Interpretation of Rectal Cancer MRI (Initial Stage)

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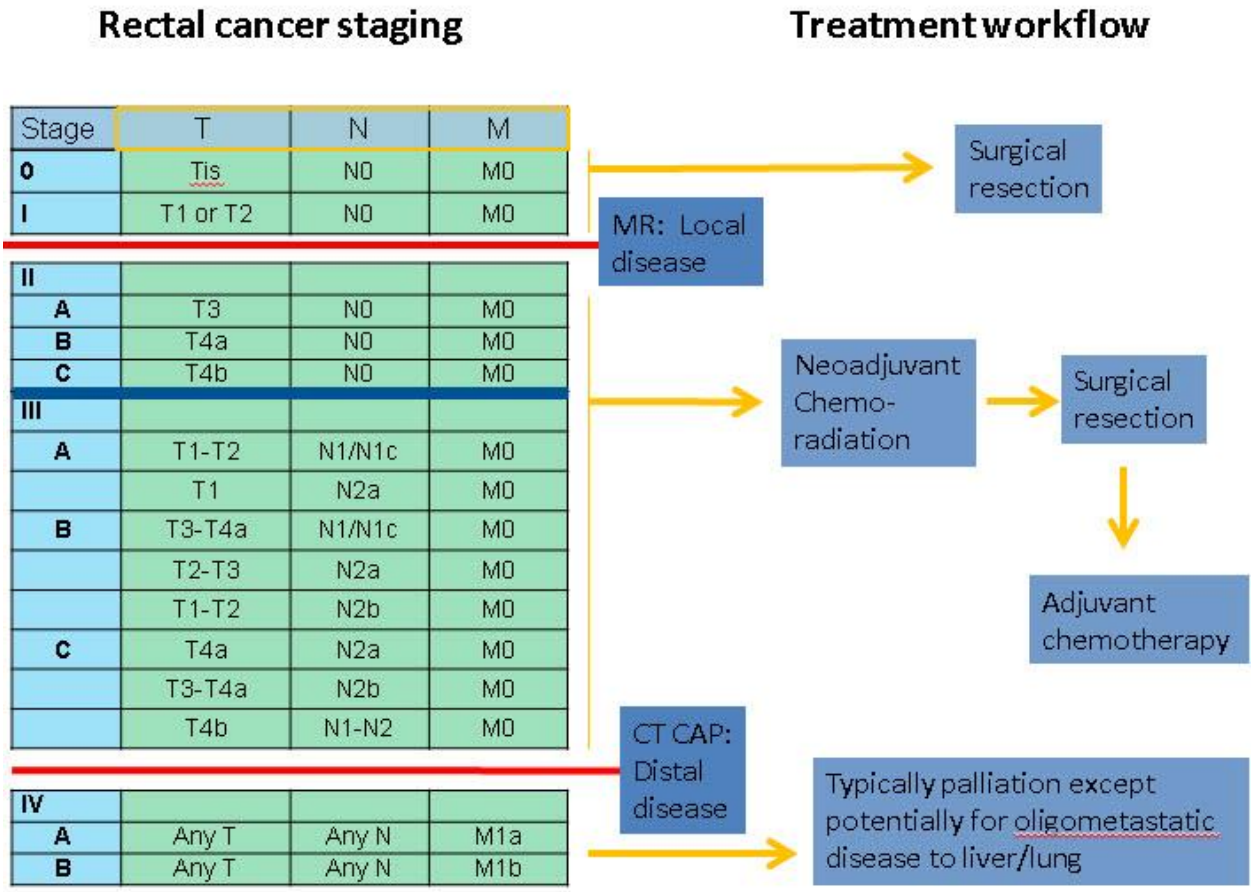
1. Baseline study- INITIAL STAGE MR
    a. Imaging is a required component of initial rectal cancer staging which is clinically-based (denoted cTNM). *Clinical staging* includes diagnostic biopsy, physical exam and imaging.
        i. cTNM staging determines whether patients receive neoadjuvant chemoradiation (or TNT-total neoadjuvant therapy) prior to surgery
        ii. After surgery, staging is based on pathology (denoted pTNM). If neoadjuvant chemoradiation was given, the staging is denoted with a prefix 'y' (ypTNM)



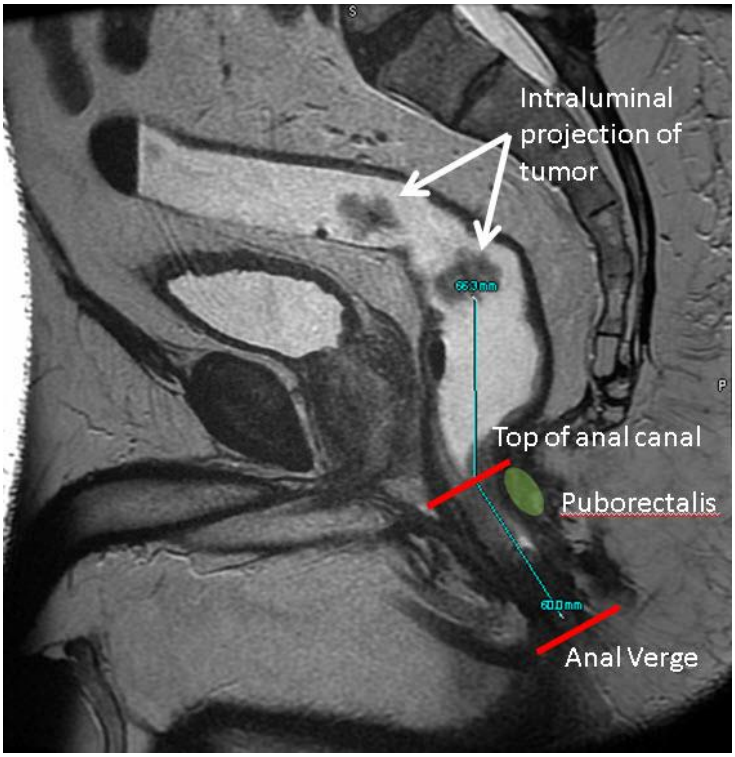
    b. Rectal MR has replaced endoscopic rectal ultrasound (ERUS) as the imaging modality of choice for rectal cancer staging due to rectal MR's superior ability in overall assessment of local extent of disease (ie, extension past the muscularis propria, relationship to the mesorectal fascia, regional lymphadenopathy). ERUS remains the modality of choice for a minority of cases with the specific question of ***T1 versus T2 status*** (cancer limited to the submucosa versus extension into the muscularis propria) to determine if an endoscopic resection is possible.[1] Rectal MR should not be used for this assessment. At

rectal MR staging, T1 and T2 are lumped into a single category (denoted 'T1/T2' or 'T1-T2').

c. Other helpful clinical information to be aware of to aid Rectal MR interpretation includes:
    i. Digital rectal exam (DRE) results for MR interpretation of low tumors. DRE can help assess for fixation to sphincters, relationship to anorectal ring and pelvic floor musculature
    ii. Rigid proctoscope or flexible sigmoidoscope findings which help to localize tumor and determine potential distal margin (see 'Tumor location and position' section)

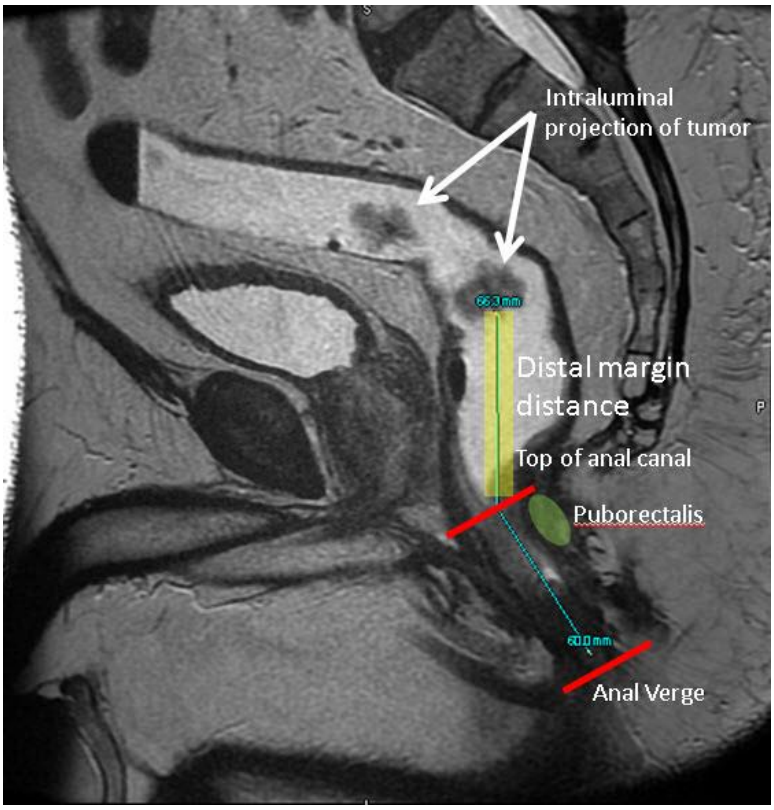
d. Tumor location and position
    i. It is important to localize and describe the relationship to several anatomic landmarks which help guide surgical approach and predict surgical margins. May impact need for neoadjuvant chemoradiation.
        1. Distance between anal verge and tumor to localize as a upper, mid, or lower rectal tumor
        2. Distance between top of anal canal (anorectal junction) and tumor to help define distal margin of the surgical resection
        3. Distance to the mesorectal fascia to determine the potential circumferential resection margin (CRM) at surgical resection
        4. Relationship to the anterior peritoneal reflection
        5. The proximal margin is typically not an issue which is determined by level of ligation of supplying arterial vasculature. Typically is well away from the location of the tumor

e. Distance from anal verge localizes tumor into upper, mid, and lower rectum
    i. Anal verge (definition): external end of the anal canal; the transitional zone between the epithelium of the anal canal and the perianal skin.
        a. Upper rectum >10-15 cm from anal verge
        b. Mid rectum >5-10 cm from anal verge
        c. Low rectum <5 cm from anal verge
    ii. How this distance is measured:
        1. Distance classically determined by rigid proctoscopy (gold standard)
        2. Flexible endoscopy may not correlate well (often overestimates distance from anal verge compared to rigid proctoscopy which straightens bends)
        3. Measured at MR along the along the long axis of the anal canal from the distal end of the *internal sphincter* to the *top of the anal canal* and the optimized distance from top of canal to *inferior edge of tumor*. The two distances should be summed.



iii. Importance of this measurement:
    1. Categorizes tumor as a high, mid, or low rectal tumor which holds implications regarding probable surgical approach
    2. Classically, high and mid rectal tumors are amenable to a sphincter sparing surgery (Low Anterior Resection; LAR) as opposed to low rectal tumors are more likely to go on to an Abdominal-Peritoneal Resection (APR) which leads to a loss of the anal sphincter and a permanent colostomy.
    3. Increasingly, LAR is a potential option for low rectal tumors — see section 'Relationship to the anal canal'
    4. High rectal tumors may be treated like distal sigmoid cancers in select cases. Discussion at multi-disciplinary conference is crucial.

f. Distance between the top of the anal canal (level of the puborectalis at the anorectal junction) and the inferior edge of tumor.
    i. Gives information regarding potential distal surgical margin. Historically, surgeons preferred a distal margin of 5 cm. This has decreased to 2 cm.[2] Evidence that a 1 cm margin may be acceptable after neoadjuvant chemoradiation.[3]
    ii. How the distance is measured
        1. Shortest linear distance between the top of the anal canal at the level of the puborectalis and the most inferior portion of the tumor



Distal margin measurement (yellow highlighted blue line)

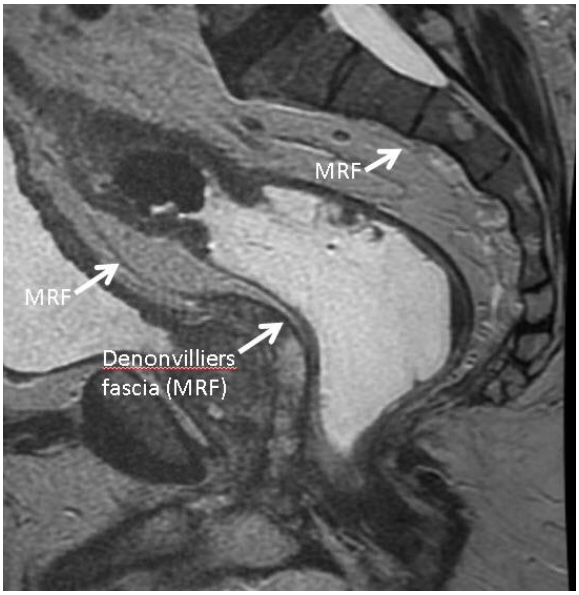
iii. Importance of the distal margin status

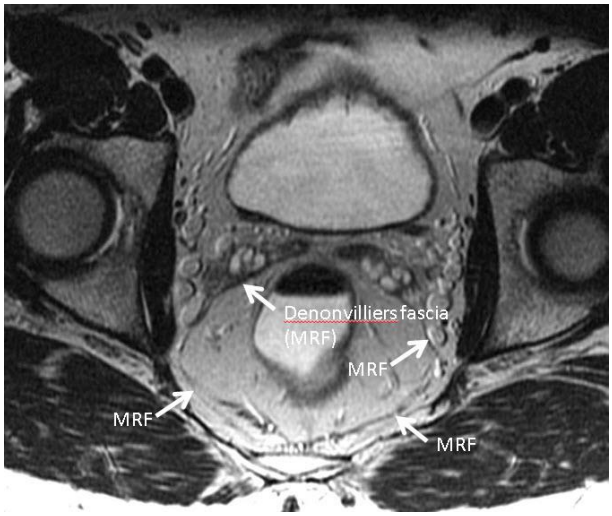
1. A positive distal margin leads to local recurrence rates of 40%[4] and decreases in 5 year survival[5] despite TME and neoadjuvant chemoradiation

g. Relationship to the mesorectal fascia (MRF) helps to determine potential circumferential resection margin (CRM)

i. MRF (mesorectal fascia): Fascial layer that encloses the rectum, mesorectal fat, lymph nodes and lymphatics to form an anatomic unit. Distance of tumor to the MRF used to predict CRM involvement.

1. MRF fuses with the presacral fascia posteriorly then encircles the rectum laterally. Anteriorly, it thickens at the level of the prostate and seminal vesicles in males (called Denonvilliers fascia). The correlate in females is fascial thickening at the rectovaginal septum. The superior extent anteriorly is demarcated by the anterior peritoneal reflection.
2. MRF completely encircles the rectum from the anterior peritoneal reflection superiorly to the level of the pelvic floor (ie, levator ani musculature) inferiorly
3. MRF is incomplete where the upper and mid rectum is partially peritonealized (see 'anterior peritoneal reflection' section)

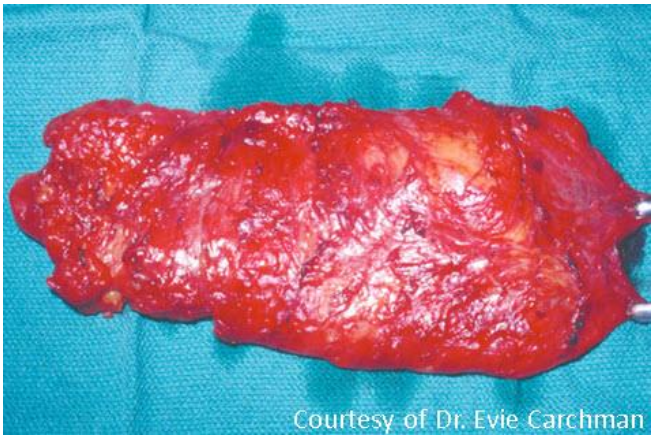


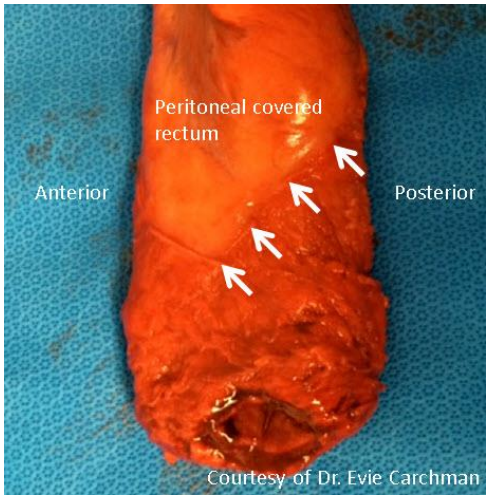


ii. CRM (circumferential resection margin) represents the distance of tumor closest to the radial edge of the surgical TME specimen.
    1. Refers to the non-peritonealized surfaces of the rectum; thus not applicable peritonealized surfaces which include the anterior and lateral walls for upper rectum and anterior walls for mid rectum. A helpful landmark is the anterior peritoneal reflection— to be discussed later).
    2. Not applicable if tumor is T1 or T2 (ie, not past the muscularis propria)
    3. Positive CRM from primary tumor extension leads to increased recurrence rates[6]
    4. Estimated by the distance of primary tumor extension to the MRF (< 1mm distance to MRF predicts CRM involvement, 1-2 mm equivocal involvement, >2 mm not involved).[7] CRM is a pathologic term and not directly assessed at imaging.
    5. Do not measure distance between a positive mesorectal lymph node and the MRF predict CRM status. Knowledge of these implants may be helpful to the surgeon to be careful in these areas during the TME resection if close to the MRF but does not impact CRM status. As EVMI is a direct extension of tumor (see below), can measure between EMVI and MRF for this assessment.

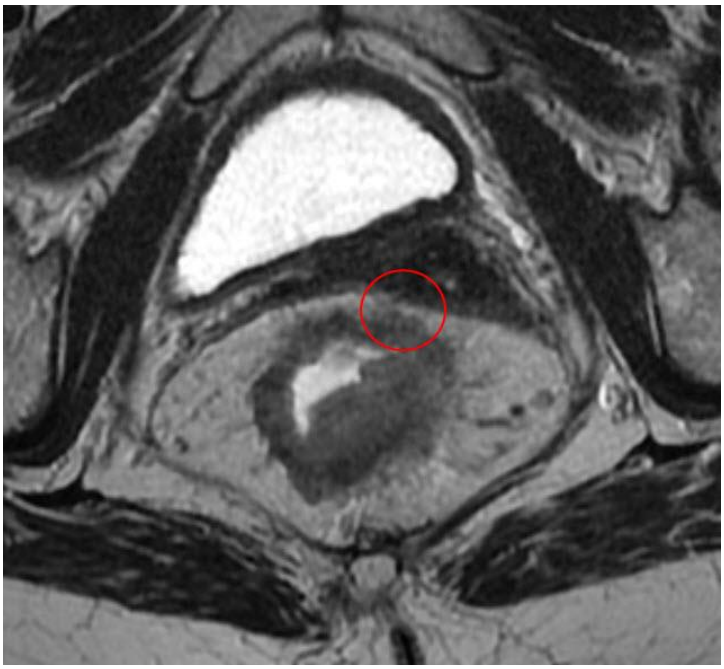
iii. TME (total mesorectal excision): Surgical technique characterized by sharp dissection in the avascular plane between the parietal and visceral pelvic fascia where the rectum and surrounding structures encapsulated by the mesorectal fascia are removed en bloc
    1. Should extend 5 cm distal to the level of the tumor. Thus, for high rectal cancers, the TME does not need to extend to the pelvic floor whereas for mid and lower tumors, the TME is extended to the pelvic floor

2. Has led to a marked decrease in local recurrence rates[8] (ie, less than 10%)





iv. How distance to the MRF is measured:
    1. Shortest linear distance between either the tumor and the MRF; typically done on the high resolution FSE T2 weighted images. It may be helpful to view from different planes.
        a. <2 mm equates to a threatened CRM
        b. <1 mm equates to an involved CRM
        c. High specificity (92%) in predicting a negative CRM[9]



<1 mm tumor to MRF so predicts 'involved CRM'

2. Distance to MRF is not applicable to peritonealized portions of the upper and mid rectum. Thus, it cannot be measured at these levels.

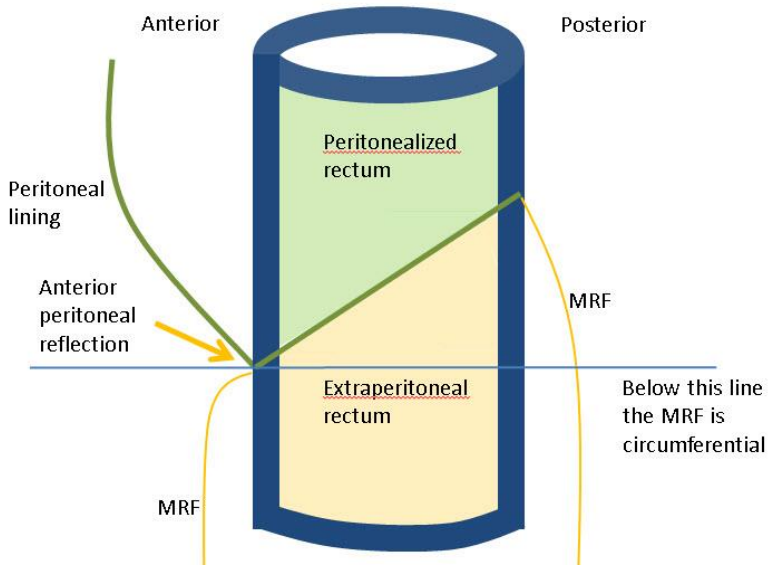
v. Clinical importance of MRF distance:

1. A threatened or involved CRM margin reinforces need for neoadjuvant chemoradiation to decrease local recurrence rates.

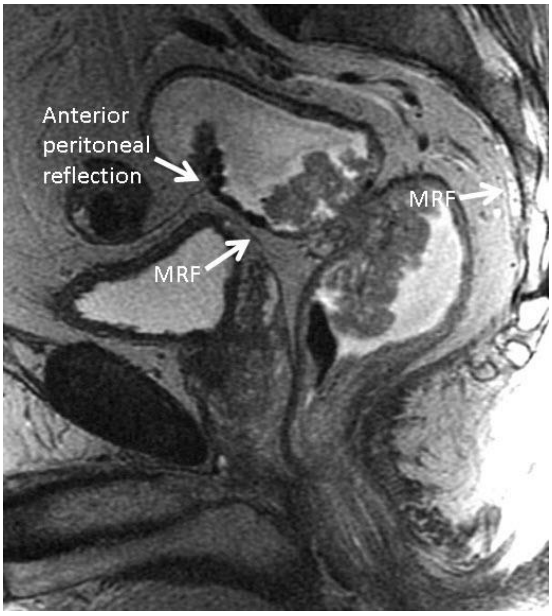
h. Relationship to anterior peritoneal reflection:

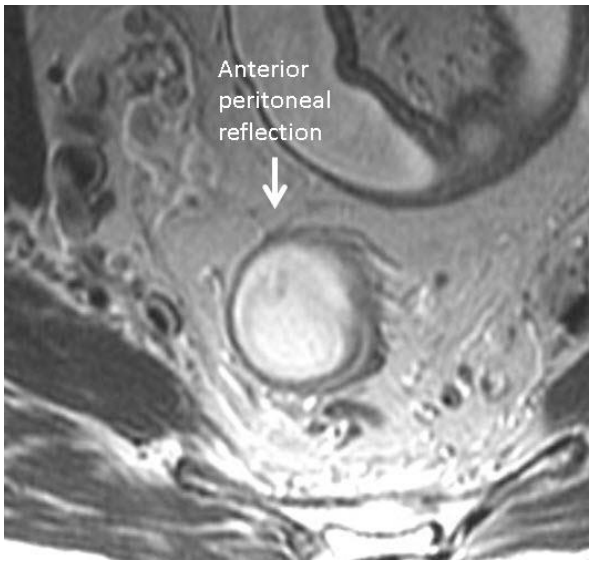
i. Anterior peritoneal reflection is a landmark seen on MR which helps to determine the peritonealized and nonperitonealized portions of the rectum. Important to delineate relationship for high and mid rectal tumors.

1. Below the anterior reflection, the rectum is completely extraperitoneal in location and the MRF completely encircles the rectum. The boundary between the peritoneal and extraperitoneal rectum courses in an obliquely superior course from anterior to posterior.



2. CRM (and MRF) does not exist for the peritonealized portions of the high and mid rectum
3. The anterior peritoneal reflection is variable in location but typically at the level of the seminal vesicles in males and at the cervical-vaginal junction in females
4. Seagull sign: the anterior peritoneal reflection on axial images is reminiscent of a seagull

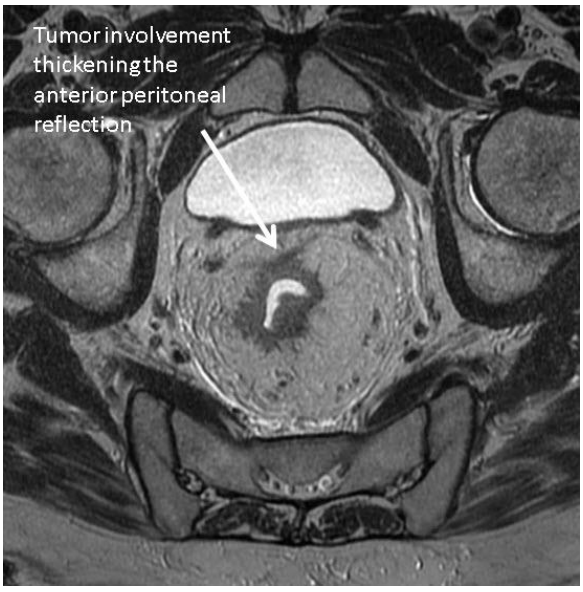


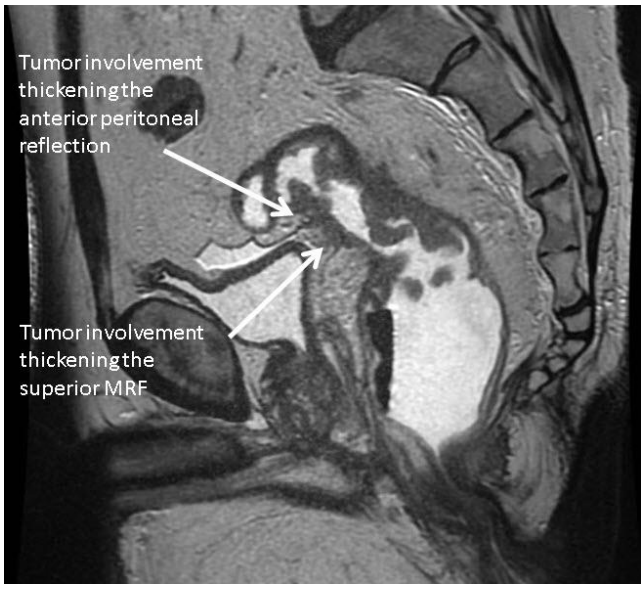


See 'seagull' sign on axial image to the right.

ii. Clinical importance

1. Tumor involvement of the anterior peritoneal reflection represents a T4a tumor and may be at risk for seeding and intraperitoneal recurrence in rectovesical space



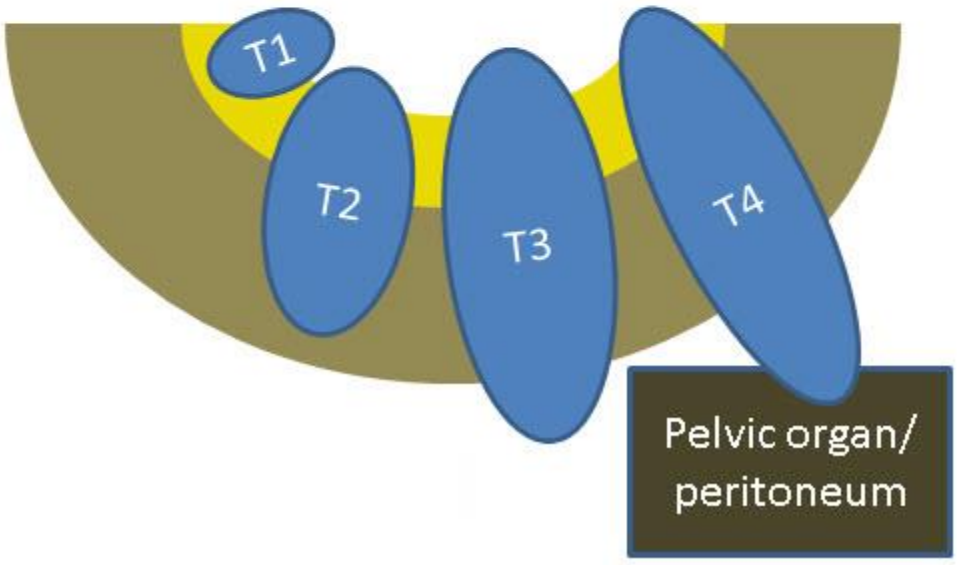


T4a cancer

2. T category

a. Based on depth of invasion. Rectal cancer begins as a mucosal process (either as an adenomatous or serrated polyp). After transformation to cancer, tumor can extend into deeper layers of the bowel wall and beyond.

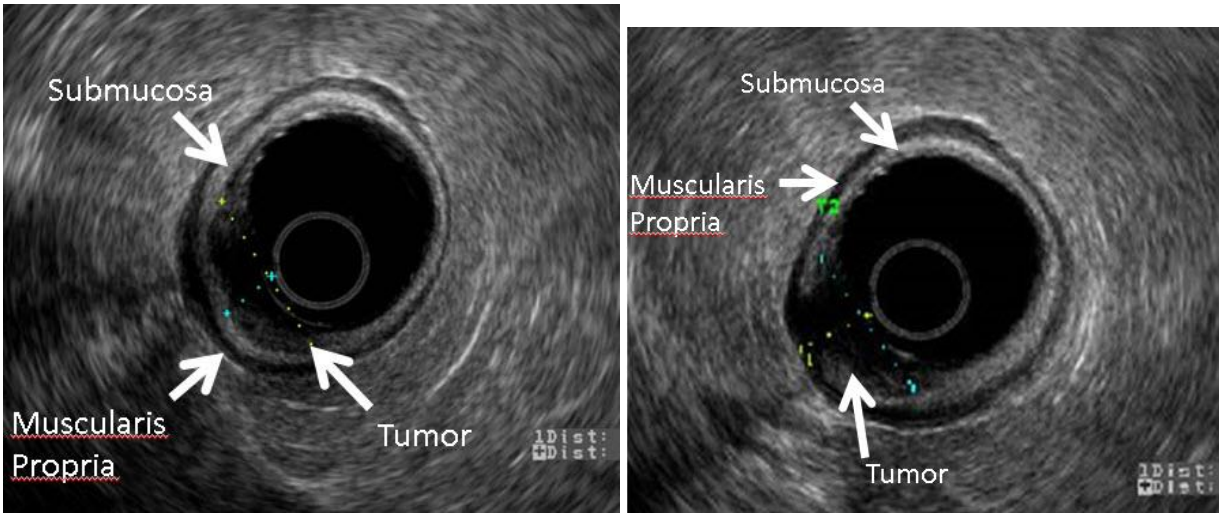
Primary tumor	
T1	Invades submucosa
T2	Invades muscularis propria
T3	Extends past muscularis propria
T4a	Penetrates visceral peritoneum
T4b	Invades adjacent organs



b. Depth of tumor wall involvement impacts treatment options. The major distinctions involve differentiation between:
    i. T1 versus T2. T1 tumors limited to within the submucosa (T1, N0, M0) are amenable to local endoscopic excision by TEMS (transanal endoscopic micro-

surgery) or TAMIS (transanal minimally invasive surgery) as opposed to more invasive surgeries (LAR- low anterior resection, APR- abdominoperineal resection).

1. Evaluated best by endoscopic rectal ultrasound which can directly visualize the layers of the bowel wall.
2. Rectal MR with a phased array coil typically cannot distinguish between T1 and T2 status as the layers of bowel wall are not resolved. Rectal MR should not be used if this is the clinical question.
    a. At MR, T1 and T2 are grouped together (T1/T2)



T1 tumor on left and T2 tumor on right on endoscopic ultrasound

ii. T2 versus T3. T2 tumors involve the muscularis propria but are contained by this muscle layer whereas T3 tumors extend past the muscular propria.
    1. Major treatment decision point whether neoadjuvant chemoradiation is given (for T3) or not (for T2) prior to surgery. (more detail to follow in next sections)

iii. Low risk T3 (≤ 5mm past the muscularis propria) v. high risk T3 (> 5mm past muscularis propria).
    1. Survival data suggest a difference in survival for T3 tumors defined by extramural extension.[10] See section on 'Extramural depth of invasion (EMD)'.
    2. Some suggest that decision for neoadjuvant chemoradiation should be made at this boundary as opposed to T2 versus T3 status.[11] Currently, decisions for neoadjuvant chemoradiation are not made as standard care in the United States for this T-category subdivision.

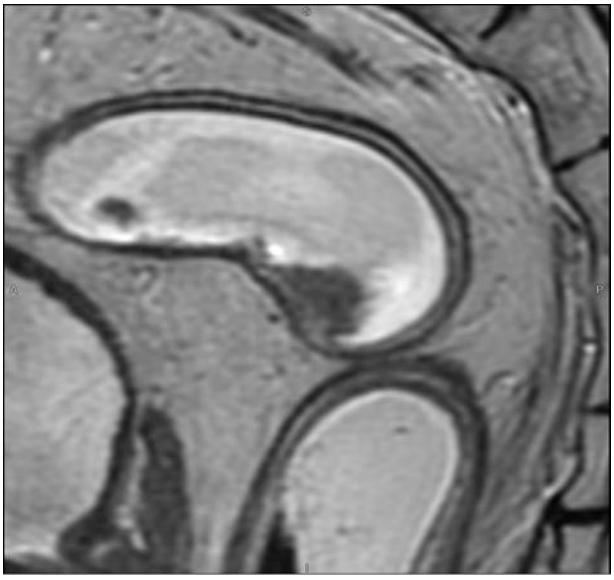
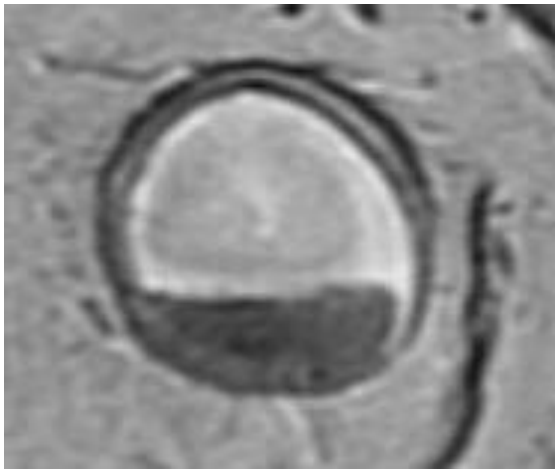
c. T2 versus T3 status
    i. Rectal MR and ERUS essentially equivalent for evaluation of T2 versus T3. However, there is increasing consensus that MR is superior to ERUS (aside from

the specific clinical question of T1 v T2 status) in assessing other features of rectal cancer staging (ie, tumor location, relationship to mesorectal fascia for CRM prediction, assessment for pelvic side wall lymph nodes, etc).

ii. Why assessment of tumor wall involvement important?
    1. Major determinant for need for neoadjuvant chemoradiation prior to surgery (positive regional lymphadenopathy and threatened circumferential resection margin are other indications). German rectal trial (n=823) showed that although neoadjuvant chemoradiation did not change 5 year survival (76% for neoadjuvant versus 74% for adjuvant therapy), it decreased local recurrence rates from 13% to 6% for clinical stage T3 or T4 or node positive disease.[12]

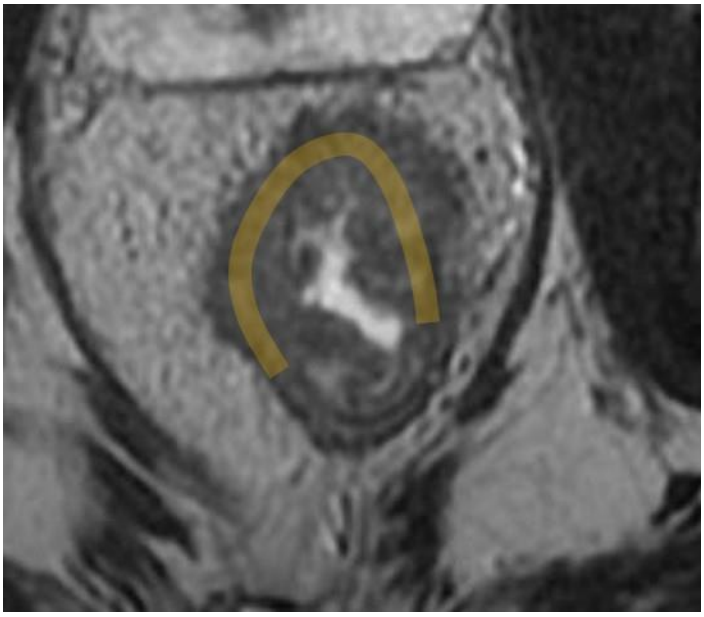
iii. How to make this determination
    1. High resolution, thin slice T2-weighted images without fat saturation
        a. Other sequences have less contrast resolution (post contrast T1, T2 with fat saturation or DWI) which impacts tumor wall assessment
    2. Including series angled to the short axis and long axis of the tumor to minimize volume averaging artifact. Otherwise, may lead to blurring and difficulty in assessment.
    3. Avoid motion (bowel and patient). Glucagon is helpful. Motion can cause blurring of the muscularis propria.
    4. Rectal gel may be helpful. Gel can minimally separate colonic walls and locate the edges of the tumor to assess the wall status

iv. Imaging characteristics:
    1. For a T2 tumor where tumor involves but is contained by the muscularis propria (MP):
        a. Smooth curving outer border of MP without lobulated outer coutour
        b. At MR, because we cannot resolve the layers of the bowel wall, we cannot differentiate between T1 and T2. Tumors should be noted T1/T2.

T1/T2 tumor. Note smoothly curving outer contour without break on sagittal and oblique axial

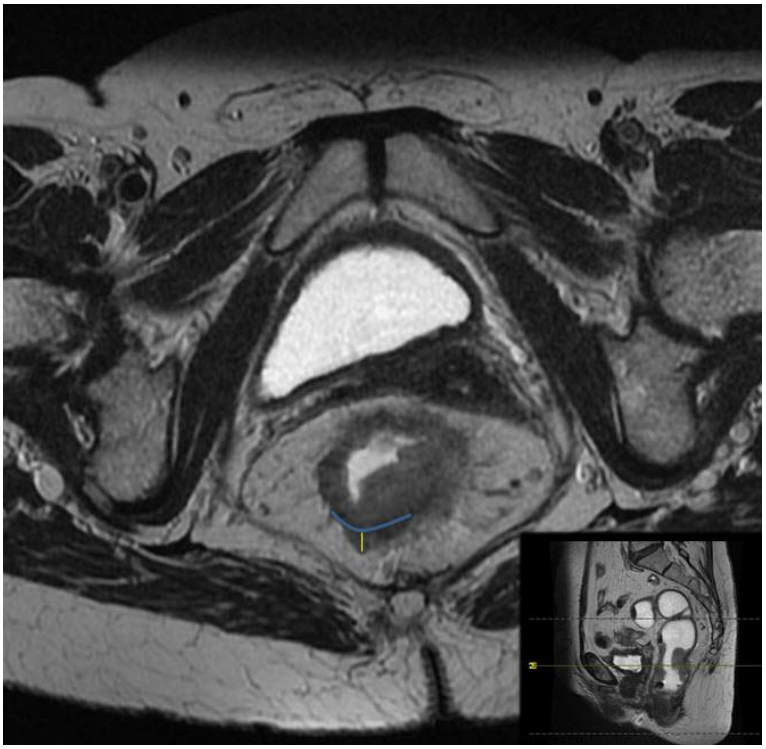
2. For a T3 where tumor extends past the MP
    a. Discontinuity/disruption of the MP (presents as a curving low signal band if intact) secondary to tumor
    b. Broad-based bulge or focal lobulation beyond expected location of MP; helpful to confirm on orthogonal planes
    c. Small vessels can pierce MP at level of tumor. Does not necessarily mean tumor extension. If the vessel is expanded, should consider extramural vessel invasion (see EMVI section)



T3 cancer. Yellow line is expected location of the MP/rectal wall which has been obliterated by tumor growth past it.

v. Peritumoral stranding into mesorectal fat
    1. Represents desmoplastic response to tumor which may or may not contain tumor.
    2. Fine low signal spicules less likely to represent tumor than thick irregular bands
    3. Controversy whether to call tumor extension past wall or not. For fine spicules, may consider fibrosis and not tumor.

d. Extramural depth of invasion
    i. Independent predictor for survival; may correlate better than wall stage
        1. Marked decrease in survival greater than 5 mm of EMD past the muscularis propria (from 85% to 59%)[10]
    ii. Not considered in AJCC staging system (7th ed) but incorporated in various MR reporting templates. T3 is subdivided into:
        1. T3a < 1mm
        2. T3b 1- <5 mm
        3. T3c 5-15 mm
        4. T3d > 15 mm
    iii. How to measure:
        1. Measure distance between outermost edge of tumor and outer edge of MP (or expected outer edge of the MP if not present due to replacement by tumor). Do not include spicules.
        2. HR resolution MR is equivalent to histology (within 0.5 mm against histology).[13] Other studies show more variability.[14]

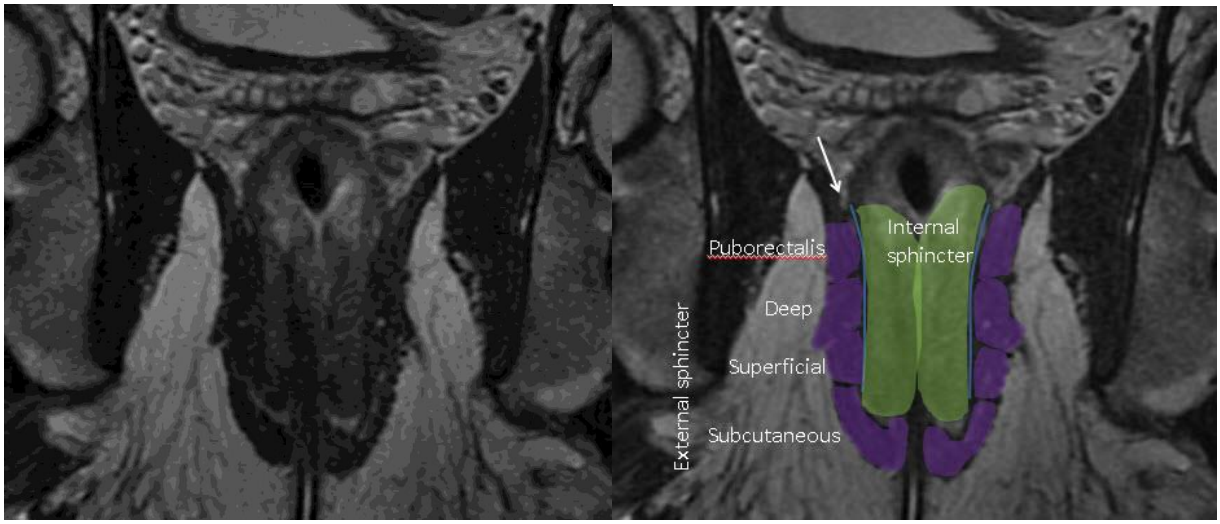


Thin blue line is the expected level of the outer rectal wall. Yellow line represents the EMD

e. Involvement of pelvic structures
    i. Potential structures include:
        1. GU: bladder, left ureter, right ureter, cervix, uterus, vagina, prostate, seminal vesicle, urethra)
        2. Pelvic sidewall: obturator internus, piriformis, ischiococcygeus
        3. Pelvic floor: pubococcygeus, ileococcygeus, puborectalis
        4. Sacrum: Sacral involvement above S2 may be unresectable
        5. Vessels: left internal iliac vessels, right internal iliac vessels, left external iliac vessels, right external iliac vessels
        6. Nerves: lumbosacral nerve roots, sciatic nerve
    ii. Classified as a T4b tumor
    iii. How to make imaging diagnosis
        1. Loss of fat plane should be noted as abutment
        2. Signal abnormality extending into structure is highly suspicious for invasion
f. Relationship to the anal canal
    i. Anal canal anatomy
        1. Surgical anal canal which includes the puborectalis (see diagram) is longer than the 'anatomic' anal canal which extends from the anal verge to the dentate line (boundary between squamous and columnar

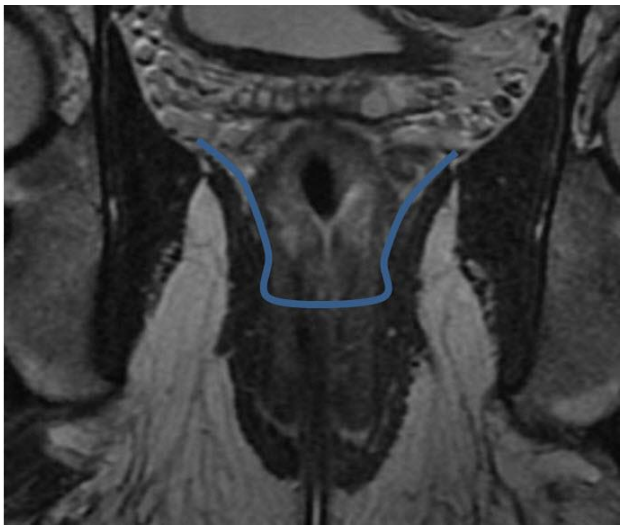
epithelium- not visualized at MR but estimated by the junction between the deep and superficial portions of the external sphincter)

2. Internal sphincter is a concentric thickening of the circular muscle layer of rectal wall
3. External sphincter is a continuation of the pelvic floor musculature/levator ani.
4. Intersphincteric space is a potential space between the external sphincter and internal sphincter which may be seen as fatty intensity cleft (The intersphincteric space is actually between the external sphincter and the conjoint longitudinal muscle—this muscle may be difficult to resolve from the outer border of the internal sphincter).



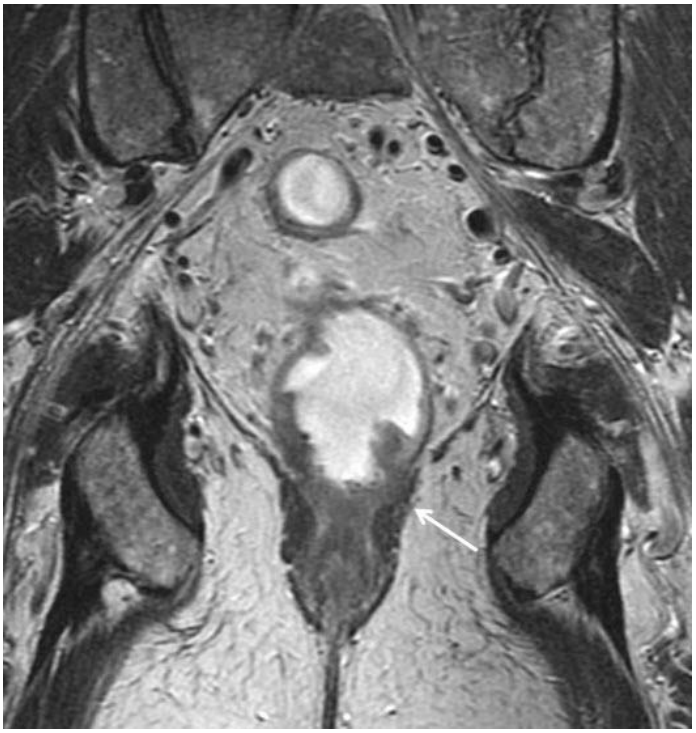
Anal canal anatomy coronal

ii. Traditionally tumor involvement of anal canal led to APR with loss of the sphincter and permanent colostomy.
iii. Newer surgical techniques to extend the distal margin such as a LAR with intersphincteric resection (ISR) where the tumor is limited to the internal sphincter may be possible in select patient groups (here the internal and external sphincters separated and the internal sphincter partially or completely removed.



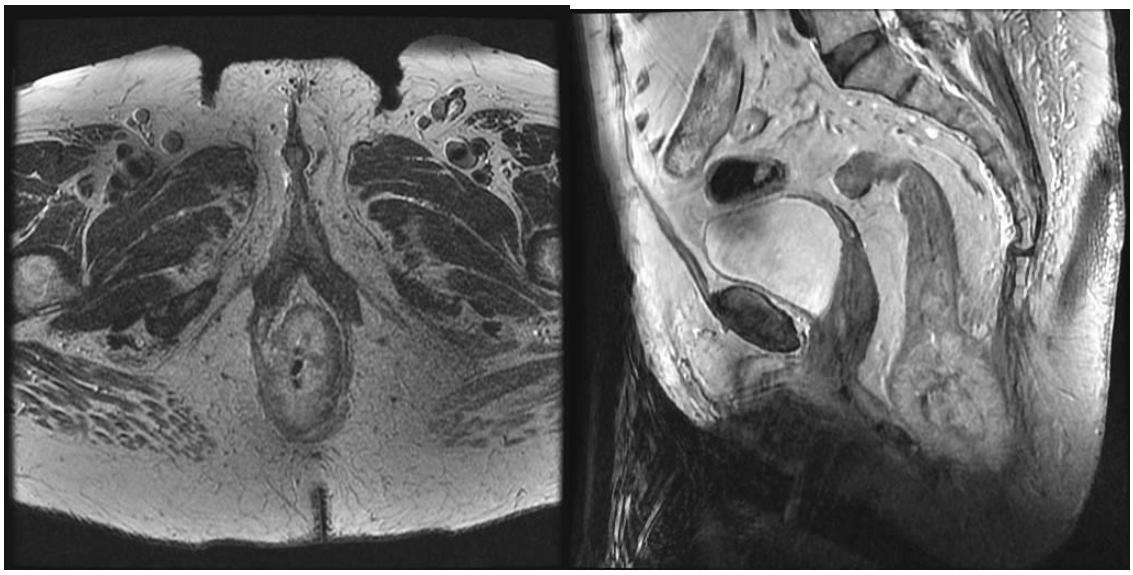
Blue line- ultralow LAR resection line

iv. How best to evaluate
    1. Coronal high resolution thin slice T2-weighted images oriented to the long axis of the anal canal
    2. Assess for intact fatty intersphincteric space free of tumor. Extension to involve intersphincteric plane and puborectalis/external sphincter leads to APR



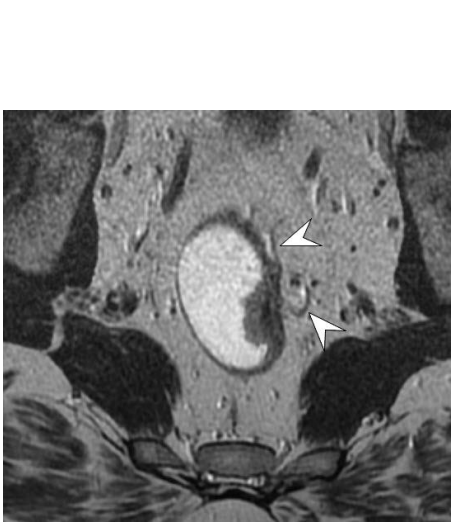
Arrow- extension past the intersphincteric fissure to involve the puborectalis on the left. Would not be a candidate for ultralow LAR

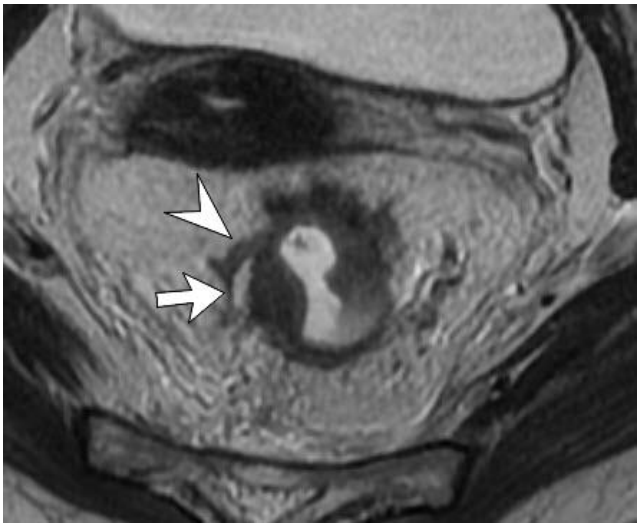
g. Mucinous subtype
    i. More likely to be invasive or present with metastatic disease.
    ii. >50% of the tumor/tumor pool has very high T2 signal intensity compared to perirectal fat/muscle



Mucinous tumor

h. Extramural venous invasion (EMVI)
    i. Presence of tumor in a mesorectal vessel extending from the primary tumor; typically a vein
    ii. By definition, EMVI makes the rectal tumor a T3 lesion.
    iii. Imaging:
        1. Assess any vessels (tubular or serpiginous structures) in the meso-rectal fat extending from the tumor
            a. A nodular contour, expansion of the lumen with tumor signal should raise suspicion for vessel involvement and EMVI
    iv. EMVI is an independent poor prognostic factor[15]
    v. MR-detected EMVI predictive of higher rates of relapse[16]



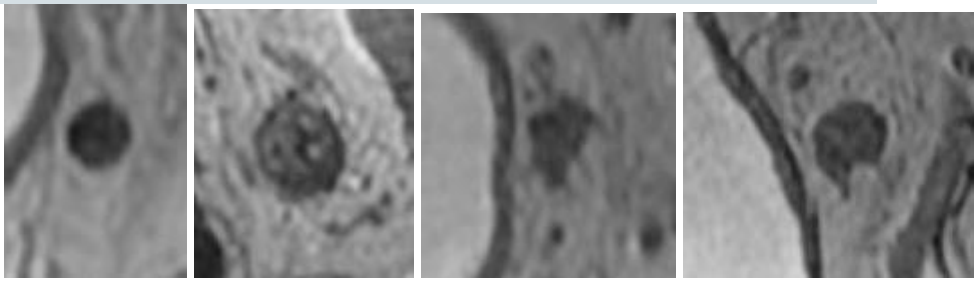


No EMVI9 normal veins without expansion EMVI

Lymph nodes

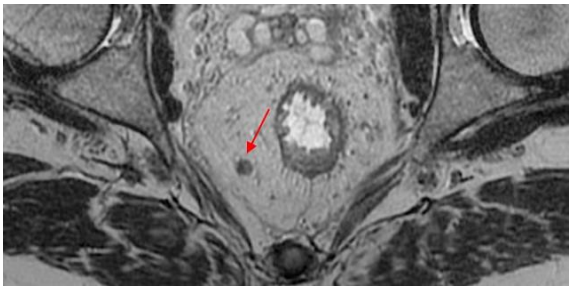
1. Sensitivity and specificity moderate (ie, 70%/70%) with available imaging biomarkers (size, internal attenuation, outer border). So make best assessment using expected drainage patterns.
    a. Lymphatic flow in mesorectum is cephalad. (90% superior back to IMA takeoff; 10% lateral to pelvic side wall lymphatics following branches of middle rectal from internal iliac.
2. Use SAR criteria to maximize sensitivity and specificity

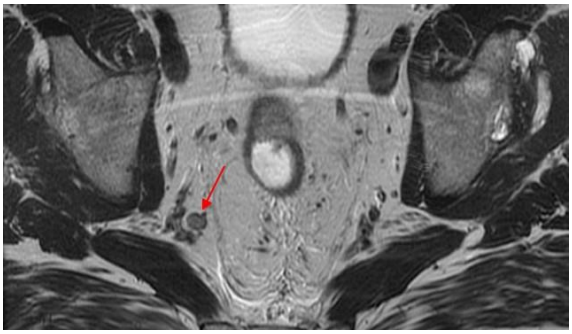
SAR criteria for positive LN
9 mm or greater
5-8 mm + 2 morphologic criteria
<5 mm + 3 morphologic criteria



Morphologic criteria: Round (first on left), internal heterogenous architecture (second from left), irregular border (last two on right)

3. Regional lymph nodes (which constitute positive 'N' status on TNM system) represent malignant involvement from direct lymphatic drainage from the tumor. These include mesorectal lymph nodes extending back to the IMA take off from the aorta and lateral pelvic lymph nodes (internal obturator and adjacent to branches of the internal iliac). Positive regional lymph nodes lead to Stage 3 disease and patients typically undergo neoadjuvant chemoradiation or TNT.


Mesorectal lymph node


Lateral pelvic lymph node

4. Metastatic lymph nodes are ones that result from hematogenous spread. If these lymph node locations are involved, this is metastatic spread and confers Stage 4 disease which is treated palliatively for the most part. So enlarged RTP lymph nodes above the level of the IMA, External iliac LN and inguinal lymph nodes are metastatic. One caveat - if the rectal cancer is low and involves the anal canal, peripheral external iliac and inguinal lymph nodes represent regional adenopathy as lymphatics can drain to these regions with anal canal involvement.

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