Early Experience with MRI-ultrasound Fusion-guided Prostate Biopsy in Japanese Men with Elevated PSA Levels

Tsutomu Tamada1*, Yoshiyuki Miyaji2, Naoki Kanomata3, Ayumu Kido1, Akira Yamamoto1, and Teruki Sone1

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Introduction
Accurate pre-treatment evaluation including prostate multiparametric MRI (mpMRI) and prostate biopsy is required to efficiently discriminate clinically significant prostate cancer (csPC) from clinically insignificant prostate cancer (cis PC). On the other hand, as one solution to the limitations of standard systematic transrectal ultrasonography (TRUS)-guided prostate biopsy including the underestimation of tumor aggressiveness PC such as the Gleason score (GS), the false negative result for anterior lesion, and the overtreatment for detection of cis PC such as small PC with GS 3 + 3, the MRI-ultrasound (US) fusion-guided biopsy is becoming a gradually used method for prostate-targeted biopsy.1

Therefore, the aim of this study was to report our early experience with MRI-US fusion-guided prostate biopsy in Japanese men with elevated prostate-specific antigen (PSA) levels.

Materials and Methods
The Institutional Review Board approved this single-center, retrospective study, and the requirement for written, informed consent was waived.

A total of 12 consecutive patients (mean age, 70 years) with elevated PSA levels who underwent prostate mpMRI followed by MRI-US fusion-guided prostate biopsy were included. In total, four of the patients underwent radical prostatectomy after the prostate biopsy.

All mpMRI examinations were performed using a 3T scanner with a 32-channel phased-array coil (Ingenia 3T CX Quasar Dual; Philips Medical Systems, Best, The Netherlands).

The MRI-US fusion-guided targeted biopsy with systematic biopsy was performed in US-guided prostate biopsy using elastic image fusion and real-time 3D tracking technology (UroStation; Koelis, Grenoble, France). A radiologist performed the segmentation of the whole prostate and MRI-defined lesions from 3D data of mpMRI images before prostate biopsy. Next, the 3D volume data of mpMRI and the real-time TRUS image were elastically fused, and then, right after the biopsy core for the target lesion on the fusion image was taken under TRUS guidance. MRI-US fusion-guided prostate biopsy was performed for lesions with prostate imaging and reporting data system version 2 categories of 3–5 or highly suspicious lesions by conventional overall mpMRI assessment.2,3 The targeted biopsy obtained was at least two cores per MRI-targeted lesion. After the targeted biopsy, standard systematic sampling (n = 12) was performed in the state that the target lesion cannot recognize. Statistical analysis was performed using the Wilcoxon signed-rank test and the Mann–Whitney U test. A two-sided value of P < 0.05 was indicated as significant.

Results
The number of biopsy cores was significantly higher in the systematic biopsy group than in the MRI-US fusion-targeted biopsy group (P = 0.003) (Table 1). The tumor detection rates of csPCs (≥GS7) and all PCs per biopsy core were higher in the MRI-US fusion-targeted biopsy group than in the systematic biopsy group (Table 1). In addition, the index of tumor size was significantly higher in the MRI-US fusion-targeted biopsy than in the systematic biopsy (P = 0.021) (Table 1).

The concordance rate with the prostatectomy GS was higher in the MRI-US fusion-targeted biopsy group than in
Table 1 Outcomes of biopsy and histopathological evaluations of MRI-US fusion-targeted biopsy and systematic biopsy in patients with elevated PSA levels

| Outcome | MRI-US fusion-targeted biopsy group ($n=12$) | Systematic biopsy group ($n=12$) | $P$-value |
|---------|---------------------------------------------|---------------------------------|-----------|
| Number of biopsy cores | 5.8 ± 3.0 | 12 ± 0 | 0.003 |
| Cancer detection rate per patient (%) | 5/12 (41) | 5/12 (41) | – |
| Cancer detection rate per PC patient (%) | 5/6 (83) | 5/6 (83) | – |
| Core positive for csPC (≥GS7) (number of cores with csPC/total number of cores) (%) | 7/69 (10.1) | 6/144 (4.2) | 0.176 |
| Core positive for all cancers (number of cores with PC/total number of cores) (%) | 18/69 (26.1) | 10/144 (6.9) | 0.044 |
| Index of tumor size (%) (total cancer core length/total core length) | 52.2 ± 29.2 | 27.5 ± 19.2 | 0.021 |

US, ultrasound; PSA, prostate-specific antigen; PC, prostate cancer; csPC, clinically significant prostate cancer; GS, Gleason score.

Table 2 Tumor aggressiveness of MRI-US fusion-targeted biopsy, systematic biopsy, and prostatectomy in patients with prostate cancer

| Patient | MRI-US fusion-targeted biopsy group Index GS* | Systematic biopsy group | Assessment of TA of systematic biopsy compared to MRI-US fusion-targeted biopsy | Prostatectomy GS | Treatment |
|---------|---------------------------------------------|--------------------------|-----------------------------------|-----------------|-----------|
| 1       | 4 + 4                                       | 3 + 4                    | Undergraded                       | 4 + 4           | Prostatectomy |
| 2       | 3 + 4                                       | 3 + 3                    | Undergraded                       | 3 + 4           | Prostatectomy |
| 3       | 3 + 3                                       | Benign                   | Undergraded                       | 3 + 3 with tertiary 4 | Prostatectomy |
| 4       | Benign                                      | 4 + 4                    | Overgraded                        | –               | HDR       |
| 5       | 3 + 4                                       | 3 + 4                    | Same                              | –               | Watchful waiting for HT |
| 6       | 3 + 4                                       | 3 + 4                    | Same                              | 3 + 4           | Prostatectomy |
| Concordance rate with prostatectomy GS | 100% (4/4)                  | 25% (1/4)                | –                                 | –               | –         |

*The index GS is the highest GS in a lesion with several GS values in multiple biopsy sampling. US, ultrasound; GS, Gleason score; TA, tumor aggressiveness; HDR, high-dose-rate brachytherapy; HT, hormonal therapy.

Discussion

In this early experience with MRI-US fusion-targeted prostate biopsy in Japan, the MRI-US fusion-targeted prostate biopsy effectively detected PCs at a smaller number of biopsy samples compared with the systematic biopsy. In addition, the tumor size within the biopsy core in the MRI-US fusion-targeted prostate biopsy was approximately twice that of the systematic biopsy. Furthermore, the concordance rate with the prostatectomy GS was perfect in the MRI-US fusion-targeted prostate biopsy, whereas the systematic biopsy GS was underestimated in 75% of patients compared with prostatectomy. With these results, MRI-US fusion-targeted prostate biopsy is expected to overcome the underestimation of not only tumor size, but also tumor aggressiveness in the systematic biopsy, and the discrimination between cis PC (≤GS6) and csPC using the MRI-US fusion-targeted prostate biopsy may be standardized in the management of patients with elevated PSA levels. However, we experienced a patient who may have had registration error of 3D data of mpMRI and TRUS. A learning curve of several patients will be required to reduce the human error in registration.

Conclusion

This early experience showed that MRI-US fusion-targeted biopsy may effectively detect csPC, and it is expected that this method will be incorporated into the algorithm of PC practice in Japan. However, further experience and investigations using Japanese patients with PC are warranted to improve the detection of csPC with MRI-US fusion-targeted biopsy.
Fig. 1 A 67-year-old man (prostate-specific antigen [PSA] of 6.33 ng/mL) with prostate cancer who underwent radical prostatectomy. (a) T2-weighted image shows an area of homogeneous hypointensity in the middle right region in the peripheral zone (11.4 mm in size) (arrow). (b) Diffusion weighted image (DWI) shows distinct hyperintensity (arrow). (c) Apparent diffusion coefficient (ADC) map shows a distinct hypointense lesion (arrow). (d) Early-phase fat suppression T1-weighted image on dynamic contrast-enhanced (DCE-MRI)-MRI shows focal moderate early enhancement (arrow). The lesion was assigned a T2-weighted imaging score of 4, DWI/ADC map score of 4, and DCE-MRI score of positive. By prostate imaging reporting and data system version 2 decision rules, the overall category is 4. MRI-US fusion-targeted biopsy detected prostate cancer with Gleason score (GS) of 4 + 4 (two positive cores: index of tumor size of 50% [GS 4 + 4] and index of tumor size of 80% [GS 4 + 4]), whereas systematic biopsy detected prostate cancer with GS of 3 + 4 (one positive core: index of tumor size of 40% [GS 3 + 4]). The prostatectomy GS was 4 + 4.

Conflicts of Interest
The authors declare that they have no conflict of interest.

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