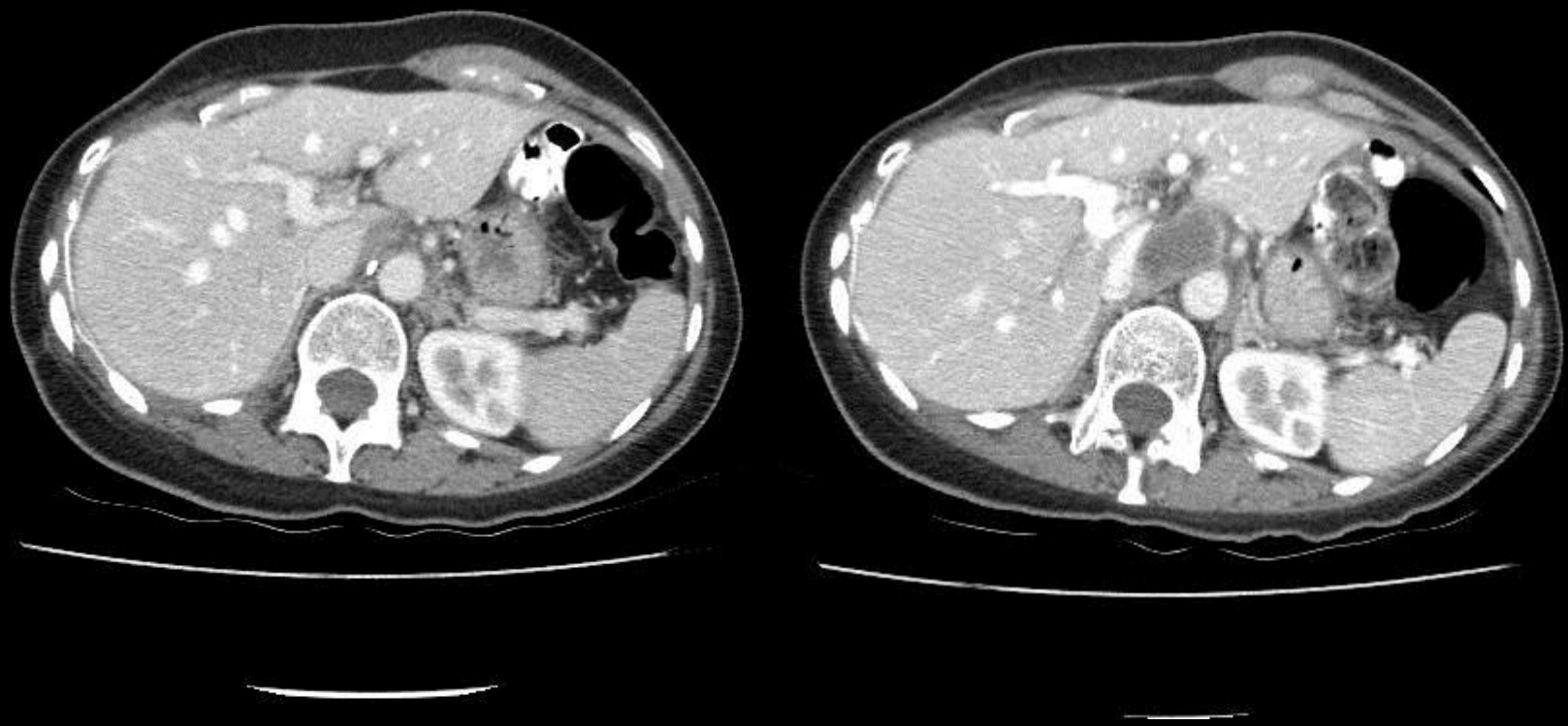
2300,0 cGy
1000,0 cGy
500,0 cGy







Acknowledgements

- Marc de Perrot
- Ron Feld
- Natasha Leighl
- Lea Dungao
- Pat Merante

Thank you for your attention