Impact of post prostate biopsy hemorrhage on multiparametric magnetic resonance imaging

Ali-Reza Sharif-Afshar, MD,[1] Tom Feng, MD,[1] Steven Koopman, MD,[1] Christopher Nguyen,[2] Quanlin Li,[3] Eugene Shkolyar,[1] Rola Saouaf, MD,[2] Hyung L. Kim, MD[1]

[1]Division of Urology, Cedars-Sinai Medical Center, Los Angeles, California, USA
[2]Department of Radiology, Cedars-Sinai Medical Center, Los Angeles, California, USA
[3]Biostatistical Core, Cedars-Sinai Medical Center, Los Angeles, California, USA

SHARIF-AFSHAR A-R, FENG T, KOOPMAN S, NGUYEN C, LI Q, SHKOLYAR E, SAOUAF R, KIM HL. Impact of post prostate biopsy hemorrhage on multiparametric magnetic resonance imaging. *Can J Urol* 2015;22(2):7698-7702.

Introduction: *Hemorrhage induced by prostate biopsy can interfere with the interpretation of prostate magnetic resonance imaging (MRI).*
Materials and methods: *We reviewed 101 patients who had prostate multiparametric MRI (MP-MRI) and radical prostatectomy.*
Results: *On MRI obtained within 4 weeks following the biopsy, hemorrhage was seen in 26/36 (72.2%) patients. Patients having a MRI between 4-6 weeks of the biopsy had hemorrhage in 8/14 (57.1%) cases. After 6 weeks, hemorrhage was less common but still present in 24/46 (52%) patients. There were five patients who had prostate MRI prior to biopsy and served as a control group. There was no significant correlation between the length of time beyond 6 weeks and the likelihood of having prostate hemorrhage on MRI.*
The overall sensitivity and specificity of MRI for predicting extracapsular extension (ECE) were 78.6% and 89%, respectively. However, if the analysis was limited to patients with MRI within 6 weeks from the time of biopsy, the sensitivity and specificity were similar: 80% and 90%, respectively. For patients with MRI obtained after 6 weeks, the sensitivity and specificity were 76.9% and 87.9%.
Conclusions: *Prostate hemorrhage is seen in the majority of cases within 6 weeks of biopsy and can be seen in nearly half the patients even beyond 6 weeks. However, hemorrhage within 6 weeks of a biopsy does not interfere with assessment for ECE.*

Key Words: prostate cancer, extracapsular extension, magnetic resonance imaging, neoplasm staging, hemorrhage, prostate

Introduction

Multiparametric magnetic resonance imaging (MP-MRI) is a commonly performed imaging modality for the detection of prostate cancer.[1,2] Preoperative prostate imaging may help determine location and extent of extracapsular extension (ECE), which can aid treatment planning. For example, patients at risk for ECE can undergo non-nerve-sparing surgery to decrease the likelihood of a positive margin. Accurate preoperative assessment of ECE may provide better risk stratification. Transrectal ultrasound-guided (TRUS) biopsy is the gold standard for diagnosing prostate cancer. However, post biopsy hemorrhage may interfere with interpretation of MP-MRI. Prostate hemorrhage has a similar appearance as tumor on T2-weighted image and can lead to overestimation of tumor burden and extent of ECE.[3] Therefore, standard practice is to delay the MRI until the hemorrhage has decreased. In our study, we assess hemorrhage on MRI obtained at various time points following a 12 core biopsy and determine its impact on detection of ECE.

Accepted for publication March 2015

Address correspondence to Dr. Hyung L. Kim, Department of Urology, Cedars Sinai Medical Center, 8635 West Third Street, Suite 1070 West, Los Angeles, CA 90048 USA

Materials and methods

Patients

We retrospectively reviewed the medical records of patients who underwent MRI of the prostate gland with no endorectal coil. OptiMARK contrast was given to patients with GFR greater than 30 cc/min. All patients underwent imaging using one MRI system. Studies were interpreted by a radiologist with expertise in prostate MRI. The analysis was based on 101 patients who had a prostate MRI followed by a radical prostatectomy. Our study was approved by the institutional review board.

MRI technique

All patients underwent imaging using a 3.0T MRI system (Verio, Siemens) equipped with a 12 channel pelvic phased array coil. Anatomical images, including T1 (0.5 x 0.5 x 3.5 mm^3, TR/TE = 4800/10 ms) and T2 (0.5 x 0.5 x 3.5 mm^3, TR/TE = 4800/125 ms) weighted turbo spin echo (TSE), were acquired in the axial, sagittal, and coronal planes following standard pelvic localizers. Diffusion-weighted imaging (DWI) was acquired using a standard single-shot echo-planar imaging (SS EPI) sequence (2.1 x 1.7 x 3.5 mm^3. TR/TE = 5000/80ms, iPat = 2, NEX = 3). Three orthogonal diffusion directions including a single b0 measurement were acquired at two nonzero b-values, (400 and 800 s/mm^2), yielding a total of seven measurements to calculate trace apparent diffusion coefficient (ADC) maps. Dynamic contrast enhanced (DCE) MRI (1.3 x 1.3 x 3.5mm^3, TR/TE = 3.02/1.09 ms, temporal resolution = 40s) was acquired and consisted of a pre scan, a series of continuous acquisition of 12 volumes post contrast delivery, and a final 9 minute delay post scan.

Image analysis

Prostate hemorrhage was identified from Tl and T2-weighted images. Prostate tumors were identified using T2WI, DWI and DCE images. ADC values were measured for all suspicious lesions. Level of suspicion for ECE was rated as none, suspicious, or definite. Our 3-point system is compatible with the 5-point prostate imaging and reporting data system (PI-RAD) proposed by the European Society of Urogenital Radiology (ESUR).[4] On our system, none, suspicious and definite correspond to PI-RAD 1-2, 3, and 4-5, respectively. Irregularity of the capsule was considered suspicious for ECE. Definitive evidence of ECE included contour bulge with loss of capsule, neurovascular bundle thickening, or measurable extracapsular disease.

Pathology

Prostate specimens were processed according to the International Society of Urological Pathology (ISUP) Consensus Guidelines on prostatectomy handling and processing.[5] Briefly, after fixation and surface capsular inking (multicolor for anatomic orientation), 5 mm bladder neck and apex shave sections were sampled as margins, as were longitudinal sections of bilateral seminal vesicles. The remainder of the gland was sectioned in 3 mm increments perpendicular to the urethra. For prostates less than 30 g, all serial sections were submitted entirely. For prostates > 30 g an ISUP guideline-compliant partial submission protocol was used, which emphasizes submission of all grossly visible tumor and any areas suspicious for ECE.[5] For all cases, the sections were submitted with ordered anatomic designations to enable three-dimensional reconstruction of the gland from histologic sections. After histological staining, all tumor foci were outlined on the microscopic slides. Presence of primary and secondary Gleason grade pattern, as well as presence of ECE and SVI involvement was documented for staging purposes.

For cases included in this study, archival H&E stained slides were retrieved from department files and re-reviewed to confirm diagnosis and staging. ECE was considered established if ECE was multifocal or involved more than five glands. ECE involving five or fewer glands was considered focal ECE. This study assessed MRI prediction of established ECE.

Results

A total of 101 patients had prostate MRI and radical prostatectomy, and their records were reviewed. Patient characteristics are summarized in Table 1. In this group, 5 had prostate MRI prior to biopsy and

TABLE 1. **Patient characteristics**

Mean age ± SD	62.4 ± 7.9
Mean PSA ± SD	8.5 ± 7.6
Clinical stage (%)	
cT1	72 (71)
cT2a	24 (24)
cT2b	3 (3)
cT2c	1 (1)
Biopsy Gleason score (%)	
6	44 (44)
7	41 (41)
8 or greater	16 (16)

TABLE 2. **Hemorrhage seen on multiparametric MRI of prostate**

Weeks following biopsy	n	Presence of hemorrhage (%)
MRI prior to biopsy	5	0
< 6 weeks	50	34 (68)
> 6 weeks	46	24 (52)

served as a control group, Table 2. On MRI obtained within 4 weeks following the biopsy, hemorrhage was present in 26/36 (72.2%) patients. Patients having a MRI between 4-6 weeks of the biopsy had hemorrhage in 8/14 (57.1%) cases. After 6 weeks, hemorrhage was less common but still present in 24/46 (52%) patients. There was no significant correlation between the length of time beyond 6 weeks and the likelihood of having prostate hemorrhage on MRI.

A critical question is whether hemorrhage interferes with the interpretation of the MRI. The presence ECE can influence plans for nerve-sparing. MRI identified ECE or was suspicious for ECE in 30 patients, of whom 21 (70%) had established ECE on final pathology. Figure 1 shows an example of hemorrhage and ECE on MRI. Of patients without evidence of ECE on MRI, 4/71 (6%) had ECE on final pathology. The overall sensitivity and specificity of MRI for predicting ECE were 78.6% and 89%, Table 3, respectively. However, if the analysis was limited to patients with MRI within 6 weeks from the time of biopsy, the sensitivity and specificity were similar: 80% and 90%, respectively. The 4-6 week group had only 14 patients and was too small to draw conclusions. Figure 2 shows that the ROC plots for these groups cluster near each other, indicating similar diagnostic performance of the MRI in the three groups shown.

When assessing for ECE, the MRI was reported on a 3-point scale, with 3 representing the highest level of suspicion. If only a score of 3 was considered positive, the MRI had a specificity of nearly 98.6% but the sensitivity was only 39%. However, the MRI had better performance when scores 2 and 3 were considered positive. The specificity and sensitivities were 89% and 78.6%, respectively. These MRI performance characteristics were similar in all groups defined by time following prostate biopsy, Table 3. Therefore, the presence of hemorrhage does not seem to interfere with detection of ECE on MRI.

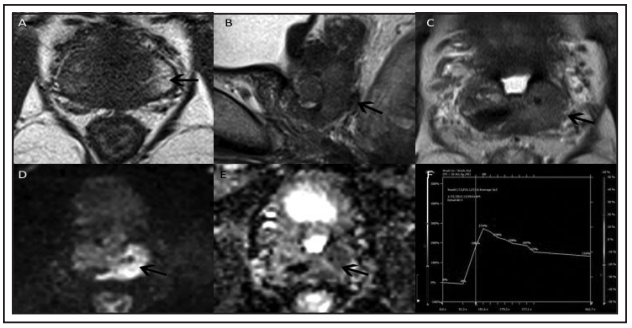

Figure 1. Example of a postbiopsy multiparametric MRI showing extracapsular extension.
A) Axial T1-weighted MRI shows hyperintense focus of hemorrhage (arrow). **B & C)** Sagittal and axial T2-weighted MRI through the site of hemorrhage demonstrate irregularity of the capsular margin (arrows) consistent with extracapsular extension. Area of intensely dark signal is due to fibrotic scar tissue and is not due to neoplasm. **D & E)** Axial DWI and ADC images through the same lesion reveal an area of diffusion restriction (arrows) due to a diffusely hypercellular tumor. Of note, region of fibrosis seen on T2 images in right gland **C)** shows no diffusion abnormalities. **F)** Dynamic contrast enhancement curve of the dominant lesion demonstrates rapid enhancement and washout, which is a pattern emblematic of malignancy.

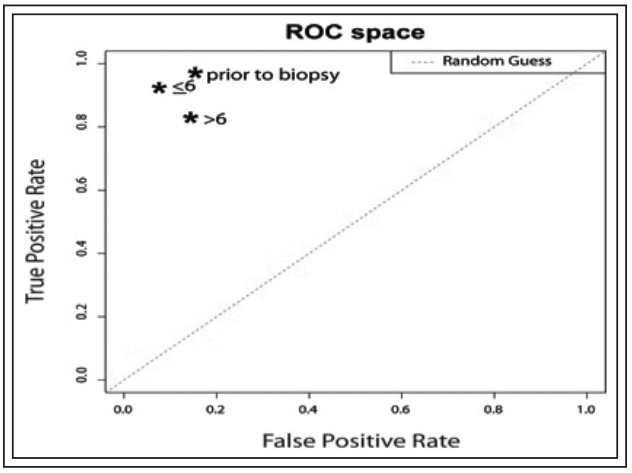

Figure 2. ROC for prediction of extracapsular extension on preoperative MP-MRI of the prostate. Each point is labeled with group based on time (weeks) following prostate biopsy.

TABLE 3. **Diagnostic characteristics of multiparametric MRI for extracapsular extension**

Group^	Fisher's exact p	Sensitivity	Specificity	PPV	NPV
< 6 weeks	< 0.0001	80	90	75	92.3
> 6 weeks	< 0.0001	76.9	87.9	71.4	90.6
All	< 0.0001	78.6	89	73.3	91.5

^weeks following biopsy
PPV = positive predictive value; NPV = negative predictive value

Discussion

MRI is commonly used to characterize prostate cancer prior to prostatectomy. The size and location of the tumor can influence the surgical approach.[6] For example the presence of ECE on MRI may indicate need for a wide resection that sacrifices the neurovascular bundle, which can decrease the likelihood of recovering sexual function. In a prospective study of 104 prostatectomy candidates, preoperative MRI altered the initial surgical plan for handling the neurovascular bundle in 27% of patients.[7] However, hemorrhage from the diagnostic biopsy can interfere with interpretation of the MRI. Therefore, it is common practice to delay the MRI until the hemorrhage has resolved.

Prior studies have documented that prostate hemorrhage can interfere with cancer detection.[3] In a study of 73 patients with biopsy-proven prostate cancer, prostate MRI findings were compared to pathology from prostatectomy. Hemorrhage persisted for as long as 4 ½ months following the biopsy, and MRI obtained within 3 weeks of biopsy tended to overestimate tumor burden and ECE. Staging accuracy improved from 46% to 83% by waiting at least 3 weeks to obtain the MRI. In a second study, 57 prostate MRIs were reviewed. The authors felt that prostate hemorrhage subjectively interfered with the interpretation in 21% of cases. They noted that this effect decreased after 21 days post biopsy and recommended that MRI be deferred for at least 3 weeks following the biopsy.[3,8]

In both of these studies, the MRI consisted of only T1 and T2-weighted images. However, modern multiparametric MRIs have improved resolution and include functional techniques such as diffusion weighted and dynamic contrast-enhanced images.[9,10] Diffusion weighted imaging allows mapping of apparent diffusion coefficients (ADC), which are useful in differentiating prostate cancer from normal tissue.[11,12] These techniques may compensate for distortion from prostatic hemorrhage. The use of MP-MRI has been shown to improve identification of ECE when compared to T2-weighted images alone.[13] T2 signal intensity and ADC values have been shown to reliably differentiate prostate cancer from hemorrhage.[14]

Therefore, we assessed the effect of prostate hemorrhage when interpreting modern MP-MRI. We found that the sensitivity and specificity of MP-MRI for predicting established ECE were similar regardless of the length-of-time between biopsy and MRI, Table 3. This suggests that post biopsy hemorrhage does not interfere with staging. To the best of our knowledge, this is the first study to assess the impact of hemorrhage on detection of ECE. Others have already assessed the effect of post biopsy hemorrhage on detection of prostate cancer on MP-MRI. In a study of 40 patients, MP-MRI had a sensitivity, specificity and accuracy of 69%, 85% and 78%, respectively, and there was no correlation between the degree of hemorrhage and time between biopsy and MRI.[10] In a second study of 44 patients, the performance of MP-MRI was compared in patients who had a delay of < 4 weeks or > 4 weeks following biopsy. There was no significant difference between the groups and the investigators concluded that a 4 week delay is not necessary.[15]

Therefore, when our results are considered along with the existing literature, we can argue that it is not necessary to defer MRI to allow post biopsy hemorrhage to diminish. We conclude that a delay is not necessary to improve cancer detection or staging. Our study has several potential limitations. The radiologist had access to the biopsy path report. However, the diagnostic biopsy can only indirectly influence assessment for ECE since the prostatectomy pathology was not available. A 5 point scale has been proposed for scoring suspicion for ECE on MRI.[4] We used a 3-point scale that is compatible with the 5-point scale, and it is preferred at our institution because it is easier for clinicians to interpret and act on.

Conclusion

Prostate hemorrhage is seen on imaging in the majority of cases within 6 weeks of biopsy and can be seen in nearly half the patients even beyond 6 weeks. However, the degree of hemorrhage within 6 weeks of a biopsy does not interfere with MP-MRI assessment for ECE. □

References

1. Epstein JI, Carmichael MJ, Pizov G, Walsh PC. Influence of capsular penetration on progression following radical prostatectomy: a study of 196 cases with long-term followup. *J Urol* 1993;150(1):135-141.
2. Outwater EK, Montilla-Soler JL. Imaging of prostate carcinoma. *Cancer Control* 2013;20(3):161-176.
3. White S, Hricak H, Forstner R et al. Prostate cancer: effect of postbiopsy hemorrhage on interpretation of MR images. *Radiology* 1995;195(2):385-390.
4. Barentsz JO, Richenberg J, Clements R et al. ESUR prostate MR guidelines 2012. *Euro Radiol* 2012;22(4):746-757.
5. Samaratunga H, Montironi R, True L et al. International Society of Urological Pathology (ISUP) Consensus Conference on Handling and Staging of Radical Prostatectomy Specimens. Working group 1: specimen handling. *Modern Pathol* 2011;24(1):6-15.
6. Tan N, Margolis DJ, McClure TD et al. Radical prostatectomy: value of prostate MRI in surgical planning. *Abdom Imaging* 2012;37(4):664-674.
7. McClure TD, Margolis DJ, Reiter RE et al. Use of MR imaging to determine preservation of the neurovascular bundles at robotic-assisted laparoscopic prostatectomy. *Radiology* 2012;262(3):874-883.
8. Ikonen S, Kivisaari L, Vehmas T et al. Optimal timing of post-biopsy MR imaging of the prostate. *Acta Radiol* 2001;42(1):70-73.
9. Hoeks CM, Barentsz JO, Hambrock T et al. Prostate cancer: multiparametric MR imaging for detection, localization, and staging. *Radiology* 2011;261(1):46-66.
10. Tamada T, Sone T, Jo Y et al. Prostate cancer: relationships between postbiopsy hemorrhage and tumor detectability at MR diagnosis. *Radiology* 2008;248(2):531-539.
11. desouza NM, Reinsberg SA, Scurr ED, Brewster JM, Payne GS. Magnetic resonance imaging in prostate cancer: the value of apparent diffusion coefficients for identifying malignant nodules. *Br J Radiol* 2007;80(950):90-95.
12. Turkbey B, Shah VP, Pang Y et al. Is apparent diffusion coefficient associated with clinical risk scores for prostate cancers that are visible on 3-T MR images? *Radiology* 2011;258(2):488-495.
13. Bloch BN, Furman-Haran E, Helbich TH et al. Prostate cancer: accurate determination of extracapsular extension with high-spatial-resolution dynamic contrast-enhanced and T2-weighted MR imaging--initial results. *Radiology* 2007;245(1):176-185.
14. Rosenkrantz AB, Kopec M, Kong X et al. Prostate cancer vs. post-biopsy hemorrhage: diagnosis with T2- and diffusion-weighted imaging. *J Magn Reson Imaging* 2010;31(6):1387-1394.
15. Rosenkrantz AB, Mussi TC, Hindman N et al. Impact of delay after biopsy and post-biopsy haemorrhage on prostate cancer tumour detection using multi-parametric MRI: a multi-reader study. *Clin Radiol* 2012;67(12):e83-e90.