

Magnetic Resonance Imaging of Penile Cancer

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KEYWORDS

• Penile cancer • MR imaging • Penile imaging • Staging

KEY POINTS

- Penile cancer, although rare in the developed world, has devastating physical and psychological consequences for the patient.
- MR imaging accurately delineates the penile anatomy and is the imaging modality of choice of accurate local staging of primary penile cancer.
- Novel MR imaging techniques such as lymphotropic nanoparticle-enhanced MR imaging may help identify metastatic lymph node disease.

INTRODUCTION

Penile cancer is a rare neoplasm with devastating physical and psychological consequences for patients. There is a wide regional variation in the incidence of penile cancer throughout the world ranging from less than 1 case per 100,000 men in Europe and the United States, to 8.3 cases per 100,000 in Brazil, to even higher in Uganda.¹ In the United States, it is estimated that there will be 1640 new cases of penile cancer and 320 cancer-related deaths in 2014.² Penile cancer tends to be a disease of older men. There is an abrupt increase in incidence in men aged approximately 60 years and the incidence peaks in men aged 80 years.

This article reviews the normal penile anatomy, MR imaging techniques for evaluation of the penis, and MR imaging features of primary and metastatic penile cancer. Recent advances in penile cancer imaging are discussed.

ANATOMY

The anatomy of the penis has important implications for the diagnosis and treatment of penile cancer. The penis can be divided into root and body. The root of the penis is located in the superficial perineal pouch and is the primary fixation point. The body of the penis is composed of three tubular endothelium-lined cavernous structures: paired corpora cavernosa, located on the dorsolateral aspect of the penis, and a single corpora spongiosum located in the midline ventrally (Fig. 1). The corpus spongiosum contains the urethra and extends anteriorly to form the glans penis. The three corpora of the penis are covered by three connective tissue layers. The innermost layer is fibrous tunica albuginea. The middle layer is the Buck fascia, a fibrous layer that surrounds the corpora cavernosa and separates them from corpora spongiosum. External to this is a layer of loose connective tissue that is covered by dartos fascia.

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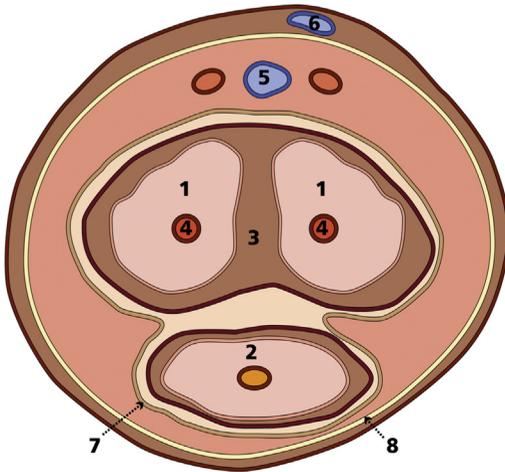


Fig. 1. Normal penile anatomy (*axial view*). 1, corpora cavernosa; 2, corpus spongiosum; 3, tunica albuginea; 4, cavernosal arteries; 5, deep dorsal vein; 6, superficial dorsal vein; 7, Buck fascia; 8, dartos fascia.

MR IMAGING

Patient positioning is paramount in MR imaging of the penis. Patient is imaged in a supine position. To elevate the scrotum and penis, a folded towel is placed between the patient's legs. The penis is taped to the abdomen in a dorsiflexed position to prevent movement and pulsation artifacts. A surface coil is placed on the penis to improve signal-to-noise ratio.

Scardino and colleagues³ suggested that MR imaging with artificial erection, achieved by injecting 10 μ g of prostaglandin E1 into the corpus cavernosum, provides a more robust local staging of the penile cancer. Artificial erection is routinely used at the authors' institute for MR imaging of the penis. However, this is avoided if there is large and painful penile tumor because of the increased risk of priapism. The MR imaging sequences used are (1) T1-axial images of the pelvis, which provide an overview of the pelvis and lymph nodes and (2) T2-axial, sagittal, and coronal images of the penis (**Box 1**). Gadolinium-enhanced sequences are not routinely used at the authors' institute. The three corpora of the penis demonstrate intermediate T1 and high T2 signal on MR imaging. Relative to the corpus spongiosum, the muscular wall of the urethra appears hypointense on both T1-weighted and T2-weighted sequences. Tunica albuginea, Buck fascia, and dartos fascia show low signal intensity on all MR imaging sequences. Tunica albuginea and Buck fascia cannot reliably be differentiated on MR imaging and appear as a hypointense rim of tissue around the corpora. T2-weighted imaging demonstrates a greater

Box 1

MR imaging protocol for penile cancer

Adequate patient positioning.

Artificial erection: injection of 10 μ g of prostaglandin E1 into the corpus cavernosum.

MR imaging Acquisition

Parameters ^a	TR	TE	FOV
T1 Axial Pelvis	679	12	400 ^b
T2 Axial Penis	5720	97	350
T2 Sagittal Penis	3750	100	250
T2 Coronal Penis	3750	100	250

Abbreviations: FOV, field of view; TE, echo time; TR, repetition time.

^a MR imaging acquisition parameters at the authors' institute.

^b Variable based on patient body habitus.

degree of contrast between the corpora and tunica albuginea. MR imaging appearances of normal penis are summarized in **Table 1** and illustrated in **Fig. 2**.

MR IMAGING OF PENILE CANCER

Primary Tumor Imaging

Most penile cancers are squamous cell carcinomas (SCCs). Other reported histologic types of penile malignancies consist of basal cell carcinoma, melanoma, sarcoma, and metastatic lesions. Moreover, several histologic subtypes of SCC have been described, each with unique clinicopathologic characteristics and outcome features.^{4,5} The most common histologic subtype of penile carcinoma is the usual-type SCC.⁶ Most penile tumors originate from the mucosal surface extending from the preputial orifice to the meatus urethralis.⁶ Tumors arising from the glans penis

Table 1

MR appearance of the normal penis

	T1-Weighted MR Imaging	T2-Weighted MR Imaging
Dartos fascia	Hypointense	Hypointense
Tunica albuginea and Buck fascia	Hypointense	Hypointense
Muscular wall of the urethra	Hypointense ^a	Hypointense ^a
Corpora cavernosa and corpus spongiosum	Intermediate	High signal

^a Hypointense relative to corpus spongiosum.

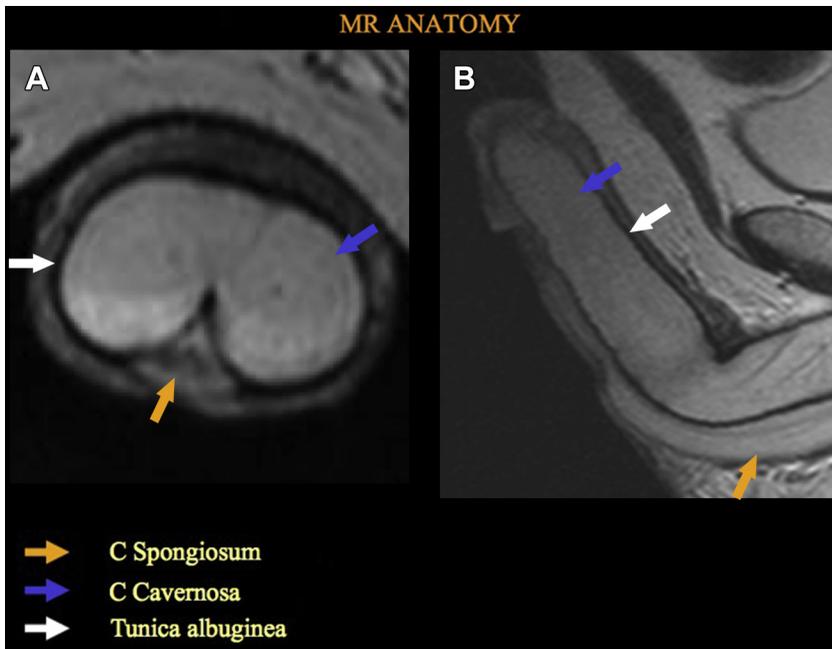


Fig. 2. Axial T2-weighted MR image (A) and sagittal T2-weighted MR image (B) show corpora cavernosa, corpus spongiosum, and tunica albuginea.

are more common than are those involving the foreskin or the sulcus.^{6,7} A recent study of about 5000 cases of invasive penile carcinoma showed that the primary site of disease was the glans penis in 34.5% of cases, prepuce in 13.2%, shaft in 5.3%, and overlapping in 4.5%, with primary site unspecified in 42.5% of cases.⁸ MR imaging is the most sensitive imaging modality for local staging of penile cancer because of its exceptional soft-tissue resolution, multiplanar capability, and excellent spatial resolution in the assessment of superficial structures. On MR imaging, primary penile cancers usually appear as solitary, ill-defined, and infiltrating mass lesions that are hypointense relative to the adjacent corpora on both T1-weighted and T2-weighted images.⁹ MR imaging enables accurate assessment of the local extent of the penile lesion, depth of tumor invasion, and involvement of tunica albuginea and other adjacent structures, including corpora, urethra, and scrotal skin. The international tumor node metastasis (TNM) staging system for penile cancer was last updated in 2009¹⁰ and is used for staging the primary tumor (Fig. 3, Table 2). MR imaging and histology appearances of various T stages of penile cancer are illustrated in Figs. 4–7.

Penile metastatic lesions are rare and most frequently occur from primary tumors in the genitourinary tract or the recto-sigmoid region.

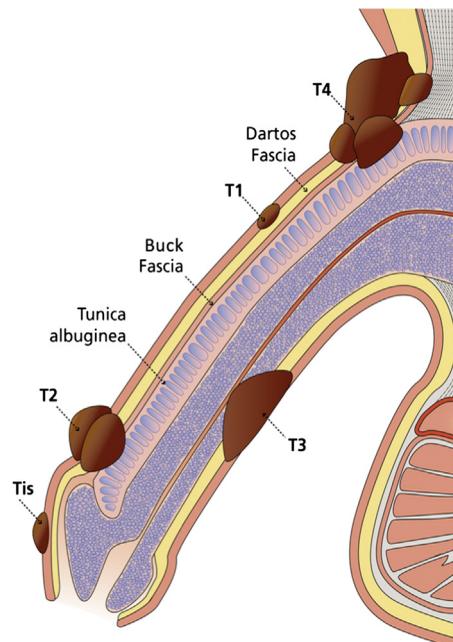


Fig. 3. Local staging of penile cancer. Tis, carcinoma in situ; T1, tumor invades subepithelial connective tissue; T2, tumor invades corpus spongiosum or corpora cavernosa; T3, tumor invades urethra; T4, tumor invades other adjacent structures.

Table 2
TNM classification of penile cancer (2009)

T—Primary Tumor	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Ta	Noninvasive verrucous carcinoma, not associated with destructive invasion
T1	<p>T1a Tumor invades subepithelial connective tissue without lymph vascular invasion and is not poorly differentiated</p> <p>T1b Tumor invades subepithelial connective tissue with lymph vascular invasion or is poorly differentiated</p>
T2	Tumor invades corpus spongiosum or corpora cavernosa
T3	Tumor invades urethra
T4	Tumor invades other adjacent structures
N—Regional Lymph Nodes (Clinical) ^a	
cNX	Regional lymph nodes cannot be assessed
cN0	No palpable or visibly enlarged inguinal lymph nodes
cN1	Palpable mobile unilateral inguinal lymph nodes
cN2	Palpable mobile multiple or bilateral inguinal lymph nodes
cN3	Fixed inguinal nodal mass or pelvic lymphadenopathy, unilateral or bilateral
N—Regional Lymph Nodes (Pathologic) ^b	
pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph metastasis
pN1	Metastasis in a single inguinal lymph node
pN2	Metastasis in multiple or bilateral inguinal lymph nodes
pN3	Extranodal extension of lymph node metastasis or pelvic lymph nodes, unilateral or bilateral
M—Distant Metastasis	
M0	No distant metastasis
M1	Distant metastasis (includes lymph node metastasis outside the true pelvis)

^a Clinical stage definition based on palpation and imaging.

^b Pathologic stage definition based on biopsy of surgical excision.

From Edge S, Byrd DR, Compton CC, et al. AJCC cancer staging manual. New York: Springer; 2010.

However, penile metastases from stomach, lung, and thyroid cancers have been described.^{11,12}

The most common lesions to metastasize to the penis are prostate and bladder cancers.^{9,13} Penile metastatic lesions can be difficult to differentiate from primary penile lesions on MR imaging. Typically, they are seen as multiple masses in the corpora cavernosa and corpus spongiosum where lesions demonstrate low signal intensity compared with to normal corporal tissue on both T1-weighted and T2-weighted images (see Fig. 6B).¹³

Lymph Node Imaging

The most important prognostic factor for survival in patients with penile cancer is the presence and extent of inguinal lymph node involvement.¹⁴ Determining the extent of lymph node involvement influences treatment strategy.¹⁵ Based on the location of the primary tumor, the site of lymph node metastasis can be predicted. Skin and prepuce lymphatics drain into the superficial inguinal lymph nodes, the glans drains into the deep inguinal and external iliac nodes, and corpora and penile urethra drains into the internal iliac nodes. Clinical examination and conventional imaging methods, including ultrasound, CT, and MR imaging, are unreliable in detecting lymph node metastasis. At the time of initial diagnosis up to 30% to 60% of patients with SCC have palpable inguinal lymph nodes,¹⁶ approximately half of which are reactive.¹⁷ Sensitivity of clinical staging of the lymph nodes have been shown to be 40% to 60% with a false-negative rate between 10% and 20%.^{18,19} Abnormal lymph nodes on CT and MR imaging are determined based of lymph node size, which results in underdetection of occult metastasis in normal-sized lymph nodes and increase in false-positive rates in patients with enlarged lymph nodes secondary to infection or inflammation. However, cross-section imaging can detect enlarged retroperitoneal and pelvic lymph nodes not identified by clinical examination.

Prophylactic lymphadenopathy has been shown to improve long-term survival.^{19–21} Recently, Ornellas and colleagues¹⁴ have shown a disease-free survival rate of 71% for subjects who underwent immediate lymphadenectomy compared with those who had a delayed lymphadenectomy with a disease-free survival rate of 30%. However, universal use of this procedure would result in overtreatment in 60% to 75% of patients.²² Moreover, it has been reported that inguinal lymphadenectomy is associated with major morbidity, including lymphedema, skin flap necrosis, and a 1% to 3% mortality rate.^{22–25} However, refinement of surgical techniques has reduced the

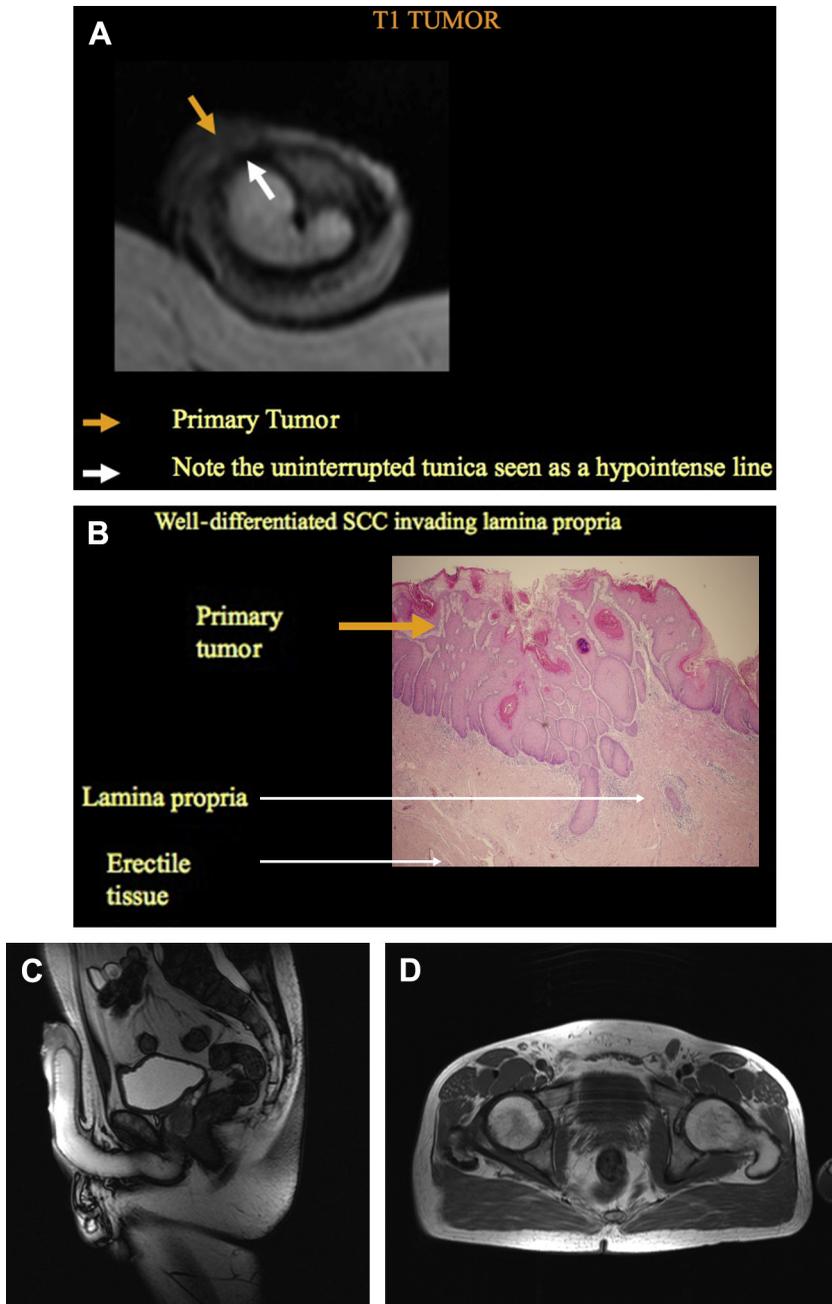


Fig. 4. T1 primary tumor of the penis. T2-weighted axial MR image (A) showing the primary tumor and an uninterrupted tunica albuginea. Histologic specimen (B) from the same patient showing well-differentiated SCC invading the lamina propria. Another patient with sagittal T2-weighted MR image of the penis (C) and axial T1-weighted MR image of the pelvis (D) showing small irregular mass involving the glans penis with intact tunica albuginea and an enlarged left inguinal lymph node (radiological classification: T1, N1).

complication rate by 50%.^{15,26} Reduction in postoperative morbidity has also been achieved by using video endoscopic inguinal lymphadenectomy.²⁷ Novel techniques such as dynamic sentinel lymph

node biopsy result in 70% reduction in the need for radical lymph node dissection,^{28,29} which remains the current gold standard for diagnosis of lymph node metastasis.

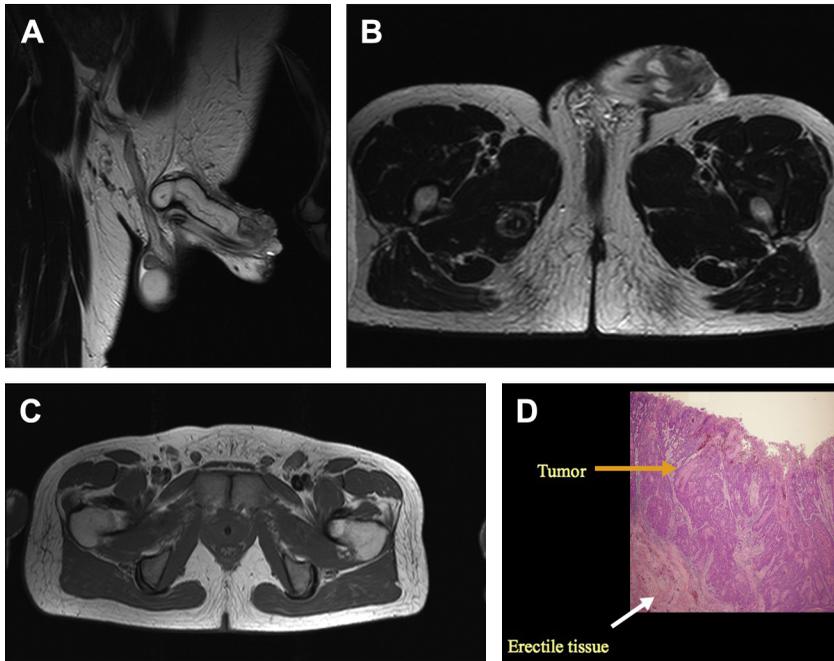


Fig. 5. T2 primary tumor of the penis. Sagittal (A) and axial (B) T2-weighted MR images of the penis showing mass originating from the glans penis. This mass is disrupting the tunica albuginea and invading the corpora cavernosa on both sides. Axial T1-weighted MR image of the pelvis (C) demonstrates bilateral enlarged inguinal lymph nodes (radiological classification: T2, N2). Histologic specimen (D) from the same patient showing moderately differentiated SCC with invasion into corpora cavernosa.

Distant Metastasis Imaging

Less than 3% of patients presenting with penile cancer have metastasis.³⁰ The lungs, liver, and retroperitoneum are the most common sites of metastasis. Distant metastasis generally occurs late in the course of the disease and is associated with a poor prognosis. The histologic subtypes of

penile SCC that are aggressive with high metastatic rates are basaloid, sarcomatoid, and pseudoglandular carcinomas.⁶ Adenosquamous carcinomas frequently metastasize to the inguinal lymph nodes but have a good prognosis. CT is the modality of choice for evaluation of distant metastases.

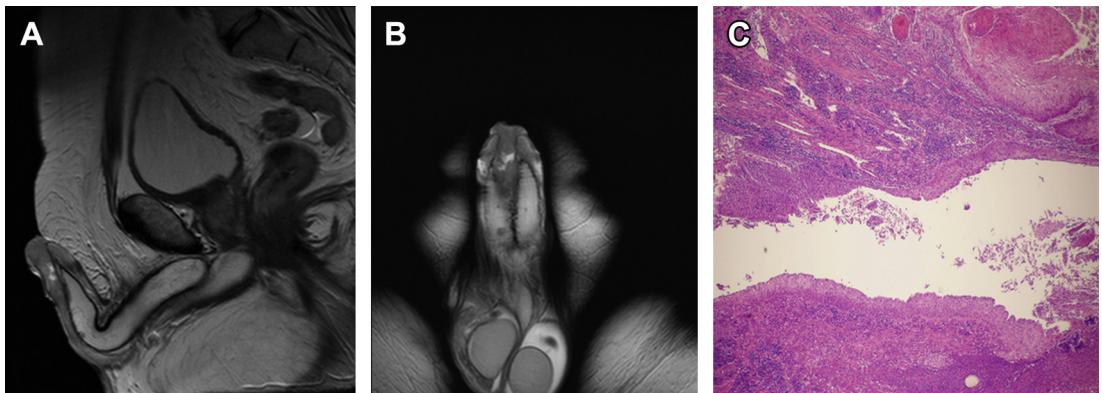


Fig. 6. T3 primary tumor of the penis. Sagittal (A) and coronal (B) T2-weighted MR images of the penis showing soft tissue mass arising in the region of the glans penis and involving the corpus spongiosum and urethra. There is a 6 mm nodule in the right corpora cavernosa. No enlarged inguinal or pelvic lymph nodes were seen (radiological classification: T3, N0, M1). Histologic specimen (C) from the same patient showing invasion of the urethra by the penile SCC.

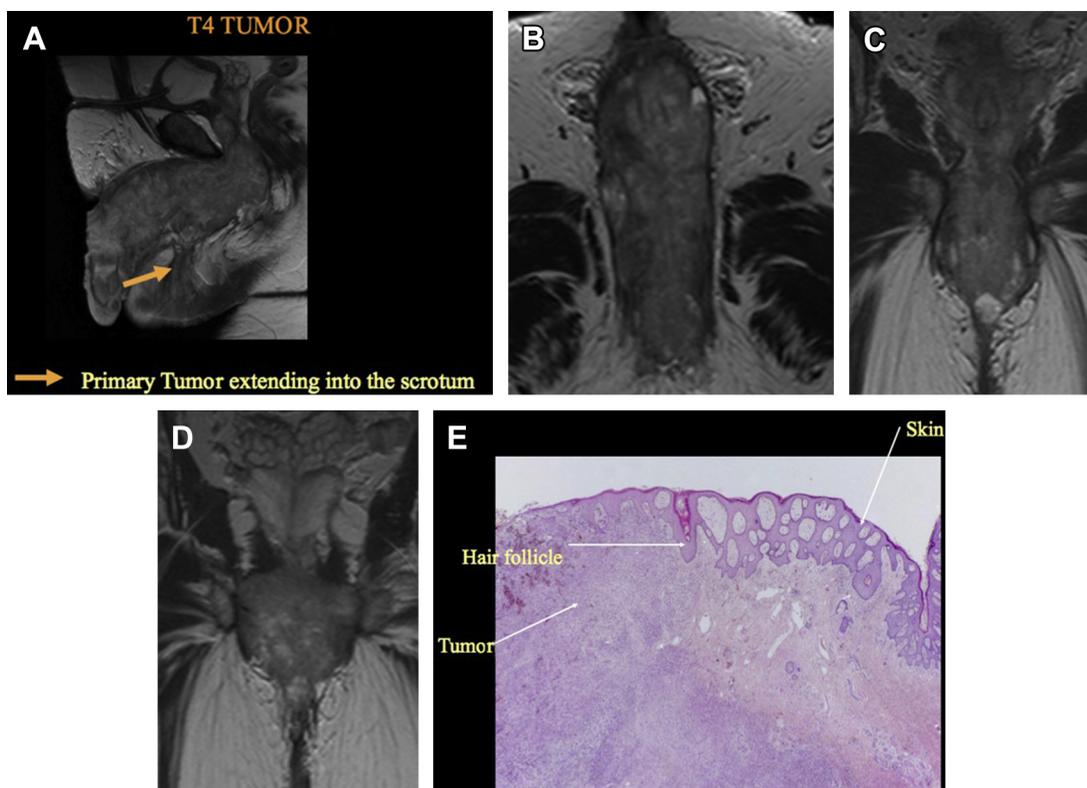


Fig. 7. T4 primary tumor of the penis. Sagittal (A) and coronal (B–D) T2-weighted MR images of the penis showing penile tumor extending into the scrotum (A) and prostate gland (C, D). Histologic specimen (E) from the same patient showing sarcomatoid SCC invading testicular skin.

Novel MR Imaging Techniques

Lymphotropic nanoparticle-enhanced MR imaging has emerged as a promising technique for regional lymph node staging of penile³¹ and various other cancers.^{32–35} This technique uses an infusion of coated ultrasmall iron oxide particles, which are taken up homogeneously by functioning macrophages in normal lymph nodes and demonstrate low signal on gradient echo T2*-weighted images, with only the center being spared in lymph nodes with hilar fat. Metastatic lymph nodes lack the normal phagocytes needed to take up the nanoparticles³⁶ and hence have high signal intensity on gradient echo T2*-weighted images. Using this technique, Tabatabaei and colleagues³¹ demonstrated a sensitivity and specificity of 100% and 97%, respectively, for detection of inguinal lymph node involvement in subjects with penile cancer after assessment of 113 lymph nodes in seven subjects.

SUMMARY

MR imaging is the modality of choice for accurate local staging of penile cancer. Moreover, penile

MR imaging helps detect lymph node involvement and metastatic disease of the penis. Familiarity with optimal imaging protocols, normal penile anatomy, and MR imaging appearances is essential for the radiologist. Emerging techniques may further enhance the abilities of MR imaging to detect lymph node metastasis.

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