ICRA 2026
Rectal Cancer Presentation

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Case: Patient CP, 52 year-old female

- **Chief complaint:** abdominal pain and change in bowel habits (difficulty evacuating stool) with associated rectal bleeding about 8 weeks ago.

- Seen by GI at OSH and went for flexible sigmoidoscopy and anoscopy
  - Two abnormal findings
    - Mass in the upper rectum extending to the rectosigmoid junction
    - Anterior anal canal mass
    - Both areas biopsied
    - Pathology
      - Upper rectal/rectosigmoid mass – adenocarcinoma, pMMR
      - Anterior anal canal mass – squamous cell carcinoma, HPV+

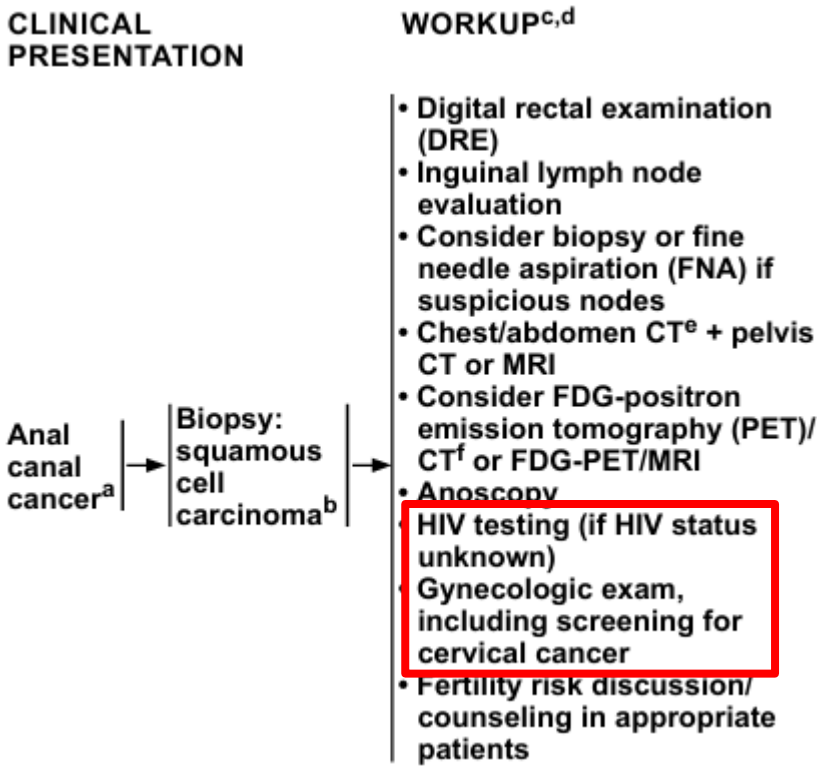
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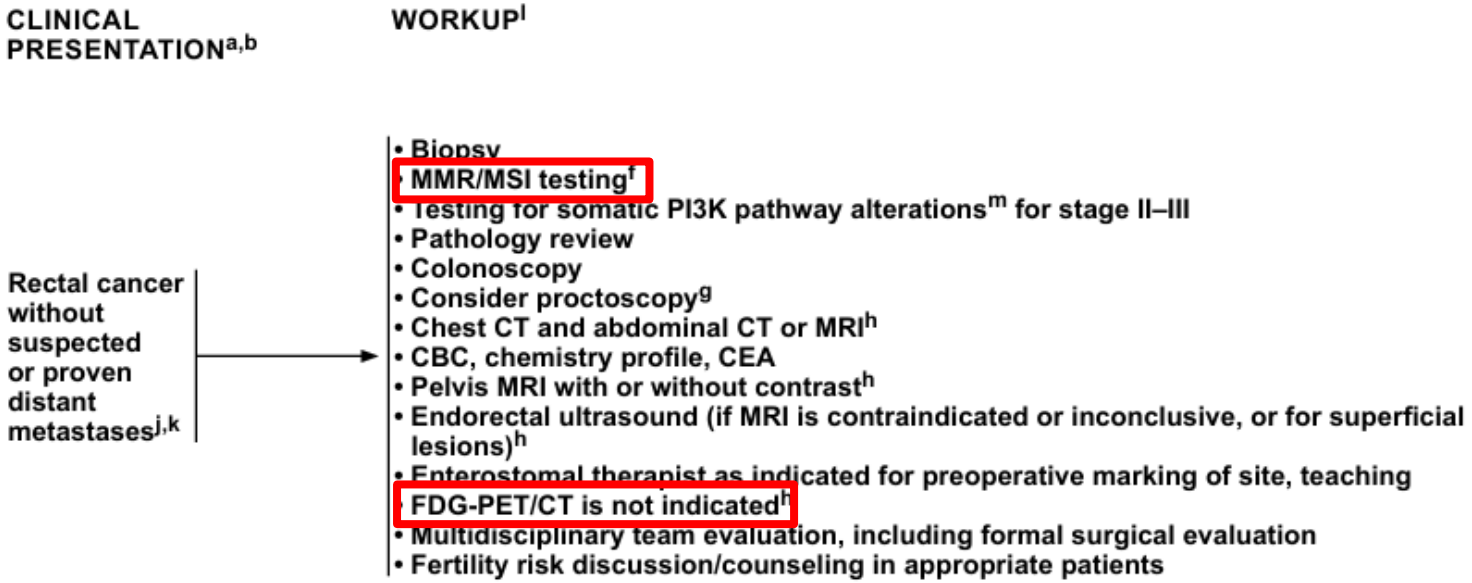
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Work Up For Anal and Rectal Cancer

- History, Physical, Anoscopy/Proctoscopy/Flexible Sigmoidoscopy
- Imaging
  - Rectal cancer: MRI pelvis w/ and w/o (rectal protocol), CT CAP w/ contrast
  - Anal cancer: CT CAP w/ contrast but personally think PET/CT very helpful





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Additional History

Additional history: In addition to bleeding, patient has had some fecal incontinence and mucus discharge as well as pain with bowel movements. No weight loss, focal bony pain. No history of IBD, no prior radiation treatments, no prior cancer diagnoses. No hx of HIV/STDs. Monogamous with her husband of 20 years.

Past Medical History

- Hypertension
- Hyperlipidemia
- T2DM
- OA

Past Surgical History

- Appendectomy
- Cholecystectomy
- b/l tubal ligation
- Carpal tunnel surgery

Social History

- Former 20 pack-year smoker (quit 6 years ago)
- Alcohol: Does not drink
- Married with four children
- Sexually active with her husband, no prior STDs, up to date on Pap testing, no prior high-risk HPV, negative HIV testing in the past

Family Cancer History:

- Father died of lung cancer at age 76 (longstanding smoker)

Medications

1. Atorvastatin
2. Hydrochlorothiazide
3. Metformin
4. Tylenol

Allergies: Tramadol

Review of Systems:

- Constitutional: + for fatigue, Negative for chills and weight loss.
- HENT: negative for dysphagia/odynophagia, lymphadenopathy ear pain and sore throat.
- Eyes: Negative for blurred vision and double vision.
- Respiratory: Negative for cough, shortness of breath, wheezing and stridor.
- Cardiovascular: Negative. Negative for chest pain and palpitations.
- Gastrointestinal: + for abdominal pain, pain defecating, blood in the stool.
- Genitourinary: Negative for dysuria and urgency.
- Musculoskeletal: Negative for back pain, myalgias and neck pain.
- Skin: Negative.
- Neurological: Negative for dizziness and headaches.
- Psychiatric/Behavioral: Negative for depression.

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Physical Exam

Vitals Within normal limits

Performance Status: ECOG 0 KPS 100

General: Healthy appearing Caucasian woman, no acute distress, pleasant

Heart: Normal rate, regular rhythm, no murmurs

Lungs: Lungs clear, no crackles, wheezes

Abdomen: Normal bowel sounds, abdomen soft and non-tender without palpable masses or organomegaly

Perianal: Perianal skin wnl, hemorrhoids apparent. Digital rectal exam revealed 3-4 cm anorectal mass starting at the verge and extending proximally and involving the left side of the anal canal from 12-6 o'clock. No extension onto the perianal skin

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Anatomy of the Anus and Rectum

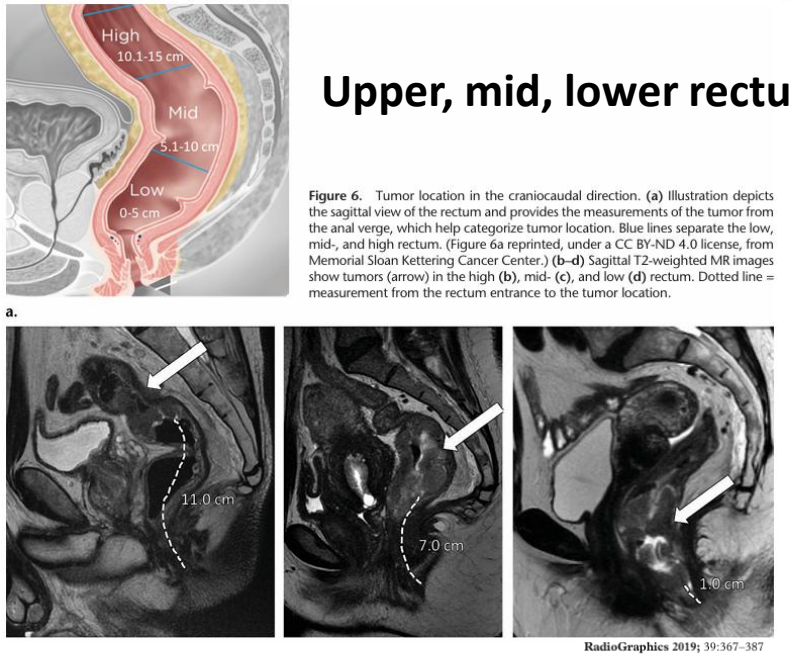
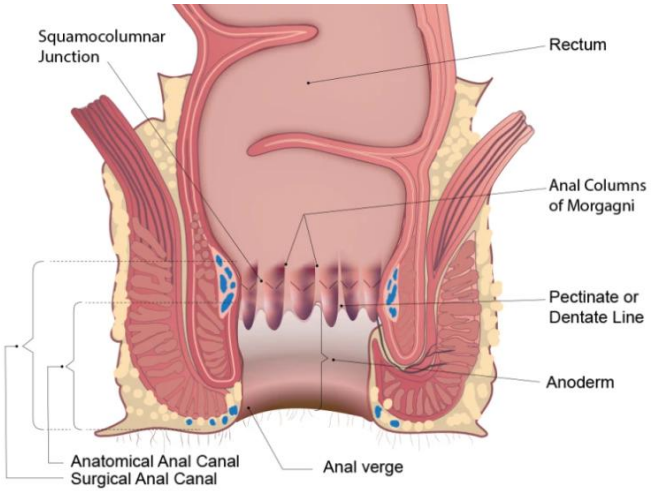


Figure 6. Tumor location in the craniocaudal direction. **(a)** Illustration depicts the sagittal view of the rectum and provides the measurements of the tumor from the anal verge, which help categorize tumor location. Blue lines separate the low, mid-, and high rectum. (Figure 6a reprinted, under a CC BY-ND 4.0 license, from Memorial Sloan Kettering Cancer Center.) **(b–d)** Sagittal T2-weighted MR images show tumors (arrow) in the high **(b)**, mid- **(c)**, and low **(d)** rectum. Dotted line = measurement from the rectum entrance to the tumor location.

a.

RadioGraphics 2019; 39:367–387

Upper, mid, lower rectum



Dentate Line – transition from columnar epithelium of rectum to the squamous epithelium of the anal canal (squamocolumnar junction)
Anal verge –most inferior aspect of anal sphincter muscles – transition from anoderm to normal perianal skin

Photomicrograph of the dentate line

Columnar epithelium with glands (rectum)

Squamous epithelium (anal canal)

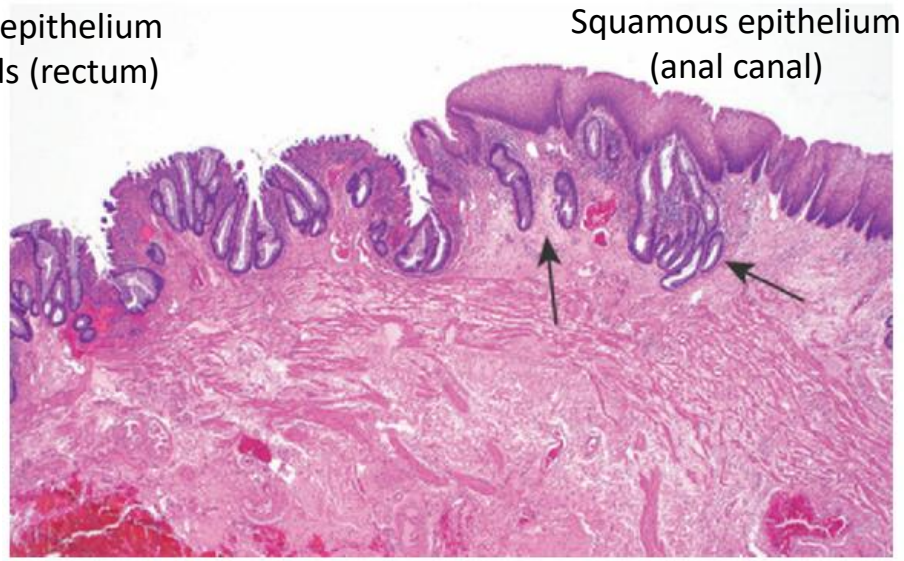


Figure 5. Photomicrograph shows the anorectal junctional mucosa, with the transition from the columnar mucinous epithelium of the rectum (left) to the simple squamous epithelium of the anal canal (right); the transition is often somewhat irregular, and the rectal columnar epithelium can extend under the squamous mucosa for a short distance in this region (arrows). (Original magnification, ×40; hematoxylin-eosin [H-E] stain.)

RadioGraphics 2015; 35:2090–2107

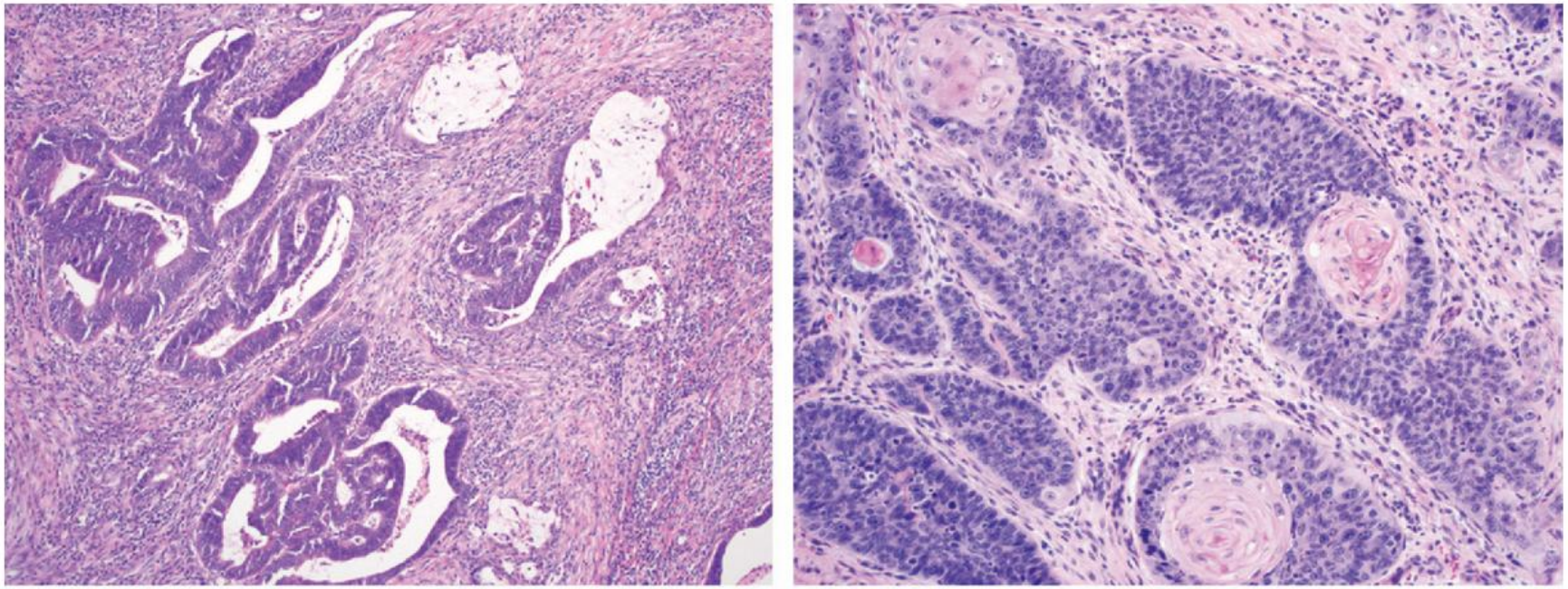
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Histology of anal cancer and rectal cancer

Rectal adenocarcinoma with abnormal gland formation

Anal squamous cell carcinoma with area of keratinization (arrows)



a. b.

Figure 6. Carcinomas of the anorectal region. **(a)** Photomicrograph shows adenocarcinoma of the rectum composed of infiltrating malignant glands, with associated desmoplastic stroma and mucin production. (Original magnification, ×100; H-E stain.) **(b)** Photomicrograph shows squamous cell carcinoma of the proximal anal canal, with predominantly basaloid morphology and foci of keratinization. (Original magnification, ×200; H-E stain.)

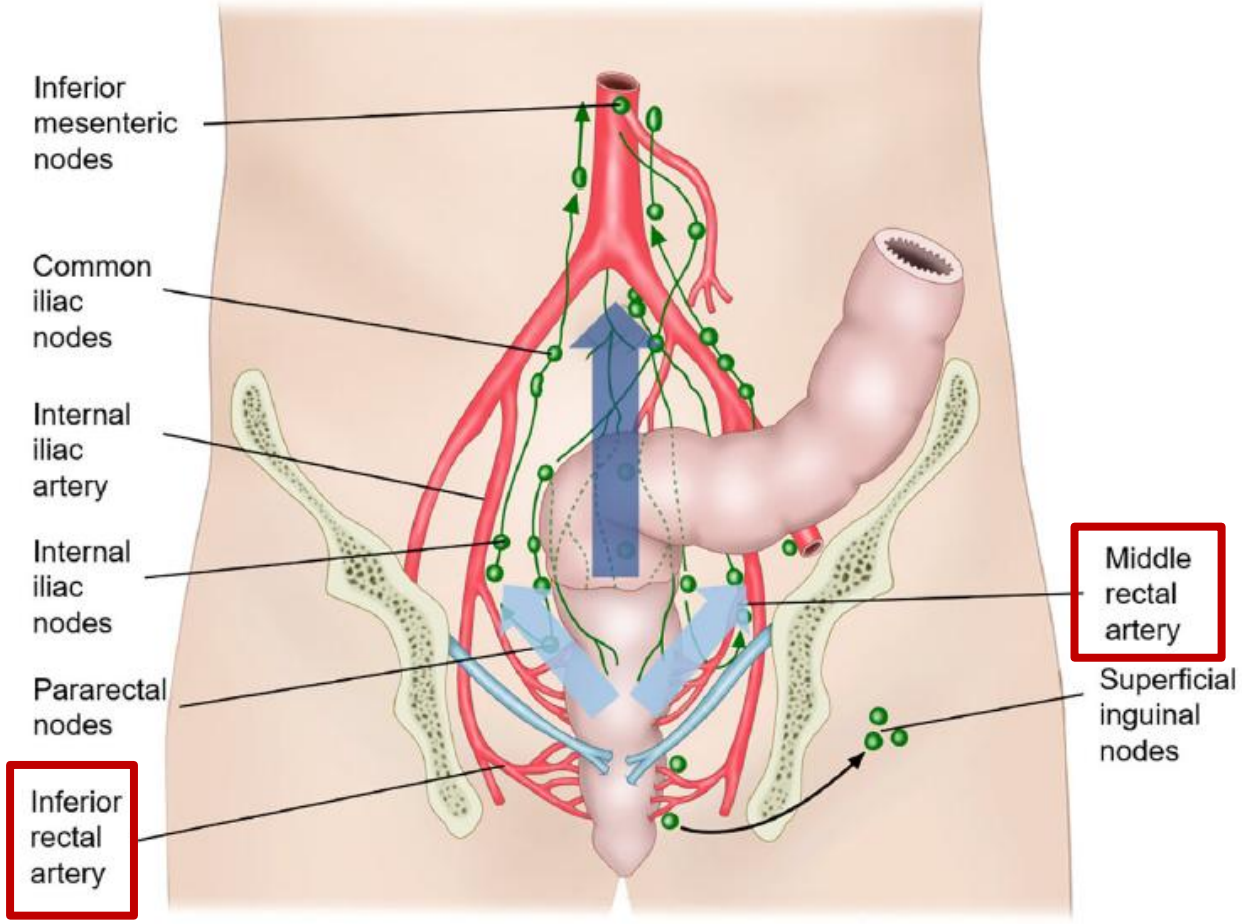
RadioGraphics 2015; 35:2090–2107

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Differential lymphatic drainage and “at risk” lymph nodes for rectal vs anal primary cancers

- Rectal cancer
  - Upper rectum
    - drainage along superior rectal vessels to mesorectal/pararectal LN
  - Lower/mid rectum
    - drainage along middle rectal vessels into internal iliac LN, obturator LN (pelvic sidewall)
- Anal cancer
  - Mesorectal, internal iliac, obturator
    - Below pectinate line, drainage along inferior rectal vessels into the superficial inguinal (groin) lymph nodes -> external iliac vessels



Front. Oncol. 12:960527.

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Clinical staging of Anal and Rectal Cancer

Anal cancer

American Joint Committee on Cancer (AJCC)
TNM Staging Classification for Anal Carcinoma (9th ed., 2022)
Table 1. **Definitions for T, N, M**

T	**Primary Tumor**
TX	Primary tumor not assessed
T0	No evidence of primary tumor
T1	Tumor less than or equal to 2 cm in greatest dimension
T2	Tumor greater than 2 cm but less than or equal to 5 cm in greatest dimension
T3	Tumor greater than 5 cm in greatest dimension
T4	Tumor of any size invades adjacent organ(s), such as the vagina, urethra, or bladder

N	**Regional Lymph Nodes**
NX	Regional lymph nodes cannot be assessed
N0	No tumor involvement of regional lymph node(s)
N1	Tumor involvement of regional lymph node(s)
N1a	Tumor involvement of inguinal, mesorectal, superior rectal, internal iliac, or obturator lymph node(s)
N1b	Tumor involvement of external iliac lymph node(s)
N1c	Tumor involvement of N1b (external iliac) with any N1a node(s)

M	**Distant Metastasis**
cM0	No distant metastasis
cM1	Distant metastasis
pM1	Microscopic confirmation of distant metastasis

Table 2. **AJCC Anatomic Stage/Prognostic Groups**

	T	N	M
Stage I	T1	N0	M0
Stage IIA	T2	N0	M0
Stage IIB	T1–T2	N1	M0
Stage IIIA	T3	N0–N1	M0
Stage IIIB	T4	N0	M0
Stage IIIC	T4	N1	M0
Stage IV	Any T	Any N	M1

Rectal cancer

American Joint Committee on Cancer (AJCC) TNM Staging Classification for Rectal Cancer 8th ed., 2017
Table 1. **Definitions for T, N, M**

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 mucosae)
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 muscularis propria into pericolorectal tissues
T4	Tumor invades* the visceral peritoneum or invades or adheres** to adjacent organ or structure
T4a	Tumor invades* through the visceral peritoneum (including gross perforation of the bowel through tumor and continuous invasion of tumor through areas of inflammation to the surface of the visceral peritoneum)
T4b	Tumor directly invades* or adheres** to adjacent organs or structures

N	**Regional Lymph Nodes**
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	One to three regional lymph nodes are positive (tumor in lymph nodes measuring ≥0.2 mm), or any number of tumor deposits are present and all identifiable lymph nodes are negative
N1a	One regional lymph node is positive
N1b	Two or three regional lymph nodes are positive
N1c	No regional lymph nodes are positive, but there are tumor deposits in the subserosa, mesentery, or nonperitonealized pericolic, or perirectal/mesorectal tissues
N2	Four or more regional lymph nodes are positive
N2a	Four to six regional lymph nodes are positive
N2b	Seven or more regional lymph nodes are positive

M	**Distant Metastasis**
M0	No distant metastasis by imaging, etc.; no evidence of tumor in distant sites or organs. (This category is not assigned by pathologists)
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 metastasis
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

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Rectal Protocol MRI for Rectal Cancer Staging

MRI showing MRF involvement with correlating pathology

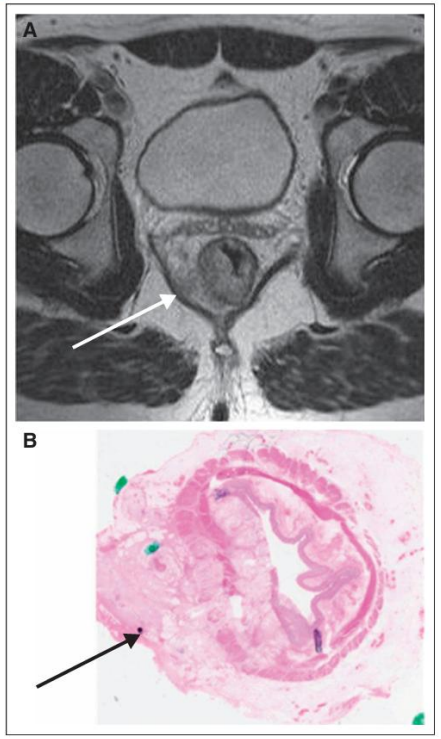
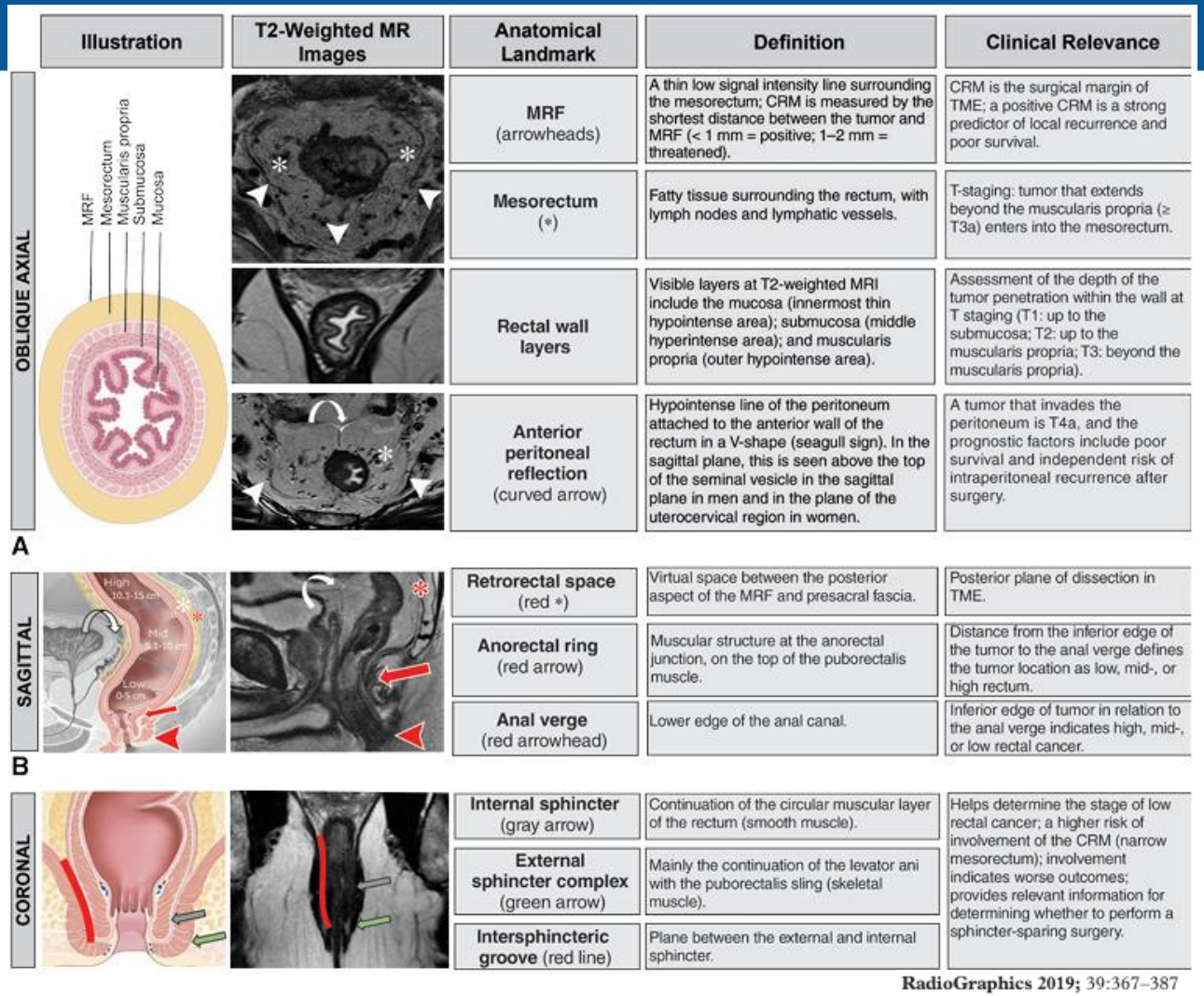


Fig 2. (A) T2-weighted axial thin section magnetic resonance imaging scan and (B) the corresponding histology section stained with hematoxylin and eosin. This scan and the corresponding histology section depict a low rectal tumor with involvement of the potential circumferential resection margin (white arrow) confirmed on corresponding histology (black arrow).

J Clin Oncol 32:34-43.



RadioGraphics 2019; 39:367–387

- Mercury trial – MRI staging better predicted outcomes (significance of MRF/CRM with poor outcomes)
- MRI also helps identify other high-risk features such as EMVI, sphincter involvement, etc

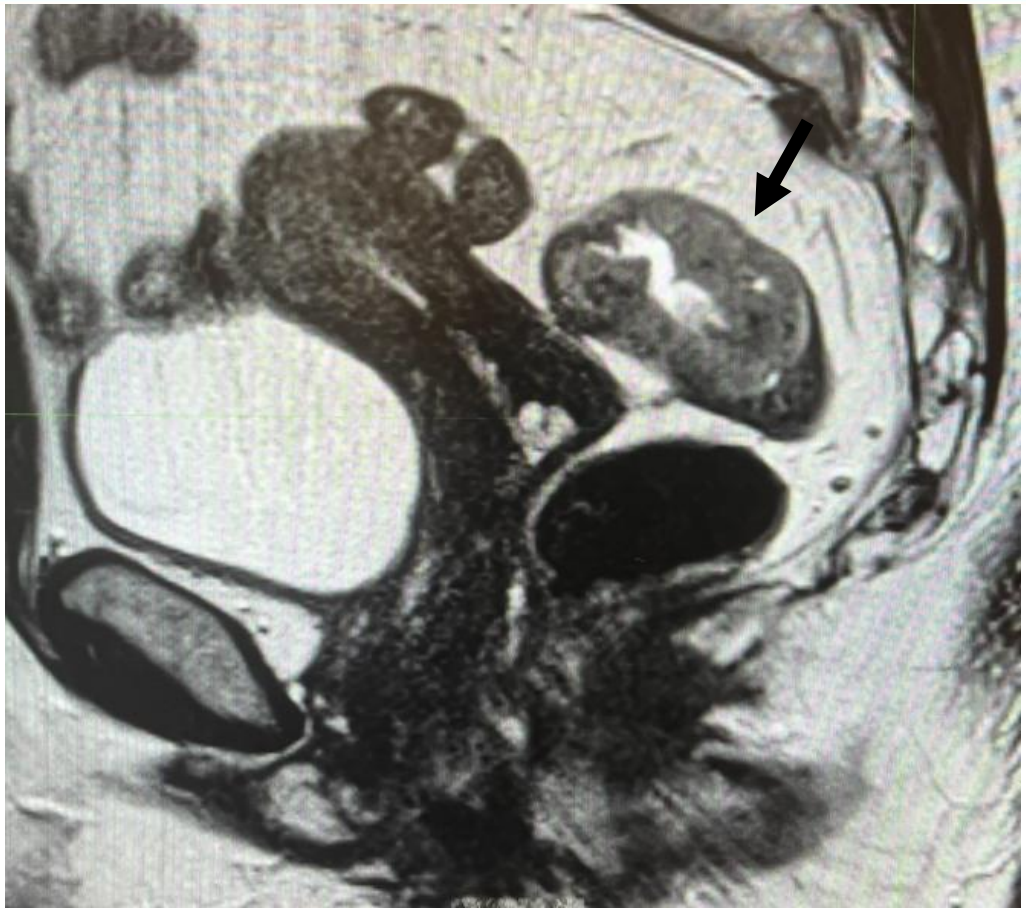
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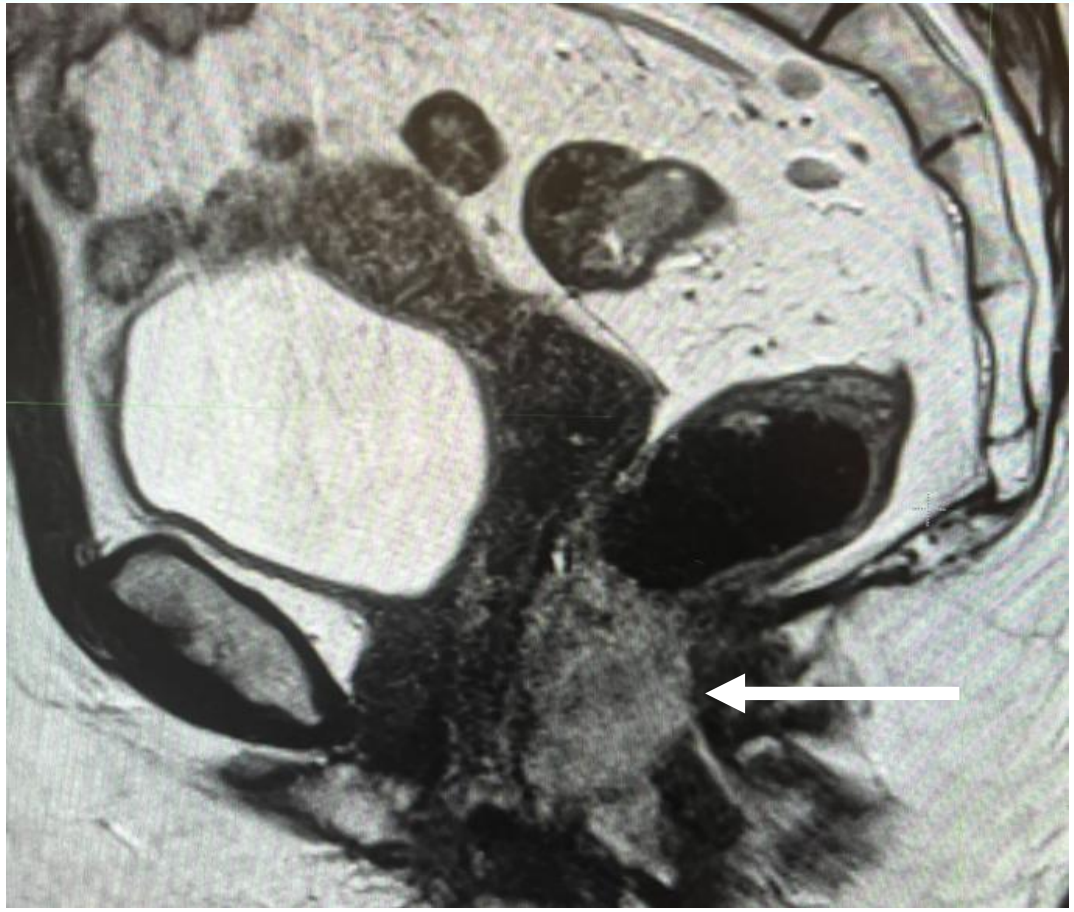
Initial staging MRI for our patient

Upper rectal/rectosigmoid mass



Upper rectal mass 5.8 cm from anorectal junction measuring 4.9 cm in craniocaudal length. Invasion into mesorectal fat and directly abuts the posterior aspect of the uterus with possible invasion of the anterior peritoneal reflection. No suspicious mesorectal or pelvic LN. cT4a N0

Anal mass



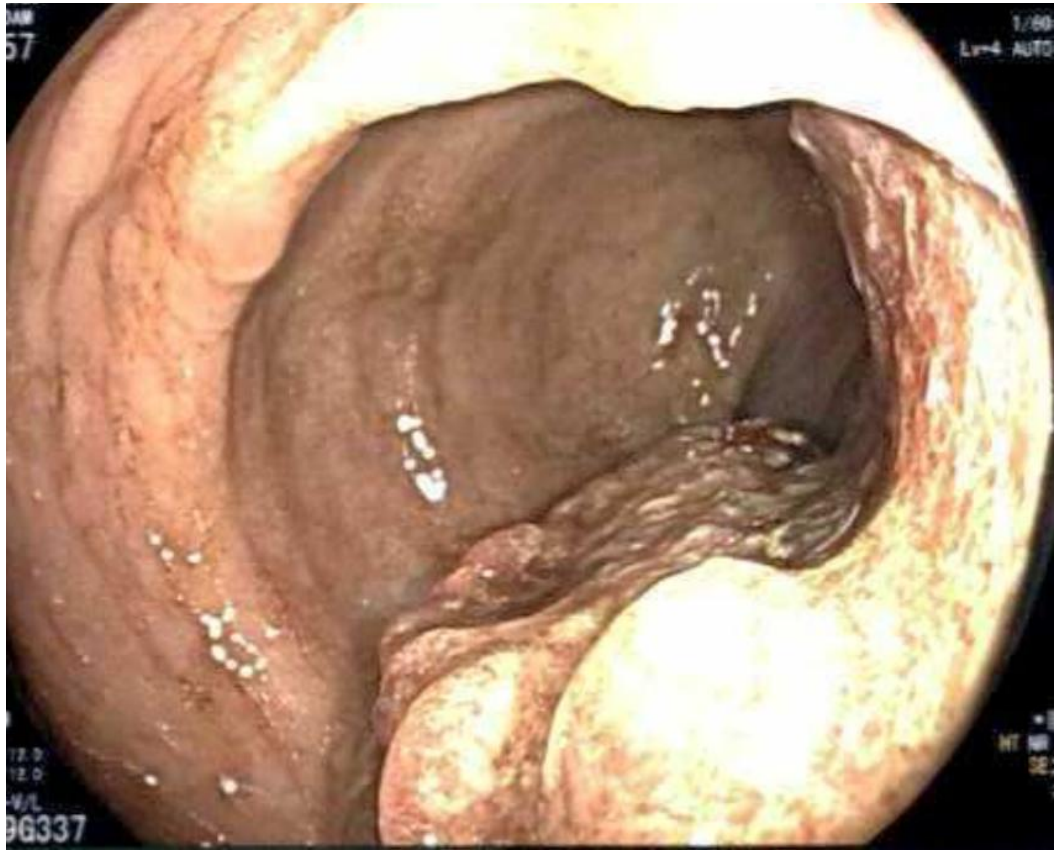
3.6 cm left anal canal mass with invasion of internal and external sphincter, no suspicious LN, cT2 N0

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Initial flexible sigmoidoscopy and anoscopy



Rectal cancer site



Anal cancer site

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Summary of initial clinical staging

- cT4a N0 M0 Rectal adenocarcinoma
  - Abutment/possible invasion of the posterior wall of uterus/peritoneum and possible invasion of anterior peritoneal reflection (cT4a)
  - No suspicious mesorectal, pelvic LN (cN0)
- cT2 N0 M0 anal squamous cell carcinoma
  - 3.6 cm primary anal tumor (cT2)
  - No pathologic inguinal, meosrectal, pelvic LN (cN0)

Two curable synchronous malignancies with different treatment paradigms. How do we address both with curative intent treatment in a timely manner?

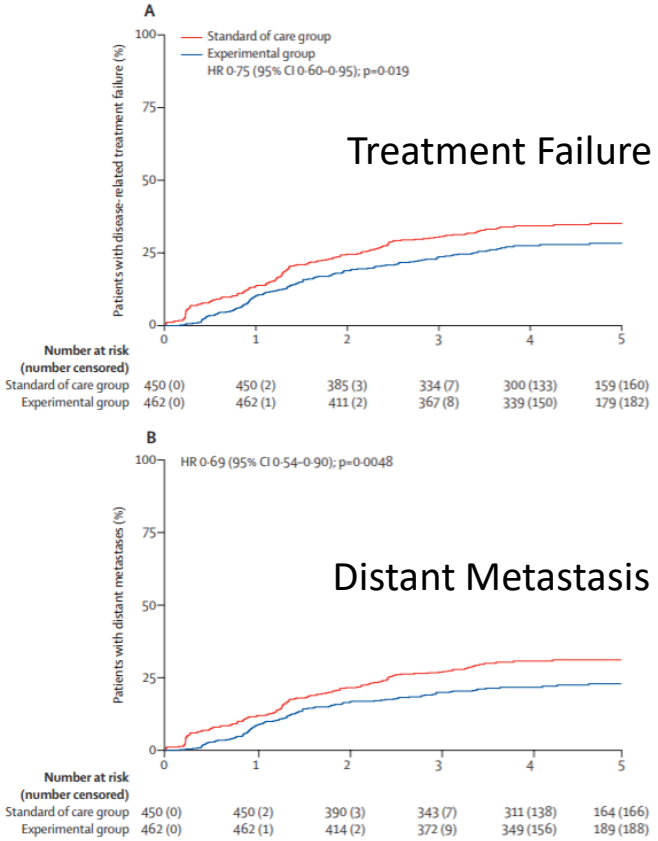
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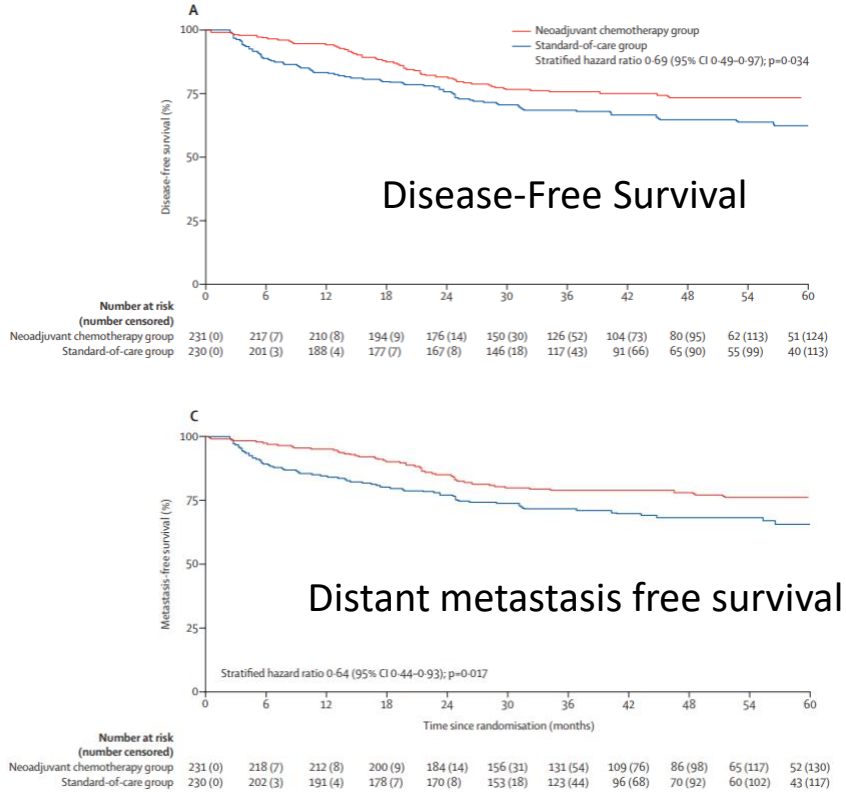
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Total neoadjuvant therapy (TNT) for locally advanced rectal adenocarcinoma

- RAPIDO



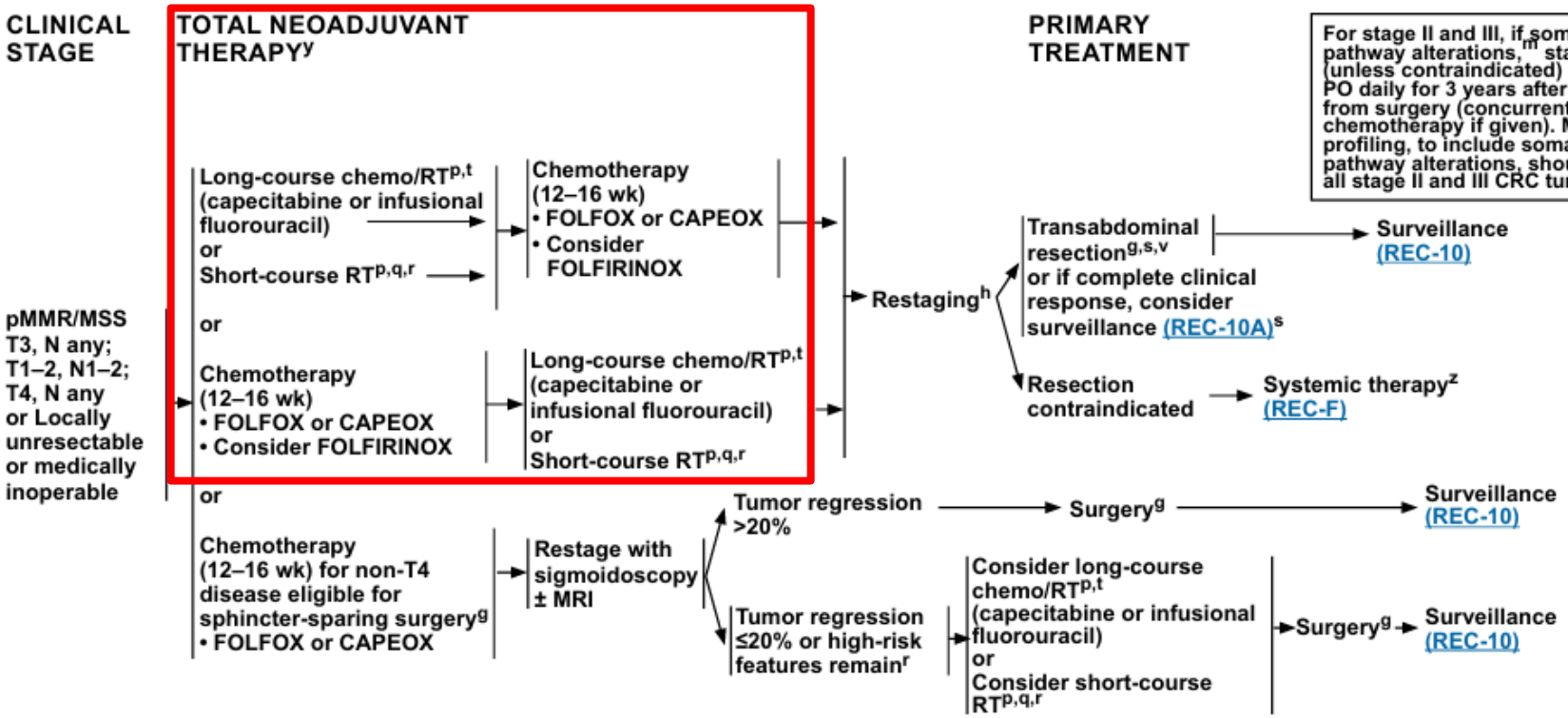
- PRODIGE 23



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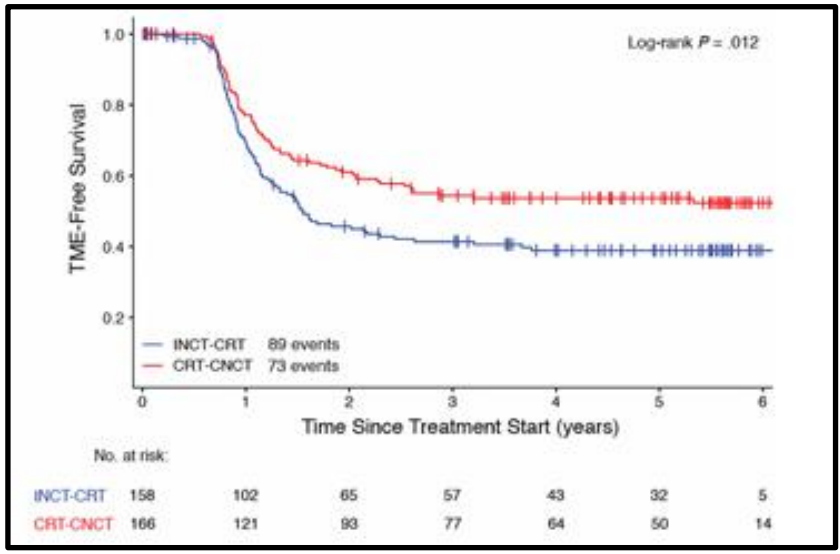
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TNT in NCCN Guidelines



Sequencing TNT – if goal is to attempt organ preservation, consider chemoRT -> chemo

OPRA trial

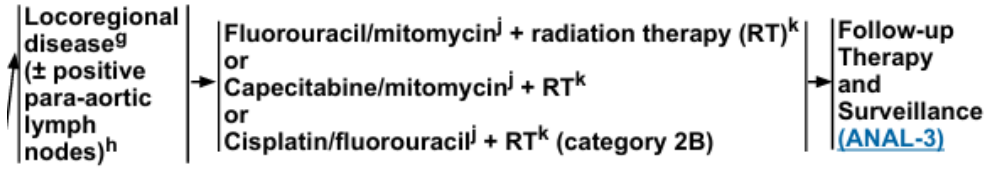


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Definitive chemoradiation for anal squamous cell carcinoma

- Based on the classic "Nigro protocol" (Nigro et al, Cancer, 1983
  - Concurrent 5-FU (continuous infusion) and mitomycin C



- Updated guidelines re: radiation per RTOG 0529 trial
  - Established reduced toxicity with IMRT planning
  - Established SIB protocol with dose specifications depending upon staging

Table 1: Dose Specification of Primary and Nodal Planning Target Volumes: RTOG-0529[4]

TNM Stage	Primary Tumor PTV Dose	Involved Nodal PTV Dose	Nodal PTV Dose
T1, N0	50.4 Gy (28 fxs at 1.8 Gy/fx)	N/A	42 Gy (28 fxs at 1.5 Gy/fx)
T2, N0	50.4 Gy (28 fxs at 1.8 Gy/fx)	N/A	42 Gy (28 fxs at 1.5 Gy/fx)
T3–4, N0	54 Gy (30 fxs at 1.8 Gy/fx)	N/A	45 Gy (30 fxs at 1.5 Gy/fx)
T any, N+ (≤3 cm)	54 Gy (30 fxs at 1.8 Gy/fx)	50.4 Gy (30 fxs at 1.68 Gy/fx)	45 Gy (30 fxs at 1.5 Gy/fx)
T any, N+ (>3 cm)	54 Gy (30 fxs at 1.8 Gy/fx)	54 Gy (30 fxs at 1.8 Gy/fx)	45 Gy (30 fxs at 1.5 Gy/fx)

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Multidisciplinary treatment recommendation

- Simultaneously treat the anal squamous cell carcinoma and rectal adenocarcinoma
- Start with chemoradiation with concurrent 5-FU and MMC
  - Radiation therapy to both anal SCC (definitive) and rectal adenocaricoma (neoadjuvant) with simultaneous integrated boost
- Proceed to neoadjuvant FOLFOX as part of TNT for rectal adenocarcinoma
- Response assessment after completion
  - Consider watch and wait if cCR to TNT for rectal adenocarcinoma, otherwise will need LAR
  - Salvage resection (APR with permanent colostomy) if incomplete response of anal squamous cell carcinoma

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Custom immobilization for radiation therapy for our patient









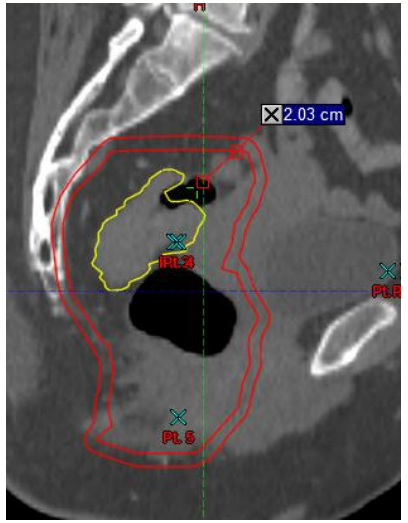
- CT simulation or planning scan
- Supine, “frog legged” in lower body vac lock, arms folded up on chest
- Full bladder

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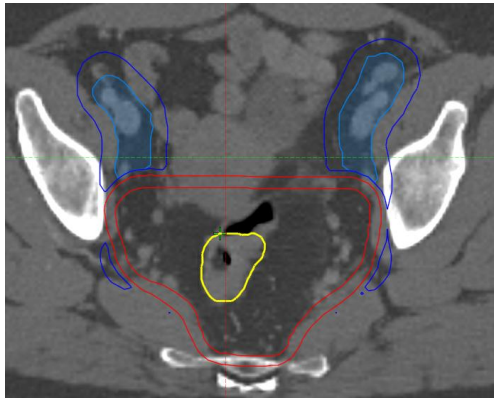
Radiation therapy for locally advanced rectal and anal cancer: Target Volume Delineation

- **Rectal cancer**
  - **Gross tumor volume (GTV)** = primary rectal tumor
  - **High dose clinical target volume (CTV_5400)** = GTV + 2-3 cm craniocaudal expansion along the mucosa (include entire mesorectum at involved levels)
  - **Low dose elective clinical target volume (CTV_4500)** = CTV_5400 + entire mesorectum + obturator LNs, internal iliac LN, presacral LN
    - Add externa iliac LN if anterior invasion into uterus, vagina, bladder or prostate
    - Consider adding groin (inguinal) LN for low tumors if involvement of anal canal
  - **Planning target volumes (PTVs)**
    - Typically a 7 mm – 10 mm expansion from the CTVs
    - Daily setup errors, different internal anatomy, etc
  - Gross lymph nodes: if mesorectal, include in the CTV_5400 volume. If other LN (e.g. internal iliac LN), clarify with surgeon whether these will be resected during surgery. If not, dose escalation to ~60-66 Gy advised



Note: Caudal expansion of CT_5400 > 2 cm due to the inclusion of the synchronous anal cancer

GTV
CTV_54 Gy
PTV_54 Gy



CTV_45 Gy
PTV_45 Gy



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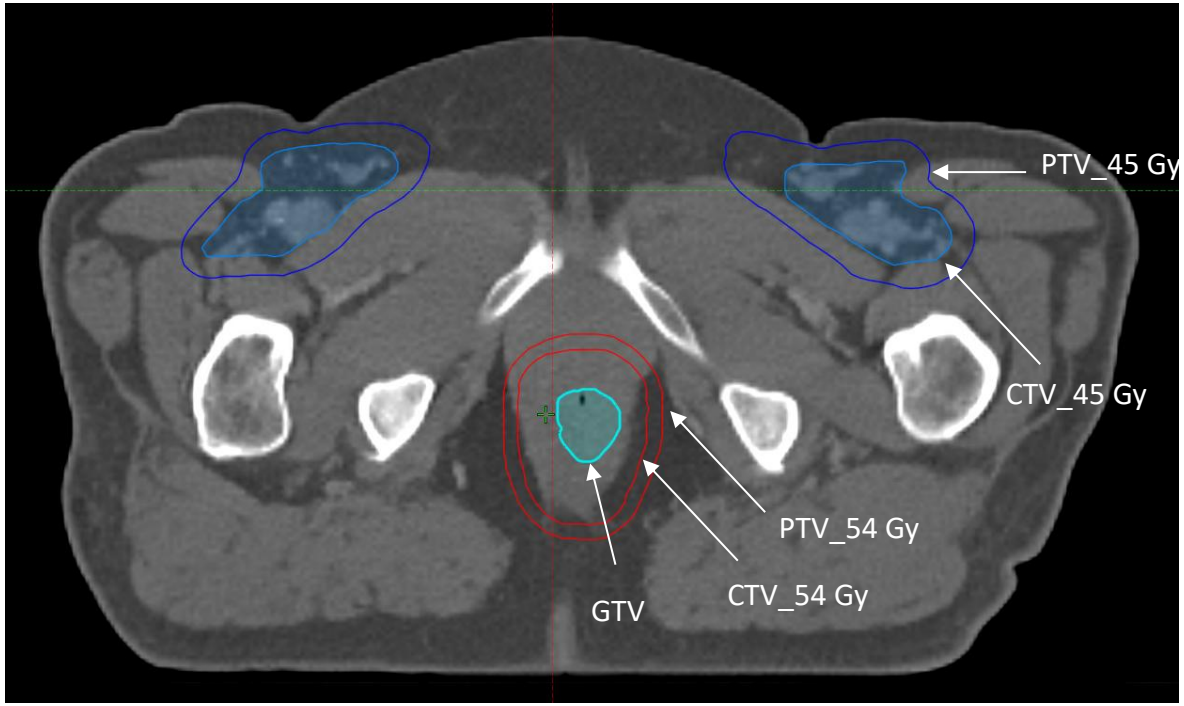
Int J Radiat Oncol Biol Phys. 2009 July 1; 74(3): 824–830.

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Radiation therapy for locally advanced rectal and anal cancer: Target Volume Delineation

- **Anal cancer**
  - **Gross tumor volume (GTV)** = primary anal tumor
  - **High dose clinical target volume (CTV_54 Gy)** = GTV + 2 cm (include entire mesorectum at involved levels)
  - **Low dose elective clinical target volume (CTV_45Gy)** = CTV_54 Gy + entire mesorectum + obturator LNs, internal iliac LN, presacral LN **external iliac LN, inguinal (groin) LN**
  - **Planning target volumes (PTVs)**
    - Typically a 7 mm – 10 mm expansion from the CTVs
    - Daily setup errors, different internal anatomy, etc
  - Gross lymph nodes: SIB boost to 50.4 – 54 Gy recommended (e.g. to gross inguinal LN)



Int J Radiat Oncol Biol Phys. 2009 July 1; 74(3): 824–830.

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Sequential radiation “boost” versus simultaneous integrated boost (SIB)

- Sequential boost or “cone down” boost
  - Two separate radiation plans
    - First plan delivers treatment to large field including areas of microscopic disease
      - e.g. rectal cancer, 45 Gy in 25 fractions to pelvis – rectal primary, mesorectum, draining lymphatics (obturator, internal iliacs))
    - Second “boost” plan or “cone down” to smaller area that requires higher dose (areas of gross disease typically)
      - E.g. rectal cancer cone down boost to the primary tumor of 5.4 Gy in 3 fx or 9 Gy in 5 fx (total dose of 50.4 Gy or 54 Gy)
- Simultaneous integrated boost (SIB)
  - Single radiation plan
    - Differential dose delivered each fraction to different areas
      - E.g. anal cancer SCC – 45 Gy in 30 fx (1.5 Gy/fx) to the anal canal/rectum and draining lymphatics (inguinal, obturator, internal and external iliacs) with an SIB of 54 Gy in 30 fx (1.8 Gy/fx) to the gross primary tumor

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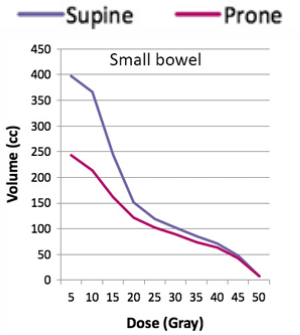
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Radiation therapy for locally advanced rectal and anal cancer: Treatment Techniques: 3D-CRT vs IMRT/VMAT

- 3D-conformal radiation (prone with belly board)
  - (3D-CRT) with 3 field box (PA, R lat, L lat fields)
  - Treatment “apertures” with static multi-leaf collimator (MLC





J Med Radiat Sci **64** (2017) 120–124

- Intensity modulated radiation (IMRT)/ Volumetric modulated arc therapy (VMAT)
  - Full arcs, dynamically moving MLCs
  - Better ability to shape dose, reduce bowel and bladder dose
  - Especially helpful for patients that need to be treated supine or for patients requiring external iliac LN coverage and inguinal LN coverage

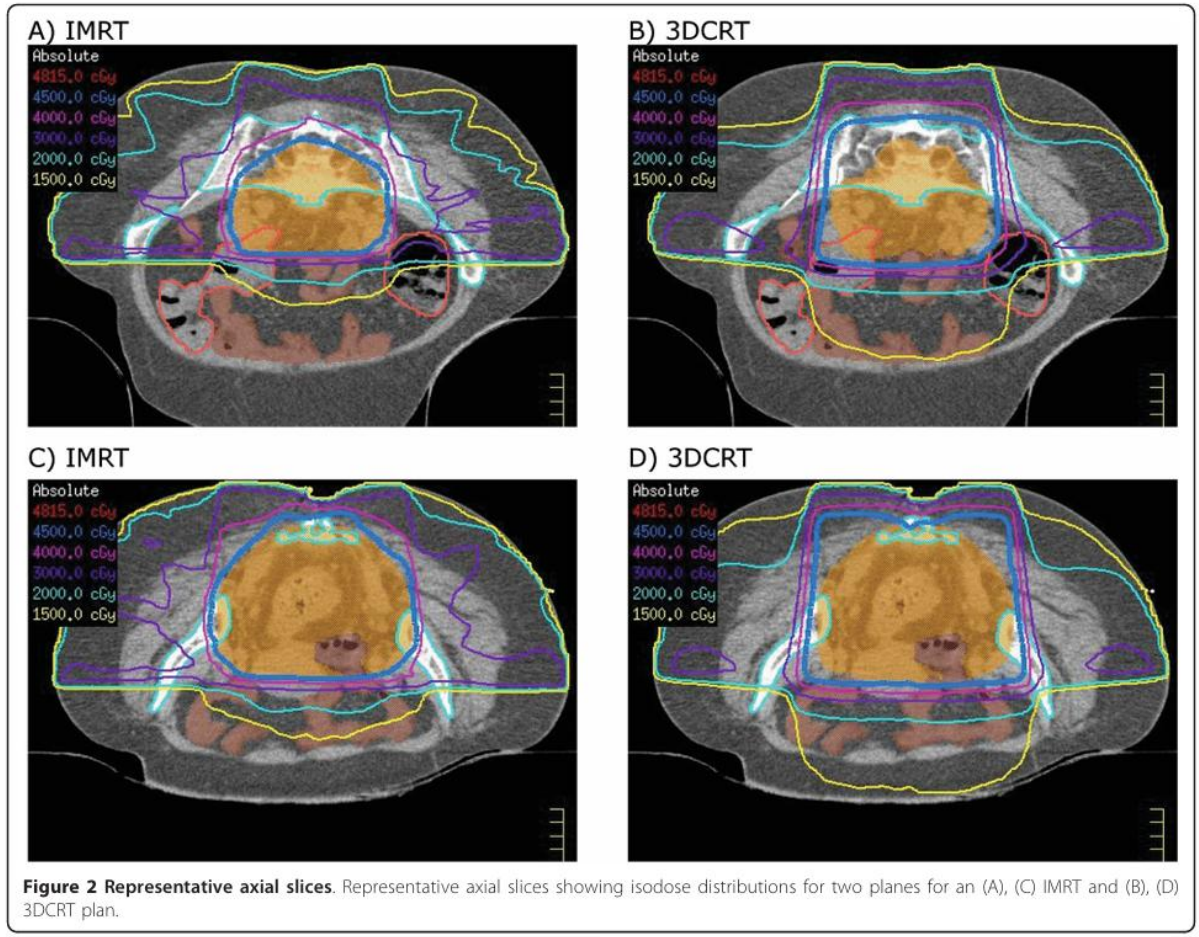


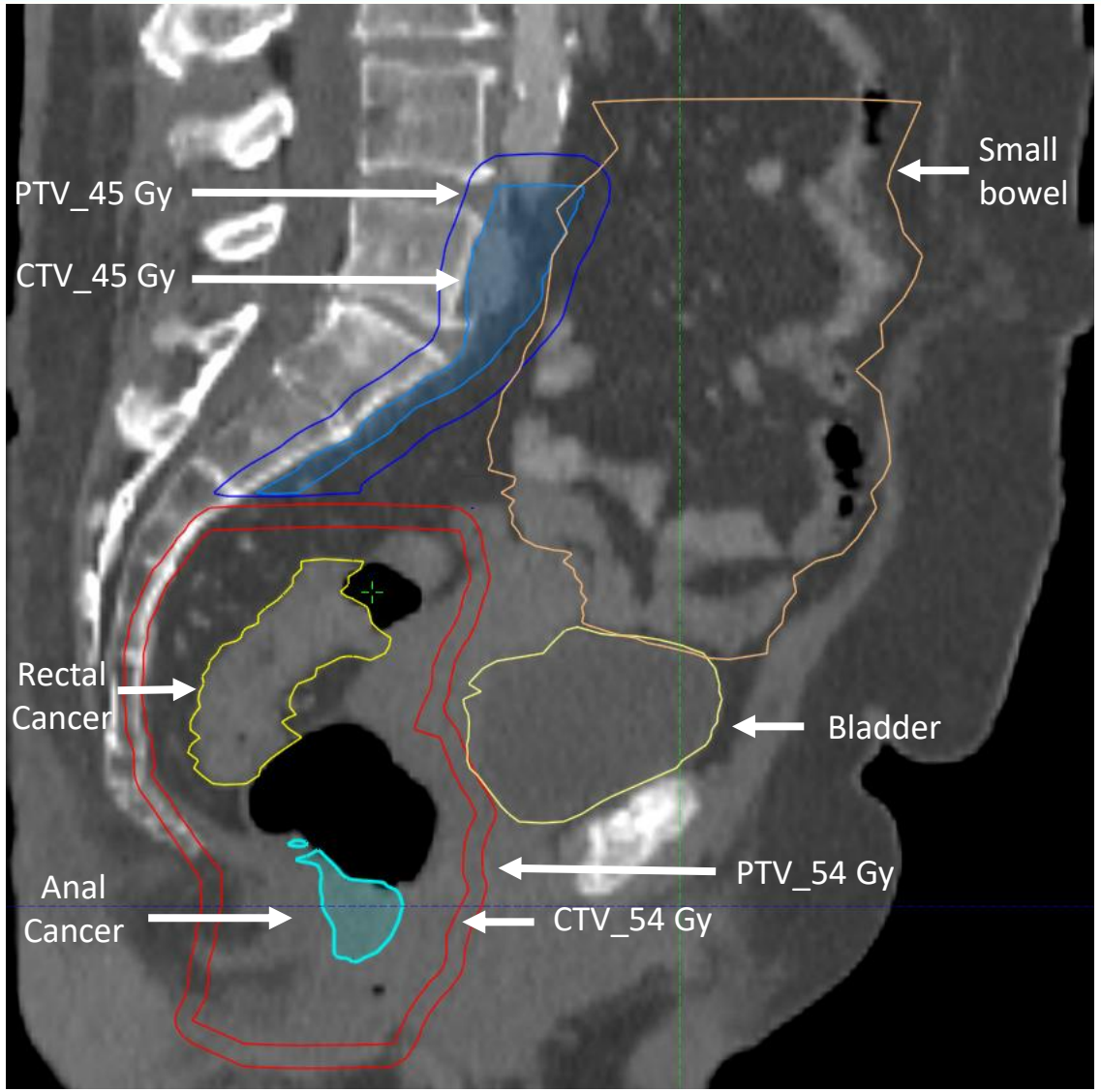
Figure 2 Representative axial slices. Representative axial slices showing isodose distributions for two planes for an (A), (C) IMRT and (B), (D) 3DCRT plan.

Mok *et al. Radiation Oncology* 2011, **6**:63

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Our patient: Final contours incorporating both anal and rectal targets



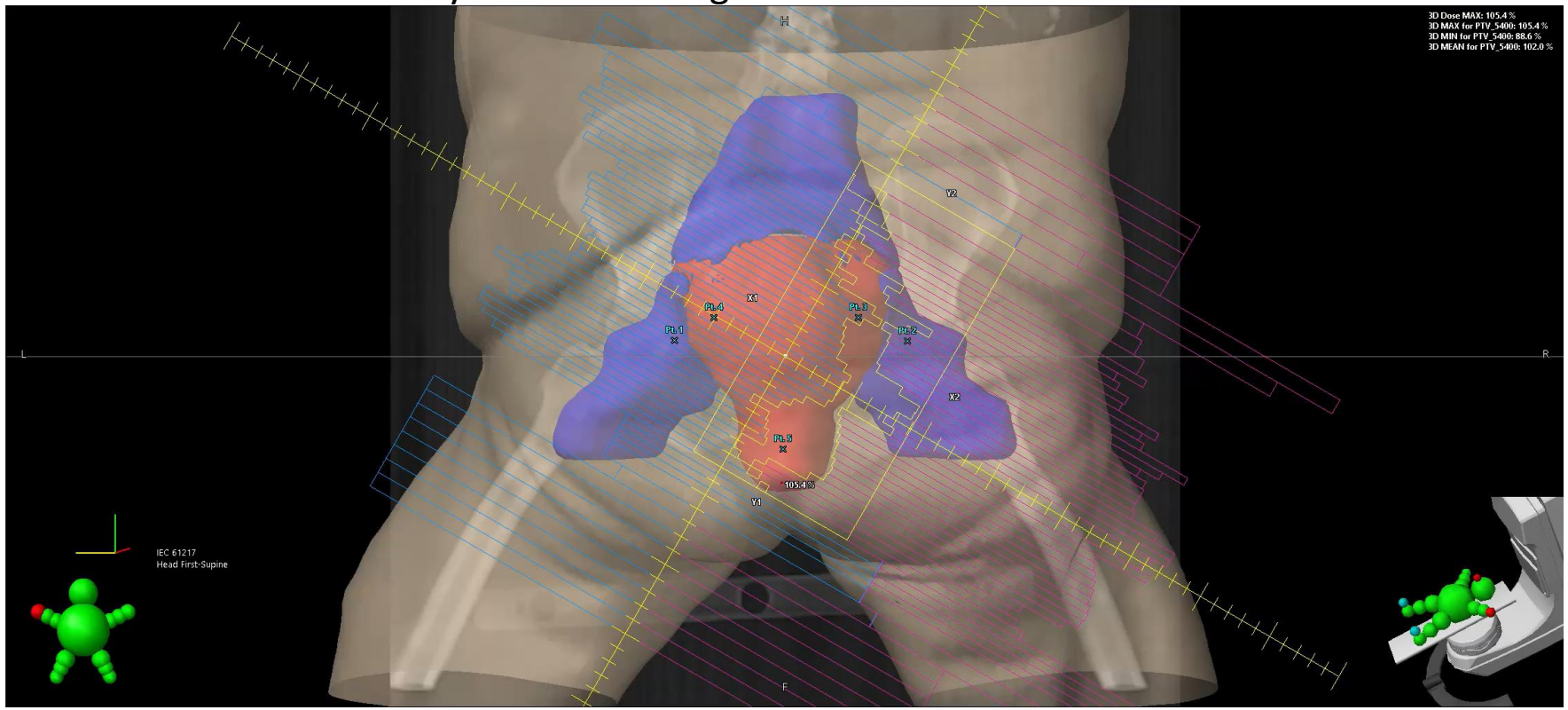
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Radiation therapy for locally advanced rectal and anal cancer: Volumetric modulated arc therapy (VMAT)

Beam's eye view showing multileaf collimator movement



RED = high dose PTV (54 Gy in 30 fx to anal and rectal primary cancer and surrounding mesorectum)

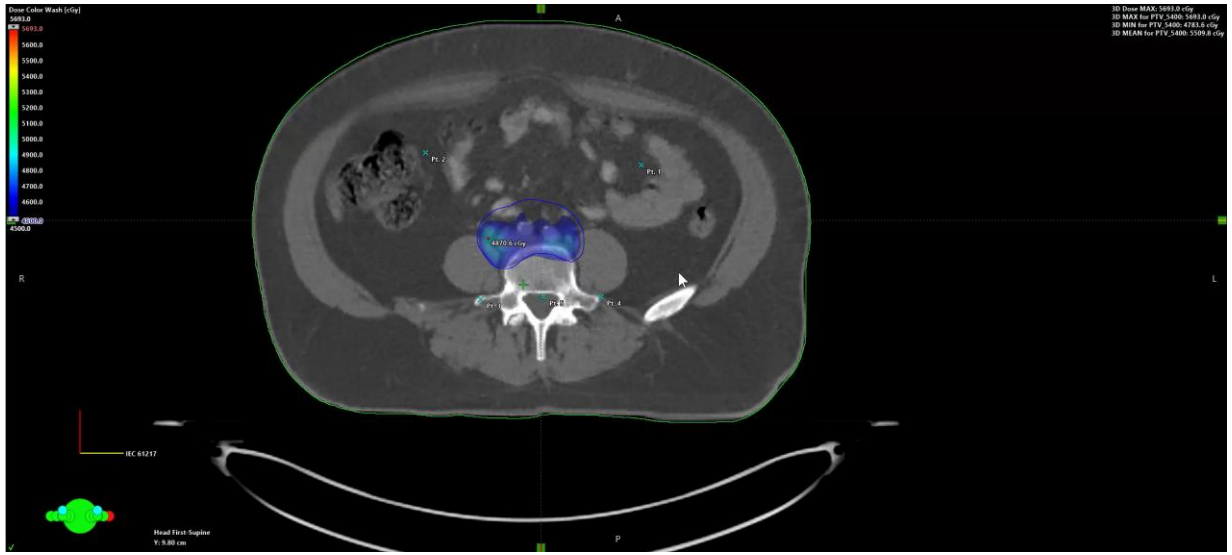
BLUE = low dose elective PTV (45 Gy in 30 fx to draining lymphatics)

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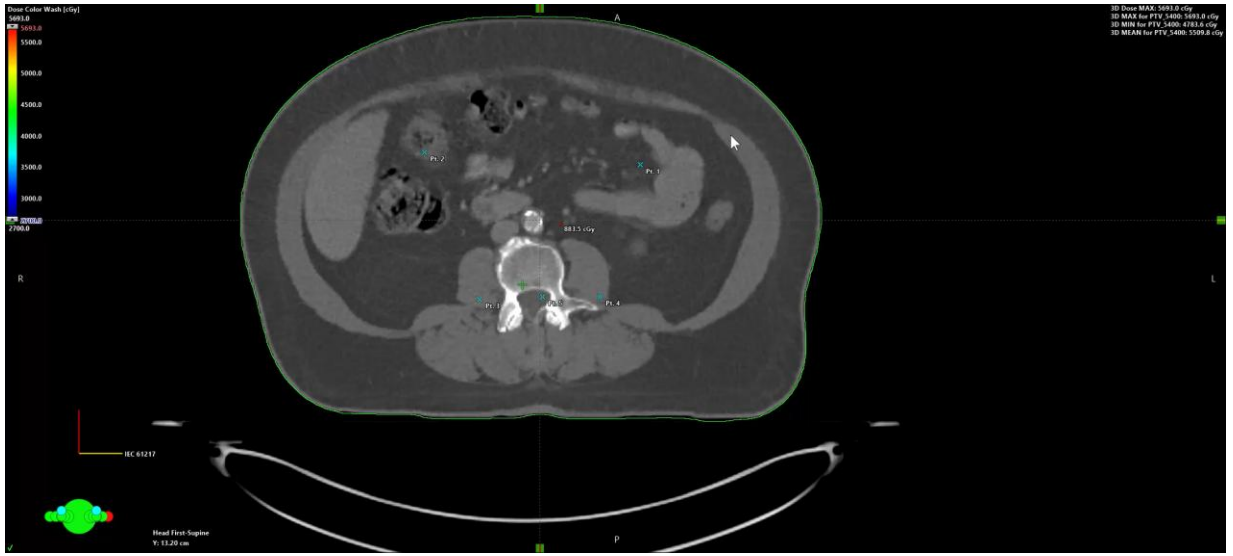
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Radiation treatment plan

45 Gy color wash



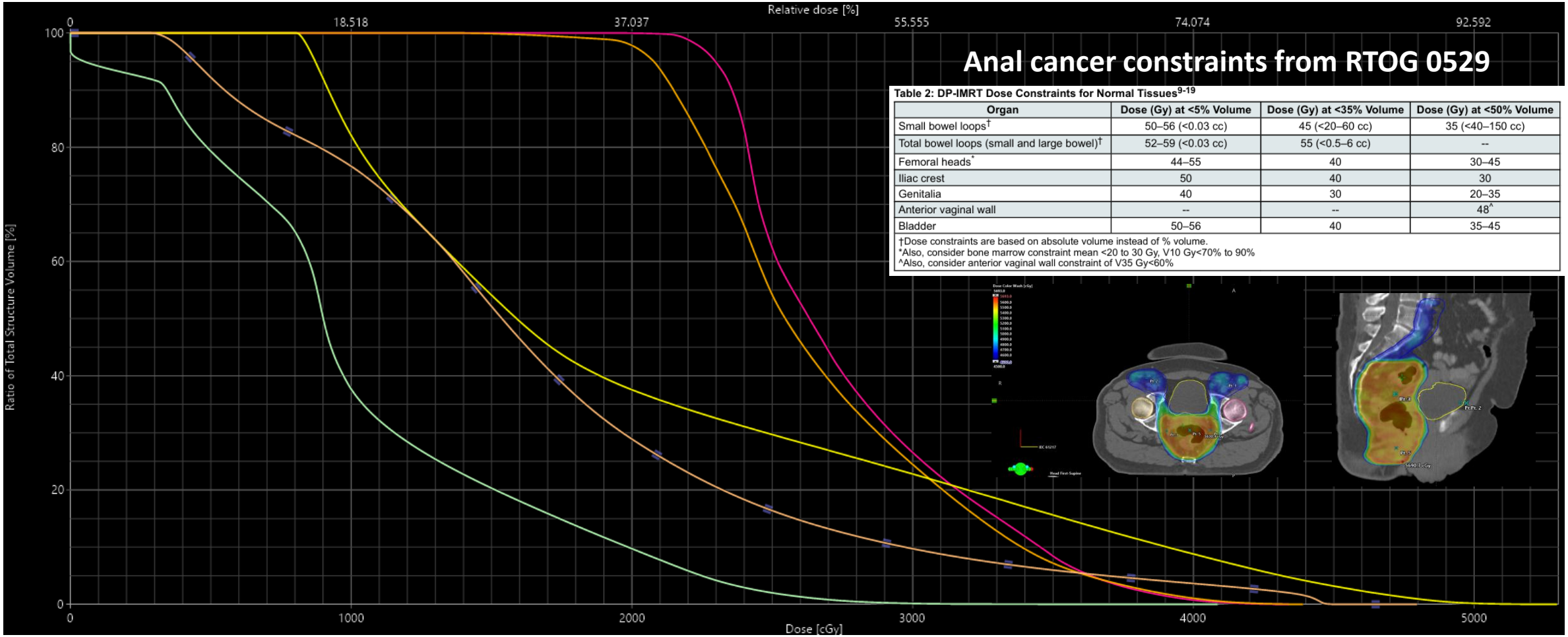
27 Gy color wash



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Radiation therapy planning and plan evaluation metrics



Anal cancer constraints from RTOG 0529

Table 2: DP-IMRT Dose Constraints for Normal Tissues[9-19]

Organ	Dose (Gy) at <5% Volume	Dose (Gy) at <35% Volume	Dose (Gy) at <50% Volume
Small bowel loops†	50–56 (<0.03 cc)	45 (<20–60 cc)	35 (<40–150 cc)
Total bowel loops (small and large bowel)†	52–59 (<0.03 cc)	55 (<0.5–6 cc)	--
Femoral heads*	44–55	40	30–45
Iliac crest	50	40	30
Genitalia	40	30	20–35
Anterior vaginal wall	--	--	48^
Bladder	50–56	40	35–45

†Dose constraints are based on absolute volume instead of % volume.
*Also, consider bone marrow constraint mean <20 to 30 Gy, V10 Gy<70% to 90%
^Also, consider anterior vaginal wall constraint of V35 Gy<60%

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Acute and late radiation toxicity for anal and rectal cancer

- **Acute**: fatigue, cytopenias, dysuria/urinary frequency, nausea, diarrhea (electrolytes), perianal dermatitis

- **Late:** urinary (frequency), GI (frequency, diarrhea, SBO, incontinence)

RTOG 0529 acute toxicity

Number of DP-IMRT Patients with an Acute Adverse Event by Category and Grade* (n=52)

	Grade				
Category	**1**	**2**	**3**	**4**	**5**
Allergy/immunology	1	1	0	0	0
Blood/bone marrow	4	8	16	14	0
Cardiac arrhythmia	0	0	2	0	0
Cardiac general	0	1	0	0	0
Coagulation	0	0	0	1	0
Constitutional symptoms	10	16	6	0	0
Dermatology/skin	5	27	11	1	0
Endocrine	1	0	0	0	0
Gastrointestinal	10	27	11	0	0
Hemorrhage/bleeding	10	1	0	0	0
Infection	0	5	11	1	0
Lymphatics	4	0	0	0	0
Metabolic/laboratory	9	6	11	0	0
Neurology	5	3	1	0	0
Pain	8	15	10	2	0
Pulmonary/upper respiratory	4	0	3	0	0
Renal/genitourinary	10	7	1	0	0
Sexual/reproductive function	2	2	2	0	0
Vascular	0	1	0	0	0
Worst overall	3	6	27	16	0

*Adverse events were scored as definitely, probably, or possibly related to protocol treatment and include adverse events where relationship to protocol treatment is missing.

Adverse events were graded with CTCAE version 3.0.

Comparisons of Acute Treatment-Related Adverse Events*

	0529 (n=52)	98-11 (Arm 1†) (n=325)	p-value (one-sided proportions test§)
Grade 2+ Adverse Events			
GI/GU‡	40 (77%)	249 (77%)	0.50
Derm	39 (75%)	271 (83%)	0.10
GI	38 (73%)	237 (73%)	0.50
GU	8 (15%)	66 (20%)	0.18
Heme	38 (73%)	275 (85%)	0.032
Overall	49 (94%)	318 (98%)	0.12
Grade 3+ Adverse Events			
GI/GU	11 (21%)	120 (37%)	0.0052
Derm	12 (23%)	159 (49%)	<0.0001
GI	11 (21%)	117 (36%)	0.0082
GU	1 (2%)	11 (3%)	0.32
Heme	30 (58%)	201 (62%)	0.29
Overall	43 (83%)	283 (87%)	0.23

Abbreviations: GI, gastrointestinal; GU, genitourinary; Derm, dermatologic; Heme, hematologic

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Her Treatment Course

- She completed therapy with no treatment breaks

- Did not need narcotics
  - Anorectal pain/pressure as well as bleeding resolved after two weeks of treatment

- On-treatment acute toxicities:
  - Grade 2 perianal dermatitis (erythema with moist desquamation)
    - Managed with skin emollient and then Silvadene cream
  - Grade 2 nausea and anorexia (particularly after 2nd cycle of 5-FU/MMC)
    - Managed with Zofran/Compazine
    - Required extra IVF and potassium repletion last week of treatment
  - Grade 2 diarrhea managed with immodium

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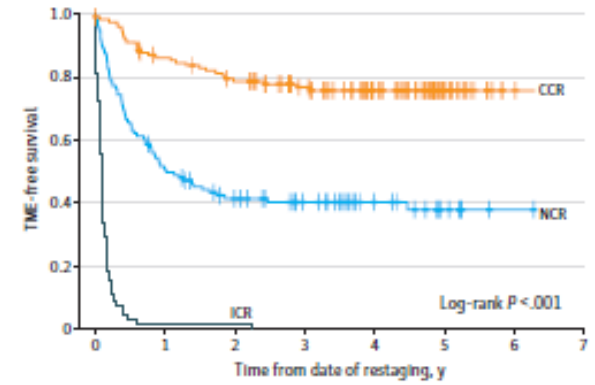
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Clinical response assessment after total neoadjuvant therapy

- After completion of TNT, obtain:
  - Rectal protocol pelvic MRI w/ and w/o contrast to assess local response
    - Post-neoadjuvant T and N stage
  - CT chest and abdomen w/ to rule out distant progression
  - Repeat endoscopy to assess endoscopic tumor response

- If considering watch and wait protocol, assess whether patient has achieved complete clinical response or near complete clinical response

Figure 2. Organ Preservation According to Clinical Tumor Response Grade by Intention-to-Treat



JAMA Network Open. 2024;7(1):e2350903.

PRINCIPLES OF NONOPERATIVE MANAGEMENT

To provide nonoperative management (NOM) for patients with rectal cancer, the multidisciplinary team's diagnostic skills are crucial. They must accurately assess clinical, radiologic, and pathologic findings, determining patient eligibility for NOM and closely monitoring progress. The team's expertise extends to tracking treatment responses, identifying surgical needs promptly, and adjusting the management plan as necessary. Additionally, the team should maintain a comprehensive understanding of the watchful waiting literature and surveillance methodology, adeptly treating patients with complete or near-complete clinical responses and regularly monitoring for potential tumor recurrence or progression. Given this, NOM is recommended only at centers with experienced multidisciplinary teams and for patients committed to intensive surveillance.

Criteria for Complete Clinical Response

- High-definition flexible endoscopy[1]
  - Pale smooth scar with or without telangiectasia
  - No ulceration, nodularity, or mucosal irregularities
  - No stricture
- DRE[1]
  - Smooth, flat scar
  - No nodularity
- Diffusion-weighted MRI[2]
  - Fibrotic, linear scar with low signal intensity on T2-weighted images
  - No diffusion restriction
  - No suspicious lymph nodes
- All of the criteria must be satisfied in order to define a complete clinical response
- Biopsy offers no added diagnostic value if the criteria are met[3,4]
- ctDNA has no proven role in the NOM of patients

Timing of Assessment for Complete Clinical Response

- For patients treated with chemotherapy first followed by radiation (induction chemotherapy), assessment should be performed no earlier than 8 weeks after completion of radiotherapy to allow time for delayed response to radiation.[5]
- For patients treated with radiation first followed by chemotherapy (consolidation chemotherapy), assessment should be completed within a month of completion of chemotherapy.

Near Complete Response[6,7]

- If the patient has had a nCR and wishes to avoid surgery, then an additional 8 weeks of observation followed by reassessment can be considered.
  - An nCR is defined by:
    - ◊ Smooth induration or superficial minor mucosal irregularity on DRE
    - ◊ Endoscopic appearance with irregular small mucosal nodules, superficial ulceration, or mild persistent erythema
    - ◊ T2-weighted MRI with downstaging with or without residual fibrosis, small area of residual signal, and complete or partial regression of lymph nodes
    - ◊ Diffusion-weighted MRI with small area of residual high signal intensity

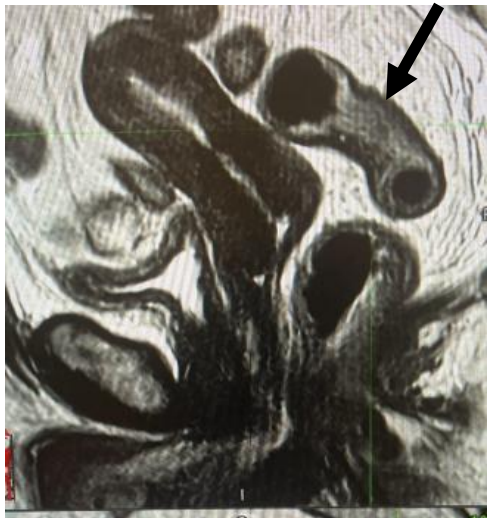
Indications for Surgery

- Radical surgery is indicated for patients who do not ultimately achieve a complete clinical response based on the above criteria or patients who have tumor regrowth after a clinical response.
- If residual tumor or regrowth is suspected at the time of assessment, it is not necessary to perform biopsies. False-negative biopsies are common in this scenario and a high degree of suspicion for tumor is sufficient as an indication for surgery.[8]

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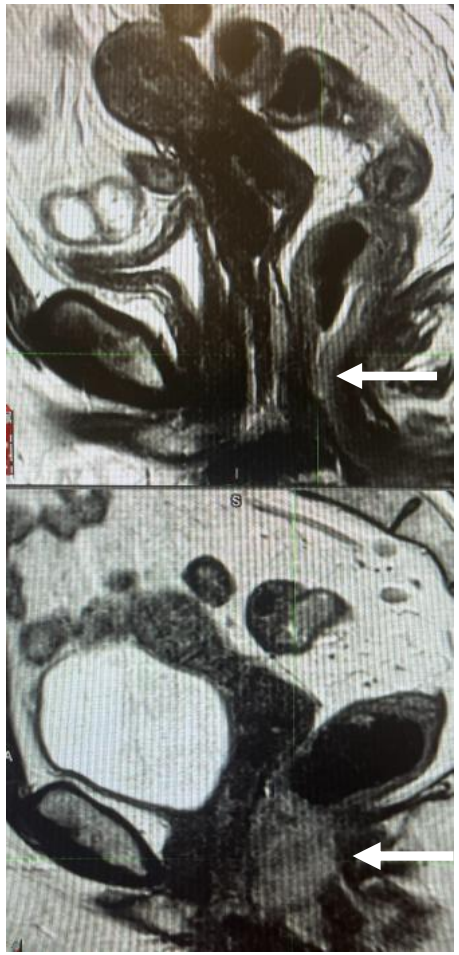
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Post-treatment MR pelvis w/ and w/o



Post-treatment

Pre-treatment



Post-treatment

Pre-treatment

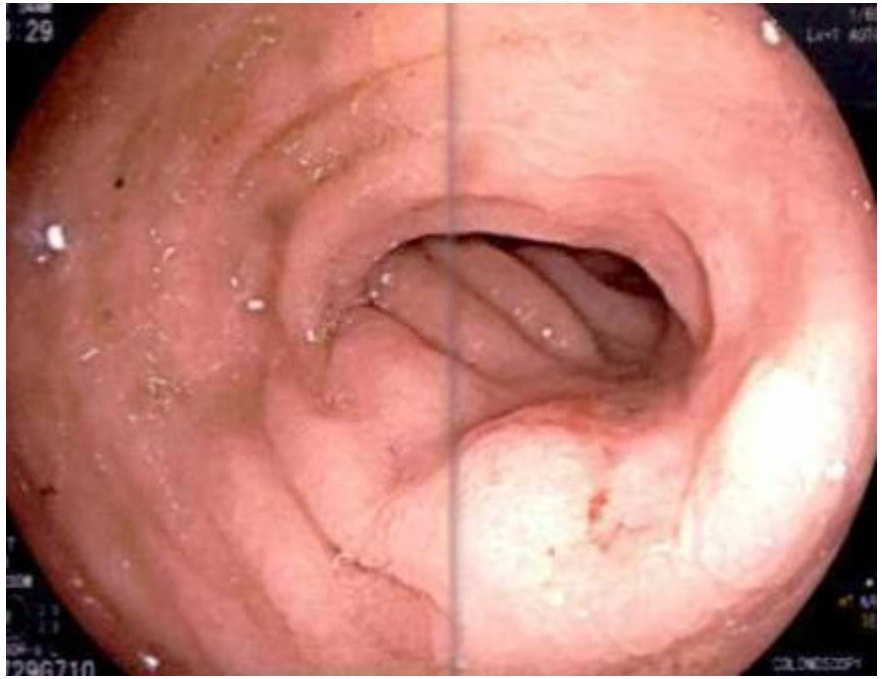
IMPRESSION:

1. No discrete anal canal mass identified.
2. Progressive scarring/fibrosis along the mid-upper rectal wall. No evidence of residual viable tumor.
3. No pathologic pelvic lymphadenopathy.

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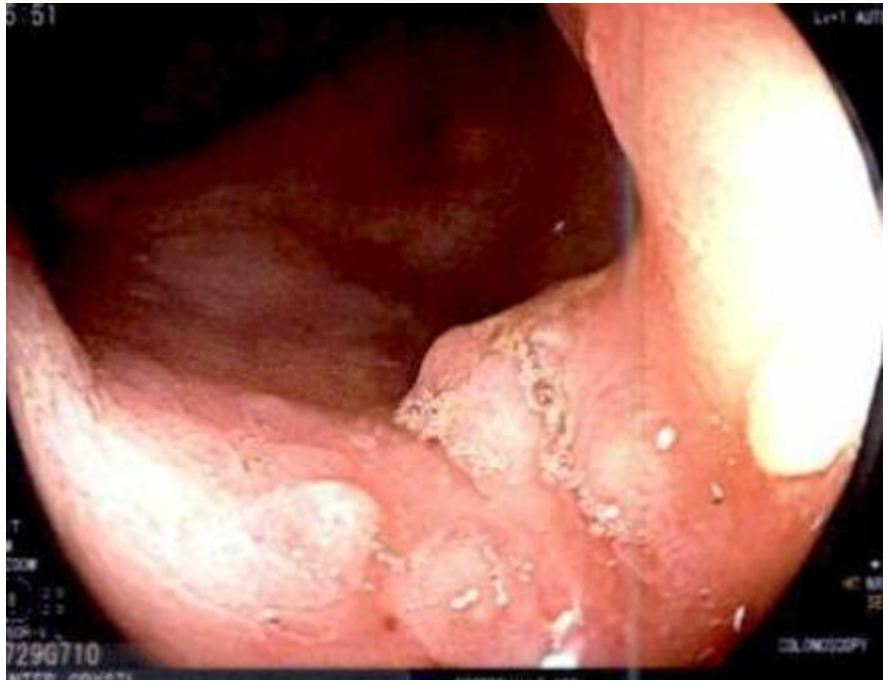
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Post-treatment flexible sigmoidoscopy



Rectal cancer site: nCR

overlying mucosa actually appeared much better. It did still feel like there was some firmness or mass underlying this. I did take a few cold forceps biopsies to try to aid with this. As of now, I would say this likely is a near-complete response, but I am concerned about the possibility of possibly having some residual disease there. In the anus, things looked pretty good actually on flex when things were cleaned up. We then withdrew the scope after performing retroflexion and performed an exam under anesthesia. She was prepped and draped in the standard sterile fashion, and a small Hill-Ferguson retractor was used to inspect the anus anteriorly in the left anterior quadrant. She had a nice flat white scar in the anal canal. On the rectal mucosal side, there was some heaped up tissue. I think this was likely just irritation; however, I did take a biopsy of this with an additional forceps and then obtained hemostasis. She was then awoken



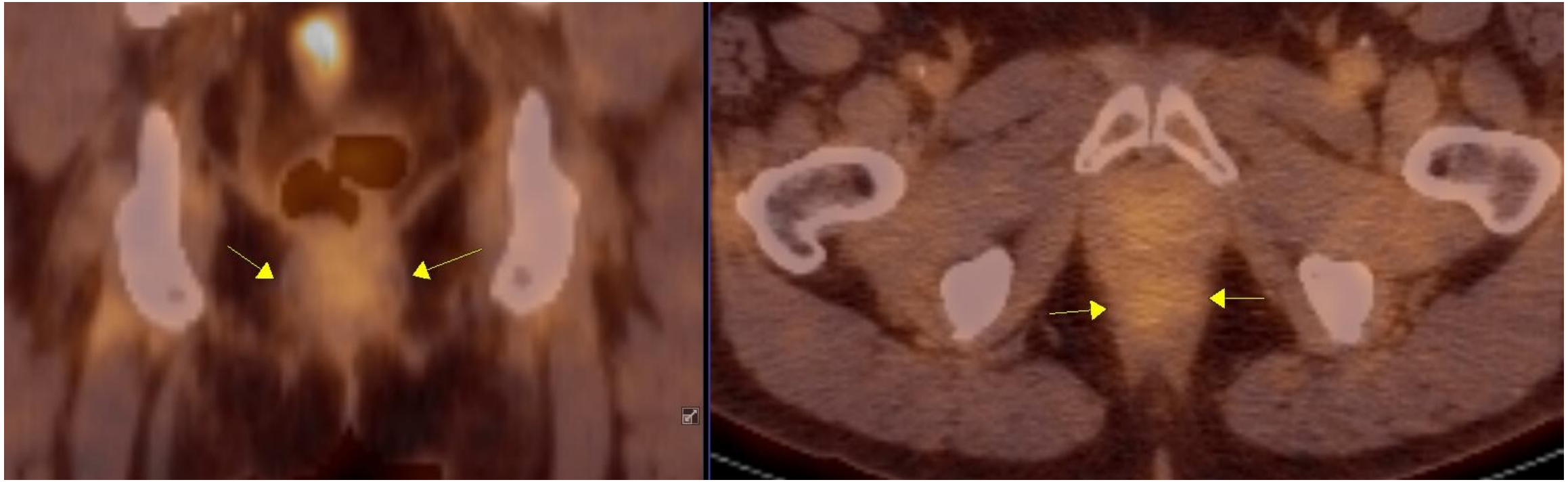
Anal cancer site: cCR

"Rectal mass," biopsy:
Superficial fragments of benign colonic mucosa (see comment).

Anal mass, biopsy:
Benign colonic mucosa (see comment).

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Post-treatment PET/CT



IMPRESSION:

PET-CT shows no evidence for metabolically active neoplasm.

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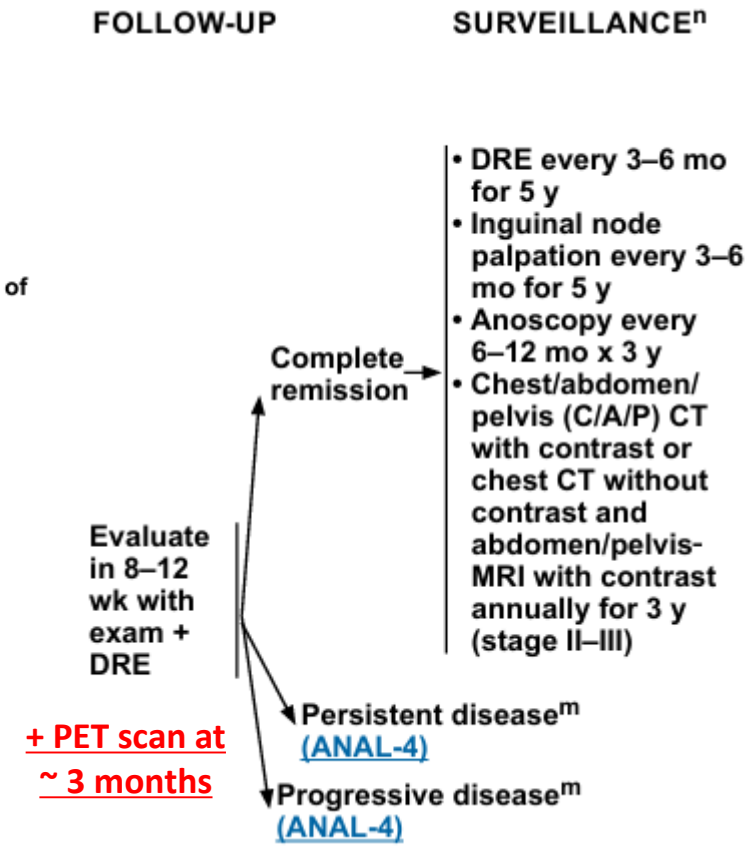
Follow up recommendations

Rectal Cancer Watch and Wait

SURVEILLANCE FOLLOWING NONOPERATIVE MANAGEMENT

- History and physical examination every 3–6 months for 2 years and then every 6 months for a total of 5 years
- CEA every 3–6 months for 2 years, then every 6 months for a total of 5 years
- Digital rectal examination (DRE) and proctoscopy or flexible sigmoidoscopy every 3–4 months for 2 years, then every 6 months for a total of 5 years
- MRI rectum every 6 months for up to 3 years
- CT chest/abdomen every 6–12 months for a total of 5 years, CT pelvis to be included once no longer doing MRI
- Colonoscopy at 1 year following completion of therapy
  - If advanced adenoma, repeat in 1 year
  - If no advanced adenoma, repeat in 3 years, then every 5 years

Anal Cancer Surveillance

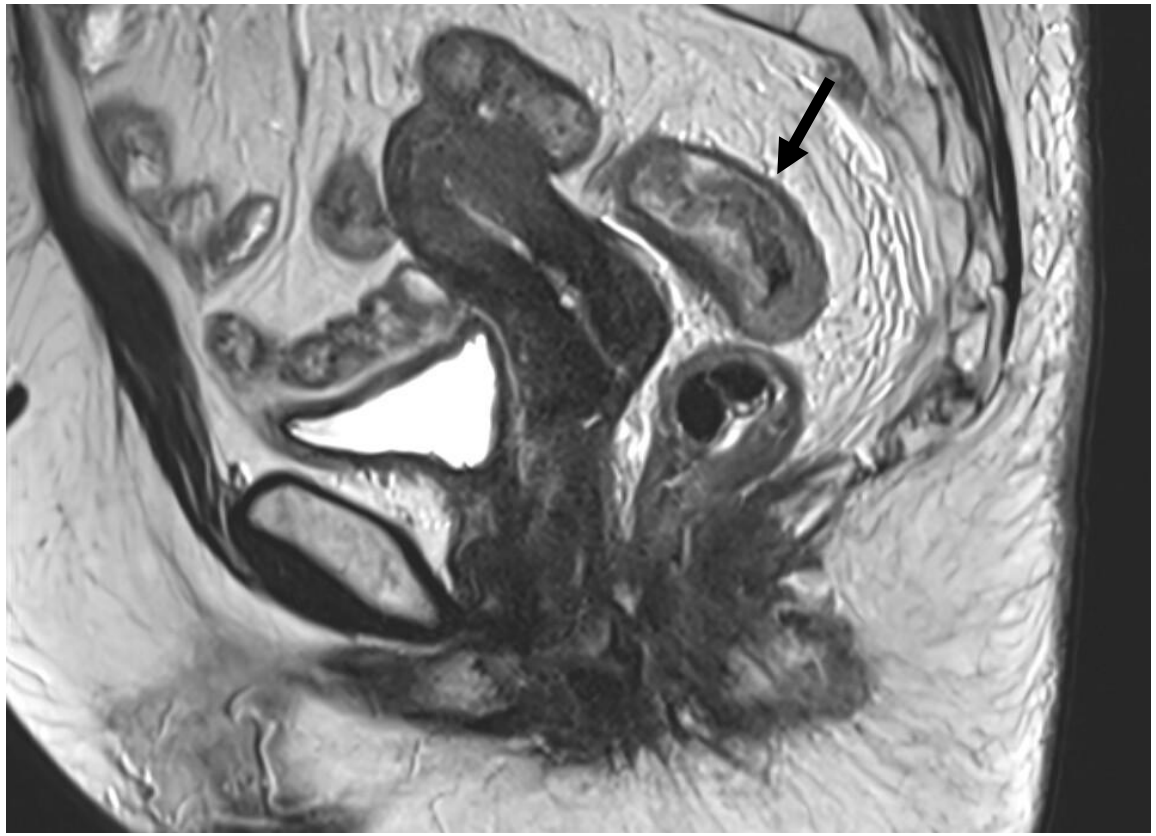


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Repeat MRI pelvis w/ and w/o 3 months later



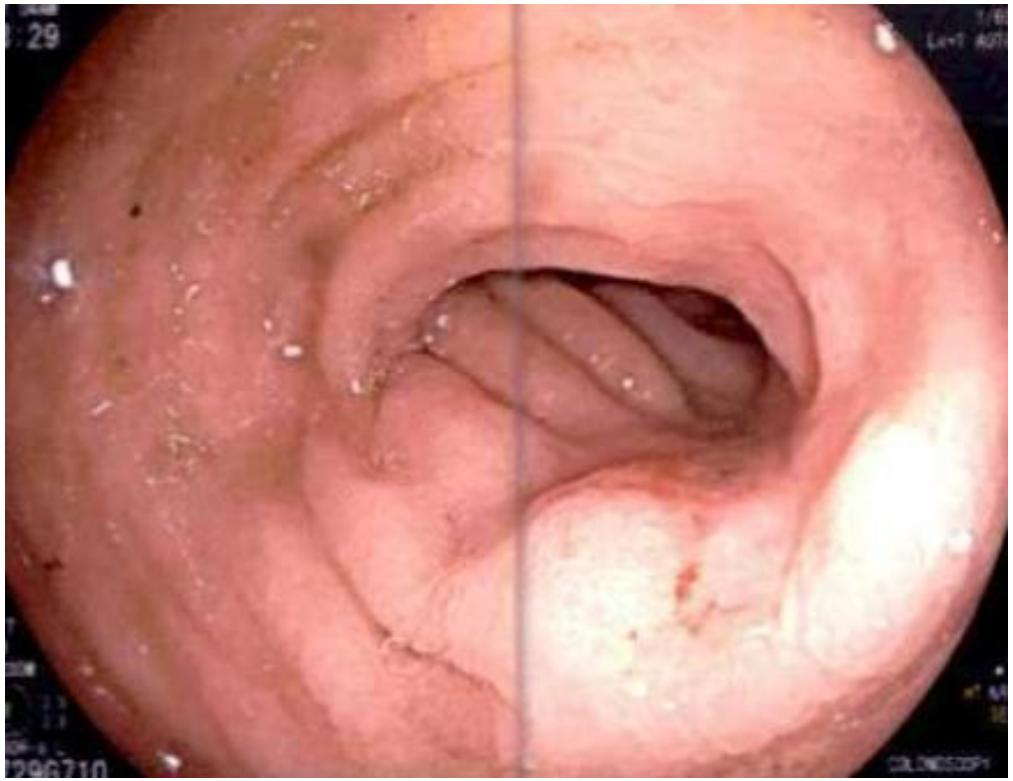
IMPRESSION:

1. Posttreatment changes involving the mid/upper rectum, without evidence of residual or recurrent viable tumor.
2. No evidence of residual or recurrent mass involving the anal canal.
3. No suspicious lymph nodes.

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Repeat flexible sigmoidoscopy



Previous flex sig image with nCR



Rectal cancer site with clear signs of disease

Proc: After informed consent was obtained, the patient was positioned in the left lateral position. A well lubricated sigmoidoscope was inserted into the anal canal and advanced to 15 cm. The findings are in the upper rectum, just proximal to third valve, has a clear recurrence/progression of rectal cancer. More distally, in anus, has flat white scar with some heaped up borders around it but no signs of recurrence. Excess air was removed while the scope was withdrawn. The prep was adequate. The patient tolerated the procedure well.

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Surgical pathology from salvage laparoscopic LAR with TME





Final Diagnosis

Sigmoid colon and rectum, low anterior resection:

Adenocarcinoma, moderately differentiated, involving the rectum with focal extension into perirectal tissues (2.6 cm, rpT3N0).

Tattoo pigment consistent with prior biopsy.

Anastomotic donuts with no significant pathologic change.

Surgical margins negative for carcinoma.

Eighteen lymph nodes negative for metastatic carcinoma (0/18).

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Prognosis/Outcomes

- ~75-80% of cure for both her rectal cancer and anal cancer based on contemporary data

Prodige 23 long term outcomes

(Ann Oncol. 2024 Oct;35(10):873-881**)**

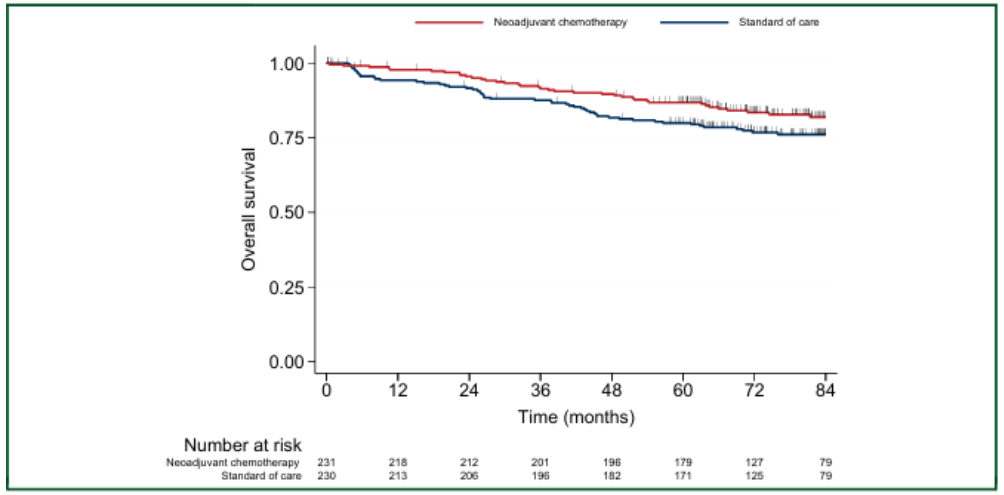


Figure 2. Overall survival.

RTOG 0529 long term outcomes

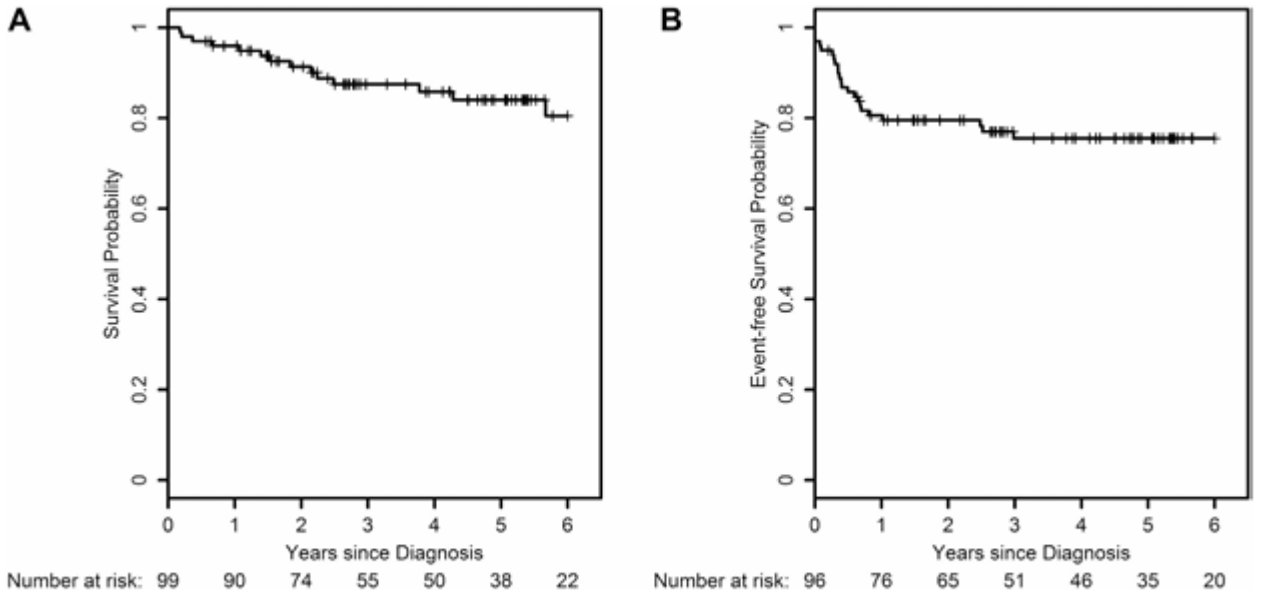


Figure 1 (A) Overall survival and (B) event-free survival (defined as absence of death, colostomy, or recurrence) for patients receiving dose-painted intensity modulated radiation therapy at our institution, as described in RTOG 0529.

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Summary:

- 52 yoF with both locally advanced cT4a N0 M0 upper rectal adenocarcinoma and cT2 N0 M0 anal squamous cell carcinoma
- Multidisciplinary treatment recommendations to simultaneously deliver definitive chemoRT to the anal cancer and total neoadjuvant therapy to the rectal cancer
- Complete response to anal cancer achieved
- Near complete response to rectal cancer but recurrent disease noted during watch and wait and salvage LAR was performed
- Long term prognosis for both cancers is good with ~80% chance of cure

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Thank you!

- Questions?



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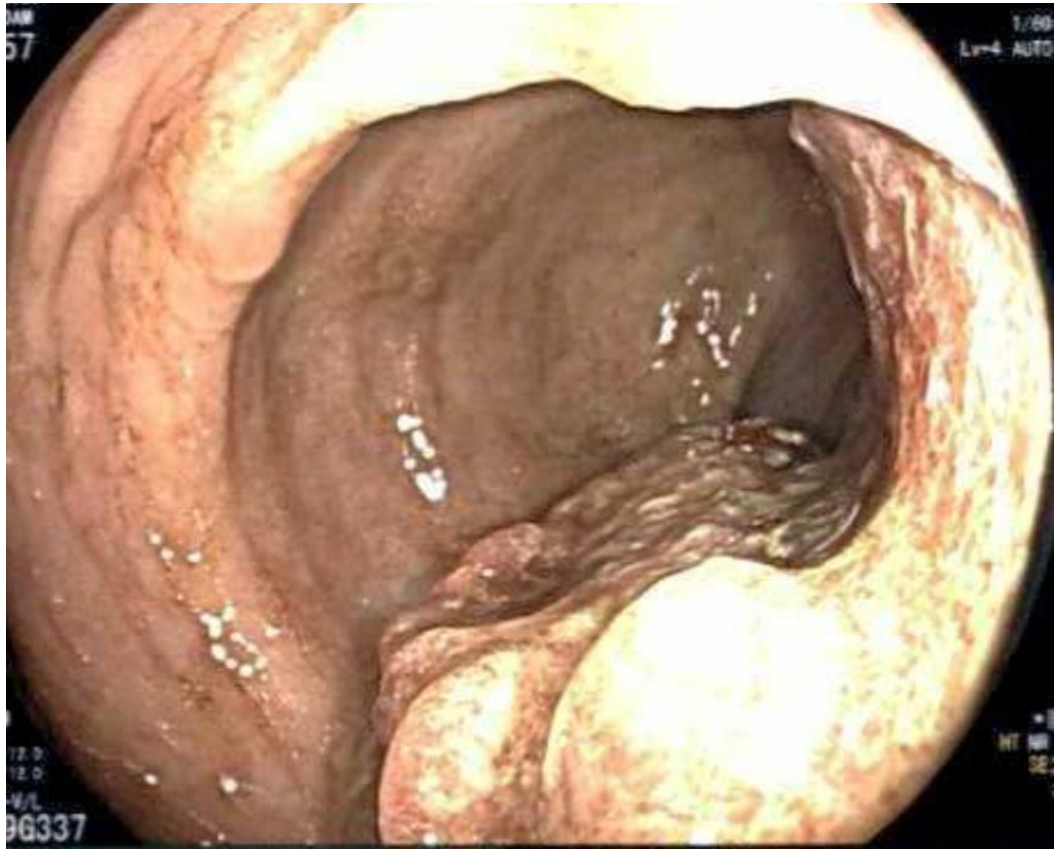
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Appendix Slides

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Pre-Treatment CS on 9/5/25



Rectal cancer site



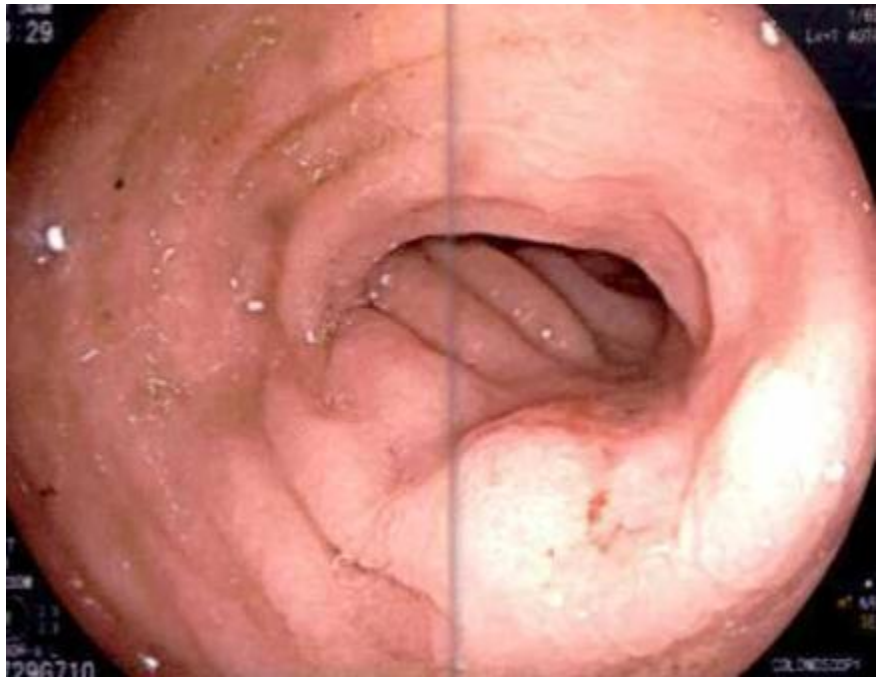
Anal cancer site

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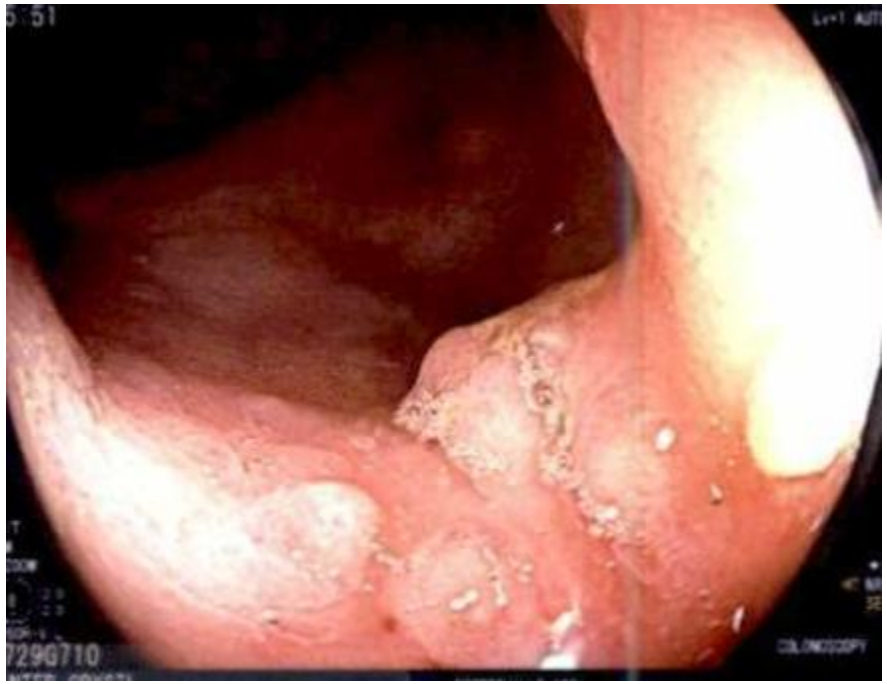
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Post-Treatment CS on 4/23/26



Rectal cancer site: nCR



Anal cancer site: cCR

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Post-Treatment Flex on 8/5/26



- Rectal cancer site with clear signs of disease

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