Mapping of Transrectal Ultrasonographic Prostate Biopsies

Quality Control and Learning Curve Assessment by Image Processing

Pierre Mozer, MD, PhD, Michael Baumann, PhD, Gregoire Chevreau, PhD, Alexandre Moreau-Gaudry, MD, PhD, Stephane Bart, MD, Raphaelle Renard-Penna, MD, Eva Comperat, MD, Pierre Conort, MD, Marc-Olivier Bitker, MD, Emmanuel Chartier-Kastler, MD, PhD, Francois Richard, MD, Jocelyne Troccaz, PhD

Objective. Mapping of transrectal ultrasonographic (TRUS) prostate biopsies is of fundamental importance for either diagnostic purposes or the management and treatment of prostate cancer, but the localization of the cores seems inaccurate. Our objective was to evaluate the capacities of an operator to plan transrectal prostate biopsies under 2-dimensional TRUS guidance using a registration algorithm to represent the localization of biopsies in a reference 3-dimensional ultrasonographic volume.

Methods. Thirty-two patients underwent a series of 12 prostate biopsies under local anesthesia performed by 1 operator using a TRUS probe combined with specific third-party software to verify that the biopsies were indeed conducted within the planned targets.

Results. The operator reached 71% of the planned targets with substantial variability that depended on their localization (100% success rate for targets in the middle and right parasagittal parts versus 53% for targets in the left lateral base). Feedback from this system after each series of biopsies enabled the operator to significantly improve his dexterity over the course of time (first 16 patients: median score, 7 of 10 and cumulated median biopsy length in targets of 90 mm; last 16 patients, median score, 9 of 10 and a cumulated median length of 121 mm; \(P = .046\)).

Conclusions. In addition to being a useful tool to improve the distribution of prostate biopsies, the potential of this system is above all the preparation of a detailed “map” of each patient showing biopsy zones without substantial changes in routine clinical practices.

Key words: image-based tracking; image processing; learning curve; prostate biopsy; quality control; 3-dimensional ultrasonography.

Mapping transrectal ultrasonographic (TRUS) prostate biopsies is of fundamental importance for either diagnostic purposes or the management and treatment of prostate cancer. At the present time, there is room for improvement in their transrectal distribution because the correlation is low between biopsy results and pathologic findings of radical prostatectomy specimens.\(^1\) This has led some operators to conduct transperineal biopsies using a template. This procedure is difficult in routine clinical use, and its accuracy is subject to caution. It is in fact well known that the prostate has considerable mobility,\(^2,3\) and the ultrasonographic planning systems do not take into account those movements at the time of puncture.\(^4\)
Modern 3-dimensional (3D) TRUS probes allow acquisition of high-quality volumes of the prostate in a few seconds. We have developed a process to track the prostate on 3D TRUS images. With a reference volume acquired at the beginning of the session and another during each biopsy, it is possible to rapidly determine the spatial relationship between the reference prostate and every biopsy volume by automatically aligning images. Thus, without changing the usual clinical practices of endorectal biopsies, in a few seconds this system provides accurate biopsy core localization by representing them in a single 3D ultrasonographic volume. The process is implemented on a computer system placed beside the ultrasound scanner during the procedure.

Our main goal was determining an operator’s ability to conduct predefined planning of 12 biopsies using the most widespread technique involving biopsy guidance with a 2-dimensional (2D) transverse TRUS image. We used our registration process to quantify sampling of the gland by measuring first, the rate of biopsies successfully reaching predefined targets and second, the length of the biopsy cores removed from the same predefined targets. To quantify the feedback contribution of the system, the operator’s learning curve was established.

**Materials and Methods**

**Patients and Operator**

After approval by an Ethics Committee, 1 operator performed 12-core TRUS biopsies on 32 patients from November 2006 to March 2007 according to a classic 12-core protocol. Informed consent was obtained from all patients. The patients were supine on a table with stirrups. Biopsies were performed with transverse 2D tracking provided by a 3D TRUS probe (RIC5-9 on a Voluson i system; GE Healthcare, Milwaukee, WI) and standard biopsy needles (18 gauge; Bard Peripheral Technologies, Covington, GA). The operator is a right-handed urologist and assistant professor, having conducted more than 100 prostate biopsies before this study.

The patient inclusion criterion was a prostate-specific antigen level of greater than 4 ng/mL; the median level was 8 ng/mL (range, 4–18 ng/mL). All patients received ciprofloxacin 2 hours before the biopsies. The average prostate volume was 45 mL (range, 20–100 mL). The biopsy was conducted after local anesthesia with 10 mL (5 mL on each side) of 2% lidocaine injected around the periprostatic nerve plexus under conventional 2D TRUS guidance.

**Biopsies**

**Intraoperative Acquisitions**

Before the first biopsy, a 3D reference volume including the prostate was acquired. The probe was then switched to the 2D mode for biopsy targeting. After each biopsy gunshot, the needle was left indwelling in the prostate for an average of 3 seconds as a 3D TRUS volume was acquired. During this acquisition, the operator paid attention to apply minimal force on the probe to minimize deformation of the prostate.

**Postoperative Registration and Measurements**

The needle was delineated in each biopsy volume and was automatically mapped into the reference volume with a rigid image-based registration algorithm. This algorithm is fully automatic and is based on the statistical analysis of the composition of images. This organ-based tracking process enables both the movements of the TRUS probe and those of the prostate to be followed. To validate registration, we pointed out clearly visible pointlike fiducials, eg, calcifications, in the prostate. The distances between corresponding fiducials after application of the registration transform were used as the reference standards to determine accuracy.

After registration, the biopsy cores can be represented in the reference volume (Figure 1), enabling their spatial distribution to be analyzed. Quantitative analyses were conducted by reslicing the reference volume in the coronal plane and the 12 preoperative square target areas were superimposed on these images. Target areas were named with the following convention: base, mid gland, or apex; lateral or parasagittal; and right or left.

For each square coronal target area mentioned above, we computed the rate of biopsies hitting the target and the biopsy length inside the target. The length measured was that of the cylinder...
removed from the target by the needle, ie, including a 20-mm-long zone starting 5 mm from the needle tip. When a biopsy overlapped several targets, the 2 greatest lengths were recorded. A biopsy was considered successful when its length within the targeted area was more than 3 mm due to the accuracy of the algorithm reported previously.5

Because the lateral apical target areas are small for preoperative planning, we merged them with the parasagittal apical targets for analysis. This merging was conducted by averaging biopsy tissue lengths in the lateral and parasagittal apical areas. Thus, for each patient, 10 targets were analyzed to study the sampling procedure and determine the operator’s capacity to perform planning. The operator was made aware of the results several days after the biopsies and was able to see where the biopsies were performed on a 3D interface.

**Statistical Analysis**
In terms of operator capacities to conduct predefined planning, a quantitative analysis of the distribution of biopsied tissue lengths was conducted with the Friedman nonparametric test. The effect of the prostate volume on the length of samples recovered from targets was determined by a linear regression. The learning curve was analyzed by separating patients into 2 groups according to chronologic order: the first 16 patients were in group 1 and the last 16 in group 2. The operator aimed at 10 targets, and a score from 0 to 10 was calculated for each patient. The Mann-Whitney nonparametric test was used to compare the score distribution between the 2 groups. The same method was applied to the analysis of sampling in the biopsied areas. The threshold of significance adopted for this study was \( P < .05 \).

**Results**
No postbiopsy complication was reported. Average pain was scored as 2 (range, 1–4) on a scale from 0 to 10.

**Analysis of Robustness and Accuracy of Image Registration**
The accuracy of the registration method was validated on 237 3D images acquired during biopsies with an average error of less than 2 mm and a maximum error of less than 4 mm. Registration between 2 volumes was computed on average in 6 seconds. The success rate for all of the registrations was 97% (375 good registrations on 384 volumes). The registration system failed 9 times, but these failures resulted from images containing artifacts caused by the presence of air between the probe and tissues.
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### Analysis of the Operator’s Capacities to Reach Planning Targets

All results are summarized in Table 1. The operator reached his target on average in 71% of the cases. The success rate was maximal in the right parasagittal mid area (100%) and minimal in the left lateral base area (53%). Overall, the ratio was maximal in the center and decreased as the planning approached the boundaries of the prostate. The distribution of biopsied tissue lengths was significantly dependent on the targeted area (\(P = 1.54 \times 10^{-10}\)). It may be noted that the lengths of the tissues sampled from the apex and the left lateral base area were less than half those expected. Finally, no effect of prostate volume on these lengths could be shown (\(P = .5\)).

### Analysis of the Operator's Learning Curve in Reaching Planning Targets

For group 1, the operator reached the target in 66% of cases compared to 77% in group 2. The median score in group 1 was 7 (minimum, 4; maximum, 9) and was significantly lower (\(P = .046\)) than in group 2 (median, 9; minimum, 2; maximum, 10). The median cumulated lengths of biopsies from inside the targets were 90 mm (minimum, 37 mm; maximum, 130 mm) for group 1 and 121 mm (minimum, 32 mm; maximum, 156 mm) for group 2. The size of the sample was statistically significant (\(P = .042\)).

### Analysis of Prostate Biopsy Sampling

The length of tissues sampled was longest in the right parasagittal mid area (median, 30 mm) and shortest in the right apex (median, 7 mm). The distribution of lengths biopsied significantly depended on the area (\(P = 5 \times 10^{-16}\)). Parasagittal zones were sampled more than lateral zones.

### Analysis of the Learning Curve in Prostate Biopsy Sampling

The median cumulated lengths of biopsies in parasagittal zones was 106 mm (minimum, 43 mm; maximum, 165 mm) for the first 16 patients and 81 mm (minimum, 51 mm; maximum, 140 mm) for the last 16 patients. The size reduction of

### Table 1. Targeting Accuracy Evaluation Results for the 32 Patients

| Target               | Biopsies, n | Biopsies inside the Target, % (n) | Biopsies Length Inside the Target, mm, Median (1st–3rd Quartile) | Biopsies, n | Biopsies inside the Target, % (n) | Biopsies Length Inside the Target, mm, Median (1st–3rd Quartile) | Biopsies, n | Biopsies inside the Target, % (n) | Biopsies Length Inside the Target, mm, Median (1st–3rd Quartile) |
|----------------------|-------------|----------------------------------|---------------------------------------------------------------|-------------|----------------------------------|---------------------------------------------------------------|-------------|----------------------------------|---------------------------------------------------------------|
|                      |             |                                  |                                                               |             |                                  |                                                               |             |                                  |                                                               |
| Right                | 32          | 72 (23)                          | 15 (12–17)                                                    | 16          | 62 (10)                          | 15 (13–17)                                                    | 16          | 81 (13)                          | 15 (12–17)                                                    |
|                      |             |                                  | 12 (8–15)                                                     |             |                                  | 8 (6–14)                                                      |             |                                  | 15 (10–16)                                                    |
|                      | 32          | 53 (17)                          | 16 (14–20)                                                    | 16          | 50 (8)                           | 15 (7–18)                                                     | 16          | 75 (12)                          | 17 (16–20)                                                    |
|                      |             |                                  | 15 (11–20)                                                   |             |                                  | 15 (14–18)                                                   |             |                                  | 16 (11–20)                                                    |
|                      | 32          | 66 (21)                          | 15 (12–17)                                                    | 16          | 81 (13)                          | 14 (12–18)                                                   | 16          | 88 (14)                          | 15 (12–18)                                                    |
|                      |             |                                  | 15 (13–17)                                                   |             |                                  | 14 (13–14)                                                   |             |                                  | 16 (16–19)                                                    |
| Right                | 32          | 100 (32)                         | 16 (12–18)                                                    | 16          | 100 (16)                         | 17 (13–19)                                                   | 16          | 100 (16)                         | 15 (13–17)                                                    |
|                      |             |                                  | 16 (14–18)                                                   |             |                                  | 17 (14–19)                                                   |             |                                  | 16 (14–19)                                                    |
|                      | 32          | 88 (28)                          | 16 (12–18)                                                    | 16          | 92 (15)                          | 16 (14–19)                                                   | 16          | 81 (13)                          | 18 (14–19)                                                    |
| Apex, lateral +      | 60          | 72 (43)                          | 7 (5–10)                                                      | 30          | 50 (15)                          | 7 (5–12)                                                      | 30          | 94 (28)                          | 7 (5–9)                                                       |
|                      |             |                                  | 8 (6–13)                                                      |             |                                  | 7 (5–8)                                                       |             |                                  | 12 (8–15)                                                      |
|                      | 59          | 59 (35)                          | 29 (6–13)                                                     | 30          | 62 (18)                          | 29 (5–8)                                                      | 30          | 56 (17)                          | 29 (5–8)                                                      |
| Sum/average          | 375         | 71 (268)                         | 187 (66)                                                     | 188         | 77 (144)                         | 188 (66)                                                     | 188         | 77 (144)                         | 188 (66)                                                     |
samples taken from these zones was statistically significant ($P = .012$). The median cumulated lengths of biopsies in lateral zones was 49 mm (minimum, 12 mm; maximum, 103 mm) for the first 16 patients and 79 mm (minimum, 20 mm; maximum, 124 mm) for the last 16 patients. The increase in length sampled from these zones was statistically significant ($P = .044$). The zones sampled thus shifted over time from the parasagittal part to the lateral part of the prostate.

**Discussion**

**Accuracy, Robustness, and Integration of the System**

One of the advantages of this system is that each biopsy is based on images of the prostate with the biopsy needle in place and not on the relative position of the puncture needle with respect to the ultrasound images acquired several minutes beforehand. This is an important finding because, in contrast to other devices such as TargetScan (Envisioneering Medical Technologies, St Louis, MO) used for transrectal biopsies and a brachytherapy template used for perineal biopsies, our system incorporates the movements of the gland. It is important to note that this approach does not rely on any external optical or magnetic tracking system or passive arm holding the probe, which means that no cumbersome additional material is required because the method uniquely involves analysis of ultrasound images.

The major drawback of the algorithm used in this study is that it does not yet integrate deformations of the prostate caused by pressure from the endorectal probe. This is why the operator paid special attention to avoid deforming the gland during acquisition of images; in addition, evaluation of the accuracy of the algorithm verified that there was little or no deformation of the prostate in contact with the probe. The mean system accuracy was determined to be 2 mm with a maximal error of 4 mm in the 3 spatial dimensions and in our opinion had no clinical relevance.

To our knowledge, a system that enables the localization of endorectal prostate biopsies with real 3D quantified accuracy has not been previously described. By increasing the biopsy time by only a few minutes, this technique leads to increased quality control of biopsy localizations specifically for each patient. System robustness should nevertheless be verified by a study involving several operators.

**Operator Accuracy, Study of Sampling, and Learning Curve**

The operator in this study had previously participated in a study using a phantom, comparing the distribution of biopsies conducted by 14 different operators. No significant difference was found between the operator in the former study and the 13 other clinicians. It can thus be considered that this operator is representative.

The success rate for reaching a target that the operator envisions mentally is relatively low (mean, 71%) and indicates the difficulties in transferring 3D coordinates while being guided only by a 2D image. Feedback given by the system in the course of this work enabled the operator to significantly improve the distribution of prostate biopsies over time. Nevertheless, the patient population in this study was too small to prove that an increase in the number of positive biopsy findings resulted from better targeting. In the same vein, the capacities of different operators should be compared to confirm these results.

**Potentials**

There are a number of potentials for this technique. It is theoretically possible to merge series of biopsies done at different times provided the volume or shape of the prostate does not vary substantially. This would, for example, verify that a suspicious zone on prior biopsies was again sampled, rather than an adjacent region. Similarly, in the context of active surveillance requiring repeated biopsies, the relative position of each biopsy at different times would increase the confidence level of this therapeutic approach. Finally, in cases of repeated biopsies resulting from a strong suspicion of cancer, it would ensure that different zones were effectively punctured.

Currently, because of the time needed to acquire a 3D TRUS volume, the system does not allow real-time feedback. Nevertheless, 3D TRUS imaging systems in research laboratories provide
about 5 volumes per second, and this algorithm should be fast enough to achieve frame rates of 5 Hz by taking advantage of the massive parallelization capacities provided by modern high-end computers, enabling continuous full 3D image-based tracking. It could be possible to select a target in the reference volume and guide the clinician to reach it. Moreover, work is in progress to take into account both deformations and merged preoperative magnetic resonance imaging and 3D TRUS reference volumes to select the target in magnetic resonance images and track it with high accuracy in this context.

Conclusions
This study has evaluated the capacities of an operator to reproduce predefined planning and also real sampling conducted during transrectal biopsies under 2D ultrasonographic guidance. In the entire patient population, the operator reached only 71% of the designated targets, with substantial variability depending on their localization. These localization errors were the cause of an undersampling of the peripheral part of the gland and an oversampling of the parasagittal part. Feedback after the procedure significantly improved the rate of targets reached and thus improved tissue sampling within the gland.

In addition to being very useful for improving prostate biopsies, the potential of this system is above all the possibility of creating a precise map of zones sampled for each patient. These biopsy localization data not only can be used to make a therapeutic decision but also can be registered for possible near-future merging with biopsies conducted at different times in the course of surveillance.

References
1. Salomon L, Colombel M, Patard JJ, et al. Value of ultrasound-guided systematic sextant biopsies in prostate tumor mapping. Eur Urol 1999; 35:289–293.
2. Artignan X, Rastkhah M, Balosso J, Fournenet P, Gilliot O, Bolla M. Quantification of prostate movements during radiotherapy [in French]. Cancer Radiother 2006; 10:381–387.
3. Padhani AR, Khoo VS, Suckling J, Husband JE, Leach MO, Dearnaley DP. Evaluating the effect of rectal distension and rectal movement on prostate gland position using cine MRI. Int J Radiat Oncol Biol Phys 1999; 44:325–333.
4. Lagerburg V, Moerland MA, Lagendijk JJ, Battemann JJ. Measurement of prostate rotation during insertion of needles for brachytherapy. Radiother Oncol 2005; 77:318–323.
5. Baumann M, Mozer P, Daamen V, Troccaz J. Towards 3D ultrasound image based soft tissue tracking: a transrectal ultrasound prostate image alignment system. Med Image Comput Comput Assist Interv 2007; 10:26–33.
6. Andriele GL, Bullock TL, Belani JS, et al. Is there a better way to biopsy the prostate? Prospects for a novel transrectal systematic biopsy approach. Urology 2007; 70(suppl):22–26.
7. Long J, Daamen V, Moreau-Gaudry A, Troccaz J, Rambeaud J, Descotes JL. Prostate biopsies guided by three-dimensional real-time (4-D) transrectal ultrasonography on a phantom: comparative study versus two-dimensional transrectal ultrasound-guided biopsies. Eur Urol 2007; 52: 1097–1104.