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PICTORIAL REVIEW

Diagnosis of recurrent prostate cancer and its mimics at multiparametric prostate MRI

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ABSTRACT

Biochemical recurrence after treatment for prostate cancer (PCa) is a significant issue. Early diagnosis of local recurrence is important for making prompt treatment decisions and is strongly associated with patient prognosis. Without salvage therapy, the average time from development of local recurrence to distant metastasis is approximately 3 years. Biochemical recurrence does not differentiate local recurrence from systemic disease; there is no reliable way to clinically diagnose local recurrence. Recent advances in multiparametric MRI (mp-MRI) techniques have markedly improved detection of local recurrence following therapy. However, a wide variety of entities can mimic recurrent PCa at mp-MRI. Therefore, the purpose of this pictorial review is to discuss the MRI findings of locally recurrent PCa and its mimics, emphasizing the key MRI features that help to differentiate local recurrence from its mimics.

INTRODUCTION

Recent advances in multiparametric MRI (mp-MRI) have markedly improved detection of local recurrence following therapy. Most local recurrences exhibit certain MR features at mp-MRI that make them readily detectable. However, a wide variety of entities can mimic recurrent prostate cancer (PCa) at mp-MRI creating a diagnostic challenge. Following radical prostatectomy, mimics may include, but are not limited to, fibrotic scar, prominent vascular structures, granulation tissue, retained seminal vesicles (SVs) and residual prostatic tissue. After radiation therapy, mimics including focal regions of severe post-treatment changes, well-preserved hypertrophic nodules in the central gland and marked hypertrophic fibromuscular stroma may be encountered. Since the early diagnosis of local recurrence is strongly associated with patient prognosis,¹ recognition of the MRI findings of locally recurrent PCa and its mimics, along with the key MRI features that help to differentiate local recurrence from its mimics, is important in guiding prompt clinical management.

MULTIPARAMETRIC MRI TECHNIQUES

Many different options exist for creating appropriate prostate mp-MRI protocols, including the use of endorectal coils, different *b*-values during diffusion-weighted imaging (DWI) and different acquisition parameters during contrast administration. Guidelines in PI-RADS™ v. 2

provide a detailed description of the protocol and also include a specific aim to establish minimum acceptable technical parameters for prostate mp-MRI.²

At our institution, prostate mp-MRI is performed with a 1.5-T whole body unit and an endorectal coil. The standard protocol includes *T*₂ weighted sequences (T2WI) acquired in axial, coronal and sagittal planes covering the SVs and prostate at 3-mm section thickness. DWI is acquired with 3 *b*-values (10, 400, 1000 s mm⁻¹), and the apparent diffusion coefficient is calculated. Dynamic contrast-enhanced MRI (DCE) images are obtained utilizing a gadolinium-based contrast agent with 26 time points during a 4-min period, so each time point is acquired in less than 10 s. DCE MRI images are acquired immediately as the contrast injection begins. If an early enhancing lesion exhibits >20% wash-out of contrast 4 min after administration of IV contrast, the lesion will be red in colour on most available DCE MRI post-processing software.

KEY FEATURES OF RECURRENT PROSTATE CANCER AT MULTIPARAMETRIC MRI

Multiple options currently exist for the treatment of newly diagnosed, clinically localized PCa. Radical prostatectomy has been the most commonly used treatment for healthy males younger than the age of 70 years, with organ-confined PCa. External beam radiation therapy in combination with

Figure 1. Recurrent prostate cancer in the surgical bed. The patient is status post radical prostatectomy with a slowly rising prostate-specific antigen to 0.7. (a) Axial T_2 shows a soft-tissue mass (arrows) in the surgical bed with slightly high T_2 signal intensity. (b) Diffusion-weighted imaging ($b = 1000$) demonstrates the lesion (arrows) in the surgical bed with high-signal intensity indicating diffusion restriction. (c) Dynamic contrast enhanced MRI demonstrates the lesion (arrows) in the surgical bed with contrast wash-in and wash-out. All findings are consistent with local recurrence.

androgen-deprivation therapy is a standard approach for intermediate- and high-risk PCa. Prostate brachytherapy is most commonly used as monotherapy for patients with low- or intermediate-risk PCa.³ Recently, focal therapies including cryotherapy, high-intensity focused ultrasound and laser treatment have emerged. In those patients in whom focal therapy is utilized for cure, the disease should be low risk and low volume in a targetable area of the prostate.⁴ Even when appropriate treatment is chosen for the patient, local recurrence may occur.

Following radical prostatectomy

Recurrent PCa in the surgical bed following radical prostatectomy is common.⁵ Early detection of local recurrence is important because these recurrences can be treated by external radiation with good response. A focus of soft tissue in the prostate surgical bed demonstrating slightly high T_2 signal compared with the pelvic muscles with contrast wash-in and wash-out at DCE MRI is suggestive of local recurrence (Figure 1).⁶ The feature of contrast wash-in and wash-out at DCE MRI is the most important finding since diffusion-weighted images may be degraded owing to surgical clips, and a small focus of soft tissue at T2WI may not be seen at an early stage. In other words, some recurrences may not be appreciated

owing to small size. In these cases, abnormal enhancement may be the only sign of disease recurrence.

Following radiation therapy

Recurrent PCa in patients after radiation therapy is also common.⁷ Accurate localization of focal recurrence allows for possible salvage radiation therapy and reduced target volume.⁸ Post-treatment changes of the irradiated prostate, including diffuse low T_2 signal and indistinctness of the peripheral, central and transition zones, make detection difficult especially on T2WI.⁹ Placement of internal radiation seeds results in degradation on T2WI and diffusion-weighted images. Given these challenges, it is important to be familiar with features of focal recurrence at mp-MRI. A mass-like lesion with low T_2 signal intensity, commonly in the same location of the pre-treatment tumour, and demonstrating early arterial enhancement with rapid wash-out at DCE MRI, with or without diffusion restriction, is highly suggestive of recurrent cancer (Figure 2).^{6,9,10}

Following focal therapy

Cryotherapy, high-intensity focused ultrasound and laser treatment are focal therapies that have received increased attention in recent years. At the site of focal treatment, a heterogeneous, but

Figure 2. The patient is status post external beam radiation therapy with recent elevation of prostate-specific antigen to 2.4. (a) Axial T_2 weighted sequence demonstrates a low T_2 signal intensity lesion (arrow) in the left apex of the peripheral zone. (b) Apparent diffusion coefficient map demonstrates diffusion restriction of the lesion (arrow) in the left apex of the peripheral zone. (c) Dynamic contrast enhanced MRI demonstrates rapid contrast wash-in and wash-out of the lesion (arrow). Target biopsy confirmed recurrent prostate cancer Gleason score 7.

Figure 3. Recurrent prostate cancer (PCa) in the central gland. The patient is status post cryotherapy with recent elevation of prostate-specific antigen to 1.5. (a) Axial T_2 weighted sequence demonstrates a homogeneous T_2 isosignal intensity lesion (arrow) in the central gland. The entire prostate (P) is deformed secondary to the prior cryotherapy. (b) Dynamic contrast enhanced MRI demonstrates rapid contrast wash-in and wash-out of the lesion (arrow) in the central gland. (c) Apparent diffusion coefficient map demonstrates diffusion restriction of the lesion (arrow) in the central gland. Ultrasound/MRI fusion biopsy confirmed recurrent PCa Gleason score 8.

predominantly low T_2 signal intensity area, may be seen with no or heterogeneous enhancement.⁶ Residual or recurrent PCa following focal therapy will exhibit a mass effect, along the edge of the prior treatment with low T_2 signal intensity, diffusion restriction and rapid contrast wash-in and wash-out (Figure 3).⁶ Knowledge of the location of previous tumour and the ability to compare the pre-treatment MRI to the post-treatment MRI may play an important role in the follow-up of patients with prior focal therapy. Of note, follow-up mp-MRI over a 6-month period after focal therapy such as high-intensity focused ultrasound may provide important information about the completeness of tumour ablation and early post-treatment changes.¹¹

Recurrent PCa following various types of treatment may be difficult to diagnose due to extensive post-treatment changes. When a local recurrent PCa is suspected on mp-MRI, an imaging (MRI or US/MRI fusion)-guided prostate biopsy may be useful in confirming the diagnosis and providing guidance for local salvage treatment. Of course, the local salvage treatment only will be performed when clinicians are certain that there are no distant metastases present. Choline positron emission

tomography-CT is a sensitive test in excluding distant metastasis, such as those in lymph nodes or bones, in these patients.

Since T2WI and DWI images are often degraded due to post-treatment changes, surgical clips and radiation seeds, DCE MRI commonly plays the most important role in detecting a local recurrence. If the DCE MRI protocol is suboptimal, due to scanning delay following IV contrast infusion or prolonged (>15 s) image acquisition for each time point, a local recurrence may be missed. The key MR features of recurrence at mp-MRI are summarized in Table 1.

MIMICS OF RECURRENT PROSTATE CANCER

Mimics following radical prostatectomy

Fibrotic scar

Fibrotic scar is commonly present in the surgical bed appearing as a soft tissue focus mimicking a recurrence. The key

Figure 4. Fibrotic scar mimicking prostate cancer. The patient is status post radical prostatectomy with a slowly rising prostate-specific antigen to 0.4. Axial T_2 demonstrates a low T_2 signal intensity mass (arrow) similar to that of the adjacent muscle (M) in the left side of the surgical bed without enhancement at dynamic contrast enhanced MRI (not shown) consistent with fibrotic scar.

Table 1. Typical MR features of recurrent prostate cancer (PCa) at multiparametric MRI

Recurrent PCa following	Typical MR features of recurrence
Prostatectomy	Soft-tissue mass in the surgical bed with slightly higher T_2 signal intensity than adjacent muscle and contrast wash-in and wash-out at DCE MRI
Radiation therapy	Mass-like low T_2 signal intensity lesion, commonly seen at the same location as the pre-treatment tumour, with diffusion restriction and rapid contrast wash-in and wash-out at DCE MRI
Focal therapy	Low T_2 signal intensity lesion, along the edge of the prior treatment, with diffusion restriction and rapid contrast wash-in and wash-out at DCE MRI

DCE, dynamic contrast enhanced.

Figure 5. Prominent venous plexus. The patient is status post radical prostatectomy with a slowly rising prostate-specific antigen to 0.4. (a) Axial T_2 weighted sequence demonstrates an elongated soft-tissue density in the lateral aspect of the surgical bed (arrows). (b) Dynamic contrast enhanced MRI demonstrates an elongated and continuous structure in the lateral aspect of the surgical bed with contrast wash-in and wash-out (arrows) consistent with a periprostatic vessel.

distinguishing feature of fibrotic scar from recurrent PCa is very low T_2 signal intensity (Figure 4) with no or slightly delayed enhancement at DCE MRI. There is no diffusion restriction in the scar although the diffusion-weighted images may be degraded due to surgical clips.⁶

Prominent vascular structure

After removal of the prostate, prominent vascular structures may be present in the surgical bed and may demonstrate rapid contrast wash-in and wash-out, mimicking recurrence, particularly on the post-processed DCE MRI images. These vascular structures do

not usually have the appearance of a soft-tissue mass in the surgical bed at T2WI and are frequently located in the anterior and lateral aspects of the surgical bed with an elongated and continuous appearance noted at DCE MRI (Figure 5). In contrast, a local recurrence appears as a rounded area with enhancement.

Granulation tissue

Granulation tissue in the surgical bed may occasionally be present, commonly in the perianastomotic region, and shows high signal on T2WI relative to muscle, mimicking a local recurrence (Figure 6).¹² However, the granulation tissue

Figure 6. Granulation tissue mimicking prostate cancer. The patient is status post radical prostatectomy with slowly rising prostate-specific antigen to 0.32. Axial T_2 shows a soft-tissue focus (arrows) with slightly high T_2 signal intensity relative to the adjacent muscle and posterior to the bladder (B) without significant enhancement at dynamic contrast enhanced MRI (not shown). Target biopsy confirmed granulation tissue.

Figure 7. Retained seminal vesicle (SV) mimicking prostate cancer. The patient is status post radical prostatectomy with slowly rising prostate-specific antigen to 0.9. Axial T_2 shows a homogeneous slightly high T_2 signal intensity area (arrow) in the expected location of the right SV without evidence of enhancement at dynamic contrast enhanced MRI (not shown). The bladder is noted (B). Target biopsy confirmed no tumour.

Figure 8. Residual normal prostate tissue mimicking recurrent prostate cancer. The patient is status post radical prostatectomy with prostate-specific antigen of 0.3. (a) Axial T_2 weighted sequence demonstrates a high T_2 signal intensity mass (arrows) in the surgical bed. (b) Apparent diffusion coefficient map demonstrates no diffusion restriction (arrows) in the high T_2 signal intensity mass in the surgical bed excluding recurrence.

demonstrates no or mild enhancement on delayed contrast images at DCE MRI, whereas a local recurrence shows early rapid contrast wash-in and wash-out.⁶

Retained seminal vesicles

After radical prostatectomy, retained SVs are observed in approximately 20% of patients.¹³ Most retained SVs are very low in signal intensity due to fibrosis and may demonstrate preservation of their convoluted tubular appearance.¹⁴ If a retained SV shows an area with focally increased T_2 signal intensity, it may mimic a recurrence (Figure 7). The clue to distinguish retained SVs from recurrent PCa is that retained SVs will not demonstrate diffusion restriction or rapid contrast wash-in and wash-out at DCE MRI.

Residual normal prostate tissue

A small amount of normal prostatic tissue may be present in the surgical bed following radical prostatectomy and can be

responsible for slight elevation of prostate-specific antigen (PSA), mimicking recurrent PCa.⁵ If the residual prostatic tissue contains a glandular hypertrophic nodule with higher signal intensity on T2WI (Figure 8), it can be differentiated from a local recurrence.⁵ The value of PSA and its increase over time may provide important clinical information. For example, residual prostatic tissue will demonstrate a low level of PSA, usually $>0.4 \text{ ng ml}^{-1}$ with little change over time.⁵ The value of PSA in a patient with a local recurrence usually gradually increases, with a doubling time of about 6–12 months.

MIMICS FOLLOWING RADIATION THERAPY

Focal region of severe post-treatment changes

Following radiation therapy, focal areas of marked low T_2 signal intensity, lower than the rest of the treated prostate, are common due to the uneven distribution of severe post-radiation

Figure 9. Focal region of severe post-treatment changes mimicking recurrent prostate cancer. The patient is status post external beam radiation therapy with prostate-specific antigen of 0.3. (a) Axial T_2 weighted sequence demonstrates two focal areas of low T_2 signal intensity (arrows) in the central gland. (b) Apparent diffusion coefficient map demonstrates no diffusion restriction (arrows) in either of these areas excluding recurrence.

Figure 10. Hypertrophic nodule in the central gland. The patient is status post external radiation therapy. Digital rectal exam demonstrated a nodule in the right side of the prostate. (a) Dynamic contrast enhanced MRI demonstrates a large area of focal enhancement (arrows) in the right central gland mimicking recurrence. (b) Axial T_2 demonstrates that the enhancement corresponds to a well-defined nodule (arrows) in the right central gland. Target biopsy confirmed no recurrence.

changes¹⁰ and treated tumour,⁶ mimicking recurrence (Figure 9a). These areas of severe post-treatment changes do not demonstrate diffusion restriction (Figure 9b) or abnormal enhancement, distinguishing them from focal recurrence.¹⁰

Well-preserved hypertrophic nodule in the central gland

Following radiation therapy, hypertrophic nodules in the central gland may be well preserved with little or no radiation-related changes. These nodules usually demonstrate diffusion restriction and rapid contrast wash-in and wash-out (Figure 10a), mimicking recurrence. These nodules can be differentiated from recurrence by well-defined margins (Figure 10b) on T2WI, a different location from the pre-treated tumour, and contrast enhancement similar to the rest of the central gland.¹⁰

Marked hypertrophic fibromuscular stroma

Following radiation therapy, the prostate may be small and atrophic. However, the anterior fibromuscular stroma may be hypertrophic with a mass-like appearance. The enlarged stroma has a low T_2 signal intensity (Figure 11a) due to fibrotic content with diffusion restriction (Figure 11b) mimicking a recurrence. The key features differentiating stroma from recurrence are that the stroma is low signal intensity on T2WI, lower than that of most recurrences; is usually located anteriorly at the midline; is symmetric or nearly symmetric; and does not enhance at DCE MRI.

SUMMARY

The mimics of focal recurrence may create a significant diagnostic challenge in daily practice. Familiarity with key MR features of mimics (Table 2) is important to avoid unnecessary intervention.

Figure 11. Hypertrophic fibromuscular stroma mimicking recurrence. The patient is status post-radiation therapy with recent elevation of prostate-specific antigen to 1.0. (a) Axial T_2 weighted sequence demonstrates a low T_2 signal intensity soft-tissue mass (arrow) near the midline in the anterior aspect of the central gland. The generalized decreased T_2 signal intensity of the peripheral zone (P) is consistent with radiation changes. (b) Apparent diffusion coefficient map demonstrates diffusion restriction of the mass (arrow). Target biopsy confirmed no tumour.

Table 2. Key MR features that will help in differentiating the mimics from recurrent prostate cancer

Mimics	Key features for differentiation
Mimics following radical prostatectomy	
Fibrotic scar	Very low T_2 signal intensity, lower than that of adjacent muscle; no or only mildly delayed enhancement
Prominent vascular structure	Lack of soft-tissue mass in the surgical bed on T2WI; located in the anterior and lateral aspects of the surgical bed with an elongated and continuous appearance at DCE MRI
Granulation tissue	No or mild enhancement on delayed contrast images at DCE MRI
Retained seminal vesicles	No diffusion restriction or rapid contrast wash-in and wash-out at DCE MRI
Residual normal prostate tissue	Low but stable prostate-specific antigen level, usually $> 0.4 \text{ ng ml}^{-1}$
Mimics following radiation therapy	
Focal region of severe post-treatment changes	No diffusion restriction or abnormal enhancement at DCE MRI
Well-preserved hypertrophic nodule in the central gland	Well-defined margins on T2WI, a different location from the pre-treated tumour and contrast enhancement which may be similar to the rest of the central gland
Marked hypertrophic fibromuscular stroma	Very low signal intensity on T2WI, lower than that of most recurrences; usually located anteriorly at the midline, symmetric or nearly symmetric, and no enhancement at DCE MRI

DCE, dynamic contrast enhanced; T2WI, T_2 weighted sequence.

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