available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Brief Correspondence

Role of Core Number and Location in Targeted Magnetic Resonance Imaging-Ultrasound Fusion Prostate Biopsy

Amanda Jane Lu, Jamil S. Syed, Kamyar Ghabili, Walter Robert Hsiang, Kevin A. Nguyen, Michael S. Leapman, Preston C. Sprenkle *

Department of Urology, Yale School of Medicine, New Haven, CT, USA

Article info

Article history:
Accepted April 9, 2019

Associate Editor:
Giacomo Novara

Keywords:
Prostate cancer
Magnetic resonance imaging-ultrasound fusion biopsy
Region of interest

Abstract

The optimal method of magnetic resonance imaging (MRI)-ultrasound (US) fusion biopsy to adequately sample regions of interest (ROIs) remains unknown. We sought to determine the number and location of cores needed to adequately detect clinically significant prostate cancer (PCa). We identified patients undergoing MRI-US fusion prostate biopsy at our institution for known history or clinical suspicion of PCa. Multiparametric MRI studies were reviewed using Likert and Prostate Imaging Reporting and Data System (PI-RADS) v2 schema. Multiple targeted cores were taken from each ROI followed by 12-core systematic biopsy. In a distinct cohort of patients, lesions were targeted using a predetermined five-core template. We estimated cancers detected through sampling of five or fewer cores, assessed by core number and core location. We identified 744 patients with 581 lesions with PCa. Seventy-seven percent (279/361) of Gleason (G) $\geq$3 + 4 tumors and 72% (137/189) of G >3 + 4 tumors were detected on two-core sampling. Relative to all targeted cores, a two-core approach missed 16% of clinically significant cancers at first biopsy, 27% in prior negative, and 32% in active surveillance patients. Detection of G $\geq$3 + 4 cancers did not differ by core location. Sampling of two cores of ROIs misses nearly one-quarter of clinically significant PCa detected on additional sampling.

Patient summary: We aimed to understand how the number of cores obtained from a suspicious area during prostate magnetic resonance imaging-ultrasound fusion biopsy affects cancer detection. We found that sampling of five cores missed substantially fewer cancers compared to two cores.

* Corresponding author. Department of Urology, Yale School of Medicine, 789 Howard Avenue, FMP 312, New Haven, CT 06519, USA. Tel. +1 203 737-8076; Fax: +1 203 785 4043.
E-mail address: Preston.Sprenkle@yale.edu (P.C. Sprenkle).

Multiparametric magnetic resonance imaging (mpMRI)-guided biopsy has increasingly been utilized in the detection of prostate cancer (PCa) [1,2]. The PRECISION trial demonstrated superior cancer detection with targeted biopsy over standard biopsy [3]. While targeted biopsy offers high accuracy in the detection of clinically significant cancer, there is no consensus regarding the number or location of targeted cores to take from a region of interest (ROI) [4].

Given procedural discomfort, incremental resource utilization, and postbiopsy infection, there is a need to define the optimal sampling technique at the time of targeted biopsy [5–7]. We examined how the number of

https://doi.org/10.1016/j.eururo.2019.04.008
0302-2838/Published by Elsevier B.V. on behalf of European Association of Urology.

cores obtained from a single ROI impacts diagnostic yield and also explored the significance of core location.

We retrospectively identified patients undergoing MRI fusion prostate biopsy through an institutional review board-approved database from December 2012 to September 2017. Patients underwent biopsy with preprocedural MRI for active surveillance or clinical suspicion of PCa. Patients underwent mpMRI with 3 T MRI without an endorectal coil. The mpMRI studies were reviewed by genitourinary radiologists using a Likert scale (through April 2015) and Prostate Imaging Reporting and Data System (PI-RADS) v2 classification schema thereafter [8,9]. Prostate biopsy was performed by two urologists experienced in targeted fusion biopsy using the Artemis device (Eigen, Grass Valley, CA, USA).

From December 2012 to October 2016, targeted biopsy cores (5 [interquartile range 3–5]) were taken sequentially from each ROI with an even distribution followed by 12-core systematic biopsy (cohort 1). From November 2016 to September 2017, patients received template five-core biopsy of each ROI followed by 12-core systematic biopsy (cohort 2). The template five cores were taken in the following sequence: central, medial, lateral, base, and apex of the lesion on a transverse view. A genitourinary pathologist reviewed all cores for final pathology. For each lesion, the number of cores needed to first detect pathology was recorded. Gleason (G) ≥3 + 4 disease was defined as clinically significant.

For cohort 1, we modeled the incremental utility of performing additional core biopsies compared with total cores in a post hoc analysis of lesions with any Gleason, G ≥3 + 4, and G >3 + 4 disease. We determined the percentage of cancers detected with all targeted cores if the operator ceased performing targeted biopsy following two, three, or four cores in an ROI. Study outcome was the percentage of cancers detected with a threshold of two cores compared with total cores taken. For lesions in cohort 2, we assessed the detection of cancers by location with a targeted five-core template.

Cohort 1: number of cores and detection of cancer in a lesion: We identified 744 patients with 1233 suspicious lesions. Of the lesions sampled, 581 demonstrated PCa of any grade, from 379 men (Supplementary Table 1). Two cores would have detected 77% (279/361) of clinically significant cancers present compared with the total number of cores taken (Table 1). In comparison, five cores would have detected 99% of cancers present (574/581). The percentage of clinically significant disease detected with two cores was greatest in the biopsy-naïve group (Fig. 1). Obtaining two cores would have detected 84% (147/176) of clinically significant cancers in biopsy-naïve, 73% (69/94) in prior negative, and 68% (60/88) in active surveillance

Table 1 – Number of cores and detection of cancer relative to total cores in cohort 1 lesions

No. of cores	No. of ≥3 + 3 cancers detected	% of ≥3 + 3 cancers detected (*n* = 581)	No. of ≥3 + 4 cancers detected	% of ≥3 + 4 cancers detected (*n* = 361)	No. of >3 + 4 cancers detected	% of >3 + 4 cancers detected (*n* = 189)
1	400	69	223	62	102	54
2	490	84	279	77	137	72
3	531	91	319	88	156	83
4	557	96	341	94	173	92
5	574	99	355	98	181	96

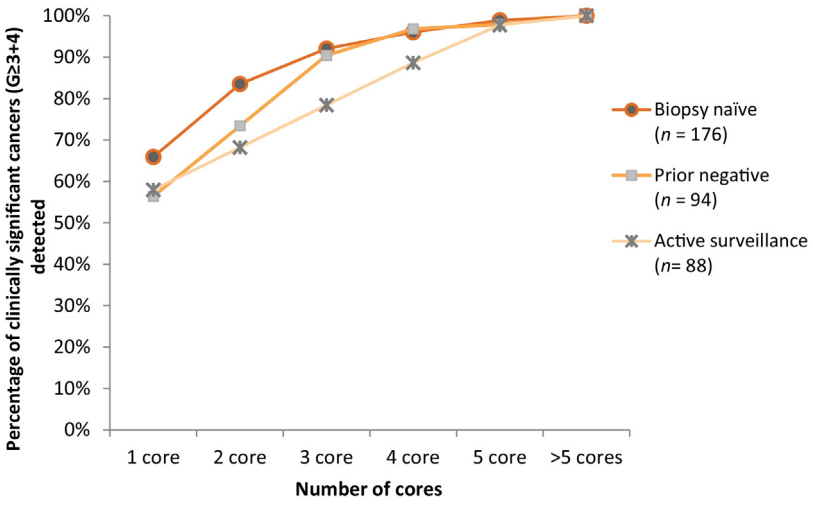

Fig. 1 – Percentage of clinically significant cancers (G ≥3 + 4) detected in cohort 1 lesions by biopsy status.

patients compared with total cores obtained ($p = 0.01$; Supplementary Table 2).

Since not all lesions were biopsied with five cores (Supplementary Table 1), we conducted a sensitivity analysis of 256 lesions that were biopsied with only five cores and found similar results. Compared with five-core biopsy, two cores detected 72.9% (102/140) of clinically significant cancers and 66.7% (42/63) of G >3 + 4 cancers (Supplementary Table 3).

Detection of clinically significant cancer at two cores compared with total cores was not different for prostate size <40 cm^3 (79% [147/185]) and ≥40 cm^3 (75% [129/173]; $p = 0.3$), or median lesion volume ≤0.33 cm^3 (77% [108/140]) and >0.33 cm^3 (80% [149/187]; $p = 0.6$). For PI-RADS 5 lesions, sampling beyond four cores did not improve the detection of G ≥3 + 4 disease ($p = 0.3$; Supplementary Table 4). Targeted biopsy of a single lesion detected the same pathology as or higher pathology than 12-core systematic biopsy for 65% (228/353) of G ≥3 + 4 disease (Supplementary Table 5).

Cohort 2: location of cores and lesion cancer detection: We identified a distinct set of 110 patients with 154 suspicious lesions. There was no association between location and presence of clinically significant PCa ($p = 0.4$). Among patients with PI-RADS 4 and 5 lesions, the location of the biopsy was not associated with the detection of clinically significant cancers (Supplementary Fig. 1; $p = 0.6$). For patients with multiple cores positive within a given lesion, we did not identify an association of location with the highest Gleason grade ($p = 0.9$), although a biopsy through the center had the highest single-core detection of cancer (46% [71/154]).

In summary, we found that a limited two-core targeted sampling strategy detects the majority of clinically significant PCa. However, nearly a quarter of cancers present are missed relative to a five-core approach. We did not observe an association between the location of biopsy core within a lesion and the detection of clinically significant PCa.

At our institution, all patients undergo both targeted and systematic 12-core biopsy, but whether more intensive sampling of each lesion could obviate systematic biopsy remains to be determined as most studies report an 8–14% risk of missing clinically significant cancer [4,10]. Limitations of our study include a lack of whole mount correlation, which restricts our ability to define gold-standard cancer detection. Whole mount pathology in the MR-targeted era has identified MR-invisible lesions missed by biopsy, but targeted biopsy may also overestimate final Gleason grade. Finally, while there may be inherent challenges with multiple biopsies of a smaller lesion, two-core biopsy of smaller lesions missed substantial clinically significant cancer. Our data suggest that more biopsies are beneficial and, considering registration error, bracketing the area is advised.

Taking five cores per ROI is needed to achieve a high clinically significant cancer detection and limit missed cancers. Our data show that the two-core standard per target, while detecting most cancers in biopsy-naïve patients, misses substantial clinically significant cancer found on further biopsy in prior negative and active surveillance patients, irrespective of lesion volume.

Author contributions: Preston C. Sprenkle 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: Lu, Sprenkle, Leapman, Ghabili.
Acquisition of data: Lu, Sprenkle, Syed, Ghabili.
Analysis and interpretation of data: Lu, Ghabili, Nguyen.
Drafting of the manuscript: Lu, Hsiang.
Critical revision of the manuscript for important intellectual content: Sprenkle, Leapman, Ghabili.
Statistical analysis: Lu, Ghabili, Nguyen.
Obtaining funding: Lu, Sprenkle.
Administrative, technical, or material support: Syed, Ghabili.
Supervision: Sprenkle, Leapman.
Other: None.

Financial disclosures: Preston C. Sprenkle certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: Research reported in this publication was supported by the National Institute of Diabetes And Digestive And Kidney Diseases of the National Institutes of Health under award number T35DK104689. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.eururo.2019.04.008.

References

[1] Moore CM, Robertson NL, Arsanious N, et al. Image-guided prostate biopsy using magnetic resonance imaging-derived targets: a systematic review. Eur Urol 2013;63:125–40.
[2] Ahmed HU, El-Shater Bosaily A, Brown LC, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet 2017;389:815–22.
[3] Kasivisvanathan V, Rannikko AS, Borghi M, et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med 2018;378:1767–77.
[4] Dimitroulis P, Rabenalt R, Nini A, et al. Multiparametric magnetic resonance imaging/ultrasound fusion prostate biopsy: are 2 biopsy cores per magnetic resonance imaging lesion required? J Urol 2018;200:1030–4.
[5] Giganti F, Moore CM. A critical comparison of techniques for MRI-targeted biopsy of the prostate. Transl Androl Urol 2017;6:432–43.
[6] Walker JT, Singla N, Roehrborn CG. Reducing infectious complications following transrectal ultrasound-guided prostate biopsy: a systematic review. Rev Urol 2016;18:73–89.
[7] Roberts MJ, Bennett HY, Harris PN, et al. Prostate biopsy-related infection: a systematic review of risk factors, prevention strategies, and management approaches. Urology 2017;104:11–21.

[8] Barentsz JO, Richenberg J, Clements R, et al. ESUR prostate MR guidelines 2012. Eur Radiol 2012;22:746–57.
[9] Weinreb JC, Barentsz JO, Choyke PL, et al. PI-RADS Prostate Imaging – Reporting and Data System: 2015, version 2. Eur Urol 2016;69:16–40.
[10] Siddiqui MM, Rais-Bahrami S, Turkbey B, et al. Comparison of MR/ultrasound fusion-guided biopsy with ultrasound-guided biopsy for the diagnosis of prostate cancer. JAMA 2015;313:390–7.