Pretreatment local staging evaluation for rectal cancer

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INTRODUCTION

Surgical resection is the cornerstone of curative therapy for patients with early stage, potentially resectable rectal cancer. The type of surgery depends on tumor stage and location within the rectum. Superficially invasive, small cancers may be effectively managed with limited surgery (such as local excision). However, most patients have more deeply invasive tumors that require low anterior resection or, in some cases, if located distally, abdominoperineal resection. Locally advanced tumors that are adherent or fixed to adjoining structures (eg, sacrum, pelvic sidewalls, prostate, or bladder) require more extensive surgery. (See "Surgical treatment of rectal cancer" and "Treatment of locally recurrent rectal adenocarcinoma".)

The combination of adjuvant radiation therapy (RT) and chemotherapy can enhance local control and cure rates in patients with either transmural invasion (T3/T4) or regional lymph node involvement (table 1). (See "Adjuvant therapy for resected rectal adenocarcinoma in patients not receiving neoadjuvant therapy".)

Increasingly, such therapy is administered preoperatively. The more favorable long-term toxicity profile and better local control with preoperative as compared with postoperative long-course chemoradiotherapy for transmural or node-positive rectal cancer were shown in the seminal German Rectal Cancer Study Group trial. Subsequently, benefit has been shown for neoadjuvant short-course RT alone, although this approach is more popular outside of the United States. More recently, the concept of "total neoadjuvant therapy," in which both RT and adjuvant systemic chemotherapy are administered preoperatively, is gaining popularity for locally

advanced tumors. (See "Neoadjuvant therapy for rectal adenocarcinoma", section on 'German Rectal Cancer Study Group trial' and "Neoadjuvant therapy for rectal adenocarcinoma", section on 'Short-course radiotherapy' and "Neoadjuvant therapy for rectal adenocarcinoma", section on 'Total neoadjuvant therapy for locally advanced tumors'.)

Although there is not universal agreement, neoadjuvant approaches are generally considered for T3/T4 and/or clinically node-positive T1/T2 tumors (table 1), distal rectal tumors (ie, tumors within 5 cm of the anal verge (figure 1)) for which preoperative chemoradiotherapy may enhance the ability to preserve the anal sphincter, and tumors that appear to invade or are in close proximity to the mesorectal fascia on preoperative imaging because of the decreased likelihood of achieving a tumor-free circumferential resection margin (CRM) with upfront surgery. (See "Neoadjuvant therapy for rectal adenocarcinoma", section on 'Indications for neoadjuvant treatment'.)

The selection of appropriate patients for initial RT or chemoradiotherapy rather than surgery is heavily dependent on accurate preoperative locoregional staging of the depth of transmural penetration, the presence or absence of suspicious perirectal nodes, and the likely status of the CRM. Locoregional tumor staging is mainly accomplished through physical examination, endoscopy, computed tomography (CT) scans, magnetic resonance imaging, and transrectal endoscopic ultrasound (TEUS).

This topic review will cover the preoperative local staging evaluation of patients with rectal cancer. The clinical presentation, diagnosis, and staging evaluation of patients with newly diagnosed colorectal cancer; the surgical treatment of rectal cancer; neoadjuvant chemoradiotherapy and RT for rectal cancer; adjuvant therapy following resection for rectal cancer; management of locally advanced, unresectable rectal cancer; and recommendations for post-treatment surveillance are discussed elsewhere.

- (See "Clinical presentation, diagnosis, and staging of colorectal cancer".)
- (See "Radical resection of rectal cancer".)
- (See "Surgical treatment of rectal cancer".)
- (See "Neoadjuvant therapy for rectal adenocarcinoma".)
- (See "Adjuvant therapy for resected rectal adenocarcinoma in patients not receiving neoadjuvant therapy".)
- (See "Treatment of locally recurrent rectal adenocarcinoma".)
- (See "Post-treatment surveillance after colorectal cancer treatment".)

SURGICAL ANATOMY

Many surgical descriptions refer to the distance of a rectal cancer from the anal verge. The upper extent of the rectum is typically defined as 12 cm from the anal verge (figure 1). While the dentate line, the point at which the squamous mucosa of the anus transitions to the columnar mucosa of the rectum, is a more reliable landmark than the anal verge, it is not visible on cross-sectional imaging. As a result, the inferior and superior margins of the anal sphincter complex are typically used as imaging landmarks. (See "Radical resection of rectal cancer", section on 'Surgical anatomy'.)

If sphincter preservation is to be achieved, the tumor has to be located high enough above the top of the anorectal ring to allow for an adequate distal margin. This is more likely with midrectal and upper rectal tumors than with distal tumors, particularly those that impinge upon or invade the sphincter complex. Preoperative chemoradiotherapy may enhance the ability to perform sphincter preservation in some patients with low-lying tumors. However:

- High-quality definitive evidence is lacking that preoperative chemoradiotherapy can consistently convert patients who need abdominoperineal resection (APR) to where low anterior resection (LAR) is feasible. The German trial of preoperative versus postoperative chemoradiotherapy demonstrated that patients undergoing preoperative chemoradiotherapy were twice as likely to undergo a sphincter-sparing operation (39 versus 19 percent [1]); however, the absolute rates of APR in the two cohorts were not significantly different. (See "Surgical treatment of rectal cancer", section on 'Low anterior resection' and "Neoadjuvant therapy for rectal adenocarcinoma", section on 'T1-2N0 tumors'.)

- Use of preoperative chemoradiotherapy for very distal early stage rectal cancer (eg, T2N0) in an attempt to convert the operation from APR to LAR, or to proctectomy and coloanal anastomosis is used at some institutions, but it is controversial and not yet a widely accepted standard of care, unless the patient declines APR. Patients with a complete clinical response might also be considered appropriate candidates for a "watch and wait" protocol rather than immediate surgery. (See "Overview of the management of rectal adenocarcinoma", section on 'Clinical T2N0 and cT1N0 not amenable to local excision' and "Neoadjuvant therapy for rectal adenocarcinoma", section on 'Nonoperative management (watch and wait)'.)

HISTORY, PHYSICAL EXAMINATION, AND ENDOSCOPY

Determining the best operative approach and the selection of appropriate patients for initial radiation therapy (RT) or chemoradiotherapy rather than surgery are heavily dependent on

accurate preoperative assessment. Digital rectal examination (DRE), rigid sigmoidoscopy, and preoperative imaging studies assist in determining the need for radical resection versus local excision, and whether the patient is a candidate for preoperative therapy.

The initial history should include information on the status of rectal and urinary function, as well as the status of sexual function in males [2].

When present, specific symptoms may assist in localizing the tumor and predicting its local extent. As examples:

- Tenesmus, the constant sensation of needing to move the bowels, usually indicates a large and possibly fixed tumor.
- Pain with defecation suggests involvement of the lower third of the rectum; most cancers located above the sphincters are painless. Very painful cancers growing directly into the anal sphincter that affect the very sensitive anal mucosa are usually not amenable to sphincter-sparing surgery. (See "Clinical presentation, diagnosis, and staging of colorectal cancer", section on 'Clinical presentation'.)

DRE is mandatory in all patients. Fixation of the lesion to the anal sphincter, its relationship to the anorectal ring (the collection of muscles that makes up the sphincters (figure 1)), fixation to both the rectal wall and pelvic wall muscles (levators), and the status of the rectovaginal septum can be assessed.

Rigid proctoscopy is more accurate than flexible sigmoidoscopy to determine the distance between the distal tumor margin, the top of the anorectal ring, and the dentate line, as well as the orientation within the rectum (eg, anterior, posterior, left, and right) [3].

Complete colonoscopy — Because of the incidence of synchronous second primary colorectal cancers (approximately 3 to 5 percent), all patients should undergo complete colonoscopy prior to surgical resection, whenever feasible. If malignant obstruction precludes a full colonoscopy (to the cecum) preoperatively, it should be performed within six months of definitive surgery, if possible. (See "Post-treatment surveillance after colorectal cancer treatment", section on 'Perioperative colonoscopy'.)

At the time of endoscopy, marking the distal end of the cancer with an India ink tattoo can allow identification of the original location of the tumor in a patient who has had a complete clinical response to neoadjuvant therapy, and it can also facilitate determination of the distal margin at the time of minimally invasive surgery.

IMAGING EVALUATION

An algorithm outlining our approach to staging evaluation for individuals with newly diagnosed rectal cancer is provided, and described in detail in the sections below (algorithm 1).

For most patients with suspected rectal cancer, thin-cut magnetic resonance imaging (MRI) with 3 mm multiplanar T2-weighted imaging and with pelvic phased-array coil is the preferred imaging modality for evaluating the extent of the primary tumor as it will be able to provide information on the depth of transmural tumor invasion, the presence of suspicious regional nodes, the status of the circumferential resection margin (CRM), and invasion of other organs and structures. The Society of Abdominal Radiology has defined a series of MRI scanner-specific protocols that are commonly used for this purpose.

Transrectal endoscopic ultrasound (TEUS) is an alternative, particularly for early stage (ie, T1-2N0) tumors, but for more advanced disease, it may be limited by the bulkiness of the tumor and the lack of depth to assess invasion of other organs. TEUS is particularly limited for posterior or posterolateral tumors in which the distance to the CRM cannot be estimated because the neighboring structures that allow assessment of the CRM are lacking.

This approach is in keeping with consensus-based guidelines from the National Comprehensive Cancer Network (NCCN) [4] and the European Society for Medical Oncology (ESMO) [5], which both state a preference for MRI over TEUS for pretreatment staging of rectal cancer, especially for intermediate and locoregionally advanced disease. Either TEUS or MRI is acceptable for a T1-2N0 tumor.

The information obtained with TEUS and MRI may be complementary, and in some cases, both procedures may be needed, particularly for mid-stage tumors where there is uncertainty about T2 versus T3N0 disease or T2N0 versus N1 status on either MRI or TEUS.

Regardless of the test that is chosen, the operating surgeon should ensure that the TEUS or MRI study is performed at an experienced center. A poor-quality MRI that is done in an inexperienced center without phased-array surface coils, without a 1.5- to 3T-field strength magnet, or without a rectal protocol can result in mismanagement because of errors in preoperative staging. The same is true for TEUS, which is highly dependent on operator experience.

Following the initial history and physical examination, digital rectal examination (DRE), rigid sigmoidoscopy, and colonoscopy, preoperative imaging studies assist in determining the optimal surgical approach and identifying patients who are candidates for preoperative

radiation therapy (RT) or chemoradiotherapy. (See "Neoadjuvant therapy for rectal adenocarcinoma", section on 'Indications for neoadjuvant treatment'.)

Rectal cancer imaging has become more critical for preoperative staging, since the order and types of treatment are often based upon pretreatment (clinical) stage as determined by imaging. Because the tumor (T) and nodal (N) categories used by the American Joint Committee on Cancer (AJCC) to assign clinical stage group were developed based upon postoperative pathology data rather than preoperative imaging findings (table 1), the currently available imaging modalities are imperfect in delineating these stages and must be selected and interpreted with care. (See "Clinical presentation, diagnosis, and staging of colorectal cancer", section on 'TNM staging system'.)

The following sections will focus on the available locoregional staging modalities. The pretreatment clinical staging evaluation to evaluate for distant disease (ie, chest computed tomography [CT], liver MRI, positron emission tomography [PET]), and the role of serum tumor markers are discussed elsewhere. (See "Clinical presentation, diagnosis, and staging of colorectal cancer", section on 'Clinical staging evaluation' and "Clinical presentation, diagnosis, and staging of colorectal cancer", section on 'Tumor markers'.)

There is debate over the utility of staging studies in early invasive cancers that are detected with a margin-negative polypectomy. Some adenomas with early invasive cancer (clinical T1 lesions) have a low (<2 percent) risk of lymphatic metastasis [6], and consensus-based guidelines from the NCCN [4] suggest observation alone for single-specimen, completely resected pedunculated polyps with invasive cancer that have favorable histologic features and clear margins (pT1) (table 2). Consensus-based guidelines from other expert groups recommend performing either high-resolution MRI or transrectal ultrasound (TRUS) to determine local T stage and assess for lymph node positivity for all patients with invasive rectal cancer, including those with pathologic T1 malignant polyps with favorable prognostic factors [5,7,8]. We agree with this approach. (See "Overview of colon polyps", section on 'High-grade dysplasia or cancer'.)

Principles of rectal cancer staging by imaging

T stage — The T stage of a rectal cancer is determined by the depth of invasion of the primary tumor, including involvement of adjacent anatomic structures (table 1). The layers of the rectum, beginning at the lumen, include the mucosa, muscularis mucosa, submucosa, muscularis propria, and subserosa/perirectal fat (figure 2). Portions of the mid and upper rectum are also covered by an external serosal layer of the peritoneum (figure 3).

Tis tumors are restricted to the mucosa, while T1 tumors have invaded the submucosa without involvement of the muscularis propria. T2 tumors (image 1) invade but do not extend beyond

the muscularis propria, while T3 tumors extend through the muscularis propria into the subserosa (image 2) or perirectal fat (image 3). T4a tumors invade a serosal equivalent layer (typically the peritoneum or mesorectal fascia), and T4b tumors invade another organ (eg, the pelvic floor muscles (image 4), prostate, or vagina).

cT1-2 tumors — Patients with a T1-2 invasive rectal cancer arising in a polyp should all undergo local staging (either MRI or TRUS) to determine primary tumor stage and assess for lymph node positivity. Given the limited accuracy of MRI in this setting [9,10], some clinicians favor TRUS.

T2 versus T3 disease — The distinction between a T2 tumor, which involves the muscularis propria, and a T3 tumor, which invades beyond the muscularis propria, is among the most important to be made in pretreatment staging because T2 tumors are typically managed initially by surgery, as long as they are clinically node negative, while T3 tumor stage may be an indication for preoperative RT or chemoradiotherapy, depending on tumor location and the degree of local invasion beyond the muscularis propria. (See "Neoadjuvant therapy for rectal adenocarcinoma", section on 'Indications for neoadjuvant treatment'.)

This distinction can be very difficult. The presence of gross tumor in the perirectal fat immediately marks that tumor as T3, but the distinction between an advanced T2 tumor and a very early T3 tumor can be very small, sometimes as small as a single cell width, and may be well beyond the resolution of any current imaging modality. However, an important point is that a patient who is thought to have a T2N0 cancer on preoperative imaging who ends up with a pathologic early T3N0 tumor with <2 mm of extramural invasion, good margins, and no poor prognostic histologic features can often be treated with observation rather than postoperative chemoradiotherapy, particularly if in the upper rectum. (See 'T3 disease and the depth of extramural invasion' below and "Adjuvant therapy for resected rectal adenocarcinoma in patients not receiving neoadjuvant therapy", section on 'T3N0 disease'.)

Locally advanced rectal cancers can invade surrounding organs. The most common sites of invasion include the prostate, urethra, urinary sphincter complex, seminal vesicles, vagina, and osseous pelvis. These sites should be specifically assessed in the imaging evaluation of T stage.

MRI and TEUS offer the greatest value for the imaging evaluation of T stage in rectal cancer. The capabilities of each of these imaging modalities are further detailed in the sections that follow. (See 'Magnetic resonance imaging' below and 'Transrectal endoscopic ultrasound' below.)

T3 disease and the depth of extramural invasion — Some have attempted to subdivide T3 disease according to the distance of tumor spread from the muscularis propria (ie, the depth of extramural invasion). While multiple thresholds have been proposed, one popular system

uses four subdivisions of the T3 stage, as determined by thin-section MRI, as follows: T3a, <1 mm; T3b, 1 to 5 mm; T3c, 6 to 15 mm; and T3d, >15 mm [11,12]. In a number of studies, T3 tumors with >5 mm of invasion beyond the muscularis propria (ie, T3c disease) had an inferior cancer-specific survival rate (approximately 54 percent, compared with 85 percent when the depth was 5 mm or less in one study) [13-16]. In addition, with increasing spread of tumor into the perirectal fat, there is increasing likelihood of nodal involvement and distant metastases at diagnosis [17,18]. These findings have led some to suggest that it is not necessarily the distinction between T2 and T3 tumors that will potentially govern treatment decisions but the identification of high-risk T3 tumors with a >5 mm depth of extramural tumor invasion [19].

However, this is a controversial area at present, and there is not uniform agreement on whether decision making for neoadjuvant therapy should incorporate depth of extramural invasion. Updated guidelines for treatment of rectal cancer from the ESMO incorporate depth of extramural invasion beyond the muscularis propria as a factor in treatment allocation using the T3 subdivision system [5]. On the other hand, the AJCC has declined to adopt such a system, even in its most recent (2017, eighth edition) modification [20]. Furthermore, consensus-based guidelines from the NCCN [4] also do not stratify decision making for T3N0 disease according to depth of extramural invasion. At present, use of the terminology for subdividing T3 disease according to depth of extravascular invasion (T3a to T3d) is nonstandard in the United States. Thus, this issue remains unsettled. This subject is discussed in detail elsewhere. (See "Neoadjuvant therapy for rectal adenocarcinoma", section on 'Contribution of depth of extramural penetration'.)

T3 versus T4a disease — The distinction between a clinical T3 and T4a tumor in the rectum requires careful assessment of the location of the peritoneal surfaces of the rectum relative to the site of tumor involvement. For rectal cancers below the level of the peritoneal reflection (typically at the level of the seminal vesicles or vaginal fornix), tumor within the mesorectal fat is evidence of T3 disease, and the tumor must extend to the mesorectal fascia to be considered a T4 lesion (figure 2). (See 'Surgical anatomy' above.)

By contrast, the anterior surface of the rectum is covered by serosa (peritoneum) at and above the peritoneal reflection. This coverage extends laterally around the rectum as we move superiorly toward the sigmoid colon (figure 3). This layer is generally not visible on imaging, so the location must be estimated based on local anatomy. In men, this reflection is typically located at the level of the seminal vesicles. In women, this is located near the posterior margin of the vagina. For tumors that extend above the peritoneal reflection, the presence of gross tumor in the pericolonic fat represents T4a disease if present in a serosally covered surface, and T3 disease if present in the uncovered surface.

Upper rectal cancers — For tumors that are located above the peritoneal reflection, it may be difficult to determine the true origin, and the term "rectosigmoid" cancer may be used. There may also be disagreement between the surgical location of the tumor, which generally relies on the linear distance from the anal verge as measured on rigid sigmoidoscopy or under tension at surgery, and the radiologic location (relative to the sacral promontory or peritoneal reflection), as assessed in nondistended, potentially folded bowel [21].

These issues may result in some confusion as to whether or not these tumors should be treated as colon or rectal cancers. The main distinction is the use of preoperative RT, which may be appropriate for transmural or node-positive rectal cancers but not primary colon cancers.

However, this distinction may not be clinically significant. The true rectum is a retroperitoneal structure that is located below the peritoneal reflection; the limitations of the bony pelvis make it difficult for the surgeon to achieve a wide soft tissue margin, and the higher rate of local recurrence that results can be mitigated through the use of RT, administered preoperatively or postoperatively. On the other hand, tumors in the upper rectum have a lower rate of local recurrence (<10 percent) after total mesorectal excision compared with mid or distal tumors, and the benefit of RT appears to be much less [22-25]. At many institutions, adjuvant RT is not offered following surgery for such tumors unless there is T4 disease or multiple positive lymph nodes. (See "Adjuvant therapy for resected rectal adenocarcinoma in patients not receiving neoadjuvant therapy", section on 'T3N0 disease'.)

Low rectal cancers — Low rectal cancers can invade the sphincter complex. Because the muscularis propria of the rectum transitions into the internal anal sphincter (figure 1), there is no anatomic boundary between this layer of the rectum and the anus. The distance of the tumor from the upper margin of the sphincter complex is used as a reasonable estimate for the likelihood of internal sphincter involvement. Tumor that extends into the low mesorectal fat may also directly invade the external sphincter muscle and pelvic floor musculature; this should be specifically reported as it may alter the surgical management of these low tumors. (See "Radical resection of rectal cancer", section on 'Intersphincteric resection for low rectal cancer'.)

Rectal cancers arising in adenomas — Rectal cancers that arise in adenomas present a special challenge for staging. Noninvasive imaging cannot reliably differentiate most invasive cancers from the adenomas in which they arise, so the extent of the adenoma-like mass may overestimate the actual area of invasive disease. Rectal MRI has been shown to commonly overstage cancers arising in rectal adenomas, with MRI T3 findings most commonly representing pathologic T2 or less disease [26,27]. In particular, the base of the adenoma's pedicle often shows irregularity of the muscularis propria layer and stranding in the mesorectal

fat of the pedicle, which may be commonly mistaken for invasive disease. TEUS may add value in these cases, and discussion in a multidisciplinary tumor board is recommended.

N stage — The N stage of rectal cancer is determined by the number of regional lymph nodes that are involved by cancer and by the presence of isolated, non-nodal, perirectal tumor deposits (table 1). The most recent (eighth edition) AJCC tumor, node, metastasis (TNM) staging classification defines N1a as involvement of one lymph node, N1b as involvement of two to three lymph nodes, and N1c as the presence of tumor deposits in the subserosa, mesentery, or mesorectal tissues without regional nodal involvement. N2a is defined as involvement of four to six lymph nodes, and N2b is defined as involvement of seven or more lymph nodes.

The regional lymph nodal stations for rectal cancer include those in the mesorectal and internal iliac drainage pathways (figure 4) [28]. According to the AJCC, the regional lymph nodes for rectal cancer include the mesorectal, superior rectal, inferior mesenteric, internal iliac (which includes the obturator nodes (figure 5)), and inferior rectal (table 3). The internal iliac lymph nodes include the lateral sacral and presacral stations. The external iliac nodes are extraregional, and if involved, they are considered to represent stage IV disease (table 1). (See "Clinical presentation, diagnosis, and staging of colorectal cancer", section on 'TNM staging system'.)

The primary lymphatic drainage of the rectum extends from the mesorectal fat superiorly along the mesorectal vessels toward the origin of the inferior mesenteric artery. This is the primary path of lymphatic metastasis in the vast majority of rectal cancers [29]. Rectal cancers can spread laterally to the internal iliac distribution via blood vessels or lymphatics that traverse the mesorectal fascia (figure 4). The cancer cells need a conduit to pass through the mesorectal fascia, unless there is direct invasion. In one series of 448 patients, 322 of whom underwent lateral lymph node dissection, 13.8 percent had lateral (internal iliac) lymph node involvement [30].

While the internal iliac nodes are a less common site of lymph node involvement from rectal cancer than is mesorectal lymphadenopathy, these are the only regional lymph nodes for rectal cancer that are not routinely excised during standard mesorectal excision. One study showed that resection of lateral lymph nodes in the internal iliac compartment measuring at least 7 mm in short axis on the initial MRI resulted in a lower rate of lateral lymph node recurrence (8.7 versus 52.3 percent, hazard ratio 6.2, 95% CI 1.4-28.5) as compared with total mesorectal excision without a lateral lymph node dissection [31]. It is, therefore, crucial that abnormal nodes in this location be specifically recognized preoperatively so that an extended (lateral)

lymphadenectomy can be considered. (See "Radical resection of rectal cancer", section on 'Lateral pelvic lymph node dissection'.)

Abnormal lymph nodes in the inguinal, external iliac, common iliac, and periaortic/paracaval nodal stations are considered extraregional and are scored as distant metastases in the AJCC TNM staging classification for rectal cancer. The distinction between regional and extraregional location can sometimes be difficult (eg, mesorectal versus iliac). Involvement of the inguinal lymph nodes should be carefully assessed whenever a low rectal cancer involves the anal sphincter since the lymphatic drainage for the sphincter flows through the inguinal stations (figure 4). (See "Radical resection of rectal cancer", section on 'Venous and lymphatic drainage'.)

Radiographic characteristics of suspicious nodes — The distinction between benign reactive nodes and nodes containing tumor is a diagnostic challenge [32,33]. In general, MRI is the modality that is most helpful for assessment of perirectal nodal involvement as it can identify involved nodes on the basis of characteristics other than size (image 5) [32,34-39]. However, especially in the setting of early rectal cancer (cT1-2), the sensitivity of MRI in detecting nodal involvement is low (21 percent in one cohort study [10]). (See 'Magnetic resonance imaging' below.)

Most centers rely on a combination of size and morphology to determine whether a node is likely to be malignant or benign. There is considerable overlap in size between normal reactive nodes and those containing tumor, and this is especially problematic with small nodes. Between 15 and 42 percent of rectal cancers have small (<5 mm) mesorectal lymph nodes containing tumor, resulting in poor diagnostic accuracy for all size-based criteria [39]. One decision analysis that weighted different size thresholds against the harms of treatment misallocation found that for perirectal lymph nodes, a cutoff of 8 mm or larger in the short axis offered the best tradeoff of benefits and harms among the possible size thresholds to call a node malignant based upon its size on pretreatment imaging [40].

The ability to detect a mixed intranodal signal and/or irregularity of the border may improve the sensitivity of MRI for detecting lymph node involvement [35,41]. Diffusion-weighted MRI sequences (image 5) may also improve the specificity and accuracy of preoperative nodal staging [42]. In 2018, the Society of Abdominal Radiology recommended the adoption of node borders, signal heterogeneity, and shape for staging of lymph nodes in rectal cancer [43]. Under the new staging recommendations, lymph nodes are to be assessed based on short axis dimension and morphologic criteria, with positive nodes counted as follows:

- Any lymph node with short axis ≥9 mm

- Lymph nodes 5 to 8 mm in short axis with at least two morphologic criteria
- Lymph nodes <5 mm and all three morphologic criteria

Suspicious morphologic criteria include round shape, irregular borders, and heterogeneous signal intensity. An example staging template is available based on these consensus guidelines. (See 'Magnetic resonance imaging' below.)

The ability to predict lymph node metastasis is particularly important for lymph nodes in the lateral compartment, which are not removed with routine total mesorectal excision. A persistently malignant-appearing lymph node in the lateral compartment despite neoadjuvant therapy may be an indication for extended lymphadenectomy, but the practice is not standardized and controversial. (See "Radical resection of rectal cancer", section on 'Lateral pelvic lymph node dissection'.)

Circumferential resection margin — The standard surgical technique for resection of a rectal cancer is total mesorectal excision, which entails removal of the entire mesorectum bounded by the mesorectal fascia. The outer boundary of this excision is known as the CRM (also called the lateral or radial margin). (See "Radical resection of rectal cancer", section on 'Radial margins'.)

Patients who have tumor involvement of the CRM at the time of surgery have significantly higher rates of local recurrence, although most of the data were derived in the era before neoadjuvant therapy [44]. The MERCURY trial showed that extension of tumor to within 1 mm of the CRM on imaging was 92 percent accurate in predicting margin involvement at the time of surgery, and that patients with CRM involvement had worse disease-free and overall survival [12,45,46], a finding that has been confirmed by others [17,44,47,48]. As a result, tumors in close proximity (1 mm) to the CRM on imaging are referred to as having a "threatened" CRM. Because of the higher risk for locoregional recurrence, patients with an involved or threatened CRM are appropriate candidates for neoadjuvant chemoradiotherapy. (See "Neoadjuvant therapy for rectal adenocarcinoma", section on 'Mesorectal fascia involvement'.)

As noted above, a number of studies have shown that T3 tumors with >5 mm of invasion beyond the muscularis propria have inferior outcomes compared with those with lesser degrees of extramural invasion (image 3). Thus, there are two major prognostic metrics related to radial tumor growth that can be determined by pretreatment local imaging: distance of growth beyond the muscularis propria and distance to the CRM. Although the T3 subdivision terminology is not used widely in the United States, we routinely report both distances, at least on rectal MRI studies. (See 'T3 disease and the depth of extramural invasion' above.)

Individual staging modalities

Magnetic resonance imaging — A typical rectal cancer staging pelvic MRI study comprises multiplanar, thin-section (3 mm), T2-weighted images [49]. The use of intravenous contrast is controversial; while the addition of contrast did not improve tumor or nodal staging with MRI in three separate studies [50-52], other studies have shown that assessment of abnormal contrast enhancement patterns in lymph nodes can add diagnostic value [41].

Diffusion-weighted images and pre- and postcontrast T1-weighted images are also frequently acquired. While endorectal coil placement was previously required, modern phased-array external coils can now provide diagnostic image quality for most patients without the need for internal coil placement [53-55]. Imaging at a 3 Tesla field strength is generally preferred due to the improved tradeoff between spatial resolution, scan duration, and tissue contrast to noise ratio at higher field strength, although the impact on diagnostic performance is modest [32,55,56]. (See "Principles of magnetic resonance imaging", section on 'MRI technology and pulse sequences'.)

A strength of MRI includes superior soft tissue contrast compared with CT and ultrasound, which can be used to differentiate malignant tissue from the muscularis propria of the rectum and to define tumor infiltration of the mesorectal fascia. The images provide examples of T2-weighted MRI images for a T2 rectal tumor (image 1), an "early" T3 rectal tumor (image 2), a late T3 rectal tumor with more than 5 mm of invasion beyond the muscularis propria (image 3), a T4b rectal tumor invading the pelvic floor musculature and perineal fat (image 4), and a T4b tumor with invasion of the anterior CRM and formation of a rectovaginal fistula (image 6).

MRI is capable of assessing all of the nodal stations of the pelvis and lower abdomen with a wider field of view than TEUS. In addition to size, MRI can demonstrate lymph node features, such as internal signal inhomogeneity, that can be predictive of tumor involvement [35]. Representative images of pathologic mesorectal (image 5) and internal iliac lymph nodes (image 7) are provided.

MRI also offers the ability to assess soft tissue features that are generally not accessible via other modalities. For example, MRI can demonstrate altered venous enhancement, which is characteristic of extramural vascular invasion [57,58]. Extramural vascular invasion is a negative prognostic factor. In one meta-analysis, MRI-detected extramural vascular invasion was associated with more frequent metastases both at diagnosis and during post-treatment follow-up [59]. Beyond its prognostic relevance, the finding of extramural vascular invasion does not alter the T stage, nor is it used to select patients for neoadjuvant RT or chemoradiotherapy. (See "Pathology and prognostic determinants of colorectal cancer", section on 'Lymphovascular invasion'.)

Another advantage of MRI over TEUS is that it allows the study of stenotic tumors. The disadvantages of MRI include a spatial resolution that is limited to approximately 1 mm with current techniques, and cost.

The accuracy of preoperative surface phased-array coil MRI in predicting rectal cancer T stage and nodal status can be illustrated by the results of a compilation of data from seven (2009 or later) systematic reviews by the Agency for Healthcare Research and Quality (AHRQ) [60].

- For T stage (T3/T4 versus T1/T2 (table 1)), the sensitivity was 87 percent (95% CI 81-92 percent), and the specificity was 75 percent (95% CI 65-80 percent).
- For lymph node involvement (any involved versus all clear), the sensitivity was 77 percent (95% CI 69-84 percent), and the specificity was 71 percent (95% CI 59-81 percent).
- For status of the CRM (involved versus clear), the sensitivity was 77 percent (95% CI 57-90 percent), and the specificity was 94 percent (95% CI 88-97 percent).

However, there was notable heterogeneity among the studies in the criteria used to define "positive" cases, particularly in assessment of nodal status. Lymph node size ≥5 mm, irregular borders, and mixed signal intensity were used in different combinations across the studies to define "involved" nodes. Status of the CRM was also variably defined, ranging from direct contiguity of tumor with the mesorectal fascia to tumor extension ≤5 mm from the mesorectal fascia.

Others note limited accuracy of MRI for both T and N staging among patients with cT1-2 tumors [9,10]. (See 'cT1-2 tumors' above.)

Diffusion-weighted MRI uses the diffusion of water molecules to generate contrast in MRI images. Combining diffusion-weighted MRI with T2-weighted imaging improves identification of metastatic lymph nodes in the pelvis (image 8). However, both sensitivity (67 to 78 percent) and specificity (60 to 67 percent) are low to moderate, and the diagnostic accuracy is only approximately 70 percent [61-63]. As a result, while diffusion-weighted MRI can facilitate lymph node detection, it is not sufficiently reliable for differentiating between benign and malignant lymph nodes [64,65]. Another potential use for diffusion-weighted MRI is in clarifying complete responses to neoadjuvant treatment, which may aid in the selection of patients for nonoperative management [66], but this is an ongoing area of investigation. (See "Neoadjuvant therapy for rectal adenocarcinoma", section on 'Tumor response assessment and follow-up'.)

Transrectal endoscopic ultrasound — Consistent with consensus-based guidelines from the NCCN [4] and ESMO, MRI is generally preferred over TEUS for pretreatment staging of rectal

cancer appropriate for resection unless MRI is contraindicated (eg, pacemaker). ESMO guidelines specifically state a preference for MRI over TEUS for intermediate and locoregionally advanced disease, but either TEUS or MRI is acceptable for a T1-2N0 tumor [5].

TEUS offers superior spatial resolution compared with standard CT and MRI techniques, which can provide more refined assessments of the depth of invasion for tumor staging. This superior resolution can be particularly useful in distinguishing T2 from early T3 tumors, which can be indistinguishable on MRI. (See 'Magnetic resonance imaging' above.)

Using TEUS, localized cancers involving only the mucosa and submucosa can usually be distinguished from T2 tumors, which penetrate the muscularis propria (image 9), or T3 tumors, which extend transmurally into the perirectal fat (image 10) [67]. The technique of TEUS is discussed in detail elsewhere. (See "Endoscopic ultrasound for evaluating patients with rectal cancer".)

The sensitivity and specificity of TEUS for rectal cancer staging were addressed in a compilation of data from seven (2009 or later) systematic reviews by the AHRQ [60]:

- For identifying T1 disease (table 1), the sensitivity was 88 percent (95% CI 85-90 percent), and the specificity was 98 percent (95% CI 98-99 percent). For identifying T2 disease, the sensitivity was 81 percent (95% CI 80-83 percent), and the specificity was 96 percent (95% CI 95-96 percent). For identifying T3 disease, the sensitivity was 96 percent (95% CI 95-97 percent), and the specificity was 91 percent (95% CI 90-92 percent). For identifying T4 disease, the sensitivity was 95 percent (95% CI 92-98 percent), and the specificity was 98 percent (95% CI 98-99 percent).

- For lymph node involvement (any involved versus all clear), the sensitivity was 73 percent (95% CI 71-76 percent), and the specificity was 76 percent (95% CI 74-78 percent).

- Data were not available on the sensitivity and specificity for evaluating the status of the CRM.

The major limitations of TEUS include its field of view and its operator dependence. Because ultrasound cannot fully assess the regional nodal stations of rectal cancer, other modalities must be relied upon for comprehensive nodal staging [68,69]. There is also considerable interobserver variability and a significant learning curve associated with performing TEUS [70].

Another challenge with TEUS is assessment of the CRM. For patients with anterior tumors, TEUS can assess the extent of tumor involvement of the mesorectal fascia, which predicts the distance of the tumor to the circumferential resection plane after surgery. However, for

posterior or posterolateral tumors, the distance to the CRM cannot be estimated using TEUS because the neighboring structures that allow assessment of the CRM are lacking. In such cases, the distance to the CRM is best estimated using MRI. (See "Endoscopic ultrasound for evaluating patients with rectal cancer", section on 'Circumferential resection margin'.)

On the other hand, the ability to perform fine-needle aspiration (FNA) biopsy of suspicious perirectal lymph nodes is a potential advantage of TEUS over MRI. However, TEUS-guided FNA does not appear to improve rectal cancer staging in most patients, and it is not routinely performed [71,72]. One reason why FNA may not add significantly to TEUS alone is that perirectal lymph nodes may be too small to be visualized by TEUS unless they contain metastatic disease. Thus, biopsy would not be expected to improve sensitivity when compared with visual criteria alone.

The comparative performance of TEUS, MRI, and CT in local staging of rectal cancers is discussed in more detail below. (See 'Comparative performance of MRI, TEUS, and CT' below.)

Computed tomography — CT scanning is a helpful modality for evaluating the presence of distant metastatic spread and for identifying tumor-related complications (eg, perforation, fistula formation), but it provides only limited local tumor and nodal staging information [2,4]. CT scans for rectal cancer staging are typically performed of the chest, abdomen, and pelvis using both oral and intravenous contrast (even if MRI of the pelvis is performed). (See "Clinical presentation, diagnosis, and staging of colorectal cancer", section on 'Computed tomography scan'.)

When examining locally advanced disease, CT determines local T stage with an accuracy of 79 to 94 percent; this falls to 52 to 74 percent when less advanced, smaller tumors are analyzed [37,73-75]. The sensitivity of CT for detecting perirectal nodal involvement depends on the size criteria used to define a node as potentially malignant, but it is generally inferior to that of TEUS and MRI. (See 'Comparative performance of MRI, TEUS, and CT' below.)

Comparative performance of MRI, TEUS, and CT — In general, transrectal endoscopic ultrasound (TEUS) and magnetic resonance imaging (MRI) are both useful for primary tumor staging. As noted above, MRI offers some advantages over TEUS: it permits a larger field of view and can visualize more proximal tumors, it tends to be less operator and technique dependent, it allows the study of stenotic tumors, it can characterize lymph nodes in a wider field of view, and as noted above, it can characterize perirectal lymph nodes on the basis of additional features beyond size. (See 'Magnetic resonance imaging' above and 'Transrectal endoscopic ultrasound' above.)

The diagnostic performance of these modalities has varied widely across studies and over time, likely due to a combination of differing populations, improving technology over time, variations in site-specific expertise, and different reference standards.

A year 2014 comparative effectiveness review by the AHRQ came to the following conclusions regarding initial staging with TEUS versus MRI versus computed tomography (CT), based upon an analysis of direct comparator studies [60]:

- The summary results are provided for preoperative tumor (table 4) and nodal staging (table 5).
- Overall:
  - TEUS is more accurate (ie, less likely to give an incorrect result; odds ratio 0.36, 95% CI 0.24-0.54), less likely to understage (odds ratio 0.63, 95% CI 0.44-0.89), and less likely to overstage rectal cancer than CT in the preoperative evaluation of T stage (13 studies, n = 595 patients, low strength of evidence).
  - There is no statistically significant difference between MRI and TEUS for preoperative rectal cancer tumor staging (six studies, n = 294 patients, low strength of evidence).
  - There is no statistically significant difference in accuracy across CT, MRI, or TEUS for preoperative nodal staging (18 studies, n = 845 patients, low strength of evidence).
  - While there is no statistically significant difference in accuracy between CT and MRI for rectal nodal staging, MRI is less likely to overstage (four studies, n = 123 patients, low strength of evidence).
- There was no comparison of MRI versus TEUS for assessment of the CRM.

The information obtained with TEUS and MRI may be complementary [76], and in some cases, both procedures may be needed, particularly for mid-stage tumors where there is uncertainty about T2 versus T3N0 disease or T2N0 versus N1 status.

As noted above, consensus-based guidelines from the NCCN [4] state a preference for MRI over TEUS for pretreatment staging of rectal cancer appropriate for resection unless MRI is contraindicated (eg, pacemaker). ESMO guidelines suggest a preference for MRI over TEUS for intermediate and locoregionally advanced disease, but either TEUS or MRI is acceptable for a T1-2N0 tumor [5]. Links to these and other society guidelines can be found elsewhere. (See 'Society guideline links' below.)

Regardless of the test that is chosen, the operating surgeon should ensure that the TEUS or MRI study is performed at an experienced center. A poor-quality MRI that is done in an inexperienced center without surface phased-array coils, without a high field strength magnet, or without a rectal protocol can result in mismanagement because of errors in preoperative staging. The same is true for TEUS, which is highly dependent on operator experience.

FDG-PET — Positron emission tomography imaging using fluorodeoxyglucose (FDG-PET) has not been shown to add significant information to conventional imaging for initial locoregional staging of rectal cancer [77,78]. The utility of FDG-PET for preoperative staging for distant metastatic disease is discussed elsewhere. (See "Clinical presentation, diagnosis, and staging of colorectal cancer", section on 'Positron emission tomography scans'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Colorectal cancer".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Colon and rectal cancer (The Basics)")
- Beyond the Basics topics (see "Patient education: Colon and rectal cancer (Beyond the Basics)" and "Patient education: Colorectal cancer treatment; metastatic cancer (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Surgical resection is the cornerstone of curative therapy for patients with early stage, potentially resectable rectal cancer. Superficially invasive, small cancers may be effectively managed with limited surgery (such as local excision). However, most patients have more deeply invasive tumors that require low anterior resection or, in some cases, if located distally, abdominoperineal resection.

  The addition of adjuvant radiation therapy (RT) and chemotherapy can enhance both local control and cure rates in patients with either transmural invasion or positive perirectal lymph nodes. Such therapy is often administered preoperatively, given the more favorable long-term toxicity profile of this approach compared with postoperative treatment. Neoadjuvant RT or chemoradiotherapy is generally considered for T3/T4 and/or clinically node-positive T1/T2 tumors (table 1), distal rectal tumors for which preoperative chemoradiotherapy may enhance the ability to preserve the anal sphincter, and tumors that appear to invade or are in close proximity to the mesorectal fascia on preoperative imaging because of the decreased likelihood of achieving a tumor-free circumferential resection margin (CRM) with upfront surgery. (See 'Introduction' above.)

- Determining the best operative approach and the selection of appropriate patients for initial RT or chemoradiotherapy rather than surgery are heavily dependent on accurate preoperative locoregional staging. Digital rectal examination (DRE), rigid proctoscopy, and preoperative imaging studies assist in determining the need for radical resection versus local excision, and whether the patient is a candidate for preoperative therapy. (See 'History, physical examination, and endoscopy' above and 'Imaging evaluation' above.)

  On DRE, fixation of the lesion to the anal sphincter, its relationship to the anorectal ring (the collection of muscles that makes up the sphincters), and fixation to both the rectal wall and pelvic wall muscles (levators) can be assessed. Rigid proctoscopy rather than flexible sigmoidoscopy can more accurately determine the distance between the distal tumor margin, the top of the anorectal ring, and the dentate line, as well as the orientation within the rectum (eg, anterior, posterior, left, and right). (See 'Surgical anatomy' above.)

- All patients should undergo complete colonoscopy to the cecum to assess for a possible synchronous second primary colorectal cancer or other polyps. (See 'Complete colonoscopy' above.)

- An algorithm outlining our approach to imaging evaluation for individuals with newly diagnosed rectal cancer is provided, and described in detail in the sections below

(algorithm 1).

Contrast-enhanced computed tomography (CT) scanning of the chest and abdomen is the most useful test for staging distant metastatic spread and for identifying tumor-related complications (eg, perforation, fistula formation). For some patients, particularly those with metastatic disease, CT alone may provide sufficient information about local staging to permit the selection of initial treatment. (See 'Computed tomography' above.)

However, in most cases, pelvic magnetic resonance imaging (MRI) or transrectal endoscopic ultrasound (TEUS) provides greater accuracy than CT for assessing the depth of tumor invasion, the presence of regional nodal metastases, and the likelihood of a positive CRM at the time of surgery, all of which may influence the choice of initial surgery versus RT or chemoradiotherapy. Either high-resolution MRI or TEUS should be performed to determine local T stage and assess for lymph node positivity for all patients with invasive rectal cancer, including those with pathologic T1 malignant polyps with favorable prognostic factors.

Consistent with consensus-based guidelines from the National Comprehensive Cancer Network (NCCN) and the European Society for Medical Oncology (ESMO), MRI is generally preferred over TEUS for pretreatment staging of rectal cancer appropriate for resection unless MRI is contraindicated (eg, pacemaker). ESMO guidelines specifically state a preference for MRI over TEUS for intermediate and locoregionally advanced disease, but either TEUS or MRI is acceptable for a T1-2N0 tumor. (See 'Principles of rectal cancer staging by imaging' above.)

The information obtained with TEUS and MRI may be complementary, and in some cases, both procedures may be needed, particularly for mid-stage tumors where there is uncertainty about T2 versus T3N0 disease or T2N0 versus N1 status. (See 'Magnetic resonance imaging' above and 'Transrectal endoscopic ultrasound' above and 'Comparative performance of MRI, TEUS, and CT' above.)

Regardless of the test that is chosen, the operating surgeon should ensure that the MRI or TEUS study is performed at an experienced center. A poor-quality MRI that is done in an inexperienced center without surface coils, without a high field strength magnet, or without a rectal protocol can result in mismanagement because of errors in preoperative staging. The same is true for TEUS, which is highly dependent on operator experience.

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Topic 2522 Version 40.0

GRAPHICS

Colorectal cancer TNM staging AJCC UICC 8th edition

Primary tumor (T)	
T category	**T criteria**
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
* Direct invasion in T4 includes invasion of other organs or other segments of the colorectum as a result of direct extension through the serosa, as confirmed on microscopic examination (for example, invasion of the sigmoid colon by a carcinoma of the cecum) or, for cancers in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria (ie, respectively, a tumor on the posterior wall of the descending colon invading the left kidney or lateral abdominal wall; or a mid or distal rectal cancer with invasion of prostate, seminal vesicles, cervix, or vagina). ¶ Tumor that is adherent to other organs or structures, grossly, is classified cT4b. However, if no tumor is present in the adhesion, microscopically, the classification should be pT1-4a depending on the anatomical depth of wall invasion. The V and L classification should be used to identify the presence or absence of vascular or lymphatic invasion whereas the PN prognostic factor should be used for perineural invasion.	
Regional lymph nodes (N)	
N category	**N criteria**
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 ▪ Nonperitonealized pericolic, or perirectal/mesorectal tissues
N2	Four or more regional nodes are positive
N2a	Four to six regional lymph nodes are positive
N2b	Seven or more regional lymph nodes are positive

Distant metastasis (M)

M category	M criteria
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

Prognostic stage groups

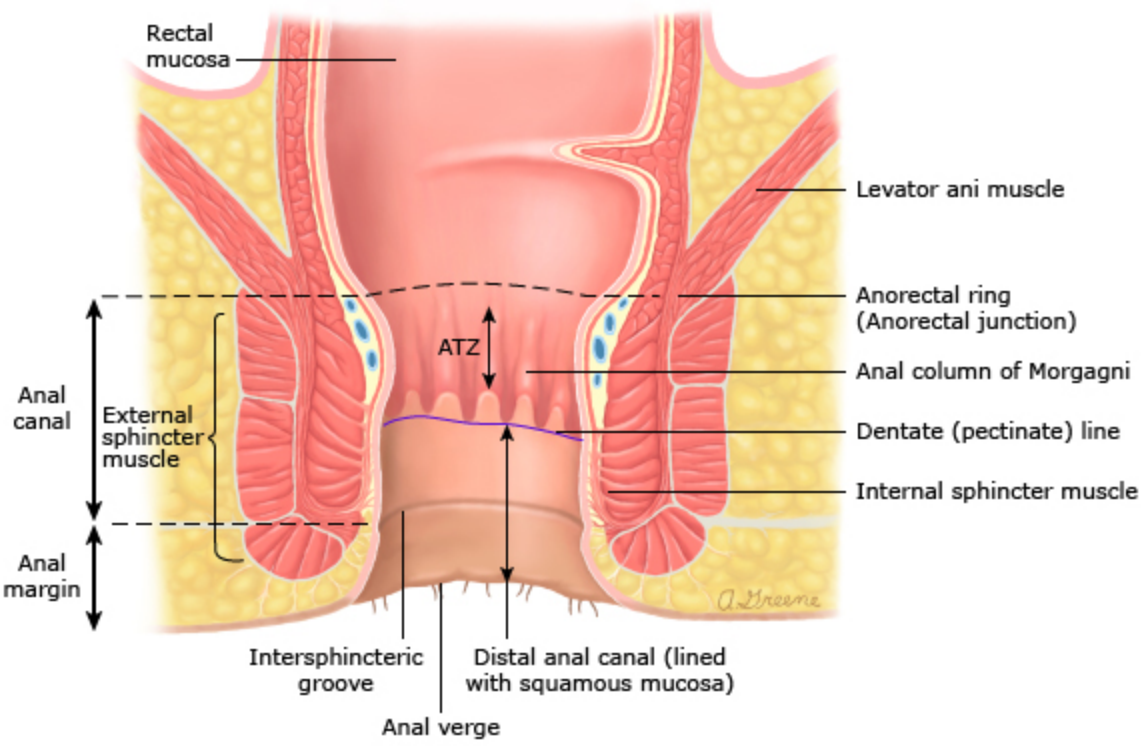
When T is…	And N is…	And M is…	Then the stage group is…
Tis	N0	M0	0
T1, T2	N0	M0	I
T3	N0	M0	IIA
T4a	N0	M0	IIB
T4b	N0	M0	IIC
T1-T2	N1/N1c	M0	IIIA
T1	N2a	M0	IIIA
T3-T4a	N1/N1c	M0	IIIB

T2-T3	N2a	M0	IIIB
T1-T2	N2b	M0	IIIB
T4a	N2a	M0	IIIC
T3-T4a	N2b	M0	IIIC
T4b	N1-N2	M0	IIIC
Any T	Any N	M1a	IVA
Any T	Any N	M1b	IVB
Any T	Any N	M1c	IVC

TNM: Tumor, Node, Metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

Graphic 111438 Version 10.0

Anatomy of the anus and rectum



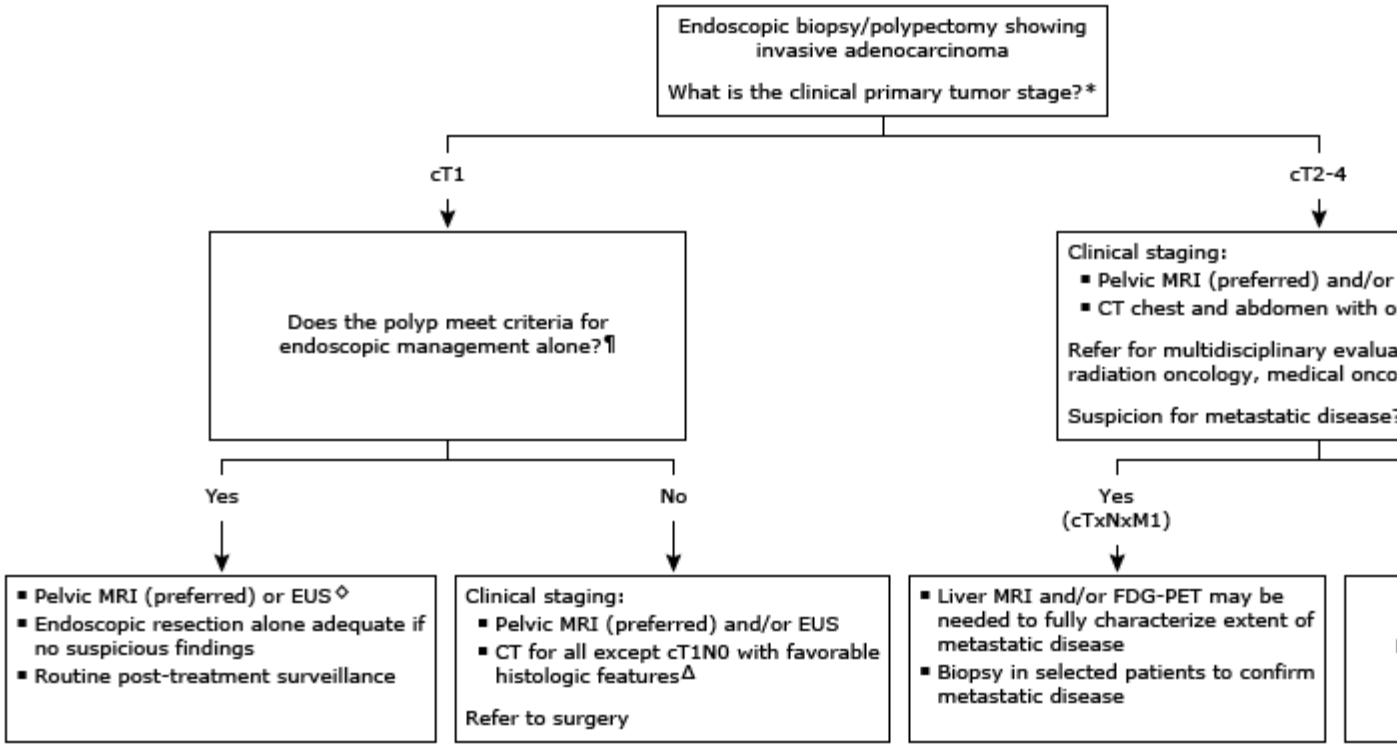
The anal canal is 2.5 to 4.0 cm long and begins superiorly where the rectal ampulla is narrowed by the anorectal ring. This palpable muscular ring is formed by fusion of the puborectalis muscle (part of the levator ani muscle complex) with the more inferior internal and external anal canal sphincters.

The external anal canal sphincter ends just distally to the internal anal canal sphincter; the intersphincteric groove is the palpable plane that can be palpated between the termination of the two sphincters. The presence of the intersphincteric groove coincides roughly with the anal verge, which marks the distal portion of the anal canal. The perianus or anal margin extends 5 cm laterally from the anal verge and is characterized by the presence of hair follicles and glands.

The interior of the anal canal can be divided into proximal and distal portions by an irregular line formed by the anal valves called the dentate (or pectinate) line (colored purple in the diagram). The portions of the anal canal proximal and distal to the dentate line have different origins of arterial supply, nerve innervation, and venous lymphatic drainage. The squamo-columnar junction (SCJ) lies within the proximal portion of the anal canal and marks the transition between rectal columnar epithelium to anal squamous epithelium. The exact position of the SCJ changes with time due to replacement of columnar epithelium with squamous epithelium in a process known as squamous metaplasia. The anal transformation zone (ATZ) is the zone where all aspects of squamous metaplasia are currently found and/or have occurred. The ATZ is marked by the SCJ proximally and extends distally to approximately the level of the dentate line.

Graphic 62539 Version 16.0

Staging workup of newly diagnosed rectal cancer



This is an overview of our approach to staging workup of newly diagnosed nonmetastatic rectal adenocarcir used in conjunction with other UpToDate content on rectal adenocarcinoma.

MRI: magnetic resonance imaging; EUS: endoscopic ultrasound; CT: computed tomography; FDG-PET: fluorc positron emission tomography.

* T1 tumors invade through the muscularis mucosa. Tumors that invade the muscularis propria or beyond a

¶ Endoscopic excision alone is NOT appropriate for malignant polyps with any of the following:

- For both pedunculated and nonpedunculated polyps:
  - Piecemeal resection
  - Poorly differentiated histology
  - Lymphovascular invasion
  - Tumor budding (foci of isolated cancer cells or a cluster of five or fewer cancer cells at the invasive
- For pedunculated polyps, a positive margin variably defined as:
  - Cancer present at the resection margin
  - Cancer within 1 mm of resection margin
  - Cancer within 2 mm of resection margin
- For nonpedunculated polyps:
  - Cancer at resection margin
  - Submucosal invasion depth ≥1 mm

Δ CT is appropriate for all except those with clinical T1N0 cancers with favorable histologic features.

- If pelvic MRI has been done, we perform CT of the chest and abdomen
- If pelvic MRI has not been done, we perform CT of the chest, abdomen, and pelvis

◇ Practice Parameters Committee of the American College of Gastroenterology (ACG) and the European Soc Oncology (ESMO), recommend performing either transrectal ultrasound or high-resolution MRI to determin stage and assess for lymph node positivity for all patients with an invasive rectal cancer, including those witl polyps with favorable prognostic factors.

Graphic 131308 Version 1.0

Guidelines for endoscopic management of a malignant polyp from the American College of Gastroenterology

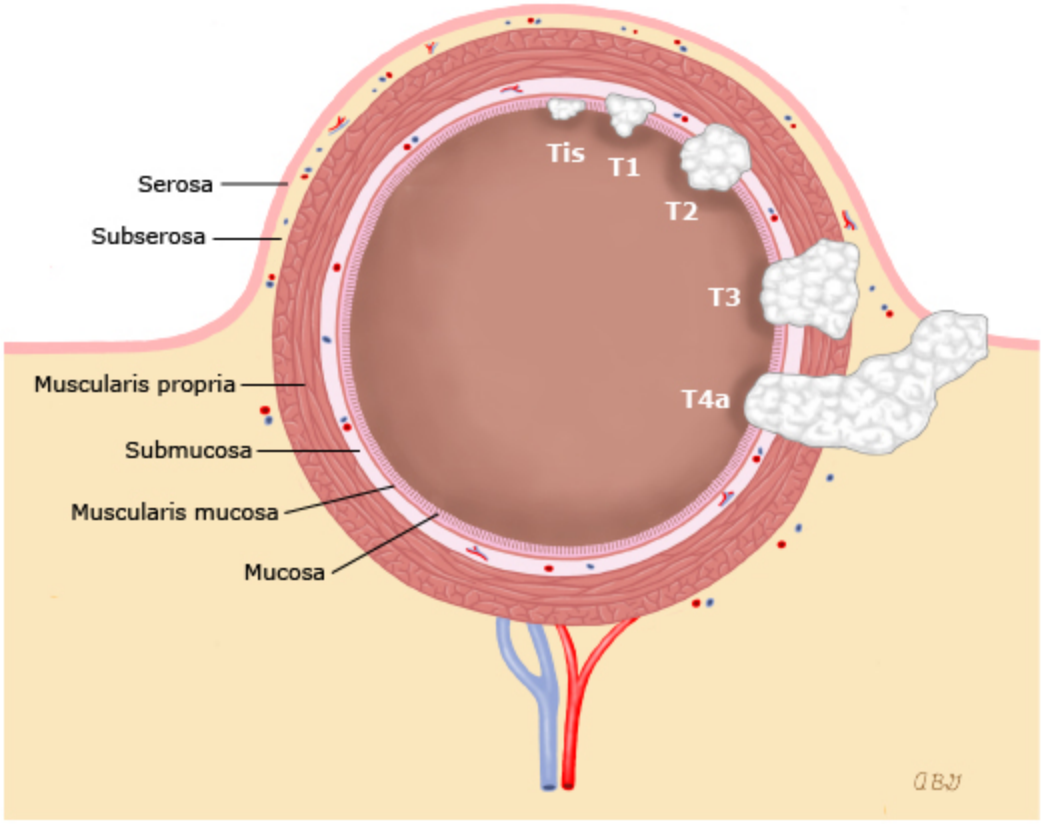
Polypectomy alone is adequate treatment for colorectal polyps with early invasive cancer if specific histologic criteria are met:
▪ The polyp is considered to be completely excised by the endoscopist and is submitted in toto for pathological examination.
▪ The polyp is fixed and sectioned so that it is possible to accurately determine the depth of invasion, grade of differentiation, and completeness of excision of the carcinoma.
▪ The cancer is not poorly differentiated.
▪ There is no vascular or lymphatic involvement.
▪ The margin of the excision is not involved. Invasion of the stalk of pedunculated polyp, by itself, is not an unfavorable prognostic finding, as long as the cancer does not extend to the margin of stalk resection.
▪ Not a sessile polyp.
▪ No extension beyond the submucosa.
▪ Local staging (MRI, ultrasound) reveals no suspicion for deeper invasion or positive lymph nodes.
▪ In addition, appropriate patients for endoscopic management of large (≥2 cm) pedunculated polyps include those in whom the concern for invasive cancer is low, and the size and location of the polyp are amenable to endoscopic resection with a relatively low risk of complications.

MRI: magnetic resonance imaging.

Bond, JH. Polyp guideline: Diagnosis, treatment and surveillance for patients with colorectal polyps. Practice Parameters Committee of the American College of Gastroenterology. Am J Gastroenterology 2000; 95:3053.

Graphic 107550 Version 1.0

Layers of the colon and rectum with associated T stages



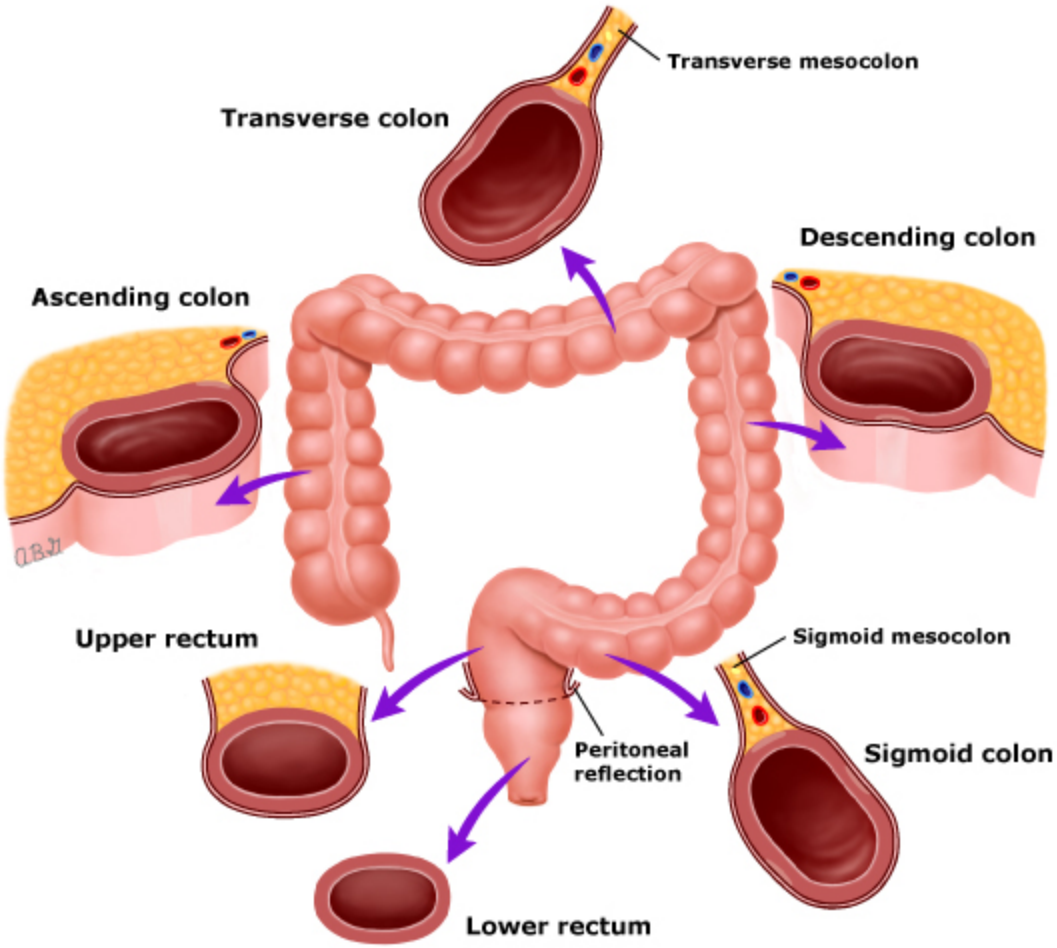
T: tumor.

Modified from:

1. *Matalon SA, Mamon HJ, Fuchs CS, et al. Anorectal cancer: Critical anatomic and staging distinctions that affect use of radiation therapy. Radiographics 2015; 35:2090.*
2. *American Joint Committee on Cancer (AJCC) Cancer Staging Manual, 8th Edition, Amin MB (Ed), Chicago: Springer Science+Business Media, LLC, 2017.*

Graphic 114851 Version 1.0

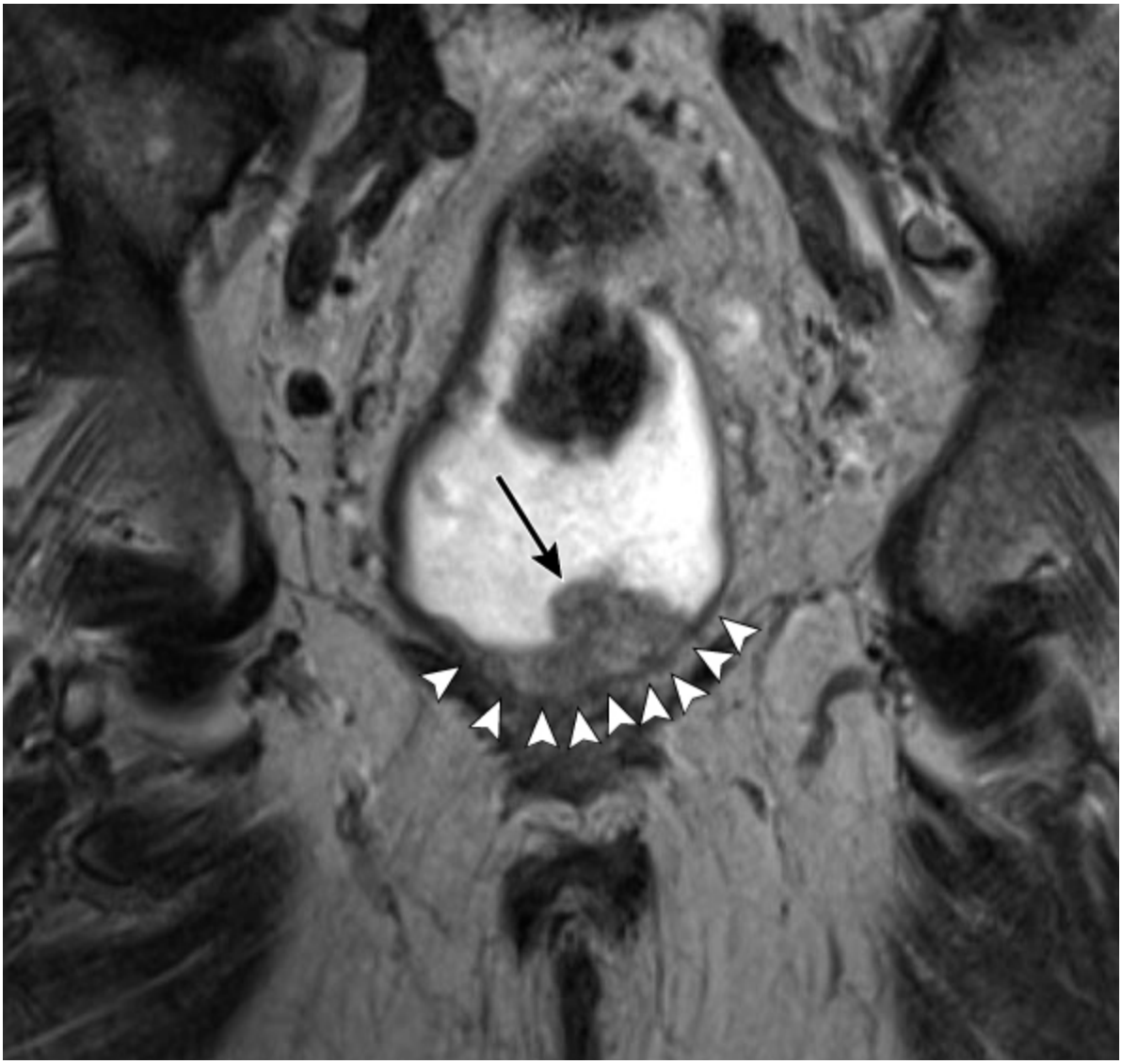
Idealized representation of the peritoneal and mesenteric relationships at various levels of the colon and rectum



Both the transverse and sigmoid colon are located intraperitoneally; at these levels, the visceral peritoneum forms a complete covering over the exterior of the bowel (the serosa), which is continuous with the mesentery (transverse and sigmoid mesocolon). In contrast, the ascending and descending colon lie within the lateral peritoneal cavity with their posterior and lateral surfaces in the retroperitoneum. At these levels, the visceral peritoneum is only present anteriorly and medially; there is no true mesentery, since the developing mesentery has fused to the posterior parietal peritoneum. The upper portion of the rectum lies above the peritoneal reflection. The anterior surface is covered by peritoneum (which forms the rectovesical pouch in men and the rectouterine pouch in women); there is no serosa over its posterior surface. The lower rectum lies beneath the peritoneum and has no serosal layer.

Graphic 81248 Version 3.0

MRI of a T2 rectal cancer

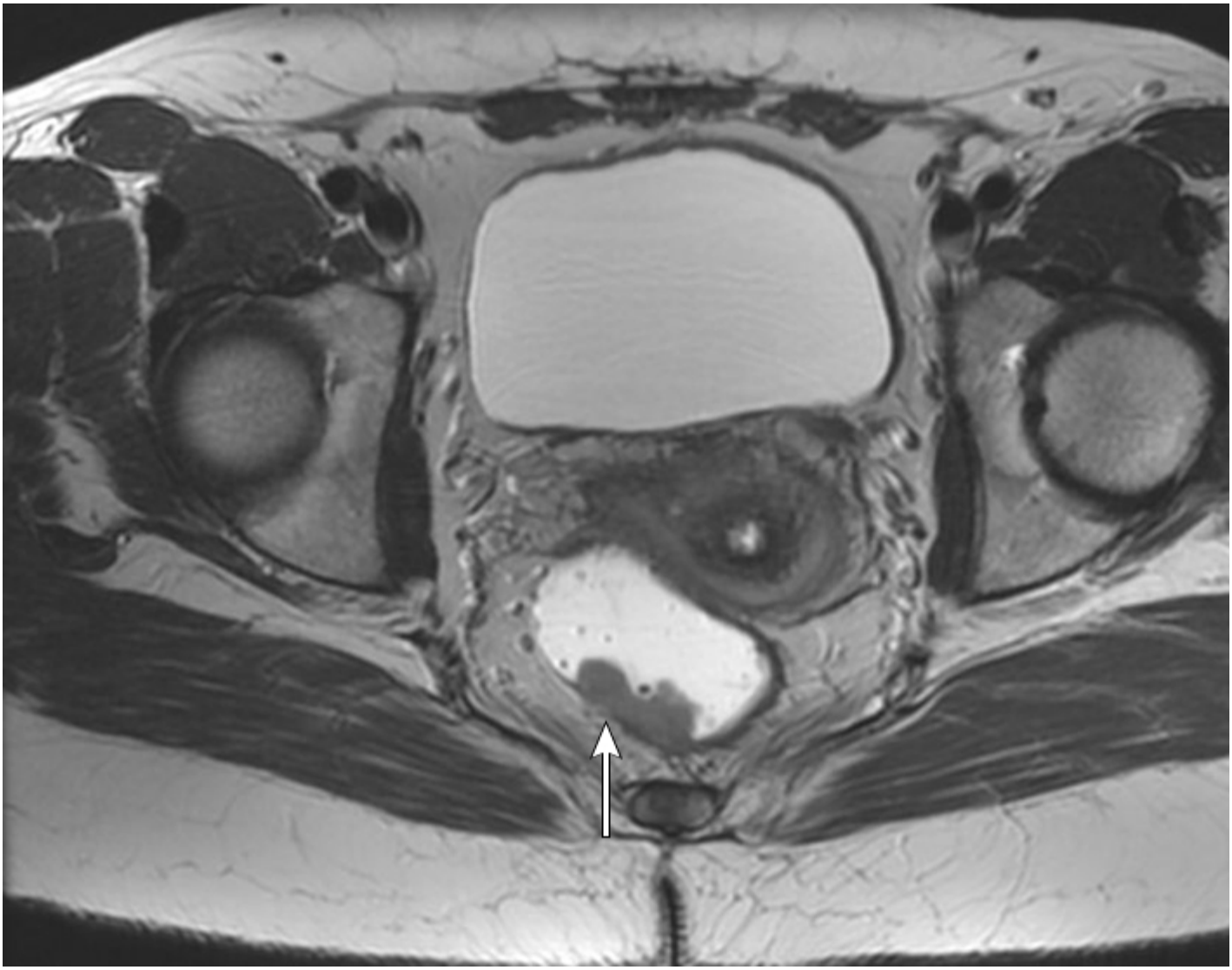


Coronal T2-weighted pelvic MRI image of a T2 cancer in the lower rectum (arrow). The thinned but intact muscularis propria is visible as a dark line (arrowheads). The patient underwent a successful margin-negative transmucosal excision.

MRI: magnetic resonance imaging.

Graphic 114585 Version 1.0

MRI of an "early" T3 rectal cancer

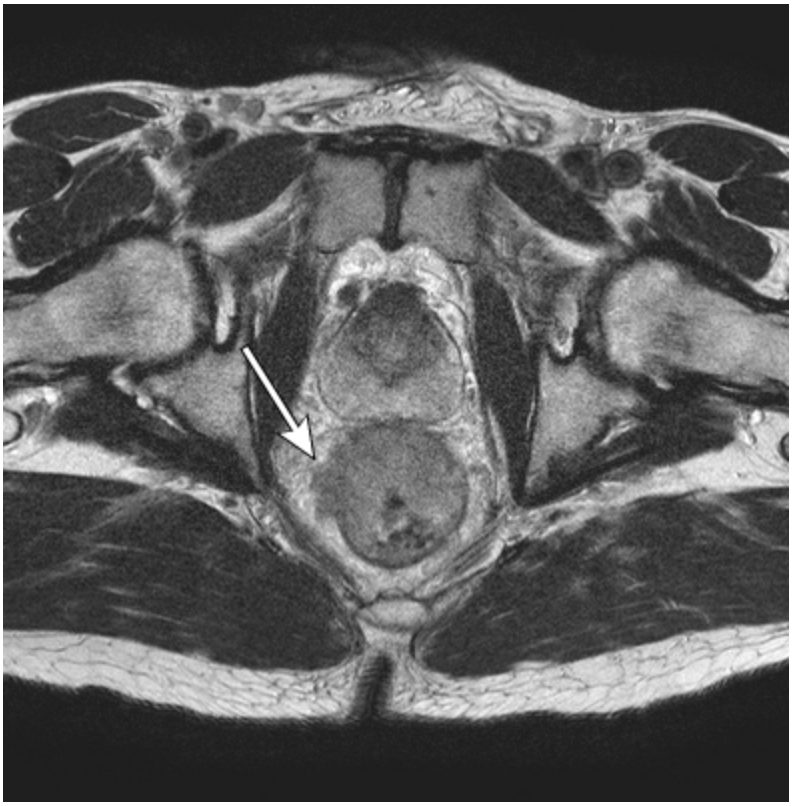


Axial T2-weighted pelvic MRI image of an early T3 rectal cancer that has barely breached the muscularis pro
The dark line of the muscularis propria is breached (arrow), but no gross tumor is visible in the mesorectal fa
This finding was confirmed using endorectal ultrasound.

MRI: magnetic resonance imaging.

Graphic 115371 Version 1.0

MRI of advanced T3 rectal cancer

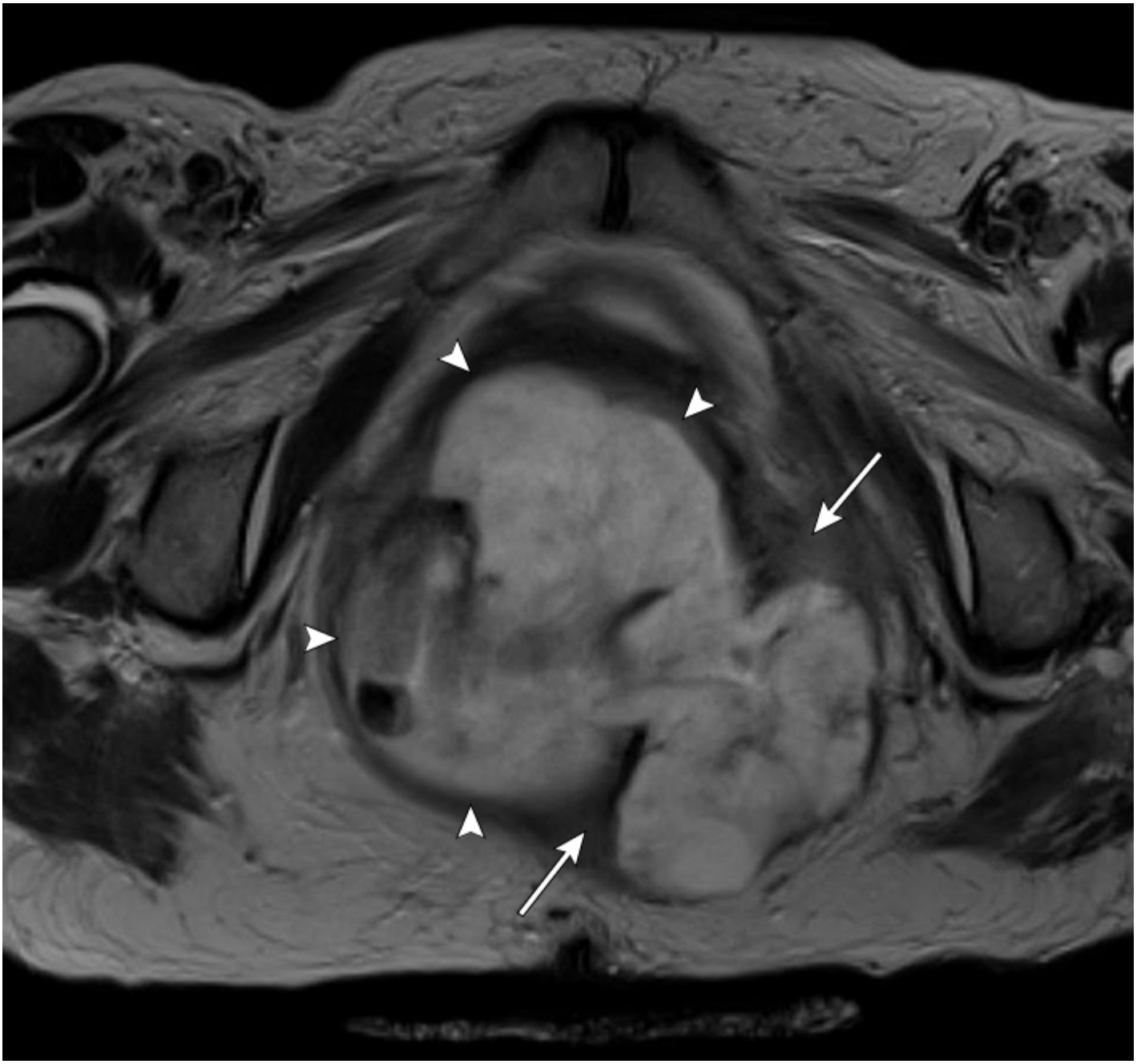


Axial T2-weighted pelvic MRI image of an advanced T3 rectal cancer. Gross tumor is visible beyond the muscularis propria in the mesorectal fat (arrow) with >5 mm of invasion beyond the muscularis propria.

MRI: magnetic resonance imaging.

Graphic 115373 Version 1.0

MRI of a T4b rectal cancer

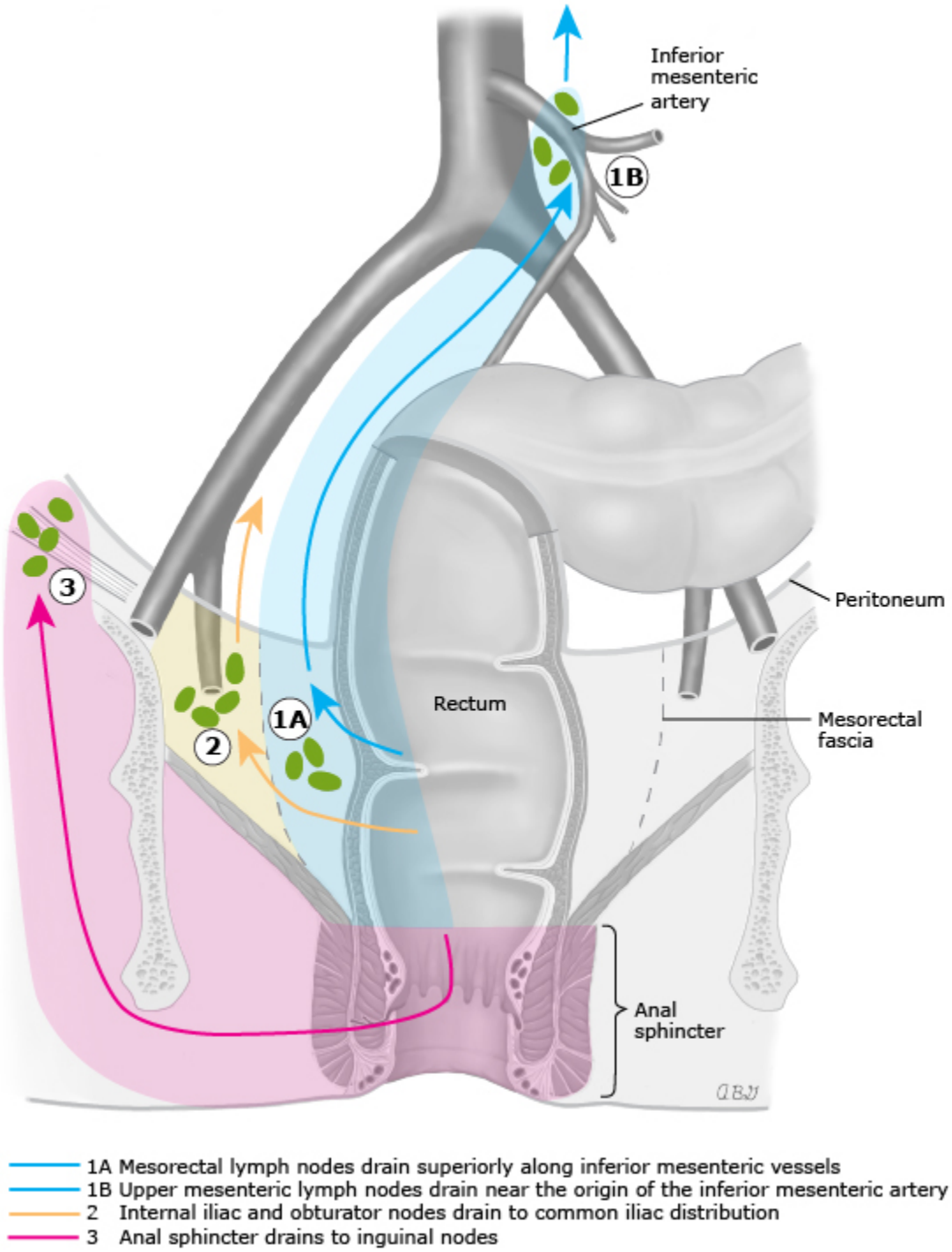


Axial T2-weighted MRI image of a T4b rectal cancer shows a large, polypoidal, T2 hyperintense mass that fill
low rectum (arrowheads). The mass breaches the bowel wall and the pelvic floor musculature (arrows) with g
extension into the perineal fat. The tumor had mucinous histology that was responsible for the T2 hyperinte
appearance.

MRI: magnetic resonance imaging.

Graphic 115374 Version 1.0

Patterns of spread of rectal cancer



Patterns of spread of rectal cancer; nodes in the distribution of 1A, 1B, and 2 represent regional nodes per the American Joint Committee on Cancer (AJCC) staging manual.

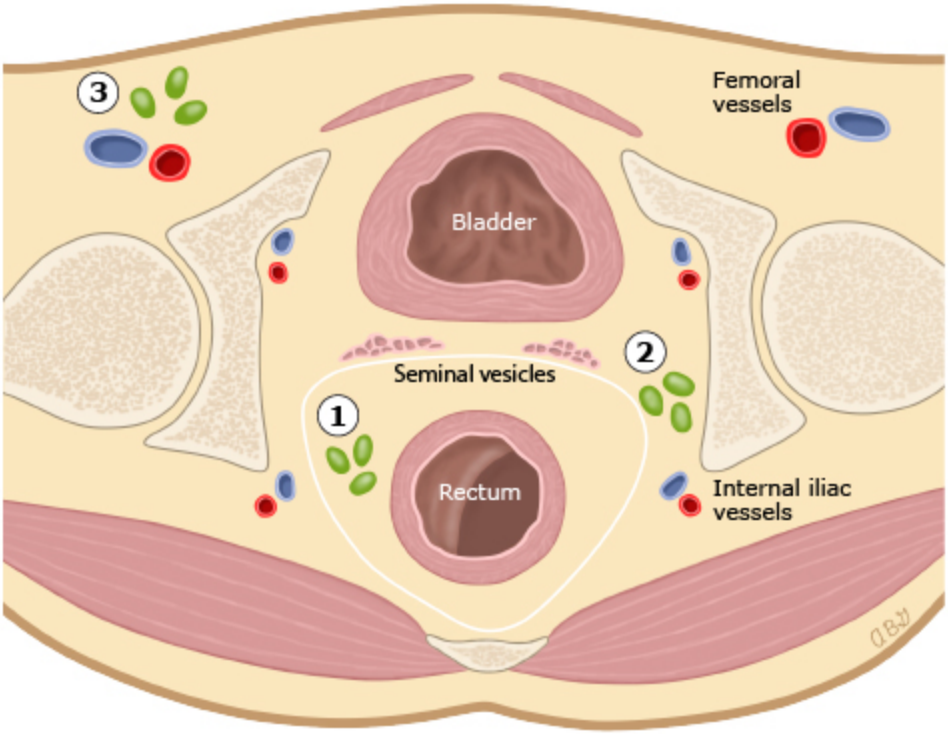
Modified from:

1. *Matalon SA, Mamon HJ, Fuchs CS, et al. Anorectal cancer: Critical anatomic and staging distinctions that affect use of radiation therapy. Radiographics 2015; 35:2090.*

2. *American Joint Committee on Cancer (AJCC) Cancer Staging Manual, 8th Edition, Amin MB (Ed), Chicago: Springer Science+Business Media, LLC, 2017.*

Graphic 114852 Version 1.0

Important nodal stations in rectal cancer



1 Mesorectal lymph nodes drain along the inferior mesenteric vessels to the mid abdominal retroperitoneum
2 Internal iliac and obturator nodes (internal iliac to common iliac drainage)
3 Femoral/inguinal (external iliac to common iliac drainage)

This axial schematic diagram of the mid rectum shows the three major lymphatic drainage regions that are relevant to rectal cancers.

Modified from:

1. *Matalon SA, Mamon HJ, Fuchs CS, et al. Anorectal cancer: Critical anatomic and staging distinctions that affect use of radiation therapy. Radiographics 2015; 35:2090.*
2. *American Joint Committee on Cancer (AJCC) Cancer Staging Manual, 8th Edition, Amin MB (Ed), Chicago: Springer Science+Business Media, LLC, 2017.*

Graphic 114850 Version 2.0

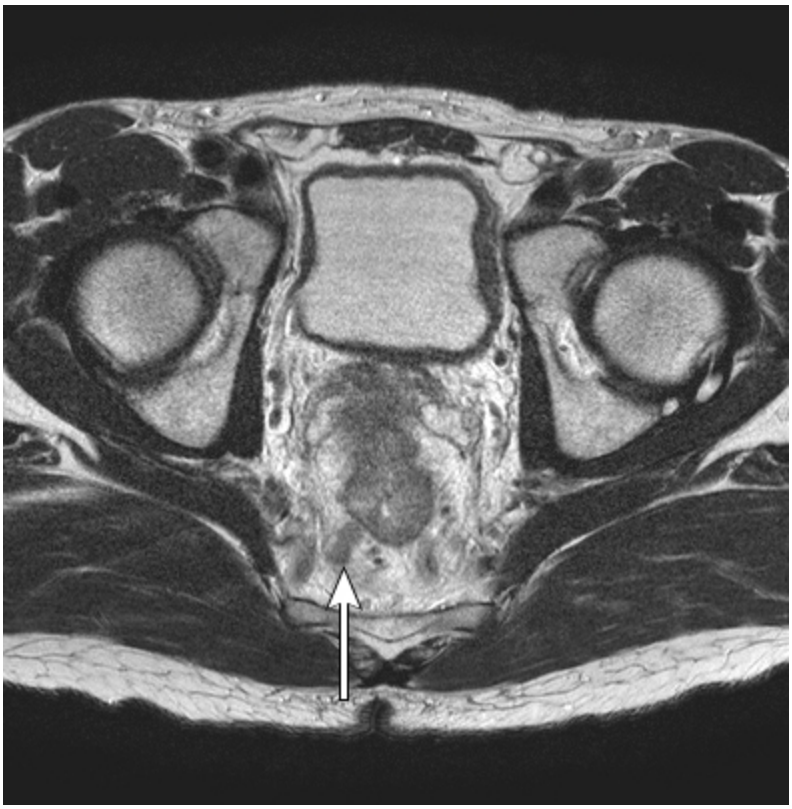
The regional lymph nodal stations for each segment of the colon and rectum

Segment	Regional lymph nodes
Cecum	Pericolic, ileocolic, right colic
Ascending colon	Pericolic, ileocolic, right colic, right branch of the middle colic
Hepatic flexure	Pericolic, ileocolic, right colic, middle colic
Transverse colon	Pericolic, middle colic
Splenic flexure	Pericolic, middle colic, left colic
Descending colon	Pericolic, left colic, sigmoid, inferior mesenteric
Sigmoid colon	Pericolic, sigmoid, superior rectal (hemorrhoidal), inferior mesenteric
Rectosigmoid	Pericolic, sigmoid, superior rectal (hemorrhoidal), inferior mesenteric
Rectum	Mesorectal, superior rectal (hemorrhoidal), inferior mesenteric, internal iliac, inferior rectal (hemorrhoidal)

Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer International Publishing.

Graphic 51172 Version 19.0

MRI of a pathologic mesorectal lymph node in a patient with rectal cancer

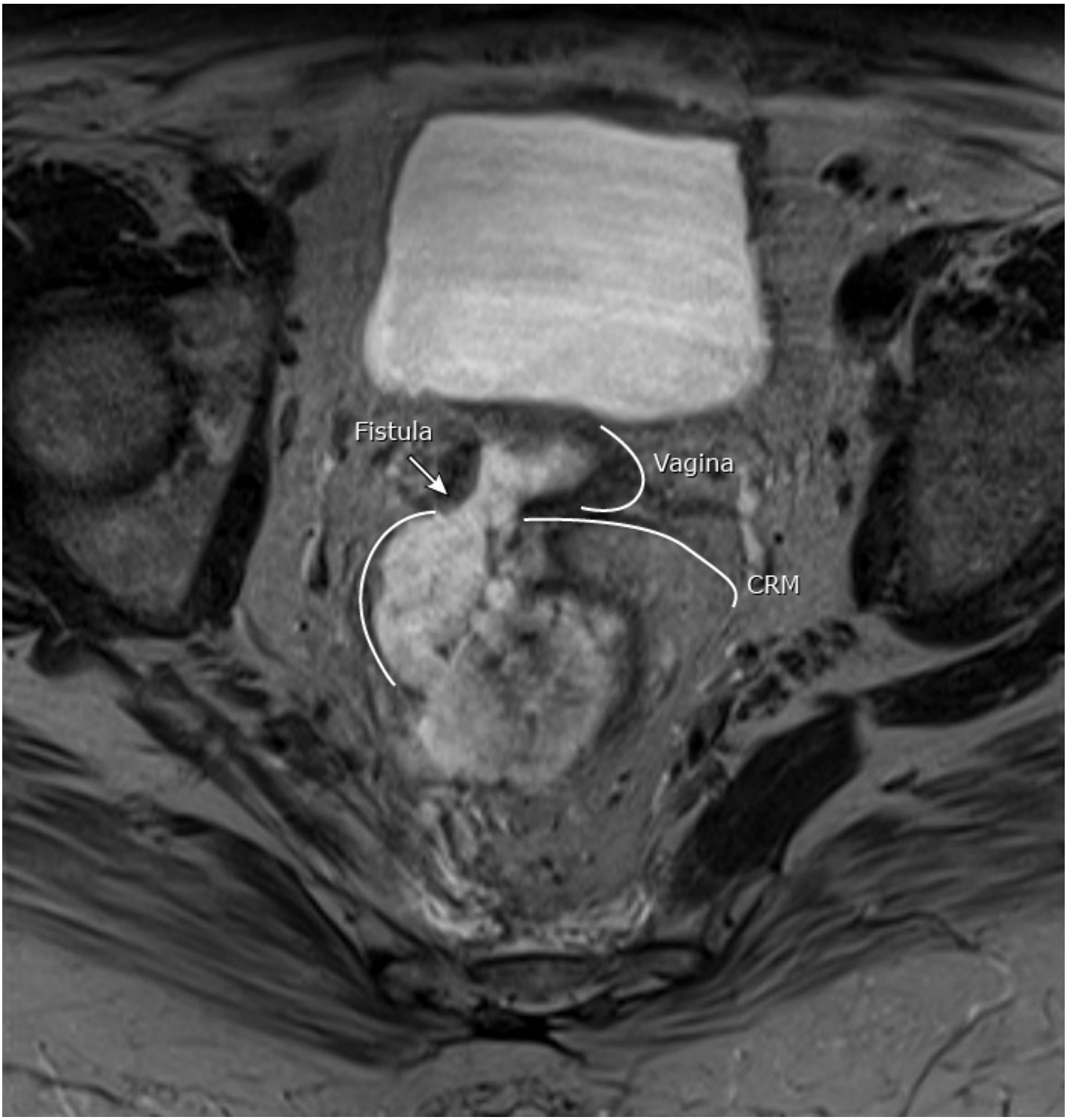


Axial T2-weighted pelvic MRI image of a node-positive rectal cancer. It shows a lymph node in the mesorectal fat at 7 o'clock that is abnormally enlarged (8 mm in short axis) and appears morphologically abnormal (arrow). The primary tumor is visible in the anterior mesorectum.

MRI: magnetic resonance imaging.

Graphic 115375 Version 1.0

MRI of a T4b rectal cancer with invasion of the anterior circumferential resecti margin (CRM) and formation of a rectovaginal fistula

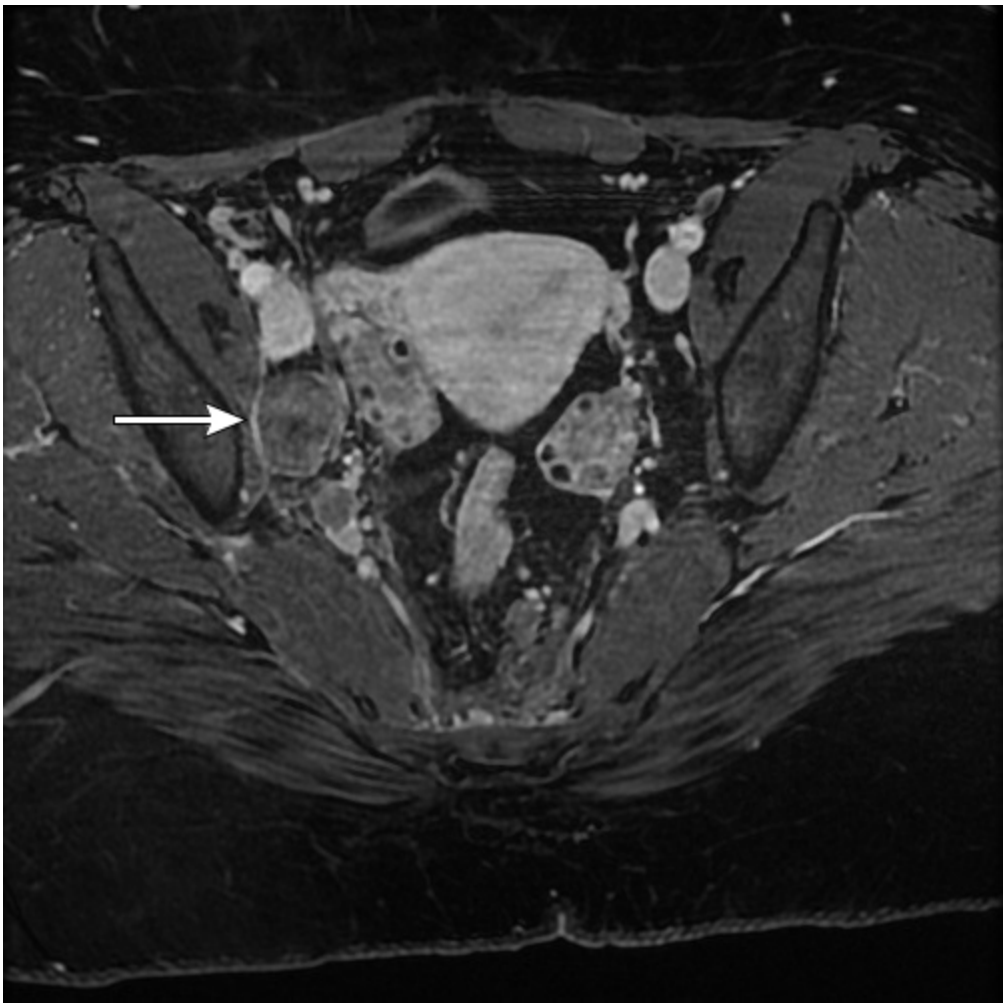


Axial T2-weighted MRI shows a T2 hyperintense rectal mass with invasion of the anterior CRM and rectovagi fistula formation. The marked T2 hyperintensity of the tumor is indicative of mucinous features.

MRI: magnetic resonance imaging.

Graphic 117815 Version 1.0

MRI of a pathologic internal iliac lymph node in a patient with rectal cancer

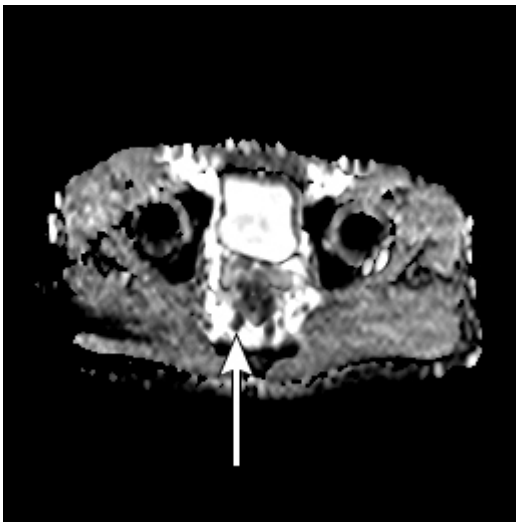


Contrast-enhanced axial MRI image shows an abnormally enlarged internal iliac lymph node at initial diagnosis of rectal cancer (arrow). While this is a less common site of lymph node involvement from rectal cancer than is mesorectal lymphadenopathy, these are the only regional lymph nodes for rectal cancer that are not routinely excised during surgery. It is, therefore, crucial that abnormal nodes in this location be specifically recognized and managed in a multidisciplinary approach to treatment.

MRI: magnetic resonance imaging.

Graphic 115377 Version 1.0

MRI of a diffusion-restricted mesorectal lymph node in a patient with rectal cancer

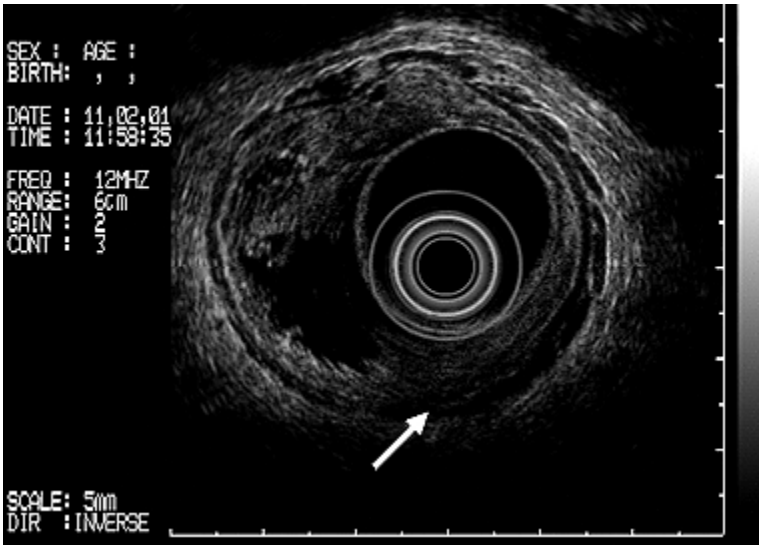


Axial apparent diffusion coefficient map from a diffusion-weighted pelvic MRI sequence shows restricted diffusion (dark signal) in a mesorectal lymph node (arrow). The mean apparent diffusion coefficient was 1096 mm^2/second.

MRI: magnetic resonance imaging.

Graphic 115376 Version 1.0

Rectal cancer seen on endoscopic ultrasound

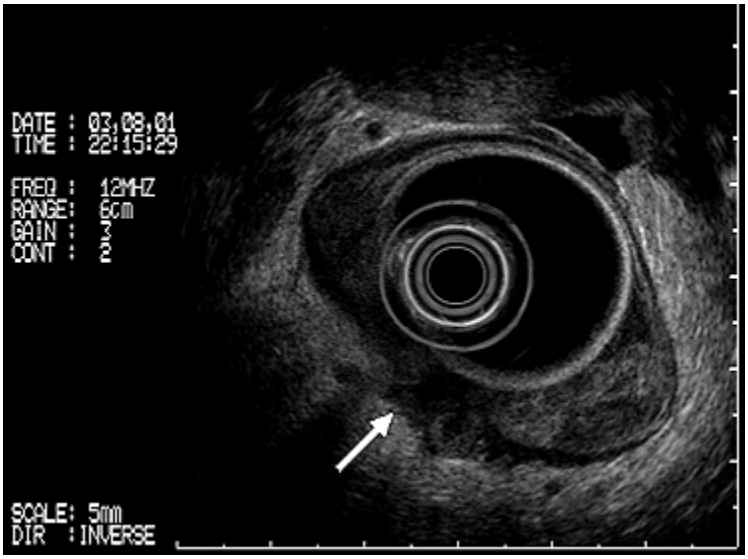


Endoscopic ultrasound image of a T2 rectal cancer with invasion of the muscularis propria (arrow).

Courtesy of Gavin C Harewood, MD, and Maurits J Wiersema, MD.

Graphic 50261 Version 4.0

Rectal cancer seen on endoscopic ultrasound



Endoscopic ultrasound image of a T3 rectal cancer with extension of the tumor into the perirectal space (arrow).

Courtesy of Gavin C Harewood, MD, and Maurits J Wiersema, MD.

Graphic 65054 Version 4.0

Summary results for primary preoperative rectal tumor (T) staging, Comparative Effectiveness Review Imaging Tests for the Staging of Colorectal Cancer, United States Agency for Healthcare Research and Quality, 2014

	MRI versus ERUS	ERUS versus CT	MRI versus CT
Sensitivity of T1/T2 versus T3/T4 (95% CI)	MRI: 88.9% (79.0-94.4) ERUS: 88.0% (80.0-93.1)	Not calculated due to insufficient data reported	Not calculated
Specificity of T1/T2 versus T3/T4 (95% CI)	MRI: 85.3% (70.6-93.4) ERUS: 85.6% (65.8-94.9)	Not calculated due to insufficient data reported	Not calculated
Accuracy (OR of getting an incorrect result [95% CI])*	1.24 (0.835-1.84)	0.359 (0.238-0.541)	0.317 (0.056-1.784)¶
Understaging OR (95% CI)*	1.571 (0.605-4.083)	0.626 (0.438-0.894)	0.317 (0.027-3.646)¶
Overstaging OR (95% CI)*	1.05 (0.518-2.16)	0.472 (0.28-0.798)	0.317 (0.028-3.653)¶
Favors	No statistically significant difference	ERUS	No statistically significant difference

MRI: magnetic resonance imaging; ERUS: endorectal ultrasound; CT: computed tomography; CI: confidence interval; OR: odds ratio.

* OR <1 indicates a lower risk of error in the first imaging modality listed in the column header; OR >1 indicates a higher risk of error in the first imaging modality listed in the column header.

¶ Study with 0.15 T magnet excluded from analyses.

Bruening W, Sullivan N, Carter Paulson E, Zafar H, Mitchell M, Treadwell J, Schoelles K. Imaging Tests for the Staging of Colorectal Cancer. Comparative Effectiveness Review No. 142. (Prepared by the ECRI Institute-Penn Medicine Evidence-based Practice Center under Contract No. 290-2012-00011-I.) AHRQ Publication No. 14-EHC046-EF. Rockville, MD: Agency for Healthcare Research and Quality; September 2014. Available at: https://effectivehealthcare.ahrq.gov/products/colorectal-cancer-staging/research (Accessed on November 12, 2021).

Graphic 116635 Version 3.0

Summary results for primary preoperative rectal cancer nodal (N) staging, Comparative Effectiveness Review Imaging Tests for the Staging of Colorectal Cancer, Agency for Healthcare Research and Quality, 2014

	MRI versus ERUS	CT versus ERUS	MRI versus CT
Sensitivity (95% CI)	MRI: 49.5% (36.0-63.1) ERUS: 53.0% (39.7-65.5)	CT: 39.6% (28.1-52.4) ERUS: 49.1% (34.9-63.5)	Not calculated
Specificity (95% CI)	MRI: 69.7% (51.9-83.0) ERUS: 73.7% (43.6-91.0)	CT: 93.2% (58.8-99.2) ERUS: 71.7% (56.2-83.4)	Not calculated
Accuracy (OR of getting an incorrect result [95% CI])*	0.882 (0.542-1.408)	1.13 (0.85-1.503)	1.316 (0.709-2.443)
Understaging OR (95% CI)*	0.972 (0.563-1.679)	1.453 (0.854-2.473)	1.743 (1.028-2.957); not robust in sensitivity analysis
Overstaging OR (95% CI)*	0.752 (0.457-1.237)	1.015 (0.571-1.801)	0.498 (0.308-0.806)
Favors	No statistically significant difference	No statistically significant difference	MRI favored for avoiding overstaging

MRI: magnetic resonance imaging; ERUS: endorectal ultrasound; CT: computed tomography; CI: confidence interval; OR: odds ratio.

* OR <1 indicates a lower risk of error in the first imaging modality listed in the column header; OR >1 indicates a higher risk of error in the first imaging modality listed in the column header.

Bruening W, Sullivan N, Carter Paulson E, Zafar H, Mitchell M, Treadwell J, Schoelles K. Imaging Tests for the Staging of Colorectal Cancer. Comparative Effectiveness Review No. 142. (Prepared by the ECRI Institute-Penn Medicine Evidence-based Practice Center under Contract No. 290-2012-00011-I.) AHRQ Publication No. 14-EHC046-EF. Rockville, MD: Agency for Healthcare Research and Quality; September 2014. Available at: https://effectivehealthcare.ahrq.gov/products/colorectal-cancer-staging/research (Accessed on November 12, 2021).

Graphic 116636 Version 3.0

Contributor Disclosures

Ronald Bleday, MD No relevant financial relationship(s) with ineligible companies to disclose. **David Shibata, MD** No relevant financial relationship(s) with ineligible companies to disclose. **Michael H Rosenthal, MD, PhD** No relevant financial relationship(s) with ineligible companies to disclose. **Kenneth K Tanabe, MD** Patent Holder: EGF SNP to determine risk for HCC [Cirrhosis, hepatocellular carcinoma]; Use of EGFR inhibitors to prevent HCC [Cirrhosis, hepatocellular carcinoma]. Consultant/Advisory Boards: Cancer Expert Now [GI cancers, melanoma]; GSK [GI Cancers]; Imvax [GI cancers]; Leidos [Melanoma, GI cancers]; Teledoc [GI cancers, melanoma]. Other Financial Interest: American Cancer Society [Honoraria as editor of Cancer]. All of the relevant financial relationships listed have been mitigated. **Herbert Y Kressel, MD** Consultant/Advisory Boards: Canon Medical Systems [MRI]. All of the relevant financial relationships listed have been mitigated. **Sonali M Shah, MD** No relevant financial relationship(s) with ineligible companies to disclose. **Wenliang Chen, MD, PhD** No relevant financial relationship(s) with ineligible companies to disclose.

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Conflict of interest policy

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