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Role of Changes in Magnetic Resonance Imaging or Clinical Stage in Evaluation of Disease Progression for Men with Prostate Cancer on Active Surveillance

Gregory T. Chesnut[a,*], **Emily A. Vertosick**[b], **Nicole Benfante**[b], **Daniel Sjoberg**[b], **Jonathan Fainberg**[c], **Taehyoung Lee**[a], **James Eastham**[a], **Vincent Laudone**[a], **Peter Scardino**[a], **Karim Touijer**[a], **Andrew Vickers**[b], **Behfar Ehdaie**[a]

[a]Urology Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA

[b]Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, USA

[c]Department of Urology, New York Presbyterian Hospital/Weill Cornell Medical Center, New York, NY, USA

Abstract

Background: Active surveillance (AS) protocols rely on rectal examination, prostate-specific antigen, imaging, and biopsy to identify disease progression.

Objective: To evaluate whether an AS regimen based on magnetic resonance imaging (MRI) or clinical stage changes can detect reclassification to grade group (GG) ≥2 disease compared with scheduled systematic biopsies.

[*]Corresponding author. Urology Service, Sidney Kimmel Center for Prostate and Urologic Cancers, Memorial Sloan Kettering Cancer Center, 353 E 68th St, New York, NY 10065, USA., Tel. +1 (212) 639-4406; Fax: +1 (929) 321-7023. chesnutg@mskcc.org (G.T. Chesnut).

***Author contributions*:** Gregory T. Chesnut had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Chesnut, Ehdaie, Vickers.

Acquisition of data: Chesnut, Benfante, Vertosick.

Analysis and interpretation of data: Chesnut, Vertosick, Sjoberg, Vickers, Ehdaie.

Drafting of the manuscript: Chesnut, Ehdaie, Vertosick.

Critical revision of the manuscript for important intellectual content: Eastham, Laudone, Scardino, Touijer, Vickers, Ehdaie.

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Design, setting, and participants: We identified a cohort of men initiated on AS between January 2013 and April 2016 at a single tertiary-care center. Patients completed confirmatory testing and prostate MRI prior to enrollment, then underwent laboratory and physical evaluation every 6 mo, MRI every 18 mo, and biopsy every 3 yr.

***Outcome measurements and statistical analysis*:** MRI results were evaluated using composite Likert/Prostate Imaging Reporting and Data System v2 scoring. MRI and clinical changes were assessed for association with disease progression. Univariable and multivariable regression models were used to predict upgrading on 3-yr biopsy.

Results and limitations: At 3 yr, of 207 men, 66 (32%) had ≥GG2 at biopsy: 55 (83%) with GG2, 10 (15%) with GG3, and one (1.5%) with GG4. Among patients with a 3-yr MRI score of ≥3, 41% had ≥GG2 disease, compared with 15% with an MRI score of <3 ($p = 0.0002$). The MRI score increased in 48 men (23%), decreased in 27 (13%), and was unchanged in 132 (64%) men. Increases in MRI score were not associated with reclassification after adjusting for the 3-yr MRI score ($p = 0.9$). Biopsying only for an increased MRI score or clinical stage would avoid 319 biopsies per 1000 men, at the cost of missing ≥GG2 disease in 169 patients.

Conclusions: An AS strategy that uses MRI or clinical changes to trigger prostate biopsy avoids many biopsies but misses an unacceptable amount of clinically significant disease. Prostate biopsy for men on AS should be performed at scheduled intervals, regardless of stable imaging or examination findings.

Patient summary: An active surveillance strategy for biopsy based only on increases in magnetic resonance imaging score or clinical stage will avoid many biopsies; however, it will miss many patients with clinically significant prostate cancer.

Keywords

Prostate cancer; Active surveillance; Prostate imaging; Progression; Magnetic resonance imaging

1. Introduction

Active surveillance (AS) for men with low-risk prostate cancer is increasingly being adopted, and its use is universally endorsed in clinical guidelines [1–5]. Inherent in most AS protocols is the requirement to repeat prostate biopsy as part of a multimodal assessment, which includes physical examination, laboratory evaluation, and, increasingly, multiparametric magnetic resonance imaging (MRI) of the prostate [6]. Studies have shown that MRI is effective both in improving biopsy accuracy and in identifying disease progression for men on AS [7,8]. Despite these improvements, scheduled systematic biopsy is still recommended in AS regimens to identify disease progression [9]. The role of changes identified during surveillance MRI, including detection of new lesions after confirmatory biopsy, has not been defined fully in the AS setting.

Less invasive methods to detect disease progression for men on AS can help reduce morbidity associated with scheduled systematic prostate biopsies. Despite advances in diagnostic technology, imaging and laboratory evaluations have yet to be proved sufficiently accurate to avoid a repeat prostate biopsy for men on AS without missing disease

progression, and the European Association of Urology recommends a follow-up strategy based primarily on clinical and biopsy evaluation [9–11]. Several studies, however, have suggested that MRI stability can help identify men at low risk for disease reclassification and those in whom repeat biopsy can be avoided [12–15]. Anecdotally, urologists are increasingly using negative or stable MRI findings to avoid performing repeat biopsy in men on AS. We reviewed our institutional experience of AS to evaluate disease progression in a contemporary cohort within a standardized AS program that involves regular physical examination, prostate-specific antigen (PSA) testing, multiparametric MRI, and biopsy follow-up. Our goals were twofold: to evaluate whether changes to MRI features or clinical stage identified using digital rectal examination (DRE) could be used to correctly identify disease progression among men with grade group (GG) 1 disease being treated on AS, and to identify the number of ≥GG2 cancers potentially missed by implementing a biopsy protocol predicated only on changes in imaging or clinical stage compared with scheduled systematic biopsies, which is our institution's standard of care.

2. Patients and methods

2.1. Patient population

After obtaining institutional review board approval, we identified 415 patients in the AS program at our institution from our prospectively maintained AS database. All patients received a diagnosis of prostate cancer between January 2013 and April 2016. This end date was chosen to ensure enough time for all patients to undergo at least two surveillance MRI scans and one scheduled prostate biopsy. Patients were excluded if they did not have GG1 disease at diagnosis ($N = 49$) or had not completed both MRI and biopsy between 2 and 4 yr after commencement of AS ($N = 159$), leaving 207 patients eligible for analysis. All patients were categorized as having National Comprehensive Cancer Network (NCCN) very low risk or low risk.

2.2. AS protocol

Prior to enrollment on AS, all men underwent confirmatory biopsy within 1 yr and underwent multiparametric prostate MRI. If MRI was not performed prior to initial biopsy, it was completed prior to confirmatory biopsy. All confirmatory biopsies were MRI guided if a targetable lesion was identified. Men with NCCN very-low-risk group disease who were referred for AS after initial or confirmatory biopsy were eligible to begin AS without repeating confirmatory biopsy. In these patients, baseline MRI was performed after AS confirmation. Based on our institution's AS protocol, patients undergo PSA testing and DRE every 6 mo, repeat multiparametric MRI every 18 mo, and follow-up MRI and biopsy at 3 yr after the initiation of AS. Images were acquired under a magnetic field of 3 T without endorectal coil, although our institutional protocol evolved over time. Sequences acquired included T1-weighted images, T2-weighted images, diffusion-weighted sequences, and dynamic contrast-enhanced sequences. Magnetic resonance (MR) images were evaluated by one of the six attending radiologists specializing in genitourinary radiology. Any lesion seen on MRI was targeted during initial, confirmatory, or surveillance biopsy. All targeted biopsies were performed under visual and software registration using a computer-assisted elastic image fusion system with real-time three-dimensional tracking technology, and two

to three biopsies were performed on targeted lesions (UroStation; Koelis, Grenoble, France). In addition to MR-targeted biopsy, all men underwent systematic transrectal ultrasound–guided 14-core prostate biopsy consisting of samples obtained from the medial and lateral aspects of the base, and middle and apical portions of the prostate bilaterally, along with two samples from the transition zone. If no region of interest (ROI) was identified with an MRI score of >2, systematic biopsy alone was performed. Prior to 2015, MR images were evaluated using a Likert Scale (0–5), which was previously validated for prostate cancer and which was shown to have low interobserver variability at our center [16–19]. Prostate Imaging Reporting and Data System (PI-RADS) v2 was used beginning in 2015. A composite MRI score was created using the Likert and PI-RADS v2 scoring systems. Owing to previously demonstrated high concordance of Likert Scale and PI-RADS v2, lesions prior to 2015 were recorded using Likert Scale, while those beginning in 2015 were scored with PI-RADS v2 [18].

2.2.1. AS biopsies—All patients underwent scheduled systematic biopsy at 3 yr. Few underwent an additional earlier biopsy, although for those who did, it was considered either “for cause” (based on MRI findings) or “not for cause” (for other reasons, including patient request, rebiopsy at a different institution, or another regularly scheduled follow-up biopsy before 3 yr). We considered 3-yr biopsy to be any biopsy performed between 2 and 4 yr after diagnosis. There were no scheduled 2- or 4-yr biopsies. We broadened the inclusion period to accommodate natural variability in scheduled biopsies based on patient and physician availability. Any biopsies performed at outside institutions were reviewed by our institution’s dedicated genitourinary pathologists. All biopsies were reported according to International Society of Urological Pathology standards [20]. Critically, no man in our cohort was advised against biopsy due to a low MRI score.

2.2.2. AS imaging evaluation—When evaluating whether changes in the MRI score or clinical stage could be used to predict which patients progress from GG1 disease, we defined change in MRI score as development of a new targetable lesion, represented by a change from an MRI score of 0, 1, or 2 to ≥3, or by any increasing MRI score from a lesion scored as ≥3 while on AS. Additionally, presence of extraprostatic extension (EPE) on 3-yr MRI among patients without EPE on baseline MRI was defined as imaging progression. Change in clinical stage was defined as any increase in clinical stage before the 3-yr MRI and biopsy.

2.3. Statistical analysis

To assess whether the 3-yr MRI score was predictive of clinically significant disease at 3-yr biopsy, we created a univariable logistic regression model using the score from the 3-yr MRI (no lesion or an MRI score of 1 or 2 vs an MRI score of ≥3) to predict whether the outcome of the 3-yr biopsy was progression to ≥GG2 disease.

If the association between lesions identified on 3-yr MRI and GG found on 3-yr biopsy was found to be significant, we planned to assess whether changes in MRI features or clinical stage added to our ability to predict ≥GG2 disease. We investigated two additional MRI-related factors: (1) any increase in MRI score from diagnosis to 3-yr MRI and (2) the

presence of EPE on 3-yr MRI among patients without EPE on the baseline MRI. We created multivariable logistic regression models for each of the additional factors, including the MRI score at 3 yr (no lesion or MRI score <3 vs MRI score ≥3), as well as change in clinical stage. To assess clinical utility, we calculated the number of biopsies that would be performed and avoided, and the number of ≥GG2 cancers diagnosed or missed, had MRI features or increase in clinical stage been used to determine which patients should be biopsied. This information was reported as the number of biopsies that would be performed or avoided, and the number of ≥GG2 cancers that would be diagnosed or missed per 1000 men in the patient population, respectively. All analyses were conducted using Stata 15 (StataCorp, College Station, TX, USA).

3. Results

Our cohort consisted of 207 men with GG1 disease who were enrolled in our institution's AS program and had both 3-yr biopsy and 3-yr MRI available. Patient demographics and disease characteristics at diagnosis and 3-yr biopsy are shown in Table 1. Twenty-five patients had an interim biopsy between the confirmatory and 3-yr biopsies. Only six had a for-cause biopsy, while all other interim biopsies were not performed for cause. There were two patients who had an upgrade to GG2 disease on a not-for-cause interim biopsy, but were not found to have GG2 disease at 3 yr: one patient had GG1 disease and one had no disease at 3 yr. These two patients have been included for the event of upgrading at 3 yr, as GG2 disease was known to be present by that time. Sixteen men (8%) with very-low-risk disease were confirmed on AS without MRI prior to AS start date. All others underwent MRI prior to confirmatory biopsy and MRI-guided biopsy of any targetable lesions. Median time on AS for patients who did not proceed to definitive treatment was 4.1 yr (interquartile range, 3.5–4.7).

Our analysis included all 207 patients in this cohort. Of 207 patients, 66 (32%) were found to have clinically significant disease at 3-yr biopsy: 55 patients (83%) with GG2 disease, 10 patients (15%) with GG3, and one patient with GG4 (1.5%). Of 207 patients, 101 underwent MRI-targeted plus systematic 3-yr AS biopsy and 106 underwent systematic biopsy alone as no targetable lesion was found on MRI. Of these 101, 39 were found to have clinically significant disease. Disease reclassification was identified by targeted biopsy alone in four patients, by systematic biopsy alone in 17 patients, and by both targeted and systematic biopsy in 18 patients.

3.1. MRI characteristics during AS

We found that presence of an MRI-detectable lesion at 3 yr was associated with disease progression. Among patients with an MRI score of ≥3 at 3 yr, 41% had ≥GG2 disease, compared with 15% of those with no lesion or an MRI score of <3, a difference of 25% (95% confidence interval, 14–37%, $p = 0.0002$). Rates of clinically significant disease are stratified by MRI score in Table 2. The use of an MRI score of ≥3 alone at 3 yr to identify men on AS for biopsy would result in 652 per 1000 men being biopsied, with 266 being diagnosed with ≥GG2 disease. It would result in avoiding 348 biopsies but would delay ≥GG2 cancer diagnosis in 53 patients.

3.2. Role of changes in MRI during AS period

After confirming that a 3-yr MRI score of ≥3 was significantly associated with the risk of clinically significant disease on 3-yr biopsy, we investigated whether including changes on surveillance MRI, or clinical stage changes in addition to MRI score, would allow us to better predict the risk of clinically significant disease. Changes in surveillance MRI findings occurred in a minority of patients and depended on baseline MRI at diagnosis (Table 3). After adjusting for the MRI score of ≥3 at 3 yr, we found no evidence that any increase in MRI score from baseline was associated with ≥GG2 disease among all patients ($p = 0.9$), and no evidence that new development of EPE on 3-yr MRI was associated with progression of disease in patients with no EPE on baseline MRI ($p = 0.11$). Twenty-one patients in our cohort had an increase in clinical stage between baseline and 3-yr biopsy, with 15 of these patients having an MRI score of ≥3. We found that increase in clinical stage was associated with ≥GG2 disease at 3 yr in addition to the MRI score at 3 yr ($p = 0.015$). Among all men who had an increase in MRI score, 42% progressed to ≥GG2. However, disease progression was also seen among men with stable or even decreasing MRI scores (Table 3).

3.3. Evaluation of MRI or clinical-change-only biopsy protocol versus scheduled biopsy

Of 50 men with a stable MRI score of 3, 16 (32%) were found to have ≥GG2 disease at 3-yr biopsy (Table 3). On average, 31% of men with stable MRI scores (regardless of the score) had ≥GG2 disease in their scheduled 3-yr biopsy specimen (range, 15–75%, depending on their baseline MRI score). If an AS protocol used “any increase in MRI score or clinical stage” as a biopsy threshold, 28% and 64% of ≥GG2 disease would be missed among men with baseline MRI scores of <3 and ≥3, respectively (Table 4). As a sensitivity analysis, we repeated these analyses excluding the six patients who had interim for-cause biopsy. Results were consistent with the main analysis and are presented in Supplementary Table 1. Additional sensitivity analysis excluding patients who underwent interim biopsy for any reason demonstrates consistent findings (Supplementary Table 2).

4. Discussion

Most men with disease progression while on AS in our study had unchanged imaging findings and stable clinical stage during the first 3 yr on AS. In our select cohort of men who completed confirmatory testing and were enrolled in the AS group, 29% had ≥3 positive biopsy cores or a PSA value of ≥10, and 60% had a targetable lesion identified on MRI at the start of AS. Higher MRI scores at 3 yr are significantly associated with a higher likelihood of finding ≥GG2 disease among men on AS. However, change in MRI score alone while on AS did not increase the likelihood of finding ≥GG2 disease at 3 yr. Importantly, we found that the absence of new ROIs or stability of lesions already seen on MRI was not sufficiently reassuring to avoid scheduled biopsy, evidenced by the findings that up to nearly a third of men with stable MRI scores were found to harbor ≥GG2 on follow-up biopsy. Overall, 15% of men with a no targetable lesion on MRI had clinically significant disease on scheduled 3-yr AS biopsy, too high a risk to warrant avoiding a scheduled biopsy in these men. Changes found during clinical examination did not alter these findings, suggesting that neither unchanged DRE nor imaging stability obviates the need for scheduled prostate biopsy. We showed that an AS protocol that calls for repeat biopsy only for changes in

clinical stage or MRI score would save many men from surveillance biopsies, but would do so at the cost of missing many clinically significant prostate cancers. Within our AS cohort, 32% of patients were found to have ≥GG2 at 3-yr biopsy, which is comparable with the 28% of men with disease progression reported by the Movember GAP3 (Global Action Plan Prostate Cancer Active Surveillance initiative) consortium, with a database of 10 296 men, at 5 yr [21]. In our study, among men properly selected for AS with confirmatory imaging and testing, those who experienced disease progression were more than five times more likely to harbor GG2 disease than ≥GG3 disease. Similar to Giganti et al [22], we found that changes in MRI scoring occurred in a minority of patients. Interestingly, a greater proportion of men with lower MRI scores at baseline were found to have new ROI or MRI score increases at 3 yr.

Incorporation of MRI into AS regimens has been proposed to increase detection of disease progression and target lesions most likely to harbor higher-grade disease. Giganti et al [22] found large variations in measured tumor volume among men with serial MRI on AS but also noted that 88% of men without an apparent lesion on initial MRI continued to have no targetable lesion at 3.6 yr of follow-up. While higher MRI imaging scores have been shown to be associated with an increased probability of detecting ≥GG2 disease, Recabal et al [9] showed that a biopsy protocol involving both MRI-targeted biopsy and systematic biopsy consistently detected more higher-grade cancers than MRI-targeted biopsy alone, regardless of the MRI score of the targeted lesion. Our study confirms the utility of combined MRI-guided biopsy and systematic biopsy in the AS population.

Frye et al [8] found MRI lesion progression useful in identifying men at risk for disease progression while on AS if they began AS with a targetable lesion. With a mean follow-up of 25.5 mo, their study showed that men with pathologic disease progression were more likely to experience MRI progression than maintaining stable imaging (79% vs 21%).However, their study included men undergoing confirmatory biopsy between 12 and 24 mo, and many men who had disease progression based on MRI changes had yet to undergo confirmatory biopsy. Uniquely, our study evaluates MRI changes among men who completed confirmatory testing prior to enrollment.

Our study has several limitations, one being that it represents a retrospective single high-volume cancer center experience. As such, this may limit the generalizability of our findings. That said, a high-volume center with specialist radiology support and reported high concordance between interpretations by radiologists provides optimal conditions to use serial MRI and avoid biopsy. While most confirmatory biopsies were performed after MRI, 8% of men in our study with NCCN very-low-risk group disease started AS prior to MRI-guided confirmatory biopsy. In these patients, baseline MRI was performed after AS confirmation. Although this is a limitation, none of these men had targetable lesions on subsequent MRI. Although the strict AS regimen strengthens our findings, the results from our 207-patient sample size require validation in larger cohorts. We broadened our inclusion criteria for 3-yr biopsies to include biopsies performed between 2 and 4 yr, and recognize this wider time interval as a potential limitation. While our AS regimen is standardized, we found it practical to accommodate patient preference in scheduling surveillance biopsies. In this study, 75% of our surveillance biopsies were performed within 6 mo of the planned 3-yr

biopsy. We did not re-review the prostate images to calculate the volume of MRI lesions. However, many regions of interest on MRI do not have a distinct and measurable lesion. It is possible that findings on MRI could have impacted decisions regarding timing for prostate needle biopsy; however, we performed a sensitivity analyses excluding the six patients who had interim for-cause biopsy, and the results were consistent with the main analysis.

These findings have important implications for patients and providers. Specifically, AS protocols increasingly incorporate MRI into serial laboratory, examination, and biopsy schedules. Routine use of MRI in AS clearly has been proved useful in guiding surveillance biopsies to increase the detection of disease progression. However, as we have shown, unchanged prostate imaging cannot be used to avoid a scheduled repeat prostate biopsy. Both repeat MRI and repeat prostate biopsy are needed, and one cannot be substituted for the other: MRI and repeat biopsy are independently important for the evaluation of patients on AS. Patients need to be counseled on the justification for scheduled, repeat prostate biopsies, regardless of imaging stability. While patients with MRI scores <3 are at lower risk than patients with scores of ≥3, they are not at low risk; the upper bound of the confidence interval indicates that up to 26% of these patients could have ≥GG2 disease at 3 yr. The risk of ≥GG2 disease is not low enough to justify performing repeat biopsy only among men with MRI scores of ≥3, and a biopsy protocol predicated on MRI score increases or clinical stage increases misses a significant portion of disease reclassification to ≥GG2 that would be identified on scheduled repeat biopsy at 3 yr.

5. Conclusions

Most men who are reclassified on AS have unchanged imaging and clinical stage during the first 3 yr of AS. Prostate MRI is effective in identifying lesions that are more likely to harbor ≥GG2 prostate cancer and in aiding the targeted biopsy of these lesions; however, lack of serial changes on MRI cannot be used to eliminate scheduled surveillance biopsies. An AS strategy for biopsy based only on increases in MRI score or clinical stage will avoid many biopsies, but will miss an unacceptable number of patients with clinically significant disease. For men on AS, surveillance biopsy should be performed at scheduled intervals; imaging or clinical stage findings cannot be used to justify the decision not to perform a biopsy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

[1]. Modi PK, Kaufman SR, Qi J, et al. National trends in active surveillance for prostate cancer: validation of Medicare Claims-based algorithms. Urology 2018;120:96–102. [PubMed: 29990573]

[2]. Cooperberg MR, Carroll PR. Trends in management for patients with localized prostate cancer, 1990–2013. JAMA 2015;314:80–2. [PubMed: 26151271]

[3]. Womble PR, Montie JE, Ye Z, Linsell SM, Lane BR, Miller DC. Contemporary use of initial active surveillance among men in Michigan with low-risk prostate cancer. Eur Urol 2015;67:44–50. [PubMed: 25159890]

[4]. Mohler J, Armstrong A, Bahanson R, et al. Prostate cancer, version 1.2016. J Natl Compr Cancer Netw JNCCN 2016;14:19–30.

[5]. Mottet N, Bellmunt J, Bolla M, et al. EAU-ESTRO-SIOG guidelines on prostate cancer. part 1: screening, diagnosis, and local treatment with curative intent. Eur Urol 2017;71:618–29. [PubMed: 27568654]

[6]. Fam MM, Yabes JG, Macleod LC, et al. Increasing utilization of multiparametric magnetic resonance imaging in prostate cancer active surveillance. Urology 2019;130:99–105. [PubMed: 30940480]

[7]. Futterer JJ, Briganti A, DeVisschere P, et al. Can clinically significant prostate cancer be detected with multiparametric magnetic resonance imaging? A systematic review of the literature. Eur Urol 2015;68:1045–53. [PubMed: 25656808]

[8]. Frye TP, George AK, Kilchevsky A, et al. Magnetic resonance imaging-transrectal ultrasound guided fusion biopsy to detect progression in patients with existing lesions on active surveillance for low and intermediate risk prostate cancer. J Urol 2017;197:640–6. [PubMed: 27613356]

[9]. Recabal P, Assel M, Sjoberg DD, et al. The efficacy of multiparametric magnetic resonance imaging and magnetic resonance imaging targeted biopsy in risk classification for patients with prostate cancer on active surveillance. J Urol 2016;196:374–81. [PubMed: 26920465]

[10]. Loeb S, Tosoian JJ. Biomarkers in active surveillance. Transl Androl Urol 2018;7:155–9. [PubMed: 29594029]

[11]. Briganti A, Fossati N, Catto JWF, et al. Active surveillance for low-risk prostate cancer: the European Association of Urology Position in 2018. Eur Urol 2018;74:357–68. [PubMed: 29937198]

[12]. Margel D, Yap SA, Lawrentschuk N, et al. Impact of multiparametric endorectal coil prostate magnetic resonance imaging on disease reclassification among active surveillance candidates: a prospective cohort study. J Urol 2012;187:1247–52. [PubMed: 22335871]

[13]. Walton Diaz A, Shakir NA, George AK, et al. Use of serial multiparametric magnetic resonance imaging in the management of patients with prostate cancer on active surveillance. Urol Oncol 2015;33:202e1–7.

[14]. Moore CM, Petrides NF, Emberton M. Can MRI replace serial biopsies in men on active surveillance for prostate cancer? Curr Opin Urol 2014;24:280–7. [PubMed: 24614348]

[15]. Eineluoto JT, Jarvinen P, Kenttamies A, et al. Repeat multiparametric MRI in prostate cancer patients on active surveillance. PLoS One 2017;12:e0189272. [PubMed: 29281647]

[16]. Vargas HA, Akin O, Franiel T, et al. Diffusion-weighted endorectal MR imaging at 3 T for prostate cancer: tumor detection and assessment of aggressiveness. Radiology 2011;259:775–84. [PubMed: 21436085]

[17]. Vargas HA, Akin O, Shukla-Dave A, et al. Performance characteristics of MR imaging in the evaluation of clinically low-risk prostate cancer: a prospective study. Radiology 2012;265:478–87. [PubMed: 22952382]

[18]. Rosenkrantz AB, Kim S, Lim RP, et al. Prostate cancer localization using multiparametric MR imaging: comparison of prostate imaging reporting and data system (PI-RADS) and Likert scales. Radiology 2013;269:482–92. [PubMed: 23788719]

[19]. Gondo T, Hricak H, Sala E, et al. Multiparametric 3T MRI for the prediction of pathological downgrading after radical prostatectomy in patients with biopsy-proven Gleason score 3+4 prostate cancer. Eur Radiol 2014;24:3161–7. [PubMed: 25100337]

[20]. Epstein JI, Zelefsky MJ, Sjoberg DD, et al. A contemporary prostate cancer grading system: a validated alternative to the Gleason score. Eur Urol 2016;69:428–35. [PubMed: 26166626]

[21]. Van Hemelrijck M, Ji X, Hellman J, et al. Reasons for discontinuing active surveillance: assessment of 21 centres in 12 countries in the Movember GAP3 Consortium. Eur Urol 2019;75:523–31. [PubMed: 30385049]

[22]. Giganti F, Moor CM, Punwani S, et al. The natural history of prostate cancer on MRI: lessons from an active surveillance cohort. Prostate Cancer Prostatic Dis 2018;21:556–63. [PubMed: 30038388]

Table 1 –

Patient demographics at diagnosis, and disease characteristics on diagnostic and 3-yr biopsies (*N* = 207)

	Diagnostic biopsy	Biopsy at 3 yr
Age (yr)	61 (57, 66)	
Race		
White	174 (84%)	
Black	20 (10%)	
Asian	3 (1.4%)	
Other/unreported	10 (4.8%)	
PSA (*N* = 196)	4.4 (3.6, 5.5)	
NCCN risk category (*N* = 197)		
Very low risk	140 (71%)	
Low risk	57 (29%)	
Clinical T classification	*N* = 207	*N* = 207
≤T1c	183 (88%)	182 (88%)
>T1c	24 (12%)	25 (12%)
Biopsy grade group		
No cancer	0 (0%)	48 (23%)
1	207 (100%)	93 (45%)
2	0 (0%)	55 (27%)
3	0 (0%)	10 (4.8%)
4	0 (0%)	1 (0.5%)
Number of positive biopsy cores	*N* = 206	*N* = 207
	1 (1, 2)	2 (1, 4)
Total number of biopsy cores taken	*N* = 206	*N* = 207
	12 (7, 13)	15 (14, 16)
Maximum percent cancer	*N* = 200	*N* = 155
	10 (5, 20)	25 (10, 50)
Total length of cancer (mm)	*N* = 196	*N* = 155
	1.5 (0.8, 3.0)	3.5 (1.5, 6.3)
MRI score		
≤2	83 (40%)	72 (35%)
3	77 (37%)	74 (36%)
4	45 (22%)	53 (26%)
5	2 (1.0%)	8 (3.9%)
Presence of EPE on MRI	5 (2.4%)	9 (4.3%)

EPE = extraprostatic extension; MRI = magnetic resonance imaging; NCCN = National Comprehensive Cancer Network; PSA = prostate-specific antigen.

Data are presented as median (quartiles) or frequency (%).

Table 2 –

Number of ≥GG2 cancers on 3-yr biopsy by MRI score on 3-yr MRI

	Rate of ≥GG2 disease, *n* (%)
No lesion or MRI score <3	11 (15)
MRI score 3	23 (31)
MRI score 4	26 (49)
MRI score 5	6 (75)

GG = grade group; MRI = magnetic resonance imaging.

Table 3 –

MRI score changes and disease progression

Baseline MRI	Change in MRI score	Number of patients	Progression to ≥GG2, *n* (%)
≤2	Stable	51	8 (16)
	Increase	32	13 (41)
3	Decrease	11	1 (9.1)
	Stable	50	16 (32)
	Increase	16	7 (44)
≥4	Decrease	16	4 (25)
	Stable	31	17 (55)
All	Decrease	27	5 (19)
	Stable	132	41 (31)
	Increase	48	20 (42)

GG = grade group; MRI = magnetic resonance imaging.

Table 4 –

Number of biopsies performed and avoided per 1000 men, and number of ≥GG2 diagnoses identified or delayed when using biopsy thresholds based on MRI features and changes in clinical stage

		Per 1000 men in patient population			
Patient population	**Biopsy threshold**	**Biopsies performed**	**Biopsies avoided**	**≥GG2 cancers diagnosed**	**≥GG2 cancers missed, *n* (%)**
All men	Any increase in MRI score or clinical stage	319	681	150	169 (53)
Baseline MRI score <3	Any increase in MRI score or clinical stage	422	578	180	72 (28)
Baseline MRI score ≥3	Any increase in MRI score or clinical stage	250	750	129	237 (64)

GG = grade group; MRI = magnetic resonance imaging.