Management of Stage III and IV Thymoma

Doctors of Thoracic Surgery

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Relationship Disclosures

- None

Clinical Presentation

- Usually 4th and 5th decades
- 1/3 - asymptomatic ant med mass on CXR or CT
- 1/3 – local symptoms: cough, “pressure”, chest pain, SVC syndrome, dysphagia
- 1/3 – found on investigation of MG
- Metastasis - pleura, distant - rare

Paraneoplastic Syndromes

- ~ 30% of thymomas – Myasthenia Gravis
- Other associated disorders:
    - Pure red cell aplasia
    - Hypogammaglobulinemia
    - SLE, dermatomyositis, RA, thyroiditis
    - others

Pathologic Classification of Thymoma

- Muller-Hermelink (Corticomedullary) : medullary, cortical, mixed, thymic ca
- Lattes/Bernatz: spindle cell, lymphocytic, mixed, thymic carcinoma
- **WHO classification: Types A, B1, AB, B2, B3, C**
- TNM system - impractical

Role for Biopsy

- MG + Ant Med Mass = Thymoma
- Regional or distant adenopathy – lymphoma?
- Young males – α–fetoprotein, βHCG (non-seminomatous germ cell)
- Small (<5cm) – excise for Dx and Rx
- Large invasive appearing tumours – biopsy to guide treatment (chemo $\pm$ RT, $\pm$ surgery)
- FNA > Core > anterior mediastinotomy (not thoracoscopy)

Staging

- Masaoka staging system
- Based on surgical and pathological findings
- Shown to be an independent predictor of recurrence and survival
- Very practical

Masaoka Staging System

I	Completely encapsulated tumour
IIa	Microscopic invasion of capsule
IIb	Macroscopic invasion – mediastinal fat or pleura
III	Macroscopic invasion – pericardium, great vessels, lung
IVa	Pleural or pericardial dissemination
IVb	Lymphatic or hematogenous metastasis

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Principles of Surgical Resection

- Complete wide resection
- Careful technique - avoid aggressive manipulation (droplet mets)
- Median sternotomy (Robotic, Not TCT, ?VATS)
- Resection of all thymic tissue (MG)
- Extended en-bloc resection as required (lung, innominate vein, cava, pleural implants)
- Phrenic nerve involvement – consider MG
- Operative mortality <1%

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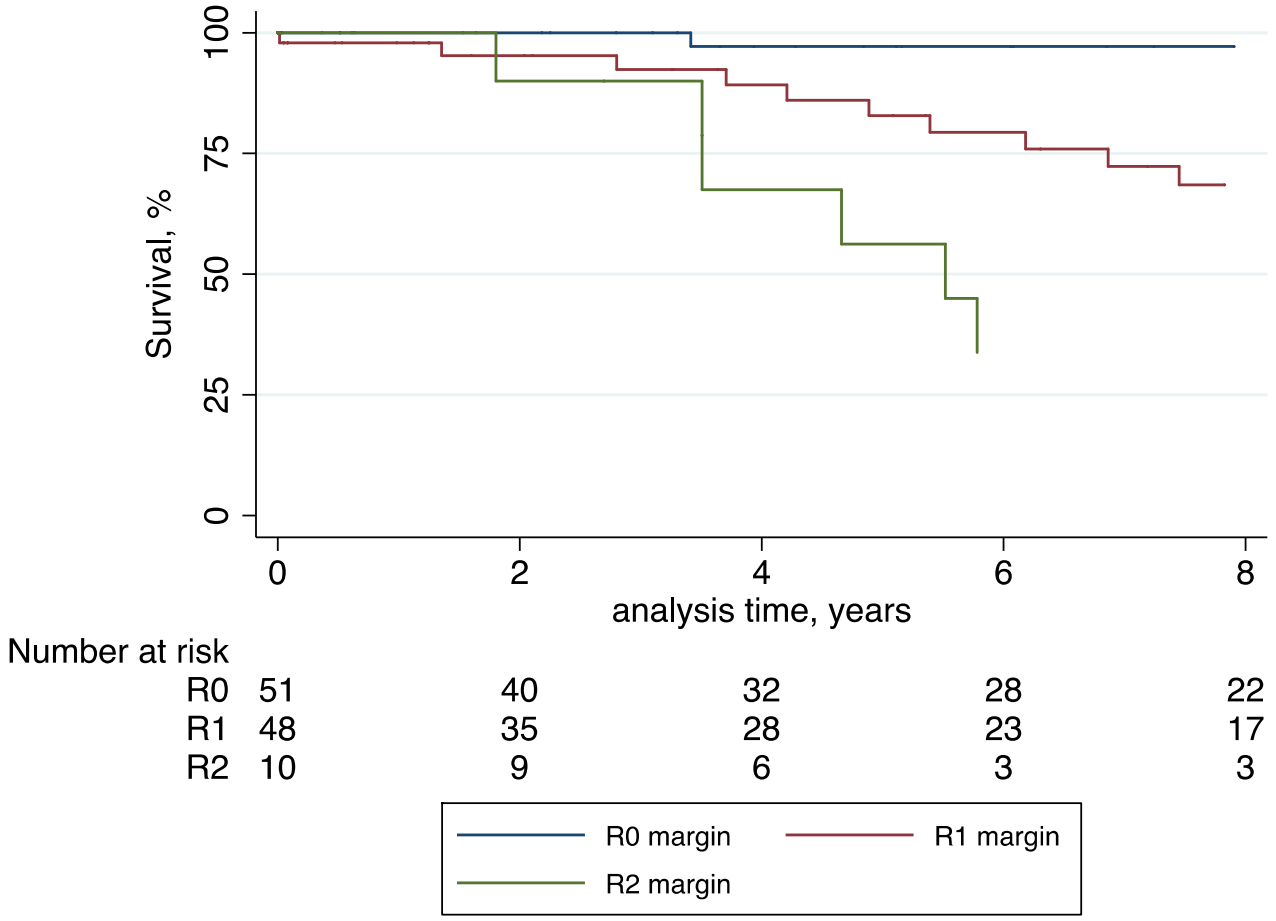
Margin Status

- Aim for complete resection
- R0, R1 do well
- No “de-bulking” intent



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Thymoma Resection TGH Experience

- 1986 - 2010
- N = 262 patients
- 51% female
- Median age 55 (16 - 86)
- Median tumour size 5.4 cm (1 - 17.5cm)
- Median follow-up 7.5 yr (1 - 25 yr)

Safieddine / Keshavjee et al. *J Thor Oncol* 2014: 9(7); 2018-22

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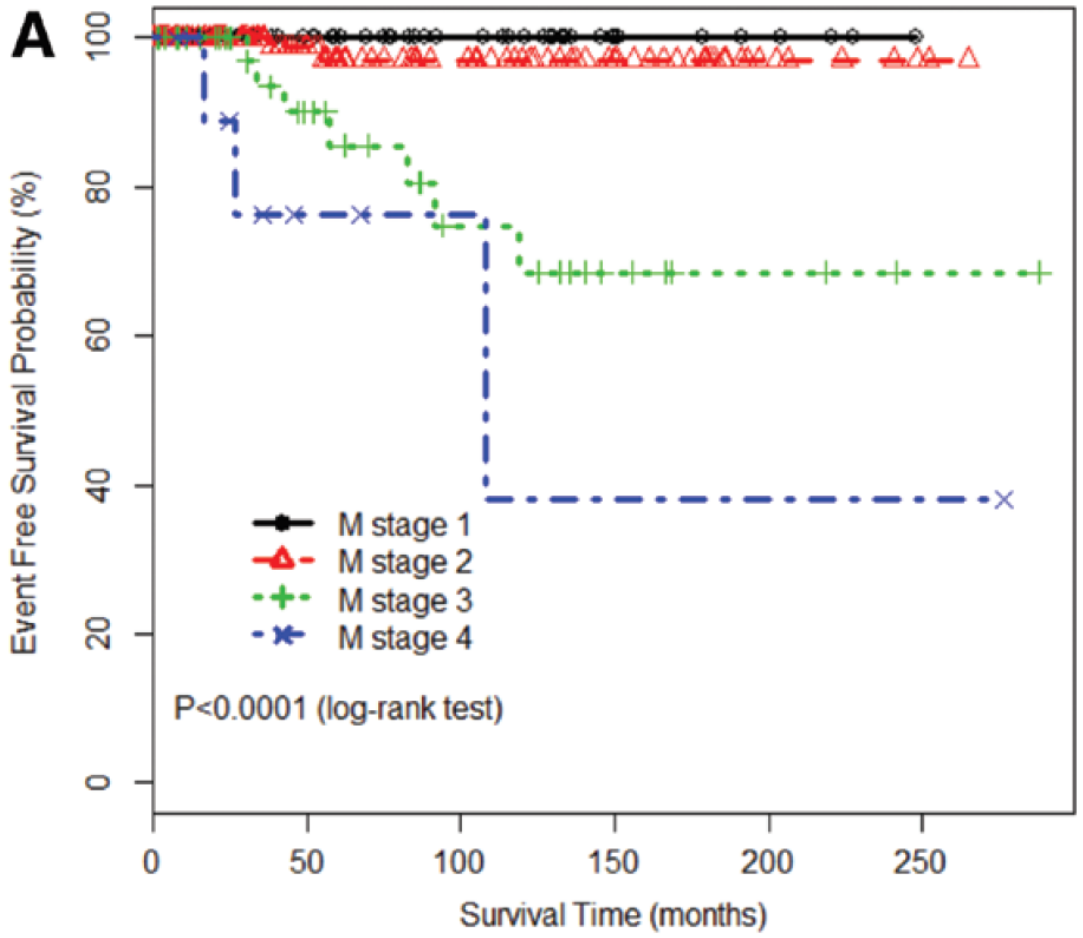
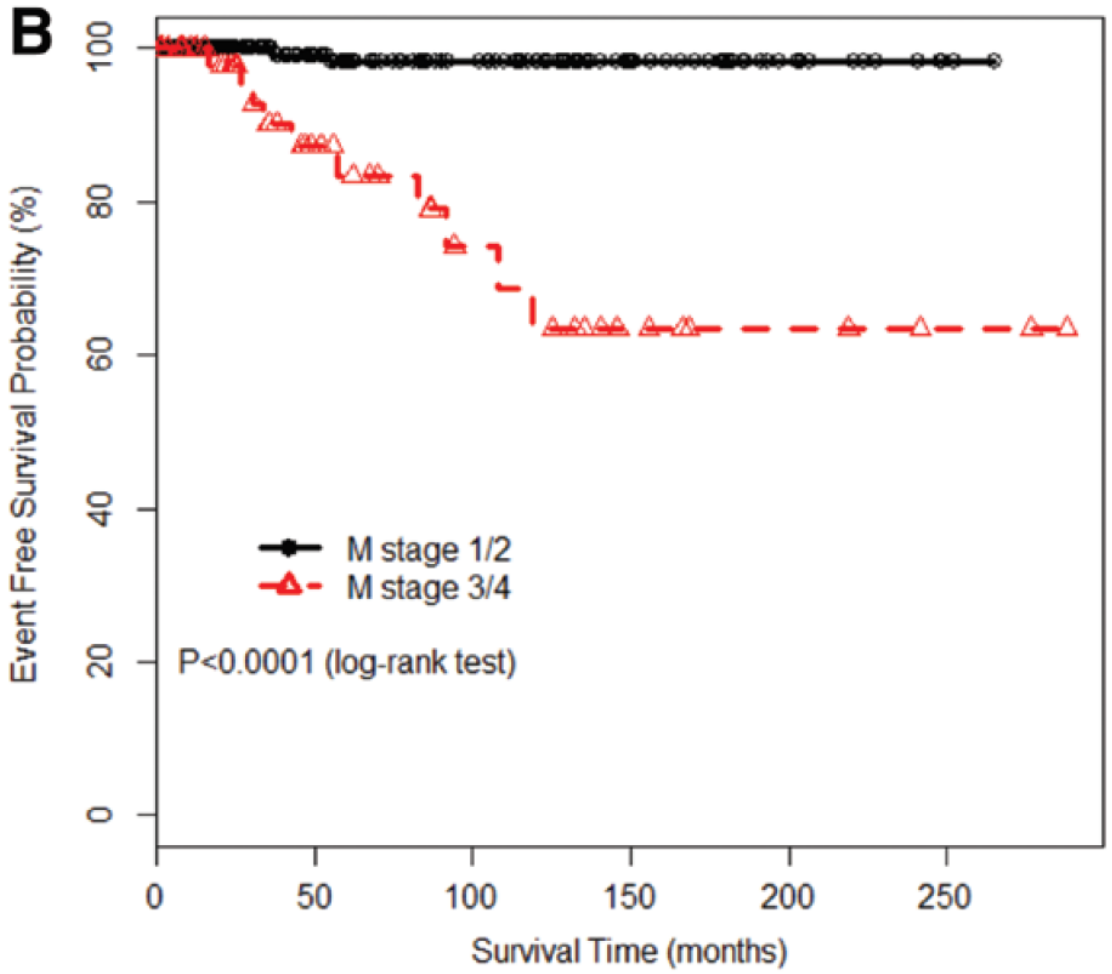
Recurrence Free Survival by Masaoka Stage

N=262

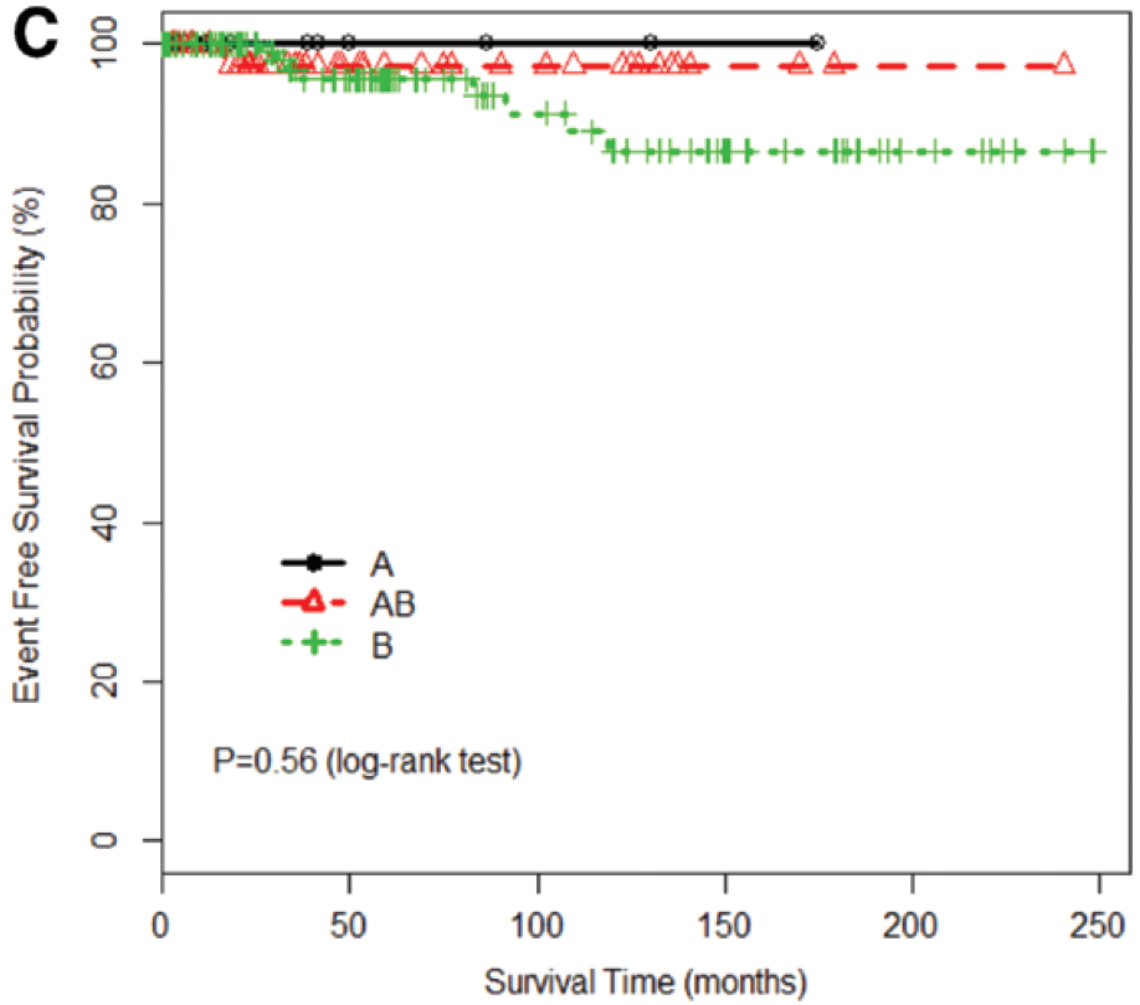


Safieddine et al. J Thor Oncol 2014: 9(7); 2018-22

Recurrence Free Survival by Grouped Masaoka Stage



Recurrence Free Survival by WHO Histology



Recurrence by tumour size

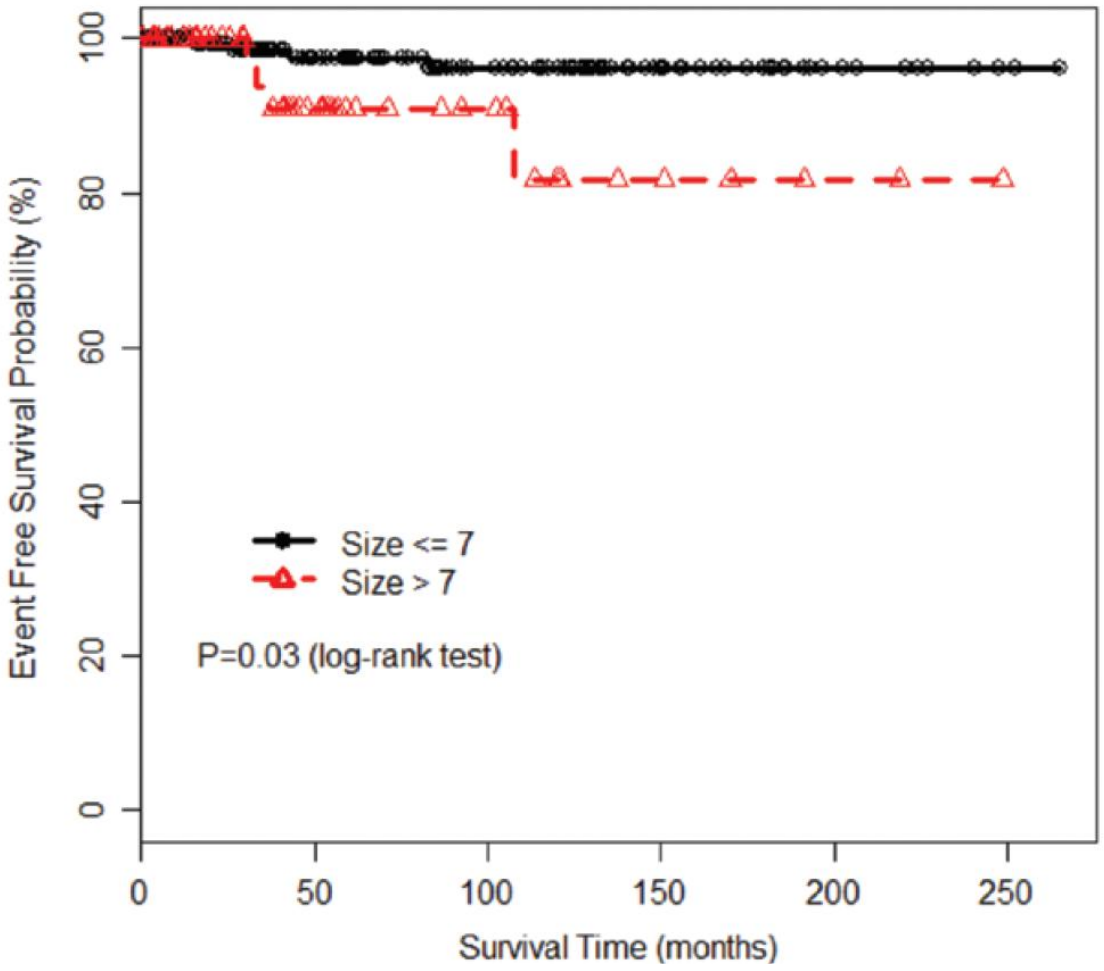


FIGURE 2. Recurrence-free survival by tumor size (dichotomized at 7 cm; $n = 262$)

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Stage III Thymoma

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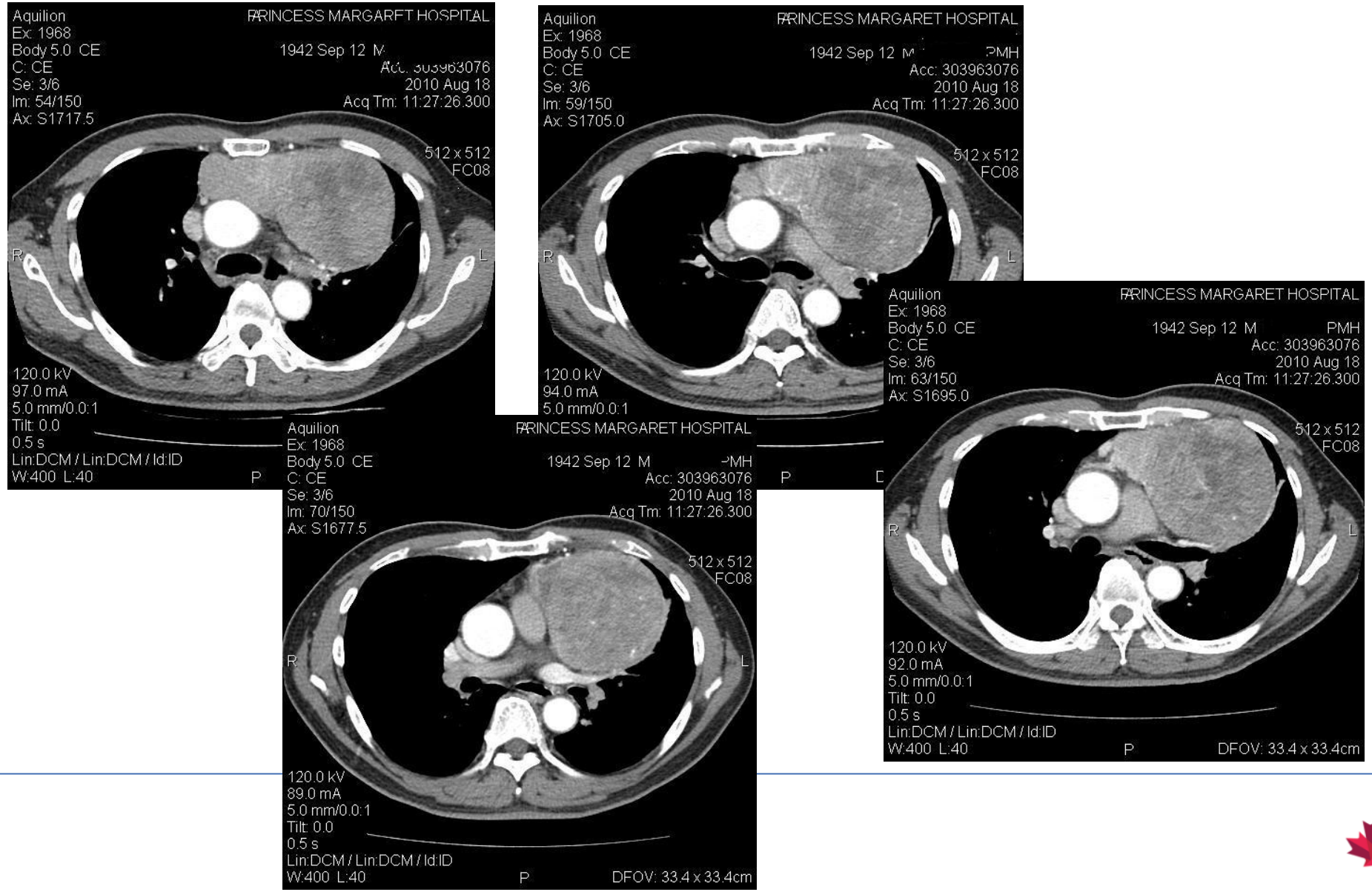
Stage II or III?



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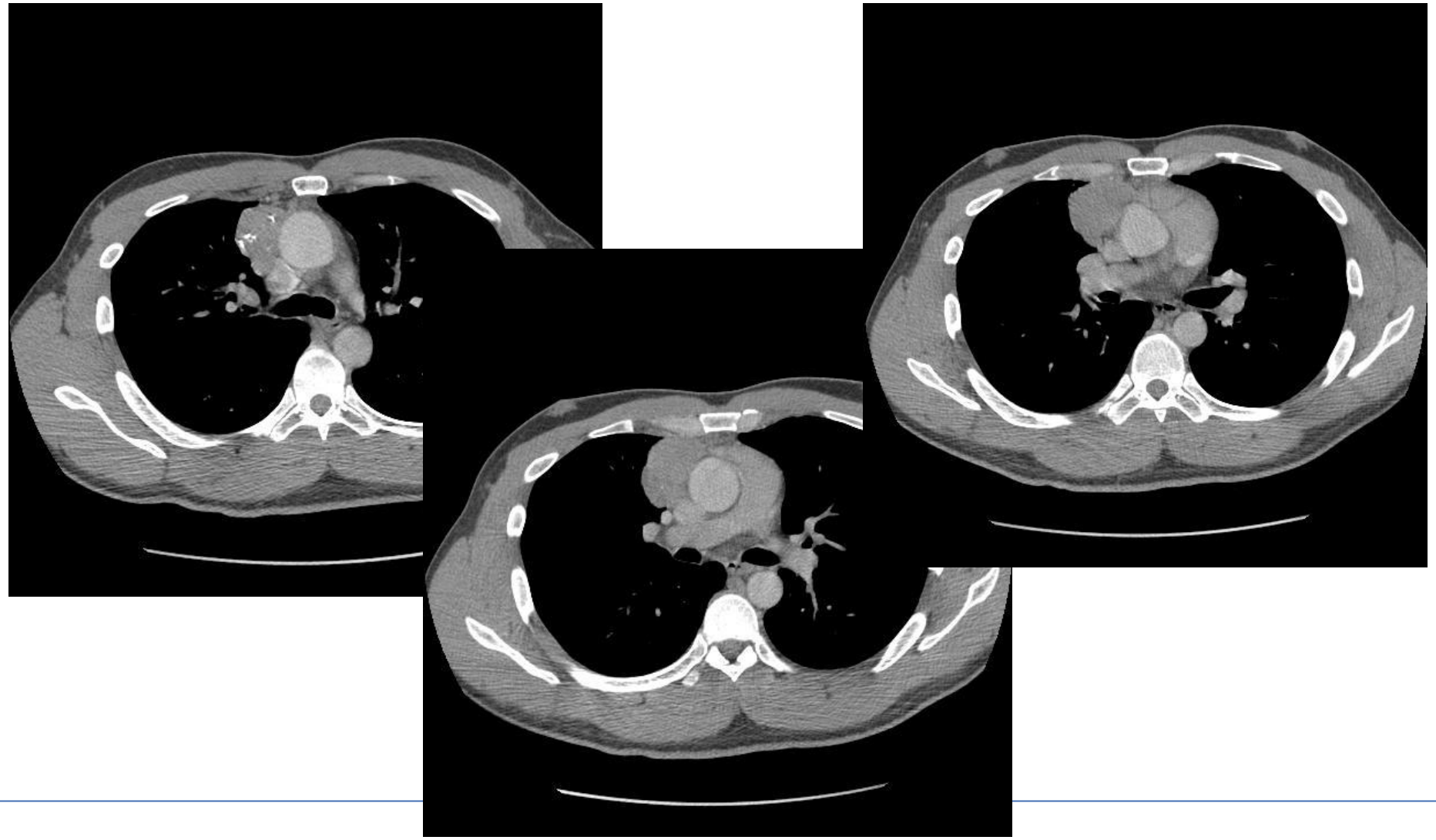
Stage III



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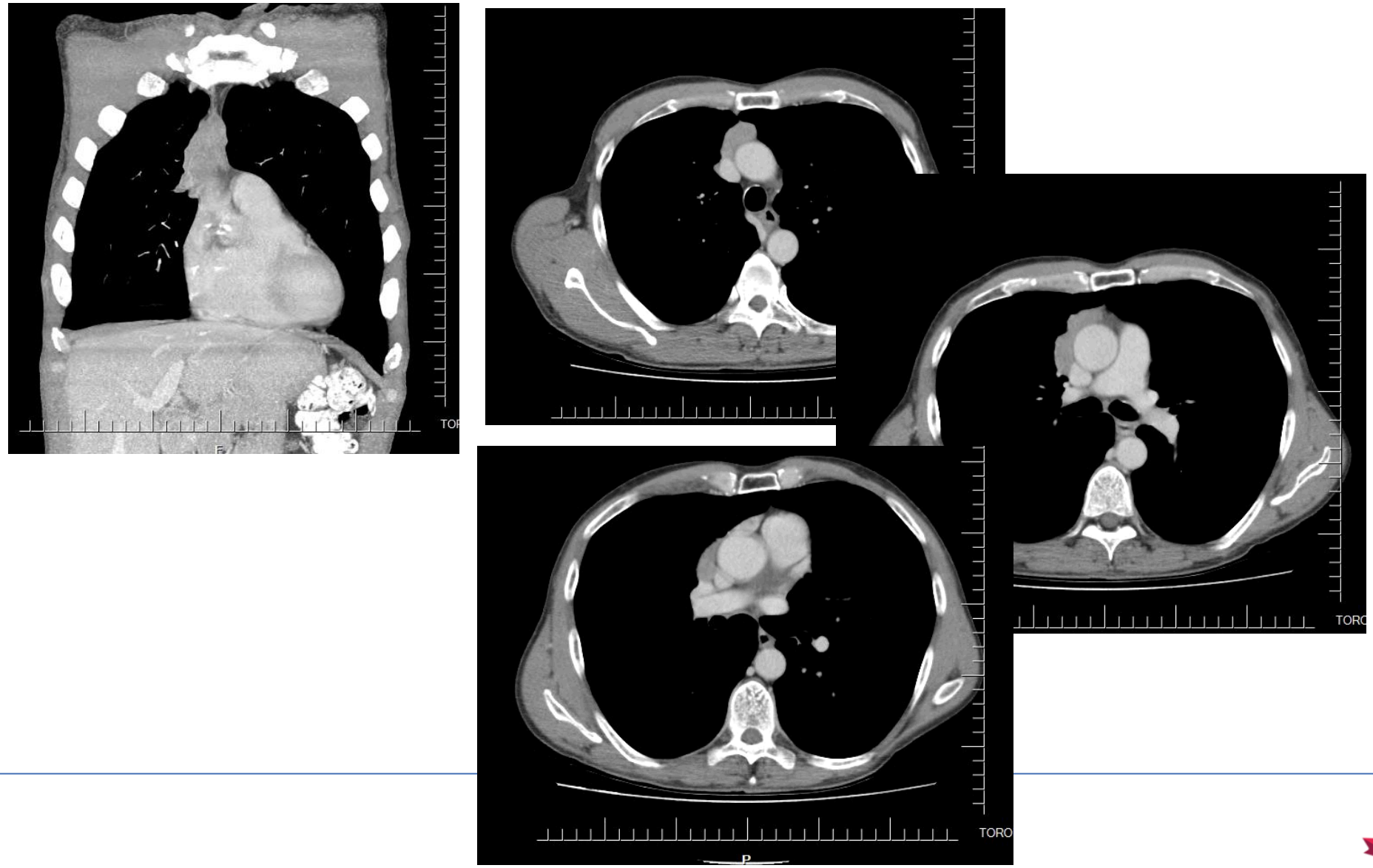
Stage III



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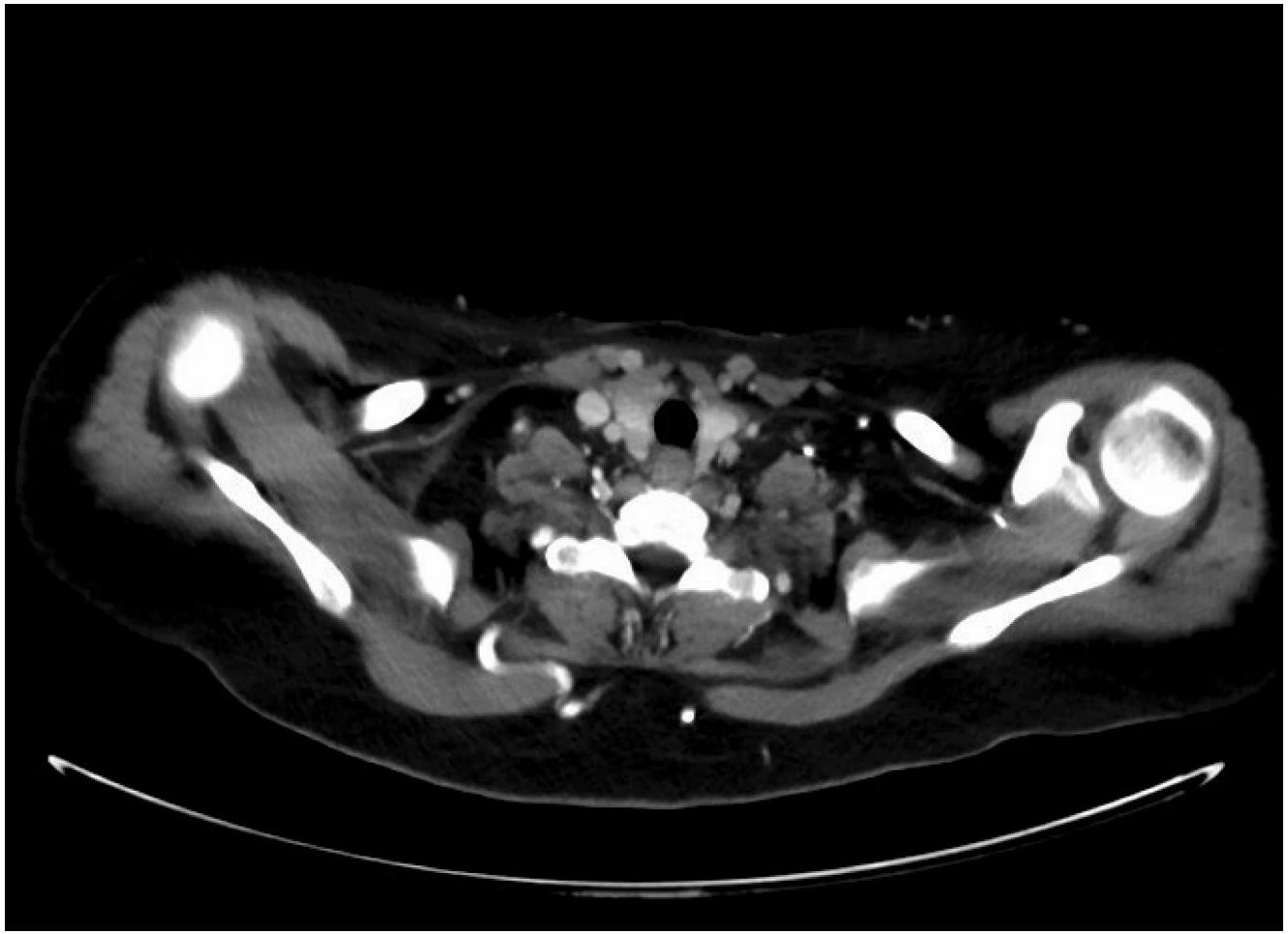
Stage III



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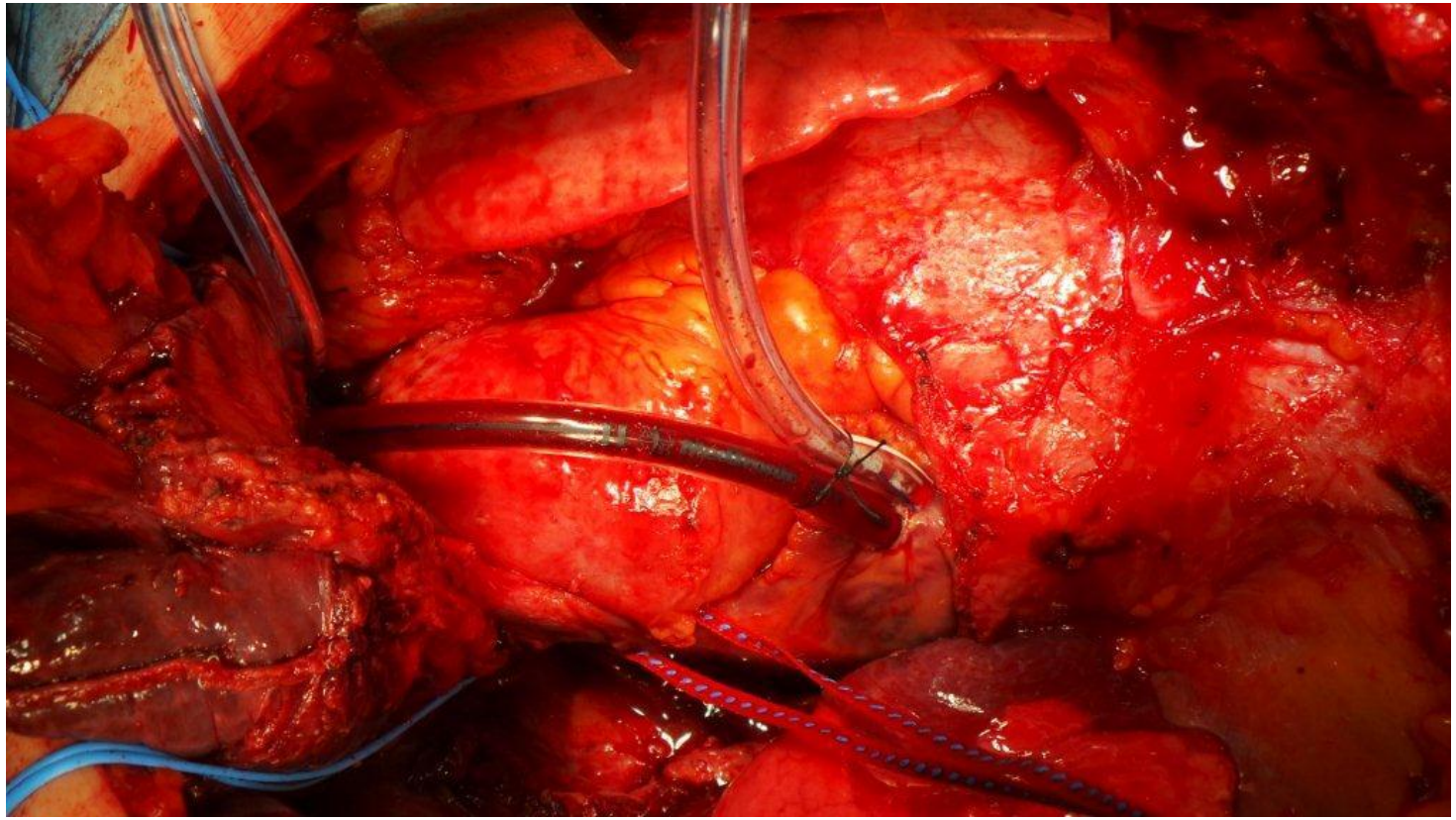
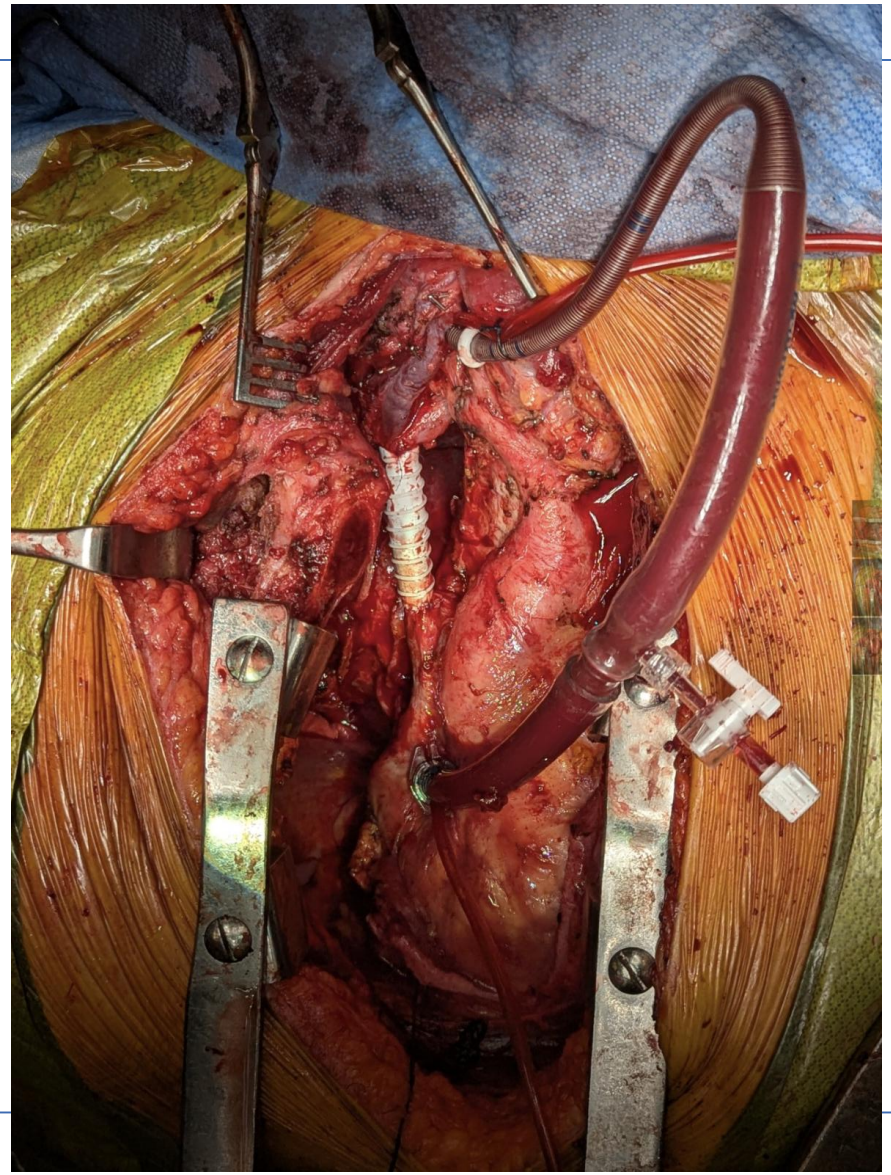
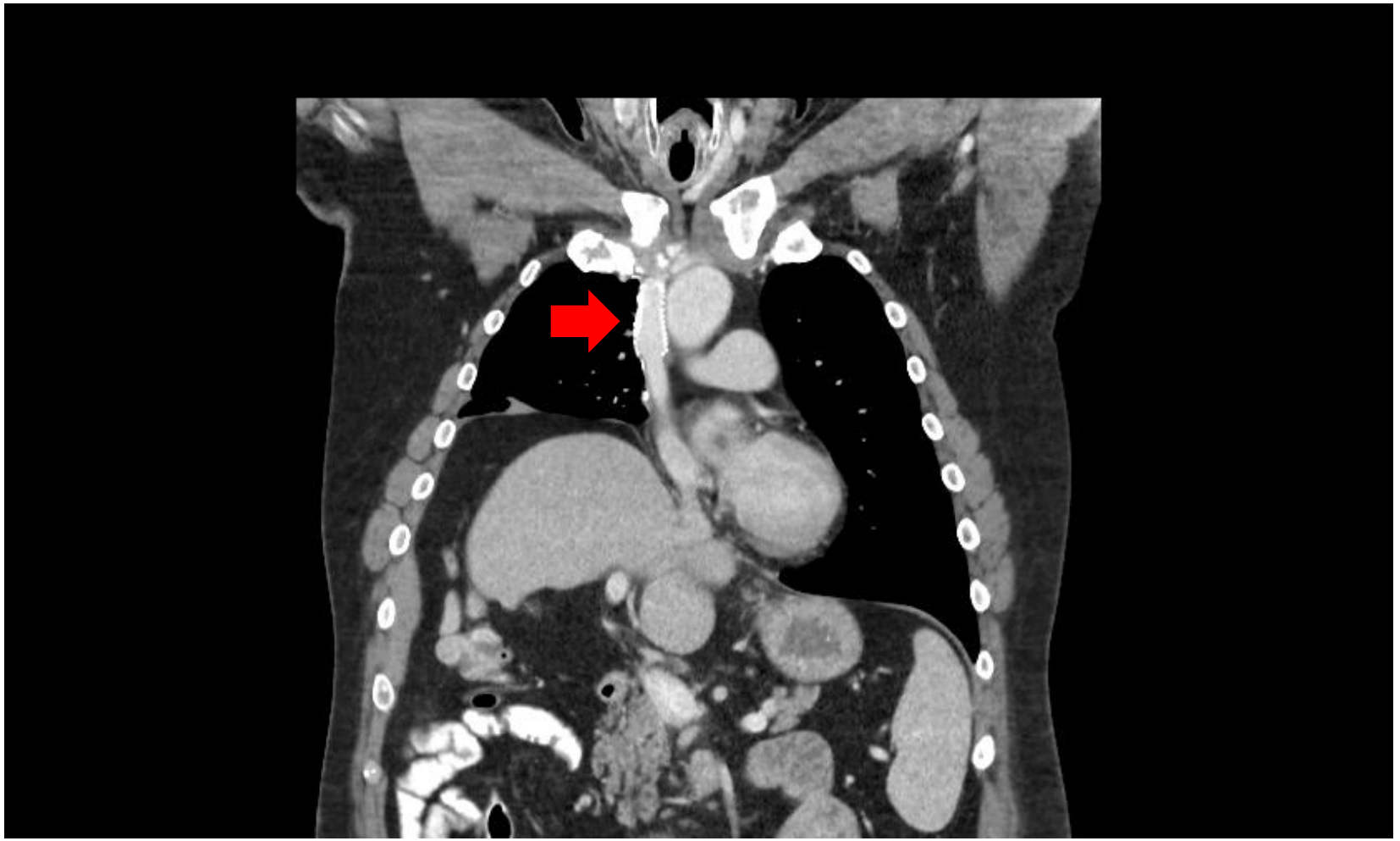
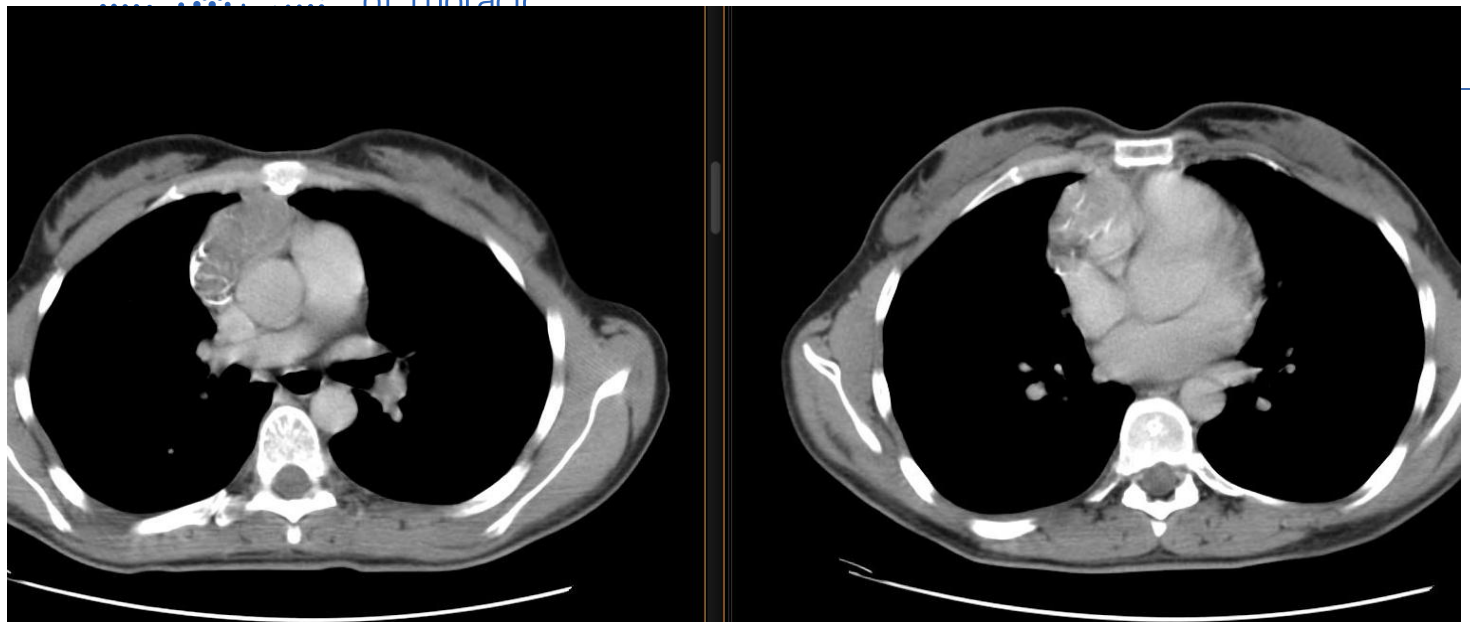


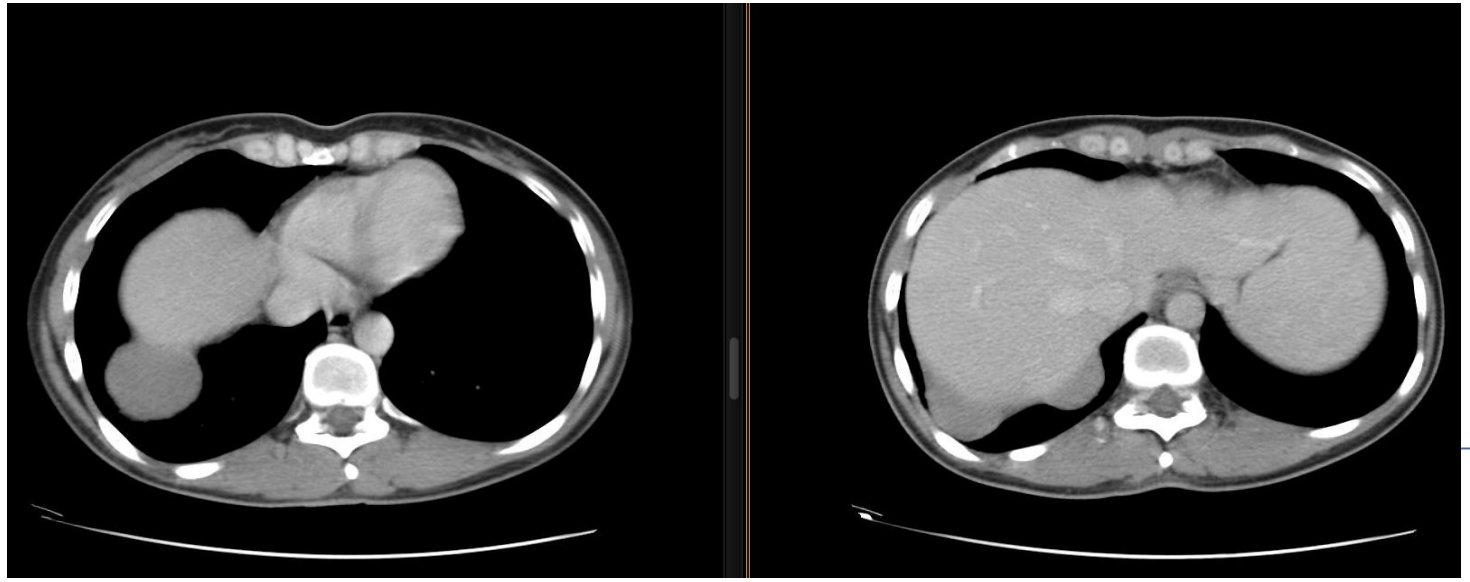


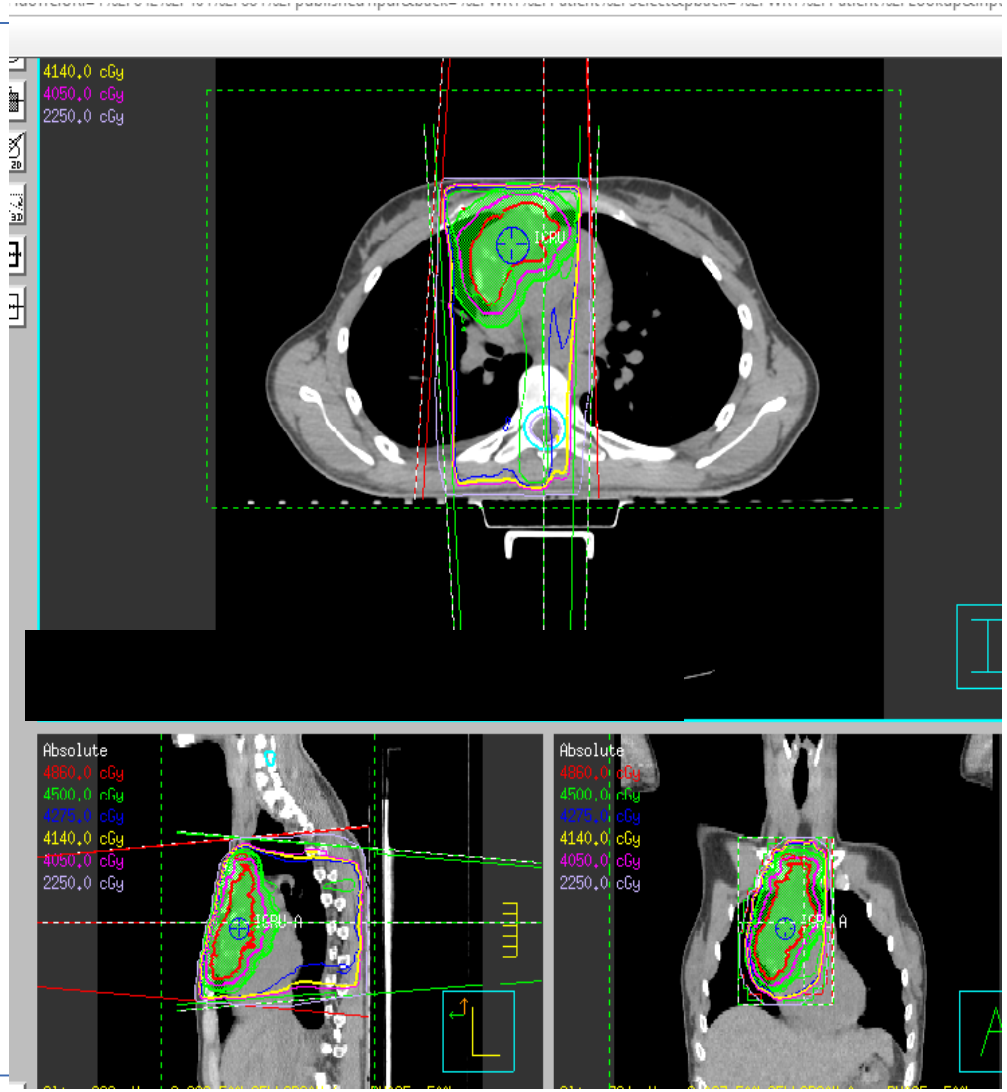


Radiation Therapy

- Incomplete resection
- Masaoka stage (II), III, IV completely resected
- (stage II controversial)
- Describe operative findings in detail in your OR note →helpful in RT decision making
- Mark areas of close margin or concern with clips for radiation therapist
- Advanced stages → decreases recurrence, improves survival






4140.0 cGy
4050.0 cGy
2250.0 cGy
Absolute
4860.0 cGy
4500.0 cGy
4275.0 cGy
4140.0 cGy
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2250.0 cGy
Absolute
4860.0 cGy
4500.0 cGy
4275.0 cGy
4140.0 cGy
4050.0 cGy
2250.0 cGy

Surgical Resection of Thymoma

- Thymomas have a favorable tumour biology → wide surgical excision → survival is measured in decades
- Adverse prognostic factors:
    - Incomplete resection
    - Larger sized tumours (>7 cm)
    - Higher Masaoka Stage (III, IV)
- Can we improve the outcome of this subgroup of patients?

Induction Therapy for Thymoma

- Controversial, heterogeneity of practice
- Appears beneficial (historical comparisons)
- Generally given in advanced (stage III and IV) thymomas (R0 resection rate ~50%)
- Cisplatinum / epirubicin / etoposide: 50-90% response rate
- Tumours > 10cm tend to be invasive, tend to recur – induction to attempt to improve resectability
- Chemo ± RT given in attempt to make an “unresectable” tumour “resectable”

Induction for technically resectable, but concerning features….

- Criteria:
  - Tumour > 8 cm in greatest axial diameter
  - Tumours 5-8cm with ≥1 additional criteria:
    - Irregular scalloped borders
    - Heterogeneous appearance
    - Ectopic calcification
    - Obvious great vessel and /or adjacent organ invasion or encirclement
  - Tumours < 5cm with obvious great vessel and or adjacent organ invasion or encirclement

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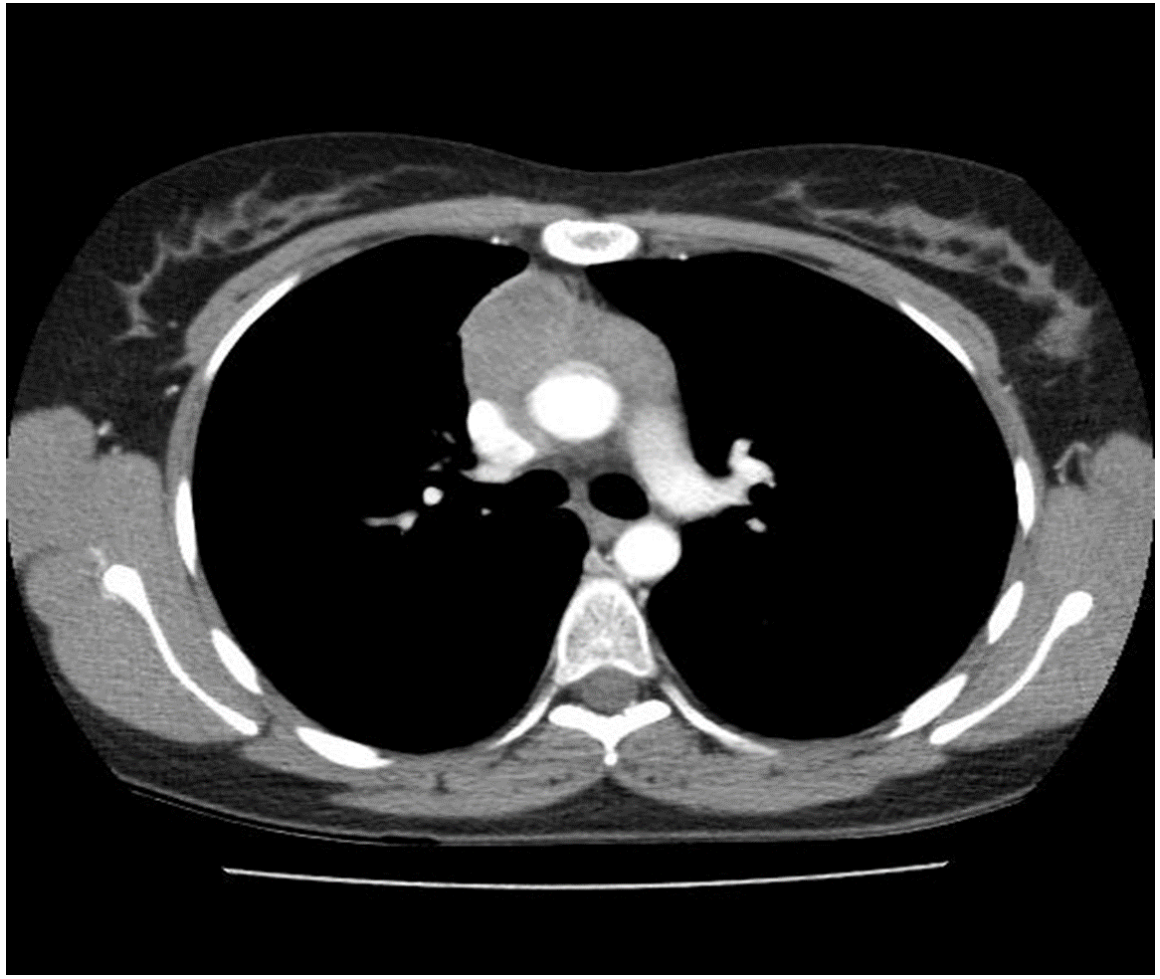
Thymoma with worrisome features



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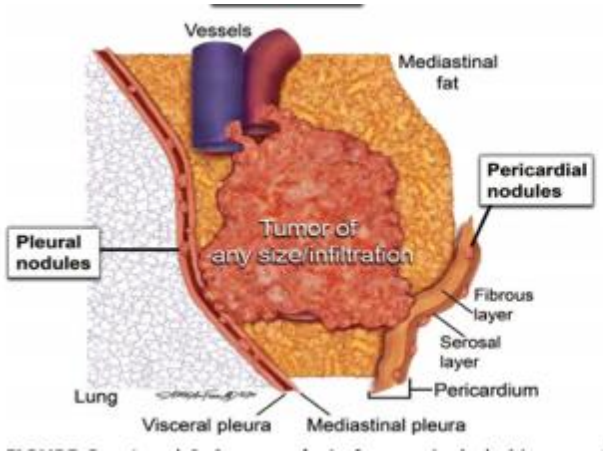
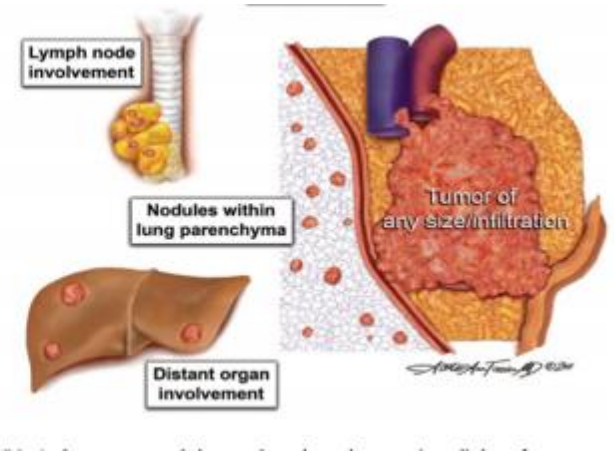
Stage IV Thymoma

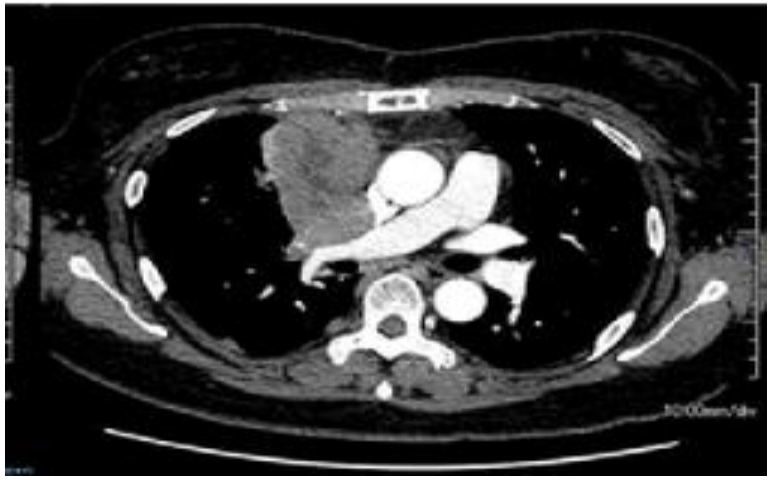
- Pleural and pericardial metastatic deposits
- Poor prognosis
- Role of surgery has been debated
- Indolent disease course
- De novo Stage IVa (vs. Stage IVa at recurrence)



Stage IVa



Stage IVb



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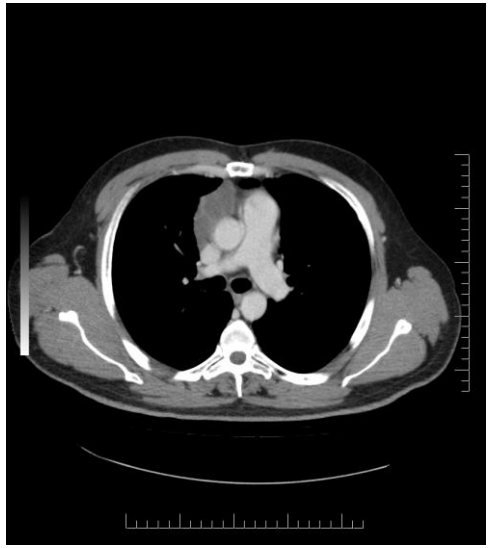
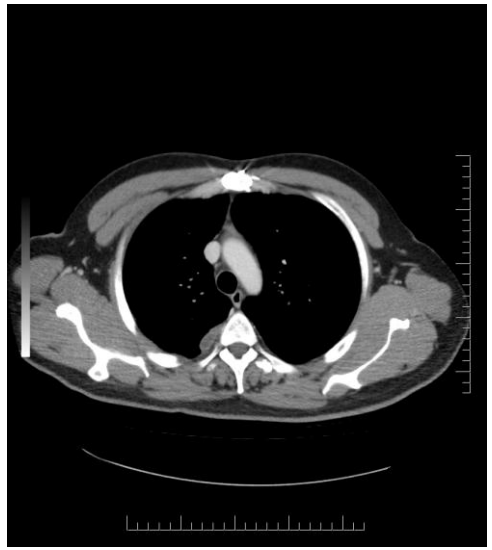
Resection of Stage IVa Thymoma

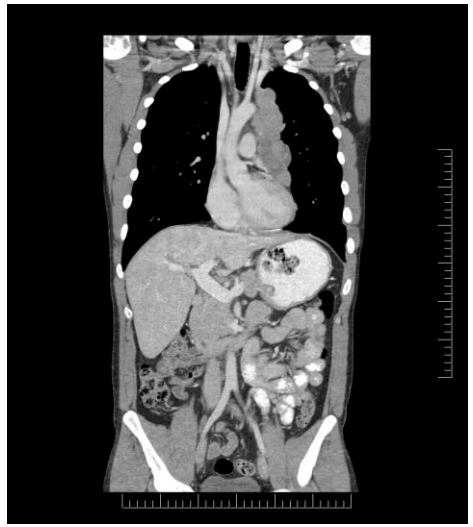


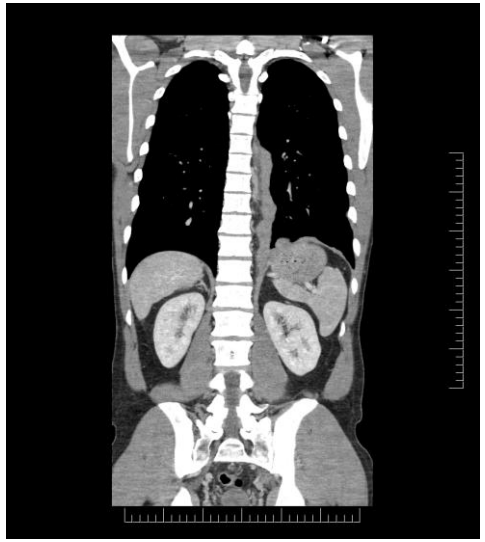


At presentation or recurrence…

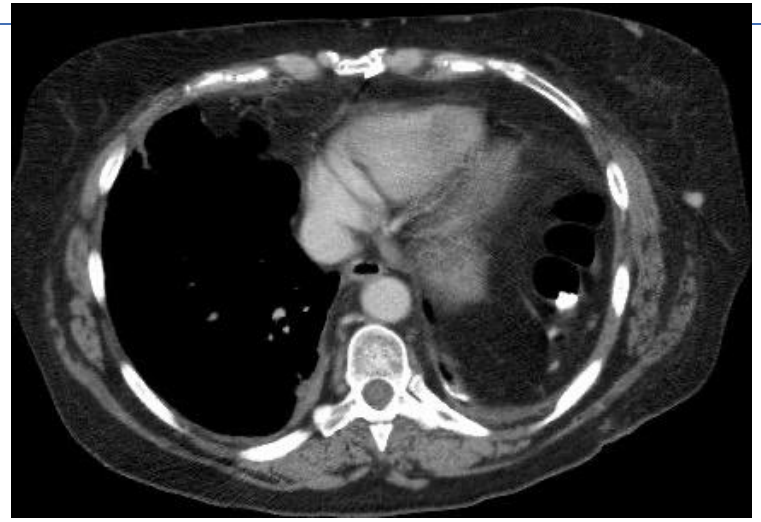
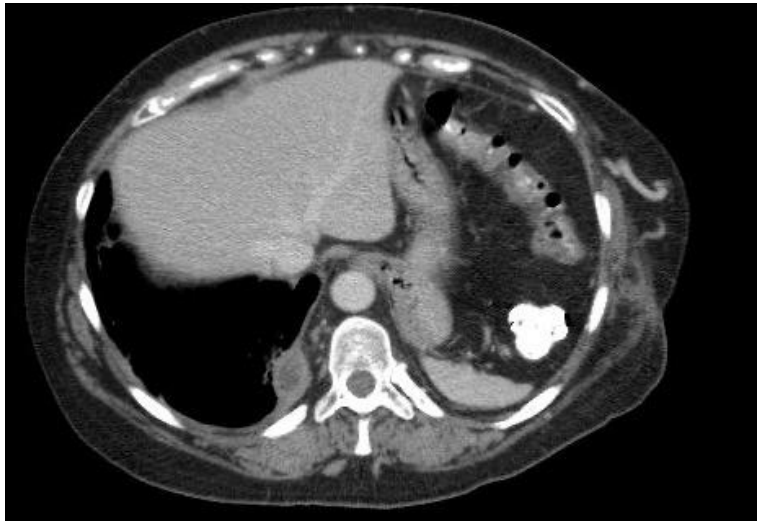
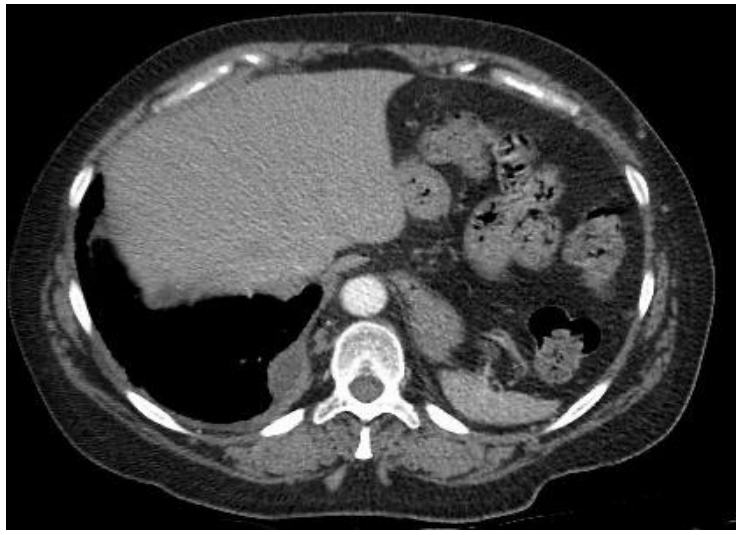
Stage IV Thymoma – Extensive Disease









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Case Presentation



- 61 yo. female
- Previously healthy
- Mild shortness of breath while playing tennis
- CXR
- 2019

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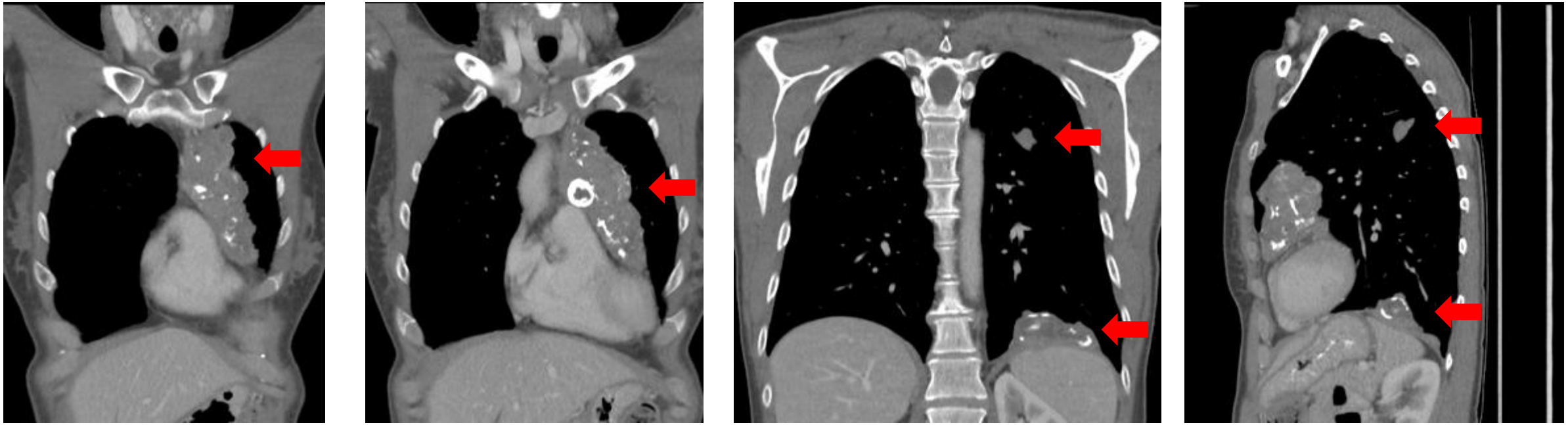
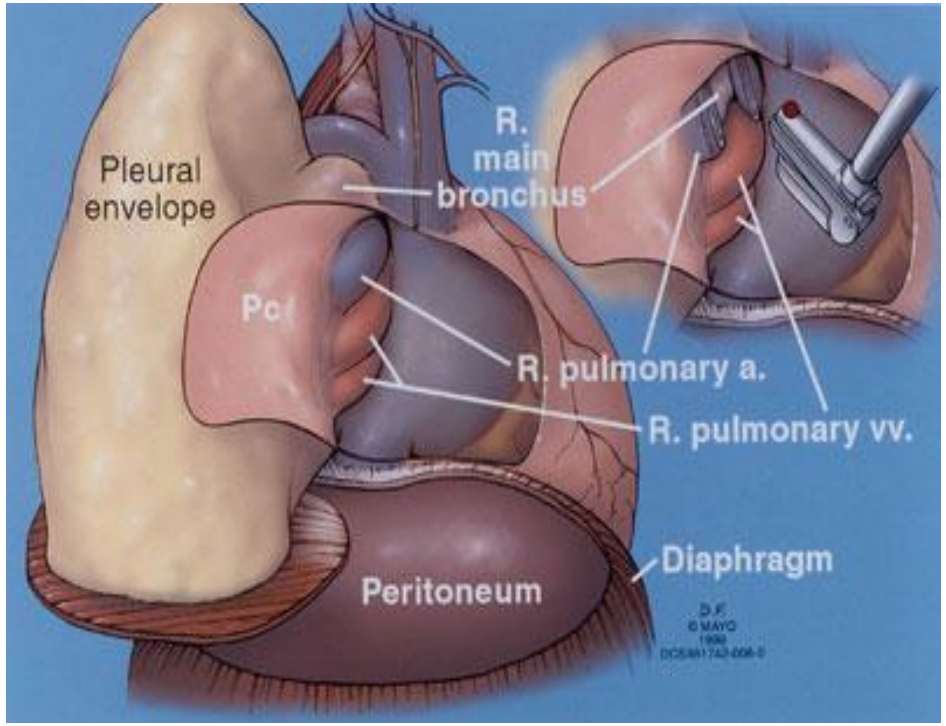
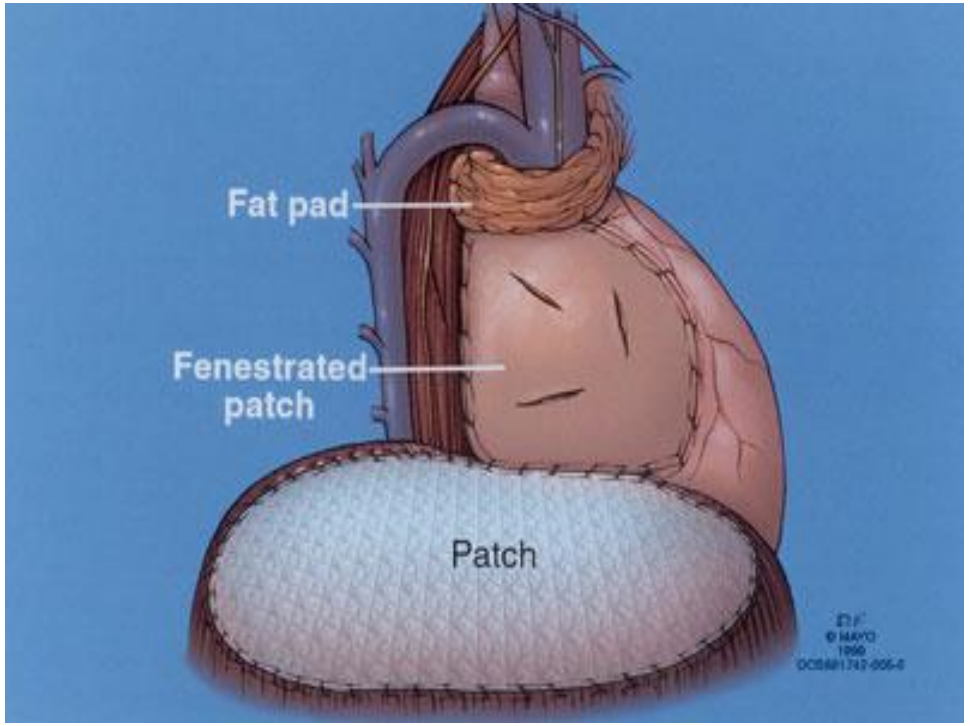
Case Presentation 2019



WHO Type B1/B2 Stage IVb Thymoma

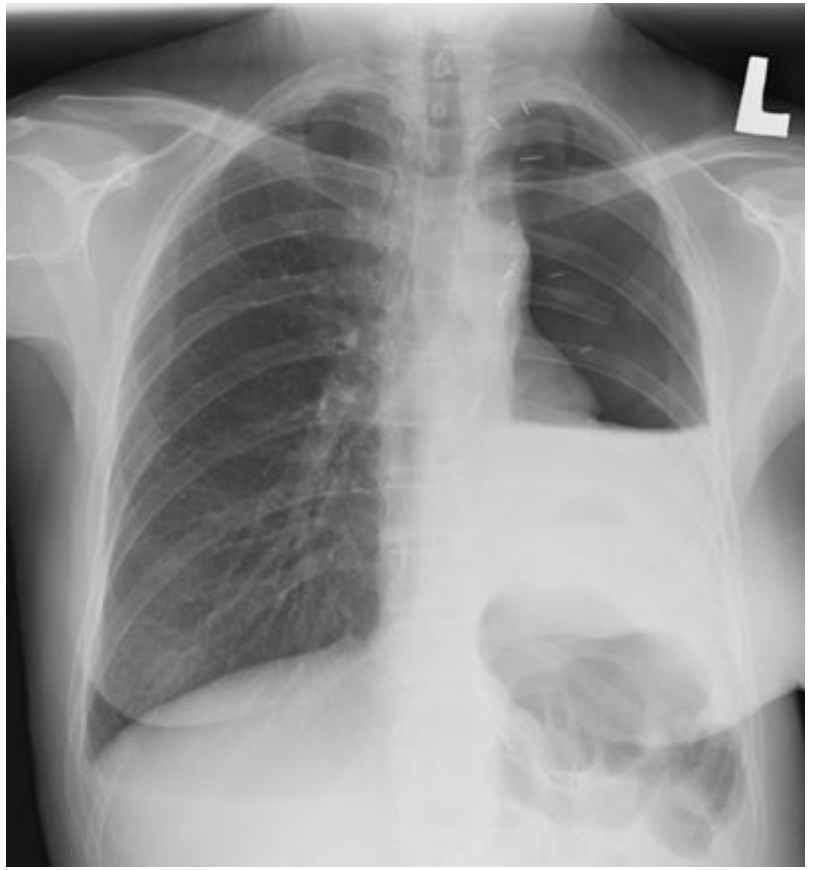
Extrapleural Pneumonectomy





Case Presentation: Treatment

- Induction chemotherapy
- CAP (3 courses)
- Minimal response
- Extrapleural Pneumonectomy
- Adjuvant hemi-thoracic Radiation



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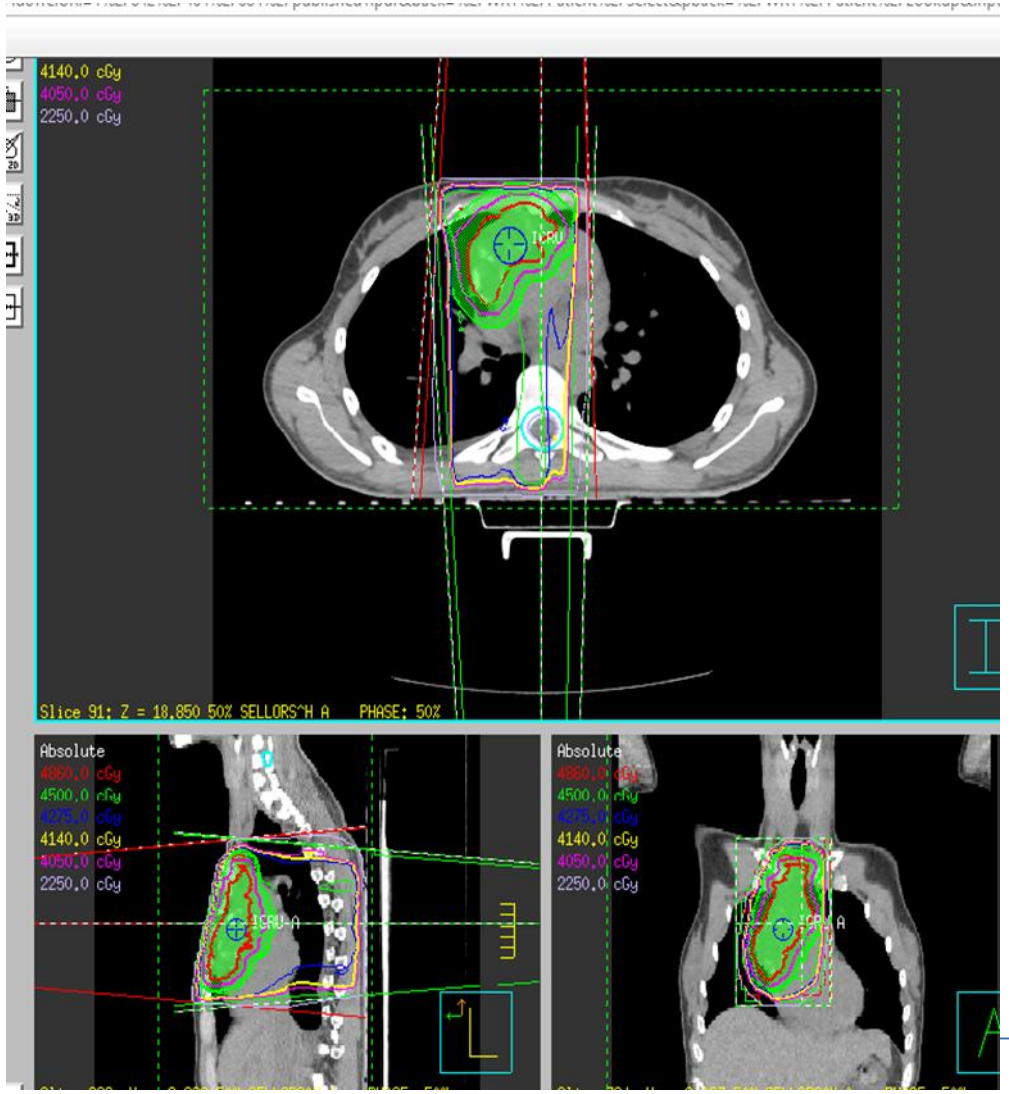

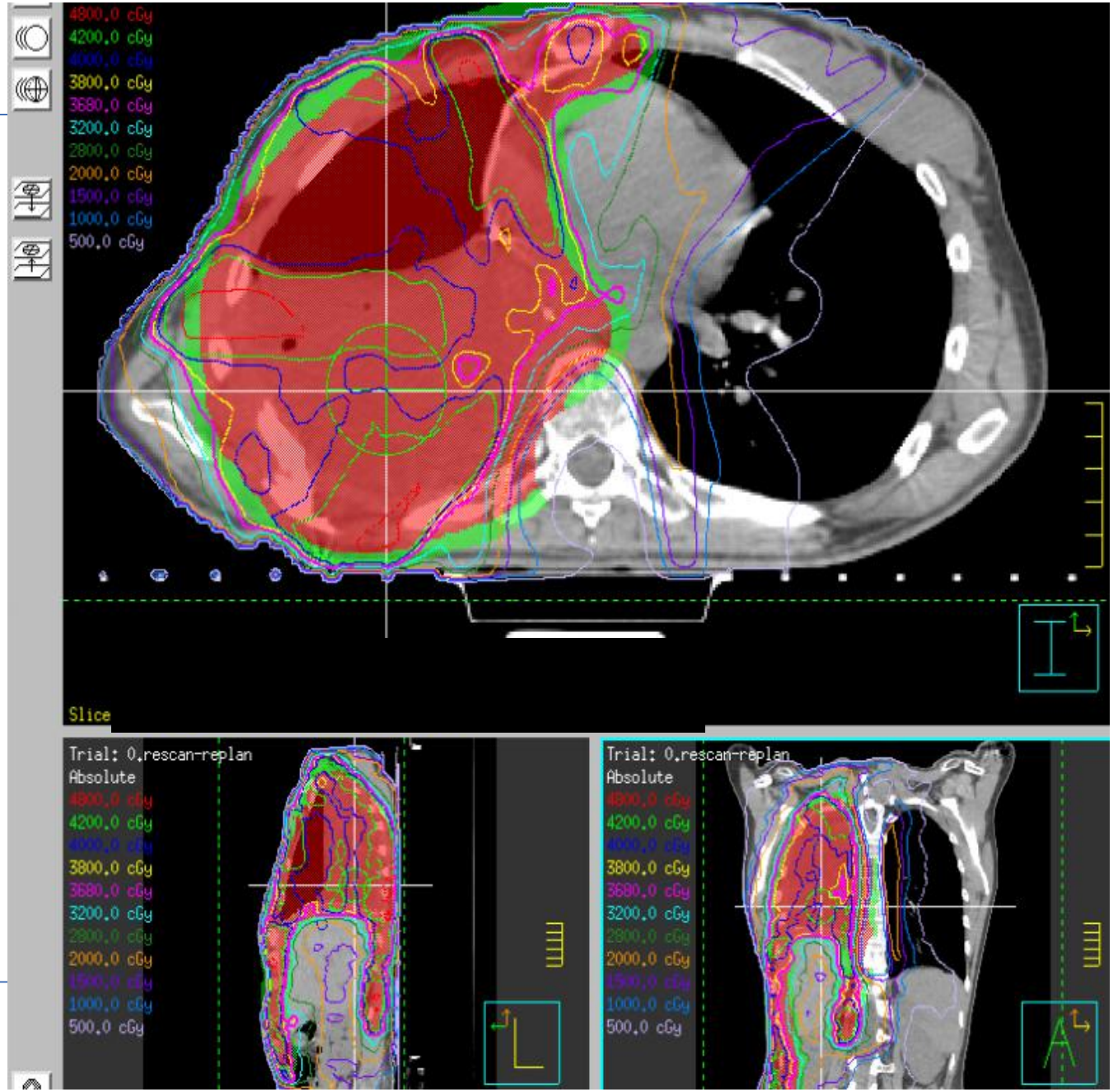

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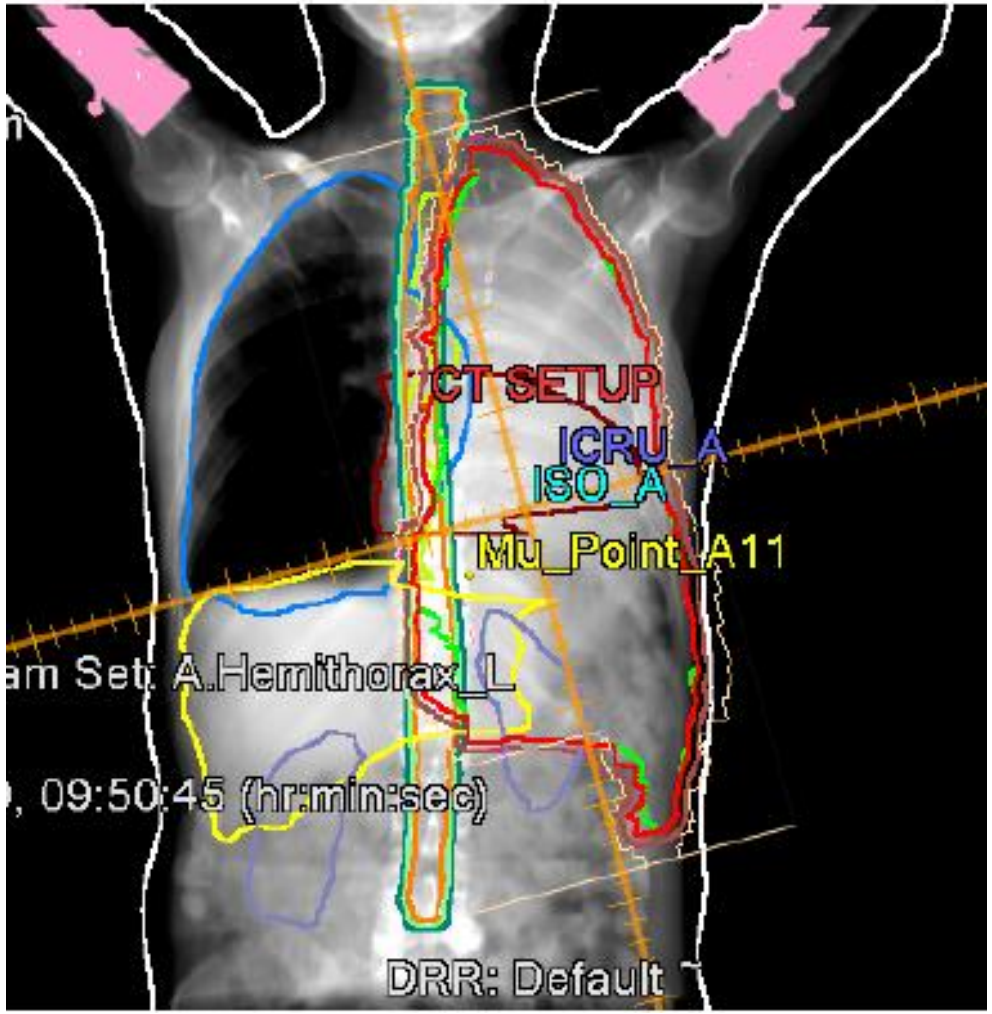
Treatment =
Chemotherapy
CAP x 3

Extrapleural pneumonectomy
ypT3N0M1b

Hemithoracic RT
50Gy/25 fr, IMRT



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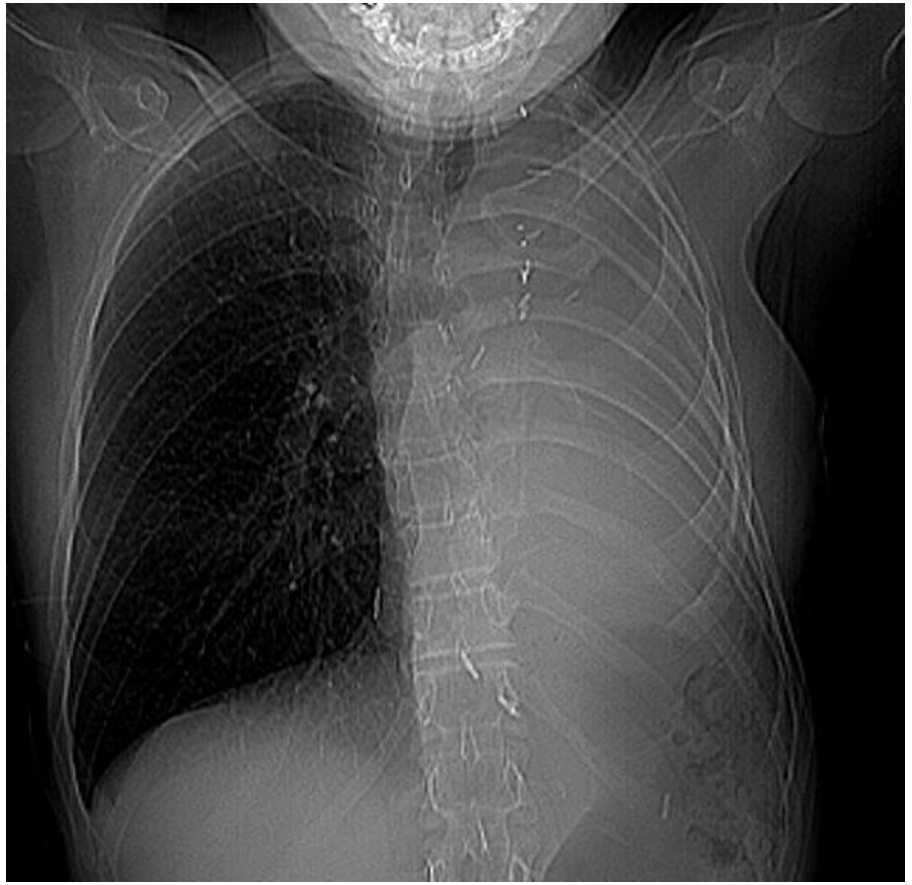
2026…7 years later, well NED





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Stage IVa Thymoma: UHN Experience

- Adult patients undergoing resection (n=122)
- Resected between 1990 to 2018
- All patients with locally advanced and recurrent thymoma and thymic carcinoma
- Recurrences of any Masaoka stage
- Diagnoses of Masaoka IVa/IVb

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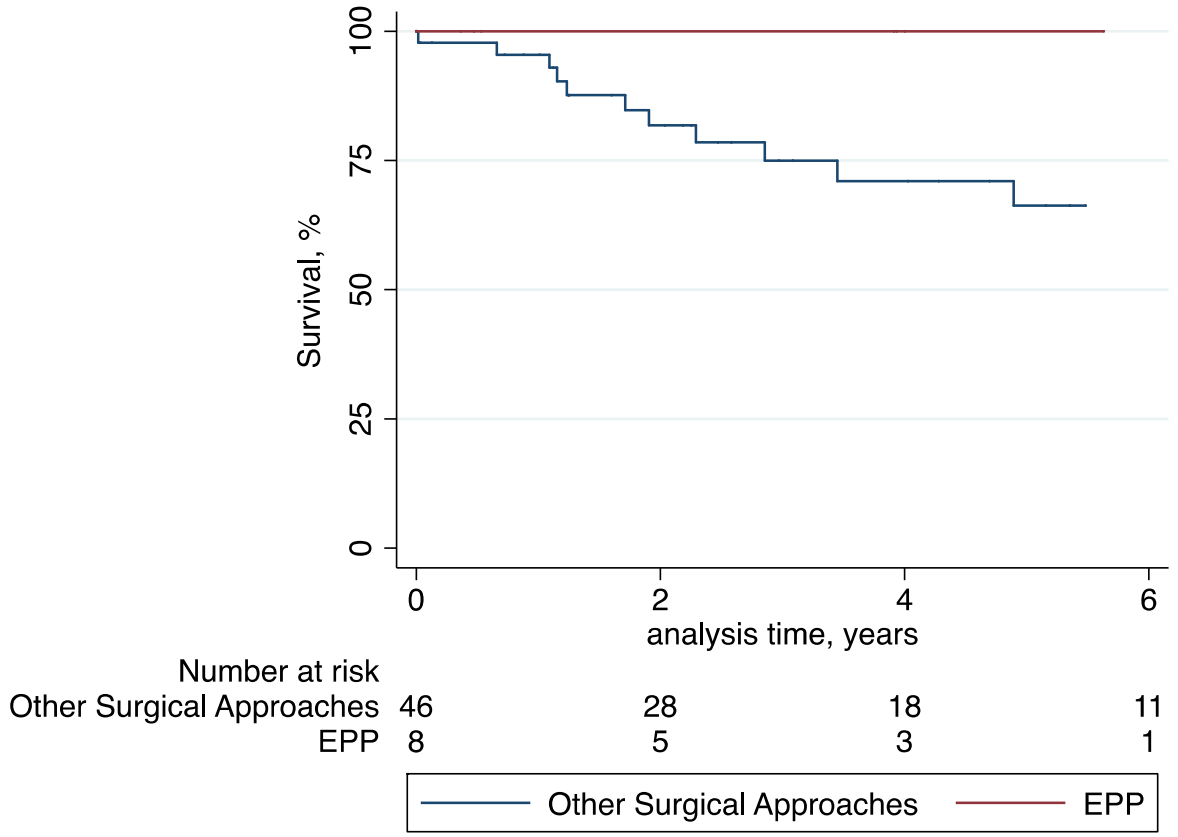
EPP vs. Other Surgical Resection Stage IVa

- EPP (n=8)
- Other resections: pleural resection/pleurectomy (n=46)



RT Considerations for stage IV thymoma

- Primary Tumor
- Long term control often achievable and likely worthwhile
- Any RT given may impact future RT considerations

- Control of Pleural Metastases
- more challenging – what are the goals?
- Control of the current pleural metastasis? SBRT
- Prevention of future metastases? EPP + hemithoracic RT

Surgery for Stage IV Thymoma: Summary

Resection



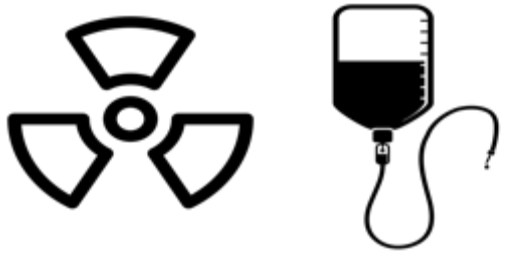
- Long Term and DFS achievable with aggressive surgery
- IV at presentation vs. recurrent

Prognostic Factors



- Complete resection
- Role of lymphadenectomy?
- Role of EPP

Adjuvant and Neoadjuvant Treatment



- Role of Adjuvant vs. Neoadjuvant Radiation

Take Home Messages

- Rare tumors - experience matters
- Multidisciplinary approach is essential
    - Thoracic Surgeon, Medical Oncologist, Radiation Oncologist
    - Also includes neurologists, immunologists, nurses, therapists, many other members of our teams
- Long term survival should be the goal

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DOTS: Division of Thoracic Surgery, Toronto General Hospital, University of Toronto



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