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Shape Analysis of the Prostate: Establishing Imaging Specifications for the Design of a Transurethral Imaging Device for Prostate Brachytherapy Guidance

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Abstract

Purpose—To examine specific prostate and urethra dimensions and prostate shape to facilitate the design of a transurethral ultrasonographic imaging device.

Methods and Materials—Computed tomographic (CT) data sets were retrospectively evaluated from 191 patients who underwent permanent prostate brachytherapy at our institution. The prostate, rectum, urethra, and bladder were each segmented with imaging software. Collected data and calculations included prostate volume at specific distances from the urethra and rectum, distances from seeds to urethra (SU), distances from seeds to rectum (SR), prostate length, and curvilinear prostatic urethra length.

Results—CT-based, postimplant mean prostate volume was 49 cm³ (range, 22–106 cm³). Mean prostate length was 4.5 cm (range, 3.1–6.0 cm). The mean curvilinear length of the prostatic urethra was 4.5 cm. The mean (standard deviation) prostatic urethra bend was 29.0° (12.2°). The mean surface distance from the prostate to the urethra was 2.9 cm and from the prostate to the rectum, 4.6 cm ($p < .001$, paired t test). The mean SU distance was 1.6 cm, and the mean SR distance was 2.3 cm ($p < .001$). In the largest prostate, the mean SU distance was 3.9 cm and the mean SR distance was 6.0 cm.

Conclusions—A urethral imaging device for prostate brachytherapy and other minimally invasive prostate therapies should ideally have a 6-cm imaging field of view to image all the prostates in this series in a single image. The mean distance from the urethra to seeds in PPB is less than 70% of the mean seed distance to the rectum.

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Keywords

brachytherapy; computed tomography; prostate; prostatic neoplasms; radiotherapy; ultrasonography; urethra

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Introduction

The American Cancer Society estimated that the incidence of prostate cancer in the United States in 2014 was nearly 233,000, with approximately 29,480 deaths caused by this disease (1). While the serum prostate-specific antigen test has been a very robust screening tool for prostate cancer (2), diagnosis and management of prostate cancer largely depend on the use of effective imaging technologies that have marginal sensitivity and specificity in the prostate. Fluoroscopy, transrectal ultrasonography (TRUS), computed tomography (CT), and magnetic resonance imaging (MRI) are the most common imaging modalities used to guide minimally invasive prostate procedures. A newer imaging modality being investigated is transurethral ultrasonography (TUUS) (3). Both traditional and new imaging methods can be optimized for examination of the prostate if there are adequate anatomical models of the prostate and associated tissue. The purpose of this study was to collect and analyze prostate shape measurements from a sampled patient population to provide prostate imaging specifications to facilitate the design of a transurethral ultrasonographic imaging device.

Image-guided prostate procedures include TRUS-guided biopsy and minimally invasive procedures. Permanent prostate brachytherapy (PPB) (4–6), a TRUS-guided procedure, involves placement of radioactive sources into the prostate through the transperineal approach. Implanted sources are imaged intraoperatively with TRUS and also frequently by fluoroscopy (7). Postoperative evaluation of the procedure includes CT scanning for purposes of determining radiation dosimetry. The variation in TRUS volume measurements and CT measurements before and after implantation has been described previously (8,9). Dubois et al (10) and Lee et al (11) determined that interobserver and intraobserver variability in prostate contouring by CT can skew postoperative assessment. With TRUS, prostate borders are identified with greater reproducibility (12), but all the implanted seeds are not accurately identified (13).

Urethral imaging can be used to visualize the prostate as a potential alternative to the conventional imaging modalities of TRUS, fluoroscopy, and CT. Examples of the utility of urethral imaging include the work by Holmes et al (3), which suggested that TUUS can be used to identify the majority of radioactive sources in PPB and provide adequate images for delineation of the prostate boundary. That investigation of TUUS used a longitudinal ultrasonographic catheter originally designed for use in cardiac applications (14). Endourethral MRI has also been used to examine the prostate (15,16). Validation studies included phantom and human work. Atalar (17) demonstrated the use of urethral MRI for guiding radiofrequency ablation in canines.

To build a custom urethral imaging device, it is necessary to accurately characterize prostate anatomy and to design devices according to the expected shape of the prostate and urethra, but there are few published data characterizing this anatomy. Early work on the subject

focused on exploring the functional anatomy of the prostate (18). At the time, there were few *in vivo* methods for assessing prostatic morphology. Instead, cadaveric and prostatectomy specimens were analyzed. Other investigators have determined prostate volume from a large cohort of patients; however, this work was limited to a volumetric rather than a morphologic analysis (7). Interest has been renewed in the shape variation of the prostate to improve predictive models for dosimetric analysis in radiotherapy (19,20). However, these methods do not address the conformation of adjacent tissues, such as the urethra, and the radiation dose to them. In addition to providing more advanced models of the anatomy for therapy planning, shape models can be used to design custom imaging devices. Specifically, the size, shape, and overall extent of the prostate and urethra provide essential information for the specification of a urethral-based device such as a TUUS or catheter-based MRI device (21).

Materials and Methods

The Institutional Review Board at our institution approved this study. To characterize the dimensionality and shape of the human prostate, automated image-processing tools were used to retrospectively evaluate CT data sets from 191 patients after PPB. All implants were performed with I-125 seeds either with loose seeds, or combined with stranded seeds. Clinical features included clinical stage (T1c, 77%; T2a/b, 22%; T3b, 0.5%); prostate-specific antigen values before therapy (mean, 6.6; range, 0.7–34.1); and Gleason score (5, 3%; 6, 83%; 7, 15%). Standard clinical evaluation of PPB at our institution includes a pelvic CT scan for dosimetric evaluation, usually on the same day as the procedure. CT scanners from 2 different manufacturers were used to obtain data: a PQ 6000 (Picker International, Inc; Cleveland, Ohio, United States) and a Lightspeed RT (GE Healthcare; Waukesha, Wisconsin, United States). The in-plane resolution of both scanners is $(0.35 \text{ mm})^2$, with a slice thickness of 3.0 mm for the Picker scanner (Picker International, Inc) and 2.5 mm for the GE scanner (GE Healthcare). CT scanners undergo monthly quality assurance consistent with AAPM Radiation Therapy Committee Task Group Report No. 66 (22), and include maintaining accuracy of spatial resolution within $\pm 1 \text{ mm}$. The current phantom used in CT quality assurance is the CatPhan^{TM} (The Phantom Laboratory, Salem, NY) and software is CT AutoQA^{TM} (IrisQA, Frederick, MD). The CT data were imported into VariSeed software, Version 7.0 (Varian Medical Systems, Inc; Palo Alto, California, United States) for calculating radiation dosimetry to the tissue.

Using the VariSeed software, the attending physician manually segmented relevant anatomical structures, which included the prostate, rectum, bladder, and urethra. Prostate brachytherapy seeds were identified and segmented automatically. After contouring on clinical workstations, the intensity data and corresponding anatomical contours were exported as DICOM-RT data sets for further analysis. Numerical preprocessing algorithms (23) were used to generate look-up tables for the distance of every pixel to the surface of the rectum and urethra. The distance look-up tables were used to calculate two specific metrics: prostate volume as a function of distance and mean distances from seeds to the defined anatomical locations. Additional data were collected on the size and shape of the prostatic urethra, including urethra length and curvature based on the presence of a 14F indwelling Foley catheter.

The data processing methods were automated with a C-callable application programmer interface developed in the Biomedical Imaging Resource at Mayo Clinic (Rochester, Minnesota) (24). Volumetric interpolation was applied to account for anisotropic data acquisition. The linear dimensions of each prostate and prostate volume were calculated. The minimum and maximum extent of the prostatic urethra in each of the three orthogonal directions was determined. For the analysis across patients, the length of the prostatic urethra was normalized by the anterior-posterior (AP) length of the prostate. The bend in the prostatic urethra was calculated from the centerline of the urethra. Because there is little left-right variation, the centerline calculation was projected onto the AP–superior-inferior (SI) plane. As with previously published methods (18), the bend in the urethra was measured as the single angle generated by use of the end points of the prostatic urethra and the point of maximal deviation from the straight line connecting the end points.

Cumulative volume-distance plots were generated. For each patient, the normalized prostate volume was plotted as a function of radial distance from the surface of the urethra and rectum. In addition, mean (standard deviation) plots were generated. The points were also calculated to represent the corresponding distances at which 100% of the prostate volume was contained. These data provided information about the minimum and maximum operating range necessary for both a transrectal and a transurethral probe. Similar plots were generated for the seed-distance data. A scatter plot was generated to show the variability of seed distance from the urethra and rectum. To evaluate the shape of the urethra, the law of cosines was used to determine the bending angle. Histograms of the bending angle and location of the bend along the prostate were generated. All statistical comparisons were conducted using a paired *t* test.

Results

Figure 1 shows the measurements for the analysis. The mean prostate volume in this cohort of brachytherapy patients was 49 cm³ (range, 22–106 cm³). Mean prostate length was 4.5 cm (range, 3.1–6.0 cm). The entire volume of each prostate was encompassed within a mean (standard deviation) radial distance of 2.9 (0.4) cm (range, 2.0–3.7 cm) from the surface of the urethra, whereas from the surface of the rectum, the mean distance was 4.6 (0.6) cm (range, 3.4–5.9 cm) (*P* < .001). Figure 2 shows the mean (standard deviation) curve for the prostate volume as a function of distance. In addition, a plot was generated for the largest and smallest prostate. The mean distance (pooled from all patients) from each seed to the urethra was 1.6 (0.9) cm (range, 0.5–1.9 cm) and to the rectum, 2.3 (1.4) cm (range, 0.8–3.2 cm) (*P* < .001). A seed-distance cumulative histogram is shown in Figure 3 along with a scatter plot showing the seed distance from both the rectum and the urethra. When the seed-distance measurement was evaluated for each patient, the distance from the individual seeds to the urethra was significantly closer (*P* < .05) than the distance from the seeds to the rectum in 188 of 191 cases. Since a portion of the cases were performed using loose seeds and local migration occurred, a small fraction of seeds were found to lie more than 6 cm from the rectum.

From the patient data, the mean curvilinear prostatic urethra length was 4.5 (0.7) cm (range, 3.0–5.9 cm), which is nearly identical to the mean SI length of the prostates. Further analysis

of individual cases suggested that the curvilinear prostatic urethra length was within 0.5 cm of the prostatic length 81% of the time. From the urethra bend data, it was determined that the mean (standard deviation) angle bend in the patient data set was 29.0° (12.2°). The mean location of the bend in the urethra was at 68% of the length of the prostate from the urethral entry point proximal to the bladder neck. Figure 4 shows the distribution of bend values for the analyzed patient population.

Discussion

We have generated unique data on the urethra-seed and rectum-seed distances in 191 I-125 prostate brachytherapy cases along with detailed prostate morphologic data. These data demonstrate that the average distance from the urethra to points of seed placement is substantially less than the average distance to the rectum. While this fact may seem obvious to brachytherapists, these results are quantitative in nature and, thus, of additional utility. Specifically, these data are relevant in considering the design and operating characteristics of intraluminal devices that image from either the rectum or the urethra.

It should be evident that the specific trajectory of the prostatic urethra may have a dramatic effect on the design of a urethral imaging device. With ultrasonography, the imaging field of view (FOV) is directly related to the frequency, aperture dimensions, and other features of the imaging device. The frequency of the imaging device is directly related to the image resolution. A higher-frequency probe can provide higher-resolution images, but at the cost of tissue penetration.

If the urethral trajectory were more proximal to the rectum than is evident from these data, the benefits of a urethral device would potentially be limited. Under such a condition, there would be only a small change in the imaging FOV. Accordingly, there would therefore be only a marginal benefit in the fidelity of the device. If the trajectory is very distal to the rectum, there is also limited benefit to a urethral imaging device. However, such a circumstance would be well-suited for combined rectum-urethra imaging, in which the two devices would be used in a complementary manner for improved imaging. Since the trajectory of the urethra is essentially through the middle of the prostate, the urethral imaging device is better suited to high-resolution ultrasonographic imaging because the required FOV is approximately only one-half of the prostate diameter. The volume-distance plots confirm the third scenario. On average, all the points within the prostate were approximately one-half the distance to the urethra compared with the rectum. Accordingly, a custom urethral imaging device could be designed to image a smaller FOV in terms of depth of penetration while still being robust to anatomical variations among patients.

The seed data provide similar results. On average, seeds are closer to the urethra than to the rectum. This is consistent with the general brachytherapy procedure guidelines in which the goal is to provide a uniform dose to the entire prostate, although there is preferential peripheral loading to avoid overdosing the urethra (25). The scatter plot highlights less variation in the seed distance locations from the urethra than from the rectum. This observation provides added support for a custom urethral imaging device with narrower margins of operation compared with a device imaging from the rectum.

The observed prostatic urethra bend is consistent with previously published results by McNeal (18); however, in contrast to previous work, the large number of complete data sets used in the present study allows for more advanced characterization of the bend. Specifically, the distribution of bending angles can be calculated to extrapolate population variation. A similar assessment can be made for the location of the bend within the prostate. Given the bending angle and the location of the bend in relation to the length of the prostate, a reasonable model of the prostatic urethra can be generated.

According to the presented data, a custom urethral imaging device must be able to image at a distance of 4 cm. In contrast, a transrectal device requires an imaging field with a depth of 6 to 8 cm. In the case of ultrasonographic imaging, the reduced FOV with TUUS would result in up to a 2-fold improvement in resolution because the imaging frequency could be as great as 10 to 20 MHz, which is nearly double that of the operating frequency of typical TRUS probes used for PPB (26). It would be beneficial to image the entire length of a prostate during a single image acquisition. Accordingly, the lateral FOV of a catheter imaging device should be 5 to 6 cm, corresponding to the maximum length of a prostate. Because this may be challenging to implement, a tracked catheter system could also be used to acquire multiple overlapped regions of data, although a single large-FOV device would be easier to work with. If possible, the urethral bend should be considered in the design of a catheter imaging device. As with many instruments, such as a flexible cystoscope, a flexible probe may be preferred if construction is feasible.

A limitation of this study is that the CT data were obtained after PPB. It is widely recognized that the prostate swells as a result of the trauma associated with PPB. Previously published work (27,28) showed that edema may persist for a month or more after PPB. Therefore, the measurements in the present study are likely larger than would be expected from a cohort of patients who have not undergone invasive therapy. However, the application for a urethral imaging device is specifically for patients undergoing prostate brachytherapy and other minimally invasive therapies, so the measurements obtained can be assumed to be appropriate for the given use. Another possible limitation of this study is the quality of the prostate contouring process. Some variation occurs among human experts for prostate segmentation from CT scans, often referred to as interobserver variability(9); however, this is currently the standard of care for post-procedural dosimetry, so it is an acceptable approach for estimating the size and shape of the prostate and associated tissues. Similarly, the CT slice thickness of 2.5 and 3.0 mm is associated with uncertainty and, thus, a limitation in the measurement precision of prostate length. Importantly, CT imaging provides comprehensive and robust seed detection. Finally, the presence of the Foley catheter may have had some influence on the orientation of the prostate and urethra, yet the presence of a catheter is common both during the procedure and in postimplant imaging, and may mimic the presence of an intraluminal measurement device such as a TUUS probe.

Conclusions

Analysis of CT data sets from 191 patients who underwent PPB yielded information on prostate and urethra volume and shape. After PPB, mean prostate volume in the cohort was 49 cm³ (range, 22–106 cm³). Mean prostate length was 4.5 cm. The mean curvilinear length

of the prostatic urethra was 4.5 cm. The mean (standard deviation) prostatic urethra bend was 29.0° (12.2°). The mean surface distance from the prostate to the urethra was 2.9 cm and from the prostate to the rectum, 4.6 cm ($p < .001$, paired t test). The mean seed-to-urethra distance was 1.6 cm, and the mean seed-to-rectum distance was 2.3 cm ($p < .001$). In the largest prostate, the mean seed-to-urethra distance was 3.9 cm and the mean seed-to-rectum distance was 6.0 cm. A urethral imaging device should have a 6-cm imaging FOV to image all the prostates in this series in a single image. A custom urethral imaging device must be able to image at a distance of 4 cm. A custom device could be useful in minimally invasive prostate procedures, including prostate brachytherapy, cryotherapy, thermal therapy, and biopsy guidance.

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Abbreviations

AAPM	American Association of Physicists in Medicine
AP	anterior-posterior
CT	computed tomography
FOV	field of view
MRI	magnetic resonance imaging
PPB	permanent prostate brachytherapy
SI	superior-inferior
TRUS	transrectal ultrasonography
TUUS	transurethral ultrasonography

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Figure 1. Computed Tomographic Measurements. All measurements were obtained automatically from the manually contoured data sets.

Figure 2.

Percentage of Prostate Volume Within Given Distances to the Urethra and the Rectum.

These plots were used to characterize the spatial extent of the prostate in relation to the urethra and rectum. A, cumulative volume-distance plots are shown for the smallest and largest prostates. All of the largest prostate is closer to the urethra than all of the smallest prostate is to the rectum. (Adapted from Holmes DR, Davis BJ, Goulet CC, Wilson TM, Mynderse LA, Herman MG, et al. Shape characterization of the prostate and urethra applicable to the design of a trans-urethral ultrasound imaging probe for prostate brachytherapy guidance [abstract]. *Int J Radiat Oncol Biol Phys*. 2005 Oct 1;63[2 Suppl 1]:S548–9. Used with permission.) B, Mean percentage of prostate volume is shown in relation to distances to the urethra and the rectum. Broken lines indicate standard deviation of the mean.

Figure 3.

Distances Between Seeds and Either the Rectum or the Urethra. A, Cumulative histogram shows that the seeds were nearly 2 times closer to the urethra than to the rectum. (Adapted from Holmes DR, Davis BJ, Goulet CC, Wilson TM, Mynderse LA, Herman MG, et al. Shape characterization of the prostate and urethra applicable to the design of a trans-urethral ultrasound imaging probe for prostate brachytherapy guidance [abstract]. *Int J Radiat Oncol Biol Phys.* 2005 Oct 1;63[2 Suppl 1]:S548–9. Used with permission.) B, Scatter plot shows all seed locations in all patients and the mean seed location for each patient. The outliers, particularly beyond 6 cm, correspond to loose seeds that tracked to the perineum or were misplaced in the bladder.

Figure 4. Histogram of Urethra Bend Angle. The mean angle of the bend was 29°. The mean location of the bend in the urethra was at 68% of the length of the prostate from the bladder neck entry point.