ACRODeck

Esophageal Cancer

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Introduction to ACRODeck

ACRODeck

- The goal of ACRODeck is to introduce standard treatments of oncologic malignancies for early radiation oncology residents

- Please note that there is often considerable variation in standard treatment recommendations

- Moreover, the landscape of oncology is ever-changing; for practice changing landmark studies and feedback, please email: resident@acro.org

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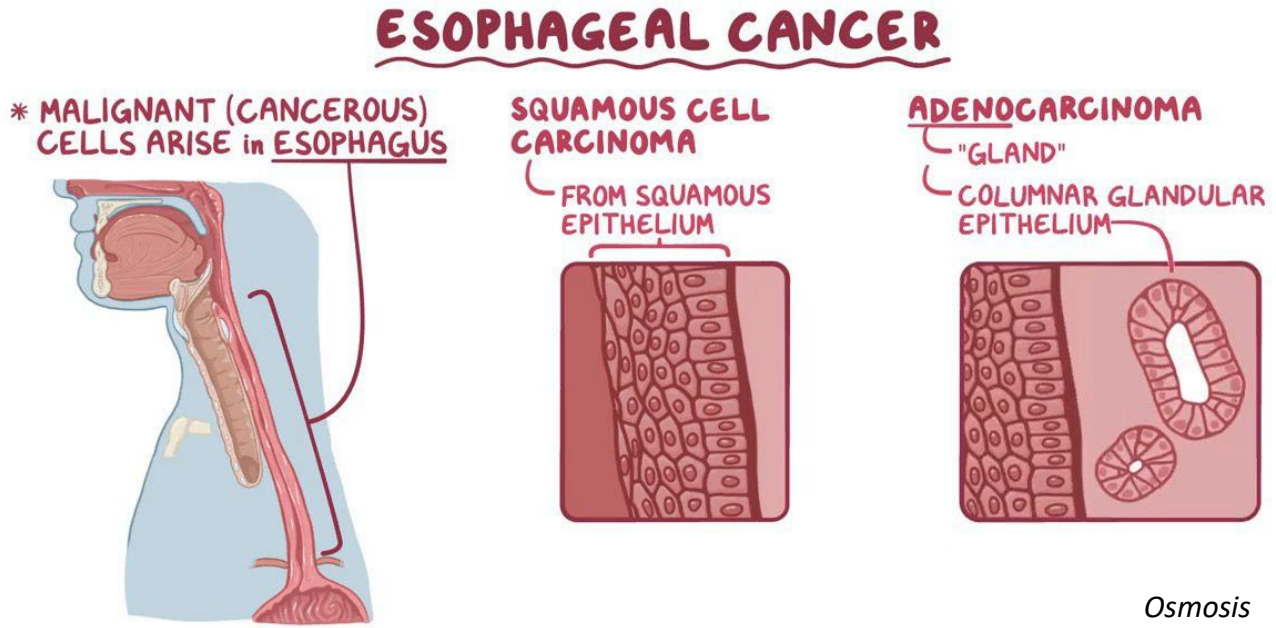
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Clinical Presentation and Differential Diagnosis

For patients with severe dysphagia, a jejunostomy tube is preferred (to a gastrostomy)

- Patients often present with progressive dysphagia and weight loss
  - Chest pain, odynophagia, cough, and hoarseness are sometimes seen as well

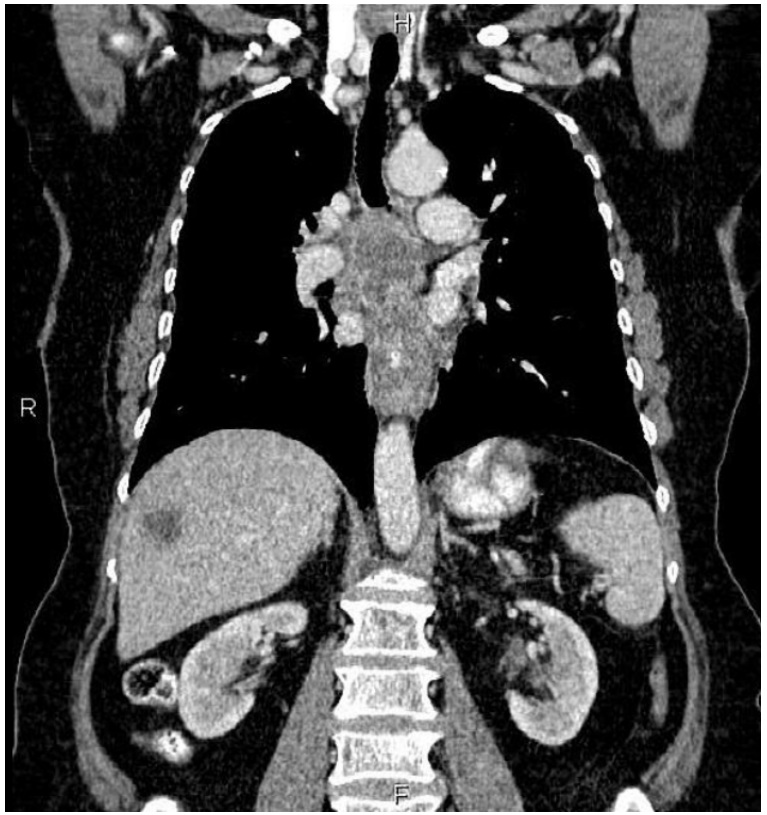
- Differential Diagnosis:
  - GERD
  - Barrett's esophagus
  - Esophageal stricture
  - Achalasia
  - Esophageal infections (candidiasis)
  - Esophageal cancer
  - Gastric cancer



Initial Workup

Endoscopic resection is recommended for T1a or Tb tumors

- H/P with labs
  - Emphasis on nutritional assessment and smoking cessation
  - CBC and CMP
- Imaging
  - CT CAP (with oral and IV contrast)
  - PET CT
- Procedures
  - Upper GI endoscopy (with biopsy)
  - EUS
  - Bronchoscopy (if tumor is at or above the carina)



Radiopaedia

Staging

Group staging is dependent on grade as well as histology

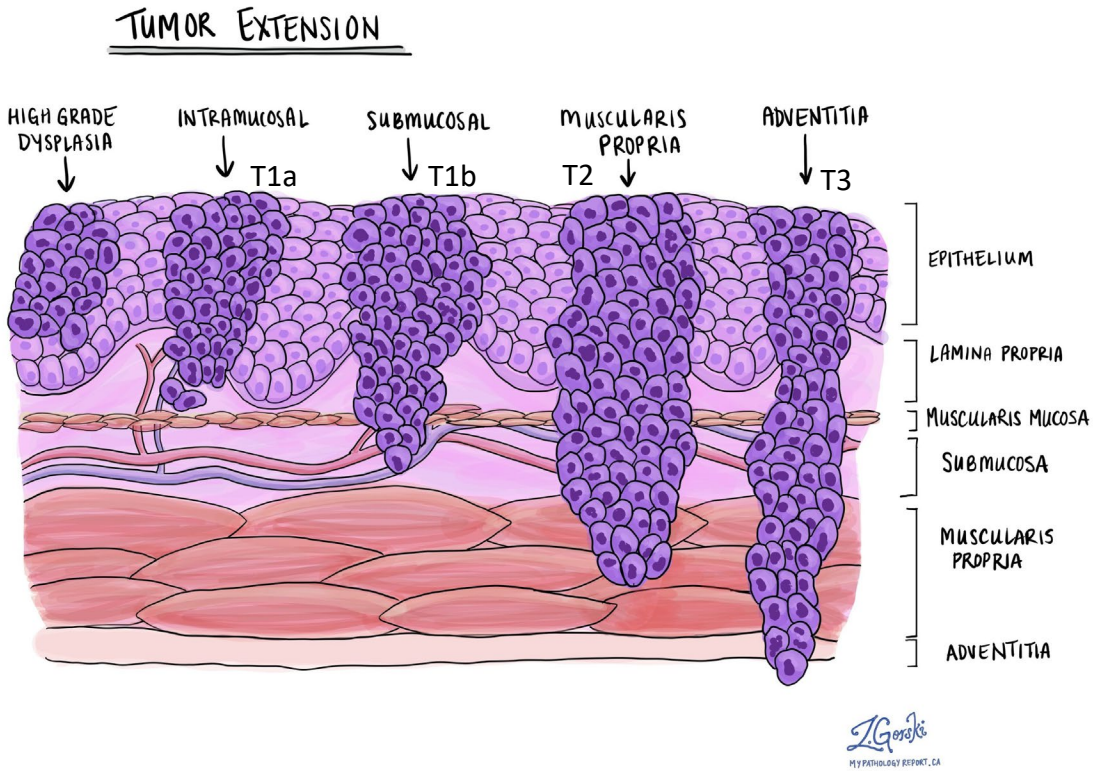


Table 32.3: AJCC 8th Edition (2017) Staging for Esophageal Cancer

Tumor		Node		Distant Metastasis		Grade	
T1	a. Invades lamina propria or muscularis mucosa	N0	• No regional LNs	M0	• No distant metastasis	G1	• Well differentiated
	b. Invades submucosa						
T2	• Invades muscularis propria	N1	• 1 to 2 regional LNs	M1	• Distant metastasis	G2	• Moderately differentiated
T3	• Invades adventitia	N2	• 3 to 6 regional LNs			G3	• Poorly differentiated
T4	a. Resectable[1]	N3	• ≥7 regional LNs				
	b. Unresectable[2]						

Notes: Resectable[1] = invades pleura, pericardium, diaphragm, azygos vein, or peritoneum. Unresectable[2] = invades aorta, vertebral body, airway. AJCC suggests ≥10 nodes removed for pT1 tumors, ≥20 for pT2, and ≥30 for pT3–4.

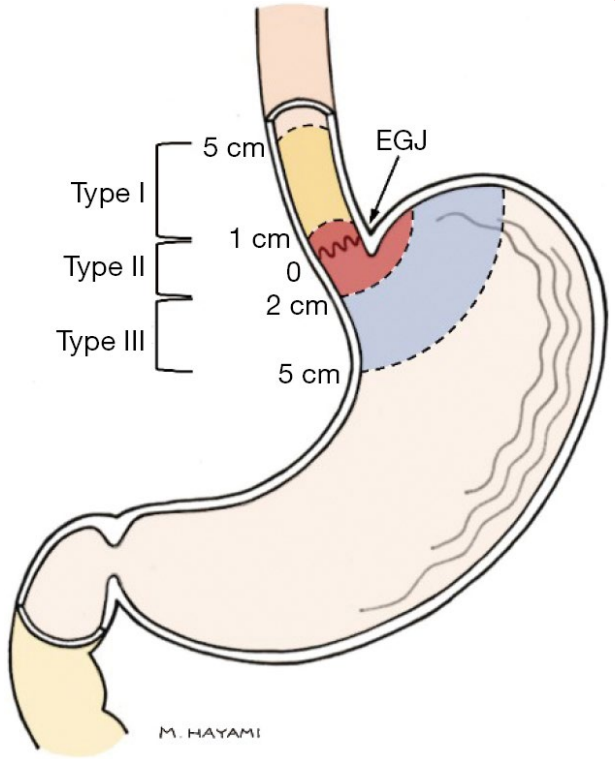
Essentials of Clinical Radiation Oncology

GEJ Tumors and the Siewert System

Peri-operative chemotherapy with FLOT is classically the mainstay for gastric cancer

- GEJ tumors are between 5 cm proximal and 5 cm distal to the GEJ

- These tumors are classified via the Siewert System:
  - Type 1: adenocarcinoma of the distal esophagus
  - Type 2: true carcinoma of the cardia arising immediately at the GEJ
  - Type 3: subcardial gastric carcinoma that infiltrates the GEJ and distal esophagus from below
    - These are considered gastric cancers per NCCN (and are treated as such)



Annals of Esophagus

Treatment Summary

Stage II - IVA

Chemotherapy
Carboplatin & Paclitaxel

Radiotherapy
41.4 Gy – 50.4 Gy in 23-28 fx

→

Surgery
Esophagectomy / Esophagogastrectomy + LND

→ < pCR →

Immunotherapy
Nivolumab

- Stage I disease (no muscularis propria involvement) can often be treated definitively with resection alone
- T4b disease (unresectable) and surgically unfit patients can be treated with definitive chemoRT
- Disease with invasion into significant OARs (heart, trachea, great vessels) can be treated with chemotherapy alone

Systemic Therapy

If a pathologic complete response is not seen on surgical pathology, nivolumab is recommended (PMID: 33789008)

- The mainstay of esophageal cancer treatment is neoadjuvant chemoRT followed by surgery
  - However: chemotherapy may be utilized in the neoadjuvant, perioperative, adjuvant, or definitive settings

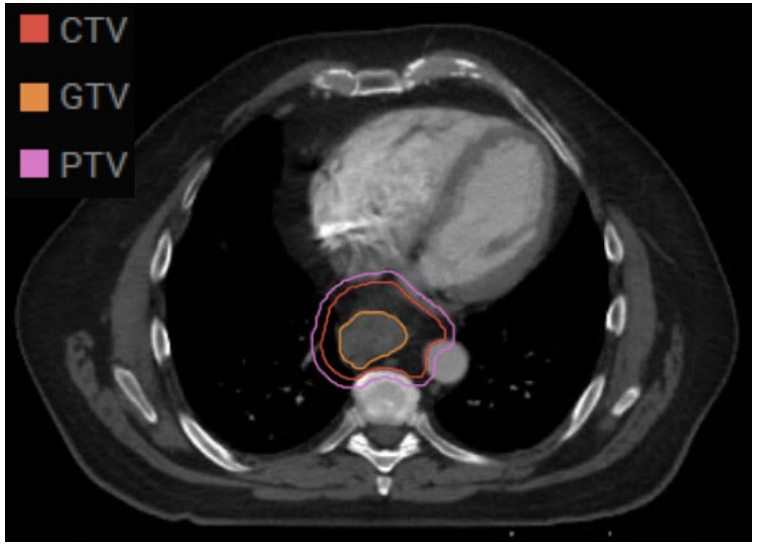
- NCCN category 1 recommendations include:
  - Carboplatin and Paclitaxel (5 cycles delivered weekly)
  - Oxaliplatin and Fluorouracil (3 cycles delivered q2 weeks)

Radiotherapy

Dose escalation had no benefit in the ARTDECO and INT 0123 trials

- The mainstay of esophageal cancer treatment is neoadjuvant chemoRT followed by surgery
  - However, radiotherapy may be utilized in the neoadjuvant, adjuvant, or definitive settings

- Radiotherapy volumes and dosing are quite variable, however:
  - A dose of around 50 Gy (with conventional fractionation) is commonly utilized for both neoadjuvant and definitive therapy
    - Lower doses (41.4 Gy as used in CROSS) are also acceptable for neoadjuvant therapy
  - Volumes include the gross tumor with a wide margin
    - See contouring atlas for details, PMID: 26104943



EContour

- Some institutions will dose escalate for tumors (i.e.: squamous cell carcinomas) in the cervical esophagus up to 74 Gy

Radiation Simulation

The supine position is generally more stable and reproducible

- 4DCT (with oral and IV contrast)
  - Other techniques of motion management are also acceptable
  - NPO 3 hours prior
- Fuse PET-CT
- Use of immobilization device is strongly recommended

Dose Constraints

Dose constraints to critical OARs (i.e.: heart) may sometimes lead to the prescription of a lower neoadjuvant dose (41.4 Gy)

OAR	Dose Constraint (Per NCCN)
Lungs	Mean < 20 Gy V20 Gy ≤ 20%
Heart	Mean < 30 Gy V30 Gy ≤ 30%
Kidneys (individual)	Mean < 18 Gy
Liver	Mean < 25 Gy
Stomach	Mean < 45 Gy Max < 54 Gy
Spinal Cord	Max ≤ 45 Gy
Small Bowel	Max ≤ 54 Gy V45 Gy ≤ 195 cc

Radiation Toxicities

Between 12 – 30% of patients develop strictures after chemoRT

- Acute:
  - Fatigue
  - Esophagitis and weight loss
    - Often, the tumor will shrink and dysphagia will improve; then, esophagitis sets in later in the treatment course
  - Pneumonitis

- Late:
  - Esophageal strictures (can develop 4 – 12 weeks after therapy)
    - Dilations are helpful to alleviate symptoms
  - Esophageal fistulas
  - Pulmonary fibrosis
  - Pericarditis and coronary artery disease

A Word on Adjuvant Treatment

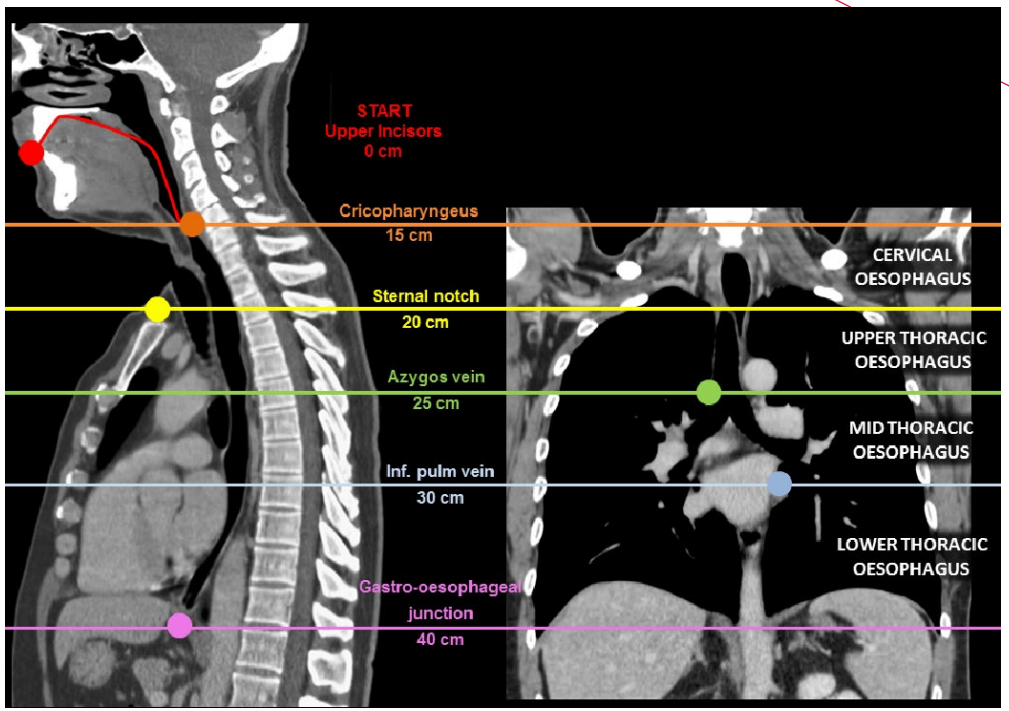
Typical radiation dose for adjuvant treatment is 50 Gy

- While neoadjuvant chemoRT is typically the mainstay of esophageal cancer treatment, adjuvant chemoRT can be considered in cases of:
  - Positive margins
  - Tumor upstaging after surgery and/or nodal positivity

Surgery

Removal of around 15 lymph nodes is typically recommended during surgery

- PET CT is performed 5-8 weeks after completion of neoadjuvant therapy to assess for surgical candidacy
  - Cervical and cervicothoracic tumors < 5 cm from the cricopharyngeus muscle are typically treated nonoperatively given the morbidity of surgery
- Surgery (esophagectomy/esophagogastrectomy) is typically done 8-12 weeks after neoadjuvant therapy
  - For most distal lesions, mediastinal and upper abdominal lymphadenectomy is also performed.
- If a pathologic complete response is not seen on the surgical specimen, adjuvant nivolumab is prescribed (for a treatment duration of 1 year)

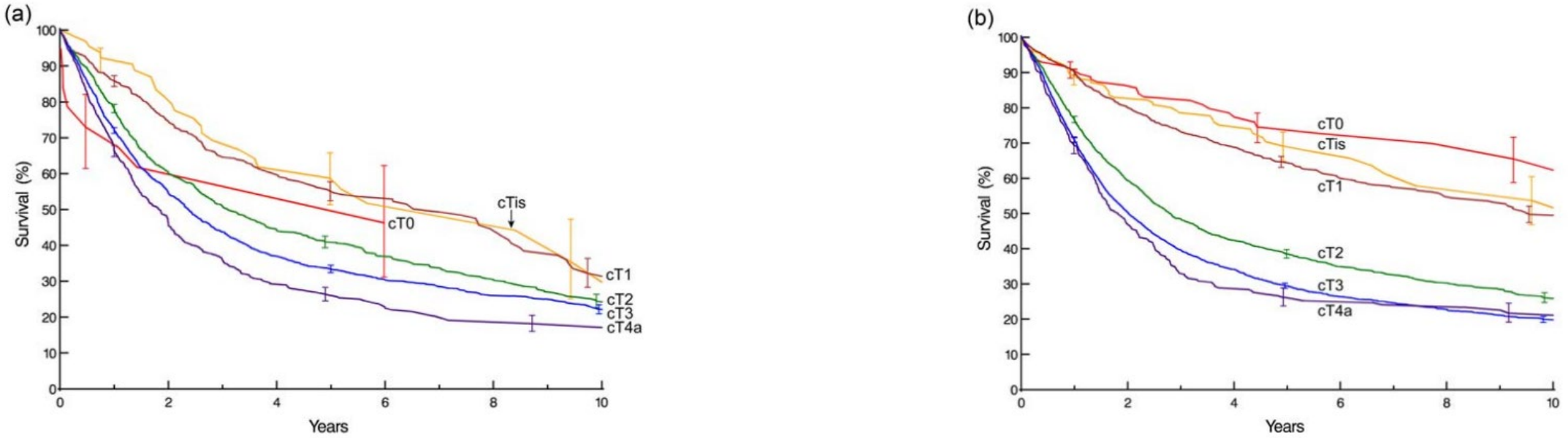


Radiopaedia: Image shows the radiological landmarks in the esophagus and their distance (in cm) from the upper incisors on endoscopy.

Prognosis

Follow-up after surgery is typically q3-6 months initially with imaging and endoscopy as clinically indicated

- Per the 2012 CROSS trial (PMID 22646630):
  - Median overall survival for SCC was 6.8 years (with a 49% pCR)
  - Median overall survival for ACA was 4.1 years (with a 23% pCR)



Survival by clinical T category: A) Squamous Cell Carcinoma B) Adenocarcinoma

Worldwide Esophageal Cancer Collaboration: clinical staging data

Review

Review #1: The CROSS Regimen

Adenocarcinoma (75%) was the more common histology seen on the CROSS trial

In the CROSS study, what was the neoadjuvant chemoradiation treatment regimen for resectable disease?

(A) 41.4 Gy with FLOT

(B) 61.6 Gy with FLOT

(C) 41.4 Gy with carboplatin/paclitaxel

(D) 61.6 Gy with carboplatin/paclitaxel

Review #2: Modern Radiation

NRG GI006 is a phase 3 RCT comparing proton therapy to IMRT

The use of IMRT in esophageal cancer has been showed to reduce toxicity of what OAR?

(A) Lung

(B) Heart

(C) Stomach

Review #3: Wu Contouring Atlas

PMID: 26104943

What is a recommended superior CTV expansion (on the primary) for a cT3N1 GEJ adenocarcinoma?

(A) 1.5 cm

(B) 3.5 cm

(C) 5.5 cm

Review #4: Checkmate 577

Nivolumab improved this metric from 11.0 months to 22.4 months ($p < 0.001$)

In the Checkmate 577 trial, which of the following was statistically improved with the addition of adjuvant Nivolumab?

(A) Disease Free Survival

(B) Overall Survival

(C) All of the above

Review #5: NEO-AGIS

The rate of neutropenia (grade 3 and 4) was 5x greater in the chemotherapy alone arm vs. the chemoRT arm (14.1% vs. 2.8%)

In the NEO-AGIS study, which of the following was significantly improved in the chemoRT arm?

(A) R0 resection rate

(B) pCR rate

(C) ypN0 rate

(D) Tumor regression (grades 1 and 2)

(E) All of the above

Answer Key

1. C
2. B
3. B
4. A
5. E

The ESOPEC trial is comparing perioperative CHT (with FLOT) with the CROSS regimen (chemoRT)