

Prostate cancer – the role of magnetic resonance imaging

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Background. This article reviews the potential of magnetic resonance imaging (MRI) in prostate cancer diagnosis.

Methods. Systematic scan of Pubmed, Ovid, Medline, Elsevier search engines was used, additional information was found through bibliographic review of relevant articles.

Results. Substantial progress has been made in the imaging of prostate cancer in MR imaging, as well as in advanced MR spectroscopy.

Conclusions. MRI is a non-invasive and direct imaging modality useful for cancer staging, therapy response, detection of recurrence and guided biopsy in previous negative biopsies. MRI with 3.0T system, whole-body MRI, dynamic contrast enhanced MRI, diffusion-weighted imaging (DWI) and MR spectroscopy (MRS) have improved tumor staging, assessment of tumor volume, aggressiveness or recurrence. Implementation of endorectal/phased array superficial MRI findings on 1.5 or 3.0T systems into nomograms for prostate pretreatment prediction is warranted. Surface phased-array coil MRI accurately defines prostate cancer with elevated risk of extraprostatic disease.

Key words: magnetic resonance imaging, prostate cancer, advanced MRI

Received: August 22, 2011; Accepted: February 21, 2012; Available online: May 10, 2012
<http://dx.doi.org/10.5507/bp.2012.025>

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INTRODUCTION

The major goal for prostatic cancer (PC) imaging is more accurate disease characterization through the synthesis of anatomic, functional and molecular imaging information¹. The high incidence of prostate cancer, combined with earlier detection and downstaging at the time of diagnosis, and slow natural progression and biological heterogeneity of the disease has made its management a complex and controversial issue. Prostate tumours have a slow growth rate and allow for prolonged survival². The downstaging resulting from prostatic serum antigen (PSA) screening has been accompanied by an unfortunate trend of over detection and over treatment of biologically indolent (low-grade, clinically insignificant) disease. Primary therapies with curative intent (surgery or radiation) provide excellent long-term cancer control, but accompanied by a risk of treatment – related morbidity². The real challenge for physicians is to differentiate patients with advanced cancer and increased risk of morbidity/mortality from those who will not require immediate or possibly delayed and therapeutic intervention². There are a number of clinical parameters and clinical nomograms to help with the choice of treatment. Defining low risk is the value of prostate serum antigen (PSA) less than 10ng/mL, Gleason score of 6 and lower, T stage of T2a or lower. High risk is define as PSA value of more than 20ng/mL, Gleason score of 8 or higher or T2c, intermediate risk is defined as PSA of 10-20ng/mL, T2b, Gleason score of 7. The Partin staging nomogram is based on clinical stage, Gleason score, serum PSA level, nomograms are widely

used for giving a prediction of the final pathologic stage, disease recurrence and estimate of biological potential. Other types of nomogram, such as Kattan ´s nomograms have been developed to predict stage, recurrence, biological potential³. Nomograms are limited by the lack of results from imaging studies that could guide interventions to control local disease. A sensitive and specific enough imaging modality is needed to help differentiate between patients with insignificant disease and patients in need of treatment. This might also decrease the need for biopsies or significantly lower the number of biopsy cores needed. Magnetic resonance imaging (MRI) is able to provide detailed anatomical images due to high spatial resolution, superior contrast resolution and multiplanar capability⁴. In the last decade MRI has improved significantly in technology and reader experience. Newer techniques, such as MR spectroscopic imaging (MRSI), dynamic contrast-enhanced MRI (DCE-MRI), perfusion MRI, diffusion-weighted imaging (DWI), high-field strength scanning, image postprocessing and picture and communication systems (PACS) improved interpretation of MR prostate cancer images. MRI and MRSI can evaluate tumor aggressiveness, SI ratios from T2WI and biochemical data from MRSI correlate with the Gleason score for PC Gleason score. Recent studies demonstrate that MRI derived parameters (apparent diffusion coefficient [ADC] and T2-relaxation time) on 3.0T system correlate with prostate tumor cellularity⁵. MRI provides noninvasively cancer staging, its biological potential, treatment planning, therapy response and local recurrence. MRSI identifies prostate cancer by an increased ratio of choline plus poly-

amines plus creatine to citrate, citrate level is reduced and choline level elevated in prostate cancer. DWI measures the Brownian motion of water molecules in tissues, while increased cellularity restricts water diffusion. ADC derived from DWI, demonstrates reduced ADC values and increased fractional anisotropy (FA) in prostate cancer. DCE-MRI visualises tumor perfusion and capillary wall permeability and hydrostatic pressure⁶.

TUMOR LOCALISATION

The staging of PC is based on tumor, node and metastasis (TNM) staging. The latest modification was made in 2010 by the American Joint Committee on Cancer (AJCC). Most important is distinguishing between patients with pathologically organ-defined prostate cancer (pT2) with good prognosis from those with non-confined prostate cancer (pT3-4). Once the cancer extends outside the prostate, the chances of cure are substantially diminished². Radical prostatectomy in organ defined prostate cancer seems to have excellent prognosis, as more than 90% (ref.²) are free from recurrence at 5 years. Nomogram prediction of organ defined prostate cancer is high with under the receiver operating characteristic (ROC) curve ranging from 0.79 to 0.82. MR findings augment significantly clinical nomograms in the prediction of PC in the organ defined stage. A prospective study of 27 patients (MRI-MRSI group and staging nomograms) reported MRI had significantly higher standardized discriminant function coefficients than the Partin tables in prediction of organ-defined prostate cancer². MRI criteria for extracapsular extension include a contour deformity with a step-off or angulated margin, an irregular bulge or edge

retraction, direct tumor extension through the capsule, obliteration of the rectoprostatic angle and asymmetry of the neurovascular bundles. MRI findings are significant pre-surgical predictors in patients with extracapsular extension in prostate cancer with augmentative value to clinical variables⁷. MR imaging has been reported to have a 13%–95% sensitivity and 49%–97% specificity for detection of extracapsular extension (ref.¹). The gold standard in 1.5 T MR system for imaging of prostate cancer is dual examination with integrate pelvic phased-array/endorectal phased array. In 3.0 T MR the recent advances with faster imaging sequences, more powerful gradient coils, post-processing correction are able to exclude using the endorectal coil, surface phased-array coil is equivalent to endorectal coil in 3.0 T system^{8,9}. However, it is expected, though not yet proven that the use of an endorectal coil at 3.0 T will allow better prostate cancer detection¹. A surface phased-array coil MRI accurately stages prostate cancer with elevated risk of extraprostatic disease. This mode of imaging may be reasonable at centres that do not have endorectal coil MRI (ref.¹⁰). MRI begins with localisation images, following submillimeter – resolution T2-weighted images (T2WI) in 3 planes for visualizing the anatomy and the architecture of the prostate gland. Prostate cancer has low signal intensity (SI) (Fig. 1), but haemorrhaging, scarring and prostatitis have a similar appearance. This method has a specificity 54-82% (ref.²) and sensitivity 46-96% (ref.²). A prospective study of 27 patients reported that MRI had significantly higher standardized canonical discriminant function coefficient than Partin tables in predicting extracapsular extension of PC (ref.¹¹). Detecting peripheral zone PC has been most effective using MR imaging. Detection of PC in the transition zone is most effective when MR imaging and MR spectroscopic imag-



Fig. 1. MRI, axial plane T2WI, bilateral hypointense lesions in peripheral zone – histologically proven prostate cancer, radical prostatectomy with robotic system was done.

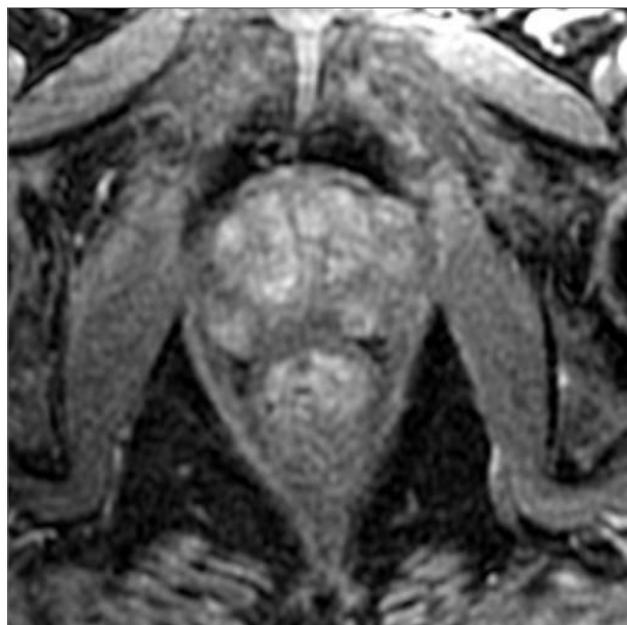


Fig. 2. DCE-MRI, axial plane, bilateral multiple nodular enhancement in early arterial phase – peripheral zone prostate cancer, histologically proven.

ing are combined. Findings supporting the diagnosis of transition zone tumor are: the presence of homogeneous low-SI region in transition zone and in the absence of dominant peripheral zone tumor. Other alternatives are poorly defined or have speculated lesion margins in transition zone, lack of a low - SI rim (associated with benign adenomatous nodules), interruption of the surgical pseudocapsule, urethral or anterior fibromuscular stromal invasion or lenticular shape.

DWI is a promising method and has recently received attention. Although DWI offers little benefit compared with T2 weighted imaging in the most prostate cancer it appears to be more effective in detection of tumor recurrence after surgery and radiotherapy. Increasing PSA levels with subtle changes in ADC raise suspicious of tumor recurrence. ADC values are found to be negatively correlated with the post-surgical Gleason grade in patients with prostate cancer¹². Our results show that ADC values might help to predict PC, especially for tumors in the peripheral zone. Given the substantial overlap in the ADC values, the addition of the other MR parameters, such as volumetry and technical improvements in DWI might improve accuracy in the stratification of patient¹². On DCE-MRI, PC shows early nodular enhancement before the rest of the parenchyma and early washout of contrast medium based on the pathologic microvasculature in the tumor (Fig. 2). These patterns are highly predictive for cancer, but not pathognomic. Some PC are mildly to moderate hypervascular and not detectable with this method. DCE-MRI has been shown to have a sensitivity of 73% and specificity of 81%, and on the 3.0T system a sensitivity of 73% and specificity of 77% (ref.¹). Analysis of the dynamic contrast - enhanced MR imaging remains controversial and requires more studies from the various institutions. DWI and the combined technique are more accurate and sensitive than DCE-MRI in the detection of PC. However DWI and DCE-MRI play complementary roles in the accurate detection¹³.

Magnetic resonance spectroscopic imaging (MRSI) measures the metabolite levels in the tumor tissue. Particular metabolites are choline, citrate, creatine and various polyamines. PC causes increased levels of choline, decrease in level of citrate, increased polyamines, but creatine values are normal. The combination of MRSI and MRI can significantly improve tumor localization within the peripheral zone and the detection of extracapsular extension significantly increases the accuracy of less-experienced readers and decreases interobserver variability¹. Further, new nomograms incorporating MR imaging and MRSI data with clinical variables for predicting of very low-risk cancer are being designed. The diagnostic accuracy of combined 1H MRSI- DCE-MRI was found to be higher than PET/CT for identifying local prostate cancer recurrence, mostly in patients with low biochemical progression after radical prostatectomy¹⁴.

TUMOR VOLUME

Apart from tumor localisation, tumor volume is helpful as well. Combining different imaging techniques has been shown to significantly increase the accuracy of MRI-calculated tumor volume^{15,16}. A safety margin of 5mm is considered in prostate cancer.

TUMOR AGGRESSIVENESS

Accurate grading of the tumor is achievable by biopsy under transrectal ultrasound guidance (TRUS) and assessment of Gleason score. Samplings are usually obtained from 10-12 areas-sextants-peripheral zone: left and apex, left and right mid-gland, left and right base, in addition cores should be obtained from any sonographically suspicious areas. To minimize the need to repeat biopsies many physicians obtain more cores the first time, obtaining 8-10-12 samplings. However, MRI can improve detection of suspected lesions directly before biopsy, in what we call "MRI guidance for prostate biopsies"¹⁷. MRI has also been used to guide and monitor ablations, as well as in high-dose-rate brachytherapy rods¹⁷. MRI has the ability to monitor thermal ablative treatment. Another form is MRI-guided percutaneous interstitial microwave thermoablation in locally recurrent tumor. Chopra et al. showed that using MRI thermometry while applying transurethral MRI guided high intensity-focused ultrasound (HIFU) allowed for stable temperature measurements¹⁸ to avoid thermal damage of surrounding tissues during the intervention. T2-weighted imaging/DCE- MRI is a promising method for guiding post-HIFU biopsy towards areas containing residual (benign or malignant) viable prostate tissue and to sensitise the detection of locally recurrent cancer in patients with biochemical recurrence. Further research is needed to improve the specificity of the technique and distinction between residual/recurrent cancer and residual benign prostate tissue¹⁹. MRI is also promising in the detection of tumor with negative biopsy and elevated PSA and this could obviate the need for repeated biopsy. Computed tomography (CT) has no role in newly diagnosed prostate cancer. Its major role is in nodal staging, detection of local and distant metastases, also in cases of local advanced disease- invasion to surrounding structures (pelvic floor, bladder, rectum and pelvic floor muscles).

DETECTION OF SEMINAL VESICLE INVASION

Seminal vesicle invasion is considered an important predictor of tumor progression and connected with increased risk of lymph node invasion, local tumor recurrence. On MRI T2 weighted images direct signs of seminal vesicle invasion are contiguous low- SI tumor extension from base of the gland to seminal vesicles, focal low- SI within the seminal vesicles disruption or loss of the normal architecture of the seminal vesicles, non-visualization

or enlarged of the ejaculatory ducts, asymmetric decrease of SI of the seminal vesicles (Fig. 3), obliteration of the angle between the prostate and the seminal vesicles and decreased conspicuity of seminal vesicles. MR imaging has been reported to have 23%-80% sensitivity and 81%-99% (ref¹) specificity for detection of seminal vesicle invasion¹. Once resection of seminal vesicles during radical prostatectomy has been done, long-term loss of urinary continence had been occurred. Recent postoperative results suggest that preservation of intact seminal vesicles during radical prostatectomy is better for long-term quality of patient's life.

DETECTION OF LYMPH NODES

The presence of lymph node involvement at the time of primary detection of the prostate cancer appears to be a poor prognostic factor associated with a high probability of progression after treatment. The conventional criterion for detection of metastatic lymph nodes on imaging is a short axis of 8 mm². MRI and CT have similar efficacy in detecting of lymph node metastases, but equally low sensitivity. Recent studies in so-called MR-lymphography using ultra-small superparamagnetic lymphotropic contrast agents allow detection of metastasis in normal - size lymph nodes, but more clinical studies are necessary^{1,2,20}.

THERAPY RESPONSE

Early selection of patients who are most likely to benefit from chemotherapy or radiotherapy may prevent the risk of toxicity in non-responding patients with prostate cancer. Early response to chemotherapy is monitored with

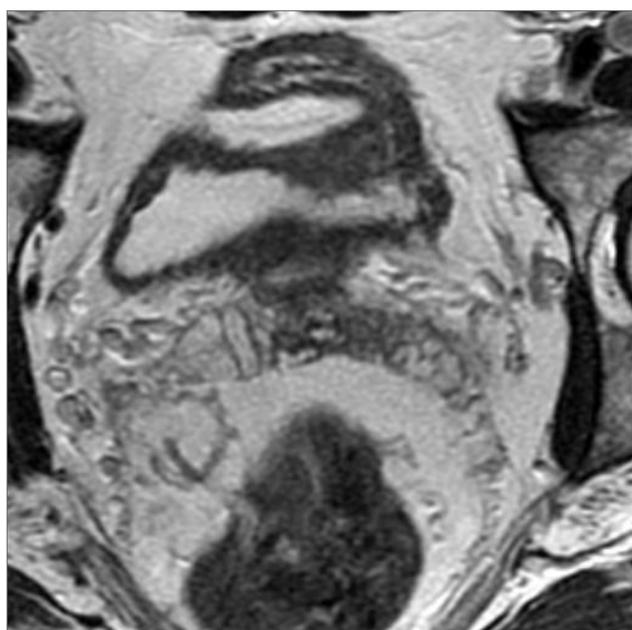


Fig. 3. MRI, sagittal plane, T2WI, direct cancer invasion to the seminal vesicles.

DWI especially in bone metastases, as well as significant changes in perfusion due to tumor vascularity and extraction coefficient derived from DCE-MRI (ref.²). For identification of local recurrence after radical prostatectomy the combination of MRI and DCE-MRI is an accurate method².

DISCUSSION

MRI is multipurpose imaging modality. Currently its role has not been exactly defined in clinical guidelines for PC. Patients with suspected prostate cancer and elevated serum markers will undergo an MRI examination and according to the results will either to go on a surveillance protocol, or MRI-guided focal ablation or radical treatment¹⁷. In patients with abnormal PSA levels and negative biopsy, there is a clinical need for a method with a high sensitivity and a high negative predictive value (unnecessary repeat biopsy could be avoided in patients with negative findings). Poor specificity and positive predictive value are less problematic since obtaining a few additional samples in false-positive areas do not seem to increase the number of biopsy morbidities²¹. MRI as a high-sensitivity high negative predictive value for guiding repeat biopsy towards aggressive cancer foci remains to be determined²². DCE-MRI imaging is a key technique for cancer detection with higher sensitivity than that of T2-weighted imaging. In order to achieve the highest possible sensitivity for detection, these two methods need to be combined in one examination. Poor specificity is explained by the presence of a high incidence of inflammation on repeat biopsies. The use of endorectal coil might not be necessary when one is interested mainly in tumor detection and localization^{8,22}. Since endorectal coils are expensive, this could have important practical consequences if MRI is to be used for routine screening in patients with elevated PSA and negative prostate biopsy.

MRSI has interesting results in cancer detection and could complement T2-weighted imaging and DCE-MRI imaging. However prostatitis is a cause of false-positive findings for MRSI as well as for DCE-MRI and T2-weighted imaging. DWI seems to be superior to DCE-MRI and is more accurate and sensitive for detection of prostate cancer. However the combination DWI and DCE-MRI does not significantly improve the accuracy or sensitivity of DWI (ref.²²), but a combination of these methods in one examination are highly recommended.

CONCLUSION

The high incidence of prostate cancer requires early detection and targeted treatment. Preoperative endorectal MR images significantly improved the accuracy of the surgeon's decision to preserve or resect the neurovascular bundle at radical prostatectomy. Most cancers are not palpable at the time of primary diagnosis. For this reason MRI in combination with MRSI, DCE-MRI and DWI

improved direct tumor visualisation. The superior efficacy of MR imaging compared with transrectal ultrasound for the prediction of tumor extraprostatic extension has been shown. There are a number of clinical parameters and nomograms, MRI makes safer, more individualized therapies possible due to high spatial resolution, multiplanar capability and superior contrast resolution. DWI, DCE-MRI, MRSI-MRI are advanced techniques for reflecting tissue biochemistry, vascular tumor feeding, biological potential, local tumor recurrence and planning for biopsies. Pelvic phased-array surface coil in 1.5T system performs well in patients with high-risk and select intermediate-risk prostate cancer. It is reasonably accurate in confirming the presence of large tumors in the prostate and detecting extraprostatic extension.

CONFLICT OF INTEREST STATEMENT

Author's conflict of interest disclosure: The authors stated that there are no conflicts of interest regarding the publication of this article.

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