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SPECIAL SECTION: RECTAL CANCER

MR staging of anal cancer: what the radiologist needs to know

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Abstract
Anal canal cancer is a rare disease and squamous cell carcinoma is the most common histologic subtype. Traditionally, anal cancer is imaged with CT and PET/CT for purposes of TNM staging. With the increased popularity of MRI for rectal cancer evaluation, MRI has become increasingly utilized for local staging of anal cancer. In this review, we focus on the necessary information radiologists need to know to understand this rare and unique disease and to be familiar with staging of anal cancer on MRI.

Keywords MRI · Anal canal · Anal cancer · Anal squamous cell carcinoma · Staging

Introduction

Anal cancer is a rare disease accounting for 2.7% of gastrointestinal tract cancers [1, 2]. While several types of malignancies can affect the anal canal, squamous cell carcinoma (SCCa) is the most common. Historically, anal cancer was surgically treated until the results of the Nigro protocol were published in 1974 [3]. The protocol showed that preoperative chemoradiation can achieve complete tumor regression on pathology. Since then, the paradigm for treating and thus staging anal cancer shifted, relying heavily on imaging for staging, most commonly with computed tomography (CT) or positron emission tomography (PET/CT). Recently, the use of magnetic resonance imaging (MRI) has increased for the initial staging of anal cancer. The superior tissue sensitivity of MRI adds clarity to the multi-disciplinary discussion required for optimal treatment planning. It is therefore important for radiologists to be familiar with the anatomy of the anal canal, be able to optimize MR imaging technique for this particular tumor and its location, as well as be familiar with accurate TNM staging including local lymph node drainage patterns. This article will discuss the key features of anal cancer and its treatment, with a focus on what the radiologist needs to know to understand this unique disease and accurately interpret MRI for anal cancer.

Clinical features and epidemiology

While anal cancer remains rare, its incidence rate has been rising at a rate of more than 2% per year for at least the past decade in the United States [4]. The American Cancer Society estimates that about 8580 new cases of anal cancer will be diagnosed and 1160 anal cancer-related deaths will occur in the United States in the year 2018 [5]. Anal cancer is usually slightly more common in women than in men but some variation exists among different racial/ethnic groups [4]. It is rarely diagnosed prior to age 35 years but is most often diagnosed between the ages of 45 and 75 [4]. Approximately 85% of primary anal canal malignancies are of squamous cell origin, whereas 10% are anal adenocarcinomas and the remaining 5% are rarer tumors such as melanoma, small cell carcinoma, or metastatic disease [6].

Nearly half of patients with anal cancer have localized disease confined to the primary site at the time of diagnosis but just over 30% have locoregional lymph node involvement

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and approximately 13% have metastatic disease [4]. Based on SEER data from 2008 to 2014, the average 5-year survival of all patients with anal cancer across cancer stages is about 67% [4]. However, survival is affected by the cancer stage at the time of diagnosis. The 5-year relative survival is greater than 81% if the cancer is localized but drops to about 64% with spread to regional lymph nodes and further down to about 30% with distant metastatic disease [4]. Patients with anal SCCa may be asymptomatic, but about half present with pain and/or anal bleeding [7]. Less commonly, these patients present with a mass or pressure sensation, itching, discharge or wetness, or a change in bowel habits or quality of stool [7].

Patients may be hesitant to seek care either because of embarrassment or because they mistake the symptoms for other benign, more common anal disease (i.e., hemorrhoids). In one study, 19% of patients waited more than 6 months after the onset of symptoms to seek treatment [8]. Even upon seeking care, appropriate treatment can be delayed because of misdiagnosis. In this same study, at the first clinic visit, a rectal exam was performed on only 54% of patients and 27% were initially misdiagnosed as having hemorrhoids [8].

Infection with the human papilloma virus (HPV) has emerged as the leading risk factor for the development of anal cancer and is thought to be associated with 65–89% of all SCCa of the anal canal [6]. A recent study from MD Anderson found that 94% (68/72) of patients treated for metastatic anal SCCa had detectable HPV [9]. Transmission of HPV occurs predominantly through sexual activity, and sexual behavior including increasing number of lifetime sex partners and anal receptive intercourse are well-known risk factors for anal SCCa [6]. However, the transmission can occur through any skin-to-skin contact with an infected area of the body.

Among the anogenital HPV serotypes, the "low-risk" genital serotypes (e.g., HPV-6 and 11) are associated with an increased risk for anogenital warts that do not progress to cancer while the ''high-risk" genital serotypes (e.g., HPV-16 and 18) are oncogenic. Nevertheless, while the anogenital warts do not progress to cancer, patients with warts are overall more likely to develop anal cancer, perhaps because of the coexistence of multiple HPV strains in individuals. The now widely available HPV vaccine in the United States targets the most four common high- and low-risk genital serotypes as well as 5 additional cancer-causing subtypes.

Although most HPV infections do not cause symptoms and clear spontaneously within a couple of years, persistent or chronic infection with high-risk, oncogenic serotypes can lead to dysplastic changes. Anal intraepithelial neoplasia (AIN) is a premalignant, precursor lesion of the anal mucosa that can progress to anal SCCa. AIN-I refers to a low-grade squamous intraepithelial lesion (LSIL) which is not considered premalignant (it can spontaneously regress and thus can be managed expectantly), but it has the potential to advance to a high-grade squamous intraepithelial lesion (HSIL) [10]. AIN-II/III refers to high-grade dysplasia/HSIL which is considered premalignant and will likely evolve to invasive cancer [10], with malignant progression shown to occur in approximately 11% of cases [11].

Patients infected with high-risk, oncogenic serotypes of HPV are also at risk for other genital-related cancers, including that of the cervix, vagina, vulva, penis, and oropharynx. Whereas HPV positivity in head and neck cancer heralds a good prognosis, the prognostic significance of HPV positivity in anal cancer is uncertain [6]. Smoking and immunosuppression, particularly coinfection with HIV or in patients who have undergone organ transplantation, also increase the risk for anal cancer, and in the setting of HIV infection the risk is not mitigated with effective anti-retroviral therapy [7].

Anatomy of the anal canal

The anal canal comprises the last few centimeters of the intestine, approximately 3 to 5 cm in length, between the rectum and the anal verge which is the external opening of the anus and is surrounded by hair-bearing perianal skin [12]. While the anatomic anal canal extends from the dentate line (or valves of Morgagni) to the anal verge, the surgical anal canal is considered to be slightly longer and extends from the anorectal junction as palpated by the surgeon to the anal verge (Fig. 1) [13].

The dentate line serves as an important junction whereby the epithelial lining changes from typical intestinal columnar cells that line the rectum to squamous cell epithelial lining down to the anal verge [12]. It is also the interchange

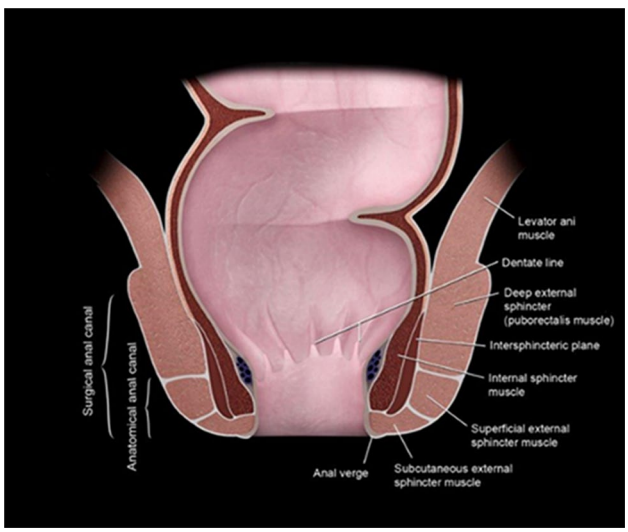

Fig. 1 Illustration of anatomy of anal canal. (Courtesy of David Bier, University of Texas MD Anderson Cancer Center, Houston, TX)

between two distinct venous and lymphatic drainage patterns which is key in understanding the typical nodal and metastatic spread of anal SCCa.

The anal sphincter complex comprises the internal anal sphincter (IAS) and external anal sphincter (EAS) complex (Fig. 2). The IAS is the continuation of thickened inner circular muscle of the rectal muscularis propria under involuntary control. On MR imaging, it appears as a homogeneous, mildly T2 hyperintense inner circular muscle layer with a thickness of approximately 3.5 mm and demonstrates avid enhancement post contrast [12]. The EAS complex is a composition of several closely related skeletal muscles (the inferior portion of the levator ani, the puborectalis, and the external sphincter muscles) under voluntary control. On MR imaging, it appears as the outermost circular layer of muscle with T2 hypointense striated appearance similar to other skeletal muscles and shows post-contrast hypoenhancement compared to the IAS.

Between the IAS and EAS complex, the conjoint longitudinal muscle (CLM), which is a fibro-fatty muscular layer in continuity with the longitudinal muscle layer of the rectum, forms an intersphincteric plane [12, 13]. The intersphincteric space between the IAS and the EAS is an important anatomic landmark as it can be entered surgically for intersphincteric resection for low rectal cancers involving the IAS [12]. On MR, it appears as a thin hyperintense column that does not enhance post contrast.

MR technique

The treatment of anal cancer is based on proper staging with knowledge of the tumor location, size of tumor, sphincter involvement, and adenopathy—best seen with the appropriate imaging technique. The accurate reporting of the primary tumor, adenopathy, and metastases guides radiation therapy, oncology, and surgery.

In this context, the successful use of MR in rectal and prostate cancer serves as a model for the imaging of anal cancer [14]. Specific techniques for MR imaging of low rectal cancer and the anal sphincter complex can be directly extrapolated to anal cancer imaging [15, 16].

Magnet selection Modern MR Scanners with improved gradient and the latest software and sequences provide the best imaging. Selection of the most modern high-field strength magnet, whether it is 1.5T or 3T, should provide adequate imaging. Low field strength magnets < 1.5T and magnets older than 20 years are not suitable for high-resolution anal imaging.

Suggested scanning protocols for rectal cancer can be found on the Society of Abdominal Radiology Rectal Cancer Disease Focus Panel website [17] and in the European Society of Gastrointestinal and in the Abdominal Radiology (ESGAR) consensus meeting paper [18]. The protocols include sequences via the major vendors including General Electric, Siemens, and Phillips 1.5T and 3T magnets.

Coils: A surface-based array coil is centered over the anal canal so that imaging of the anal cancer can be performed in the isocenter of the magnet where imaging is optimum. The placement of the receiver coil somewhat lower than the normal pelvic imaging placement may result in minimally degraded images of metastatic adenopathy in the retroperitoneum of the upper pelvis. The imaging of metastases to common iliac and para-aortic nodes may not be covered by the surface coil and can be evaluated with concurrent CT or PET/CT.

Unlike rectal cancer which has known drainage usually superior to the tumor, pathways of anal cancer include the

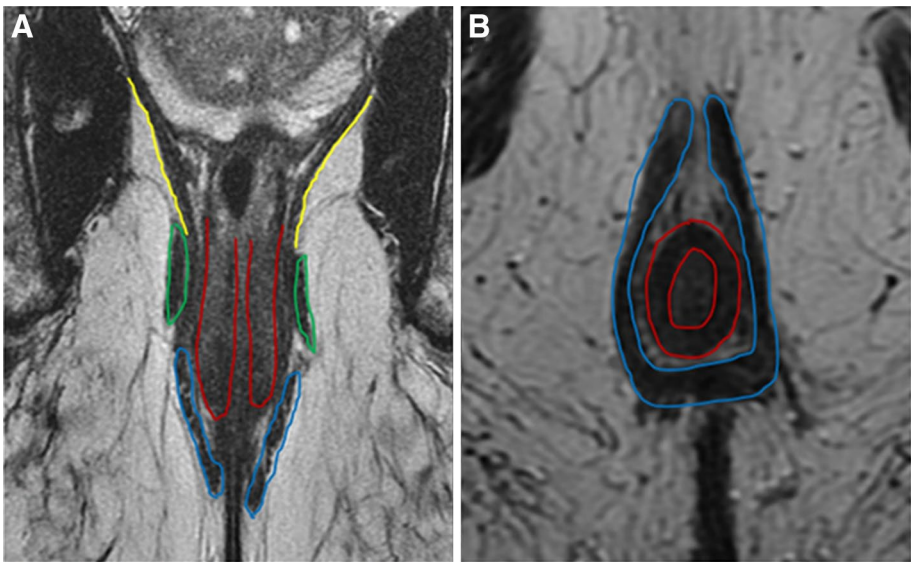

Fig. 2 Normal anal canal on MRI. **a** T2-weighted coronal oblique image. **b** T2-weighted axial oblique image, just above the anal verge. Red line—internal anal sphincter. Blue line—external anal sphincter. Green line—puborectalis muscle (deep external sphincter). Yellow line—levator ani muscles

pelvic sidewalls and inguinal regions. Saturation bands placed over the anterior pelvic wall to reduce respiratory motion from subcutaneous fat in rectal imaging should thus be removed or repositioned to better evaluate the inguinal nodes (Fig. 3d).

Switching phase direction from AP to right to left can reduce the breathing artifact. However, right to left phase limits the rectangular field of view (FOV) and may increase scan time. A larger FOV may be helpful to evaluate for local regional pelvic sidewall and inguinal adenopathy.

Parallel imaging may degrade high-resolution T2 images and may not be important in pelvic imaging, compared to abdominal imaging where motion is a major problem.

An endorectal coil cannot be used because it is too painful and may even push the tumor away from the coil. Patients cannot tolerate an endoanal probe due to painful friable mucosa from tumor.

Sagittal, axial images orthogonal to the anal canal and coronal imaging of anus are the mainstay for diagnosis. As in rectal MRI, obtaining high-resolution T2, small FOV 3 mm oblique images perpendicular to the anus is the most important sequence and coronal oblique images parallel to the anal canal are useful for imaging sphincter involvement (Fig. 3).

Contrast-enhanced gradient T1-weighted imaging may be helpful in characterizing the tumor or other anal pathology; however, as in rectal imaging, it is not mandatory. 3-D T2-weighted images, such as General Electric Cube or Siemens Space, are helpful if orthogonal images are needed in a different plane for viewing the sphincters. If volumetric measurements are needed for determining response to therapy, 3-D imaging will help [19, 20]. Diffusion-weighted images are useful for tumor and lymph node localization and characterization.

Staging

Standard initial work-up of the anal cancer includes a detailed physical examination (which includes inspection of perianal area for visible lesions), a digital rectal exam (DRE), and a proctoscopy with biopsy. The physical exam includes palpation of the inguinal regions for possible inguinal lymphadenopathy. As part of the physical exam, a vaginal examination in women is performed to determine

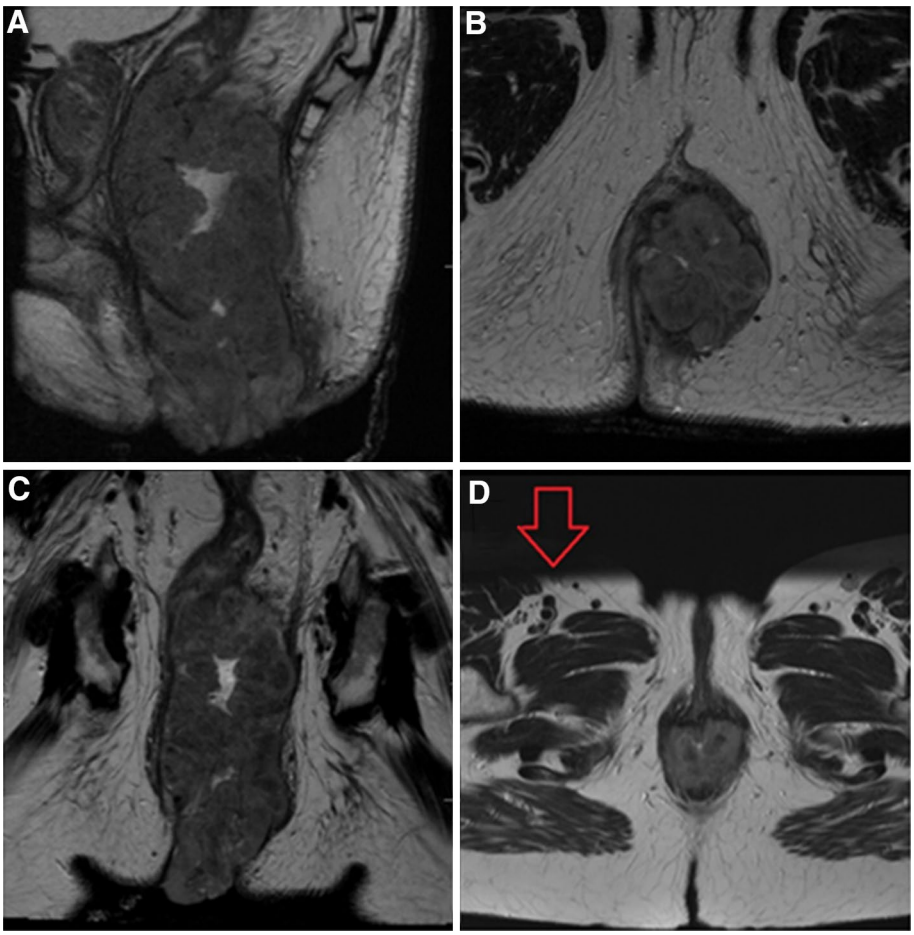

Fig. 3 **a** Sagittal and **b** axial high-resolution MRI: similar to rectal MRI, high-resolution T2-weighted, small FOV 3 mm slice thickness oblique imaging perpendicular to anus is an important sequence for evaluation of anal cancer and adjacent structures. **c** Coronal oblique images parallel to anal canal are useful for anal sphincter evaluation. **d** Axial T2-weighted image shows improper placement of saturation band resulting in partial visualization of right inguinal node (red arrow), important for appropriate staging

vaginal involvement and the presence of fistulas. The DRE involves the evaluation of the primary anal lesion, invasion of local structures and/or anal sphincter, and perirectal nodal involvement. A proctoscopy is usually performed under anesthesia to allow for direct assessment of the lesion and tissue sampling to confirm diagnosis.

Guidelines by the American Society of Colon and Rectal Surgeons and joint guidelines by European Society of Medical Oncology, European Society of Surgical Oncology, and European Society of Radiotherapy and Oncology (ESMO-ESSO-ESTRO) recommend MRI and endoanal ultrasound (EAUS) for the initial imaging evaluation of the primary anal cancer [21, 22]. Pelvic MRI is the preferred modality. EAUS is usually reserved for small superficial lesions (T1 stage) due to its small FOV which limits the evaluation of lymph nodes and local structures and if MRI is not available [21–23].

CT of the chest, abdomen, and pelvis with intravenous contrast is universally accepted for the evaluation of distant metastatic disease and lymphadenopathy. ^{18}F-FDG PET/CT has been increasingly used for the systemic staging of anal cancer, showing especially high sensitivity for nodal disease detection [24–28]. Recent studies showed that FDG PET/CT changes anal cancer staging in 17–25% of patients when compared to CT [29]. FDG PET/CT is currently accepted as an optional adjunct imaging modality for anal cancer staging in addition to CT. Given its high sensitivity for detection of regional nodal involvement, the National Comprehensive Cancer Network (NCCN) recommends FDG PET/CT for radiation treatment planning [2].

TNM staging of anal cancer follows the guidelines by the American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) [30]. Cancer staging is determined by the assessment of size and local organ involvement (T), regional lymph node metastasis (N), and distant metastatic disease (M) (Table 1) [30]. MRI is the primary imaging modality for evaluating the size of the primary anal carcinoma and involvement of the local organs. CT, FDG PET/CT, and MRI have been used for regional nodal staging.

Primary tumor imaging (T staging)

High-resolution multiplanar MR imaging allows for excellent visualization of the anal canal, sphincter complex, local structures, and regional lymph nodes. It is the preferred imaging modality for primary anal cancer staging when available. The reported sensitivity of MRI for anal cancer diagnosis is 90–93%; it is limited for visualizing small superficial lesions which can be detected with 100% sensitivity by EAUS [31–34]. Both modalities have a high concordance in tumor size and high accuracy for evaluation

Table 1 TNM staging

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	High-grade squamous intraepithelial lesion (previously termed carcinoma in situ, Bowen disease, anal intraepithelial neoplasia II–III, high-grade anal intraepithelial neoplasia)
T1	Tumor ≤ 2 cm
T2	Tumor > 2 cm but ≤ 5 cm
T3	Tumor > 5 cm
T4	Tumor of any size invading adjacent organ(s), such as the vagina, urethra, or bladder
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in inguinal, mesorectal, internal iliac, or external iliac nodes
N1a	Metastasis in inguinal, mesorectal, or internal iliac lymph nodes
N1b	Metastasis in external iliac lymph nodes
N1c	Metastasis in external iliac with any N1a nodes
Distant metastasis (M)	
MX	Distant metastasis cannot be assessed
cM0	No distant metastasis
cM1	Distant metastasis
pM1	Distant metastasis, microscopically confirmed

American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) eighth edition TNM classification of anal cancer
Reprinted with permission from the AJCC Cancer Staging Manual, Eighth Edition, AJCC Cancer Staging Form Supplement, 2018

of sphincter involvement (while the latter is not part of T staging, it is an important prognostic factor) [31–34]. MRI is superior for the evaluation of the involvement of local structures and regional lymph nodes [31–34].

At MR imaging, anal cancer shows high-to-intermediate signal intensity on T2-weighted images (higher than that of skeletal muscles and lower than that of normal ischioanal fat); low-to-intermediate signal intensity on T1-weighted images; and avid post-contrast enhancement. Anal cancer usually has an infiltrative or lobulated intraluminal annular or semiannular growth pattern (Figs. 4, 5). Anal cancer usually arises within the anal canal, may extend to the rectum even above the anorectal junction, and have a similar appearance to rectal cancer (Fig. 5).

T staging of the anal cancer is based on the longest diameter of the lesion, with tumors larger than 5 cm associated with worse prognosis [21]. Multiplanar capabilities of MRI make it an excellent imaging modality for the accurate measurement of the longest size of the tumor on one of the 3 available planes and for the accurate anatomical visualization of lesions at baseline for radiation therapy planning as well as for follow-up of treatment response. It is important to keep in mind that the T4 stage of the anal cancer does not include involvement of the external/internal sphincter muscles, rectal wall, puborectalis muscle, or levator ani muscle (Fig. 6). However, involvement of these structures has prognostic significance and may influence radiation planning. MRI allows for the detection of the involvement of the adjacent organs, such as the bladder, vagina, urethra, etc., thereby allowing for accurate T4 staging of anal cancer. Metastatic lesions to the rectum above the primary site can be seen (Fig. 7). Anal cancer may arise in condylomas (Fig. 8) especially in patients with pre-existing AIN lesions.

Nodal drainage pathways (N staging)

Nodal metastases significantly impact prognosis. Toubul et al. reported that the 5-year survival rate is 76% for N0 disease but is lower at 53.5% for N1 nodal involvement in anal carcinomas [35].

The location of nodal metastases in anal carcinomas depends on the site of the primary tumor [36–39]. External iliac, inguinal, and deep inguinal nodal metastases occur in anal carcinomas located inferior to the dentate line while mesorectal and internal iliac nodal metastases are seen more often in anal carcinomas located superior to the dentate line

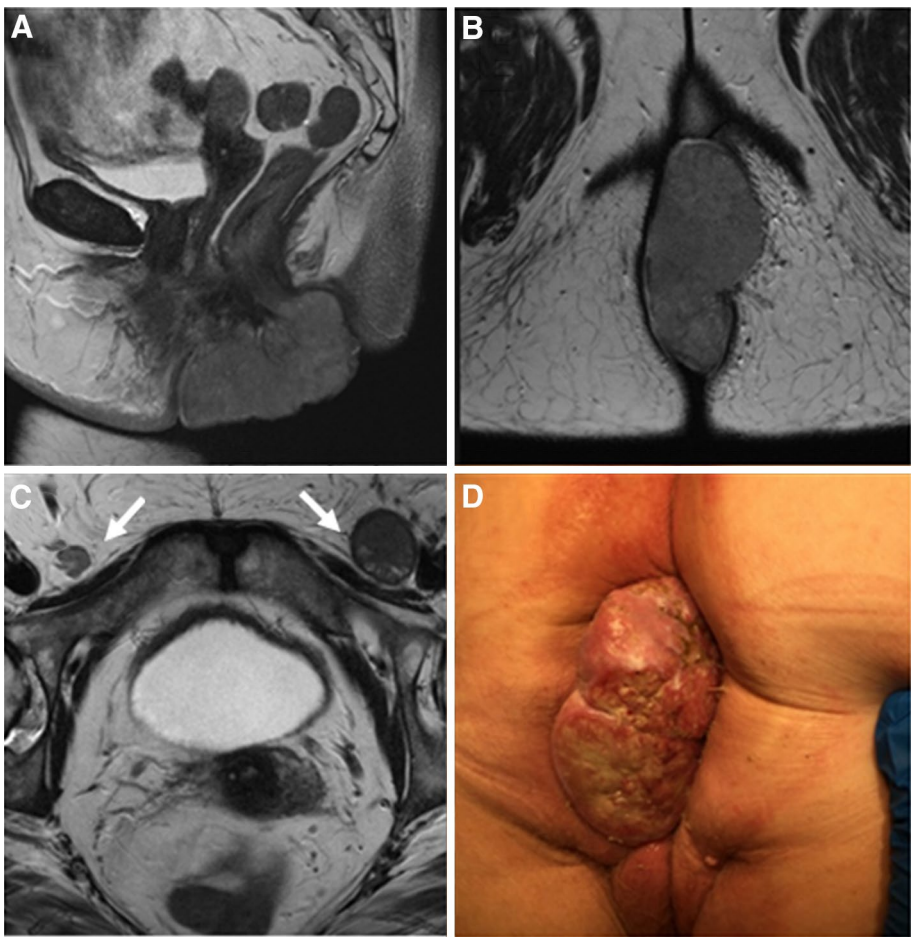

Fig. 4 **a** Sagittal and **b** axial T2-weighted images: anal squamous cell carcinoma measuring 7.8 × 3.9 × 5.0 cm without invasion of vagina or urethra, T3. **c** Axial T2-weighted image: multiple enlarged heterogeneous inguinal nodes bilaterally (arrows), greater on left; however, there was no intrapelvic adenopathy, N1a. **d** Physical exam: large fungating mass prolapsing from anus is seen

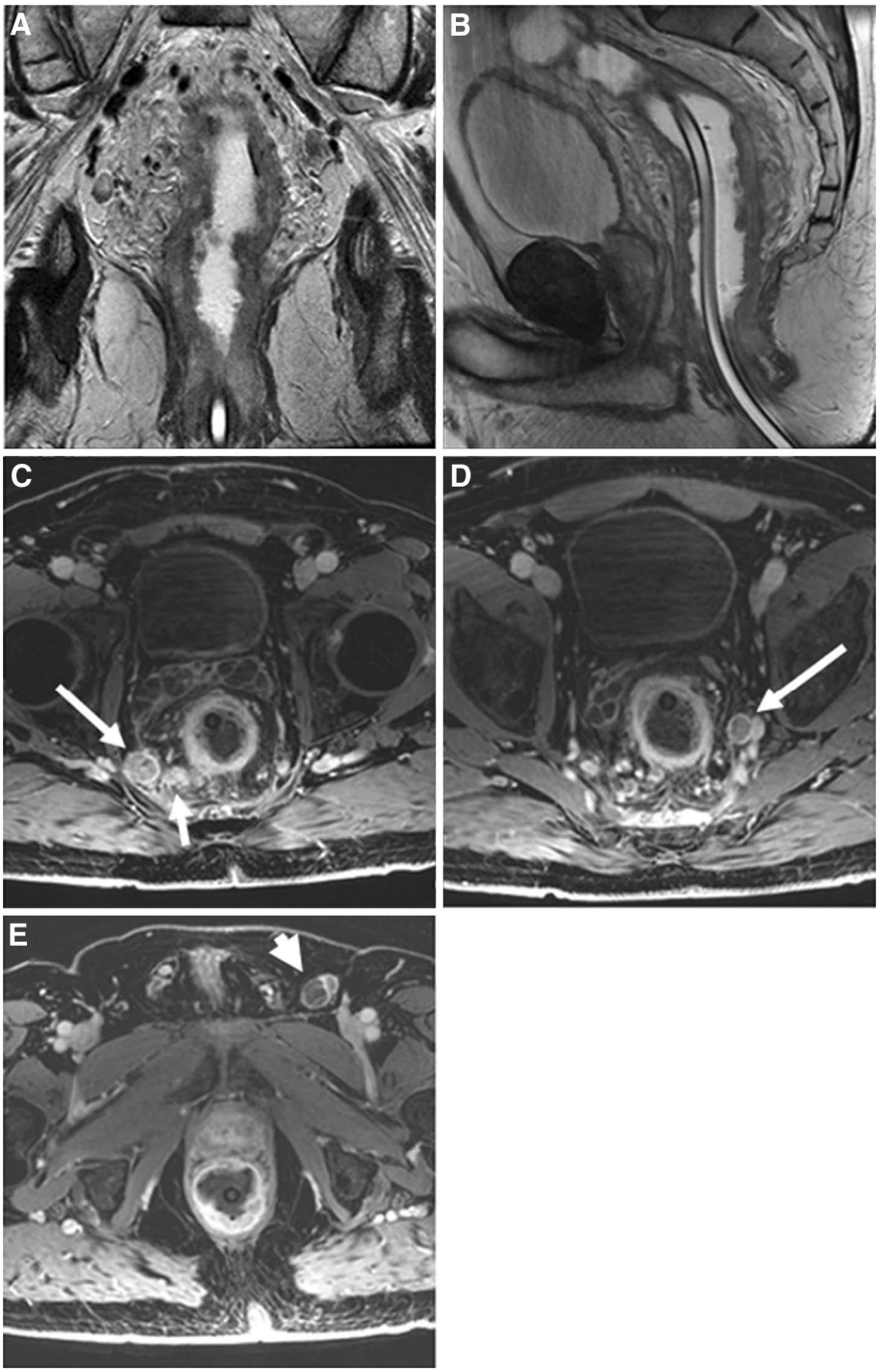

Fig. 5 **a** Oblique coronal and **b** sagittal T2-weighted images: poorly differentiated anal SCCa with infiltrative appearance, measuring up to 13.4 cm in length without invasion of local structures, T3. This appearance could be mistaken for rectal cancer. **c**–**e** Axial post-contrast 3D T1-weighted fat saturated images: heterogeneous mesorectal (short arrow), internal iliac (long arrow), and inguinal adenopathy (arrowhead), N1a

[40]. However, tumors extending both above and below the dentate line can spread to any of the above-described nodal regions.

The newest AJCC guidelines for TNM staging for anal cancers introduced significant changes in nodal staging; the N2 and N3 categories from the prior edition have been removed while the N1 category has been sub-classified into N1a, N1b, and N1c [30]. In the latest TNM staging, N0 refers to lack of regional of regional nodal metastases. N1a corresponds to metastasis in inguinal, mesorectal, or internal iliac lymph nodes; N1b corresponds to metastasis in external iliac lymph nodes; and N1c refers to metastasis in external iliac with any N1a nodes.

Imaging plays an important role in the evaluation of nodal involvement. Although metastatic nodes may demonstrate sonographic features such as round shape, irregular cortical

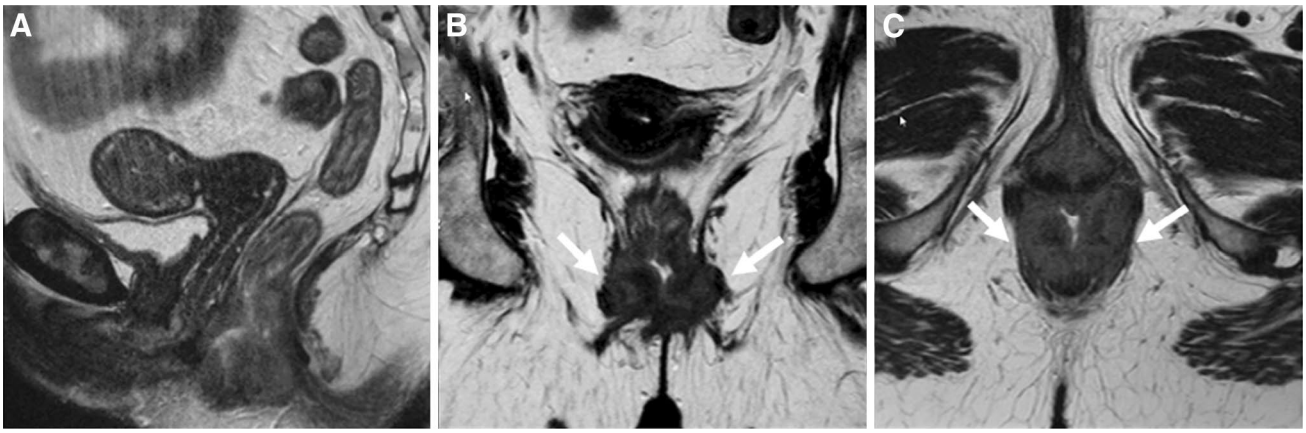

Fig. 6 **a** Sagittal, **b** oblique coronal, and **c** axial oblique T2-weighted images through anal canal: anal SCCa with sphincter invasion (arrows pointing to puborectalis) measuring 4.2 × 3.6 × 4.1 cm, T2 N0

outline, and lack of normal fatty hilum/hilar blood flow, ultrasound has limited diagnostic sensitivity and specificity for this purpose [39]. Thus, currently, CT and/or MRI pelvis is used for imaging anal carcinoma.

Size criteria for nodal metastases in anal carcinoma are yet to be validated. Although enlarged nodes with a short axis > 1 cm are often considered to be suspicious for metastatic adenopathy, the assessment of nodal involvement based on size is fraught with error [31, 41]. Benign reactive nodes may appear significantly enlarged while nodal micrometastases can occur in nodes measuring < 5 mm [13, 42].

Given the limitations of the size criteria, MR nodal morphologic features may be more helpful for determining nodal involvement. The presence of necrosis or heterogeneity, irregular nodal outline or spiculated border, and strong nodal enhancement are reported to be useful features suggestive of nodal involvement in anal cancers [13, 31, 41–43]. Biopsy may be required for definitive diagnosis, especially when this would impact management.

The latest NCCN guidelines report that PET/CT may be added to the staging of anal carcinoma, given its superior performance for identifying metastatic disease compared to traditional morphological imaging [44]. Winton et al. reported that FDG-PET had a sensitivity of 89% for nodal regional disease compared to 62% sensitivity with conventional CT and MR imaging [45]. A meta-analysis showed that PET/CT led to a change in nodal staging in 28% of patients [24]. Another meta-analysis involving 17 studies reported an overall sensitivity of 93% and specificity of 76% for PET/CT in the detection of metastatic inguinal adenopathy [25]. Furthermore, this meta-analysis reported that PET/CT played a critical role in management as it resulted in treatment modification in 12–59% of the patients [25]. Given the emergence of hybrid PET/MRI in oncologic imaging, PET/MRI may have a promising role in the staging of anal carcinoma in the future, but further research is warranted before this can be used as a standard of care.

M staging

Distant metastatic disease is relatively rare at initial diagnosis (5–11%) and is usually associated with post-treatment recurrence [4]. The para-aortic lymph nodes, liver, and lung are the most common sites for distant metastasis. CT with intravenous contrast is the modality of choice for the evaluation of distant metastatic disease [21, 22, 25]. Recent studies showed that FDG PET/CT had a higher sensitivity than CT imaging, identifying additional sites of distant metastasis in 3–5% of cases [25–27]. Therefore, FDG PET/CT is recommended as an optional adjunct modality to CT for anal cancer staging [22].

Reporting template

With the increased use of structured and synoptic reporting, the Society of Abdominal Radiology Disease Focused Panel for rectal and anal cancer developed a reporting template for use in initial staging of anal cancer with MRI (Table 2). This template may serve as a possible guide for radiologists to be used for reporting anal cancer MRI, and as a tool to improve communication of important staging information to clinicians.

Treatment

As with most gastrointestinal cancers, the most important prognostic factors in anal cancer are the T and N stage. In patients treated with radiation with or without chemotherapy, the most striking difference in results is seen when

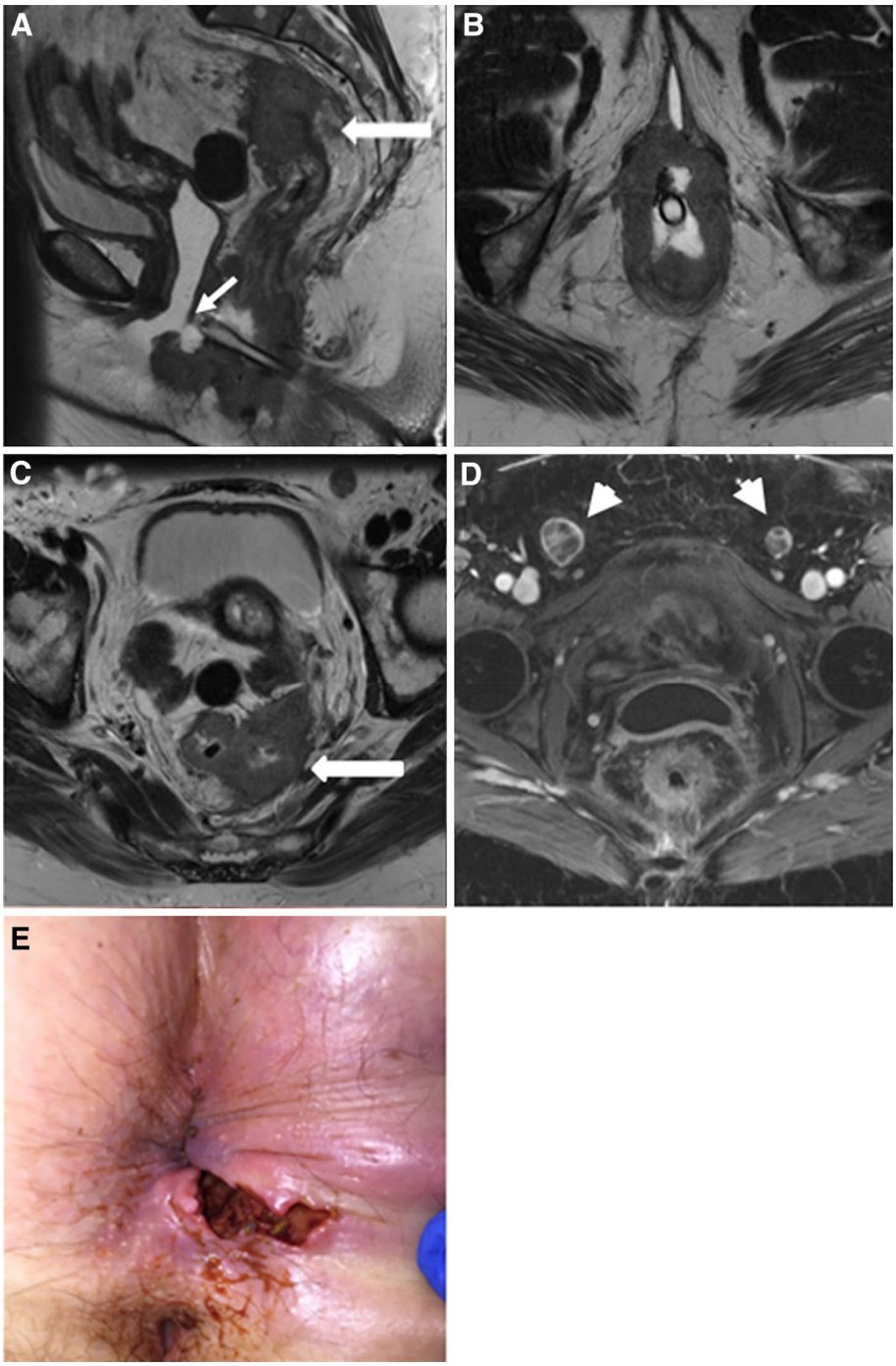

Fig. 7 **a** Sagittal and **b** axial T2-weighted images: invasive moderately differentiated squamous cell carcinoma, with involvement of vagina and complicated by large anovaginal fistula (small arrow), T4. **c** Axial T2-weighted and **d** axial post-contrast 3D T1-weighted FS images: bilateral inguinal nodal metastases (arrowheads), N1a. Large rectal metastasis is seen in high rectal region (horizontal arrows) (**a**, **c**). **e** Physical examination: perianal fistulization of anal SCCa

comparing T1–2 primary cancers (≤ 5 cm) versus T3–4 primary cancers (> 5 cm). The local failure rates with T3–4 primary cancers are approximately 50% following chemoradiation (CMT); when a complete response is achieved, the local failure rate is 25% [46].

In contrast to the T-stage, the impact of positive lymph nodes is less clear. Unlike rectal cancer, inguinal lymph nodes involvement in anal cancer are considered nodal (N) metastasis rather than distant (M) metastasis and patients should be treated in a potentially curative fashion. Cummings et al. reported that patients with negative nodes who received CMT had a higher 5-year cause-specific survival compared with those with positive nodes (81% vs. 57%) [47]. The RTOG 87-04 trial reported a higher colostomy rate (which is an indirect measurement of local failure) in N1 versus N0 patients (28% vs. 13%) [48]. In node-negative and possibly node-positive patients, the addition of mitomycin-C decreased the overall colostomy rates. The

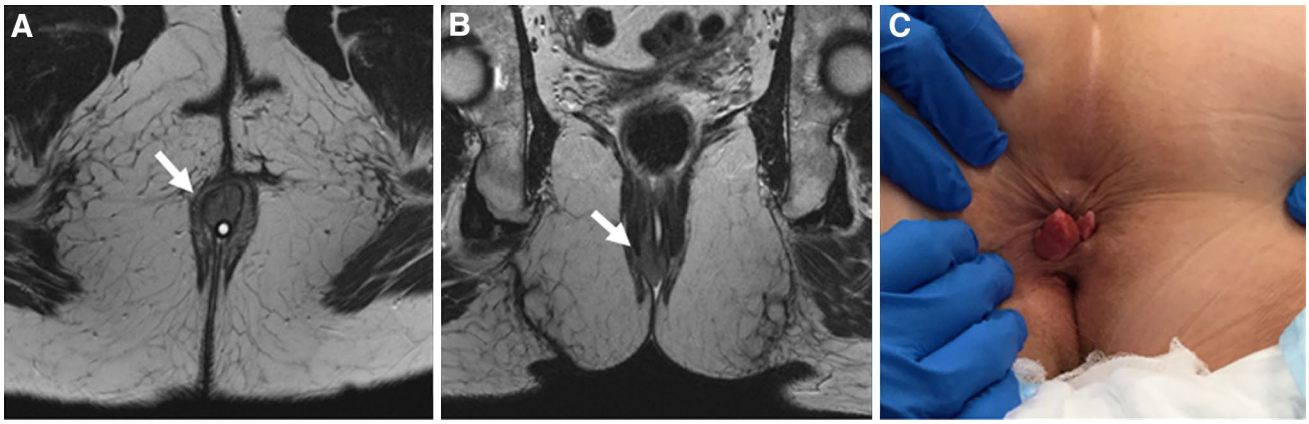

Fig. 8 **a** Axial and **a** oblique coronal T2-weighted images: anal SCCa arising from condyloma measuring 3.8 cm (arrow), T2. No evidence of nodal metastasis, N0. **c** Physical exam (prone positioning): anal condyloma with large 3 cm mass at anterior midline and additional 1 cm lobe at right posterolateral quadrant

EORTC randomized trial of 45 Gy ± 5-FU/mitomycin-C also reported that patients with positive nodes experienced significantly higher local failure ($p = 0.035$) and lower survival ($p = 0.038$) rates compared to those with negative nodes [49].

Chemoradiation therapy

The conventional treatment for anal canal cancer was abdominoperineal resection (APR) until the late 1970s. This standard was challenged by Nigro et al. in his initial report of 3 patients with squamous cell cancer of the anal canal who, following preoperative treatment with 30 Gy plus concurrent 5-FU and mitomycin-C, were found to have a pathologic complete response at the time of surgery [3]. Since that time, many single-arm phase II studies have indicated that initial CMT yields an 80–90% complete response rate with APR reserved for salvage [46]. Even in patients with large (≥ 5 cm) primary cancers, although the complete response rate is lower (50–75%), the majority of patients may be spared a colostomy and have an excellent overall survival [46].

Results of two prospective randomized trials from Europe of CMT versus radiation alone (EORTC [49] and UKCCCR ACT 1 [50]) support the use of CMT. Although neither trial revealed a significant overall survival advantage, given the improvement in local control and colostomy-free survival, they helped to establish CMT as the standard treatment. Mitomycin C-based conventional CMT remains the standard of care in most institutions. Despite these results, a number of investigators still advocate the use of cisplatin-based CMT based on its lower acute toxicity profile [51]. New CMT approaches including the use of cytotoxic agents such as capecitabine, oxaliplatin, and cetuximab have been investigated [52, 53]. To date, these approaches, as well as the use of 3-drug regimens [54] have not shown benefits compared with 5-FU/mitomycin C-based CMT.

Intensity modulated radiation therapy

Intensity modulated radiation therapy (IMRT) is a method to deliver pelvic radiation therapy with lower acute and long-term toxicity. By identifying the dose-limiting tissues surrounding the primary tumor and pelvic nodes and using multiple radiation fields to avoid them, IMRT allows for dose escalation with less toxicity.

The RTOG 0529 phase II trial examined IMRT in a cooperative group setting [55]. Compared with RTOG 98-11 patients who received conventional radiation/5FU/mitomycin-C, patients who received IMRT had fewer treatment breaks (49% vs. 62%) and lower acute toxicity (grade 2 + heme [73 vs. 85, $p = 0.032$], grade 3 + GI [21% vs. 36%, $p = 0.0082$] and Grade 3 + skin [23% vs. 49%, $p < 0.0001$]). Based on both single institution and RTOG data, IMRT has become the standard of care for CMT treatment of anal cancer.

In conclusion, CMT involving pelvic radiation with IMRT and concurrent chemotherapy (5-FU combined with either mitomycin-c or cisplatin) have resulted in 5-year survival rates of approximately 80% while allowing sphincter preservation for most patients. Surgery is reserved for selected patients with T1M0 disease who can undergo resection with acceptable functional outcomes or an APR for salvage following CMT.

Summary

Anal canal cancer is a rare and unique tumor type that can benefit from modern radiologic imaging techniques such as MRI for local tumor extent and lymph node staging. PET/CT

Table 2 MRI anal squamous cell cancer baseline staging template

CLINICAL INFORMATION: [FREE TEXT]
(Note: Use this template ONLY for primary anal cancer, not for adenocarcinoma of the rectum involving anal canal)

TECHNIQUE: [FREE TEXT]

COMPARISON:

FINDINGS:

TUMOR SIZE: [ ] cm × [ ] cm (largest measure in any plane x perpendicular measure)
T-STAGE:
- □ Tx/T0 (primary tumor cannot be assessed/no evidence of primary tumor)
- □ T1 (≤ 2 cm)
- □ T2 (> 2 cm ≤ 5 cm)
- □ T3 (> 5 cm)
- □ T4* (adjacent organ(s), NOT including sphincter, rectal wall, skin, subcutaneous tissue)

*Structures with invasion/possible invasion: [None/FREE TEXT]

FUNCTIONAL SEQUENCES:
DWI:
- □ Restricted diffusion
- □ No restricted diffusion
- □ N/A

LYMPH NODES*: [*locoregional*: internal iliac/obturator, external iliac, mesorectal, inguinal, superior rectal/hemorrhoidal]
- □ N0: No visible or no suspicious regional lymph nodes
- □ N1a: Suspicious inguinal, mesorectal AND/OR internal iliac lymph node(s)
- □ N1b: Suspicious external iliac lymph node(s)
- □ N1c: Suspicious external iliac AND any N1a lymph node (inguinal, mesorectal, or internal iliac)

OTHER: [FREE TEXT other pelvic organs, bones, other incidental findings]

IMPRESSION:
1. [FREE TEXT]
2. mr T [ ] N [ ]

*Suggested criteria for malignant lymph node, primary staging

Mesorectal and superior rectal (any of the following)
≥ 9 mm short axis diameter
5–8 mm short axis diameter AND ≥ 2 morphologically suspicious characteristics ¥
< 5 mm short axis diameter AND 3 morphologically suspicious characteristics¥
Internal iliac and obturator:
≥ 5 mm short axis diameter
Inguinal lymph nodes (deep and superficial)
Non-HIV: ≥ 1 -cm short axis diameter
HIV: ≥ 1 -cm short axis diameter and asymmetric
External and common iliac nodes
≥ 1 cm short axis diameter

¥Morphologically suspicious criteria
Round shape
Irregular border
Heterogeneous signal

NB The criteria above are intended as a practical guideline and are based on expert opinion by the SAR DFP panel. The panel acknowledges lack of sufficient scientific data regarding imaging criteria for nodal staging in anal cancer

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and CT are the mainstay for staging and detection of distant metastases in patents with anal cancer. As MRI for initial staging of anal canal cancer is becoming more widely utilized, it is important for radiologists to be familiar with the anatomy of the anal canal, be able to optimize MR imaging technique for this particular tumor and its location, and be comfortable with TNM staging including local lymph node drainage patterns. Additionally, as radiology is increasingly moving towards structured or synoptic reporting, we propose an MRI template which can be used to accurately convey useful information to our clinical colleagues.

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