ORIGINAL ARTICLE

Clinical Trials Study

Role of serial multiparametric magnetic resonance imaging in prostate cancer active surveillance

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Abstract

AIM: To examine whether addition of 3T multiparametric magnetic resonance imaging (mpMRI) to an active surveillance protocol could detect aggressive or progressive prostate cancer.

METHODS: Twenty-three patients with low risk disease were enrolled on this active surveillance study, all of which had Gleason score 6 or less disease. All patients had clinical assessments, including digital rectal examination and prostate specific antigen (PSA) testing, every 6 mo with annual 3T mpMRI scans with gadolinium contrast and minimum sextant prostate biopsies. The MRI images were anonymized of patient identifiers and clinical information and each scan underwent

radiological review without the other results known. Descriptive statistics for demographics and follow-up as well as the sensitivity and specificity of mpMRI to identify prostate cancer and progressive disease were calculated.

RESULTS: During follow-up (median 24.8 mo) 11 of 23 patients with low-risk prostate cancer had disease progression and were taken off study to receive definitive treatment. Disease progression was identified through upstaging of Gleason score on subsequent biopsies for all 11 patients with only 2 patients also having a PSA doubling time of less than 2 years. All 23 patients had biopsy confirmed prostate cancer but only 10 had a positive index of suspicion on mpMRI scans at baseline (43.5% sensitivity). Aggressive disease prediction from baseline mpMRI scans had satisfactory specificity (81.8%) but low sensitivity (58.3%). Twenty-two patients had serial mpMRI scans and evidence of disease progression was seen for 3 patients all of whom had upstaging of Gleason score on biopsy (30% specificity and 100% sensitivity).

CONCLUSION: Addition of mpMRI imaging in active surveillance decision making may help in identifying aggressive disease amongst men with indolent prostate cancer earlier than traditional methods.

Key words: Active surveillance; Treatment triaging; Magnetic resonance imaging; Indolent disease; Prostate cancer

Core tip: Multiparametric magnetic resonance imaging (mpMRI) has the potential to distinguish more aggressive prostate cancer even when indolent prostate cancer is the biopsy diagnosis. Addition of mpMRI to active surveillance protocols would benefit decision making.

INTRODUCTION

Prostate cancer is one of the most common solid organ cancers and the third leading cause of cancer-related death in men[1]. Introduction of and widespread utilization of serum prostate specific antigen (PSA) screening has increased the incidence of low-risk prostate cancer with about 25%-50% of newly diagnosed patients having low-risk disease[2]. For the majority of these patients, the prostate cancer will behave as an indolent disease and only have clinically significant effects or cause death in a relatively small proportion of men[3-5]. This subgroup of patients often does not require immediate treatment and can be managed with an active surveillance protocol. This has become an increasingly popular strategy for men with low-risk prostate cancer, as it allows up to 65% of patients to avoid unnecessary treatments and their inherent risk of toxicities[6]. Patients on active surveillance are monitored regularly for signs of disease progression[4,7,8]. A dilemma currently encountered by physicians that counsel patients with prostate cancer is differentiating indolent malignancies from aggressive disease. Current assessments are based on clinical stage, the Gleason score of prostate biopsies, and serum PSA levels but these assays have been shown to have an accuracy of less than 75% in predicting indolent disease confined to the prostate[9-11]. This means that there is a subpopulation of patients within the low-risk category who will have disease progression during active surveillance and better methods of identifying early progression on active surveillance are needed.

Magnetic resonance imaging (MRI) is increasingly demonstrating its effectiveness in determining the location, size and grade of prostate cancer[12,13]. Higher field strength MRI can be advantageous due to an increased signal to noise ratio which has led some preliminary investigations to identify extracapsular disease in up to 88% of cases[14]. In addition it has been demonstrated that combining the information from multiple MRI sequences [*i.e.*, T2 weighted imaging and diffusion weighted imaging (DWI)] can increase the accuracy of detecting prostate cancers by a magnitude of 10%, presumably due to the complementary information provided by the different sequences[15]. This has resulted in the addition of baseline multiparametric MRI (mpMRI) to some of the recommendation guidelines for stratification of risk[16,17].

In this study, we performed serial mpMRI scans on patients with indolent prostate cancer who were enrolled in an active surveillance protocol. The objectives of the study were to examine the accuracy of mpMRI in detecting and localizing low-risk prostate cancer and to determine the ability of mpMRI to differentiate indolent prostate cancer from aggressive disease at baseline. The serial scans were also examined to determine if mpMRI was able to identify disease progression earlier than standard methodology.

MATERIALS AND METHODS

Patient population

Patients eligible for enrollment were men aged 18 years or older with histologically proven low-risk adenocarcinoma of the prostate. Low-risk classification was composite Gleason score ≤ 6, and either clinical stage ≤ T2a or PSA ≤ 10 ng/mL. Additional inclusion criteria included: Adequate kidney function; no

Table 1 Parameters of magnetic resonance imaging

Protocol	Sequence	Repetition time (ms)	Echo time (ms)	Flip angle (°)	Slice thickness (mm)	Field of view (AP × RL) (mm × mm)	Matrix size	Voxel size (mm × mm)	Reconstructed voxel size (mm × mm)	Averages	Acquisition time (min:s)
Sagittal T_2-weighted	FSE (18 echoes)	3000	100	90 exc. 135 refoc.	5	160 × 160	224 × 216	0.71 × 0.74	0.63 × 0.63	6	3:42
T_1-weighted	FSE (7 echoes)	700	11	90 exc. 145 refoc.	5	160 × 160	400 × 319	0.4 × 0.5	0.4 × 0.4	3	4:54
T_2-weighted	FSE (17 echoes)	3000	100	90 exc. 145 refoc.	5	160 × 160	400 × 317	0.4 × 0.5	0.4 × 0.4	3	5:48
Diffusion weighted	Single-shot EPI	2500	64	90 exc.	4 1 mm gap	160 × 144	80 × 59	2.00 × 2.42	1.25 × 1.24	6[1]	4:02
dynamic contrast-enhanced	3D-FFE	4.4	2.1	15 exc.	5	260 × 260	128 × 102	2.03 × 2.52	1.02 × 1.02	2	6:37
T_2 map	TSE (6 echoes)	1300	N × 30	90 exc. 180 refoc.	5	160 × 160[2]	160 × 160	1.00 × 1.25	0.63 × 0.63	2	10:32[3]

[1]Twelve averages were acquired for b = 500 s/mm². [2]Field of view of 160 × 200 was used for larger patients to avoid fold over. [3]Acquisition time was 13:08 min if the larger field of view of 160 × 200 was used. FSE: Fast spin echo; EPI: Echo planar imaging; FFE: Fast field echo; exc.: Excitation pulse; refoc.: Refocusing pulse; N: Echo number; AP × RL: Anterior posterior by right left.

contraindications for MRI scans; no history of previous malignancies except non-melanoma skin tumors; and reliability for follow-up.

Study design
This single-institution, prospective, phase Ⅱ clinical trial was designed and performed at the Cross Cancer Institute. This trial was registered at ClinicalTrials.gov with the registration identifier NCT00676286. Research ethics approval was obtained from the local Alberta Cancer Research Ethics Committee. All patients provided written informed consent prior to enrollment and participation in this trial.

Studies monitoring similar patient populations have demonstrated that 20%-30% of patients with indolent prostate cancer demonstrate disease progression within the first two years of follow-up[6,18,19]. For the sample size calculation we assumed that there would be a 25% rate of disease progression and a 50% rate of detecting disease progression utilizing mpMRI[19,20]. This study was designed with a sample size of 24 to have a power of 80% and a significance level of 5% to detect at least one patient with disease progression.

All patients had clinical assessment, including digital rectal examination, and PSA testing performed at or within 8 wk of enrollment and then every 3 mo for the first year and biannually thereafter. Prostate biopsies were performed at baseline or within 16 wk of enrollment (minimum of sextant biopsies) and annually thereafter. MRI scans were performed at baseline and annually for the duration of the study, with caution taken to ensure that imaging was performed prior to biopsies to prevent artifact.

Evidence of disease progression was identified during follow-up by: Gleason pattern ≥ 4 (composite Gleason score ≥ 7); clinical stage ≥ T3a; or PSA doubling time less than 2 years. Patients with progressive disease were offered treatment with any one or a combination of standard treatment options.

3.0 Tesla MRI
Patients had a bowel preparation prior to the MRI scan and were asked to have an empty rectum and empty bladder for the MRI scan. Prior to imaging, Buscopan® 1 mL (20 mg/mL) was administered intramuscularly to decrease bowel peristalsis and allow for clear visualization of the prostate.

All measurements were performed with a 3T Philips Healthcare Intera whole body MRI scanner. The scanner's built in body coil was employed for RF (radiofrequency) transmission while a Philips six element SENSE-TORSO coil was used for signal reception. It was ensured that the patient was positioned such that the prostate was at iso-centre and at the centre of the receiver RF coil. Axial, coronal and sagittal scout images were acquired. A set of sagittal T_2-weighted images were acquired with parameters indicated on the first line of Table 1. The images were employed to align all the axial images perpendicular to the long axis of the prostate gland.

Table 1 shows the parameters used for the axial T_1-weighted, T_2-weighted, diffusion weighted, dynamic contrast-enhanced (DCE) and T_2 map pulse sequences. All axial sets consist of 12 slices each 5 mm thick (or as with the diffusion weighted images 4 mm with a gap of 1 mm) so that the images could be registered with each other. The diffusion weighted sequence acquisition time was reduced by using a 0.667 half scan factor and a sense factor of 2 in the RL direction. Acquisitions with five b-values were acquired, namely, 0, 125, 251, 376 and 501 s/mm². The diffusion weighted sequence also employed SPAIR fat suppression with an inversion delay of 90 ms. The DCE pulse sequence used a keyhole factor of 58.75%. ProHance gadolinium contrast (0.2 mL/kg) was administered to the patient over 20 s and acquisition of data began after approximately four dynamics. A total of 50 dynamic scans were acquired.

Table 2 Qualitative determination of index of suspicion

Procedure step	Structure examined		Index of suspicion assessment
1	Assign region	Base	Superior most margin of prostate to the widest transverse diameter
		Midgland	Widest transverse diameter to ejaculatory ducts at verumontanum
		Apex	Inferior to midgland
2	Peripheral zone	Consider T$_2$ features	4: Moderate low signal with mass like appearance
			3: Mild low signal with mass like appearance
			2: Mild low signal which is focal but not clearly mass like, moderate diffuse low signal
			1: Mild low signal, diffuse and/or feathered, linear low signal
			0: Normal signal
		Consider DWI features	4: Definite abnormality (high DWI and low ADC relative to background)
			3: Probable abnormality (low ADC)
			2: Possible abnormality (mild decrease ADC or increase DWI)
			1: Mottled
			0: Homogeneous ADC or low DWI
		Consider DCE features	4: Rapid early enhancement, wash out
			3: Rapid early enhancement, remaining strong and prolonged
			2: Mild early enhancement, plateau or progressive
			1: No early upstroke, progressive enhancement
			0: No enhancement
			Assign combined score
3	Central gland	Consider T$_2$ features	4: Mass like low T$_2$ signal with invasion into AFMS or peripheral zone/disrupted surgical capsule, irregularly or poorly marginated mass like low T$_2$ signal without a capsule
			3: Mass like homogeneous low T$_2$ signal with no capsule, preserved surgical capsule
			2: Diffuse heterogeneous signal with intact surgical capsule
			1: Encapsulated nodules
			0: Normal
4	Fibromuscular stroma		Assess for presence of disease
5	Extracapsular extension		Assess for presence of disease
6	Seminal vesicles		Assess for presence of disease

ADC: Apparent diffusion coefficient; DWI: Diffusion weighted imaging; DCE: Dynamic contrast-enhanced.

The entire MRI session lasted approximately 45 min. T$_2$ maps and apparent diffusion coefficient (ADC) maps were calculated on the console using Philips analysis software.

DCE processing and analysis

All processing of the DCE data was performed using in-house software written in Matlab. In conjunction, a graphical user interface was developed to handle the DCE data flow. After data for one patient and time-point was loaded, tissue of interest was contoured in the view window on one of the dynamic images. These pixels were then targeted for analysis. Each pixel was analyzed independently. First, an enhancement curve was generated for the pixel in question by normalizing the signal level through-time to the average of the first five pre-contrast dynamics. This curve was then fit to an enhancement model (modified Brix model[21]) whose shape is controlled by four parameters: A, k$_{ep}$, k$_{el}$, and t$_{arr}$. The A is an amplitude factor, which can be related to the size of the extravascular extracellular space (EES)[22]. The parameters k$_{ep}$ and k$_{el}$ are rate constants which describe the transfer of contrast from the EES to plasma (k$_{ep}$), and the elimination of contrast from the plasma (k$_{el}$). The t$_{arr}$ parameter is simply the time at which the contrast is seen to arrive at the pixel. This model is described in the equation:

$$\{[S(t - t_{arr})]/[S(0)]\} = 1 + A \times k_{ep} \times \{\exp[-k_{ep}(t - t_{arr})] - \exp[-k_{el}(t - t_{arr})]\}/(k_{el} - k_{ep})$$

For each data set, one or more of the pixels were selected for initial analysis to better adjust the seed parameters used in the optimization routine. This optimization routine determined the four parameters described above that lead to the best fit of the model to the data. Changing the seed parameters was not found to affect the final result in this context, but it did increase the efficiency of the solver. The optimization code utilized the Matlab function "fminsearch", which uses a Nelder-Mead method appropriate for multi-dimensional nonlinear optimizations.

Interpretation of biological imaging

The MRI images were anonymized of patient identifiers and clinical information to ensure that there was an unbiased interpretation of each investigation. Each scan underwent radiological review and was reported upon without the other results known. The radiologist reported the presence of characteristics consistent with malignancy (Table 2) and defined the index of suspicion (IOS) for each lesion using a score of 1-5 (1: most probably benign; 2: probably benign; 3: indeterminate; 4: probably malignant; 5: highly suspicious of malignancy). IOS of 3 or higher was used as the cut-off for identification of malignant disease[23].

Table 3 Patient's demographics and disease characteristics at baseline

Characteristic	Value
Age (yr), median (range)	65 (51-75)
PSA (ng/mL), median (range)	6.4 (1.4-14.3)
Clinical stage, *n* (% of total)	
cT1c	20 (87.0)
cT2a	2 (8.7)
cT2b	1 (4.3)
Gleason score 6 (3 + 3), *n* (% of total)	23 (100%)
% of cores positive per patient, median (range)	8.3 (0[1]-58.3)
Density of tumor in positive biopsy cores (% of core), median (range)	10 (1-60)
HGPIN, *n* (% of total)	6 (26.1)
PNI, *n* (% of total)	4 (17.4)
LVI, *n* (% of total)	0 (0.0)

[1]Three patients had benign biopsies at study enrollment but previous positive biopsies. HGPIN: High grade prostate intraepithelial neoplasia; PNI: Perineural invasion; LVI: Lymphovascular invasion.

The radiologist reviewed the serial scans for each patient to examine if there were signs of disease progression over time including imaging characteristics (increased exchange on DCE, decreases in the ADC on DWI), growth of lesions, new lesions identified or other changes suggestive of disease progression.

RESULTS

Patient demographics

Over 40 mo (January 2009-May 2012), 24 active surveillance patients consented to and were enrolled on the study. One patient was not evaluable as they did not have evaluable MRI scans. The baseline characteristics of the 23 evaluable patients are described in Table 3. All patients enrolled had low-risk Gleason 3 + 3 = 6 disease and the majority were clinical stage T1c (87%). Three patients had no positive cores on their enrollment biopsy but had at least one positive biopsy previously. Nine patients on this active surveillance study had ≥ 3 cores positive (or ≥ 25% positive cores) from their baseline biopsy. Six of these patients had subsequent disease progression during the course of follow-up.

Amongst the study patients, 67 sets of biopsies were analyzed and the median number of biopsies was 3 per patient. The median number of cores per biopsy at baseline and during active surveillance was 12. In total there were 809 cores [median 12 cores per biopsy set (7-17)], with 143 cores positive for prostate cancer [median 1 positive core per biopsy set (range: 0-9)] with 5 sets of biopsies having greater than 50% positive cores over the course of the study. During the study 21 biopsies in 8 patients had biopsies with no positive cores. Of these only one patient had subsequent disease progression during the course of follow-up.

Disease progression

The median follow-up time was 24.8 mo (6.2-50.8 mo). During the study 11 patients had disease progression

Table 4 Prostate cancer visualization with magnetic resonance imaging

	n = 23
Number of scans with baseline IOS of:	
1	8
2	5
3	3
4	2
5	5
Number of follow-up MRI scans, median (range)	3 (0-4)
Number of follow-up scans with signs of disease progression	3
Number of follow-up scans with changed IOS	1

MRI: Magnetic resonance imaging; IOS: Index of suspicion.

and the median time from enrollment to progression was 21.7 mo (6.2-37.9 mo).

The primary cause for patients being categorized as having disease progression was upstaging to a higher Gleason score on biopsy (all 11 patients). In combination with the higher Gleason score, 5 of the 11 patients also had ≥ 50% of cores involved and 2 of these additionally had PSA doubling time less than 2 years. All of the patients with progressive disease were offered treatment. Two patients declined therapy and choose to remain on active surveillance, 5 had low dose rate prostate brachytherapy, 2 had external beam radiation treatment, and 2 underwent radical prostatectomies.

Prostate cancer imaging with MRI

Although all patients had previously positive biopsies of Gleason score 6 prostate cancer only 10 of the 23 patients had positive identification of malignancy (IOS 3-5) on mpMRI at baseline (Table 4 and Figure 1). The sensitivity of prostate cancer detection at baseline was 43.5%.
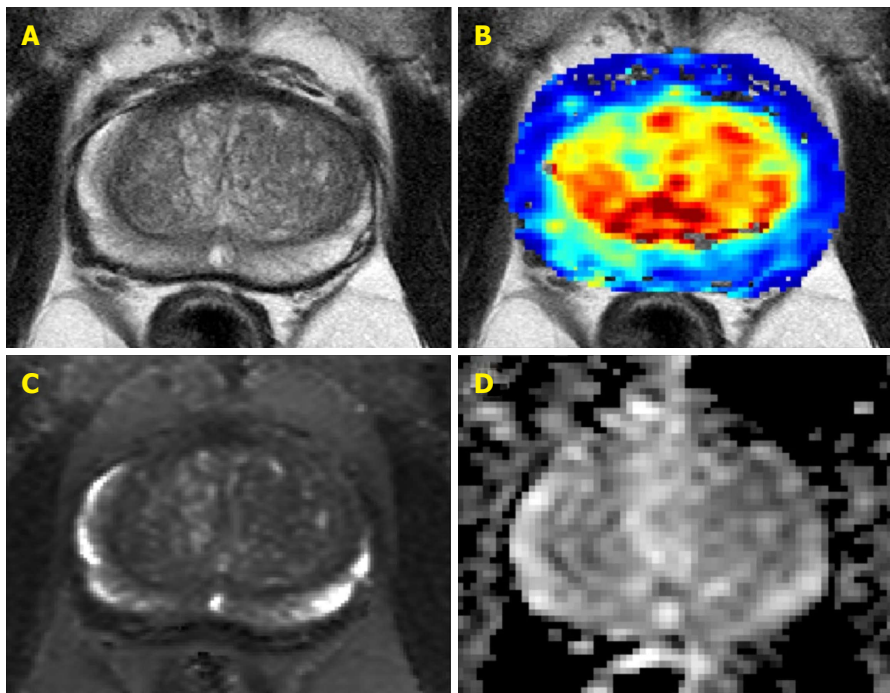
Seven of the ten patients with IOS greater than or equal to 3 at baseline had disease progression during the study. The aggressive disease prediction from baseline mpMRI scans had specificity of 81.8% and sensitivity of 58.3%.

Twenty-two patients had serial mpMRI scans and the median number of scans was 3 scans per patient (range 1-5). One patient had only a baseline scan with an IOS of 5 before disease progression was detected on biopsy. The IOS of mpMRI scans remained the same for all but one patient whose fourth scan had an IOS of 2 rather than 1 but remained below the threshold of 3 and this patient did not have disease progression on biopsy. Additionally during follow-up only 3 patients had scans with signs of disease progression and all 3 had baseline IOS of 4 or 5. The sensitivity to detect disease progression was 100% but the specificity was only 30% as 7 patients did not exhibit signs of disease progression on mpMRI but had Gleason score 7 disease on biopsy.

DISCUSSION

Low-risk prostate cancer can behave like an indolent
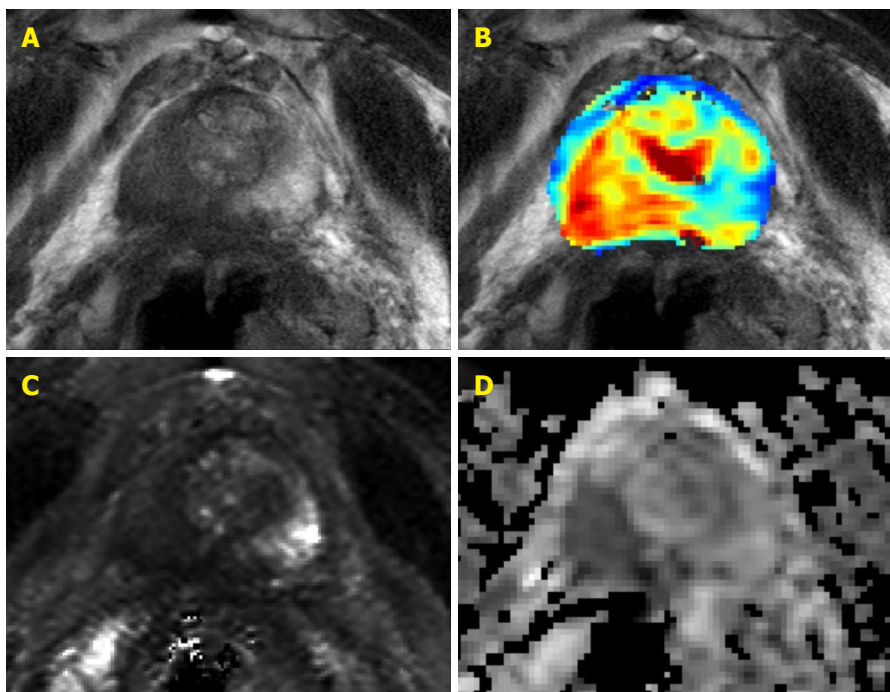
Patient 1

Patient 2

Figure 1 Baseline multiparametric magnetic resonance imaging images of two patients with Gleason score 6 low-risk prostate cancer but with different index of suspicion from multiparametric magnetic resonance imaging. Patient 1 had an IOS of 1 on their baseline MRI scan and Patient 2 had an IOS of 5 on their baseline MRI scan. The mpMRI images shown for each patient are: A: T2-weighted image; B: DCE-parameter overlay (Amplitude); C: Quantitative T2 map; D: ADC map. mpMRI: Multiparametric magnetic resonance imaging; MRI: Magnetic resonance imaging; IOS: Index of suspicion; ADC: Apparent diffusion coefficient; DCE: Dynamic contrast-enhanced.

disease and causes death in only a small subpopulation of patients[3-5]. Extensive work is being done to distinguish aggressive low-risk prostate cancer from indolent disease that doesn't require treatment but current surveillance protocols lack accurate tools. In addition to low accuracy due to undersampling, prostate biopsies cause discomfort and carry a risk of infection (including rare cases of sepsis leading to death). Addition of a sensitive and specific non-invasive method for monitoring patients would allow active surveillance to be a

more attractive management approach for men with prostate cancer. To the best of our knowledge, this is the first study that utilized serial mpMRI scans to predict disease aggressiveness.

We examined whether mpMRI IOS was related to larger lesions and found that 75% of the patients with IOS 3-5 had 25% or greater positive cores on baseline biopsy. This was regardless of future disease progression status although higher positive cores were also predictive of more aggressive disease. Six of the 11 patients that had subsequent progressive disease had 25% or higher positive cores at baseline compared with only 3 of 12 patients without signs of disease progression.

Gleason score remains the best available predictive factor for prostate cancer mortality and the presence of Gleason pattern 4 is often an indication that a patient should receive intervention[5]. mpMRI has been shown to have high detection accuracy for Gleason pattern 4 disease (97.4%)[24] and some of our patients with positive baseline scans may have had higher Gleason score disease that was missed on biopsy due to sampling inadequacy[11]. We performed sextant biopsies which, although standard practice, are subject to inaccuracy and inconsistency. This would be consistent with studies that showed better detection of Gleason score 7 disease and increased incidence of upstaging on MRI guided biopsies[24-27]. In one study 41% of Gleason score 6 patients were reclassified to higher Gleason score based on mpMRI targeted biopsy[28] and in another study 20% of patients were reclassified to a higher Gleason score upon repeat biopsy focused on MRI results[23].

This study was a pilot, feasibility study and as such was limited to a small sample size which resulted in limited power to correlate quantitative MRI parameters with disease progression. The standard b-value for the diffusion weighted MRI protocol changed from 500 to 1000 to 1400 s/mm^2 during the course of this work. For consistency, we kept it at 500 s/mm^2, which is the value we used at initiation. Also since study initiation, mpMRI technology and analyses have improved as well as increased experience by radiologists. Combined, these factors may have resulted in lower sensitivity for detection than desired at baseline and during follow-up.

In this study we only examined whether or not a prostate cancer lesion was identified on MRI. However, extracapsular extension, SV involvement, and LN involvement can also be examined through mpMRI. Utilization of imaging techniques may also improve detection of prostate cancer in the central or anterior aspect of gland which can often be missed on biopsy because of anatomical and technical limitations[9,29].

In this pilot study we found that baseline mpMRI was able to predict disease aggressiveness in 7 of 11 patients who had biopsy proven disease progression while on study. Three patients who did not have disease progression while on study were also predicted to have aggressive disease. If the mpMRI protocol utilized in this study were added to decision making in active surveil-

lance protocols this would have resulted in 7 patients receiving earlier therapy which could benefit clinical outcome. There would however be 3 patients treated without disease progression and 4 patients who would have missed earlier therapy and not be treated until after biopsy proven disease progression.

Active surveillance protocols are still evolving and there is currently no gold standard. Follow-up with PSA serum levels and repeat biopsies requires improvement and imaging modalities are being examined. The use of fluoro-deoxyglucose and choline positron emission tomography has been examined and they appear to have moderate ability to distinguish aggressive from indolent disease[30-32]. Here we demonstrate the potential of mpMRI to detect prostate cancer with increased risk of progression although alone it has limited sensitivity and specificity. The future of active surveillance will likely include molecular imaging in combination with less frequent biopsies and novel serum or urine biomarkers of disease progression[33].

COMMENTS

Background
Prostate cancer is one of the most common solid organ cancers and the third leading cause of cancer-related death in men. Introduction of and widespread utilization of serum prostate specific antigen (PSA) screening has increased the incidence of low-risk prostate cancer with about 25%-50% of newly diagnosed patients having low-risk disease. For the majority of these patients, the prostate cancer will behave as an indolent disease and only have clinically significant effects or cause death in a relatively small proportion of men. Many patients with low-risk indolent prostate cancer are choosing to delay treatment and as a result many are managed with active surveillance. This management strategy involves the monitoring of PSA values and prostate biopsies, but these tests lack accuracy for predicting aggressive or progressive disease. In this study the authors examined whether the addition of 3T multiparametric magnetic resonance imaging (mpMRI) at 3T to an active surveillance protocol could increase the detection of aggressive or progressive prostate cancer.

Research frontiers
Active surveillance protocols are still evolving and there is currently no gold standard. Follow-up with PSA serum levels and repeat biopsies requires improvement and imaging modalities including positron emission tomography and MRI are being examined. Novel serum or urine biomarkers of disease progression are being examined to supplement PSA monitoring.

Innovations and breakthroughs
Numerous studies with mpMRI of patients with prostate cancer have shown its utility to detect intermediate risk prostate cancer. To the best of the authors' knowledge, this is the first prospective study that utilized serial mpMRI scans during active surveillance of patients with low risk prostate cancer to predict disease aggressiveness.

Applications
Although this study was a small pilot trial, it supports further examination of mpMRI during active surveillance decision making. With the recent improvements in technology and clinical experience it is likely that a larger trial

could show the ability of mpMRI to predict indolent disease and thus stratify patients to active surveillance or definitive treatment.

Terminology

mpMRI provides a non-invasive way of measuring a range of possible quantitative physiological parameters in addition to conventional anatomical information. With regards to this study into prostate cancer, the T2 weighted imaging provided detailed soft tissue anatomical features and dynamic contrast enhanced provided physiological exchange parameters through the rate of intake and washout of the gadolinium contrast agent which is different in prostate cancer than normal prostate tissue. The measurement of apparent diffusion coefficient provided yet another quantitative parameter. Gleason score is the sum of primary and secondary Gleason patterns. The Gleason patterns are assigned by a pathologist examining the cellular features on the biopsy. The range of scores is 1 for cancer that closely resembles normal prostate tissue and glands are present through 5 for prostate cancer in which there are sheets of cells and few or no glands visible.

Peer-review

The authors evaluated the role of multiparametric MRI in detecting aggressive tumors during active surveillance in 23 low-risk prostate cancer patients.

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