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Seminar article

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

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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.

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%

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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