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Original Article

Pathologic findings in patients with targeted magnetic resonance imaging-guided prostate needle core biopsies

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Abstract: In contrast to the routine (non-targeted) sampling approach of transrectal ultrasound guided biopsies (TRUS-GB), targeted magnetic resonance imaging-guided biopsies (TMRI-GB) target regions of the prostate suspicious for prostate cancer (PCa), based on findings on multiparametric MRI. We sought to examine the pathologic findings identified on TMRI-GB, due to the fact that there are limited studies on this in the Pathology literature. A search was made through our Urologic Pathology files for prostate needle core biopsies that were obtained via TMRI-GB. Forty-six patients were identified. Mean patient (PT) age was 62 years (range: 50-78 years). Twenty one of 46 PTs (46%) had a history of PCa, 10/46 PTs (22%) had a history of negative TRUS-GB and rising PSA, and the remaining 15/46 PTs (32%) had never undergone biopsy. Cancer detection rate on TMRI-GB was 57% for PTs with a prior diagnosis of PCa, 50% for PTs with a history of benign biopsy, and 67% who were biopsy naïve. An average of 3.16 cores were sampled from malignant lesions and an average of 2.74 were sampled from benign lesions (P=0.02). TMRI-GB has a higher cancer detection rate than TRUS-GB. TMRI-GB may have a critical role as a tool for active surveillance, tumor mapping, and primary detection of PCa, which will likely evolve as the ability to identify malignant lesions improve. The roles of pathologists and radiologists in the validation of this procedure will continue to be even more vital in the future.

Keywords: Prostate, prostatic adenocarcinoma, MRI, targeted, needle core biopsies

Introduction

Prostate cancer (PCa) is a major health problem in men, representing an estimated 27% (233,000) of all new men's cancer cases and 10% (29,480) of all men's cancer related deaths in the United States in 2014 [1]. To establish a definite diagnosis of PCa in patients with elevated prostate specific antigen (PSA) levels or an abnormal digital rectal exam (DRE), a systematic (non-targeted) sampling approach of transrectal ultrasound-guided biopsies (TRUS-GB) remains the accepted standard of care.

The prostate is the only solid organ which is sampled in a standardized, non-targeted manner. In all other solid organs, suspicious areas are identified with the aid of direct visualization or radiologic imaging prior to biopsy [2]. Because prostate cancer is often multifocal and the volume of prostate sampled is relatively small, sampling error is common in TRUS-GB. The collection of 10 to 14 cores during standard TRUS-GB results in PCa detection rates that range from 22% to 44.3% [3-5]. Although collection of up to 14 cores decreases false negative rates (when compared to the sextant protocol), the morbidity and infection associated with such biopsies is not insignificant. In the past decade, hospital admission rates associated with complications following TRUS-GB have quadrupled [6]. In addition, several cases of prostate cancer are missed on the first TRUS-GB, and the likelihood of detecting prostate cancer decreases with each subsequent negative TRUS-GB. One study showed that the rate of cancer detection decreases from 22% on first TRUS-GB to 4% by fourth TRUS-GB [3].

Figure 1. Interventional radiologist obtaining targeted magnetic resonance imaging-guided prostate needle core biopsies.

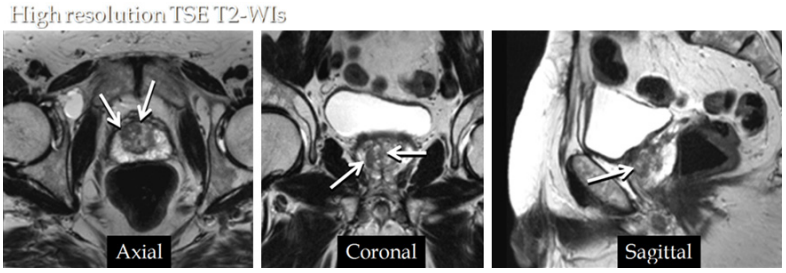

Figure 2. Different views of multiparametric diagnostic MRI scan showing suspicious lesions within the prostate gland.

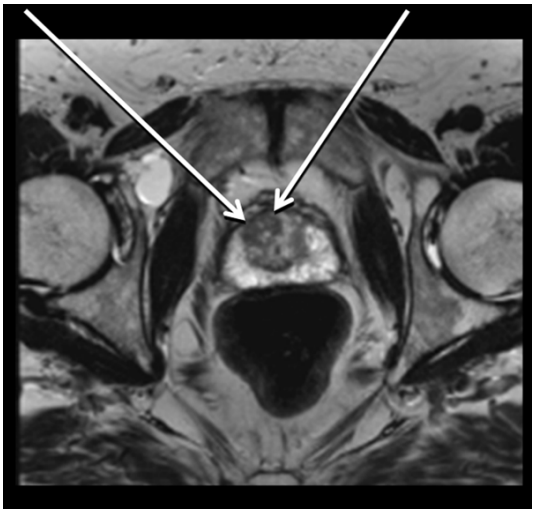

Figure 3. Higher magnification of axial view of multiparametric diagnostic MRI scan shows suspicious lesions within the prostate gland.

In this setting, TMRI-GB has emerged as a technique which could improve cancer detection rates and potentially limit number of biopsy procedures performed in patients with a high clinical suspicion for cancer. Recent studies have demonstrated that multiparametric MRI effectively localizes PCa lesions, and that targeted biopsies of the lesions accurately detect cancer in clinically suspicious patients [7]. Yet, there is a dearth of literature exploring the pathologic findings of men who have undergone TMRI-GB. In this study, we examined the cancer detection rate in patients with clinical suspicion of PCa and evaluated the histopathologic characteristics of all lesions sampled.

Materials and methods

Magnetic resonance imaging and TMRI-GB

To identify cancer suspicious lesions for subsequent targeted biopsies, all patients underwent a dedicated preprocedure multiparametric diagnostic MRI scan which utilized a high resolution 32-channel surface pelvic coil. Patients with suspicious lesions underwent their biopsy procedures on the same MRI scanner, typically within 1-60 days following the diagnostic scan. Preliminary imaging consisted of fast axial and sagittal TSE T2-weighted, high resolution axial TSE T2-weighted, and Diffusion-weighted (b=2000) scans to re-demonstrate the target lesions.

TMRI-GB was performed on a 0.3T MRI scanner (Magnetom Trio, Siemens, Germany). The patients were placed in the prone position in the MRI scanner. Transrectal placement of the rectal piece of the Dyna-TRIM system (Invivo, USA) was inserted following lubrication with lidocaine gel. The transrectal piece was then connected to the rest of the system. Preliminary imaging was obtained to identify the transrectal fiducial line, the target lesion(s), and to calculate the trajectory angles in 3 planes. Subsequently, an 18-gauge core biopsy needle was introduced into the target lesion to collect

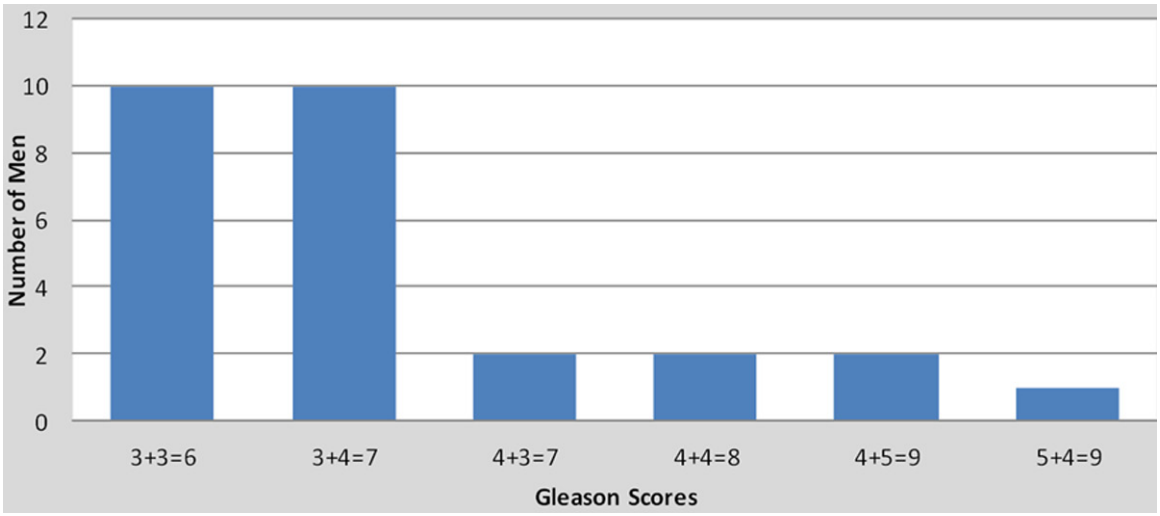

Figure 4. Number of men with each Gleason score identified by TMRI-GB.

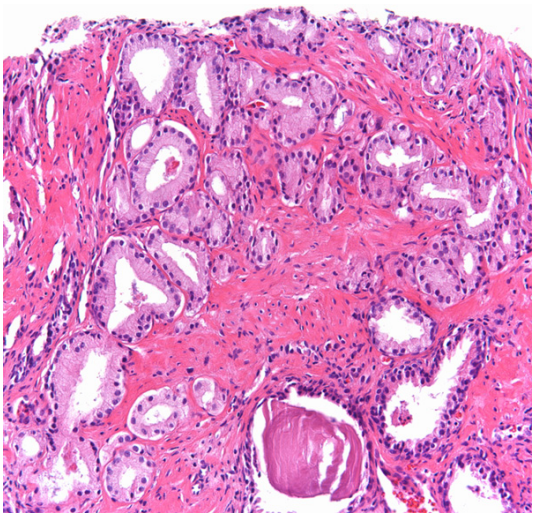

Figure 5. Targeted magnetic resonance imaging-guided prostate needle core biopsy showing prostatic adenocarcinoma, Gleason score 3+3=6.

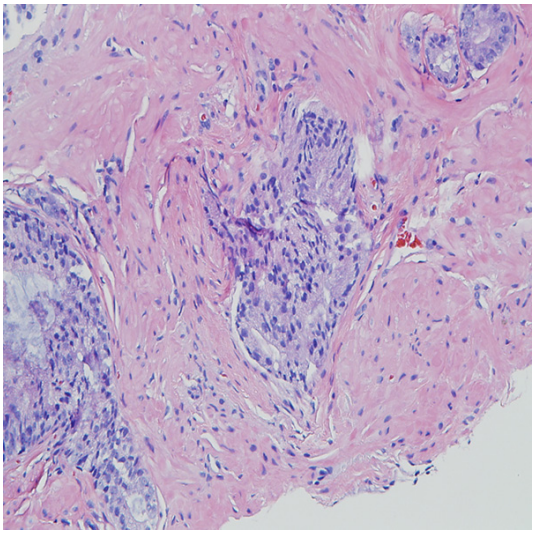

Figure 6. Targeted magnetic resonance imaging-guided prostate needle core biopsy showing prostatic adenocarcinoma, Gleason score 4+3=7.

between 1 and 6 cores per lesion (**Figures 1**-**3**). Interpretation of the biopsy results was performed by a urologic pathologist.

Pathology

A search was made through our Urologic Pathology files for prostate needle core biopsies that were obtained via TMRI-GB. Patients had either previously undergone prostate biopsies, with either benign or malignant results, or had never undergone previous prostate biopsies. All slides were re-reviewed by a Urologic Pathologist and the histologic findings were documented.

This study was completed following the guidelines of and with approval from our institutional review board.

Results

Patient characteristics

Forty-six cases were identified. Mean patient age was 62 years (range: 50-78 years). Mean PSA at the time of TMRI-GB was 9.25 ng/ml (range: 0.49-69.71 ng/ml) and median 5.6 ng/ml. Fifteen of 46 patients (32%) had never undergone prior biopsy at the time of TMRI-GB.

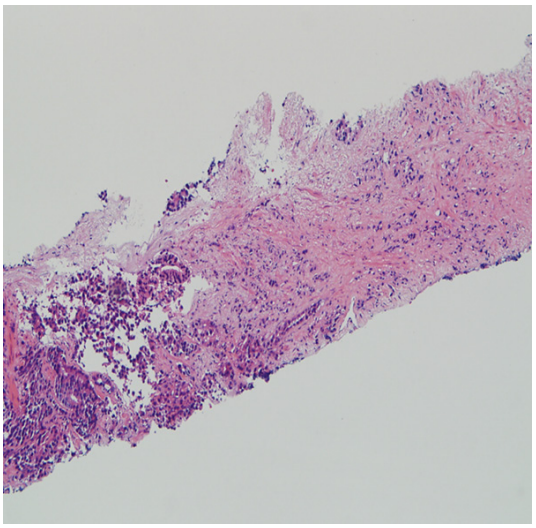

Figure 7. Targeted magnetic resonance imaging-guided prostate needle core biopsy showing prostatic adenocarcinoma, Gleason score 4+5=9.

Of the 31 patients (67%) with a prior biopsy, 3/31 (10%) had a TMRI-GB and 28/31 (90%) had a TRUS-GB. Twenty-one of these 31 patients (68%) had a history of PCa, and 10/31 patients (32%) had at least one negative TRUS-GB.

Of the 21 patients with previous PCa diagnosis, 15 patients had a Gleason score of 3+3=6 and were on active surveillance. Four patients had a Gleason score of 7 (3+4 or 4+3), 1 patient had ductal PCa (4+4=8), and 1 patient had a Gleason score of 4+5=9. All patients were described as having at least 1 focal abnormality suspicious for PCa on the dedicated multiparametric diagnostic MRI, with an average of 4.6 lesions identified per patient (range: 1-7 lesions).

Biopsy results

An average of 13 cores (range: 3-23 cores) were collected per patient per TMRI-GB procedure with an average of 3 cores (range: 1-6) sampled from each lesion. In this study, TMRI-GB detected cancer in 27/46 patients (59%). Forty-nine of 212 suspicious lesions identified on MRI were cancerous. One hundred fifty five cores were biopsied from these cancerous lesions, and 113/155 cores (73%) contained malignant glands. The highest Gleason score documented for each of the 27 PTs with PCa identified by TMRI-GB is shown in **Figures 4**-**7**. Five of 10 (50%) PTs with a history of benign biopsy had PCa identified by TMRI-GB. Ten of 15 PTs (67%) with no prior biopsy had a malignant TMRI-GB. Twelve of 21(57%) PTs with a prior diagnosis of PCa had PCa identified by TMRI-GB. These results grouped according to baseline characteristics are described in **Figure 8**.

All TMRI-GB findings were benign in 19/46 patients (41%). A total of 163 of all 212 (76.8%) lesions sampled contained benign pathologic findings. An average of 3 cores was removed from each benign lesion. Non-cancerous findings included: inflammation in 38 lesions, atypical small acinar proliferation (ASAP) in 4 lesions, high grade prostatic intraepithelial neoplasia (HGPIN) in 10 lesions, benign prostatic hyperplasia (BPH) in 2 lesions, BCG therapy effect in 8 lesions, no prostatic tissue identified in 5 lesions, and otherwise unremarkable benign prostatic tissue in the remaining 95 lesions. Graphical representation of histology findings in each of 212 lesions sampled by TMRI-GB, is depicted in **Figure 9**.

Discussion

TMRI-GB appears to have improved cancer detection rates when compared to TRUS-GB in patients with high clinical suspicion of PCa. Other studies have described TRUS-GB cancer detection rates ranging from 10% to 17%, after an initial negative biopsy [3, 7, 8]. In our patients with history of negative prostate biopsies, cancer detection rate was 50% on TMRI-GB. These findings are similar to those of a 2012 Dutch study, which described a TMRI-GB cancer detection rate of 41%, and a 2011 German study, which described a TMRI-GB cancer detection rate of 52%, in patients with a prior negative TRUS-GB [9, 10].

In patients with no prior prostate biopsy and high clinical suspicion for PCa, our cancer detection rate was 67%. While a 2014 study demonstrated a cancer detection rate of 53.1% in biopsy naïve patients, a prospective study by Pokorny et al. demonstrated a cancer detection rate in biopsy naïve men of (69.7%), which is similar to our findings [11, 12]. Overall, our cancer detection rate in all patients is 59%, which is similar to the detection rates of recent studies and within the range of previously reported values [13]. Prior studies have stratified patients as low, moderate, and high according

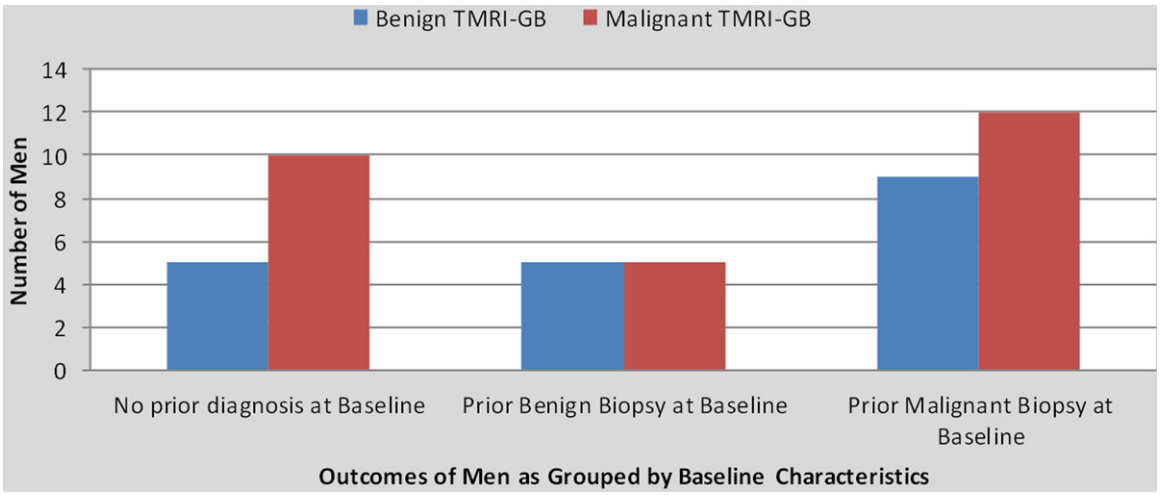

Figure 8. TMRI-GB results grouped according to baseline characteristics.

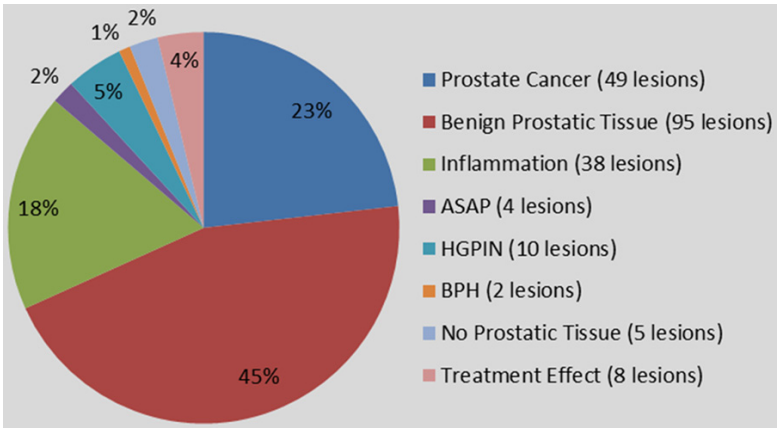

Figure 9. Histology of each lesion identified by TMRI-GB.

to number of MRI sequences suspicious lesions identified by MRI, with increasing numbers of sequences correlating with higher risk categories [14]. We have not stratified our patients according to radiologic risk during this investigation. However, upon data analysis a curious statistically significant finding was revealed. The mean number of cores sampled from lesions deemed malignant by a urologic pathologist was 3.16 and the mean number of cores sampled from lesions deemed benign by a urologic pathologist was 2.74. Number of cores was extrapolated from the number of passes performed by the interventional radiologist as indicated in the radiologic procedure note. We believe more cores were retrieved from malignant lesions due to radiologic findings that raised the suspicions of the interventional radiologists. These particular characteristics have not yet been elucidated, but we intend to characterize them in future studies. As we also document benign histologic findings in our pathology reports, we may also be able to characterize findings which are more likely associated with benign prostatic hyperplasia, high grade prostatic intraepithelial neoplasia or atypical small acinar proliferation, and less likely associated with cancer.

In conclusion, as cancer detection rates improve with TMRI-GB (and as specific radiologic characteristics of suspicious lesions become elucidated) we may be able to decrease the number of unnecessary biopsies performed on patients with a high clinical suspicion for PCa, and focus more on targeted lesions within the prostate gland. We predict that increasingly targeted biopsies will ultimately decrease the number of biopsy sessions required to diagnose PCa as well as decrease the number of cores sampled per biopsy session, there by decreasing cost and risk of infection. TMRI-GB may have a critical role as a tool for active surveillance, tumor mapping, and primary detection of PCa, and Pathologists and Radiologists will continue to play even more critical roles in the validation of this procedure.

Disclosure of conflict of interest

None.

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References

[1] Siegel R, Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. CA Cancer J Clin 2014; 64: 9-29.

[2] Moore CM, Robertson NL, Arsanious N, Middleton T, Villers A, Klotz L, Taneja SS, Emberton M. Image-guided prostate biopsy using magnetic resonance imaging derived targets: a systematic review. Eur Urol 2013; 63: 125-140.

[3] Djavan B, Ravery V, Zlotta A, Dobronski P, Dobrovits M, Fakhari M, Seitz C, Susani M, Borkowski A, Boccon-Gibod L, Schulman CC, Marberger M. Prospective evaluation of prostate cancer detected on biopsies 1, 2, 3, and 4: When should we stop? J Urol 2001; 166: 1679-1983.

[4] Presti JC, O'Dowd GJ, Miller MC, Mattu R, Vetri RW. Extended peripheral zone biopsy schemes increase cancer detection rates and minimize variance in prostate specific antigen and age related cancer rates: results of a community multi-practice study. J Urol 2003; 169: 125-129.

[5] Patel AR, Setphen JJ. Optimal biopsy strategies for the diagnosis and staging of prostate cancer. Curr Opin Urol 2009; 19: 232-237.

[6] Nam RK, Saskin R, Lee Y, Liu Y, Law C, Klotz LH, Loblaw DA, Trachtenberg J, Stanimirovic A, Simor AE, Seth A, Urbach DR, Narod SA. Increasing hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy. J Urol 2013; 189: s12-s18.

[7] Hambrock T, Somford DM, Hoeks C, Bouwense SA, Huisman H, Yakar D, van Oort IM, Witjes JA, Fütterer JJ, Barentsz JO. Magnetic resonance imaging guided prostate biopsy in men with repeat negative biopsies and increased prostate specific antigen. J Urol 2010; 183: 520-528.

[8] Roehl KA, Antenor JA, Catalona WJ. Serial biopsy results in prostate cancer screening study. J Urol 2010; 167: 2435-2439.

[9] Hoeks CM, Schouten MG, Bomers JG, Hoogendoorn SP, Hulsbergen-van de Kaa CA, Hambrock T, Vergunst H, Sedelaar JP, Fütterer JJ, Barentsz JO. Three-tesla magnetic resonance-guided prostate biopsy in men with increased prostate-specific antigen and repeated, negative random, systematic, transrectal ultrasound biopsies: detection of clinically significant prostate cancers. Eur Urol 2012; 62: 902-909.

[10] Roethke M, Anastasiadis AG, Lichy M, Werner M, Wagner P, Kruck S, Claussen CD, Stenzl A, Schlemmer HP, Schilling D. MRI-guided prostate biopsy detects clinically significant cancer: analysis of a cohort of 100 patients after previous TRUS biopsy. World J Urol 2012; 30: 213-218.

[11] Quentin M, Blondin D, Arsov C, Schimmöller L, Hiester A, Godehardt E, Albers P, Antoch G, Rabenalt R. Prospective evaluation of magnetic resonance imaging guided in-bore prostate biopsy in biopsy naïve men with elevated prostate specific antigen. J Urol 2014; 192: 1374-1379.

[12] Pokorny MR, Van de Ven W, Barentsz J, Thompson L. Prospective study of diagnostic accuracy comparing prostate cancer detection by transrectal ultrasound-guided biopsy versus magnetic resonance (MR) imaging with subsequent MR-guided biopsy in men without previous prostate biopsies. Eur Urol 2014; 66: 22-9.

[13] Overdun CG, Futterer JJ, Barentsz JO. MRI-guided biopsy for prostate cancer detection: a systematic review of current clinical trials. Curr Urol Rep 2013; 14: 209-213.

[14] Pinto PA, Chung PH, Rastinehad AR, Baccala AA Jr, Kruecker J, Benjamin CJ, Xu S, Yan P, Kadoury S, Chua C, Locklin JK, Turkbey B, Shih JH, Gates SP,Buckner C, Bratslavsky G, Linehan WM, Glossop ND, Choyke PL, Wood BJ. Magnetic resonance imaging/ultrasound fusion guided prostate biopsy improves cancer detection following transrectal ultrasound biopsy and correlates with multiparametric magnetic resonance imaging. J Urol 2011; 186: 1281-1285.