UPDATE

Usefulness of magnetic resonance imaging in prostate cancer

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Abstract

In the last decade, technical advances in magnetic resonance imaging (MRI) have made it the technique of choice in the overall management of patients with suspected or confirmed prostate cancer. MRI makes it possible to acquire information about morphology and function in the same examination by using techniques like spectroscopy, diffusion, and dynamic sequences with intravenous contrast material administration. Moreover, MRI enables both focused study of the prostate gland and of regional and/or whole-body involvement, depending on the clinical indications, in less than an hour. The main clinical indications for MRI of the prostate are a) staging local, regional, and/or remote disease; b) detecting prostate cancer or guiding prostate biopsy in cases of clinical suspicion or negative findings in previous biopsy specimens; and c) monitoring the response to treatment. It is important to know the different protocols with specific MRI sequences for the prostate, depending on the different clinical indications, to ensure that they are performed and interpreted correctly. This article provides up-to-date information about the use of MRI for the study of the prostate to show how the morphological and functional information can be used in clinical practice.

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Utilidad de la resonancia magnética en el cáncer de próstata

Resumen

Los avances técnicos de la resonancia magnética (RM) en la última década hacen que se considere la técnica de elección en el manejo global del paciente con sospecha o diagnóstico de cáncer de próstata. La RM permite combinar información morfológica y funcional al mismo...
Introduction

Prostate cancer is a large-scale public health problem and the most common malignancy in men in industrialised countries. Despite these data, there are no accurate tools currently available for prostate cancer diagnosis. Clinical suspicion of prostate cancer is based on digital rectal examination (DRE) and on elevated prostate-specific antigen (PSA). There are two forms of PSA in the serum: free form and attached to proteins. PSA produced by normal tissue is less likely to bind to proteins, while neoplastic tissue and attached to proteins. PSA produced by normal tissue is less likely to bind to proteins, while neoplastic tissue produces more of the attached form. Thus, patients with a free-to-total PSA ratio > 30% are rather unlikely to have cancer, whereas for ratio < 25% the probability increases. There is no consensus regarding the pathological level of total PSA, although values higher than 4 ng/ml are considered suspicious. The accepted approach with PSA > 4 ng/ml is to take a prostate biopsy. Excessive use of PSA levels entails a great number of unnecessary biopsies; with 60-70% of biopsies with negative results. Low positive predictive value of PSA is due to overlap with benign prostatic pathology and prostatitis, where elevated PSA may also be found. In addition, the presence of multiple negative biopsies before establishing a definite diagnosis of cancer is not infrequent.

Traditionally, imaging techniques have been of little relevance for prostate cancer management. Only transrectal ultrasound (US) as guide for biopsy, and computerized tomography (CT) for abdominopelvic staging have been used, but with limited accuracy for local or regional staging. Incidentally, the new technological advances in MR have proved useful to detect cancer in patients with clinical suspicion (change in PSA values, free PSA ratio or rate of PSA increase) and to attain a more reliable local, regional or systemic staging. Technological progress of MR provides a detailed morphological image in high resolution that is used as a map and guidance to direct biopsy using transrectal US, increasing significantly the diagnostic accuracy in the detection and localization of cancer. In addition to anatomical information, MR imaging provides metabolic information by means of spectroscopy (MR spectroscopy), molecular information, using diffusion MR imaging (DMR), and also information about the vascularization using dynamic sequences obtained after the intravenous administration of a contrast agent (CMR). The possibility to integrate this information allows not only locating the lesion, but also determining the degree of differentiation or aggressiveness of the tumor. Today, it is possible to perform a complete MR study for the different clinical indications by applying adequately different protocols. Although prostate MR is not yet widely used, it is being used routinely in certain institutions and clinical environments. In this paper, we review and update the role of RM in the management of patients with clinical suspicion or diagnosis of prostate cancer and we describe a practical approach for implementing and integrating morphological and functional information into clinical practice.

MR examination technique

Equipment and preparation

MR examination of the prostate needs high field units with no lower than 1.5T. Nonetheless, 3T units — recently introduced — offer a better signal-to-noise ratio. An optimal MR study for localization and detection of prostate cancer requires the use of an endorectal coil and a pelvic multi-channel phased-array coil; endorectal coil is more uncomfortable and makes the exploration more expensive. Depending on the clinical indications, e.g. staging of a previously diagnosed prostate cancer, a morphological study with a pelvic multi-channel phased-array coil may be enough. For 3T units, the need of using an endorectal coil has not been determined yet. Preparation for the endorectal study requires bland diet 12h before the study and avoiding stimulating drinks such as caffeine and theine. Enema or glucagon administration may be used, but it is not indispensable. Bladder repletion is not needed; in fact, given the duration of the examination, it is better if the use of a contrast agent (CMR) offers a better signal-to-noise ratio. An optimal MR study for localization and detection of prostate cancer requires the use of an endorectal coil and a pelvic multi-channel phased-array coil; endorectal coil is more uncomfortable and makes the exploration more expensive. Depending on the clinical indications, e.g. staging of a previously diagnosed prostate cancer, a morphological study with a pelvic multi-channel phased-array coil may be enough. For 3T units, the need of using an endorectal coil has not been determined yet. Preparation for the endorectal study requires bland diet 12h before the study and avoiding stimulating drinks such as caffeine and theine. Enema or glucagon administration may be used, but it is not indispensable. Bladder repletion is not needed; in fact, given the duration of the examination, it is better if the
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Patient urinates before to avoid having to urinate during the procedure. A DRE using urological lubricant is done before the introduction of the US MR probe in order to prepare the sphincter and rule out rectal stenosis which may hamper anal probing. Next, the probe is inflated with 80-100 cc of liquid air. Different liquids have been used such as barium sulphate suspension that reduces susceptibility artifacts. If there is a history of previous biopsies, MR examination has to be postponed 8–10 weeks to avoid that glandular hemorrhagic changes (fig. 1) or periglandular fibrotic changes may interfere with the correct interpretation of the study.

Morphological MR imaging. Anatomy

Morphological sequences consist of spin-echo (SE) or fast spin-echo (FSE) acquisitions (table 1).

1. Transverse T1-weighted FSE images were obtained from the aortic bifurcation to the symphysis pubis using the following parameters: repetition time (RT), 400–500 ms; echo time (ET), minimum; section thickness, 5 mm; intersection gap, 1 mm < field of view (FOV), 34 cm; matrix, 256 × 192; number of excitations, 1; and frequency direction, transverse to prevent motion artifact from the intestinal loops. This sequence allows assessment of pelvic lymph nodes and of the pelvis bone to rule out metastasis and to assess hemorrhagic changes after biopsy (table 2) (fig. 1).

2. T2-weighted FSE images in the three planes were obtained from the prostate and seminal vesicles. RT, 6000–7500 ms; ET, 96–130 ms; echo train length, 16; section thickness, 3 mm; intersection gap, 0 mm; FOV, 14–16 cm; matrix, 256 × 192, frequency direction, antero-posterior (in axial acquisition); and number of excitations, three. This sequence allows the evaluation of the normal prostate anatomy (table 2). Interpretation has not been proved better using fat saturation imaging. The prostate consists of four zones: peripheral posterior or peripheral gland, central, transitional and anterior fibro stromal. The central and transitional zones form.

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<th>Table 1</th>
<th>Acquisition parameters of the prostate MR protocol in our 1.5T unit</th>
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<td>Sequence</td>
<td>T1 (SE)</td>
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<tr>
<td>Plane</td>
<td>Axial</td>
</tr>
<tr>
<td>Coil</td>
<td>ATD-TORSO</td>
</tr>
<tr>
<td>Anatomical coverage</td>
<td>Aortic bifurcation</td>
</tr>
<tr>
<td>ET (ms)</td>
<td>Minimum</td>
</tr>
<tr>
<td>RT (ms)</td>
<td>400-500</td>
</tr>
<tr>
<td>Section thickness (mm)</td>
<td>5</td>
</tr>
<tr>
<td>FOV (cm)</td>
<td>34</td>
</tr>
<tr>
<td>Matrix</td>
<td>256 × 192</td>
</tr>
<tr>
<td>Acquisitions</td>
<td>1</td>
</tr>
<tr>
<td>Echo train</td>
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</tr>
<tr>
<td>Acquisition time</td>
<td>3:26</td>
</tr>
<tr>
<td>Flip angle (º)</td>
<td>–</td>
</tr>
<tr>
<td>Bandwidth</td>
<td>20.83</td>
</tr>
<tr>
<td>b-value (s/mm²)</td>
<td>–</td>
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</tbody>
</table>

ATD-TORSO: integrated (ATD) endorectal (ENDO) + pelvic coil (TORSO) connection; DWI: diffusion weighted imaging; FRFSE: fast recovery fast spin echo; FSE: fast spin echo; GE FAST SPGR: echo gradient fast spoiled gradient; SE: spin echo; PRESS: point resolved spectroscopy.
the central gland. In adulthood, benign prostatic hypertrophy arises from the transitional zone, compressing the central zone and forming the pseudo-capsule or surgical capsule (fig. 2). The transitional zone is called either central zone or central gland in adulthood. The peripheral gland shows homogeneous high signal intensity in contrast to the heterogeneous low signal intensity of the central-transitional zone, although high intensity areas of adenoma may be observed in the central zone. The neurovascular bundle is located postero-laterally to the peripheral gland-zone (fig. 2). The diagnostic criterion for prostate cancer on T2-weighted MR images is the presence of nodular areas of low signal intensity within the normal high signal intensity of the peripheral gland or zone (fig. 3). T2-weighted imaging has limitations for identifying cancer in the transitional zone due to the difficulty to define tumoral zones of low signal intensity within the normal low signal intensity of the central tissue. The findings suggesting cancer in the transitional

<table>
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<th>Imaging type</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tr>
<td>MR</td>
<td>Allows anatomical and functional images of the prostate. MR is more accurate in lesion detection and staging than any other method.</td>
<td>Expensive</td>
</tr>
<tr>
<td>T1 MR</td>
<td>Detection of hemorrhages post-biopsy as zones of high intensity. Detection of nodes and bone lesions.</td>
<td>Prostate gland appears homogeneous.</td>
</tr>
<tr>
<td>T2 MR</td>
<td>Differentiation of anatomical zones. Cancer shows low signal intensity. Peripheral zone tumors appear as not well defined foci of low intensity. Allows assessment of ECE. SVI appears as foci of low signal intensity within the high signal intensity of the seminal vesicles.</td>
<td>Prostatitis, hemorrhages, atrophy, BPH and post-treatment changes may look like cancer. Central gland tumors signal is similar to the normal gland signal and to the central gland hypertrophy. Transitional zone hyperplasia with cystic and fibrotic nodes may show similar signal pattern as cancer. Lymph nodes staging is complicated and should be based on their morphology and enlargement.</td>
</tr>
<tr>
<td>CMR</td>
<td>Detection of vascularization. Increased specificity in comparison with T2 MR only; early tumoral enhancement, with rapid washout of contrast agent.</td>
<td>Small low grade tumors may not show increased vascularization. Patients with BPH may show an abnormal increase of the pattern similar to that of patients with central gland tumors. Contrast agent with gadolinium may caused nephrogenic systemic fibrosis in patients with severe renal failure.</td>
</tr>
<tr>
<td>MRS</td>
<td>Provides concentrations of citrate, choline and creatine; high levels of choline and low levels of citrate may be indicative of cancer.</td>
<td>Technological challenge and may required physicists expert in MR. Overlap between the metabolic profile of prostatitis and cancer.</td>
</tr>
<tr>
<td>DMR</td>
<td>Prostate cancer may appear as a focus of high intensity and then as a low signal in the ADC map.</td>
<td>Findings may not be specific since hyperplasia may also have low diffusion. Susceptibility problems due to postbiopsy hemorrhage.</td>
</tr>
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zone are: diffuse low signal intensity with poorly defined margins, absence of a margin with (commonly seen in adenomas) and disruption of the surgical pseudocapsule. Low signal intensity lesions in the peripheral zone may also be observed in benign lesions such as prostatitis, hyperplasia, fibrosis, subacute post-biopsy hemorrhage, post-radiation therapy changes, and hormone deprivation therapy (fig. 4). The prostate does not have a real capsule, but a fibro-muscular band named prostatic capsule (fig. 2). More than 70% of prostate cancers arise in the peripheral gland and the rest in the central gland. In prostates with large hypertrophic areas in the transitional zone, where the peripheral tissue is compressed, cancer localization may be difficult using systematic blind biopsies.

MR spectroscopy

MR spectroscopic imaging provides information on the gland metabolism. Sequence is acquired using the multivoxel technique, programming a volume on T2-weighted imaging and according to the guidance parameters specified for our MR unit (table 1). For three-dimensional spectroscopic acquisition we use selective bands to achieve water and lipid suppression and to optimize citrate and lipid choline detection. Six saturation-bands are used to eliminate signals from the adjacent tissue. Field homogenization is automatically calculated. Spatial resolution of 0.24–0.34 cm³, RT/ET: 1000/130 ms, 16 × 8 × 8 phase-encoded spectral arrays, and 19 min acquisition time. The dataset should be processed using specific software for quantification of the values of the metabolic ratios. Generally, the peaks calculated are for choline, creatine and citrate. Despite other metabolites can be also identified such as polyamines, they are better detected in 3T units. Good signal-to-noise ratio needs to be confirmed (> 5:1) as well as the absence of contamination by fat or water. Normal prostatic tissue has high citrate values and low choline and creatine values; whereas neoplastic tissue has high choline values and low citrate values (fig. 3).

Suspicion criterion is a ratio [(creatine + choline)/citrate] (CCo/Ci) > 0.7 obtained in the study of the peripheral gland in a 1.5T unit; however, there is no consensus regarding which metabolic ratio determines the presence of prostate cancer, due to the variability among patients and MR units. Parameters of the metabolic ratio for the central gland have not been established due to the overlap in CCo/Ci ratio between the normal, or hypertropic, and the neoplastic tissue in the central zone. In any case, the most specific finding for diagnosis of neoplasia in the central zone is the absence or very low values of citrate and the elevation of choline.

Diffusion MR

The technological advances of MR have allowed an expansion in the use of the diffusion sequence (DMR) to organs other than the brain, since spectroscopic imaging was first used for diagnosis of stroke. Diffusion sequence provides information about random brownian motion of the free water molecules in the interstitial space and through the cellular membrane. In general, neoplastic
tissue has more restricted diffusion than normal tissue because of its higher cellular density, which hampers normal diffusion of water molecules. Diffusion sequence provides information about cellular density, the tortuosity of the extracellular space, the integrity of the cellular membranes, and the degree of glandular organization. For our unit, the diffusion sequence is spin echo—single shot echo planar image (TR/TE: 6000–6500/minimum ms, b value: 0 and 1.000 s/mm² in the axial plane) (table 1). The sequence must include the whole pelvis, prostate and seminal vesicles in order to simultaneously achieve regional staging and detect a potential glandular lesion in the same acquisition. The low mobility of molecules appears as a high signal on DMR; similarly, molecules with high mobility show a loss of signal. Sequence interpretation requires processing and quantification of the diffusion images using the ADC (apparent diffusion coefficient) in the parametric map (fig. 5). For quantification, the 5–10 mm² region of interest (ROI) is placed on the region of choice. Factor b value varies since there is no consensus regarding its optimal value. Nonetheless, values = 0 and ≥ 1000 s/mm² are recommended for the prostate. The use of higher b values may increase the sensitivity of the sequence by eliminating the high signal intensity of tissues with long T2 relaxation times (edema or fluid due to the high density of their protons), phenomenon known as “T2 shine-through”. Lesions with serious diffusion restrictions appear as low signals on grey-scale ADC maps or blue on color maps (fig. 5). There is no a clearly defined ADC value to differentiate between cancer and absence of cancer; however, values < 1.2 x 10⁻³ mm²/s are a quite indicative threshold of neoplastic process. In order to avoid misinterpretations, diffusion images need to be evaluated along with anatomical images. Advantages of diffusion are short acquisition time and high contrast resolution between tumor and normal tissue. However, its drawbacks are poor spatial resolution and the potential susceptibility artifacts caused by postbiopsy hemorrhage (table 2).

Dynamic MR

Dynamic contrast-enhanced MR imaging (CMR) allows evaluation of tumor vascularization and also indirectly of the angiogenesis. For the prostate, a T1-weighted 3D gradient-echo sequence of the whole gland and seminal vesicles is normally used, with a high temporal resolution. In our unit, we use a 3D fast gradient-echo sequence (table 1) (TR/TE: 14/2; angle: 12°; thickness: 4 mm; FOV: 26; matrix: 256 x 160) with a 4-9 s temporal resolution. The sequence is repeated until reaching a 3-5 min total length. Analysis of the values of the contrast signal intensity over time ratios can be done in three ways: qualitative (curve profile), semi-quantitative (changes in the signal intensity) or quantitative. Qualitative values measure the types of curve profile: type I (progressive enhancement), type II (in plateau) or type III (rapid washout) similar to perfusion imaging studies of breast. Semi-quantitative values measure and quantify the relative signal intensity (higher postcontrast signal intensity/prescontrast signal ratio), slope of the intensity-time curve (that shows speed of enhancement) or the area under the intensity-time curve. These measurements are easy to obtain in the workstations, but cannot be compared among different units (fig. 6). For obtaining quantitative parameters, pharmacokinetics parameters are used, which allow quantification of various...
parameters: $k_{\text{trans}}$ (transit of the contrast from the vascular compartment to the interstice through the endothelium), $k_p$ (return to the vascular compartment) and $V_e$ (fraction of extracellular space of tumor)\textsuperscript{26}. In addition, using these data we can generate parametric maps representing the intratumoral heterogeneity of the vascular distribution. Nonetheless, we should take into account the complexity behind these parameters, the lack of standardization and of universal post-processing software. In areas where the tumor shows high vascular permeability (as the peripheral zone), $k_{\text{trans}}$ values depend mainly on the flow; whereas in the centre of the tumour (where permeability is the limiting factor), $k_{\text{trans}}$ values depend on the permeability surface\textsuperscript{27}. Interpretation difficulties arise from the lack of standardization. However, some authors have proved that the most reliable parameter for neoplasm detection is a rapid washout rate\textsuperscript{14,28}.

Whole body MR imaging

Today, advances in MR technology allow performing a whole body study for the screening of bone metastases in less than 30 min. The examination includes: diffusion sequence in the axial plane of all the stations, whole-body coronal T1-weighted sequence and STIR; and sagittal T1-weighted sequence of the whole spine. Detailed description of the protocol and of the whole-body technique is beyond the scope of this review, but this information can be obtained from the specific referenced publication about the whole-body MR technique and diffusion sequence\textsuperscript{29}.

Clinical indications

Diagnosis and localization

Guides do not recommend yet MR for prostate cancer detection\textsuperscript{30}. However, MR usefulness has proved a tool to guide the biopsy to a focal area in patients with elevated PSA and previous negative biopsies\textsuperscript{31}. MR has proved more useful for prostate cancer detection than DRE or systematic blind biopsy\textsuperscript{32}. MR is also useful for cancer detection in the peripheral zone as well as in the central zone (fig. 5), which is actually a difficult access zone from where samples are not usually obtained in routine biopsies\textsuperscript{33}.

High resolution T2-weighted imaging is relatively sensitive but not very specific for prostate cancer localization\textsuperscript{33}, as described in the examination technique section (fig. 4) (table 2). Combination of T2-weighted sequence with one or two functional sequences, MR spectroscopy, DMR or CMR (table 2), may improve cancer detection\textsuperscript{32,34-36}. The optimal combination of functional sequences to complement T2-weighted images and the efficacy combining all functional sequences has not been proven. Integration of DMR imaging into the study protocol should be done routinely, since its usefulness has been demonstrated if combined with T2-weighted imaging\textsuperscript{37,40}, without increasing the cost of the procedure, unlike spectroscopy or dynamic contrast-enhanced MR imaging. Integration of the morphological and functional information in a single MR study points to an improvement in the diagnostic capability of the technique (fig. 6), particularly in the central transitional zone\textsuperscript{28,41}. In fact, MR diagnostic accuracy of cancer for the central gland is lower than that for the peripheral gland. This is due to the presence of similar findings in morphological MR and functional MR in benign hypertrophy, prostatitis and cancer\textsuperscript{31-42}. Functional technique has the advantage of providing information to predict the degree of tumor differentiation, which correlates with the values of the specific tumor markers for prostate cancer\textsuperscript{43,44}. Preliminary studies seem to put in objective terms the correlation between elevated values of tumor markers and functional imaging parameters that are pathological and suggestive of more differentiated neoplasias. Recently, it has been demonstrated the usefulness of combining the integrated information in MR with clinical parameters such as free PSA levels or PSA density (PSA value-prostate size ratio) in order to select the patients who are good candidates for biopsy, in contrast with the current indication of undergoing biopsy for patients with PSA > 4 ng/ml\textsuperscript{37,45}. The idea is to select patients with high clinical risk of cancer in order to perform a MR examination, to perform more accurate biopsies in patients with tumor suspicion on functional MR. These new proposed algorithms would obviate a significant number of unnecessary biopsies in patients with elevated PSA, due to the high negative predictive value of MR for prostate cancer. Moreover, performing a prebiopsy MR would avoid artifacts caused by postbiopsy hemorrhage or fibrosis that may interfere in the correct interpretation of the prostate MR study (table 2)\textsuperscript{13,14}.

Likewise, the use of MR as prebiopsy tool allows obtaining information about tumor localization to help us direct the needle into the lesion. However, it is complicated to transfer the MR information to the US screen upon biopsy\textsuperscript{30}. To that end there are different options. First, we can specify tumor localization by using a morphological diagram, although this approach does hold operator-related errors. Second, we can use a coregistration of the MR image on the US screen in real time; nonetheless, it is technically difficult to integrate a static image, such as a MR image, into a dynamic US image\textsuperscript{46}. Third, we can perform a MR-guided biopsy in the MR room; however, availability, costs and complexity of the procedure may be a problem due to the amount of equipment needed. Probably, the most feasible option, and there are already some prototypes, is to coregistrate the MR image on the US screen upon biopsy.

One of the main difficulties in the diagnostic assessment of the prostate is to differentiate between chronic prostatitis and cancer. In both cases, the peripheral gland shows low signal intensity at T2-weighted sequences (fig. 7). In the MR spectroscopic sequence, the CCo/Ci ratio appears elevated, similar to what happens in neoplastic tissue\textsuperscript{47}. In dynamic contrast-enhanced sequences overlap may also occurs since hypervascularization appears in both prostatitis and cancer\textsuperscript{18}. Some findings suggest prostatitis, particularly bilateral diffuse or patchy low signal intensity of well defined margins or triangular at T2-weighted imaging (fig. 7). Diffusion sequence may be useful to differentiate prostatitis from prostate cancer. Chronic prostatitis generally has intermediate ADC values, unlike the lower ADC values of cancer; nonetheless, there is overlap in ADC values
between benign hypertrophy and cancer (table 2), specially in the central gland.

Staging

The TNM classification is the reference standard for prostate cancer staging. The aim is to determine the anatomical extent of cancer and to differentiate intraglandular from locally invasive or metastatic lesions, in order to decide treatment: curative (prostatectomy, brachytherapy, cryotherapy, HIFU [High Intensity Focused Ultrasound]) or palliative (radiotherapy, hormonotherapy).

Cancer without extraglandular extension is considered T2 stage and T3 when it spreads outside the capsule. Due to its high contrast and spatial resolution, MR is the most reliable method for prostate cancer staging, in comparison with computed tomography (CT), echography and DRE.

MR criteria for extracapsular extension (ECE) of a prostatic tumor are (fig. 8): irregular and spiculated focal bulging of the capsule, loss of the normal low signal intensity of the capsule, obliteration of the rectoprostatic angle, asymmetry and involvement of the neurovascular bundle; and tumor extension into the seminal vesicles (table 3). The invasion of the seminal vesicle is demonstrated by the presence of low signal within the vesicles. Diffusion sequence has proved useful as a parameter of seminal vesicle infiltration (fig. 9).

In order to obtain the maximum accuracy of MR in prostate cancer staging, it is essential to use an endorectal or a multichannel pelvic coil to obtain high-resolution studies of the pelvis.

It is important to be aware that capsule irregularity may be observed after biopsy (fig. 10), but this fact does not mean extension to the capsule or postbiopsy artifacts. For instance, a previous study reported a decrease in the accuracy of local staging from 83% to 46% due to MR postbiopsy artifact. It is difficult to objectively assess the data published on MR reliability in prostate cancer local staging, due to the different techniques and methods employed. However, a meta-analysis performed on 74 studies on prostate cancer staging concluded that the best results are obtained with high-resolution MR multiplanar imaging using endorectal coil.

The most specific criterion for extracapsular extension (ECE) is the asymmetry of the neurovascular bundle (38% sensibility, 95% specificity) and the most sensitive is the overall assessment of all the criteria of ECE (68% sensitivity, 72% specificity).

The studies that have analyzed the selection criteria for MR studies on prostate cancer staging suggest including patients with an intermediate clinical risk of T3 stage (PSA, 10–20 ng/ml; Gleason 5–7). This approach has a good cost-effectiveness ratio for patients with intermediate risk and with high risk of ECE (PSA > 20 ng/ml and Gleason > 7).

<table>
<thead>
<tr>
<th>Table 3</th>
<th>MR criteria for ECE</th>
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<tr>
<td>Irregular focal bulging and spiculated of the capsule</td>
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<tr>
<td>Loss of the normal low signal intensity of the capsule</td>
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<tr>
<td>Obliteration of the rectoprostatic angle</td>
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<tr>
<td>Involvement or asymmetry of the neurovascular bundle and periprostatic fat</td>
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<tr>
<td>Extension into the seminal vesicles</td>
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![Figure 7](image1.png) Chronic prostatitis in a 45 years old patient with 17 ng/ml PSA. Axial T2-weighted image shows bilateral patchy low signal intensity in the peripheral zone with regular margins. MR spectroscopy sequence shows elevated [(choline + creatine)/citrate] (CCo/Ci) ratio. Parametric map does not show low ADC values and there are no focal areas in blue. CMR sequence shows bilateral hypervascularization in zones of suspicion at the axial T2 image, predominantly on the right. Histological examination showed chronic prostatitis in all the biopsy cylinders.

![Figure 8](image2.png) MR criteria for ECE. A) Irregular and spiculated focal bulging of the capsule (arrow). B) Obliteration of the rectoprostatic angle (arrow). C) Involvement and asymmetry of the neurovascular bundle and periprostatic fat (arrow). D) Extension into the left seminal vesicle (arrow).
agreement regarding which node size is considered pathological, but a maximum value of 8 mm for round nodes and 10 mm for oval ones, measured in the short axis, is accepted. In order to improve reliability, organ-specific contrast agents have been developed. Ultrasound superparamagnetic particles of iron oxide (USPIO) are injected intravenously and taken up by macrophages of the reticuloendothelial system of the node, causing a decrease in the MR signal intensity. Metastatic nodes, where the macrophages are replaced by the tumor, do not capture the iron particles and, as a result, there is no modification of the MR signal. Initial experience suggests that USPIO used in MR lymphography improves the sensitivity and specificity for detection of metastatic nodes \(^{57}\). In any case, the use of this organ-specific contrast has not been approved in the clinical practice.

Bone metastases screening is recommended in patients with PSA \(> 20 \text{ ng/ml}\) or with high levels of alkaline phosphatase in blood\(^{58}\). Although the technique for bone metastases detection is bone scintigraphy, the development of the MR technology makes possible to perform a whole-body MR study during the study of local staging, using the same coil \textit{antenna} without moving the patient. The addition of the diffusion sequence of the whole pelvis to the examination protocol of prostate cancer allows a more accurate diagnosis of bone lesions (fig. 9). Results show that MR imaging is more accurate than bone scintigraphy\(^{59}\). Maybe in the future, a whole body MR will be performed as the method of choice instead of bone scintigraphy, when there will be more MR resources and availability. The option of screening for bone metastases using only a MR study of the spine is also considered\(^{60}\).

**Therapeutic monitoring**

Nowadays, the post therapeutic monitoring method for diagnosis of tumoral relapse is elevated PSA, which is considered a biochemical relapse\(^{58}\). MR imaging can be useful for detection and localization of local relapse for surgical treatment\(^{61}\), radio bacytherapy\(^{62}\), hormonotherapy\(^{63,65}\), cryotherapy\(^{64,65}\) or High-Intensity Focused Ultrasound (HIFU)\(^{66}\).

After different treatments, MR findings may be difficult to interpret due to the presence of glandular atrophy and fibrosis caused by radiation, brachytherapy seeds, scar or post-surgical clips (table 2). T2-weighted sequence has low sensitivity for tumoral relapse detection due to a diffuse low signal intensity caused by atrophy\(^{67}\) that prevents differentiating neoplastic tissue from atrophic tissue (fig. 4).

In these cases, it is advisable to use functional sequences such as MR spectroscopy, DMR and CMR to improve the detection of the lesion\(^{51,62,68}\) (fig. 11).

Conventional MR sequences have proved useful for localization of potential post-prostatectomy relapse, although an endorectal coil is required\(^{69}\). T2-weighted sequence and CMR are effective for assessing the response to HIFU treatment (fig. 11)\(^{66}\). Diffusion sequence may differentiate tumoral relapse from post-radiation changes based on the different ADC values; however, its role in prostate cancer management is yet to be determined\(^{21}\).
Future prospects

The clear ongoing progress in the development and application of MR technology in the management of prostate cancer suggests that it will be included in the routine clinical practice. Platforms of computer-aid design (CAD) are now also being developed and will allow integration of all the information gathered from the RM studies in one screen. In other words, we have at our disposal the morphological information at T2-weighted sequences, combined with functional information from the spectroscopy, diffusion and vascular studies (fig. 6). One technological challenge is to improve parameters standardization and interpretation of the different sequences obtained from the different units available in the market. In addition, we should have the tool to transfer the MR information to the US screen to perform the prostate biopsy efficiently.

Conclusion

Prostate MR imaging is the technique of choice for prostate cancer management in the diagnosis, staging and therapeutic monitoring. The use of MR as a prebiopsy technique in patients with risk of prostate cancer has advantages and a significant benefit in patient management. Functional MR imaging allows improving the accuracy of the method, and an understanding of its advantages and disadvantages is required for a correct interpretation (table 2). Ongoing progress and improvement of the technology should increase the efficacy for patient management so that MR could be included in clinical practice guidelines.

Authorship

J.C. Vilanova has made contributions to the conception and design of the article.

All the authors have been involved in drafting the paper or in its critical review, making important intellectual contributions.

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