

# *ARROCase*

# Esophageal Cancer

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# Case: Clinical Presentation

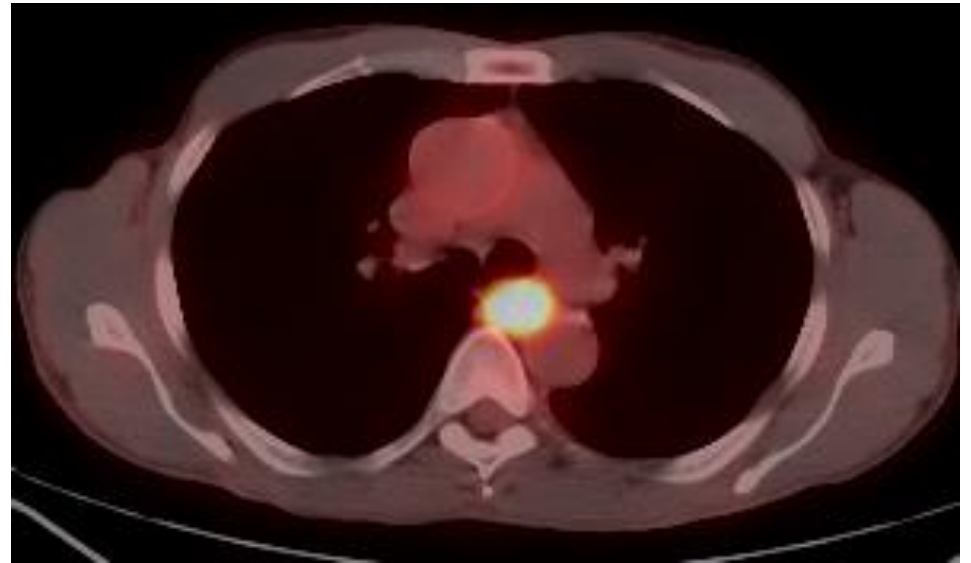
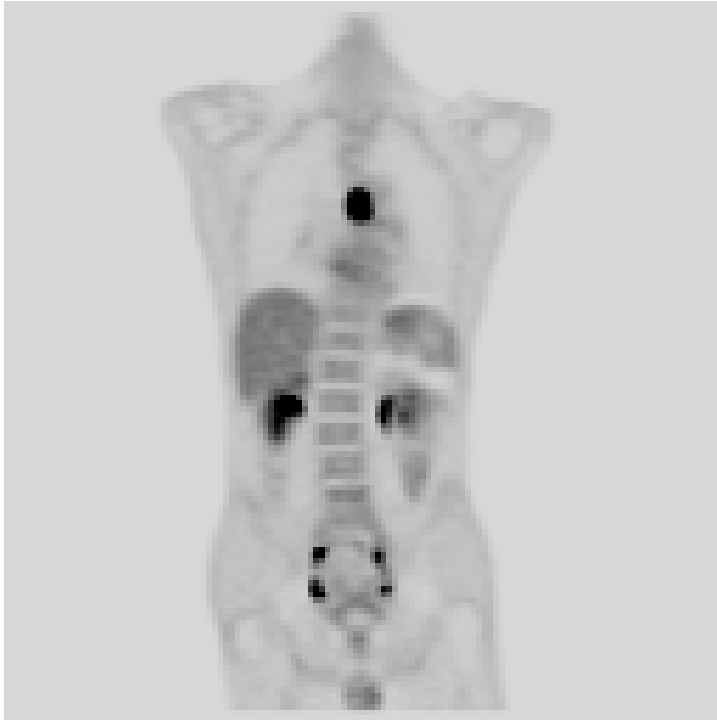
- 58 y/o male with 3 month history of dysphagia initially to solids, progressing to liquids
- Odynophagia
- Vague mid-chest discomfort
- 15 pound weight loss over the past 3 months
- Denies vomiting or regurgitation of food
- Denies cough/SOB
- KPS 80

# Work-Up: Upper Endoscopy

- Large, friable, malignant-appearing mass noted spanning 25-31 cm from the incisors
- Occupying 50-60% of the lumen
- Remainder of endoscopic exam including stomach and duodenum were normal
- Biopsy was obtained, revealing moderately differentiated squamous cell carcinoma

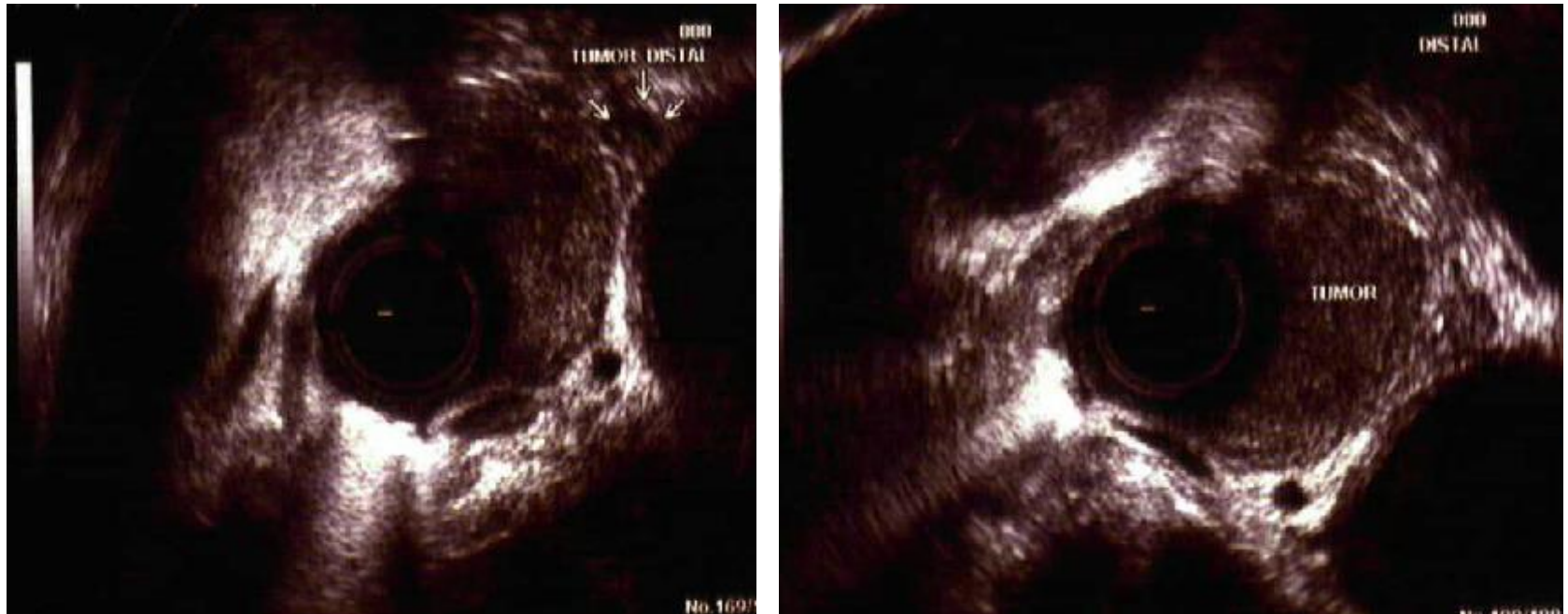


# Work-Up: PET/CT Scan



- Large area of FDG avid wall thickening seen in mid esophagus, with a maximal SUV of 12.7
- No FDG avid lymphadenopathy is identified to suggest metastatic disease
- The distribution of the FDG is otherwise within physiological limits

# Work-Up: Endoscopic Ultrasound



- Hypoechoic lesion extending through the muscularis propria
- No abnormal lymphadenopathy was noted, confirming the lesion to be **T3 N0**
- No frank invasion into the surrounding structures was noted

# Epidemiology

- Two distinct histopathologic types: squamous cell carcinoma and adenocarcinoma
- Relatively uncommon in the US
- Lifetime risk of being diagnosed with the disease is less than 1%
- 18,170 new cases in 2014
- 15,450 patients expected to die of the disease

# Risk Factors

- Tylosis
- Plummer-Vinson Syndrome
- Caustic injury
- HPV (SCC)
- Tobacco
- Alcohol
  - 90% of SCC in Western Europe and North America can be attributed to tobacco and alcohol use
- Obesity, GERD, Barrett's Esophagus (adenoca)
- Raw fruits and vegetables are protective

# Anatomy

- Cervical esophagus
  - Cricopharyngeus to the thoracic inlet
  - 15-18 cm from the incisors
- Upper third
  - Thoracic inlet to the carina
  - 18-24 cm from the incisors
- Middle third
  - Carina to the inferior pulmonary veins
  - 24-32 cm from the incisors
- Lower third
  - Traversing the remaining distance to the GE junction
  - 32-40 cm from the incisors



# Lymphatic Drainage

- Rich mucosal and submucosal lymphatic system which may extend long distances (reason why proximal/distal margins used for radiation planning have traditionally been a minimum of 5 cm)
- Submucosal plexus drains into internal jugular, peritracheal, hilar, subcarinal, periesophageal, periaortic, and pericardial lesser curvature lymph nodes
- Left gastric and celiac nodes for lower third lesions

# Histology

- Squamous cell carcinomas
  - Majority of cases throughout the world
  - 40% of esophageal cancer in the US
  - 70% in the proximal and middle third
- Adenocarcinoma
  - Frequently arise in the context of Barrett's esophagus
  - Mainly occur in the distal third of the esophagus
  - Rate of adenocarcinoma rising in US (obesity & GERD)
- No significant survival differences have been noted between various histologies

# Clinical Presentation

- Dysphagia
  - Most common
  - Initially to solids, then progressing to liquids
  - Large impact on QOL
- Odynophagia
- Weight loss (Anorexia)
- Pain
- Cough/Hoarseness (Recurrent laryngeal nerve)
- Vomiting

# Diagnosis/Work-Up

- Upper endoscopy - allows for biopsy and diagnosis
- Bronchoscopy in patients with tumors above the level of the carina
- Barium esophagram (optional) – can identify a tracheoesophageal fistula
- CT chest and abdomen – can identify extension beyond the esophageal wall, enlarged lymph nodes, and visceral metastases
- For cervical primaries, a neck CT should be performed to evaluate for cervical lymph node involvement
- Endoscopic ultrasound – highly accurate in determining depth of invasion as well as lymph node involvement
- FDG-PET scan for staging and response to pre-operative treatment

# TNM Staging, AJCC 7<sup>th</sup> Edition

## Primary Tumor

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	High-grade dysplasia
T1	Tumor invades lamina propria, muscularis mucosae, or submucosa
T1a	Tumor invades lamina propria or muscularis mucosae
T1b	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades adventitia
T4	Tumor invades adjacent structures
T4a	Resectable tumor invading pleura, pericardium, or diaphragm
T4b	Unresectable tumor invading other adjacent structures, such as aorta, vertebral body, trachea

## Regional Lymph Nodes

Nx	Regional nodes not assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1-2 regional lymph nodes*
N2	Metastasis in 3-6 regional lymph nodes*
N3	Metastasis in 7 or more regional lymph nodes*

## Distant Metastasis

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

\*Regional lymph nodes extend from cervical nodes to celiac nodes.

# Group Staging, AJCC 7<sup>th</sup> Edition

## Adenocarcinoma

Stage 0	Tis, N0, M0, grade 1 or X
Stage IA	T1, N0, M0, grade 1-2 or X
Stage IB	T1, N0, M0, grade 3
	T2, N0, M0, grade 1-2 or X
Stage IIA	T2, N0, M0, grade 3
Stage IIB	T3, N0, M0, any grade
	T1-2, N1, M0, any grade
Stage IIIA	T1-2, N2, M0, any grade
	T3, N1, M0, any grade
	T4a, N0, M0, any grade
Stage IIIB	T3, N2, M0, any grade
Stage IIIC	T4a, N1-2, M0, any grade
	T4b, any N, M0, any grade
	Any T, N3, M0, any grade
Stage IV	Any T, any N, M1, any grade

## Squamous Cell Carcinoma

Stage 0	Tis, N0, M0, grade 1 or X, any location
Stage IA	T1, N0, M0, grade 1 or X, any location
Stage IB	T1, N0, M0, grade 2 or 3, any location
	T2-3, N0, M0, grade 1 or X, lower esophagus or X
Stage IIA	T2-3, N0, M0, grade 1 or X, upper and middle esophagus
	T2-3, N0, M0, grade 2 or 3, lower esophagus or X
Stage IIB	T2-3, N0, M0, grade 2 or 3, upper and middle esophagus
	T1-2, N1, M0, any grade, any location
Stage IIIA	T1-2, N2, M0, any grade, any location
	T3, N1, M0, any grade, any location
	T4a, N0, M0, any grade, any location
Stage IIIB	T3, N2, M0, any grade, any location
Stage IIIC	T4a, N1-2, M0, any grade, any location
	T4b, any N, M0, any grade, any location
	Any T, N3, M0, any grade, any location
Stage IV	Any T, any N, M1, any grade, any location

# Treatment: T1 Disease (Localized to the Mucosa)

- Little or no risk of lymph node metastases
- T1a (lamina propria or muscularis mucosa)
  - Endoscopic mucosal resection followed by ablation (preferred)
  - Esophagectomy
- T1b (Invades submucosa)
  - Esophagectomy

# Treatment: Locally Advanced Disease (Resectable)

- T1bN+, T2-T4aN0-N+
  - Trimodality therapy with neoadjuvant chemoradiotherapy (CRT) followed by surgical resection
- RT dose 41.4 - 50.4 Gy in 1.8 Gy daily fractions
  - No utility in dose escalation
    - RTOG 94-05 (Minsky et al) 50.4 v. 64.8 Gy (w/ cis/5-FU)
    - Closed after interim analysis showed no probability of superiority in the high-dose arm
- Multiagent chemotherapy with cisplatin and 5-FU or paclitaxel and carboplatin typically used



# CROSS Trial

- Preoperative Chemoradiotherapy for Esophageal or Junctional Cancer
- 366 patients w/ T1N1 or T2-3N0 GE junction or esophageal cancer
- Randomized
  - Preoperative CRT (41.4 Gy & Carboplatin/Paclitaxel) followed surgery
  - Surgery alone

# CROSS Trial Results

- R0 resection
  - 92% in CRT v. 69% in surgery arm ( $p < 0.001$ )
- pCR (ypT0N0)
  - 29% CRT arm
  - 28% in adenoca v. 49% in SCC ( $p = 0.008$ )
- +LN in resection specimen
  - 31% (CRT) v. 75% ( $p < 0.001$ )
- Median OS
  - 49 months (CRT) v. 24 months ( $p = 0.003$ )
- Overall Survival (5-year)
  - 47% (CRT) v. 34%

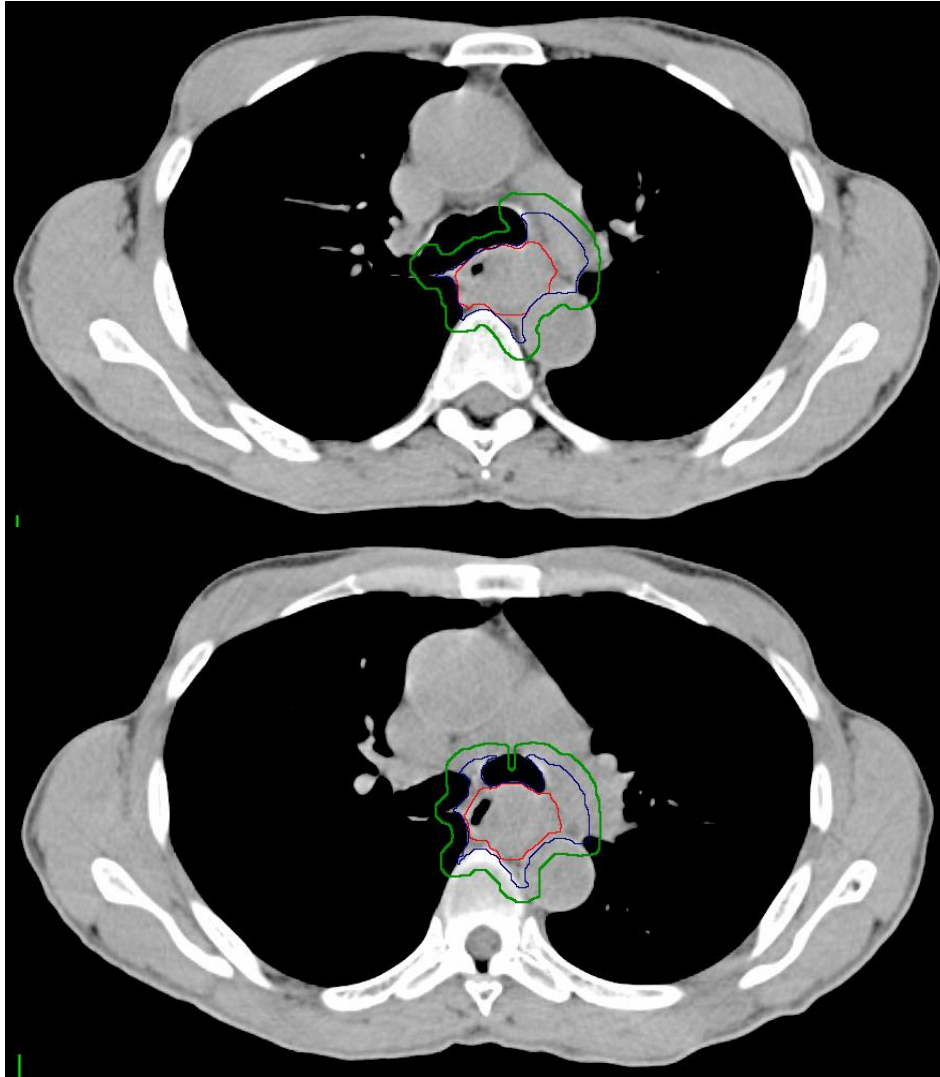
# Treatment Planning

- CT Simulation
  - IV and/or esophageal contrast may be used to aid in target localization
  - Arms above head to maximize number of beam arrangements
  - Immobilization cradle
  - Consider 4D-CT for GE junction tumors

# Target Volumes (RTOG 1010)

- GTVp: primary tumor in the esophagus
- GTVn: grossly involved regional lymph nodes
- CTV = GTVp with a 4 cm expansion sup/inf along the length of the esophagus and gastric cardia and a 1.0-1.5 cm radial expansion plus the GTVn with a 1.0-1.5 cm expansion in all dimensions
- The celiac axis should be covered for tumors of the distal esophagus or GE junction
- PTV (45Gy) expansion should be 0.5 to 1.0 cm and does not need to be uniform in all dimensions
- Boost PTV (50.4Gy) = GTVp and GTVn with an expansion of 0.5 to 1.0 cm

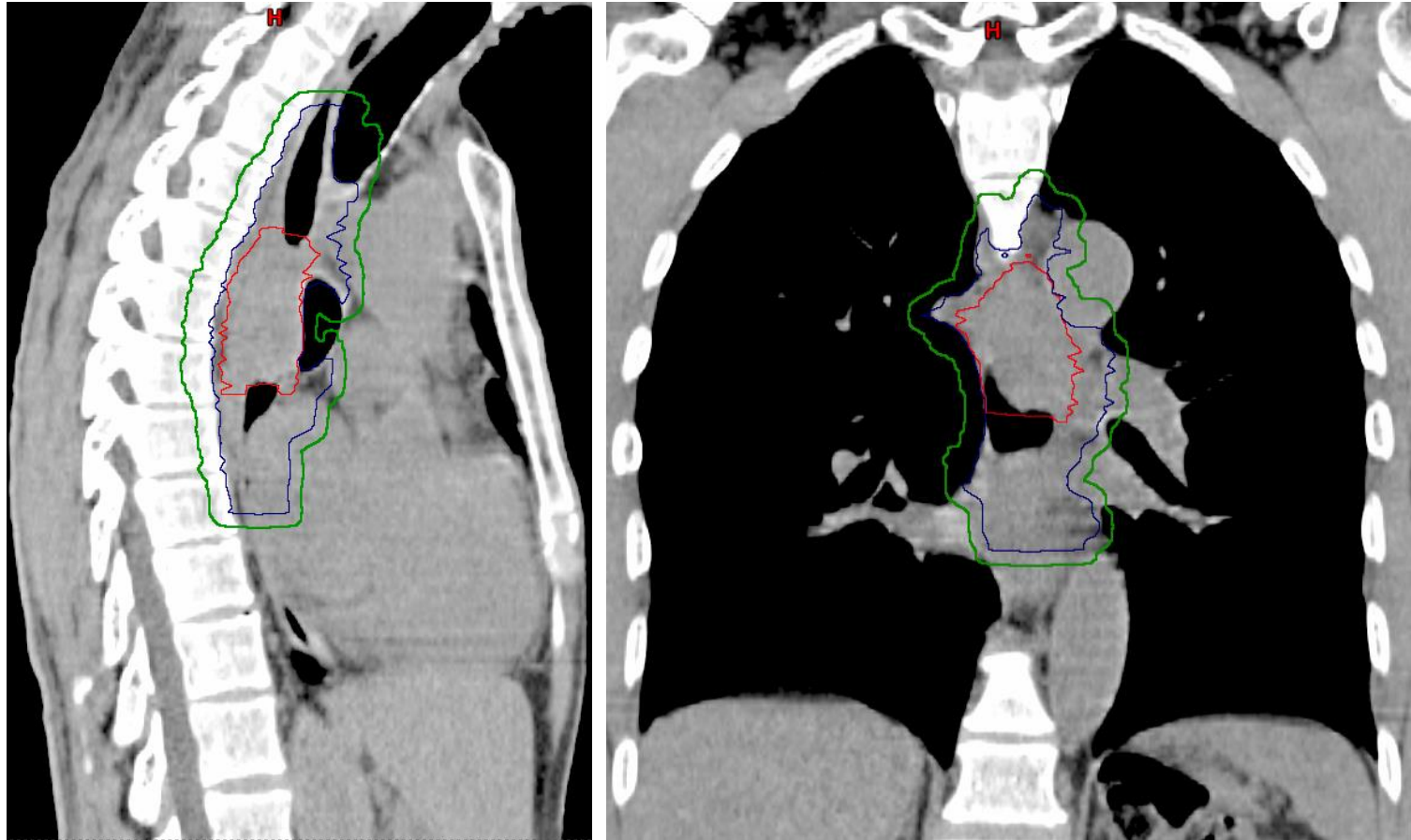
# Target Volumes



- GTV
- CTV
  - Cropped off anatomic structures in which invasion is not likely (i.e. vertebrae, trachea/bronchi, aorta, lung)
- PTV

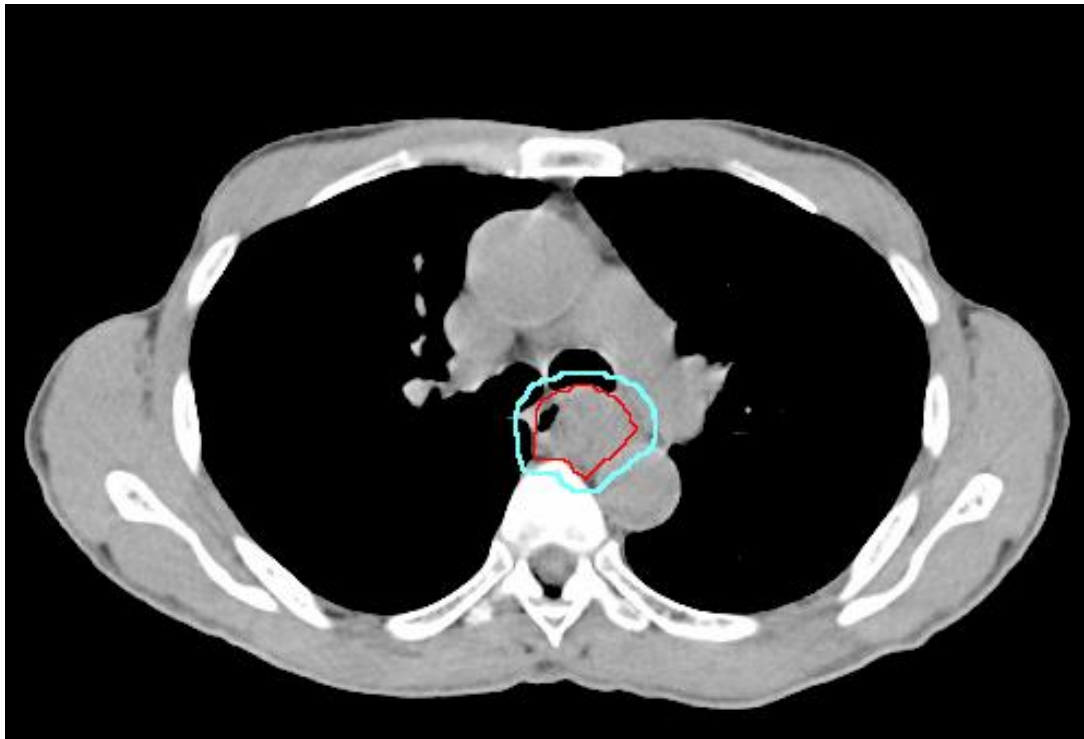
# Target Volumes

- GTV
- CTV
- PTV  
(45Gy)



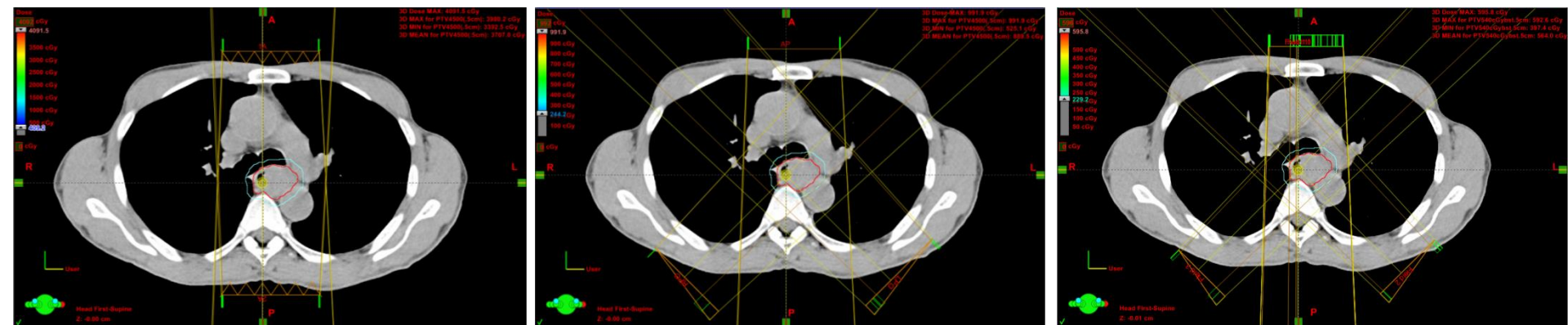
# Boost Volumes

- Boost PTV (50.4Gy) = GTV with an expansion of 0.5 to 1.0 cm



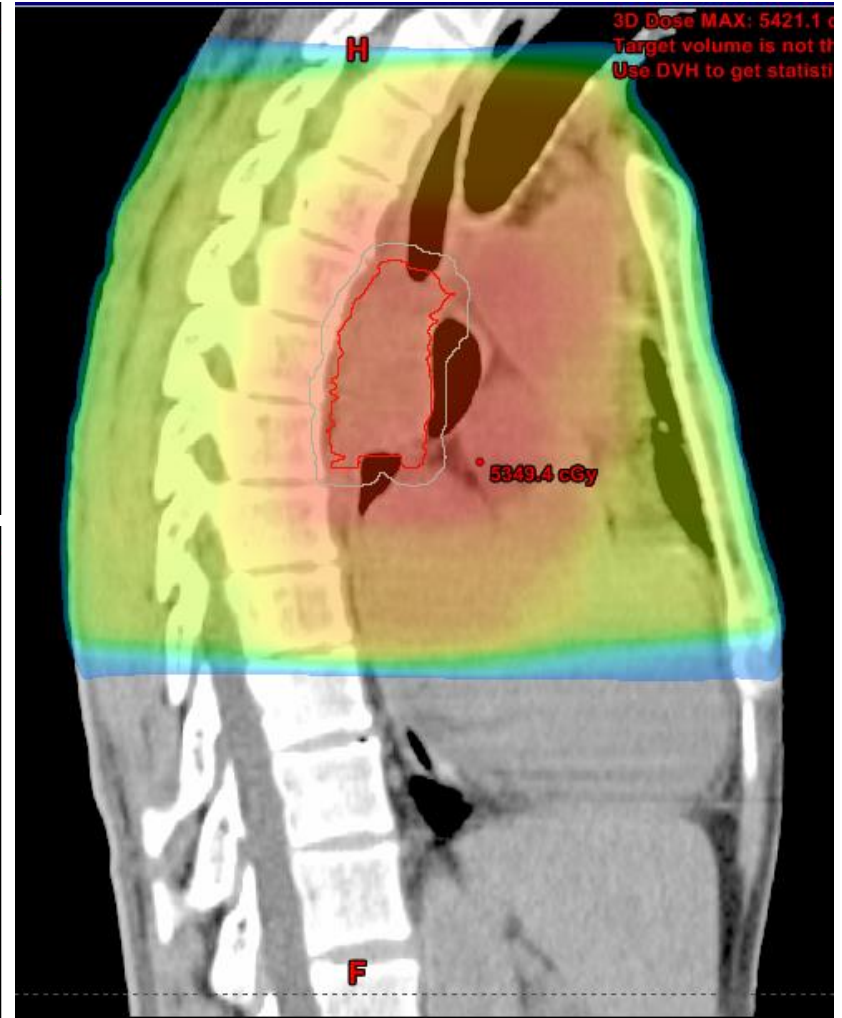
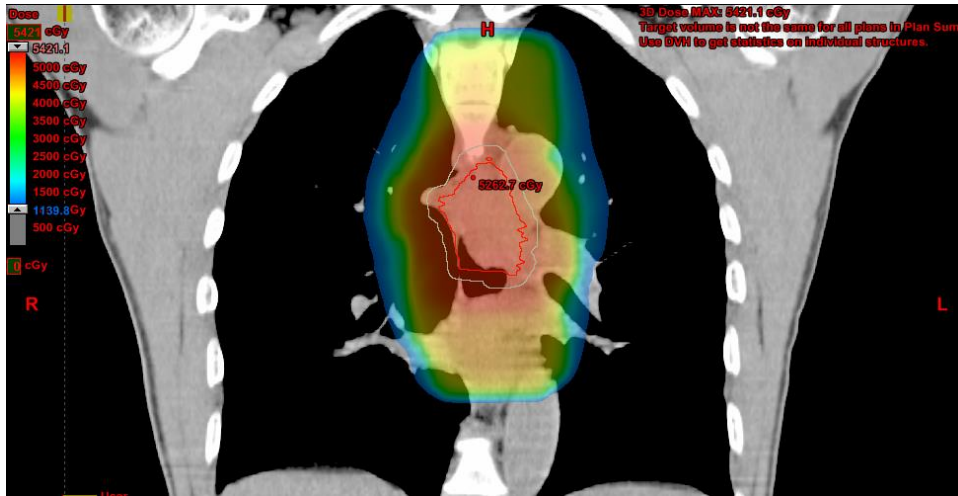
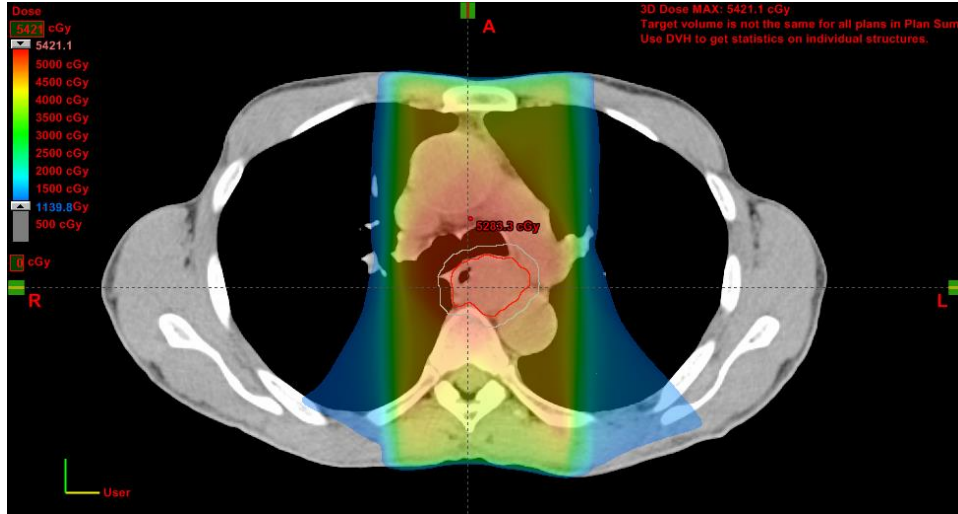
# Treatment Plan

- 3D-CRT with daily CBCT
- AP/PA to 36 Gy followed by 3-field boost to 45 Gy
- Additional cone down (Boost PTV) to 50.4 Gy
- Concurrent chemotherapy with carbo/taxol





# Plan Sum

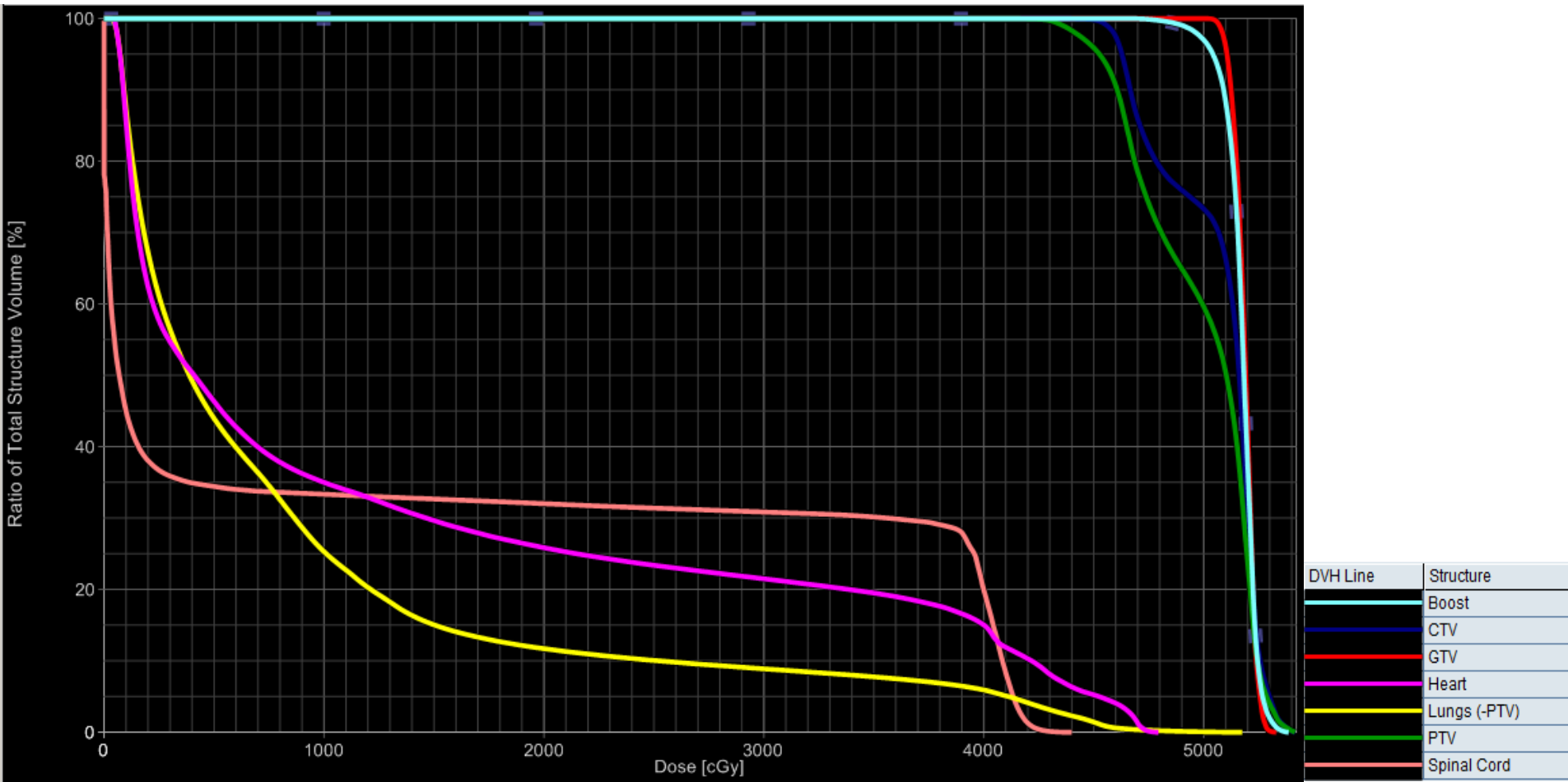


# Dose Constraints (RTOG 1010)

Structure	Metric	Per Protocol	Acceptable Variation
<b>Lungs (- PTV)</b>	Max Dose (0.03 cc)	≤ 110% Rx Dose	≤ 113% Rx Dose
	Mean Dose	≤ 20 Gy	≤ 21 Gy
	V30	≤ 20%	≤ 25%
	V20	≤ 25%	≤ 30%
	V10	≤ 40%	≤ 50%
	V5	≤ 50%	≤ 55%
<b>Heart (&amp; pericardium)</b>	Max Dose (0.03 cc)	≤ 52 Gy	≤ 54 Gy
	Mean Dose	≤ 32 Gy	≤ 34 Gy
	V40	≤ 50%	≤ 55%
<b>Kidneys</b>	Max Dose (0.03 cc)	≤ 45 Gy	≤ 50 Gy
	V20	≤ 30%	≤ 40%
<b>Spinal Cord</b>	Max Dose (0.03 cc)	≤ 45 Gy	≤ 50 Gy
<b>Liver</b>	Mean Dose	≤ 21 Gy	≤ 25 Gy
	V30	≤ 30%	≤ 40%

# Cumulative DVH

Including dose to PTV1 and Boost PTV2



# References

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