ACRODeck

Rectal 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

Table of Contents

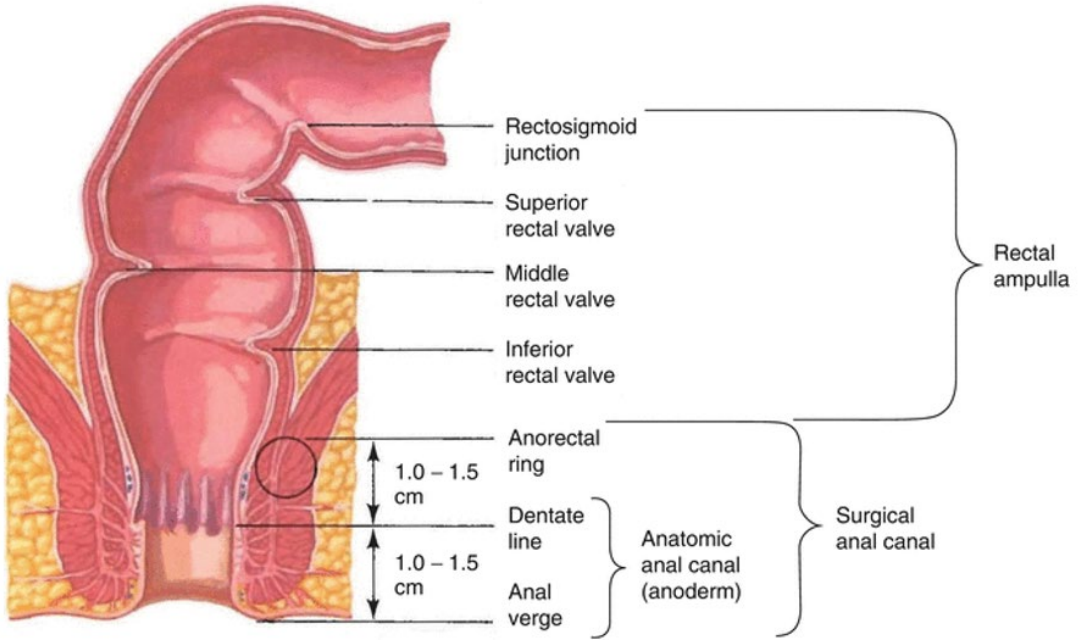
ACRODeck

Clinical Presentation and Differential Diagnosis

As of 2023, NCCN recommends colonoscopy starting at age 45 and every 10 years if negative (for average-risk patients)

- Patients often present with hematochezia
  - Iron deficiency anemia, constipation, diarrhea, abdominal pain, and rectal urgency may be present as well

- Differential Diagnosis:
  - IBS/IBD
  - Hemorrhoids
  - Diverticulosis
  - Colonic carcinoid/neuroendocrine tumors
  - Gastrointestinal lymphoma
  - Rectal adenocarcinoma



The rectum begins at the rectosigmoid junction and ends where the rectal ampulla narrows at the anorectal ring

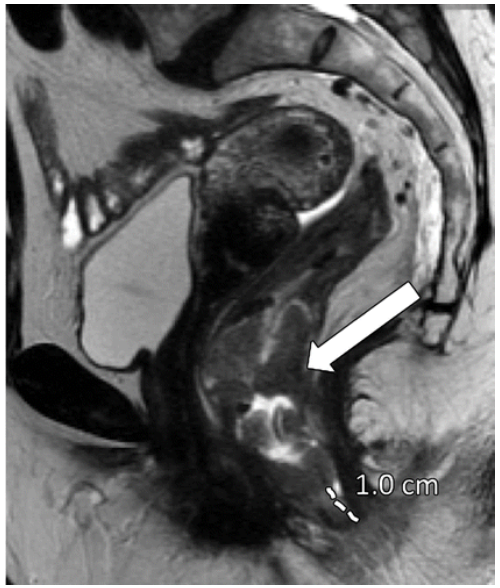
Surgical Anatomy of the Colon, Rectum and Anus

Rectal Anatomy

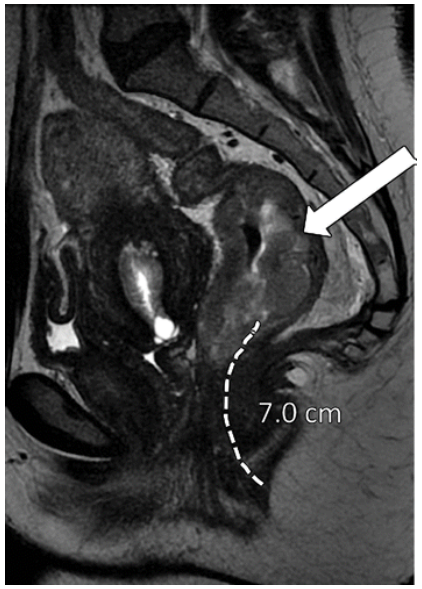
Colon cancer is treated primarily with surgery (± CHT)

- Rectal cancers are defined as lesions inferior (or at) to the peritoneal reflection; they are also sometimes defined as lesions within 12 - 16 cm of anal verge
  - If the tumor is completely above these levels, the patient is treated under the paradigm of colon cancer

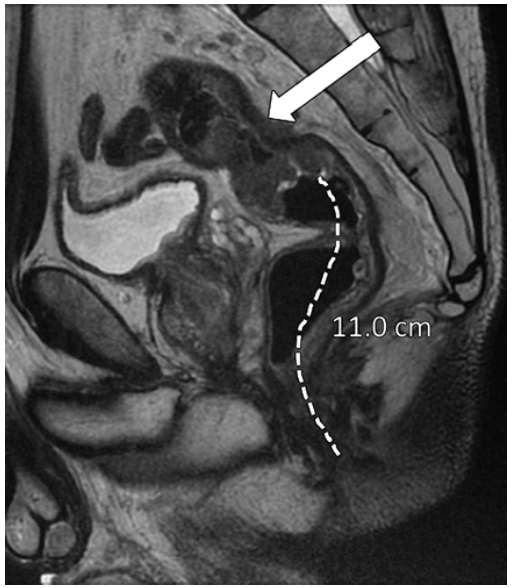
- Within the rectum, tumors are sometimes categorized as:
  - Low (less than 6 cm from the anal verge)
  - Middle (6-12 cm from the anal verge)
  - High (12-16 cm from the anal verge)



Low



Mid



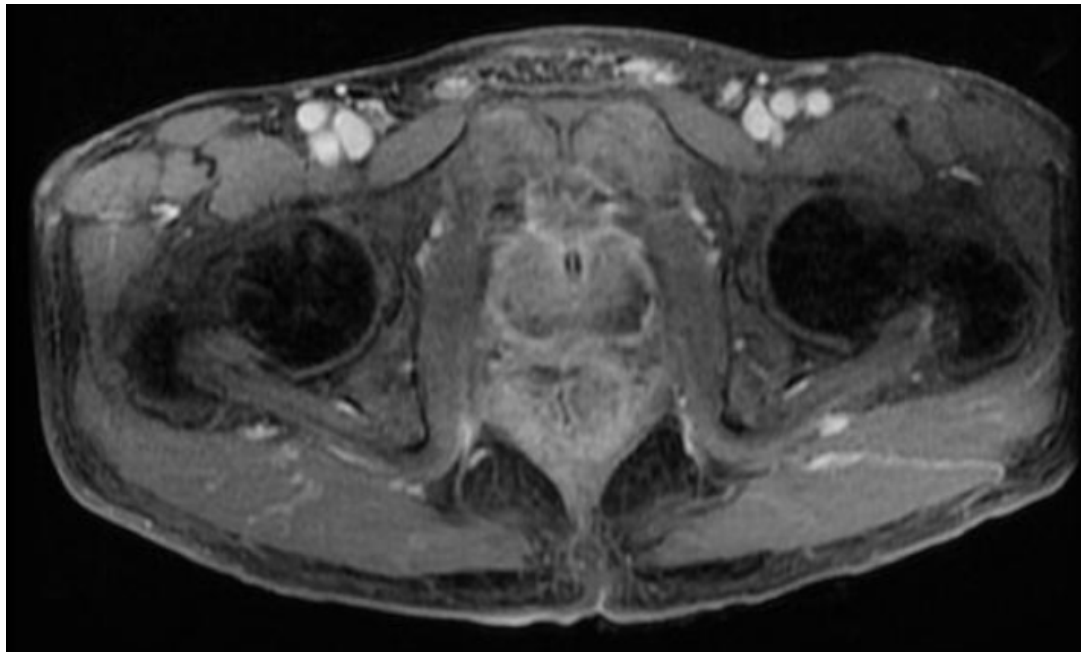
High

(PMID: 30768361)

Initial Workup

- H/P with labs
  - DRE
  - CBC, CMP, CEA
- Imaging
  - CT CAP
  - MRI pelvis
    - T2 is often the most helpful sequence
  - Endorectal US can be considered for patients in whom MRI is contraindicated or inconclusive
- Procedures
  - Colonoscopy with biopsy (with MMR/MSI testing)

A colonoscopy helps assess the presence of satellite lesions elsewhere in the colon



Radiopaedia: T4 rectal cancer with invasion into the prostate

Staging

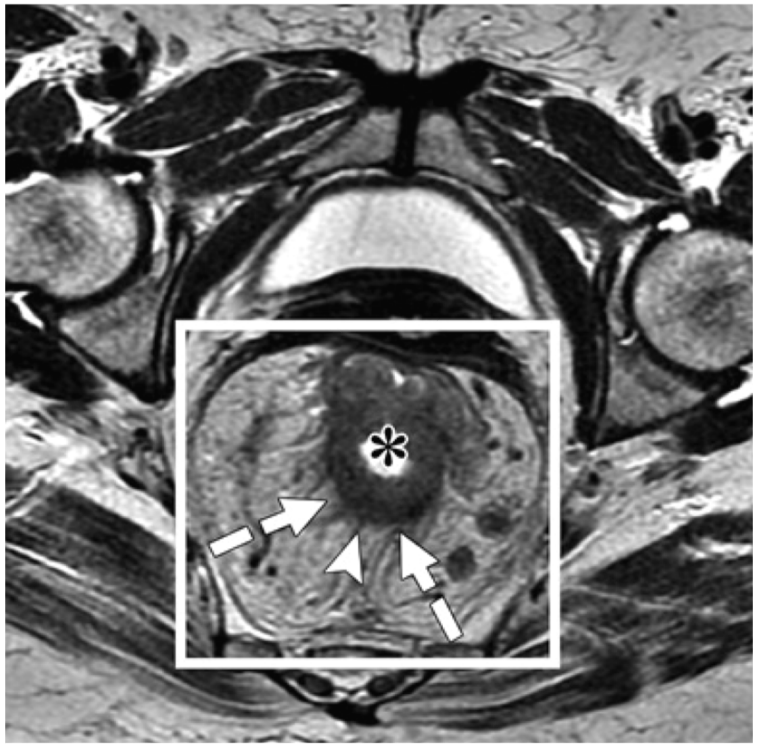
In rectal cancer, involvement of the external iliac or common iliac nodes is considered M1a disease

Table 36.3: AJCC 8th ed. (2017): Staging for Rectal Cancer

T/M \ N		cN0	cN1a	cN1b	cN1c	cN2a	cN2b
T1	Invades submucosa	I	IIIA				
T2	Invades muscularis propria						
T3	Invades into pericolorectal soft tissue	IIA	IIIB				
T4	a. Invades into visceral peritoneum[1]	IIB					
	b. Invades or adherent to adjacent organs/structures	IIC	IIIC				
M1a	Distant metastasis to 1 organ without peritoneal metastasis	IVA					
M1b	Distant metastasis to 2 organs without peritoneal metastasis	IVB					
M1c	Metastasis to peritoneal surface with or without other organ or site	IVC					

Notes: Peritoneum[1] = Includes gross perforation of bowel through tumor and continuous invasion of tumor through areas of inflammation to surface of visceral peritoneum.
cN1a, 1 regional LN; cN1b, 2–3 regional LNs; cN1c, no positive regional LNs, but subserosal, mesenteric, non-peritoneal peri-colic or peri-rectal tumor deposits; cN2a, 4–6 regional LNs; cN2b, ≥7 regional LNs.

Essentials of Clinical Radiation Oncology



T2 MRI: Tumor infiltrates beyond the muscularis propria into the mesorectum; also depicted are two round mesorectal lymph nodes (PMID: 30768361)

Treatment Summary

Stage II – III: There are a myriad of regimens to treat rectal cancer; here is one:

- Stage I disease can often be treated with surgery alone
- For dMMR/MSI-H tumors, immunotherapy alone can be used (if no complete clinical response after 6 months, treatment with radiotherapy and/or chemotherapy is considered)
- 25 Gy in 5 fx (SC-RT) can be considered instead of capecitabine and 50.4 Gy
- The sequence of chemoRT and chemotherapy is interchangeable (however, the OPRA trial demonstrated increased organ preservation with chemoRT first)

Radiotherapy

- Neoadjuvant chemoRT (within a total neoadjuvant regimen (TNT)) has become the standard of care for most locally advanced rectal cancers
  - Adjuvant RT is not standard of care, but may used in cases of unexpected tumor upstaging after surgery

- There are two common dose regimens:
  - Long Course RT (LC-RT) = 50.4 Gy in 28 fx
    - Given with capecitabine
    - The initial volume is given 45 Gy, with a boost (between 5.4 - 9 Gy) delivered sequentially
  - Short Course RT (SC-RT) = 25 Gy in 5 fx
    - Given alone

- There are two common methods to deliver RT
  - 3DCRT
  - IMRT/VMAT

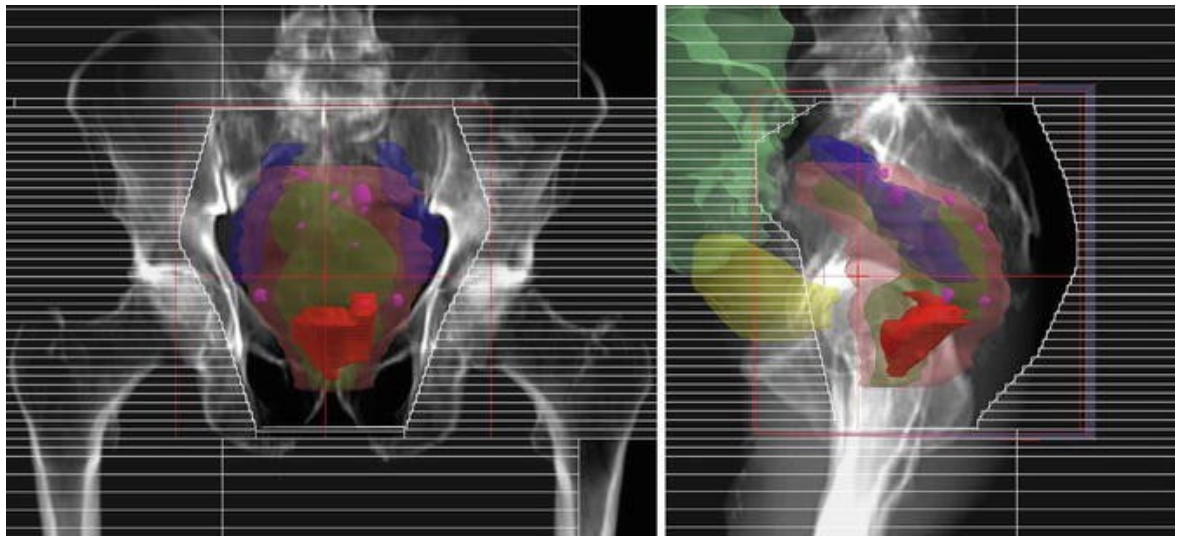
The 2023 publication of RAPIDO demonstrated a higher rate of locoregional recurrence with SC-RT

https://twitter.com/dremmaholliday/status/1649787962064871426?s=46&t=AnAHaVIO70NdPkrw8VRyzA

RT Delivery

Although RTOG 0822 did not show benefit of IMRT (likely due to the utilization of CAPEOX), many centers will utilize IMRT due to dosimetric benefits

- 3DCRT
  - Beam Arrangement:
    - 2 laterals beams
    - 1 posterior beam
  - Borders
    - Superior: L4/L5 or L5/S1
    - Inferior: level of the ischial tuberosities or 3 cm below the caudal-most extent of the tumor
    - Lateral: 2 cm beyond the pelvic inlet
    - Anterior: depends if the external iliacs are being included
      - If they are: the border is anterior to the pubic symphysis
      - If they are not: the border is posterior to the pubic symphysis
    - Posterior: 1 cm past the posterior sacral bony contour
- IMRT
  - Refer to RTOG contouring atlas (PMID: 19117696)



Radiation Therapy for Gastrointestinal Cancers

Radiation Simulation

The prone position may be beneficial in limiting the amount of small bowel receiving RT dose

- CT (with oral and IV contrast)
  - NPO 3 hours prior
- Fuse MRI
- Use of an immobilization device is strongly recommended

Selected Dose Constraints

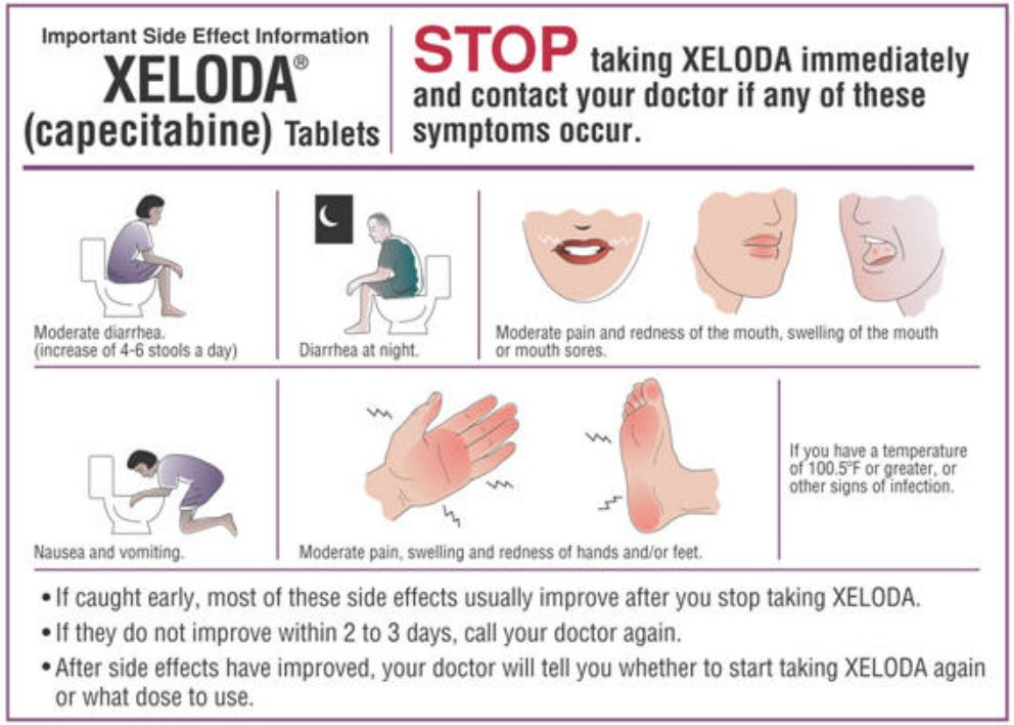
Detailed constraints for both SC-RT and LC-RT are provided by the VA and ASTRO Expert Panel (PMID 35907764)

OAR	Dose Constraint (for LC-RT)
Bladder	Mean < 40 Gy
Small Bowel	Max < 50 - 54 Gy
Femoral Head	$D_{5\%}$ < 45 Gy Max < 50 Gy (per RTOG 0822)

Chemotherapy

Capecitabine is contraindicated in individuals with DPD deficiency

- Neoadjuvant chemoRT (within a total neoadjuvant regimen (TNT)) has become the standard of care for most locally advanced rectal cancers
  - Adjuvant chemotherapy is not standard of care, but may used in cases of unexpected tumor upstaging after surgery
- For chemoRT, oral capecitabine is given concurrently with LC-RT (5-FU infusion is also an option)
  - Capecitabine is given BID on each day of RT (M-F)
- For the chemotherapy portion of TNT (3-4 months), two options include:
  - FOLFOX: q2 weeks
  - CAPEOX: q3 weeks
- Adjuvant chemotherapy is not standard of care, but may used in cases of unexpected tumor upstaging after surgery



Side effects of capecitabine may include hand/foot syndrome as well as GI effects

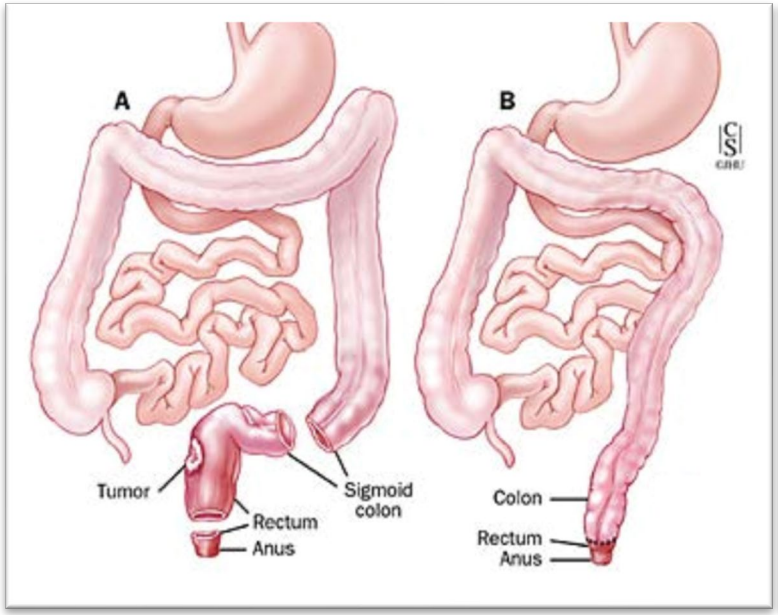
Surgery

If a patient is upstaged based on pathology after a transanal excision, the initial surgery is considered a large biopsy and a full treatment regimen (i.e.: TNT) is required afterwards

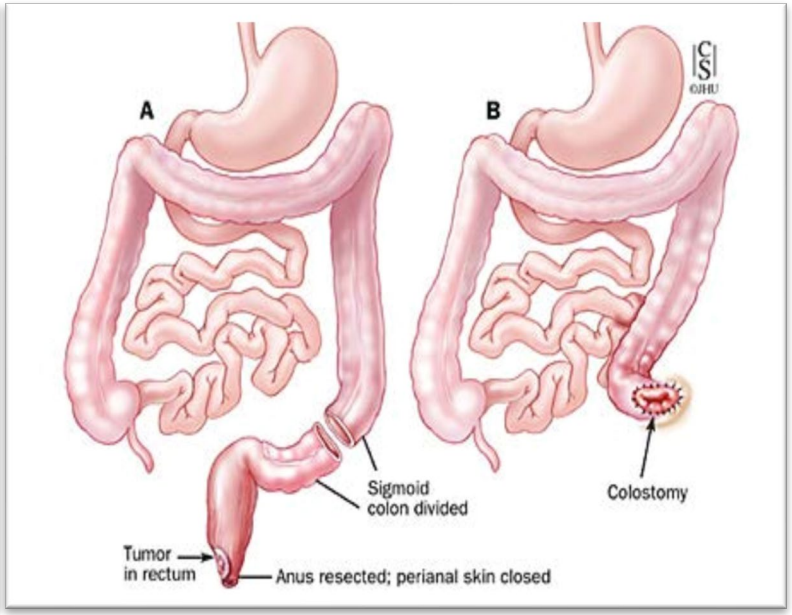
- A transanal excision can be considered for tumors that are:
  - < 3cm, <30% rectal circumference, grades 1-2, within 8 cm of the anal verge, and a margin > 3mm

- However, particularly after neoadjuvant treatment, surgical standard is a **total mesorectal excision**
  - **LAR = low anterior resection** (sphincter sparing)
    - The end goal is lack of an ostomy (although one may be required temporarily)
  - **APR = abdominoperineal resection** (sphincter complex is resected)
    - An APR is indicated for tumors located close to the anal verge, where resection would result in incontinence
    - It is characterized by a permanent colostomy

LAR



APR

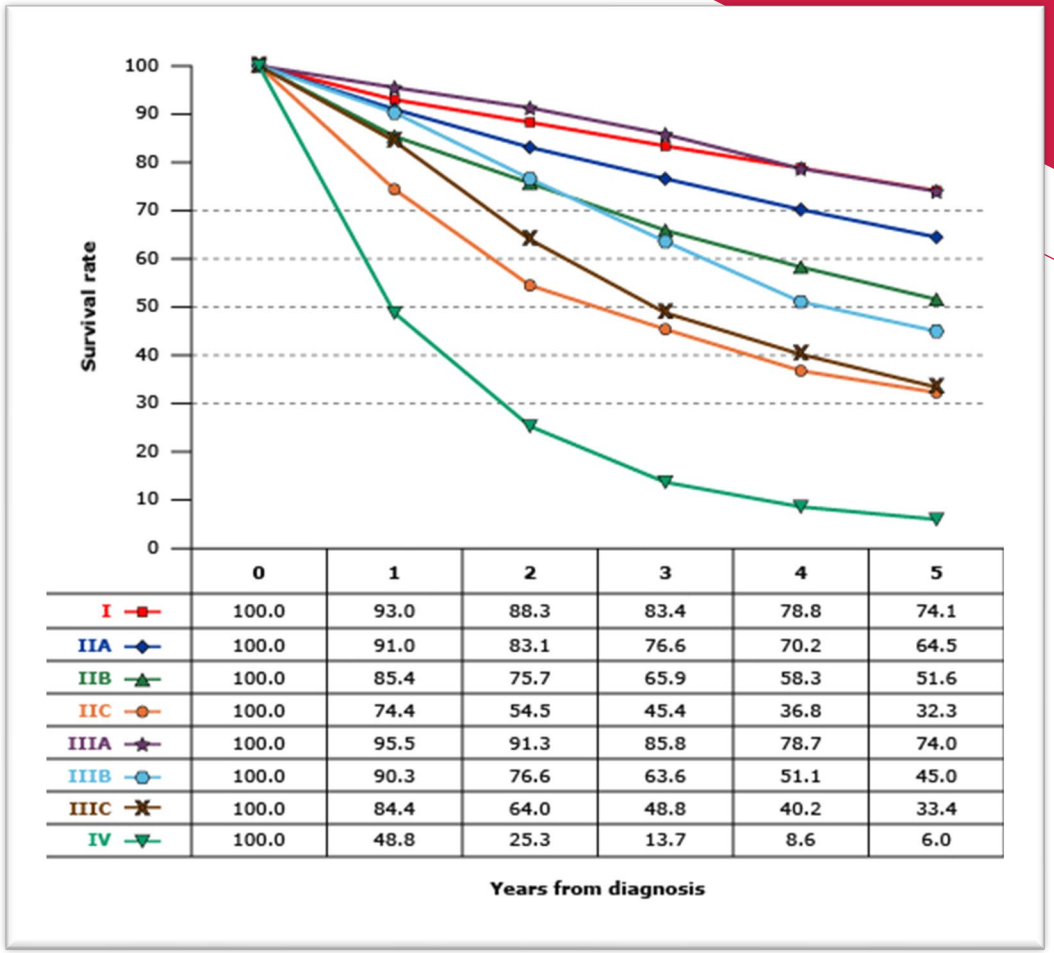


JHU

Prognosis

- Treatments in rectal cancer are rapidly evolving
  - With recent advances, a complete clinical response with organ preservation is a very reasonable goal for a sizable portion of our patient population

The liver is the most common site of metastases



	0	1	2	3	4	5
I	100.0	93.0	88.3	83.4	78.8	74.1
IIA	100.0	91.0	83.1	76.6	70.2	64.5
IIB	100.0	85.4	75.7	65.9	58.3	51.6
IIC	100.0	74.4	54.5	45.4	36.8	32.3
IIIA	100.0	95.5	91.3	85.8	78.7	74.0
IIIB	100.0	90.3	76.6	63.6	51.1	45.0
IIIC	100.0	84.4	64.0	48.8	40.2	33.4
IV	100.0	48.8	25.3	13.7	8.6	6.0

Observed survival rates for 9,860 cases with adenocarcinoma of the rectum (Data from the SEER 1973-2005)

Review

Review #1: Organ Preservation for Rectal Adenocarcinoma

At three years, 53% of patients were able to be spared of a TME with this approach

Per the OPRA trial (PMID: 35483010), what sequence was associated with the highest rate of organ preservation?

(A) Long course chemoRT followed by consolidation chemotherapy (FOLFOX or CAPEOX)

(B) Short course RT followed by consolidation chemotherapy (FOLFOX or CAPEOX)

(C) Induction chemotherapy (FOLFOX or CAPEOX) followed by long course chemoRT

(D) Induction chemotherapy (FOLFOX or CAPEOX) followed by short course RT

Review #2: Pathologic Complete Response

Preoperative chemoRT had improved compliance and toxicity profile (compared to postoperative chemoRT)

On the German rectal trial (PMID 22529255), what was the pCR rate in the preoperative chemoRT arm?

(A) 9%

(B) 19%

(C) 29%

Review #3: CTV Coverage

Remember, external iliac lymph nodes are not considered regional in rectal cancer

Which of the following is an indication for including the external iliac lymph node chain in the radiation volume?

(A) Adenocarcinoma histology

(B) T4 tumors invading anterior GYN/GU organs

(C) History of HNPCC

Review #4: Complete Clinical Response

For patients treated with CHT first and then RT, the assessment should be performed no earlier than 8 weeks

For patients treated with radiation first followed by chemotherapy (in total neoadjuvant treatment), when should the assessment for a complete clinical response occur?

(A) Within 1 week

(B) Within 1 month

(C) Within 1 year

Review #5: Watch and Wait

For the first three years, MRI rectum is recommended every 6 months

Which of the following is recommended (per NCCN) for surveillance of rectal cancer following a nonoperative management approach?

(A) CEA

(B) DRE

(C) Proctoscopy / Flexible Sigmoidoscopy

(D) MRI Rectum

(E) CT Chest and Abdomen

(F) Colonoscopy

(G) All of the above

Answer Key

1. A
2. A
3. B
4. B
5. G

NRG –GI002 is exploring the addition of immunotherapies to TNT