

# Diagnosis and Diagnostic Imaging of Anal Canal Cancer



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## KEYWORDS

- Anal canal cancer
- Magnetic resonance imaging
- 18F-fluorodeoxyglucose positron emission tomography
- Anoscopy
- Endoanal ultrasound

## KEY POINTS

- Anal canal cancer can present with rectal bleeding, pain, or change in bowel habits and is often a delayed diagnosis owing to the similarity of symptoms to common benign conditions.
- Staging procedures for anal canal cancer can include anoscopy, biopsy, computed tomography, MRI, endoanal ultrasound imaging, and/or 18F-fluorodeoxyglucose-PET.
- Imaging modalities for detection, staging, evaluation of treatment response and surveillance of anal canal cancer are sensitive and robust.

## INTRODUCTION

Anal canal cancer is a relatively uncommon malignancy, with an incidence of approximately 30,000 cases annually worldwide.<sup>1</sup> Owing to the unique location and anatomy of this malignancy, careful examination and diagnostic procedures are necessary for optimal staging and treatment. This article focuses on the underlying anatomy of the anorectal region, important imaging characteristics of the anus, common clinical presentations of anal canal cancer, and the diagnostic procedures required for adequate staging and treatment of this cancer type.

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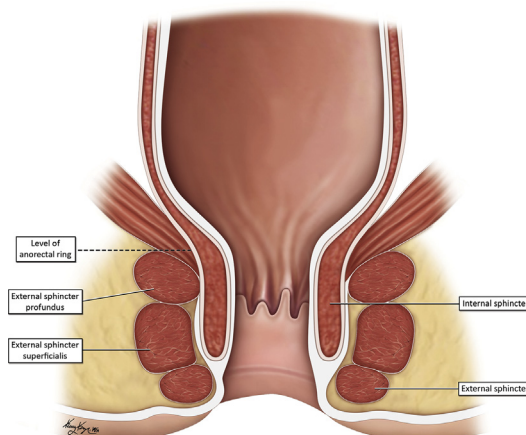
## ANATOMY OF THE ANUS

The anus drains the last 3 to 5 cm of the gastrointestinal tract through the internal and external anal sphincters, extending from the dentate line to the anal verge and perineum (**Fig. 1**). The anatomic anal canal goes from the dentate line or valves of Morgagni to the anal verge (**Fig. 2**). The surgical anal canal is longer than the anatomic canal and starts at the level of the anorectal ring just above the anal columns of Morgagni and extends to the anal verge or margin.<sup>2</sup> The muscular wall of the rectum, the muscularis propria, is covered with columnar epithelium. This columnar epithelium overlies the upper one-half or two-thirds of the internal sphincter and internal hemorrhoid plexus. The lining changes from columnar to transitional epithelium and at the free edge of the columns of Morgagni to squamous epithelium. The irregular junction indicates the dentate or pectinate line, with biopsy showing islands of squamous epithelium in between columnar epithelium.<sup>2</sup>

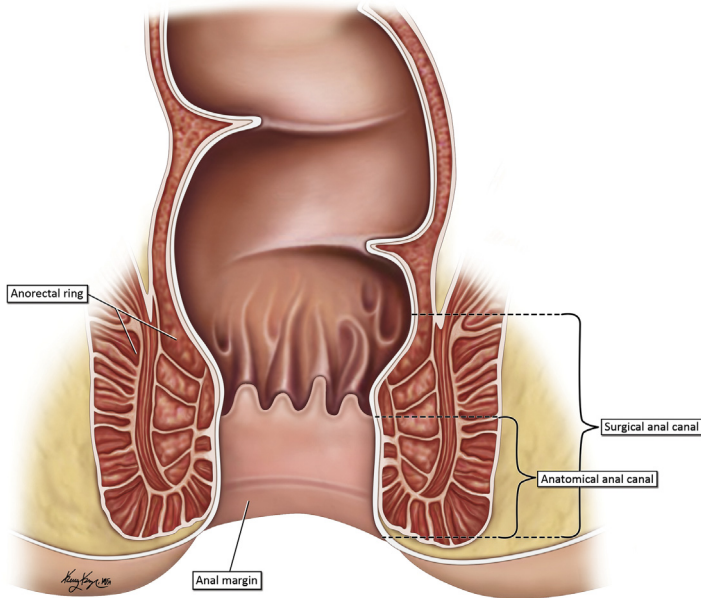
The inner circular muscle of the muscularis propria becomes the internal sphincter in the anus and is covered by squamous epithelium. The conjoined longitudinal muscle of the muscularis propria becomes the intersphincteric plane. The external sphincter complex is composed of the most inferior part of the levator ani muscle, the puborectalis sling, and the external sphincter muscles. The upper border of the puborectalis sling forms the upper edge of the surgical anal canal. True squamous skin with sweat glands and hair follicles covers the anal verge.<sup>3,4</sup>

## CLINICAL PRESENTATION

Patients diagnosed with anal canal cancer often present with anorectal pain or bleeding, but these symptoms occur in only approximately one-half of patients. Other clinical manifestations of anal canal cancer include anorectal fullness, pruritus, and change in bowel habits.<sup>5,6</sup> More advanced tumors can cause fecal incontinence or weight loss. Many patients with anal cancer come to the attention of physicians with complaints of hemorrhoidal-type bleeding or pain, and about one-half are not diagnosed until more than 24 months after symptom onset.<sup>6</sup> Because the symptoms of anal cancer can mimic those of more common, benign conditions, the diagnosis of anal cancer is often delayed. In some cases, patients are entirely asymptomatic from their anal cancer.



**Fig. 1.** Anatomy of the anal canal, including relevant musculature. (Courtesy of Kelly M. Kage, BS, MFA, University of Texas MD Anderson Cancer Center, Houston, TX.)



**Fig. 2.** Anatomy of the anatomic and surgical anal canal. (Courtesy of Kelly M. Kage, BS, MFA, University of Texas MD Anderson Cancer Center, Houston, TX.)

Patients being evaluated for anal cancer should have a thorough history of potential risk factors taken, including human immunodeficiency virus (HIV)/AIDS, non-HIV-related immunosuppression, organ transplantation, chronic steroid use, receptive anal intercourse, cigarette smoking, and human papilloma virus infection.<sup>7</sup> In addition to these, a history of cervical, vulvar, or vaginal cancer can be a significant risk factor as well. In high-risk populations, some advocate for anal cancer screening to decrease the incidence of anal cancer,<sup>8</sup> although no formal guidelines currently exist for routine anal cancer screening.

## DIAGNOSIS AND PROCEDURES

In patients with worrisome anorectal complaints, a thorough physical examination, including visual inspection of the perirectal area and a digital rectal reexamination, must be undertaken. A digital rectal reexamination can identify the primary lesion, determine whether there is sphincter invasion, and/or fixation of the tumor, and identify perirectal lymphadenopathy, if present.<sup>9</sup> In addition, the presence or absence of inguinal lymphadenopathy must be assessed. After a complete physical examination has been performed, histologic diagnosis of anal cancer is generally determined through biopsies obtained during an examination under anesthesia with anoscopy or proctosigmoidoscopy; this is also often necessary to ensure patient tolerance of a complete examination.<sup>9</sup> Further information about the primary tumor, such as anal cancer size, depth, sphincter involvement, and local lymph node involvement, can be elicited from endoanal ultrasound or MRI, if desired.<sup>10–12</sup>

With respect to MRI, the recent widespread success of this imaging modality for rectal cancer staging could benefit anal cancer staging given the similar tumor location. In primary rectal cancer, high-resolution T2-weighted imaging is the best MRI

sequence. The T2 sequence consists of thin section (3 mm) axial images obtained orthogonal to the tumor plane, with an in-plane resolution of 0.5 to 0.8 mm. This technique allows differentiation between rectal tumors confined within the rectal wall (stage T2 tumors) and those that extend beyond the muscularis propria (stage T3 tumors). Most important, the depth of invasion outside the muscularis propria can be assessed with a high degree of accuracy.<sup>13</sup> In addition, high-resolution T2-weighted images allow the morphologic assessment of pelvic nodes, thereby improving accuracy in the characterization of nodes as benign or malignant, because size criteria have proved to be of limited value.<sup>3,14</sup> Furthermore, MRI may be better for localization of suspicious lymph nodes outside of the field of view of endoscopic ultrasound imaging.

Once evaluation of the primary tumor has been completed, computed tomography of the chest, abdomen, and pelvis should be performed to evaluate for lymphadenopathy and distant metastasis. Any clinically enlarged or radiographically abnormal inguinal lymph nodes must be histologically evaluated through biopsy, as this determines staging and potential radiation dosing required. 18F-fluorodeoxyglucose PET/computed tomography can also identify suspicious lymph nodes or distant metastases not detected by physical examination,<sup>15,16</sup> and pretreatment PET/computed tomography maximum standardized uptake value is strongly associated with primary tumor stage and histology.<sup>17</sup> Future hybrid PET-MRI scanners may improve the diagnostic performance of 18F-fluorodeoxyglucose PET.<sup>18</sup>

In addition to imaging, patients with a new diagnosis of anal cancer should undergo basic laboratory studies, including a complete blood count, renal and hepatic function tests, and HIV status, if not already known. Women should also undergo a Papanicolaou test to screen for precancerous and cancerous lesions in the cervix, and men should undergo penile examination to exclude premalignant or malignant lesions there as well.

## **ANORECTAL ANATOMY AND IMAGING**

### ***The Sphincter Complex and Pelvic Floor***

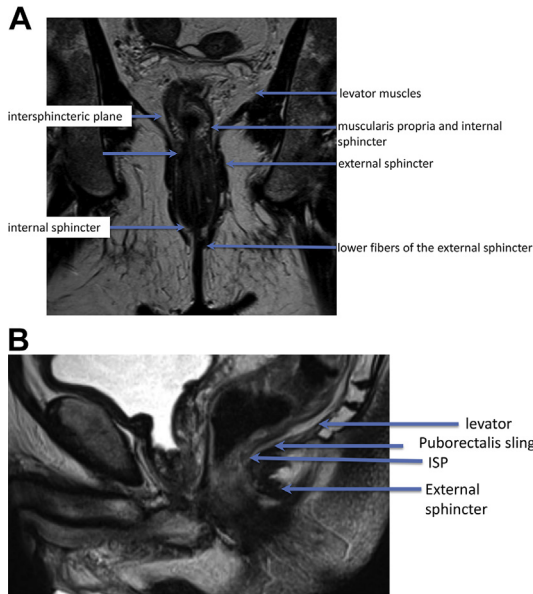
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The continuity of the muscularis propria and internal sphincter is well depicted on a coronal MRI (**Fig. 3A**). The intersphincteric plane that separates internal sphincter from the somatic muscle “sheet” is contiguous with the external sphincter. The most proximal portion of this sheet is made up of the levator muscles, which are attached at the sacrum, lateral pelvic sidewall, and symphysis pubis to form a hammocklike muscular diaphragm of the pelvic floor. The most distal fibers of the levator blend with the uppermost fibers of the puborectalis muscle (**Fig. 3B**). The latter forms a sling that creates the acute angle of the anorectal junction and is anchored to the inferior pubic rami. Fibers of the puborectalis sling in turn blend with the external sphincter. The lower fibers of the external sphincter terminate 3 to 4 mm below the internal sphincter at the anal verge.

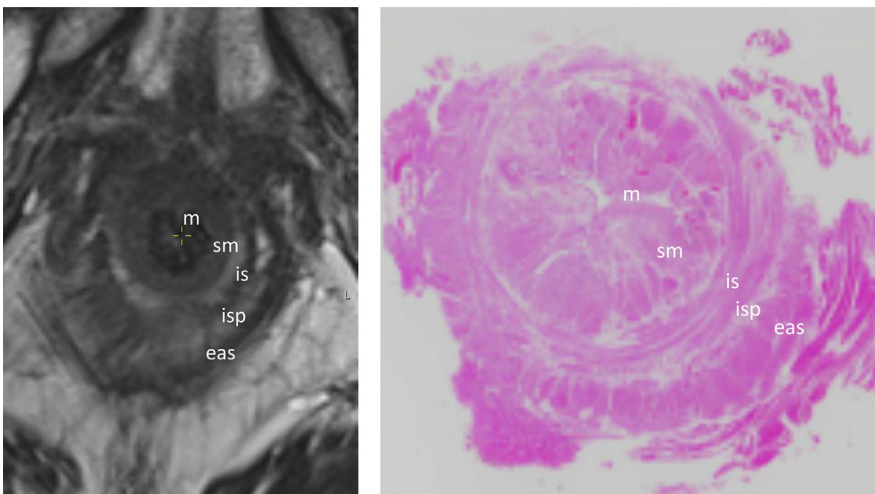
### ***The Anal Canal***

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The surface mucosal layer in the anal canal is less than 1 mm in thickness and is seen as a discrete, low signal intensity layer. Below this is the thicker submucosal layer containing lymphatics and vasculature, which is of intermediate signal intensity compared with fluid or muscle and has a thickness of several millimeters. The internal sphincter is a thin, 1- to 2-mm layer of low signal intensity that is contiguous with the muscularis. Below the level of the lowermost fibers of the internal sphincter, the anal canal forms the vertical columns of Morgagni, marking the junction between columnar and squamous epithelium (**Fig. 4**).



**Fig. 3.** (A) The continuity of the muscularis propria and internal sphincter is well depicted on a coronal MRI. The intersphincteric plane that separates internal sphincter from the somatic muscle “sheet” that is contiguous with the external sphincter. (B) Sagittal MRI showing the levator muscles attached at the sacrum the most distal fibers of the levator blend with the upper most fibers of the puborectalis muscle. Fibers of the puborectalis sling in turn blend with the external sphincter.



**Fig. 4.** Anatomy of the anal canal on high resolution MRI with corresponding hematoxylin and eosin histopathology. eas, external anal sphincter; is, internal sphincter; isp, intersphincteric plane; m, mucosa; sm, submucosa

### Adjacent Structures

The anatomic hindgut is separated from the anterior visceral compartment by the urogenital septum (a fibromuscular embryonic remnant; **Fig. 5A**). Inferiorly, the horizontal fibers of the transverse perineal muscle separate the anal canal from the urethra in females (**Fig. 5B**) and the crus of the penile bulb in males. More superior, the septum separates the anal canal wall from the apex of prostate and distal vagina in males and females respectively. Laterally, the obturator internus muscles are separated from the lower anal canal by the ischioanal fossa containing fat and the lymphatics and vascular branch supply and drainage to the external sphincter complex.

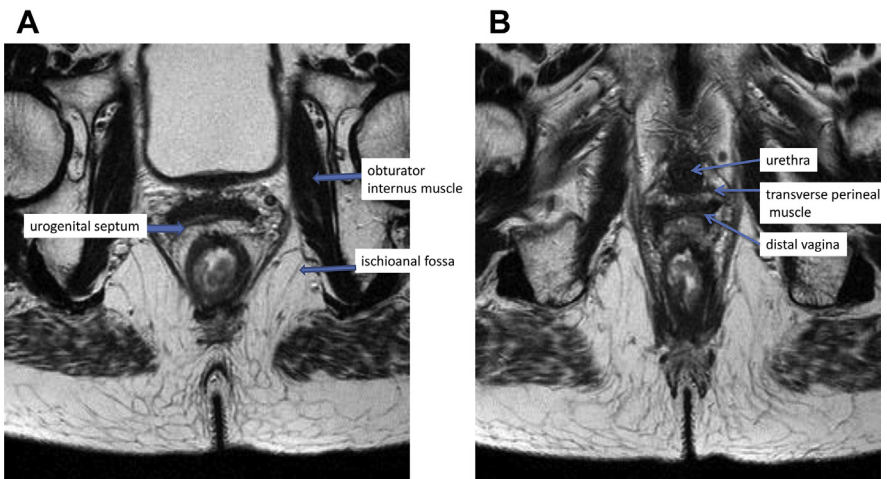
### STAGING

Staging of anal canal cancers follows the American Joint Committee on Cancer/Union Internationale Contre le Cancer system and is determined by size of the primary tumor, presence of local invasion, presence of regional lymphadenopathy, and presence of metastatic disease (**Table 1**).<sup>19</sup> In a study of 19,199 patients with anal carcinoma diagnosed between 1985 and 2000, 25.3% were stage I, 51.8% were stage II, 17.1% were stage III, and 5.7% were stage IV at the time of diagnosis.<sup>20</sup> Staging clearly impacts necessary treatment and prognosis in this tumor type.

### IMPACT OF IMAGING ON STAGING OF ANAL CANAL CANCER

#### Primary Anal Cancer Staging by Imaging

Primary invasive anal cancer is readily depicted on high-resolution MRI as an intermediate signal intensity mass. Most commonly, as with rectal adenocarcinoma, these lesions tend to present as annular or semiannular infiltrating mass lesions and arise within the anal canal (**Fig. 6A**). On occasion, squamous cell carcinoma presents higher and above the anorectal junction, but the TNM classification for squamous cell carcinoma is still used. This separates prognosis according to the maximum length of the tumor. It was originally derived for classification of tumor length by digital rectal examination, but the advent of high-resolution MRI has made it easier to provide objective



**Fig. 5.** (A) Embryology and resultant development of the anal canal. (B) Anatomy of the female anal canal.

Table 1 Staging of anal canal cancer			
AJCC Stage	Primary Tumor (T) Stage	Lymph Node Status (N)	Distant Metastasis (M)
I	T1	N0	M0
II	T2	N0	M0
	T3	N0	M0
IIIA	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
	T4	N0	M0
IIIB	T4	N1	M0
	Any T	N2	M0
	Any T	N3	M0
IV	Any T	Any N	M1

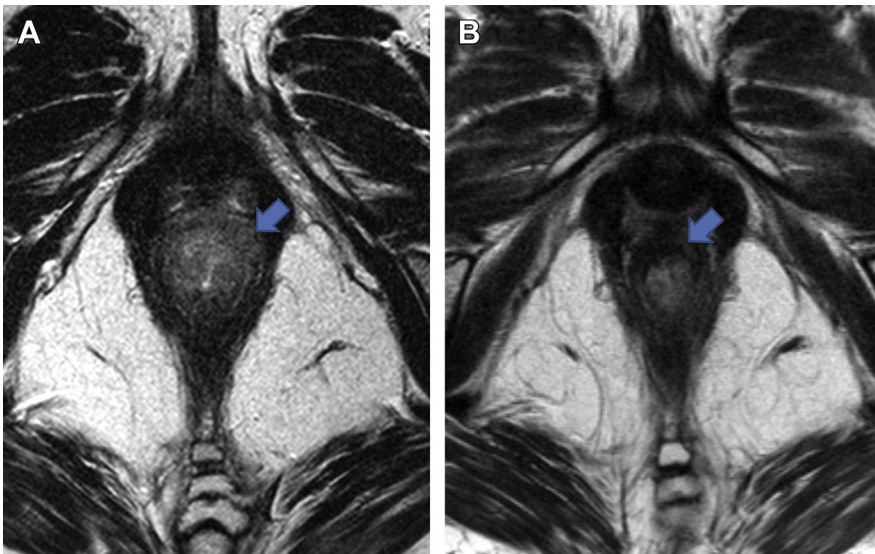
Primary tumor staging of anal canal cancer: T1:  $\leq 2$  cm in greatest dimension, T2:  $2 <$  tumor  $< 5$  cm in greatest dimension, T3:  $> 5$  cm in greatest dimension, T4: tumor that invades adjacent organs (vagina, urethra, bladder, prostate).

Nodal staging of anal canal cancer: N0: no regional lymph node metastasis, N1: metastasis in perirectal lymph node(s), N2: metastasis in unilateral internal iliac and/or inguinal lymph node(s), N3: metastasis in perirectal and inguinal lymph nodes and/or bilateral internal iliac and/or inguinal lymph nodes.

Distant Metastatic Staging of Anal Canal Cancer: M0: no distant metastasis, M1: distant metastasis.

*Abbreviation:* AJCC, American Joint Committee on Cancer.

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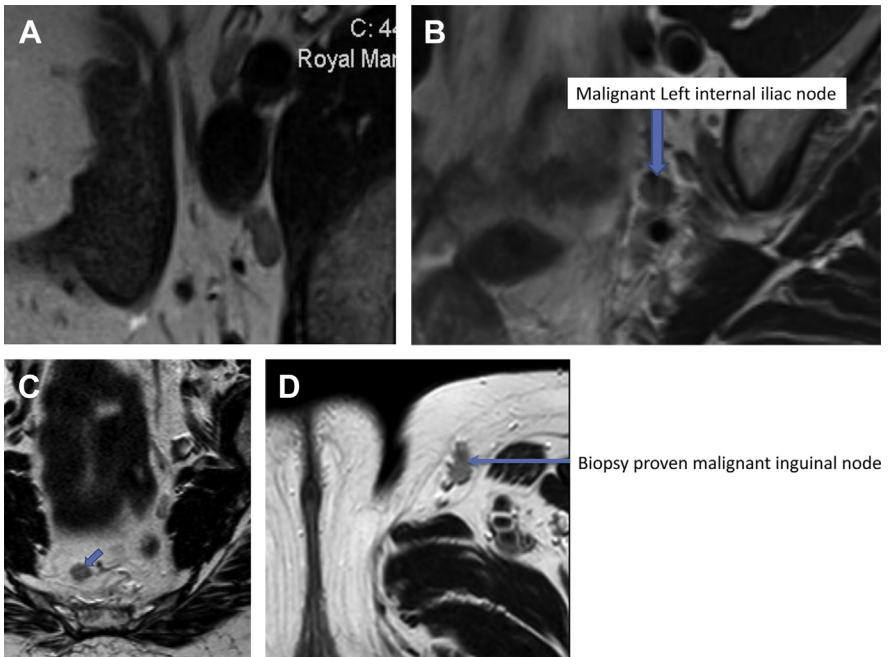


**Fig. 6.** (A) Axial high-resolution MRI in a female patient with a newly diagnosed anal cancer. The primary tumor is seen as a semiannular mass of higher signal intensity (*arrow*) than the anal sphincter and occupies the anterior quadrant. There is extramural spread of 11 mm at the 2 o'clock position which infiltrates inner fibers of left puborectalis and posterior wall of the vagina. (B) After chemoradiotherapy, the treated tumor/scar is present in the anterior quadrant (*arrow*). There is no longer any abnormal intermediate signal intensity to indicate residual active tumor and the sphincter anatomic layers, puborectalis and vagina show no evidence of disruption by tumor signal.

measurement. Because chemoradiotherapy is the mainstay of treatment, an accurate anatomic depiction of the radial as well as craniocaudal extent of tumor enables optimal radiotherapy planning and permits a baseline series of imaging for comparison with posttreatment scans to verify response and to monitor the treated tumor and nodal deposits for any suspected recurrence (Fig. 6B).

### ***Nodal Spread of Anal Canal Cancer***

Nodal spread in anal cancer can be challenging, particularly if perianal inflammation results in reactive lymphadenopathy. Both benign reactive nodes (Fig. 7A) and malignant nodes (Fig. 7B–D) regress after chemoradiotherapy, and so disappearance of nodes cannot be used as an indicator. Reliance on size criteria is also known to result in overestimation of nodal spread, and the most accurate results are achieved by evaluating the morphologic characteristics that are associated with metastatic infiltration. Nodal infiltration by tumor can result in a breach of the normally smooth lymph node capsule, leading to spiculated irregularity of the node border. Squamous cell infiltration in nodes is often associated with necrosis, which will result in focal high signal intensity within the node giving rise to mixed signal intensity characteristics. Inguinal nodal enlargement is a frequent finding but not always related to malignancy, so targeted ultrasound guided fine needle aspiration of inguinal nodes is a helpful and relatively straightforward means of determining the inguinal nodal status. MRI assessment should include high resolution evaluation of the mesorectal nodes up to the L5/S1 level, the inguinal nodal territory and the external, obturator fossa, internal iliac nodes and common iliac nodes. These are all classified as locoregional lymph nodes but the N stage grouping depends on the sites of nodal spread.



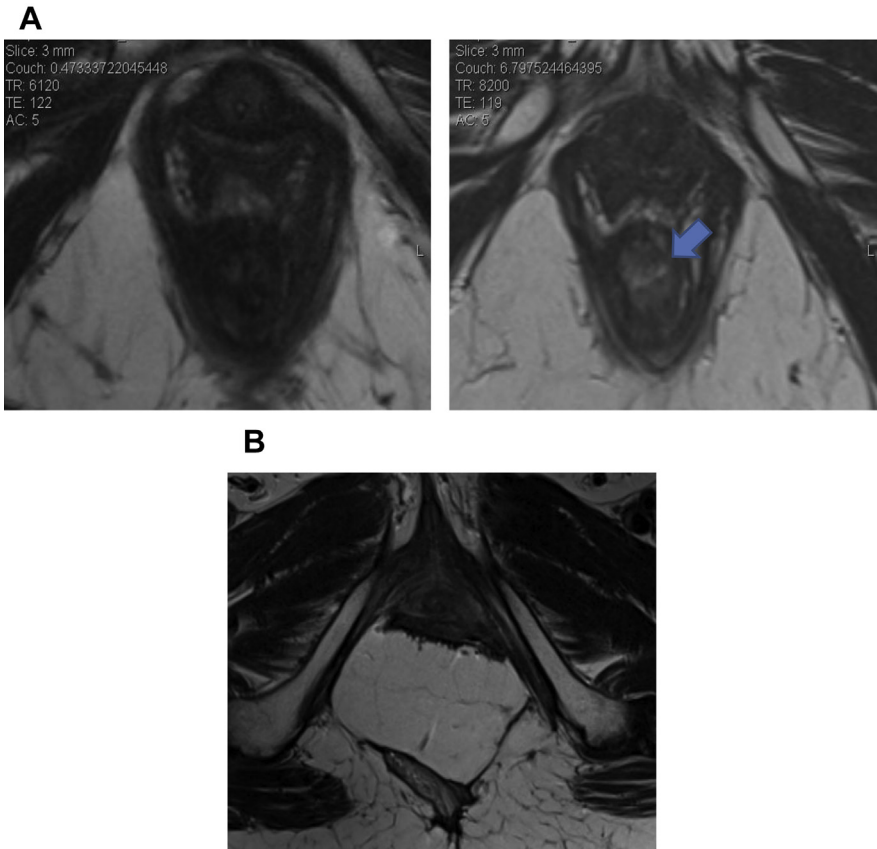
**Fig. 7.** (A) Benign reactive lymph nodes. (B) Malignant left internal inguinal lymph node (arrow). (C) Malignant mesorectal lymph node characterized by nodal capsule irregularity (arrow). (D) Biopsy-proven malignant inguinal lymph node.



## IMAGING CHARACTERISTICS OF CLINICAL OUTCOMES

### *Imaging Appearances After Treatment*

Traditional imaging has been undertaken at 3 months from the completion of chemoradiotherapy, when treatment related fibrosis established and the low signal intensity of fibrosis can be more readily distinguished from the intermediate signal intensity of residual tumor (Fig. 8A). It is now recognized that anal cancers may continue to regress after this initial 3-month assessment, and the majority should have fully regressed by 6 months after completion of treatment. The vast majority of tumors respond fully to treatment and require surveillance only. In a minority of patients,



**Fig. 8.** (A) Serial imaging after chemoradiotherapy for squamous cell carcinoma of the anal canal. The images on the left were undertaken as part of annual follow-up and showed treated tumor as demonstrated by a crescentic low signal scar visible at the level of the puborectalis in the anterior quadrant. At a surveillance scan the following year, the low signal intensity scar was no longer visible; there was instead marked thickening and new intermediate signal along the anterior quadrant of the anal canal. The recurrent tumor was infiltrating the muscularis propria but did not extend into the posterior vaginal wall (*arrow*). (B) Postoperative appearance of the anal canal after the patient's surgical excision and flap reconstruction. Histology showed an anterior quadrant ulcerated invasive moderately differentiated squamous cell carcinoma that was present at the anorectal junction. The tumor was present in the submucosa and the muscularis propria but did not extend into the levators or the attached vaginal wall.

the tumor fails to regress and in those instances salvage surgery is required to render the patient disease free. The close proximity of neighboring viscera (prostate, urethra, and vagina) means that radical exenterative surgery with or without radical nodal dissection may be necessary.

### ***Imaging Features of the Pelvis During Surveillance***

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The combination of clinical follow-up assessment, serial imaging, and careful comparison with the initial posttreatment baseline has enabled the earlier diagnosis of recurrence and the consequent radical salvage of pelvic recurrence (see **Fig. 8**). Recurrence within the treated scar can be seen as reemergence of intermediate signal intensity in or around the tumor scar. Emergence of new or progressively enlarging nodes is also readily diagnosed on surveillance MRI and may be treated with radical intent. Imaging is also helpful in the diagnosis of some of treatment related complications, such as fistula formation and insufficiency fracture.

### **SUMMARY**

Anal canal cancer is a tumor type that depends on accurate anatomic staging for optimal treatment planning and cure. In addition to standard diagnostic procedures, including history and physical, laboratory assessment, and endoscopy, modern radiologic imaging techniques are extremely helpful in the assessment of this cancer. The use of multiple robust radiographic modalities has improved staging, response evaluation, and surveillance of this cancer.

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