View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Archivio della ricerca- Università di Roma La Sapienza

ELSEVIER

CrossMark

Urologic Oncology: Seminars and Original Investigations 34 (2016) 303–310

UROLOGIC ONCOLOGY

Seminar article

Magnetic resonance imaging for localization of prostate cancer in the setting of biochemical recurrence

Valeria Panebianco, M.D.[a,*], Flavio Barchetti, M.D.[a], Marcello Domenico Grompone, M.D.[a], Anna Colarieti, M.D.[a], Vincenzo Salvo, M.D.[a], Gianpiero Cardone, M.D.[b], Carlo Catalano, M.D.[a]

[a] *Departement of Radiological Sciences, Oncology and Pathology, Sapienza University of Rome, Rome, Italy*
[b] *Radiology Department, IRCCS San Raffaele Turro, Milan, Italy*

Received 10 December 2015; received in revised form 20 January 2016; accepted 23 January 2016

Abstract

The clinical suspicion of local recurrence of prostate cancer after radical treatment is based on the onset of biochemical failure. The use of multiparametric magnetic resonance imaging (MRI) for prostate cancer has increased over recent years, mainly for detection, staging, and active surveillance. However, suspicion of recurrence in the set of biochemical failure is becoming a significant reason for clinicians to request multiparametric MRI. Radiologists should be able to recognize the normal posttreatment MRI findings. Fibrosis and atrophic remnant seminal vesicles (SV) after radical prostatectomy are often found and must be differentiated from local relapse. Moreover, brachytherapy, external beam radiotherapy, and focal therapies tend to diffusely decrease the signal intensity of the peripheral zone on T2-weighted images due to the loss of water content, consequently mimicking tumor and hemorrhage. The combination of T2-weighted images and functional studies like diffusion-weighted imaging and dynamic contrast-enhanced imaging improves the identification of local relapse. Tumor recurrence tends to restrict on diffusion images and avidly enhances after contrast administration. The authors provide a review of the normal findings and the signs of local tumor relapse after radical prostatectomy, external beam radiotherapy, brachytherapy and focal therapies. © 2016 Elsevier Inc. All rights reserved.

Keywords: MRI; Prostate; Cancer; Recurrence; Prostatectomy; Radiotherapy; Brachytherapy; Cryosurgery

Introduction

Multiparametric magnetic resonance imaging (mp-MRI) has been used for detection, localization, and staging of prostate cancer (PCa) over the last few years. It combines T1-weighted images (T1WI) and T2-weighted images (T2WI) with at least 2 functional techniques such as dynamic contrast-enhanced imaging (DCEI), diffusion-weighted imaging (DWI), and MR spectroscopy (MRS) [1]. The role of mp-MRI on PCa has, however, been extended to cases of active surveillance, patients who refused biopsy, MRI-guided or MRI-Ultrasound fusion biopsy, posttreatment surveillance, and diagnosis of recurrence after treatment [2]. Radical prostatectomy (RP) and radiotherapy (RT), either by external beam radiotherapy (EBRT) or brachytherapy (BT), have curative intent in patients with localized PCa. Other alternative treatment options like focal ablative therapies are minimally invasive procedures with reduced toxicity. However, they are not completely established yet [3]. The aim of this article is to review the fundamentals of mp-MRI in the setting of biochemical recurrence (BR) after primary treatment. Moreover the authors provide an overview of the currently available data concerning this new imaging technology on the normal findings and the signs of local tumor relapse after RP, EBRT, BT and focal therapies.

Imaging approach to biochemical failure

Recurrence PCa after curative intent treatment is not uncommon. Among patients undergoing RP or RT, 27% to 53% develop biochemical failure (BF), which is defined as a rise in prostate-specific antigen (PSA) level, and 16%

* Corresponding author. Tel.: +39-06-446-8587; fax: +39-06-49-0243.
E-mail address: valeria.panebianco@uniroma1.it (V. Panebianco).

http://dx.doi.org/10.1016/j.urolonc.2016.01.004
1078-1439/© 2016 Elsevier Inc. All rights reserved.

to 35% need second-line treatment. The definition of BF differs between RP and RT. After RP, it is defined by 2 consecutive PSA values of >0.2 ng/ml. After RT, with or without short-term hormonal manipulation, it is defined by a PSA increase >2 ng/ml higher than the initial PSA nadir value [4,5]. However, it must be stressed that some poorly differentiated tumors do not secrete PSA and laboratorial follow-up should not constitute an isolated parameter in these patients. BF is not synonymous of local recurrence in the prostatic bed. It can be also due to distant metastases. Moreover, a persistently elevated PSA serum level could be also due to residual glandular healthy tissue in the post-prostatectomy bed. Therefore, in patients with BF after primary treatment, a diagnostic imaging procedure is often carried out to distinguish between local cancer recurrence and distant spread of disease [6]. Currently, in agreement with literature data, the sensitivity (Se) and specificity (Spe) of positron emission tomography/computed tomography (PET/CT) using ^{11}C-labeled or ^{18}F-labeled Cho compounds or the new radiotracer 68 Ga prostate-specific membrane antigen 11, in restaging patients with PCa after primary treatment, are greater in detecting metastatic lymph nodes, distant metastases, and local neoplastic recurrences when serum PSA values are >1 ng/ml, PSA doubling time is <6 months, and PSA velocity is >2 ng/ml/y [7–10]. Although PET/CT is recommended in patients with high PSA serum values, in patients who experience low biochemical alterations after RP (PSA serum values between 0.2 and 1 ng/ml) it is very important to exclude the presence of locoregional recurrence, being this information essential for radiation oncologists to target salvage treatment. To date, the role of PET/CT in detecting local recurrence in postprostatectomy bed or radiotreated prostate in patients with BF and low PSA values is still incompletely defined, probably because of the poor detection rate of small lesions, which may be due to the limited spatial resolution (5–6 mm) of PET scanners. mp-MRI—thanks to its inherent superior contrast and spatial resolution, especially with an endorectal coil—and the use of functional techniques, represents an emerging and promising modality for the evaluation of recurrent PCa after primary treatment [11]. The main mp-MRI findings after primary treatment are summerised in the Table.

mp-MRI: Technical aspects

Morphological T2WI is acquired with a high spatial resolution technique (3–4 mm thickness) in order to identify very small pathological tissues [12]. In DCEI the prostate bed is repetitively acquired with a gradient-echo T1W sequence before and after intravenous injection of contrast medium over a period of time. DCEI, in addition to qualitative assessment of the images, allows the calculation of semiquantitative parameters such as peak enhancement, time to peak, wash-out slope, area under the contrast enhancement curve, and quantitative parameters, such as *K*trans, *Ve*, and *K*ep [12]. PCa shows neoangiogenesis and is, therefore, associated with early and high peak enhancement, wash-out slope, high area under the contrast enhancement curve, and higher *K*trans, *K*ep, and *Ve*.

DWI is based on an echo-planar sequence and depicts the diffusivity of water molecules along the 3 space directions within the tissue. It provides qualitative and quantitative information about “cell density” and cell membrane integrity. In neoplastic prostatic tissue extracellular space is decreased; therefore, the movement of water molecules is restricted and the so-called apparent diffusion coefficient (ADC) values are low compared with healthy prostatic tissue. DWI can be performed without the administration of exogenous contrast agent and it does not require long acquisition times [13]. MRS imaging (MRSI) provides 3-dimensional data set of the prostate gland, with volume voxels ranging from 0.24 cm to 0.34 cm. This functional technique evaluates the relative concentration of metabolites within voxels. The main metabolites in the prostate gland are citrate (Cit, a marker of benign tissue), creatinine (Cr, insignificant for diagnosis, but difficult to resolve from choline), and choline (Cho, involved in the cellular membrane synthesis and degradation, a marker of malignant tissue). The peak integral ratio of Cho plus Cr to Cit (CC/C ratio) can distinguish PCa tissue from healthy glandular tissue. Conforming to the literature, in a nontreated prostate gland, each voxel can be defined as follows: fibrotic or scar tissue when the ratio is <0.2, residual healthy prostatic glandular tissue when the ratio is between 0.2 and 0.5, probably recurrent PCa when the ratio is between 0.5 and 1, and definitely recurrent PCa tissue when the ratio is >1 [14].

Table
mp-MRI findings after prostate cancer primary treatment.

	T2WI	DWI	DCEI
Recurrent PCa after prostatectomy	Slightly high signal intensity	Restricted diffusion	Rapid wash in and wash out
Recurrent PCa after radiotherapy	Low signal intensity	Restricted diffusion	Rapid wash in and wash out
Recurrent PCa after focal therapies	Low signal intensity	Restricted diffusion	Rapid wash in and wash out
Fibrotic tissue	Low signal intensity	No restricted diffusion	Slightly delayed enhancement
Granulation tissue	High signal intensity	No restricted diffusion	Mild or no enhancement
Retained seminal vesicles	High signal intensity	No restricted diffusion	Delayed wash in and wash out
Residual glandular healthy tissue after prostatectmy	High signal intensity	No restricted diffusion	Mild or no enhancement

mp-MRI after radical prostatectomy

When a post-RP BF is recognized, salvage RT is generally performed without histological confirmation of local relapse, as transrectal ultrasound (TRUS) is neither sensitive nor specific and a negative biopsy does not rule out a local recurrence [6]. With the development of intensity-modulated RT and image-guided RT, there is the potential to escalate the dose in areas of known disease recurrence after RP, so that accurate identification of local recurrence with pelvic imaging might improve the effectiveness of tumor eradication, improving therefore the chance of long term control [15]. mp-MRI represents an emerging and promising modality for the evaluation of prostatic fossa after RP. Moreover, mp-MRI after RP is a very useful tool to discriminate between locoregional relapse and small amount of residual glandular healthy tissue, scar/fibrosis, retained seminal vesicle and granulation tissue and it may even be able to assess the aggressiveness of nodule recurrence by means of ADC values [10,11,16–18]. A recurrent PCa can be recognized as a soft tissue mass in the surgical bed with slightly high T2 signal intensity (SI) than the adjacent muscle, with restricted diffusion and rapid wash in and wash out at DCEI (Fig. 1). The presence, on T2WI, of a lobulated, semicircumferential, nodular-like, or plaque-like soft tissue thickening in the prostatectomy bed that appear slightly hyperintense compared to pelvic muscles should be considered to be strongly suggestive of local recurrence [3]. The most common site of postoperative local recurrence is the vesicourethral anastomosis around the urinary bladder or membranous urethra [3]. Other common sites of local recurrence are retrovesical (between the urinary bladder and rectum), at the anterior or lateral surgical margins of the prostatectomy bed (e.g., abutting the levator ani muscles) and at the resection site of the vas deferens [19]. In most cases local recurrence can be readily distinguished from normal perianastomotic scar/fibrotic changes, which appears of low SI compared with muscle on T2WI with no or slightly delayed enhacement at DCEI. Granulation tissue may occasionally be present in the perianastomotic region, where it can mimic the appearance of tumor recurrence because of its high SI relative to the pelvic muscles, however, it shows no or mild enhancement on delayed contrast images at DCEI, whereas local PCa recurrence shows early rapid contrast wash in and wash out [20]. After RP retained SVs are observed in approximately 20% of patients. Most retained SVs are very low in SI because of fibrosis and may demonstrate preservation of their convoluted tubular appearance. If a SV shows an area of focally increased T2 SI it can mimic a recurrence. The clue to distinguish retained SVs from recurrent PCa is that retained SVs would not demonstrate diffusion restriction or rapid contrast wash in and wash out at DCEI [20].

The role for spectroscopy after RP remains controversial and needs to be defined further. Indeed, spectroscopy is limited by its poor spatial resolution and its high sensitivity to field inhomogeneities and susceptibility artefacts caused by surgical clips in the anastomotic area, which decrease the spectroscopic

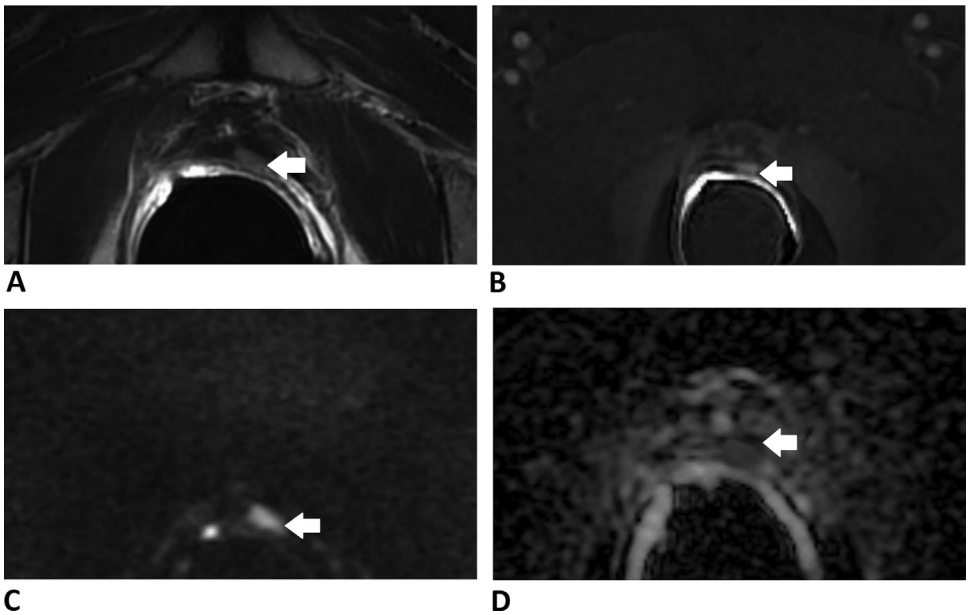

Fig. 1. Multiparametric-MR images of a 64-year-old man with prostate-specific antigen progression (PSA serum level = 0.65 ng/ml) after radical retropubic prostatectomy, with suspected local recurrence. (A) Axial T2-weighted fast spin-echo image shows a soft tissue nodule of 1 cm in size on posterior left perianastomotic location in front of the rectal wall at approximately 30 mm from the ureteral meatus, which is slightly hyperintense compared to pelvic muscles (white arrow). (B) Axial gradient-echo T1-weighted perfusion image showing a remarkable enhancement of the pathological tissue (white arrow). (C) Axial native DWI image at $b = 3{,}000$ s/mm^2 showing marked restricted diffusion of water molecules (white arrow). (D) Axial ADC map reconstructed from images obtained at $b = 0$, 500, 1,000, and 3,000 s/mm^2 shows a dark area corresponding to the abnormal hyperintense tissue seen on T2-weighted images and hypervascular nodule seen on color map (black arrow). All these findings are consistent with locoregional relapse. Color version of figure is available online.

quality and can preclude successful spectroscopic measurements. Nevertheless in case of larger lesions in the prostatectomy fossa (>10 mm) MRSI can play a role as problem solving technique in doubtful cases when the other techniques are borderline. A high Cho concentration in the lesion is more suggestive of PCa recurrence than residual benign gland or fibrosis [10,11]. Wu et al. [21] in a meta-analysis carried out to assess the effectiveness of mp-MRI in detecting local recurrent PCa after RP found that DCEI, compared with T2WI, showed higher pooled Se (85%) and Spe (95%) and when combined with MRSI had the highest pooled Se (92%). Panebianco et al. [18] assessed the role of 3T-DWI in the detection of local PCa recurrence analyzing a large number of patients (262 men) with BF after RP. The patient population was divided into 2 groups according to recurrent lesion size detected on MRI and PSA serum level. Group A included 126 patients with PSA ranging from 0.5 to 1.7 ng/ml and a lesion size ranging from 4 to 8 mm. Group B included 116 patients with PSA serum level ranging from 1.4 to 2.9 ng/ml and a lesion size ranging from 9 to 15 mm. In group A, the presence of local disease was ascertained on the basis of TRUS-guided biopsy, whereas in group B a reduction of PSA serum values higher than 50% following RT was used to validate mp-MRI results. For the identification of local recurrence in group A, combined T2WI and DCEI (T2 + DCEI) displayed Se 98%, Spe 94%, positive predictive values (PPV) 97%, negative predictive values (NPV) 96%, and accuracy of 93%; combined T2WI and DWI with a $b = 3{,}000\ mm^2/s$ (T2 + DW3) had Se 97%, Spe 95%, PPV 96%, NPV 95%, and accuracy of 92%; combined T2WI and DWI with a $b = 1{,}000\ mm^2/s$ (T2 + DW1) showed Se 93%, Spe 89%, PPV 94%, NPV 91%, and accuracy of 88%. The area under the receiver operating characteristic curve for T2 + dynamic contrast enhanced [DCE] was 0.917, for T2 + DW3 was 0.823, and for T2 + DW1 was 0.724. In group B T2 + DCE had Se 100%, Spe 97%, PPV 96%, NPV 95%, and accuracy of 91%; T2 + DW3 showed Se 98%, Spe 96%, PPV 93%, NPV 91%, and accuracy of 89%; T2 + DW1 displayed Se 94%, Spe 92%, PPV 91%, NPV 89%, and accuracy of 86%. The A_z for T2 + DCE was 0.875, for T2 + DW3 was 0.783, and for T2 + DW1 was 0.679. The authors supposed that the overall accuracy of DCEI is superior to that of DWI because DWI are more affected by distortion artefacts because of surgical clips and background noise than DCEI are, though there are some cases in which DCEI is doubtful and DWI is of paramount importance for local recurrence depiction. For instance, a prominent periprostatic venous plexus may sometimes mimic the appearance of enhancing recurrent tumor on DCEI; therefore, when there is this potential pitfall DWI is mandatory to exclude the presence of abnormal tissue in the postprostatectomy bed. Moreover, the authors in order to evaluate the aggressiveness of local recurrent PCa, compared ADC values of locoregional recurrences with the histological results. The mean and standard deviation of ADC values were $0.5 \pm 0.23\ mm^2/s$ for high-grade aggressiveness, $0.8 \pm 0.09\ mm^2/s$ for intermediate-grade aggressiveness, and $1.1 \pm 1.17\ mm^2/s$ for low-grade aggressiveness; ADC values higher than $1.3\ mm^2/s$ (mean ADC = 1.4; range: 1.3–1.7) were found in patients with a histological finding of prostatic gland remnants.

Roy et al. [22] in a recent study evaluated the Se of the 3 types of functional MRI techniques in the detection of local PCa recurrence after RP and after EBRT. They enrolled 60 consecutive patients with BF after RP or after EBRT. TRUS-guided biopsy was used to validate MRI results. The patient population was divided into 2 groups according to the therapy delivered. Group A included 28 patients (serum PSA value range: 0.3–2.8 ng/ml) who underwent RP, and group B included 32 patients (PSA serum level range: 2.2–4.8 ng/ml) who received EBRT. In group A the Se was highest for T2WI plus DCE (97%) followed, in decreasing order, by DCEI alone (94%) and T2WI plus DWI plus DCEI (94%), T2WI plus DWI plus DCEI plus MRSI (74%), DWI alone (65%) and T2WI plus DWI (65%), T2WI alone (56%), T2WI plus MRSI (53%), and lastly MRSI (50%). The worst results were obtained with isolated T2WI and MRSI; the lower performance of MRSI may reflect a partial volume effect due to the voxel size.

In patients scheduled for local salvage EBRT after RP, accurate anatomic localization of tumor deposits within the postprostatectomy bed, by means of mp-MRI, may allow for an individualized field of irradiation, thereby maximizing efficacy and minimizing toxicity to normal surrounding tissues. In this setting mp-MRI findings could be used to apply a stereotactic boost to the recurrence site, potentially improving in this way the control of local disease and avoiding further locoregional relapses over time. Furthermore, the differential diagnosis between residual glandular healthy tissue and locoregional neoplastic recurrence is of paramount importance for the radiation oncologist because the dose of RT delivered in the prostate bed is quite different [23]. The recent development of the new hybrid PET/MRI scanners, with simultaneous acquisition of mp-MRI and PET images, can yield combined structural, functional, and metabolic information that can potentially affect patient management and outcome [24]. Cho-PET/MRI might improve RT planning by enabling more precise target volume delineation of local recurrence as well as of PCa involved lymph nodes [25].

mp-MRI after EBRT

In patients with local recurrence after RT, if local salvage therapy is not undertaken early, then the median time to development of distant metastases is ≈ 3 years [26]. Local salvage therapies with curative intent include additional irradiation of the prostate, RP, and other new treatment options such as cryosurgery, transrectal high-intensity focused ultrasound trans-rectal ultrasonography guided (TRUS-guided) and laser therapy [27]. As the exact location of the recurrent tumor within the prostate is generally unknown, the general practice of salvage therapies involves treatment of the

entire prostate [27]. Currently, there is an increasing need of imaging techniques able to identify and localize recurrent PCa in order to perform focal salvage therapies effectively with minimal complications.

At present mp-MRI is widely considered to be the state of the art in detecting and localizing PCa recurrence in patients with BP after definitive RT. After RT, the entire prostate and the SVs show decreased size and diffusely decreased SI on T2WI, and the peripheral, central, and transition zones appear less distinct from each other [28]. PCa also show changes, which may include decreased size, reduced capsular bulging, capsular irregularity, or decreased extracapsular extension. These changes are caused by RT induced glandular atrophy and fibrosis. The effects of RT on the T2WI appearance of adjacent anatomic structures include increased bladder or rectal wall thickness, thickening of the perirectal fascia, and increased SI of the pelvic sidewall musculature [29]. In addition, there may be increased SI in the bone marrow on T1WI due to post-RT fatty replacement [29]. T2WI alone is of a limited diagnostic accuracy because the recurrent tumor and the normal surrounding parenchyma both appear hypointense [12]. It has been hypothesized that cancer can be detected under such circumstances if it produces an additional focal reduction in SI [30] or if appears as a hyperintense region compared to surrounding prostate tissue [31]. Moreover, a focal T2 hypointense region may represent the treated nonviable tumor and not necessarily cancer recurrence [12].

A recurrent PCa tumor after EBRT is seen as an area, commonly seen at the same location of the pretreatment tumor, with diffusion restriction and rapid contrast wash in and wash out at DCEI, usually isointense to the surrounding parenchyma on T2WI (Fig. 2). Following RT even though the gland is usually small and atrophyc, the anterior fibromuscolar stroma may be hypertrophic with a mass like appearance. The enlarged stroma has a low T2 SI due to fibrotic content with diffusion restriction mimicking a recurrence, but on DCEI it shows no enhacement [20].

Identifying a recurrent disease using DCEI is easier, paradoxically, than the initial detection of cancer—this is because of the very different patterns between recurrence and postradiation fibrosis. After RT, recurrent tissue can be recognized as hypervascular early enhancing homogeneous nodule, whereas in the surrounding prostatic tissue the enhancement is homogeneous, slow, and low [6]. Hence, DCEI is more reliable than T2WI for the detection of recurrent PCa. A serious drawback of DCEI is that its Spe in depicting the recurrence in the central gland is almost always reduced. Following RT hypertrophic nodules in the central gland may be well preserved with little or no radiation induced changes. These nodules usually show restricted diffusion and rapid contrast wash in and wash out mimicking recurrence. These nodules can be differentiated

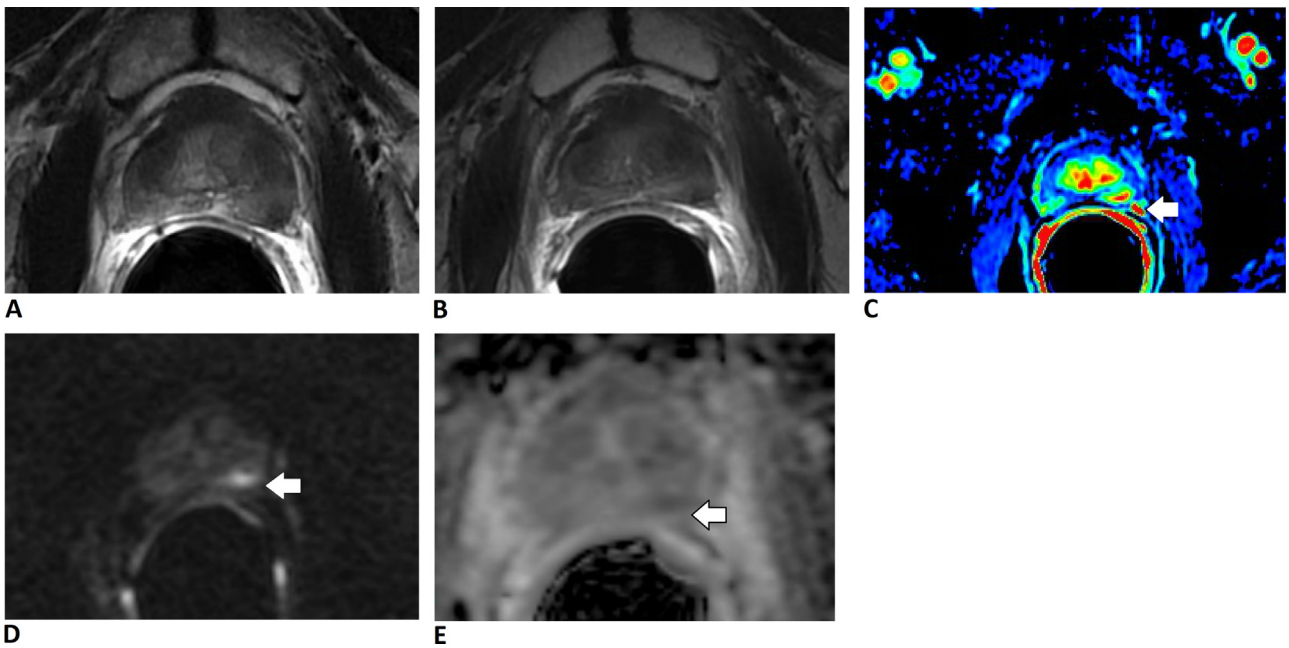

Fig. 2. A 64-year-old man with TRUS-guided biopsy-proved PCa of the left third middle peripheral zone (Gleason score, 3 + 4). (A) Axial T2-weighted images before EBRT showing a hypointense focus on the left third middle peripheral zone corresponding to cancerous lesion. (B–E) Multiparametric-MR images obtained after 14 months after external beam radiation therapy. (B) Axial T2-weighted fast spin-echo image shows shrinkage of the prostate gland, which appears diffusely hypointense because of radiation induced atrophy and fibrosis with a hypointense focus in the same location of the treated cancer. (C) Axial gradient-echo T1-weighted color map image showing a remarkable nodular enhancement at the left third midgland (white arrow). (D) Axial native DWI image at $b = 3{,}000$ s/mm^2 showing a focus with marked restricted diffusion of water molecules (white arrow). (E) Axial ADC map reconstructed from images obtained at $b = 0$, 500, 1,000, and 3,000 s/mm^2 shows a dark area corresponding to the hypervascular nodule (white arrow). All these findings are consistent with local recurrent PCa.

from recurrence by well defined margins on T2WI, a different location from pretreatment tumor and contrast enhacement similar to the central gland. DCEI should be performed at least 3 months after RT because an increase in perfusion and blood volume due to an inflammatory reaction of the tissue to RT can be found immediately after treatment. MRSI in evaluating the response to RT and in detecting local recurrence yielded promising result. The use of an endorectal coil is essential for spectroscopic imaging even at high field strength, because it increases signal-to-noise ratio by a factor of 10, which results in higher spatial and spectral resolution [32]. Panebianco et al. [33] in a recent study showed that MRSI follow-up, using CC/C ratio, shows a greater potential compared to PSA in monitoring patients after EBRT because MRSI can demonstrate PCa recurrence or residual disease before the BR occurs, leading to the possibility to deliver salvage local therapy, and thus the chance for cure as early as possible. Wu et al. in a meta-analysis carried out to assess the effectiveness of T2WI, DCEI, and MRSI in detecting local recurrent PCa after EBRT found that DCEI, compared with T2WI, showed higher pooled Se (90%) and Spe (81%). DCEI combined with MRSI had the highest pooled Se and Spe (90%) [21]. Furthermore, a comparison of pre-EBRT and post-EBRT MRI has shown that most recurrent cancers occurred at the site of primary tumors [34].

Local PCa recurrence appears as an area of high SI on DWI native images and of low SI on ADC maps relative to the surrounding healthy prostate tissue. Many false-positive can occur. Similar findings may be observed in various benign conditions of the prostate, including hemorrhage, hyperplasia, adenoma, and chronic inflammation. Postbiopsy hemorrhage has been also reported to reduce ADC values [35]. In a recent study, Donati et al. [36] analyzed a patient population of 53 men with BR after EBRT. TRUS-guided biopsy was used as the standard of reference. They showed that in detecting recurrent tumor the addition of DCEI to T2WI plus DWI did not improve diagnostic accuracy, thus eliminating the risks and costs associated with the intravenous administration of gadolinium-based contrast agents. Roy et al. [22] in a recent study evaluated the Se in the detection of post-RT local PCa recurrence of the 3 types of functional MRI techniques, with TRUS-guided biopsy as the standard of reference. They enrolled 32 patients with BR after EBRT (PSA serum level range: 2.2–4.8 ng/ml). The Se was highest for T2WI plus DWI plus DCEI plus MRSI (100%) followed by, in decreasing order, T2WI plus DWI, DCEI alone and DWI alone (94%), T2WI plus DCEI (91%), T2WI plus DWI plus DCEI plus MRSI (76%), T2WI and MRSI alone (74%), and lastly T2WI plus MRSI (44%).

mp-MRI after transperineal brachytherapy

BT is a type of RT in which the radiation source is placed near or inside the treatment area. This technique could be TRUS or MRI guide. A large number of ^{125}I or ^{192}Ir seeds are implanted in the prostate via transperineally inserted catheters. There is no consensus on BF after BT. A PSA bounce, defined as a temporary increase of the PSA level followed by a further decrease, occurs in 30% to 60% of patients 12 to 24 months after implantation, without clinical relevance. PSA bounce typically persists for approximately 12 months and PSA levels usually do not increase more than 1.0 ng/ml [6]. BT may produce several levels of magnetic susceptibility artefacts on both morphological and functional sequences, hampering cancer detection. When visible, BT seeds appear as dark dots on T2WI and ADC map. Similarly to EBRT, post-BT prostate tends to appear diffusely hypointense on T2WI, with loss of the normal zonal anatomy. BT seeds are often seen outside the gland, in the surrounding fat planes and less commonly at the base of the penis. According to Rouvière et al. [6], recurrent foci may be identified on DCEI as early-enhanced nodules. The use of DWI and MRSI is not well established in the detection of intraglandular recurrence after BT mainly due to local artefacts [37].

mp-MRI after focal therapies

RP and EBRT can lead to significant complications, such as incontinence and impotence, and can have a substantial effect on quality of life. Consequently, promising techniques such as cryosurgery, high-intensity focused ultrasound, and laser-induced thermal therapy have emerged as feasible minimally invasive focal treatment options able to preserve uninvolved prostatic tissue with the aim of preserving genitourinary function [38]. Focal therapy is controversial as PCa is multifocal in approximately 70% to 80% of patients [39]. However, it is the largest tumor focus (index tumor) that is, presumed to be the main factor for tumor progression and prognosis [40]. There are no validated criteria for BF after focal therapies. Some centers consider a PSA cutoff of around 1 ng/ml, which may be combined with a posttreatment biopsy [6,41]. At the site of focal treatment a heterogenous but low T2 SI may be seen with no contrast enhancement. Data in literature are scarce regarding PCa recurrence after focal therapies. Residual or recurrent PCa following focal therapies exhibits a mass effect along the edge of the previous treatment, with low T2 SI, diffusion restriction and rapid contrast wash in and wash out.

Conclusions

mp-MRI could be currently considered as the most reliable imaging tool to detect local PCa recurrence in patients with BF after primary treatment. mp-MRI after RP is indicated to diagnose small local cancer recurrence in a range of PSA serum values between 0.2 and 1 ng/ml when PET/CT is not eligible. Moreover, mp-MRI, thanks to functional techniques, allows the differentiation between

residual glandular healthy tissue, scar/fibrotic tissue, granulation tissue, and tumor recurrence and it may also be able to assess the aggressiveness of nodule recurrence. Moreover, the recent development of hybrid PET/MRI scanners could improve the diagnostic accuracy in depicting local PCa relapses in postprostatectomy fossa. mp-MRI findings could be used to boost the dose of salvage RT to the recurrent PCa nodule and potentially improve the control of local disease, thus avoiding an eventual locoregional relapses. The precise detection and localization of local tumor recurrence after EBRT are of utmost importance for following purposes: (1) for guiding targeted TRUS-guided biopsy of suspicious areas, thus reducing the false-negative rate associated with systematic biopsies, (2) to perform MR-guided biopsy leading to a higher detection rate of recurrent PCa with a minimum number of biopsy cores compared to TRUS-guided systemic biopsies and, consequently, leading to higher patient satisfaction, (3) appropriate treatment selection and planning, (4) to guide surgery, and (5) to improve the targeting of salvage RT (external beam or interstitial) or minimally invasive ablative techniques in order to perform focal salvage therapies effectively with minimal complications. To minimize time for mp-MRI data acquisition, we hypothesize that a combination of T2WI and DWI could be sufficient to detect local recurrence. This observation derives from the evidence that DWI and DCEI are similar in terms of Se and accuracy for recurrent PCa detection and localization both after RP and EBRT [18,36]. Therefore, as DWI requires a short imaging time, without the need for intravenous contrast medium and has relatively simple postprocessing requirements, it could be assumed to be a valid alternative to DCE. However, DCEI can be helpful in patients with seed placement after BT, as DWI is prone to susceptibility artifacts and distortion in these cases. mp-MRI in detecting locoregional relapse after focal therapies in not yet investigated and need further studies in order to confirm its role.

References

[1] Barentsz JO, Richenberg J, Clements R, et al. ESUR prostate MR guidelines 2012. Eur Radiol 2012;22:746–57.

[2] Kirkham APS, Haslam P, Keanie JY, et al. Prostate MRI: who, when, and how? Report from a UK consensus meeting. Clin Radiol 2013;68:1016–23.

[3] Heidenreich A, Bellmunt J, Bolla M, et al. EAU guidelines on prostate cancer. Part 1: screening, diagnosis, and treatment of clinically localised disease. Eur Urol 2011;59:61–71.

[4] Roach MR III, Hanks G, Thames H Jr, et al. Defining biochemical failure following radiotherapy with or without hormonal therapy in men with clinically localized prostate cancer: recommendations of the RTOG-ASTRO Phoenix Consensus Conference. Int J Radiat Oncol Biol Phys 2006;65:965–74.

[5] Boorjian SA, Thompson RH, Tollefson MK, et al. Longterm risk of clinical progression after biochemical recurrence following radical prostatectomy: the impact of time from surgery to recurrence. Eur Urol 2011;59:893–9.

[6] Rouvie‘re O, Vitry T, Lyonnet D. Imaging of prostate cancer local recurrences: why and how? Eur Radiol 2010;20:1254–66.

[7] Giovacchini G, Picchio M, Coradeschi E, et al. Predictive factors of [11C]choline PET/CT in patients with biochemical failure after radical prostatectomy. Eur J Nucl Med Mol Imaging 2010;37:301–9.

[8] Reske SN, Blumstein NM, Glatting. G. [11C]choline PET/CT imaging in occult local relapse of prostate cancer after radical prostatectomy. Eur J Nucl Med Mol Imaging 2008;35:9–17.

[9] Sachpekidis C, Eder M, Kopka K, et al. 68-Ga-PSMA-11 dynamic PET/CT imaging in biochemical relapse of prostate cancer. Eur J Nucl Med Mol Imaging 2016.

[10] Panebianco V, Barchetti F, Musio D, et al. Advanced imaging for the early diagnosis of local recurrence prostate cancer after radical prostatectomy. Biomed Res Int 2014;2014:827265.

[11] Barchetti F, Panebianco V, Multiparametric MRI. For recurrent prostate cancer post radical prostatectomy and postradiation therapy. Biomed Res Int 2014;2014:316272.

[12] Westphalen AC, Reed GD, Vinh PP, et al. Multiparametric 3 T endorectal MRI after external beam radiation therapy for prostate cancer. J Magn Reson Imaging 2012;36:430–7.

[13] Haghighi M, Shah S, Taneja SS, et al. Prostate cancer: diffusion-weighted imaging versus dynamic contrast-enhanced imaging for tumor localization—a meta-analysis. J Comput Assist Tomogr 2013;37:980–8.

[14] Kirkham APS, Emberton M, Allen C. Howgood is MRI at detecting and characterising cancer within the prostate? Eur Urol 2006;50:1163–75.

[15] King CR, Spiotto MT. Improved outcomes with higher doses for salvage radiotherapy after prostatectomy. Intl J Radiat Oncol Biol Phys 2008;71:23–7.

[16] Casciani E, Polettini E, Carmenini E, et al. Endorectal and dynamic contrast-enhanced MRI for detection of local recurrence after radical prostatectomy. Am J Roentgenol 2008;190:1187–92.

[17] Vargas HA, Wassberg C, Akin O, Hricak. H. MR imaging of treated prostate cancer. Radiology 2012;262:26–42.

[18] Panebianco V, Barchetti F, Sciarra A, et al. Prostate cancer recurrence after radical prostatectomy: the role of 3-T diffusion imaging in multiparametric magnetic resonance imaging. Eur Radiol 2013;23:1745–52.

[19] Sella T, Schwartz LH, Swindle PW, et al. Suspected local recurrence after radical prostatectomy: endorectal coil MR imaging. Radiology 2004;231:379–85.

[20] Notley M, Yu J, Fulcher AS, Turner MA, et al. Diagnosis of recurrent prostate cancer and its mimics at multiparametric prostate MRI. Br J Radiol 2015;88:20150362.

[21] Wu LM, Xu JR, Gu HY, et al. Role of magnetic resonance imaging in the detection of local prostate cancer recurrence after external beam radiotherapy and radical prostatectomy. Clin Oncol 2013;25:252–64.

[22] Roy C, Foudi F, Charton J, et al. Comparative sensitivities of functional MRI sequences in detection of local recurrence of prostate carcinoma after radical prostatectomy or externalbeam radiotherapy. Am J Roentgenol 2013;200:361–8.

[23] Sefrova J, Odrazka K, Paluska P, et al. Magnetic resonance imaging in postprostatectomy radiotherapy planning. Int J Radiat Oncol Biol Phys 2012;82:911–8.

[24] Panebianco V, Giove F, Barchetti F, et al. High-field PET/MRI and MRS: potential clinical and research applications. Clin Transl Imaging 2013;1:17–29.

[25] Thorwarth D, Leibfarth S, M̈onnich D. Potential role of PET/MRI in radiotherapy treatment planning. Clin Transl Imaging 2013;1:45–51.

[26] Bianco FJ Jr., Scardino PT, Stephenson AJ, et al. Long-term oncologic results of salvage radical prostatectomy for locally recurrent prostate cancer after radiotherapy. Int J Radiat Oncol Biol Phys 2005;62:448–53.

[27] Gravina GL, Tombolini V, Di Staso M, et al. Advances in imaging and in non-surgical salvage treatments after radiorecurrence in prostate cancer: what does the oncologist, radiotherapist, and radiologist need to know? Eur Radiol 2012;22:2848–58.

[28] Coakley FV, Hricak H, Wefer AE, et al. Brachytherapy for prostate cancer: endorectal MR imaging of local treatment-related changes. Radiology 2001;219:817–21.
[29] Sugimura K, Carrington BM, Quivey JM, et al. Postirradiation changes in the pelvis: assessment with MR imaging. Radiology 1990;175:805–13.
[30] Nudell DM, Wefer AE, Hricak H, et al. Imaging for recurrent prostate cancer. Radiol Clin North Am 2000;38:213–29.
[31] Yakar D, Hambrock T, Huisman H, et al. Feasibility of 3T dynamic contrast-enhancedmagnetic resonance-guided biopsy in localizing local recurrence of prostate cancer after external beam radiation therapy. Invest Radiol 2010;45:121–5.
[32] Fütterer JJ, Scheenen TWJ, Huisman HJ, et al. Initial experience of 3 tesla endorectal coil magnetic resonance imaging and 1H-spectroscopic imaging of the prostate. Invest Radiol 2004;39:671–80.
[33] Panebianco V, Barchetti F, Musio D, et al. Metabolic atrophy and 3T 1H-MR spectroscopy correlation after radiation therapy for prostate cancer. Br J Urol Int 2014;14:852–9.
[34] Pucar D, Hricak H, Shukla-Dave A, et al. Clinically significant prostate cancer local recurrence after radiation therapy occurs at the site of primary tumor: magnetic resonance imaging and step-section pathology evidence. Int J Radiat Oncol Biol Phys 2007;69:62–9.
[35] Rosenkrantz AB, Kopec M, Kong X, et al. Prostate cancer versus post-biopsy hemorrhage: diagnosis with T2- and diffusion-weighted imaging. J Magn Reson Imaging 2010;31:1387–94.
[36] Donati OF, Jung SI, Vargas HA, et al. Multiparametric prostate MR imaging with T2-weighted, diffusionweighted, and dynamic contrast-enhanced sequences: are all pulse sequences necessary to detect locally recurrent prostate cancer after radiation therapy? Radiology 2013;268:440–50.
[37] Lucas R, Magalhães Pina J, et al. Post-treated prostate cancer: normal findings and signs of local relapse on multiparametric magnetic resonance imaging. Abdom Imaging 2015;40:2814–38.
[38] Bomers JG, Sedelaar JP, Barentsz JO, et al. MRI-guided interventions for the treatment of prostate cancer. Am J Roentgenol 2012;199:714–20.
[39] de la Rosette J, Ahmed H, Barentsz J, et al. Focal therapy in prostate cancer: report from a consensus panel. J Endourol 2010;24:775–80.
[40] Da Rosa MR, Trachtenberg J, Chopra R, et al. Early experience in MRI-guided therapies of prostate cancer: HIFU, laser and photodynamic treatment. Cancer Imaging 2011. http://dx.doi.org/10.1102/1470-7330.2011.9003.
[41] Han K, Belldegrun A. Third-generation cryosurgery for primary and recurrent prostate cancer. Br J Urol 2004;93:14–8.