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Endorectal multi-parametric MRI of the prostate: Incremental effect of perfusion imaging on biopsy target identification

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Abstract

Purpose—To evaluate the incremental effect of perfusion imaging on biopsy target identification at endorectal multi-parametric prostate MRI.

Method and materials—We retrospectively 52 patients who underwent endorectal multi-parametric prostate MRI for suspected or untreated prostate cancer. Two readers independently identified biopsy targets without and with perfusion images.

Results—Reader 1 identified 36 targets without and 39 targets with perfusion imaging ($p > 0.05$). The corresponding numbers for reader 2 were 38 and 38, respectively ($p = 0.5$).

Conclusion—Perfusion imaging does not significantly increase the number of biopsy targets identified at endorectal multi-parametric prostate MRI.

Keywords

MRI; prostate cancer; prostate biopsy; diffusion; perfusion

Introduction

Recent growth in the use of MRI for the local assessment of known or suspected prostate cancer has been driven by the development of increasingly robust and accurate multiparametric approaches, particularly with the incorporation of diffusion and perfusion imaging, and the emergence of MRI-targeted biopsy as a novel diagnostic method, whether by cognitive, MRI/ultrasound “fusion” or direct “in-bore” techniques [1]. Multiparametric prostate MRI is an important and widely used adjunct to standard clinical assessment by digital rectal examination and serum prostatic specific antigen level determination for the approximately one million men who currently undergo prostate biopsy in the United States every year [2, 3]. Imaging can stratify such patients by likelihood of cancer, assist with

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biopsy target identification and guide biopsy of targets that appear likely to be malignant [4, 5]. This represents a sea-change in our approach to studying prostate MRI, because biopsy target identification is becoming a major research endpoint in addition to the traditional endpoints of tumor localization, tumor characterization, and outcome correlation [6, 7]. This change coincides with increasing pressure in the broader healthcare context for imaging services to be personalized, patient-friendly, and of added value. These issues raise new questions for how we perform prostate MRI.

Diffusion imaging is widely recognized to be of great utility in the MRI evaluation of prostate cancer, but the role of perfusion imaging is more controversial [8, 9]. Perfusion imaging adds time to study acquisition, poses a small risk of contrast reactions [10], and adds to the duration and complexity of interpretation by the radiologist tasked with reading the study. Although diffusion and perfusion play a complementary role in the accurate detection of prostate cancer, diffusion is more accurate and sensitive than perfusion imaging alone in the detection of prostate cancer [11]. In this context, the added value of perfusion imaging is questionable with respect to biopsy target identification and the increased time required for study interpretation, both of which are endpoints that have received little attention. Therefore, we undertook this study to evaluate the incremental effect of perfusion imaging on biopsy target identification at endorectal multi-parametric prostate MRI.

Materials and methods

Subjects

This was a retrospective single institution study approved by our Institutional Review Board with waiver of the requirement for informed consent. The study was compliant with the Health Insurance Portability and Accountability Act. We performed a search of our radiology information system to identify all men with suspected or known untreated prostate cancer who underwent endorectal multiparametric MRI of the prostate, including T2, diffusion, and perfusion sequences, at our institution over a three year period. Of the 52 men who met these inclusion criteria, 48 were scanned on at 3T and 4 on at 1.5T whole body MRI scanner (Achieva and Ingenia; Philips Healthcare, Netherlands). There were no exclusion criteria.

MRI technique and interpretation

Endorectal multiparametric MRI sequence protocol parameters are shown in Table 1. Two attending radiologists (---, ---), with 20 and 5 years of experience in multiparametric MRI of the prostate, respectively, and unaware of patient clinical data, independently reviewed MR images on a picture archiving and communication system workstation (Impax; Agfa, Mortsel, Belgium) and identified biopsy targets in all of the study patients. For purposes of interpretation, a randomly sequenced worklist of the 52 patients was generated. During the first of two review sessions that were separated by a minimum interval of two weeks, each radiologist interpreted the odd-numbered cases using all sequences except the dynamic contrast enhanced perfusion images and the even-numbered cases using all images including the perfusion images. During the second review session, the process was reversed so that at the end of the interpretation process, both readers had identified biopsy targets on all studies

twice, once with perfusion images and once without. During each review session, the first author (--; not one of the readers) electronically recorded the location of each target and the time required in seconds to identify the biopsy target(s). Using an amalgam of published experience, biopsy targets were defined as foci of low T2 signal intensity with an ellipsoid or crescentic sub-capsular morphology in the peripheral zone or infiltrative non-encapsulated appearance in the central gland accompanied by focal reduction in apparent diffusion coefficient or accompanied by focal early intense enhancement or rapid washout on perfusion imaging [12-15]. No minimum size was required or specified.

Post-MRI data collection

The first author reviewed all available clinical and histopathological records of the study subjects. Age, serum prostatic specific antigen level and findings from any prostate biopsies performed before multiparametric MRI were recorded. After MRI, the first author recorded the findings of any subsequent prostate biopsy. In particular, in order to validate the process used to identify biopsy targets, we specifically tracked those patients who proceeded to direct MR-guided biopsy of the prostate following the identification of an actionable target at diagnostic multiparametric MRI study. Direct MR-guided biopsy of the prostate is a clinical service that has been provided at our institution for the past two years, using previously described methodology [5]. The first author correlated biopsy targets identified by MRI during this study with targets that were clinically identified by MRI and underwent MR-guided biopsy to determine if they were the same lesion and to establish the resulting tissue diagnosis.

Data analysis

Descriptive statistical analysis was conducted to evaluate all continuous and categorical variables. We used paired t-test to compare the time required within each reader to identify biopsy target(s) with and without perfusion imaging, and McNemar's test to determine whether adding perfusion imaging significantly affects the identification of one or more targets for each reader. Kappa statistic and the corresponding 95% confidence interval were computed to assess the agreement between the readers for biopsy target identification with or without perfusion imaging [16]. All statistical analysis was conducted using SAS 9.4 (Cary, NC: SAS Institute Inc.).

Results

Patients

The final study population consisted of 52 men with a mean age of 66 years (range, 53-84) and a mean serum prostatic specific antigen level of 25.6 ng/mL (range, 0.4-50.6). In 28 men, the prostate MRI was requested for further evaluation of known and untreated biopsy proven prostate cancer, with a median Gleason score of 6 (range, 6-10). In the remaining 24 men, the MRI was requested to evaluate suspected prostate cancer based on an elevated serum prostatic specific antigen level or an abnormal digital rectal examination.

MR findings

At MRI review, reader 1 identified 36 targets without perfusion imaging, and three additional targets for a total of 39 targets with perfusion imaging (NS; $p = 0.3$). Reader 2 identified the same 38 targets on review of MRI studies without and with perfusion images (NS; $p = 0.5$). The mean time required by reader 1 to review each study for targets was 70 seconds without perfusion imaging and 131 seconds with perfusion imaging ($p < 0.001$). The corresponding numbers for reader 2 were 86 and 118 seconds, respectively ($p < 0.001$). Representative cases are shown in Figures 1 and 2. Kappa values indicated substantial inter-reader agreement for target identification, whether without ($\kappa = 0.75$; 95% confidence interval 0.56 to 0.94) or with ($\kappa = 0.64$; 95% confidence interval 0.41 to 0.87) perfusion imaging. Specifically, without perfusion imaging readers agreed on the presence or absence of targets in 46 of 52 patients; in the remaining 6 patients, 2 had one target each identified by reader 2 but not reader 1, and 4 had one target each identified by reader 1 but not reader 2. With perfusion imaging, readers agreed on the presence or absence of targets in 44 of 52 patients. In the remaining 8 patients, 3 had one target each identified by reader 2 but not reader 1, and 5 had one target each identified by reader 1 but not reader 2.

Post-MRI biopsy results

Fourteen of the 52 patients in the study proceeded to direct MR-guided biopsy of clinically identified targets by MRI, including 11 patients with no prior diagnosis of prostate cancer and 3 patients with known Gleason 6 prostate cancer. In all 14 patients, these clinically identified targets corresponded to targets identified during the MRI exam by one or both readers. Overall, 6 of the 14 targets biopsied had a positive result, with a median Gleason score of 7 (range, 6 to 8). In the 11 patients with no prior diagnosis of prostate cancer, 4 of the direct MR-guided biopsies were positive. In the 3 patients with known Gleason 6 prostate cancer, 2 of the direct MR-guided biopsies were positive. An additional three patients had a new diagnosis of prostate cancer established after MRI, two at systematic transrectal ultrasound guided biopsy of the prostate and one at transurethral resection of the prostate. That is, of the 24 patients who originally underwent MRI for suspected disease, 7 received a new diagnosis of prostate cancer (4 at direct MR-guided biopsy, 2 at transrectal ultrasound guided biopsy, and 1 at transurethral resection). When these 7 patients are combined with the 28 patients who underwent MRI for known prostate cancer, a total of 35 of the 52 patients in our study currently have a tissue diagnosis of prostate cancer.

Discussion

This study, evaluating the incremental effect of perfusion imaging on biopsy target identification at endorectal multiparametric prostate MRI, has three important results. First, this study suggests that perfusion imaging does not significantly increase the number of possible biopsy targets identified at multiparametric MRI. The clinical implication is that when checking a prostate MR study for the presence of a possible target, a reader can reasonably focus on reviewing the T2 and diffusion imaging alone. This would allow rapid assessment in a busy clinical setting. In addition, review for biopsy target presence need not be delayed while waiting for complex post-processing or time-curve analyses of the perfusion data. This would have important implications if diagnostic imaging and targeted

Our study has several limitations. The primary limitation is that most of the targets we identified were not confirmed pathologically, with only a small number of cases proceeding to a positive direct MR-guided biopsy. From a scientific perspective, it would have been ideal for all of our targets to have been histologically validated. However, from a pragmatic perspective, this criticism is tangential to our central finding. Our aim was to investigate the effect of perfusion imaging on target identification, irrespective of whether those targets were true or false positives. The histopathological accuracy of target identification would be a more important limitation if we had shown a significant difference in target detection between MRI without and with perfusion, since then it would have determined which technique was providing better information. But given that perfusion did not significantly change target identification, the histopathological nature of the targets becomes of secondary importance. The high degree of interobserver agreement in our study also provides some reassurance that target definition and identification was at least reproducible between readers, and not completely arbitrary. We did not utilize the PI-RADS scoring system as part of our reader interpretation process. However, our definition of a biopsy target largely

corresponds to PI-RADS version 2 scores of 4 and 5 [8]. Our sample size is relatively small. Patients were identified retrospectively from the population of men referred clinically for endorectal multiparametric prostate MRI which may have introduced selection bias in this process. Identified targets did not undergo systematic histopathological correlation. However, the frequency with targets were identified was 69-75% (36 to 39 of 52 patients), which is comparable to the general rate of approximately 60% seen across other similar populations [19]. The rate of positive biopsy in the subset that proceeded to MR-guided biopsy (43%; 6 of 14) in our study is also comparable to the positive biopsy rate in a large series with similar inclusion criteria from the National Institute of Health (46%; 461 of 1003) [14]. Such comparisons suggest our approach is broadly similar to other work in this field. While we did use PI-RADS as the basis for target definition, these corollaries with other similar work also suggests our methodology is analogous. Our study of interpretation time could be criticized as an artificial endpoint, since we were entirely focused on biopsy target definition. Clearly, complete interpretation of a prostate MR study requires much more time and involves many other observations, such as assessment of extracapsular extension, seminal vesicle invasion, lymphadenopathy, bony lesions and incidental pathology. The interpretation time endpoint, however, is relevant if an MRI study was to be followed in quick succession by a biopsy procedure, as discussed above. Another limitation of our study is that we asked readers to decide if a biopsy target was present or absent in each patient, forcing a binary yes/no response. This was intentional since we wished to mimic the clinical scenario where an MR-targeted biopsy is considered either appropriate or not. Such a binary response and analysis may have failed to detect more subtle effects of perfusion imaging on reader confidence. It is possible that a larger series or a study with a more quantitative response might have captured such minor effects. That said, if the effect of perfusion imaging on biopsy target identification is so small, it is difficult to see how it would have any major clinical importance. Larger and more comprehensive studies will be required to address all these limitations.

In conclusion, when considering prostate biopsy target identification as an endpoint, perfusion imaging is of limited utility during multi-parametric prostate MRI, and adds significantly to the time required for reader interpretation.

Acknowledgments

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Fig. 1.

A:- Axial T2-weighted MR image in a 56 year old man with a serum prostate specific antigen of 35.2 ng/ml, a benign digital rectal exam, and 3 previous negative transrectal ultrasound guided biopsies shows a large non-encapsulated focus (arrow) of infiltrative low T2 signal intensity in the right central gland.

B:- Corresponding axial apparent diffusion coefficient map shows matching focal restricted diffusion on the right anterior base central gland (arrow). Both readers identified this target at multiparametric MR imaging, both without and with perfusion images.

C:- Corresponding axial perfusion image from the arterial phase of enhancement shows an ill-defined ellipsoidal matching focus (arrow) of questionable early enhancement.

D: - Oblique axial T2-weighted MR image obtained after direct MR-guided biopsy of the target focus (grey arrow) confirms a needle track (white arrow) within the lesion. Two cores were obtained from this target and demonstrated Gleason 3+4 prostate cancer in 100% of the tissue obtained.

Fig. 2.

A:- Axial T2-weighted MR image in a 68 year old man with a serum prostate specific antigen level of 1.8 ng/ml and hematospermia shows a small somewhat geographic focus (arrow) of low T2 signal intensity in the right apical peripheral zone.

B:- Corresponding apparent diffusion coefficient map shows a matching focus (arrow) of mildly restricted diffusion.

C:- Corresponding axial perfusion image from the arterial phase of enhancement shows a matching focus (arrow) of early enhancement. This target was identified by reader 1 alone and only with perfusion images. This lesion did not proceed to targeted biopsy.

Table 1

Details of the diagnostic endorectal multiparametric MR imaging protocol. Studies were performed on a 1.5 or 3T whole body MR scanner (Ingenia; Philips Healthcare, Netherlands) with patients in the supine position using a body coil for signal excitation and a flexible multi-element phased-array surface coil (Philips 32 channel SENSE torso/cardiac coil) combined with a balloon-covered expandable endorectal coil (Medrad Prostate eCoil) inflated to 80-100 cm³ for signal reception (all MR images were routinely post-processed to compensate for the reception profile of the endorectal coil).

Parameter	T1	T2	Diffusion	Perfusion
Sequence	Axial fast spin echo	Axial & coronal fast spin echo	Axial single-shot echoplanar	Axial steady-state gradient echo
Anatomic coverage	Pelvis	Prostate	Prostate	Prostate
TR/TE (msec/msec)	400-600/10	Minimum/120	Minimum/Minimum	Minimum/Minimum
Echo train length	4	26	NA	NA
Acceleration factor	1.6	1.3	2	4
Matrix	352 × 352	560 × 560	176 × 176	232 × 168
Field of view (cm)	30	18	18	18
Number of excitations	2	3	3	
Slice thickness/gap (mm)	5/0.5	3/0	3/0 × 25	3.2/0 × 20
Specific to sequence	Transverse frequency direction.	Anteroposterior frequency direction for axials.	Frequency-selective inversion recovery fat suppression. B values of 0, 600, and 1000 s/mm ² . Apparent diffusion coefficient maps created and exported to PACS.	Flip angle = 150°, 35 phases pre and post of 20 cm ³ IV gadodiamide (Omniscan; GE Healthcare, Milwaukee, WI) injected at 3 cm ³ /s. Post-processed multiparametric perfusion maps for relative enhancement, maximum enhancement, maximum relative enhancement, time of contrast media arrival (T0), time to peak, wash in rate, wash out rate, brevity of enhancement, and area under the curve created on an independent workstation (IntelliSpace Portal; Philips Healthcare, Netherlands) and exported to PACS.