Rectal Cancer: Management Overview & Optimizing the Patient Experience

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3/23/19
Outline

• How is rectal cancer diagnosed and evaluated?
• Why is radiation considered for the care plan?
• What is radiation therapy, and how is it delivered?
• How are radiation, chemotherapy, and surgery integrated as part of the care plan for locoregionally advanced rectal cancer?
• What are the side effects of treatment, with a focus on radiation therapy?
• What is the patient experience entail from the time of consultation to treatment completion?
• What are some main concerns with rectal cancer survivorship?
Rectal Cancer: Signs/Symptoms

- Abdominal or rectal pain
  - May be associated with tenesmus
    - Feeling of incomplete defecation, accompanied by pain, cramping and straining
- Change in bowel habits
  - Thinner stools
  - Incomplete emptying
  - Diarrhea and/or constipation
    - Quantify # of bowel movements at presentation & before symptoms started
- Gastrointestinal (GI) bleeding
- Fatigue/Anemia
- Weight loss
Work-Up

- Colonoscopy with Biopsy
- Rigid proctoscopy/Sigmoidoscopy
  - Establish distance of tumor from anus/sphincter
  - Abdominoperineal resection (APR) vs low anterior resection (LAR)
- CT Chest/abdomen/pelvis (ideally with oral & IV contrast)
- Labs:
  - CBC, CMP, & the cancer marker CEA
- Pelvic MRI and/or Endoscopic Ultrasound (EUS)
- Enterostomal therapist as indicated for pre-op marking of ostomy site & teaching
- PET/CT not routinely indicated
T-Stage: Depth of Invasion

- **T-stage**
  - Depth of invasion starting from intestinal lumen
  - Not based on size

Chen & Anker; Colon & Rectum from *Radiation Oncology: Imaging and Treatment* 2013
Rectal Nodal Distribution

Draining nodal regions:

- All patients
  - Internal iliac
  - Mesorectal
  - Presacral

- If tumor invades anterior organ (T4b)
  - External iliac b/c drains organs like uterus/prostate
### Rectal Staging AJCC 8th Edition

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>T1</strong></td>
<td>Tumor invades submucosa</td>
</tr>
<tr>
<td><strong>T2</strong></td>
<td>Tumor invades muscularis propria</td>
</tr>
<tr>
<td><strong>T3</strong></td>
<td>Tumor invades through muscularis propria into pericolorectal fat</td>
</tr>
<tr>
<td><strong>T4a</strong></td>
<td>Tumor penetrate to the surface of the visceral peritoneum</td>
</tr>
<tr>
<td><strong>T4b</strong></td>
<td>Tumor invades or is adherent to other organs or structures</td>
</tr>
<tr>
<td><strong>N1a</strong></td>
<td>1 node</td>
</tr>
<tr>
<td><strong>N1b</strong></td>
<td>2-3 nodes</td>
</tr>
<tr>
<td><strong>N1c</strong></td>
<td>Tumor deposit(s) in subserosa, mesentery, or non-peritonealized pericolic or perirectal tissues without regional nodal mets</td>
</tr>
<tr>
<td><strong>N2a</strong></td>
<td>4-6 nodes</td>
</tr>
<tr>
<td><strong>N2b</strong></td>
<td>≥7 nodes</td>
</tr>
<tr>
<td><strong>M1a</strong></td>
<td>Distant mets confined to one organ or site without peritoneal metastases</td>
</tr>
<tr>
<td><strong>M1b</strong></td>
<td>Mets in &gt;1 organ/site or in the peritoneum without peritoneal metastases</td>
</tr>
<tr>
<td><strong>M1c</strong></td>
<td>Mets to peritoneal surface alone or with other organ mets</td>
</tr>
</tbody>
</table>
Rectal Staging AJCC 8th Edition

Always refer to the specific chapter for rules on clinical and pathological classification of this disease.

<table>
<thead>
<tr>
<th>When T is...</th>
<th>And N is...</th>
<th>And M is...</th>
<th>Then the stage group is...</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>N0</td>
<td>M0</td>
<td>0</td>
</tr>
<tr>
<td>T1, T2</td>
<td>N0</td>
<td>M0</td>
<td>I</td>
</tr>
<tr>
<td>T3</td>
<td>N0</td>
<td>M0</td>
<td>IIA</td>
</tr>
<tr>
<td>T4a</td>
<td>N0</td>
<td>M0</td>
<td>IIB</td>
</tr>
<tr>
<td>T4b</td>
<td>N0</td>
<td>M0</td>
<td>IIC</td>
</tr>
<tr>
<td>T1-T2</td>
<td>N1/N1c</td>
<td>M0</td>
<td>IIIA</td>
</tr>
<tr>
<td>T1</td>
<td>N2a</td>
<td>M0</td>
<td>IIIB</td>
</tr>
<tr>
<td>T3-T4a</td>
<td>N1/N1c</td>
<td>M0</td>
<td>IIIA</td>
</tr>
<tr>
<td>T2-T3</td>
<td>N2a</td>
<td>M0</td>
<td>IIIB</td>
</tr>
<tr>
<td>T1-T2</td>
<td>N2b</td>
<td>M0</td>
<td>IIC</td>
</tr>
<tr>
<td>T4a</td>
<td>N2a</td>
<td>M0</td>
<td>IIC</td>
</tr>
<tr>
<td>T3-T4a</td>
<td>N2b</td>
<td>M0</td>
<td>IIC</td>
</tr>
<tr>
<td>T4b</td>
<td>N1-N2</td>
<td>M0</td>
<td>IIC</td>
</tr>
<tr>
<td>Any T</td>
<td>Any N</td>
<td>M1a</td>
<td>IVA</td>
</tr>
<tr>
<td>Any T</td>
<td>Any N</td>
<td>M1b</td>
<td>IVB</td>
</tr>
<tr>
<td>Any T</td>
<td>Any N</td>
<td>M1c</td>
<td>IVC</td>
</tr>
</tbody>
</table>

- **Stage II**
  - Tumor invades through muscular wall of rectum (T3-T4)
- **Stage III**
  - Positive lymph nodes (N+)
- **Stage IV**
  - Metastatic disease (M+)
Work-up/Staging

Stage II A (T3 N0 M0)

(Left) Colonoscopy shows a nonobstructing polypoid mass in the distal, anterior rectum in a 36-year-old woman who presented with hematochezia. On rigid proctoscopy, it is 6.5 cm from the anal verge. Biopsy revealed a moderately differentiated adenocarcinoma. (Right) Endorectal ultrasound (7.5 and 10 Mhz) shows a 4 cm lesion extending through the rectal wall into adventitia (T3). No peritumoral adenopathy was identified.

Chen & Anker; Colon & Rectum from Radiation Oncology: Imaging and Treatment 2013
Work-up/Staging:
T3 Disease

Stage II A (T3 N0 M0)

Stage II A (T3 N0 M0)

[Left] Axial CECT shows concentric wall thickening with tumor extending into perirectal tissue in a patient with tumor located 8 cm from the anal verge based on rigid proctoscopy. [Right] Coronal T2W FS MR shows a partially obstructing tumor starting approximately 8 cm from the anal verge and extending over approximately 5.1 cm of rectum. The tumor is hyperintense on diffusion-weighted imaging.

Stage II A (T3 N0 M0)

Stage II A (T3 N0 M0)

[Left] Axial T1WI C+ MR shows an enhancing rectal tumor predominantly in the posterior wall but circumferential in area causing tumor narrowing. [Right] Axial T2W FS MR in the same patient shows a T3 N0 rectal tumor extending into perirectal fat, which directly abuts the mesorectal fascia on the right. There is no evidence of invasion of the coccyx.
Work-up/Staging: T4b Disease

(Left) Flexible sigmoidoscopy in a 28-year old man who presented with rectal pain and bleeding shows friable, infiltrated mucosa in the rectum, extending proximally from the anorectal junction. Biopsy confirmed adenocarcinoma. (Right) Endorectal ultrasound (7.5 and 10 MHz) shows a large rectal mass invading into the prostate, evidenced by the loss of the fat plane between the structures.

(Left) Axial OCT in same patient shows circumferential thickening of distal rectum and anal canal. Note the perirectal stranding with fat plane loss between posterior bladder, prostate, and right seminal vesicle with the anus. (Right) Axial T2W FSE MR in same patient shows T2 hyperintense tumor at the right anterolateral rectosigmoid with invasion of perirectal muscles and seminal vesicles. There is an enlarged node of G3 up.

Chen & Anker; Colon & Rectum from Radiation Oncology: Imaging and Treatment 2013
Pattern of Failure: University of Minnesota

- 1974 - Retrospective study
  - 74 patients with rectal adenocarcinoma
  - All but 1 was T3-4 or LN(+) at initial curative resection
    - 91% Abdominoperineal resection
  - Second or Symptomatic look surgery 6-12 mos. later
  - Repeated Third & Fourth times
- No post-op RT or chemo
- 70% eventually recurred
  - Of those patients, 40% by 7 months, 85% by 2 years, 98% by 4 years

<table>
<thead>
<tr>
<th>Pattern of Failure</th>
<th>Only failure</th>
<th>Any</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local/Regional</td>
<td>48%</td>
<td>92%</td>
</tr>
<tr>
<td>Distant</td>
<td>8%</td>
<td>50%</td>
</tr>
<tr>
<td>Peritoneal seeding</td>
<td>0%</td>
<td>6%</td>
</tr>
</tbody>
</table>

Gunderson & Sosin; Cancer. 34:1278-1292, 1974
Pattern of Failure: University of Minnesota

- Pattern of failure in 52 pts.
  - * = lung met
  - † = liver met
  - Δ = wound implant
  - ● = local failure
  - O = lymph node failure

- Majority of recurrences would have been encompassed by a standard radiation pelvic field
  - Delineated above by solid-lined octagon

- CONCLUSIONS
  - Vast majority (92%) of failures for T3/4 or N+ rectal cancer have locoregional component
  - Pelvic radiation may prevent these recurrences

Gunderson & Sosin; *Cancer.* 34:1278-1292, 1974
What is Ionizing Radiation?

Unit for Ionizing Radiation Dose = Gy = Joule/Kilogram

1 Gy = 100 cGy
How does radiation kill cancer cells?

- Photon ejects electron from atom

- Indirect Action (75%)
  - Electron breaks up $\text{H}_2\text{O}$ into ions
  - Water ions damage DNA

  OR

- Direct Action (25%)
  - Electron damages DNA
How Radiation Works

• Radiation damages DNA of healthy cells & cancer cells
• Healthy cells stop trying to divide & repair the damage
• Cancer cells try to divide and can’t complete cell division
  – DNA is too abnormal so they die a mitotic death
Why Give Radiation: Dutch Trial = Surgery (TME) +/- RT

- Eligibility Criteria
  - Non-metastatic rectal adenocarcinoma
  - ≤15 cm from anal verge
- 119 centers enrolled from 1996 - 1999
  - 1748 patients total
  - 1382 patients with R0 circumferential margin
- Schema: +/- Short Course RT
  (5 x 5 Gy to pelvis)
  ≤1 week
  Total Mesorectal Excision (TME)
Dutch Results: Benefit in Local Control

- Median f/u 11.6 years
- 6% benefit in local control for all patients
  - Larger benefit for more advanced stages
- No benefit to overall survival or preventing distant mets
Distant Spread Locations

**INITIAL SITE OF RECURRENCE**

<table>
<thead>
<tr>
<th>Location</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>14%</td>
</tr>
<tr>
<td>Lung</td>
<td>9%</td>
</tr>
<tr>
<td>Local Regional</td>
<td>9%</td>
</tr>
<tr>
<td>Intraabdominal</td>
<td>8%</td>
</tr>
<tr>
<td>Retroperitoneal</td>
<td>4%</td>
</tr>
<tr>
<td>Peripheral Lymph Node</td>
<td>2%</td>
</tr>
</tbody>
</table>

### Summary of Effect of Adjuvant Treatment on Outcome

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Overall Survival</th>
<th>Local Recurrence</th>
<th>Distant Metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemo RT</td>
<td>10-15%</td>
<td>10-15%</td>
<td>10-15%</td>
</tr>
<tr>
<td>Chemo</td>
<td>10%</td>
<td>0</td>
<td>10-15%</td>
</tr>
<tr>
<td>RT</td>
<td>0</td>
<td>5-10%</td>
<td>0</td>
</tr>
</tbody>
</table>
When to Give RT? Pre-op vs. Post-op

• Eligibility Criteria
  – ≤75 years old
  – Non-metastatic Rectal Adenocarcinoma
  – T3/4 or N+
  – ≤16 cm from anal verge

Schema:
  Arm 1: Pre-op RT
  • XRT to 50.4 Gy /28 fractions → TME → 5-FU
  Arm 2: Post-op RT
  • TME → XRT to 54 Gy /30 fractions → 5-FU

Sauer et al. JCO 2012
Outcomes of Pre/Post-op ChemoRT

- Median f/u 11.2 years
- Significantly more patients completed treatment in pre-op arm & had decreased local failure
- No difference in OS, distant mets free survival (DMFS), or disease-free survival (DFS) between arms
- Of local recurrences
  - 28% local alone & 72% also had mets
- Less acute & late side effects with pre-operative therapy: Favored CRT → S → C
## Common Side Effects

<table>
<thead>
<tr>
<th>Acute</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>Minor persistent fatigue</td>
</tr>
<tr>
<td>Skin irritation/erythema</td>
<td>Increased bowel movement frequency</td>
</tr>
<tr>
<td>Abdominal cramping</td>
<td>Increased bowel movement urgency</td>
</tr>
<tr>
<td>Abdominal bloating</td>
<td>Sexual dysfunction</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Decreased Libido</td>
</tr>
<tr>
<td>Increased flatulence</td>
<td>Menopause</td>
</tr>
<tr>
<td>Frequent urination</td>
<td>Infertility</td>
</tr>
<tr>
<td>Nausea</td>
<td>Vaginal dryness</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>Vaginal narrowing</td>
</tr>
<tr>
<td>Mild pain</td>
<td>Pain with intercourse</td>
</tr>
<tr>
<td>Worsening/development of hemorrhoids</td>
<td>Impotence</td>
</tr>
<tr>
<td>Hair loss in radiated site</td>
<td>Orgasm Changes (decreased ejaculate)</td>
</tr>
<tr>
<td>Cytopenias (leukopenia, lymphopenia, and thrombocytopenia)</td>
<td></td>
</tr>
</tbody>
</table>
# Less Common Side Effects

<table>
<thead>
<tr>
<th>Acute</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>Severe persistent fatigue</td>
</tr>
<tr>
<td>Mucous/Stool discharge/incontinence</td>
<td>Loss of bone density</td>
</tr>
<tr>
<td>Severe pain (e.g. from Sores/Ulcers on skin or near cancer &amp; rectal inflammation)</td>
<td>Muscular stiffness/discomfort from fibrosis (tissue stiffening/scarring)</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>Persistent urinary frequency/urgency/discomfort</td>
</tr>
<tr>
<td>Anemia which might require transfusion</td>
<td>Fecal incontinence (due to damage to pelvic nerves &amp; muscles)</td>
</tr>
<tr>
<td>Infections (fungal, viral, or bacterial)</td>
<td>Persistent sexual dysfunction</td>
</tr>
<tr>
<td>Severe diarrhea</td>
<td>Blood in ejaculate</td>
</tr>
<tr>
<td>Dehydration</td>
<td>Permanent hair loss</td>
</tr>
<tr>
<td>Death</td>
<td>Damage to the intestines that could require surgery to repair (e.g. perforation, fistula, adhesions, and obstruction)</td>
</tr>
<tr>
<td></td>
<td>Abnormal opening in internal organ (e.g. fissure) that could cause pain and bleeding (e.g. bowel including rectum [proctitis] or urinary [cystitis])</td>
</tr>
<tr>
<td></td>
<td>Bone fractures</td>
</tr>
<tr>
<td></td>
<td>Tumor/cancer caused by radiation</td>
</tr>
<tr>
<td></td>
<td>Death</td>
</tr>
</tbody>
</table>
Fig. 1. Fecal incontinence for liquid stools in RT+ and RT− patients without stoma.

- Patients received long course preoperative chemoradiation
- Comparable toxicity to short course
Table 2. International Index of Erectile Function Scores in irradiated (RT+) and nonirradiated (RT−) patients

<table>
<thead>
<tr>
<th>Domain (valid answers n, RT+/RT−)</th>
<th>Range</th>
<th>RT+ group Mean (SD)</th>
<th>RT- group Mean (SD)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexual desire</td>
<td>2–10</td>
<td>5.0 (2.0)</td>
<td>5.4 (2.0)</td>
<td>0.23</td>
</tr>
<tr>
<td>(n = 104/130)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erectile function</td>
<td>1–30</td>
<td>6.9 (7.9)</td>
<td>14.3 (11.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(n = 100/125)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orgasmic function</td>
<td>0–10</td>
<td>2.9 (3.8)</td>
<td>5.2 (4.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(n = 103/128)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercourse satisfaction</td>
<td>0–15</td>
<td>7.6 (3.5)</td>
<td>10.1 (2.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>(n = 32/65)†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall satisfaction with sex life</td>
<td>2–10</td>
<td>4.3 (2.2)</td>
<td>5.7 (2.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(n = 96/120)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Mann-Whitney U test.
† Patients who had sexual intercourse during the previous month.

- RT negatively impacted sexual function
- Associated with low serum testosterone
Norwegian: Female Sexual QOL

- **Effect of RT**
  - No change in libido
  - Increased dyspareunia (35% vs. 11%)
  - Increased vaginal dryness (50% vs. 24%)
  - Reduced vaginal dimension (35% vs. 6%)
    - Consider vaginal dilators post-RT
Multi-Institution Trial Assessing RT (Accrual Complete)

- Patients randomized to receive RT or not
- Hope is to preserve outcomes despite exclusion of RT
- Just recently completed accrual
- Results still pending
<table>
<thead>
<tr>
<th>CLINICAL STAGE</th>
<th>NEOADJUVANT THERAPY</th>
<th>PRIMARY TREATMENT</th>
<th>ADJUVANT TREATMENT&lt;sup&gt;c,p,q&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3, N any with clear circumferential margin (CRM) (by MRI,&lt;sup&gt;1&lt;/sup&gt; T1-2, N1-2)</td>
<td>Chemo/RT&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Consider restaging&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Surveillance (See REC-11)</td>
</tr>
<tr>
<td></td>
<td>• Capecitabine/long-course RT&lt;sup&gt;f&lt;/sup&gt; or infusional 5-FU/long-course RT&lt;sup&gt;g&lt;/sup&gt; (category 1 and preferred for both) or</td>
<td>Transabdominal resection&lt;sup&gt;h,u,v&lt;/sup&gt;</td>
<td>Surveillance (See REC-11)</td>
</tr>
<tr>
<td></td>
<td>• Bolus 5-FU/leucovorin/long-course RT&lt;sup&gt;o,q&lt;/sup&gt; or RT&lt;sup&gt;q&lt;/sup&gt;</td>
<td>Restaging&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Surveillance (See REC-11)</td>
</tr>
<tr>
<td></td>
<td>• Short-course RT&lt;sup&gt;t&lt;/sup&gt; or</td>
<td></td>
<td>Systemic therapy&lt;sup&gt;w&lt;/sup&gt; (See REC-F)</td>
</tr>
<tr>
<td></td>
<td>Chemotherapy&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Capecitabine/RT&lt;sup&gt;e&lt;/sup&gt; (preferred) or infusional 5-FU/RT&lt;sup&gt;d&lt;/sup&gt; (preferred) or bolus 5-FU/leucovorin/RT&lt;sup&gt;e&lt;/sup&gt; or Short-course RT&lt;sup&gt;t&lt;/sup&gt;</td>
<td>Transabdominal resection&lt;sup&gt;h,u&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>• FOLFOX (preferred) or CAPEOX (preferred) or 5-FU/leucovorin or capcitabine</td>
<td></td>
<td>Resection contraindicated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Systemic therapy&lt;sup&gt;w&lt;/sup&gt; (See REC-F)</td>
</tr>
</tbody>
</table>

See Evidence Blocks on REC-6A

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<sup>e</sup>See Principles of Imaging (REC-A).
<sup>f</sup>See Principles of Surgery (REC-C).
<sup>1</sup>CRM measured at the closest distance of the tumor to the mesorectal fascia.
Clear CRM: Greater than 1 mm from mesorectal fascia, levator muscles and not invading into the intersphincteric plane.
<sup>g</sup>Bolus 5-FU/leucovorin/RT is an option for patients not able to tolerate capecitabine or infusional 5-FU.
<sup>p</sup>See Principles of Adjuvant Therapy (REC-D).
<sup>q</sup>See Principles of Radiation Therapy (REC-E).
<sup>t</sup>Evaluation for short-course RT should be in a multidisciplinary setting, with a discussion of the need for down-staging and the possibility of long-term toxicity.

Note: For more information regarding the categories and definitions used for the NCCN Evidence Blocks™, see page EB-1.
All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.
NCCN Guidelines Version 3.2018
Rectal Cancer
NCCN Evidence Blocks™

CLINICAL STAGE

NEOADJUVANT THERAPY

Primary Treatment
(6 MO PERIOPERATIVE TREATMENT PREFERRED)

ADJUVANT TREATMENT

T3, N any with clear circumferential margin (CRM) (by MRI), T1-2, N1-2

Chemo/RT
- Capecitabine/long-course RT\textsuperscript{4} or infusional 5-FU/long-course RT\textsuperscript{9} (category 1 and preferred for both) or
- Bolus 5-FU-leucovorin/long-course RT\textsuperscript{9} or RT\textsuperscript{9}
- Short-course RT\textsuperscript{1} or

Consider restaging\textsuperscript{c}

Transabdominal resection\textsuperscript{h,u,v}

5-FU/leucovorin or capecitabine or FOLFOX (preferred) or CAPEOX (preferred)

Surveillance
(See REC-11)

Systemic therapy\textsuperscript{w}
(See REC-F)

CT3, N0 before chemo/RT

Resection contraindicated

CT1-3, N1-2 before chemo/RT

FOLFOX or CAPEOX

Surveillance
(See REC-11)

Systemic therapy\textsuperscript{w}
(See REC-F)

Chemotherapy
- FOLFOX (preferred) or CAPEOX (preferred) or
- 5-FU-leucovorin or capecitabine

Capecitabine/RT (preferred) or infusional 5-FU/RT (preferred) or bolus 5-FU-leucovorin/RT\textsuperscript{9} or Short-course RT\textsuperscript{1}

Restaging\textsuperscript{c}

Resection contraindicated

Transabdominal resection\textsuperscript{h,u}

Systemic therapy\textsuperscript{w}
(See REC-F)

See Evidence Blocks on REC-6A

---

\textsuperscript{c}See Principles of Surgery (REC-C).

\textsuperscript{4}CRM measured at the closest distance of the tumor to the mesorectal fascia.

\textsuperscript{5}Clear CRM. Greater than 1 mm from mesorectal fascia, levator muscles and not invading into the intersphincteric plane.

\textsuperscript{9}Bolus 5-FU-leucovorin/RT is an option for patients not able to tolerate capecitabine or infusional 5-FU.

\textsuperscript{w}In those patients who achieve a complete clinical response with no evidence of residual disease on digital rectal examination, rectal MRI, and direct endoscopic evaluation, a "watch and wait," nonoperative management approach may be considered in centers with experienced multidisciplinary teams. The degree to which risk of local and/or distant failure may be increased relative to standard surgical resection has not yet been adequately characterized. Decisions for nonoperative management should involve a careful discussion with the patient of his/her risk tolerance.

\textsuperscript{v}FOLFOXIRI is not recommended in this setting.

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Note: For more information regarding the categories and definitions used for the NCCN Evidence Blocks™, see page EB-1.

All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.
Non-Operative Management Study (Accrual Complete)

- All trial patients are evaluated to continue non-operative management
- Received either chemo or chemoRT first, but all therapy given before assessing response
- Closed to accrual
- Results pending
Active Research Protocol (NRG GI-002): Search for Novel Systemic Agents

- High risk patients
- Search for systemic agents to give with RT that may improve outcomes
- All patients receive systemic therapy (chemo, targeted agents, and/or immunotherapy), RT & surgery
Initial Consultation with Rad Onc:

• Discuss goals of care & specifically goals of RT
  – Improve local control?
  – Definitive therapy via non-operative management?

• Does patient want RT?
  – If yes, consent patient
CT Simulation for RT Planning

- Position/Immobilize Patient
- Tattoos placed for daily setup/alignment
- Set initial borders of radiation treatment region
Simulation Instructions & RT Targets

**CT Simulation**
- Reproducible set up
- Displace bowel superiorly out of field
  - Prone
  - Belly board
  - Full bladder
- Anal marker to delineate anal verge
  - Helps avoid anus when appropriate & for tumor localization
- Consider PO contrast if significant small bowel volume falls into pelvis
- Consider IV contrast if need help identifying nodes (rare)

**RT Plan**
- Usually 3D conformal
  - 3 or 4 fields
- Consider IMRT for select cases
  - Small bowel avoidance
Simulation Instruction Details:
Full Bladder to Protect Small Bowel

- 1 hour before simulation and all subsequent treatments
  - Empty bladder & quickly drink 16 oz of water
  - Encourage patient to practice before the sim day to make sure they can hold urine for that long

Chen & Anker; Colon & Rectum from Radiation Oncology: Imaging and Treatment 2013
Empty Bladder Appearance

- Bowel falls into pelvic radiation fields
- Increased GI Toxicity
ANATOMY

Aorta bifurcates at L4
Common Iliacs bifurcate at L5/S1

External Iliac Nodes run in a straight line from L4/L5 to pubic symphysis (so to include give 2 cm sup margin On the aforementioned line), 1 cm ant to pubis, 3 cm ant to femoral head

Internal Iliac Nodes dive posteriorly (so to include ant border is at post margin of pubis, but give at least 2 cm on vertebral bodies!)

Obturator nodes lie anterior To internal iliac nodes, in sup lat Obturator foramen on AP film
Fields using Bony Landmarks

<table>
<thead>
<tr>
<th></th>
<th>AP</th>
<th>Lateral (T3)</th>
<th>Lateral (T4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LAR</strong></td>
<td><img src="image1" alt="Diagram LAR AP" /></td>
<td><img src="image2" alt="Diagram LAR T3" /></td>
<td><img src="image3" alt="Diagram LAR T4" /></td>
</tr>
<tr>
<td><strong>APR</strong></td>
<td><img src="image4" alt="Diagram APR AP" /></td>
<td><img src="image5" alt="Diagram APR T3" /></td>
<td><img src="image6" alt="Diagram APR T4" /></td>
</tr>
</tbody>
</table>

- Larger fields if post APR
Perineal Scar Boost/Bolus

- Radiation field is larger post APR to cover scar (frequent site of recurrences)
  - Adds to toxicity
Dosimetrists Perform

- Dose Calculation
- Dose/Plan Optimization
- Plans take from hours if emergency (e.g. bleeding) up to 10 business days (IMRT)
What if Anterior Organ Invasion (T4b)?

- 3D Conformal RT fields
  - T3 Top rom & T4b bottom row
  - For T4b: Increased bowel dose due to larger region at risk

(Left) PA DRR showing the pelvic field for treatment of T3 rectal cancer includes coverage of internal iliac vessels (magenta) within the expanded CTV (dark green), not the external iliac CTV (light green). (Right) Lateral DRR shows T3 rectal pelvic field indicating coverage of internal iliac vessels (magenta) with CTV margin without intentional coverage of the external iliac CTV (light green). Classically, the anterior border is the base of pubis.

(Left) PA DRR showing the pelvic field for a T4b rectal cancer involving an anterior structure shows coverage of both the external (light green) and internal (dark green) iliac LN CTVs. (Right) Lateral DRR showing the pelvic field for a T4b rectal cancer shows CTV coverage of both the external iliac LNs (light green) and internal iliac LNs (dark green). Classically, the anterior border is 1 cm anterior to the pubis.

University of Vermont Cancer Center
What is Intensity Modulated Radiation Therapy (IMRT)?

- Beam divided into hundreds of “beamlets”
- Computer treatment planning software optimizes beamlet intensities
- Allows fulfillment of challenging dose constraint requirements

3D Conformal RT
- Uniform dose across entire beam

IMRT
How is dose modulation accomplished for IMRT?

- Multi-Leaf Collimator is moving while the beam is on
- Most of the field is blocked at any time
When is IMRT helpful?

- IMRT best for concave targets
  - Can “paint” dose where needed, avoiding normal tissue such as bowel
When is IMRT not helpful?

- For this IMRT plan, dose is spread out into bowel and bladder
- 3D CRT is more efficient and less expensive
# RT Plan Evaluation: Dosimetry Goals

<table>
<thead>
<tr>
<th>Organ</th>
<th>Ref.</th>
<th>Volume</th>
<th>Dose (Gy or %)</th>
<th>Priority</th>
<th>Achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PTV</strong></td>
<td>£</td>
<td>≥95%</td>
<td>≥95%</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>α</td>
<td>&lt;0.03 cc</td>
<td>&lt;85%</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Femoral heads</strong></td>
<td>£</td>
<td>&lt; 50%</td>
<td>&gt;30 Gy</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>£</td>
<td>&lt; 40%</td>
<td>&gt;40 Gy</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>£</td>
<td>&lt; 5%</td>
<td>&gt;45 Gy</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>£</td>
<td>Max</td>
<td>&lt;50 Gy</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>Bladder</strong></td>
<td>£</td>
<td>Mean</td>
<td>&lt;40 Gy</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>Small bowel/Peritoneal Cavity (Contour to 1 cm above PTV)</strong></td>
<td>&amp;</td>
<td>&lt;200 cc (&lt;1000)</td>
<td>V30 Gy</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&amp;£</td>
<td>&lt;150 cc (&lt;500)</td>
<td>V35 Gy</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>£</td>
<td>&lt;70 cc (&lt;425)</td>
<td>V40 Gy</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&amp;£</td>
<td>&lt;35 cc (&lt;250)</td>
<td>V45 Gy</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&amp;£</td>
<td>D0.03cc</td>
<td>&lt;50 Gy</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>
Additional Considerations: Avoiding the Ovaries

- Typically oophoropexy considered if ≤40 years old
- Still experience premature menopause
  - Timing may be estimated from dose received, as there is no safe RT dose that spares oocytes
Quality Assurance

- Performed by Physicists
- Multiple confirmations that data transferred correctly
  - Planning computer → Linac
- Physicists may give a “dummy” treatment to a patient surrogate
  - a.k.a phantom, usually container of water
  - Confirms correct calculations of dose to be delivered to a patient
  - Important for IMRT - see comparison between plan & actual below:

![Gamma Analysis Graphs]

**Summary (Gamma Analysis)**
- Total Points: 1138
- Passed: 1033
- Failed: 105
- % Passed: 90.8
Treatment Console

- RT Plan is transferred to treatment machine consoles
- Therapists check for all required information/instructions
Treatment

- Both RT linear accelerator gantry and “couch” where patient lays can move
Duration of Treatment

- RT given daily, 5 days per week
  - Long course RT: 27 – 30 treatments
  - Short course RT: 5 treatments
- Daily appointment duration ~15 minutes
  - Set-up: 3-5 minutes
  - Imaging: 3 minutes
  - Treatment:
    - 3D conformal
      - 30 seconds to 3 minutes per radiation field & often 3-5 fields
    - IMRT
      - 3-4 minutes given via arc around patent
Radiation Plan

• Consider offering patient opportunity to see his/her RT plan
  – Helps increase comfort & confidence with process
Pre-Treatment Setup Verification: Planning vs. Treatment Scans

- Compare imaging from time of simulation to pre-treatment scan
- Goal:
  - around 200-300 cc
  - Larger filling might not be reasonable
    - ~550 cc shown here
- Successful bladder filling achieved!
Pre-Treatment Setup Verification: Overlay
During RT: 
On-Treatment Visit

- Patients seen weekly by both nurse & physician
- Side effect management
  - Skin care, medical management, hydration, treatment breaks, etc.
- Emotional support/encouragement
# Acute Side Effect Management

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatitis</td>
<td>Aquaphor/Aloe Vera&lt;br&gt;Betamethasone&lt;br&gt;Post RT: Consider silvadene</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Low residue/fiber diet&lt;br&gt;Imodium → Lomotil → Morphine&lt;br&gt;Severe: octreotide (needs admission)</td>
</tr>
<tr>
<td>Dysuria</td>
<td>Hydrate&lt;br&gt;Baking soda (1 tsp) &amp; water (32 oz) – mix &amp; divide into 4 servings/day&lt;br&gt;Pyridium</td>
</tr>
<tr>
<td>Difficulty emptying bladder</td>
<td>Tamsulosin (Flomax)</td>
</tr>
<tr>
<td>Urinary Incontinence</td>
<td>Ditropan</td>
</tr>
<tr>
<td>Pain</td>
<td>Tylenol 1000 mg (ideally TID or less)&lt;br&gt;Ibuprofen 400 mg (ideally TID or less) if no significant bleeding&lt;br&gt;Narcotics if needed</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>Zofran, Compazine &amp; Ativan&lt;br&gt;If persists, consider olanzapine &amp; reglan</td>
</tr>
<tr>
<td>Flatulence/Cramping</td>
<td>Simethicone</td>
</tr>
</tbody>
</table>
Severe Side Effect Management

• If Grade 3 toxicity
  – Hold RT until Grade ≤2 or less
    • Unless not from RT (e.g. hand/foot from capecitabine)
  – Reassure patient treatment breaks (unless extensive) will not affect outcomes

• Grade 3 diarrhea/dehydration
  – IV fluids
  – Make sure to check labs & replete deficiencies prn
  – Consider admission to hospital
  – Consider imaging if refractory to standard management
    • CT imaging may show inflammation (<1% risk):

  ![](image1.png)

Before ChemoRT: Normal Appearing Bowel
2/3 Way Through ChemoRT: Inflamed Bowel Loops
Survivorship Considerations

• Develop long-term surveillance plan
  – Combination of H&P, CEA lab draws, CT chest/abdomen/pelvis scans, and colonoscopies
  – Routine CEA monitoring & CT scans not recommended past 5 years

• Bowel function changes
  – Chronic diarrhea, incontinence, stool frequency, stool clustering, urgency, cramping
    • Consider anti-diarrheals, bulk forming agents, diet manipulation, pelvic floor rehabilitation/physical therapy, and protective undergarments
  – Ostomy care

• Neuropathy
  – Consider duloxetine for painful neuropathy (not useful for numbness, tingling, cold sensitivity)
  – Consider referral to pain specialist for refractory cases

• Urogenital dysfunction
  – Screen for sexual dysfunction, erectile dysfunction, dyspareunia, and vaginal dryness
  – Screen for urinary incontinence, frequency & urgency
  – Consider referral to urologist or gynecologist for persistent symptoms

• Consider bone density monitoring due to potential for pelvic fractures

• Encourage healthy diet & exercise
  – Limit alcohol consumption (≤ 1 for women & ≤2 for men)
  – Consider daily aspirin 325 mg for secondary prevention

• Encourage continued therapeutic relationship with PCP
  – Help patient establish care with one if not presently involved

Adapted from NCCN Guidelines Version 3.2018
<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fecal frequency/urgency/incontinence</td>
<td>Anti-diarrheal Meds</td>
</tr>
<tr>
<td></td>
<td>Pelvic Physical Therapy</td>
</tr>
<tr>
<td>Urinary frequency/urgency/incontinence</td>
<td>Ditropan</td>
</tr>
<tr>
<td></td>
<td>Pelvic Physical Therapy</td>
</tr>
<tr>
<td>Persistent Fatigue</td>
<td>Physical Activity (e.g. Steps to Wellness)</td>
</tr>
<tr>
<td>Muscular stiffness/discomfort/fibrosis</td>
<td>Pelvic Physical Therapy</td>
</tr>
<tr>
<td>Rectal pain</td>
<td>Analgesics</td>
</tr>
<tr>
<td></td>
<td>Pelvic PT</td>
</tr>
<tr>
<td>Pelvic fractures</td>
<td>Rest</td>
</tr>
<tr>
<td></td>
<td>Referral to endocrinology</td>
</tr>
<tr>
<td></td>
<td>Vit D/Calcium</td>
</tr>
<tr>
<td>Small Bowel Obstruction</td>
<td>Send to Emergency Dept.</td>
</tr>
<tr>
<td></td>
<td>Nasogastric Tube &amp; bowel rest</td>
</tr>
<tr>
<td></td>
<td>Surgery evaluation</td>
</tr>
<tr>
<td>Hematuria/Hematospermia</td>
<td>Urology Evaluation</td>
</tr>
<tr>
<td></td>
<td>May need to coagulate ulcer in bladder</td>
</tr>
<tr>
<td>Dysparunia</td>
<td>Consider gynecology evaluation</td>
</tr>
<tr>
<td></td>
<td>Topical Estrogen Cream</td>
</tr>
<tr>
<td>Vaginal Stenosis</td>
<td>Vaginal Dilator</td>
</tr>
<tr>
<td>Erectile Dysfunction</td>
<td>PCP/Urology consult (prostaglandin injections, prosthesis)</td>
</tr>
<tr>
<td>Rectal Bleeding</td>
<td>Endoscopic coagulation/electrocautery via gastroenterology</td>
</tr>
<tr>
<td></td>
<td>Sulfacrate enema</td>
</tr>
</tbody>
</table>
Summary

• Staging studies help establish a diagnosis, prognosis, and treatment options
• Radiation preferentially kills cancer cells rather than normal tissue
  – Advances in radiation technology are improving outcomes
  – Decreased toxicity and improved efficiency
• Multidisciplinary input is essential from the time of diagnosis through the follow-up period
• Treatment plans are individualized
  – Based on a patient’s goals and disease characteristics
• Encourage patients to seek and utilize resources
  – Numerous options available to support their care plan
Thank you!

• Questions?