Rectal Cancer: Definitive Management

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Outline

- Case Presentation
  - Workup
  - Management
    - Simulation
    - Contours
    - Plan Evaluation
    - Follow-up

- Background
- Workup
- Staging
- Management
  - Treatment Sequencing
  - Chemotherapy
  - Surgery
  - Radiation

Case: Clinical Presentation

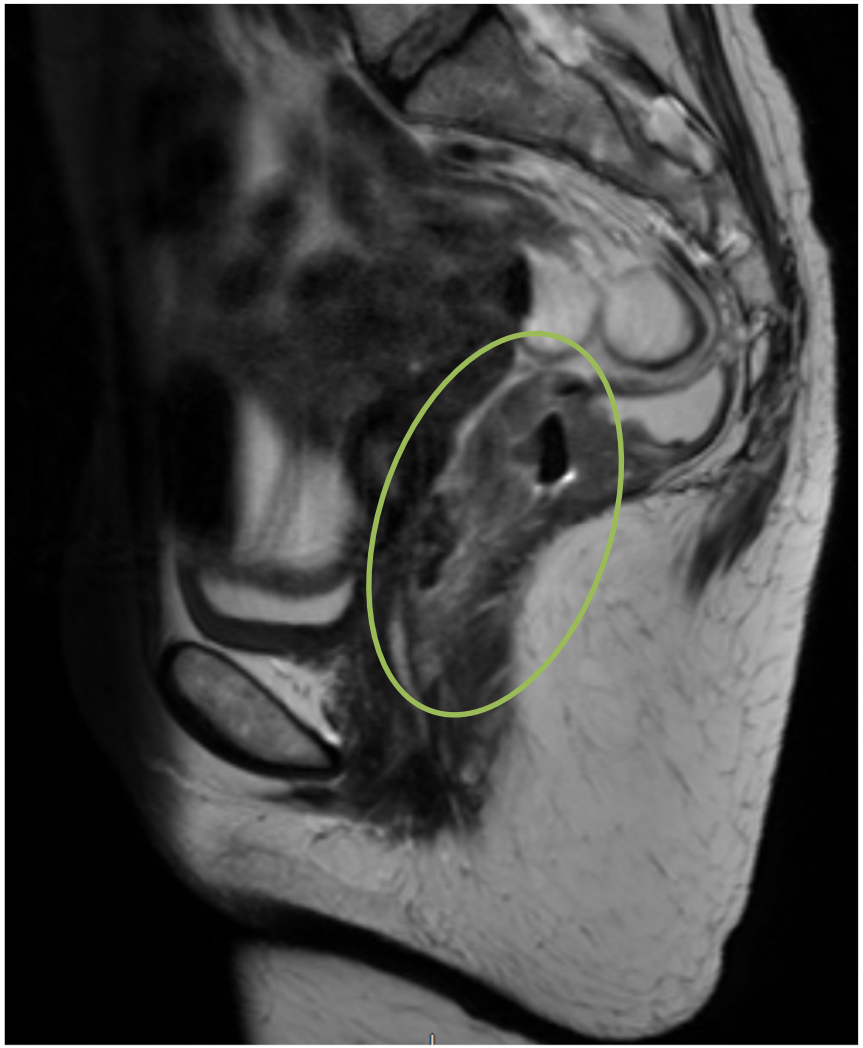
61 year old woman who had a positive screening fecal immunochemical test (FIT) and was referred for a colonoscopy. She denies bright red blood per rectum. She denies significant weight loss. She denies having previous colonoscopies.

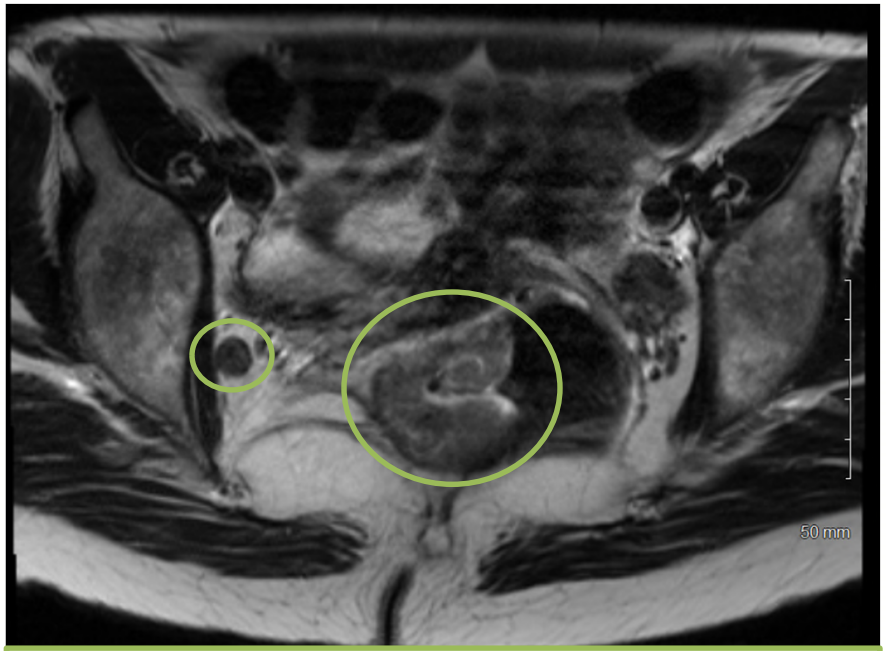
- **Past Medical Hx**: migraines
- **Surgical Hx**: appendectomy
- **Medications**: None
- **Allergies**: NKDA
- **Family Hx**: non-contributory
- **Social Hx**: Current smoker- 1ppd for 40 years.

Case: Diagnostic Workup

- **CEA:** 0.9
- **Colonoscopy**
  - Severe stenosis in sigmoid colon. Fungating, infiltrative and ulcerated non-obstructing large mass in the low rectum. Mass is partially circumferential. The mass is 4 cm in length.
  - Biopsy: Moderately differentiated adenocarcinoma
- **CT Chest/Abd**
  - No evidence metastatic disease

Case: Imaging





MRI

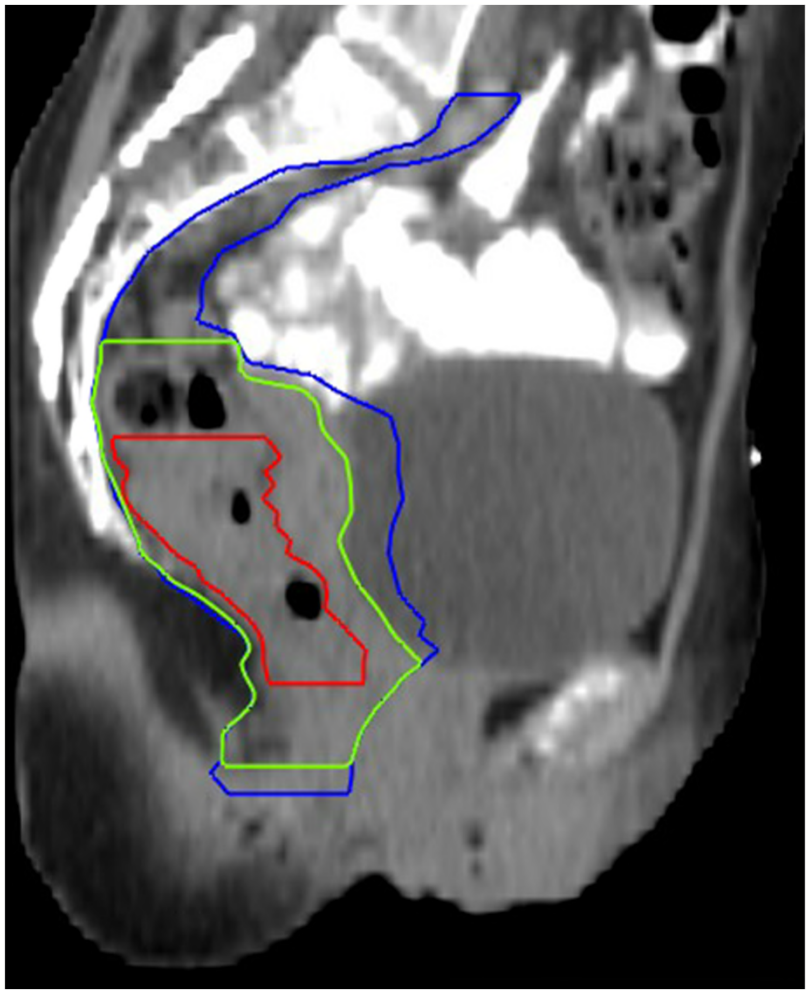
-Low rectal mass with possible extension of the inferior anterior portion of the mass into the posterior uterine wall and multiple abnormal lymph nodes

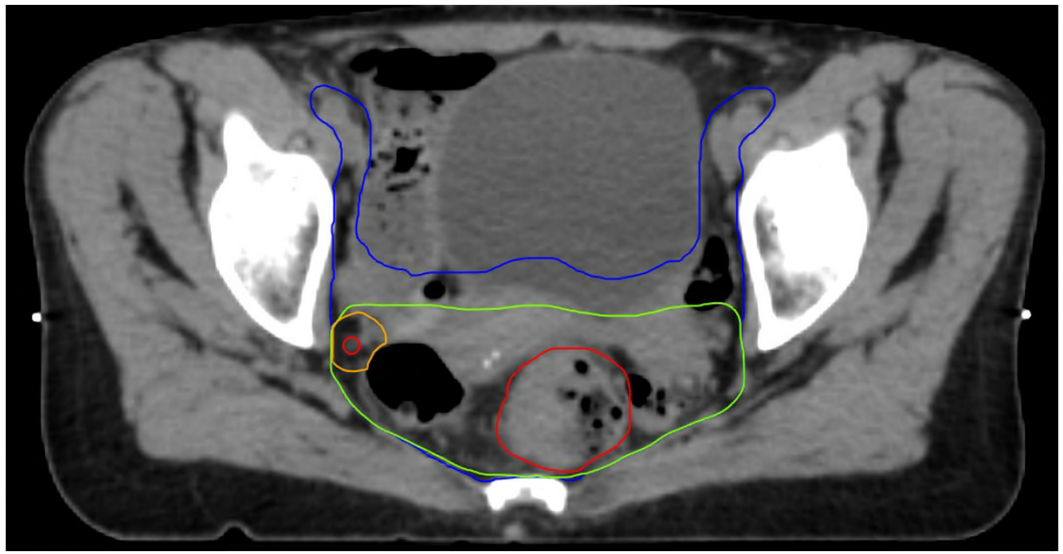
-Multiple abnormal lateral pelvic lymph nodes

Case: Management

- **Stage**: cT4bN2bM0 rectal adenocarcinoma
- After multidisciplinary discussion, decision was to proceed with total neoadjuvant therapy (TNT) followed by surgery (likely LAR)
  - CRT with Xeloda → Chemotherapy → Surgery
  - Lateral pelvic lymph nodes will likely not be removed at time of surgery

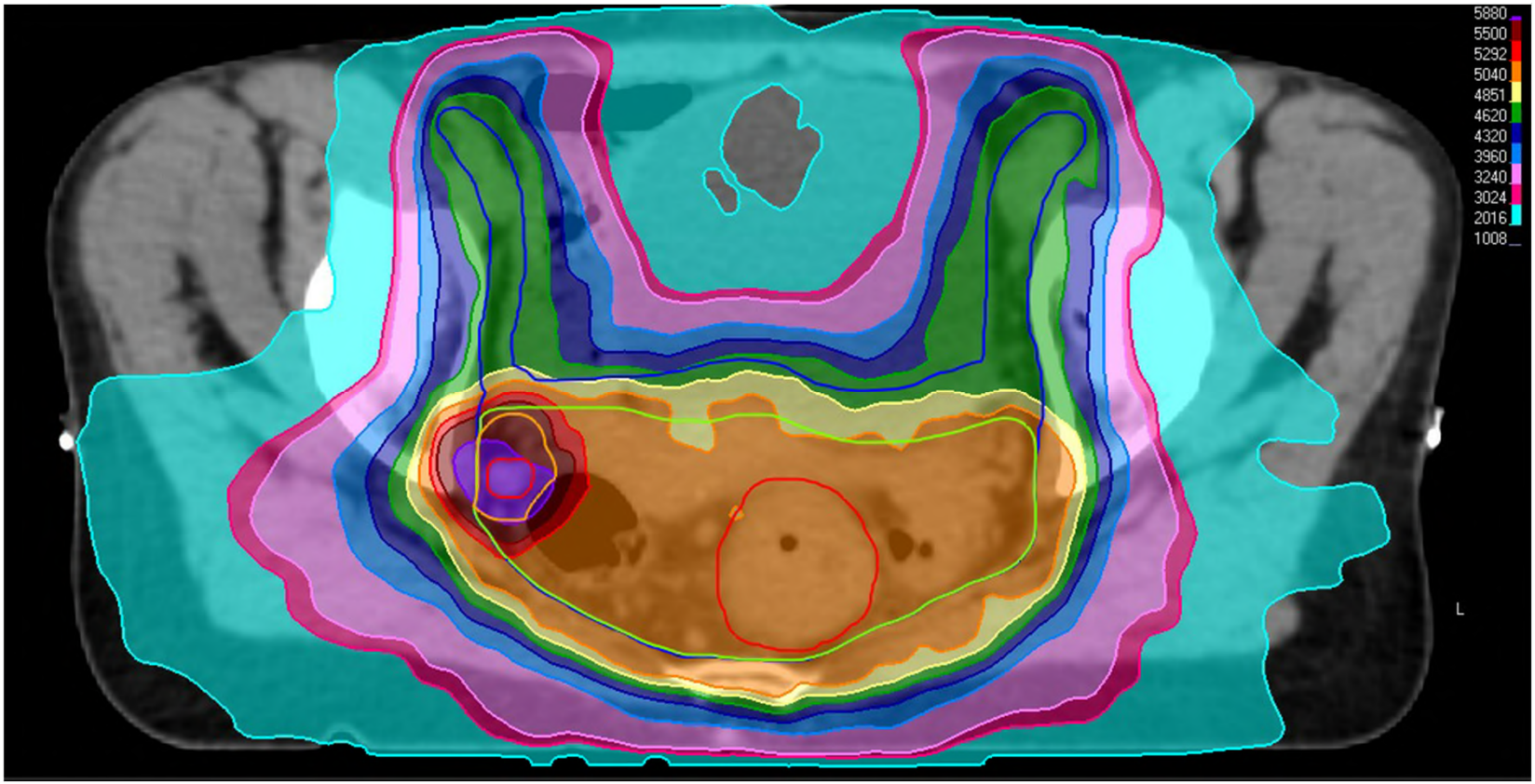
Case: Contours



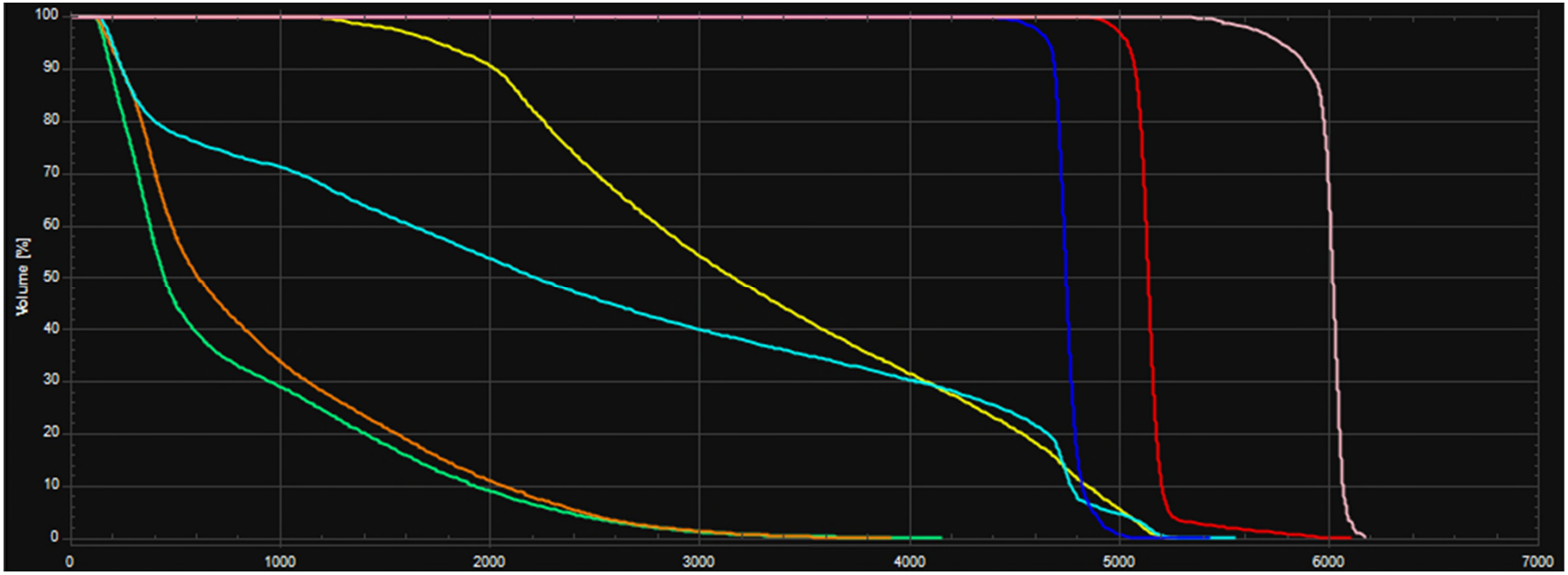


GTV (primary and nodal)
Elective Nodal CTV (46.2 Gy)
Primary CTV (50.4 Gy)
Nodal CTV (58.8 Gy)
28 fractions (SIB)

Case: Plan Evaluation



Case: Plan Evaluation



Bowel_Small

$D_{0.02cc}$: 54 Gy
V45: 139 cc

Bladder

Mean: 33 Gy

Femur_Head_L

V40: 0.1%

Femur_Head_R

V40: 0.0%

PTV_4620

99% at 95% Rx

PTV_5040

99% at 95% Rx

PTV_5880

98% at 95% Rx

Case: Follow-Up

- Patient did well through CRT and only occasionally required Imodium for loose stool
- Currently getting FOLFOX and tolerating treatment well
- Seen 1 month after completion of RT
  - No residual acute toxicities
- Patient will proceed with resection (likely LAR) after completion of chemotherapy

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- Background
- Workup
- Screening
- Staging
- Management
  - Chemotherapy
  - Surgery
  - Radiation
  - Treatment Sequencing

Background

- Colorectal cancer is the 3rd most common cancer in the U.S. among men and women
- Estimated cases in 2022:
  - 106,180 colon cancer
  - 44,850 rectal cancer
- Incidence is decreasing amongst older adults, but increasing in younger adults
  - 2012-2016 incidence increased by 2% per year in <50 year old age group
- CRC is the 3rd leading cause of cancer death in U.S. for both men and women with estimated 52,580 deaths in 2022

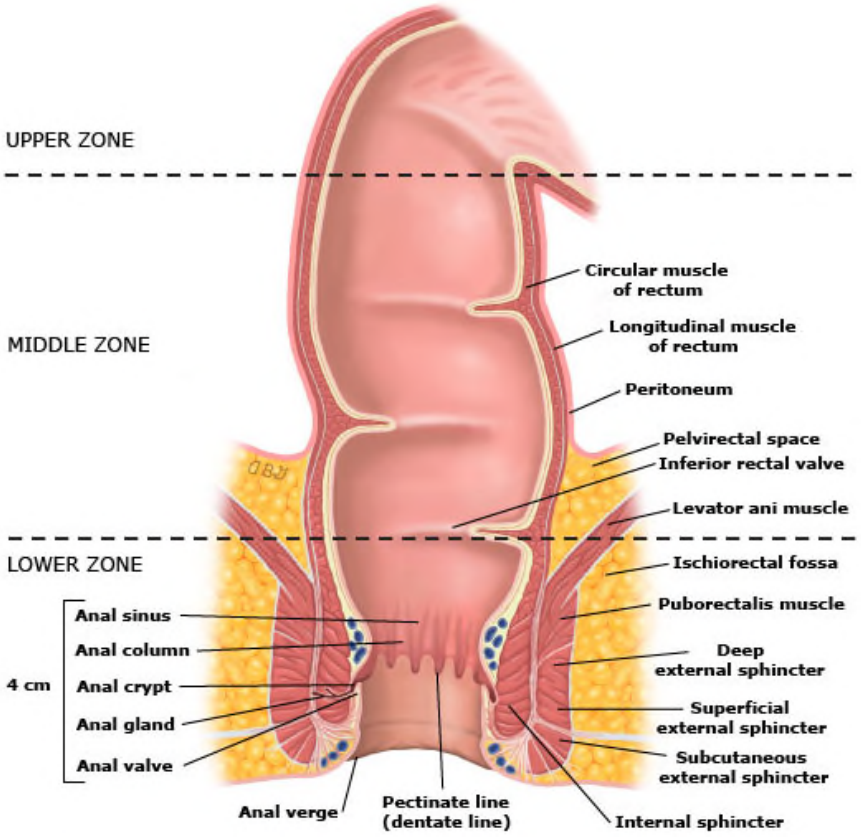
Risk Factors

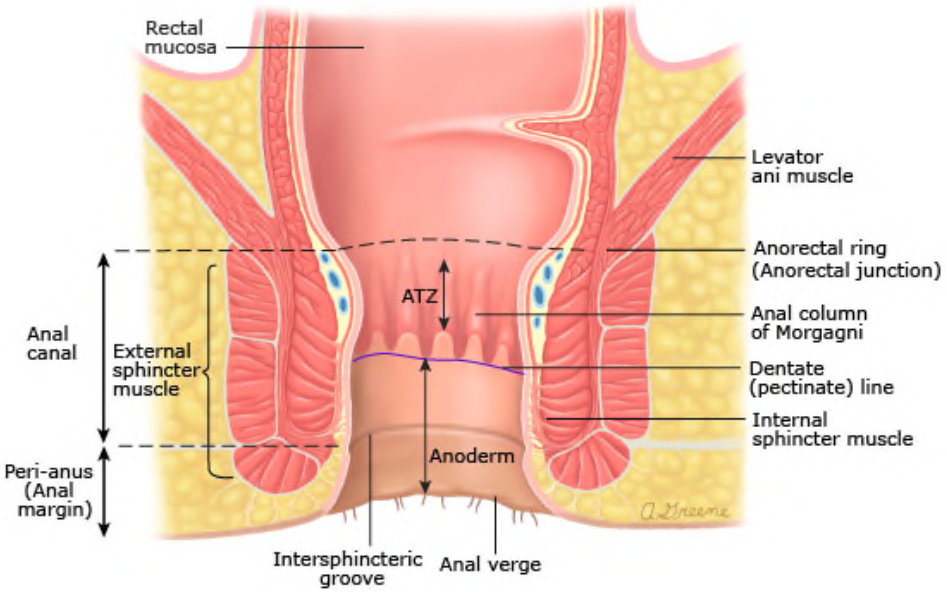
Modifiable	Non-Modifiable
- Obesity - Decreased physical activity - Metabolic syndrome - Consumption of red meat and processed meats - Tobacco - Alcohol use - High fat, low fiber diet	- Increased age - IBD (UC, Crohn's) - Family history - Inherited syndrome (FAP, HNPCC) - Diabetes

Anatomy

- Rectum extends approximately 15 cm from the peritoneal reflection (S3) to the anorectal ring
  - Anorectal ring: level of the puborectalis sling and levators
  - Dentate line: transition from columnar epithelium to nonkeratinized squamous epithelium
- Tumor is often referenced by distance from the anal verge or dentate line/anorectal ring
- Rectum can be subdivided into thirds based on distance from the anal verge:
  - Upper third (12-16 cm)
  - Middle third (6-12 cm)
  - Lower third (0-6 cm)

Anatomy





Source: UpToDate

LN Drainage and Metastasis

- **Superior third of rectum** → perirectal, presacral, sigmoidal, and inferior mesenteric nodes
- **Middle third of rectum** → internal iliac nodes
- Tumors extending **below dentate line** → superficial inguinal nodes
- Liver is most common site of CRC metastatic disease via portal venous system
- Increased propensity for metastasis to lungs for rectal cancer (lower rectum drains to internal iliac veins and then to IVC)

Screening

- The American Cancer Society and USPSTF recommend CRC screening for ages 45-75 for individuals of average risk:
  - Colonoscopy every 10 years (preferred)
  - Flexible sigmoidoscopy every 5 years
  - Fecal occult blood test (FOBT) or fecal immunochemical testing (FIT) every year
- Individuals with IBD: colonoscopy 8 years after diagnosis and every 1-3 years thereafter

Workup

- **H&P**
  - DRE – evaluate sphincter function (predictor of subsequent continence)
- **Rigid Proctoscopy** – assess primary tumor and biopsy
- **Colonoscopy** – detect possible synchronous primaries
- **CT chest, abdomen, and pelvis** – detect metastatic disease
- **Endorectal ultrasound (ERUS)** – accurate in predicting T category, assess depth of tumor penetration and adjacent mesorectal and pelvic LNs
- **MRI** – accurate in predicting T-category and mesorectal fascial involvement (circumferential resection margin [CRM] positivity), assess involvement of LNs based on size criteria
- **PET** – helpful for LN involvement when indicated
- **CBC, CEA**

Staging

T	Primary Tumor
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma *in situ*: intramucosal carcinoma (involvement of lamina propria with no extension through muscularis mucosa)
T1	Tumor invades the submucosa (through the muscularis mucosa but not into the muscularis propria)
T2	Tumor invades the muscularis propria
T3	Tumor invades through the muscular propria into the pericolorectal tissues
T4	a: Tumor invades through the visceral peritoneum (includeding gross perforation of the bowel through tumor and continuous invasion of tumor through areas of inflammation to the surface of the visceral peritoneum) b: Tumor directly invades or adheres to adjacent organs or structures

N	Regional Lymph Nodes
NX	Not assessed
N0	No regional LN metastasis
N1	1-3 LNs positive
N1a	One regional LN positive
N1b	Two or three regional LNs positive
N1c	No regional LNs are positive, but there are tumor deposits in the subserosa, mesentery, or nonperitonealized pericolic, or perirectal/mesorectal tissues
N2	4+ LNs positive
N2a	4-6 LNs positive
N2b	7+ LNs positive

Staging

M	Distant Metastasis
M0	No distant metastasis by imaging, etc; no evidence of tumor in distant sites or organs
M1	Metastasis to one or more distant sites or organs or peritoneal metastasis is identified
M1a	Metastasis to one site or organ is identified without peritoneal metastsis
M1b	Metastasis to two or more sites or organs is identified without peritoneal metastasis
M1c	Metastasis to the peritoneal surface is identified alone or with other site or organ metastases

American Joint Committee on Cancer (AJCC)
TNM Staging System for Rectal Cancer 8th ed., 2017

Table 2. **Prognostic Groups**

	T	N	M
Stage 0	Tis	N0	M0
Stage I	T1, T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T4a	N0	M0
Stage IIC	T4b	N0	M0
Stage IIIA	T1-T2	N1/N1c	M0
	T1	N2a	M0
Stage IIIB	T3-T4a	N1/N1c	M0
	T2-T3	N2a	M0
	T1-T2	N2b	M0
Stage IIIC	T4a	N2a	M0
	T3-T4a	N2b	M0
	T4b	N1-N2	M0
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b
Stage IVC	Any T	Any N	M1c

General Management

- **cT1N0**: transanal excision
  - If R0 → observe
- **cT1-2N0**: TME (LAR or APR)
  - If R0 → observe
  - If pT3+ or N+ → adjuvant therapy
- **cT3-4, N+**: multiple options (typically tri-modality therapy)
  - *See next slide*

Treatment Sequencing

LC-CRT → TME → Adjuvant Chemotherapy

SC-RT → TME → Adjuvant Chemotherapy

LC-CRT → Chemotherapy → TME

SC-RT → Chemotherapy → TME

Chemotherapy → LC-CRT → TME

Chemotherapy → SC-RT → TME

LC-CRT → Chemotherapy → NOM

SC-RT → Chemotherapy → NOM*

Chemotherapy → LC-CRT → NOM

Chemotherapy → SC-RT → NOM*

Key

LC-CRT: long course chemoradiation

SC-RT: short course radiotherapy

TME: total mesorectal excision

NOM: non-operative management

* SCRT TNT does not have a lot of evidence in the NOM setting. Current trials are underway.

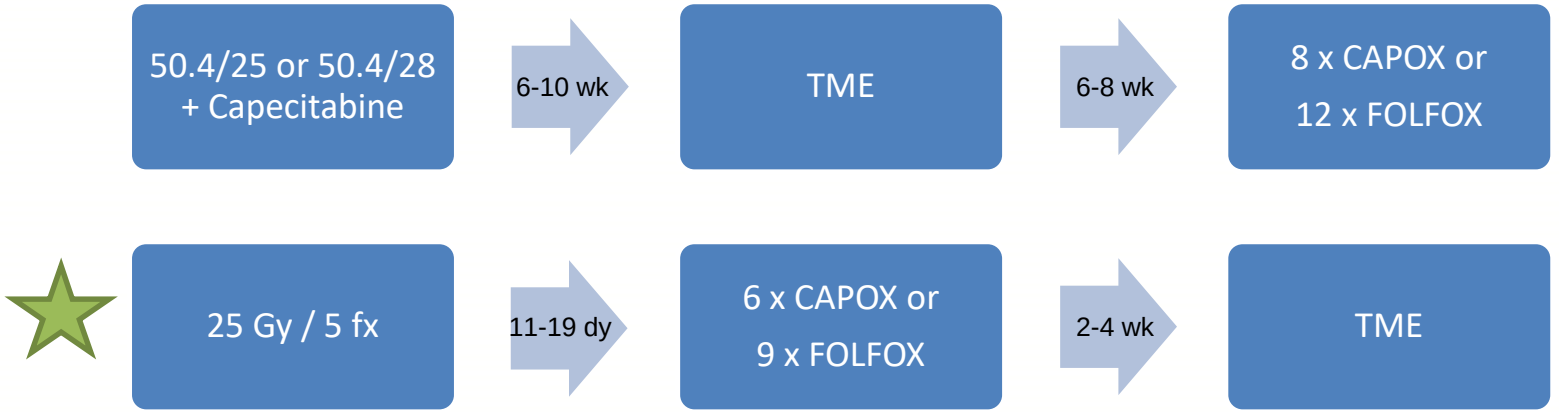
Total Neoadjuvant Therapy (TNT)

Benefits

- Improved compliance with systemic therapy
- Improves pCR→ may facilitate non-operative management
- Less time with diverting ostomy
- Treats possible circulating micrometastases
  - Potential decreased risk of distant metastases

Evidence for TNT

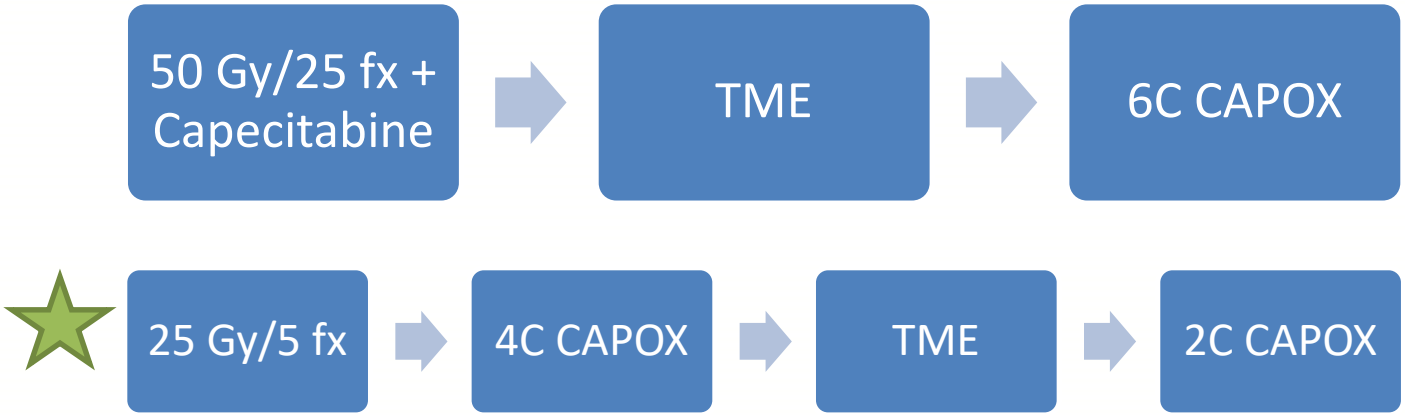
- **RAPIDO**
  - Eligibility: cT4, cN2, extramural venous invasion (EMVI), <1 mm to mesorectal fascia, lateral lymph nodes >1 cm
  - Randomized 1:1



  - 3-year disease related treatment failure: 30.4% (standard arm) vs 23.7% (TNT), p=0.02
  - pCR improved with TNT (14 → 28%)
  - Improved chemotherapy completion rate with TNT (84% vs 57%)

Evidence for TNT

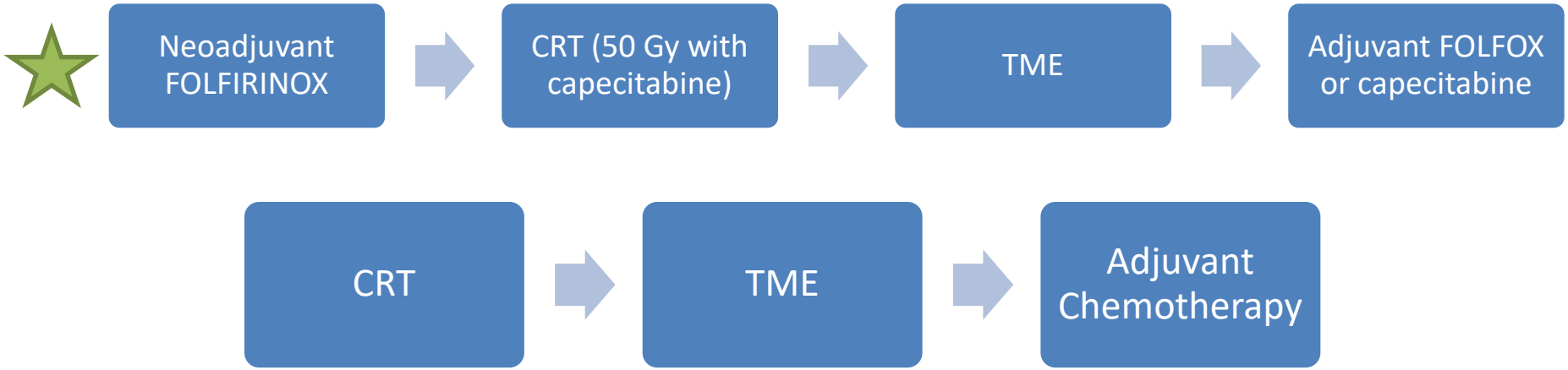
- **STELLAR**
  - Eligibility: distal or middle third, T3-T4 and/or N+ rectal adenocarcinomas



  - pCR (12 → 17%) and cCR (13 → 23%) improved with TNT
  - Full-dose completion rates of preoperative treatment improved with TNT (82.6% vs 95.2%)
  - Probability of OS at 3 years improved with TNT (86.5% vs 75.1%)

Evidence for TNT

- **PRODIGE 23**
  - Eligibility: cT3 or cT4 M0 rectal adenocarcinoma



  - 3-year disease-free survival: 76% TNT and 69% standard (p=0.03)

Concurrent Chemotherapy

- **Xeloda (Capecitabine)**
  - Fluorouracil prodrug that inhibits thymidylate synthase → interfering with DNA synthesis
  - Concurrent dose: 825 mg/m^2 BID 5 days per week
    - Take 1 hour prior to RT
  - Possible side effects: hand foot syndrome, mucositis, cardiotoxicity, fatigue, GI symptoms, neuropathy, cytopenias
- **5-Fluorouracil (5-FU)**
  - Thymidylate synthase inhibitor → interrupts nucleotide synthesis needed for DNA replication
  - Concurrent dose
    - Continuous IV infusion: 225 mg/m2 5-7 days per week
    - Bolus: 400 mg/m2 over 4 days on weeks 1 and 5
  - Side effects: cardiotoxicity, mucositis, alopecia and nail changes, dermatitis, GI symptoms, cytopenias

Consolidative/Adjuvant Chemotherapy

- **FOLFOX**
  - 2-week cycles
  - 2-hr infusion of oxaliplatin + leucovorin → bolus injection of 5-FU and 46-hour continuous infusion of 5-FU
- **CAPOX**
  - 3-week cycles
  - 2-hour infusion of oxaliplatin on day 1 and oral capecitabine 1000 mg/m^2 BID daily on days 1-14

Surgery

- **Total Mesorectal Excision (TME)**
  - Sharp en bloc removal of the mesorectum, including associated vascular and lymphatic structures, fatty tissue, and mesorectal fascia
  - Removes lymphatic drainage regions of tumors located above the level of the levator muscles
  - Spares autonomic nerves
  - At least 12 LNs for staging
  - Standard of care combined with either LAR or APR

Surgery

APR

- Abdominoperineal resection
- Not sphincter sparing
- Option if adequate distal margin (1cm) cannot be obtained
- Patients with poor pre-op anorectal sphincter function
- Permanent colostomy

LAR

- Low anterior resection
- Sphincter sparing
- Negative distal margin required
- Patients with adequate pre-op anorectal sphincter function
- More amenable to coloanal anastomosis or colonic J-pouch, but colostomy may be required

Transanal Excision

- **GRECCAR 2**
  - Eligibility: cT2-T3 lower rectal carcinoma, maximum size 4 cm with good clinical response to neoadjuvant chemotherapy (residual tumor < 2 cm)
  - Randomized before surgery to local excision or TME
    - In the local excision group, completion TME was required for ypT2-3
  - Failed to show superiority of local excision over TME because many patients in the local excision group received a completion TME

Transanal Excision

- Organ preservation can be considered in certain patients that have a good response to neoadjuvant therapy to avoid morbidity of rectal excision
- **ACOSOG Z6041**
  - Eligible: cT2N0 rectal adenocarcinoma measuring < 4 cm in greatest diameter, involving < 40% of the circumference of the rectum, located within 8 cm of the anal verge
  - Treatment: Neoadjuvant CAPOX + 50.4 Gy → transanal excision
  - Results
    - 49% pCR, 3-year DFS 87% (per protocol)

Non-Operative Management

Benefits of NOM

- Improved quality of life
- Potentially avoid colostomy
- Prevent surgical complications
- Many recurrences can be salvaged with subsequent surgery

Non-Operative Management

Habr-Gama et al. ***Operative vs Nonoperative Treatment for Stage 0 Distal Rectal Cancer Following Chemoradiation Therapy***

- Eligible: distal rectal adenocarcinoma considered resectable, treated with neoadjuvant chemoradiation (50.4 Gy with 5-FU and Leucovorin)
- Incomplete clinical response → surgical resection
- Patients with complete clinical response were not immediately operated on
    - Year 1: Monthly physical, DRE, proctoscopy, biopsies (when feasible), CEA; CT A/P and chest radiograph q 6 months during 1st year
    - Year 2: Follow-up visits q 2 months
    - Year 3: Follow-up visits q 6 months
- Results
    - 27% of patients had cCR at 8 weeks after completion of CRT
    - 8% of patients in resection group had pT0N0 disease on surgical path

Non-Operative Management

MSKCC OPRA

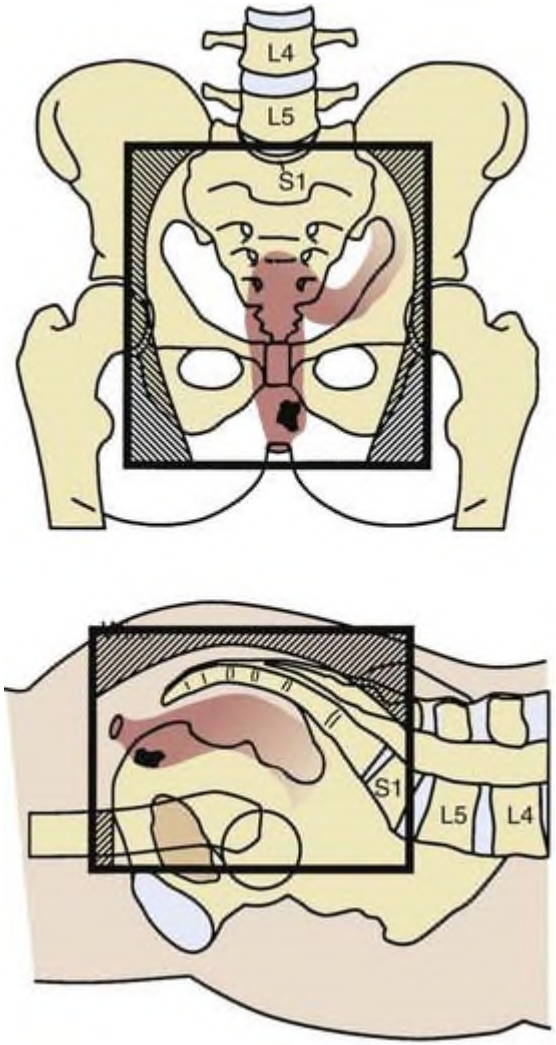
- Eligible: Stage II and III rectal adenocarcinoma
- Treatment: 4 months FOLFOX or CAPEOX before or after chemoradiation
  - Patients re-staged 8-12 weeks after finishing TNT with DRE, flexible sigmoidoscopy and MRI
  - Patients with complete or near-complete clinical response were offered Watch and Wait
- Results: Up-front CRT followed by consolidation chemotherapy resulted in numerically higher Watch and Wait rate compared to induction chemotherapy followed by CRT

Omission of Radiation

- **MSKCC Pilot Trial**
  - Eligible: cT3N0 or cT3N+ disease, tumor amenable to sphincter-preserving TME and distal edge located between 5 and 12 cm of the anal verge
  - Treatment: 4C mFOLFOX6 + bevacizumab → 2C mFOLFOX6
    - Patients with progression during chemo proceeded to CCRT
    - Those without progression proceeded to TME without CCRT
  - Results: pCR 25%, 94% proceeded to TME without CCRT
- **PROSPECT**
  - Eligible: T2N1, T3N0, T3N1
  - Standard Arm: CCRT → TME → FOLFOX
  - Experimental Arm: FOLFOX → (CRT if <20% response on MRI or ERUS) → TME → FOLFOX
  - Results pending

Principles of Radiotherapy

- **3D CRT most commonly used**
  - RTOG 0822: Treatment with IMRT
    - 51.5% with a ≥ grade 2 GI adverse events compared to 40% on RTOG 0822 (3D CRT)
- Reasonable to use IMRT when inguinal lymph nodes are treated or boosting lateral pelvic LNs



Radiotherapy: Simulation

- **Option 1**: Supine, head first, Vac-Lock for immobilization
  - Frog leg position if treating inguinal LNs (anal or vaginal involvement)
- **Option 2**: Prone with a belly board
  - Ideal for patients with larger body habitus
    - Decreases small bowel dose
- Treat with full bladder
    - Decreases small bowel dose
- Consider treating with vaginal dilator to decrease risk of vaginal stenosis

Radiotherapy: Contours

- **GTVp**: primary tumor (use colonoscopy, imaging)
- **GTVn**: involved lymph nodes (boost to ~60Gy for lateral pelvic LNs)
- **CTVp**: include entire circumference of rectal lumen at involved levels. GTVp + 2.5 cm craniocaudal, 1.5 cm radial. Cover entire mesorectum to the pelvic floor.
- **CTVn:** GTVn + 1-1.5 cm
  - Consider boosting lateral pelvic nodes unless planned to be removed at time of surgery
- **CTV_LN**: include common iliac, internal iliac, presacral, peri-rectal and obturator lymph nodes, 7 mm around vessels
  - Include external iliac LNs for T4 tumors extending anteriorly
  - Include external iliac LNs and inguinal LNs for anal involvement

Radiotherapy: Dose & Fractionation

- Short Course: 25 Gy / 5 fx
  - **Swedish Rectal Cancer Trial**
    - Pre-op RT with surgery vs. surgery alone (blunt dissection, not TME)
    - Pre-op RT improved 13-yr OS, CSS, and LR
  - **Dutch TME Study** (2011 Lancet)
    - Pre-op RT with TME vs TME alone
    - Pre-op RT improved 10-yr LR
    - No difference in OS
- Consider Short Course RT for upfront LAR candidates
  - Suggestion that LC-RT has better conversion to sphincter sparing

Lateral Pelvic Lymph Nodes

- **Lateral Node Study Consortium**
  - Retrospective multicenter study
  - Patients with enlarged lateral lymph nodes (≥ 7mm) have a considerable change of local recurrence (~20%) despite neoadjuvant treatment
  - Lateral lymph node dissection lowers the rate of local recurrence considerably, but it is a difficult surgical technique
    - Not standardly performed at every institution
      - **Important to discuss with surgeons at multidisciplinary conferences!**

Lateral Pelvic Lymph Nodes

- If lateral lymph nodes are not dissected, consider boosting with radiation
  - Chen et al (PRO 2020). *Effect and Safety of Radiation Therapy Boost to Extramesorectal Lymph Nodes in Rectal Cancer*
    - Patients with clinically positive lateral pelvic LNs that would not be removed during TME received an additional boost (up to 54.0 - 59.4 Gy)
    - There was no difference in 3-year OS and PFS in the lateral lymph node negative group and the group with treated lateral lymph nodes
    - They did not observe any lateral pelvic nodal recurrences
    - There were no differences in acute grade 3+ or chronic toxicities

Radiotherapy: Side Effects

Acute

- Fatigue
- Diarrhea, increased bowel frequency
- Acute proctitis
- Dysuria

Late

- Persistent bowel changes
- Strictures at the anastomotic site
- Small bowel obstruction
- Urinary incontinence
- Radiation cystitis
- Vaginal stenosis
- Secondary malignancy

Follow-Up

- **Transanal local excision only**
  - Proctoscopy (with EUS or MRI with contrast) q3-6 mos for 2 years, then q6 mos until 5 years
  - Colonoscopy at 1 year after surgery
    - If advanced adenoma, repeat in 1 yr
    - If no advanced adenoma, repeat in 3 yrs then q5 yrs
- **Stage I with full surgical staging**
  - Colonoscopy at 1 year after surgery
    - If advanced adenoma, repeat in 1 yr
    - If no advanced adenoma, repeat in 3 yrs then q5 yrs

Follow-Up

- **Stage II-IV**
  - H&P with CEA q3-6 mos for 2 yrs, then q6mos until 5 years
  - Stage II, III: CT CAP q6-12mos for 5yrs
  - Stage IV: CT CAP q3-6mos for 2 yrs, then q6-12 mos until 5 yrs
  - No PET/CT recommended
  - Colonoscopy at 1 year after surgery
    - If no pre-op colonoscopy due to obstruction, then colonoscopy in 3-6 mos post-op
    - If advanced adenoma, repeat in 1 yr
    - If no advanced adenoma, repeat in 3 yrs then q5 yrs

References

- Minsky BD, Rodel CM, Valentini V. Rectacl Cancer. Gunderson and Tepper's Clinical Radiation Oncology. 58, 1011-1036.e8
- NCCN Rectal Cancer Guidelines Version 2.2021
- Folkesson J, Birgisson H, Pahlman L, et al. Swedish Rectal Cancer Trial: Long Lasting Benefits from Radiotherapy on Survival and Local Recurrence Rate. J Clin Oncol 2005;23:5644-50.
- Kapiteijn E, et al. Preoperative Radiotherapy Combined with Total Mesorectal Excision for Resectable Rectal Cancer. N Engl J Med. 2001; 345:638-46.
- Kusters M, et al. Patterns of local recurrence in rectal cancer; a study of the Dutch TME trial. Eur J Surg Oncol. 2010;36:470-6.
- Ngan SY, et al. Randomized trial of short-course radiotherapy versus long-course chemoradiation comparing rates of local recurrence in patients with T3 rectal cancer: Trans-Tasman Radiation Oncology Group Trial 01.04. J Clin Oncol. 2012;30:3827-33.
- Cisel B, Pietrzak L, Michalski W, et al. Long-course preoperative chemoradiation versus 5 x 5 Gy and consolidation
- RTOG Contouring Atlas- Rectal Cancer
- Hong TS, Moughan J, Garofalo MC, et al. NRG Oncology Radiation Therapy Oncology Group 0822: A Phase 2 Study of Preoperative Chemoradiation Therapy Using Intensity Modulated Radiation Therapy in Combination with Capecitabine and Oxaliplatin for Patients with Locally Advanced Rectal Cancer. Int J Radiat Oncol Biol Phys. 2015;93:29-36.
- Chin, R. I., Roy, A., Pedersen, K., Huang, Y., Hunt, S., Glasgow, S. C., Tan, B., Wise, P. E., Silviera, M. L., Smith, R., Suresh, R., Badiyan, S. N., Shetty, A., Henke, L. E., Mutch, M. G., & Kim, H. (Accepted/In press). Clinical Complete Response in Patients With Rectal Adenocarcinoma Treated With Short-Course Radiation Therapy and Nonoperative Management. *International Journal of Radiation Oncology Biology Physics*. https://doi.org/10.1016/j.ijrobp.2021.10.004
- Garcia-Aguilar J, Patil S, Kim JK, et al. Preliminary results of the organ preservation of rectal adenocarcinoma (OPRA) trial. J Clin Oncol 2020; 38:s4008.
- Habr-Gama A, Perez RO, Sao Juliao GP, Proscurshim I, Gama-Rodrigues J. Nonoperative approaches to rectal cancer: a critical evaluation. Semin Radiat Oncol. 2011. Jul;21(3):234-9.
- Ronal Bleday, David Shibata. UpToDate: Surgical treatment of rectal cancer. Aug. 2021. Accessed 1/27/2022.
- Cercek A, Roxburgh CSD, Strombom P, et al. Adoption of Total Neoadjuvant Therapy for Locally Advanced Rectal Cancer. JAMA Oncology. 2018;4(6):e180071.
- Conroy T, Bosset J, Etienne P, et al. Neoadjuvant chemotherapy with FOLFIRINOX and preoperative chemoradiotherapy for patients with locally advanced rectal cancer (UNICANCER-PRODIGE 23). Lancet Oncol. 2021.
- AJCC Cancer Staging Manual- 8th Edition

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References

- Conroy T, Bosset JF, Etienne PL, Rio E, François É, Mesgouez-Nebout N, Vendrely V, Artignan X, Bouché O, Gargot D, Boige V, Bonichon-Lamichhane N, Louvet C, Morand C, de la Fouchardière C, Lamfichekh N, Juzyna B, Jouffroy-Zeller C, Rullier E, Marchal F, Gourgou S, Castan F, Borg C; Unicancer Gastrointestinal Group and Partenariat de Recherche en Oncologie Digestive (PRODIGE) Group. Neoadjuvant chemotherapy with FOLFIRINOX and preoperative chemoradiotherapy for patients with locally advanced rectal cancer (UNICANCER-PRODIGE 23): a multicentre, randomised, open-label, phase 3 trial. Lancet Oncol. 2021 May;22(5):702-715. doi: 10.1016/S1470-2045(21)00079-6. Epub 2021 Apr 13. PMID: 33862000.
- Rullier E, Vendrely V, Asselineau J, Rouanet P, Tuech JJ, Valverde A, de Chaisemartin C, Rivoire M, Trilling B, Jafari M, Portier G, Meunier B, Sieleznieff I, Bertrand M, Marchal F, Dubois A, Pocard M, Rullier A, Smith D, Frulio N, Frison E, Denost Q. Organ preservation with chemoradiotherapy plus local excision for rectal cancer: 5-year results of the GRECCAR 2 randomised trial. Lancet Gastroenterol Hepatol. 2020 May;5(5):465-474. doi: 10.1016/S2468-1253(19)30410-8. Epub 2020 Feb 7. PMID: 32043980.
- AJCC Cancer Staging Manual- 8th Edition
- Ansari N, Solomon MJ, Fisher RJ, Mackay J, Burmeister B, Ackland S, Heriot A, Joseph D, McLachlan SA, McClure B, Ngan SY. Acute Adverse Events and Postoperative Complications in a Randomized Trial of Preoperative Short-course Radiotherapy Versus Long-course Chemoradiotherapy for T3 Adenocarcinoma of the Rectum: Trans-Tasman Radiation Oncology Group Trial (TROG 01.04). Ann Surg. 2017 May;265(5):882-888. doi: 10.1097/SLA.0000000000001987. PMID: 27631775.
- Clinicaltrials.gov

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