Natural History of Pathologically Benign Cancer Suspicious Regions on Multiparametric Magnetic Resonance Imaging Following Targeted Biopsy

Darren J. Bryk,* Elton Llukani, William C. Huang and Herbert Lepor

From the Department of Urology, Smilow Comprehensive Prostate Cancer Center, New York University School of Medicine, New York, New York

Abbreviations and Acronyms

ADC = apparent diffusion coefficient

ASAP = atypical small acinar proliferation

CSR = cancer suspicious region

DCE = dynamic contrast enhancement

DRE = digital rectal examination

DWI = diffusion weighted imaging

GLM = greatest linear measurement

HGPIN = high grade prostatic intraepithelial neoplasia

mpMRI = multiparametric MRI

MRI = magnetic resonance imaging

PCa = prostate cancer

ss = suspicion score

US = ultrasound

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Study received institutional review board approval.

* Correspondence: Department of Urology, New York University School of Medicine, 150 East 32nd St., 2nd Floor, New York, New York 10016 (telephone: 917-833-4676; FAX: 646-825-6397; e-mail: Darren.Bryk@med.nyu.edu).

Purpose: We determined the natural history of pathologically benign cancer suspicious regions on multiparametric magnetic resonance imaging following targeted biopsy.

Materials and Methods: Between January 2012 and September 2014, 330 men underwent prostate multiparametric magnetic resonance imaging. A total of 533 cancer suspicious regions were identified and scored on a Likert scale of 1 to 5 based on suspicion for malignancy with 5 indicating the highest suspicion level. Following multiparametric magnetic resonance imaging all men underwent magnetic resonance imaging-ultrasound fusion targeted prostate biopsy using ProFuse software and the ei-Nav|Artemis system (innoMedicus, Cham, Switzerland), and a computer generated 12-core random biopsy. We analyzed a cohort of 34 men with a total of 51 cancer suspicious regions who had benign prostate biopsies and underwent repeat multiparametric magnetic resonance imaging and prostate specific antigen testing at 1 year. Changes in the greatest linear measurement, the suspicion score and serum prostate specific antigen were ascertained.

Results: During 1 year the suspicion score distribution and the mean greatest linear measurement of the cancer suspicious regions decreased significantly ($p < 0.0001$) while mean prostate specific antigen did not significantly change ($p = 0.632$). Two (3.9%), 15 (29.4%) and 34 cancer suspicious regions (66.7%) showed an increase, no change and decrease in suspicion score, respectively. No (0%), 21 (42.0%) and 29 cancer suspicious regions (58.0%) showed an increase of 20% or greater, no change and a decrease of 20% or greater in greatest linear measurement, respectively. Of the 2 cancer suspicious regions exhibiting an increased suspicion score neither showed a prostate specific antigen increase of 0.5 ng/ml or greater.

Conclusions: Our study provides compelling evidence that few benign cancer suspicious regions increase in suspicion score and/or the greatest linear measurement within 1 year independent of the baseline suspicion score. Therefore, routinely repeating multiparametric magnetic resonance imaging at 1 year in men with pathologically benign cancer suspicious regions should be discouraged since it is unlikely to influence management decisions.

Key Words: prostate, prostatic neoplasms, magnetic resonance imaging, diagnostic imaging, biopsy

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THE standard of care in the United States for PCa screening and detection has been to perform a transrectal ultrasound guided random systematic biopsy for men with elevated PSA and life expectancy exceeding 10 years.[1,2] This pathway has resulted in over detection and overtreatment of PCa.[3,4] Random systematic biopsies of the prostate were performed since transrectal ultrasound lacked sensitivity and specificity for identifying the sites of significant PCa.[5,6] There is now an abundance of evidence that mpMRI, which includes T2-weighted imaging, DCE and DWI, reliably identifies significant PCa and can facilitate targeted prostate biopsy.[7–12]

Many CSRs detected on mpMRI are pathologically benign when targeted biopsy strategies are used.[9,13–17] There are several explanations for a benign targeted biopsy of a CSR. The CSR could be caused by prostatitis (acute, chronic or granulomatous), atrophy or benign prostatic hyperplasia, or the biopsy did not adequately sample the CSR. Thus, the true negative predictive value of a targeted biopsy of a CSR can only be ascertained by long-term followup of these cases. To date the natural history of biopsy negative CSRs has not been well described in the literature.

The objective of this study was to assess the short-term natural history of pathologically benign CSRs based on repeat mpMRI and PSA levels at 1 year.

MATERIALS AND METHODS

Patient Selection

This is an institutional review board approved, retrospective review of the medical records of a consecutive cohort of 330 men who underwent prostate mpMRI due to elevated levels of PSA and/or abnormal DRE between January 2012 and September 2014. Our group of radiologists reviewed all images and recorded the size and ss of all observed CSRs using a 5-point Likert scale.[18,19] A total of 533 CSRs were identified. MRI-US fusion targeted biopsy was done using Profuse software and the ei-Nav|Artemis system by 2 uro-oncologic surgeons (HL or WCH) at a single institution. Four biopsies were directed into each CSR and an additional 12 cores were obtained using a computer generated random template. We identified 34 men with a total of 51 CSRs with no evidence of PCa, HGPIN or ASAP on targeted and random biopsies who subsequently underwent repeat mpMRI and serum PSA measurement at 1 year. None of these men had a prior biopsy showing PCa.

MRI Technique and Review

Multiparametric MRI was performed with a 3.0 Tesla system using a torso phased-array coil. Prostate images included multiplanar turbo spin-echo T2-weighted images, axial turbo spin-echo T1-weighted images, axial single-shot echo-planar DWI including an apparent diffusion coefficient map constructed from b-values of 50 and 1,000 seconds per mm^2, and volumetric DCE images using a 3-dimensional fat suppressed spoiled gradient-echo T1-weighted sequence with a temporal resolution of less than 6 seconds.[14,20] Parameters for locating a CSR and determining its ss have been described in prior studies.[7,11,12,21] All images were reviewed by a group of 9 radiologists who interpret more than 2,000 images annually using a standardized reporting template. The ss and GLM of all CSRs were reported in a standardized radiology report.

Data and Statistical Analyses

Demographics, medical history, serum PSA levels at baseline and 1 year, mpMRI interpretations at baseline and 1 year, and prostate biopsy reports were extracted from the medical records and stored on a secure database.

Since the primary objective of our study was to characterize the short-term natural history of pathologically benign CSRs, it was necessary to define at the onset changes that might trigger a decision to repeat a biopsy. The relationship between prostate cancer detection rates and ss has been consistently observed.[9,10,14] Therefore, any interval change in ss was considered meaningful. We arbitrarily selected a 20% change in GLM as the threshold for a change in CSR size. Since the mean baseline GLM in our cohort was 10.2 mm, a 20% increase in GLM would correspond to an approximately 2 mm change. Assuming that the CSR is a sphere, a change in GLM from 10 to 12 mm would represent approximately a 70% change in volume. There is also evidence that a PSA velocity of 0.5 ng/ml per year is a risk factor for detecting significant PCa.[22,23] Therefore, for the purposes of this study a single unit change in ss, a 20% change in GLM or a 0.5 ng/ml change in serum PSA between baseline and 1 year were considered changes in these parameters.

The statistical test used to analyze the data was determined based on the results of the Kolmogorov-Smirnov test for normality. The Wilcoxon signed rank test was used to compare baseline and 1-year GLM and ss of the CSRs. The paired samples t-test was used to compare baseline and 1-year PSA. Statistical significance was considered at $p < 0.05$. Statistical analysis was performed with IBM® SPSS® Statistics, version 20.

RESULTS

Table 1 shows the pathological diagnoses of the 533 CSRs that were subjected to fusion targeted biopsies stratified according to ss. Overall 157

Table 1. *Pathological diagnoses of fusion targeted biopsies stratified by ss*

	No. ss 2 (%)	No. ss 3 (%)	No. ss 4 (%)	No. ss 5 (%)	Total No. (%)
PCa	23 (12.5)	42 (21.5)	59 (50.0)	33 (91.7)	157 (29.5)
HGPIN	8 (4.3)	12 (6.2)	10 (8.5)	0	30 (5.6)
ASAP	2 (1.1)	2 (1.0)	0	0	4 (0.7)
Benign	151 (82.1)	139 (71.3)	49 (41.5)	3 (8.3)	342 (64.2)
Totals	184	195	118	36	533