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Prostate Mechanical Imaging: A New Method For Prostate Assessment

Robert E Weiss^a, Vladimir Egorov^b, Suren Ayrapetyan^b, Noun Sarvazyan^b, and Armen Sarvazyan^{b,*}

^a*Division of Urology, Department of Surgery, Robert Wood Johnson Medical School/University of Medicine and Dentistry of New Jersey, New Brunswick, New Jersey (REW)*

^b*BARTANN Laboratories, West Trenton, New Jersey*

Abstract

Objectives—To evaluate the ability of Prostate Mechanical Imaging (PMI) technology to provide an objective and reproducible image and to assess the prostate nodularity.

Methods—The PMI device developed by Artann Laboratories was evaluated in a pilot clinical study. For the 168 patients (ages 44 to 94) presented to an urologist for prostate evaluation, PMI-produced images and assessment of prostate size, shape, consistency/hardness, mobility, nodularity, and was compared with digital rectal examination (DRE) findings. The PMI and DRE results were further tested for correlation against a transrectal ultrasound of the prostate (TRUS) guided biopsy for a sub-group of 21 patients with an elevated PSA level.

Results—In 84% of the cases the PMI device was able to reconstruct 3-D and 2-D cross-sectional images of the prostate. The PMI System and DRE pre-tests were able to determine malignant nodules in 10 and 6 patients, respectively, of the 13 patients with biopsy-confirmed malignant inclusions. The PMI System findings were consistent with all 8 biopsy negative cases, while the DRE had 1 abnormal reading for this group. The correlation between PMI and DRE detection of palpable nodularity was 81%, as indicated by the area under the receiver operating characteristic (ROC) curve. Estimates of the prostate size provided by PMI and DRE were found to be statistically significantly correlated.

Conclusions—The PMI has the potential to enable a physician to obtain, examine and store a three dimensional image of the prostate based on mechanical and geometrical characteristics of the gland and its internal structures.

Keywords

prostate imaging; mechanical imaging; tissue elasticity; elastography; prostate cancer

Introduction

A surge in prostate cancer screenings by prostate specific antigen (PSA) widely adopted in the early 1990s resulted in a 49% increase in prostate cancer detection¹ that lead to a new challenge of managing prostate cancer: detection of the clinically significant disease and determination

* Correspondence: Armen Sarvazyan, 1459 Lower Ferry Road, West Trenton, NJ 08618; Phone (609) 883 0100; Fax: (609) 858 5233; E-mail: artann@artannlabs.com.

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of the individualized treatment therapy²⁻⁴. Most men with an elevated level of PSA have a nonpalpable clinically localized disease, detected approximately 10 years ahead of the symptomatic history, that otherwise would not ever be manifested in approximately 30% to 50% of the cases⁵⁻⁷. All current screening methods for prostate cancer have their limitations. The highest sensitivity, specificity, and positive predictive value are reported for the PSA at 72.1%, 93.2% and 25.1%, respectively⁸. Yet, as many as 43% of prostate cancer patients have normal PSA levels⁹⁻¹¹. A digital rectal examination (DRE) allows a physician to palpate the gland and is routinely integrated into the urological evaluation. A DRE can potentially access tumors above stage T1 in the posterior and lateral aspects of the prostate gland that constitute about 65% to 75% of the detected cancers. DRE effectiveness, however, is limited by its highly subjective nature and dependence on the examiner's training, experience, and ability to interpret the results. Despite the low 5% to 30% positive predictive value of the DRE¹²⁻¹⁶, a 26% increase in the detection of prostate cancer was reported when PSA testing was supplemented with manual palpation¹².

The clinical application of a Prostate Mechanical Imaging (PMI) technique for prostate assessment was examined in this study. PMI technology is based on the visualization of internal structures and dimensions of the prostate by measuring mechanical stress patterns on the gland surface with pressure sensor arrays¹⁷⁻²⁰. Temporal and spatial changes in the stress pattern provide information on the hardness of the prostate. Evaluation of tissue hardness (shear elasticity modulus) by various elasticity imaging techniques have demonstrated that the elastic properties of tissues could potentially be used to differentiate between normal and diseased tissues and characterize inclusions, such as benign or malignant²¹⁻²⁴. Measurements of excised prostate specimens demonstrated that normal prostate tissue has a lower modulus value than the prostate cancer tissue, yet higher than a modulus of benign prostatic hyperplasia²⁵. In essence, the PMI performs an electronic palpation that captures the subjective sense of touch of the DRE, but with the additional benefits of reconstructing and recording an image and a higher sensitivity.

Materials and Methods

PMI System

The PMI system (Artann Laboratories, NJ) consists of a transrectal probe shown on Figure 1 with two separate pressure sensor arrays (Pressure Profile Systems, CA) and an orientation sensor (Honeywell, NJ), a data acquisition and processing unit, and a laptop computer. The first pressure sensor array installed on the head of the probe collects a sequence of pressure patterns while the probe is pressed against the prostate. The obtained data are translated into 2-D and 3-D prostate images through a complex temporal and spatial filtering and subsequent signal processing²⁶. The second sensor array located on the shaft of the probe measures the forces applied on the sphincter and tracks the location of the probe head relative to the sphincter. The 3-D orientation sensor located in the handle of the probe provides data on the relationship between acquired stress patterns and the position of the probe.

Study protocol

168 men were enrolled in the study. A standard DRE was performed by a single attending urologist. Results were recorded using a DRE chart, specifically designed for the study. For the PMI examination, a patient was asked to place his chest on a table and to bend at a 90-degree angle at his waist. The rectum did not need to be evacuated prior to the examination. A lubricated probe covered with a disposable sheath was inserted into the rectum with the sensor surface held downward. Scanning began by collecting data to establish an image of the sphincter as a reference point. The probe was inserted further until the prostate was visualized on the computer screen. The prostate scan was performed through a set of multiple

compressions. The examiner was able to observe and inspect, in real-time, two orthogonal cross-sections of the prostate with the relative location of the probe head pressure sensitive area marked in both projections. The PMI scan took approximately 40 to 60 seconds and the collected data were saved in a digital format. After each examination, the patient was given a questionnaire to ascertain the overall comfort level of the procedure. Transrectal ultrasound of the prostate (TRUS) images and biopsy data were obtained for those patients who were undergoing TRUS-guided biopsy.

Statistical analysis

Statistical assessment of the clinical data was performed using the MATLAB 6.5 (MathWorks, MA). The PMI data were divided into 3 samples corresponding to the prostate size (small, medium, large) and 2 samples of prostate nodularity (no nodule, nodule) as determined by the DRE. The Jarque-Bera test was utilized to evaluate the hypothesis that the sample has a normal distribution with an unspecified mean and variance, while a t-test was applied to compare the means of these samples. A receiver operating characteristic (ROC) plot provided an evaluation of the accuracy of the PMI System in finding palpable lesions that were identified by the DRE.

Results

Population characteristics

The mean patient age was 69 (ranging from 44 to 94) with a racial distribution of 84% White, 6% African-American, 8% Asian and 2% others. As documented by the DRE, prostate size distribution was 35% for small, 53% for medium, and 12% for large. In 17% of patients, the DRE detected nodularity or an induration. The patient's appraisal of the procedure comfort revealed that 46% of the respondents described the sensation of the probe to be similar to that felt during a DRE; 31% noted more discomfort caused by PMI, while 23% thought the DRE was more uncomfortable.

PMI Data Quality

In 84% of the cases (141 patients) the PMI provided data sufficient for quantitative assessment and image reconstruction of the prostate. Four potential causes of the 16% failure became apparent: anatomical limitations such as position of the prostate relative to sphincter and/or bladder (5%); insufficient pressure applied (5%); excessive noise from sensors (4%); and inability of the examiner to locate the prostate upon insertion of the probe (2%). It was found that patient's age or extended duration of the exam did not affect the quality of data, or capability of the system to attain data or to produce an image of the prostate.

Prostate Size

Prostate size was calculated directly from the normalized 2-D or 3-D PMI images. The PMI data were categorized by the DRE estimated volume of the prostate as small, medium and large. A box plot analysis, a graphical equivalent of t-test, demonstrated the linear correlation of the PMI and DRE assessments of the prostate size.

Prostate Nodularity

The ROC analysis plot, Figure 2, evaluated the ability of the PMI to reveal DRE palpable nodules by using a DRE detected nodule to indicate a true positive and the absence as a true negative. The area under the ROC curve was calculated to be 81%, with a 95% confidence interval from 74% to 88%. The subgroup of the study was referred for further TRUS-guided biopsy testing due to the patients having an elevated PSA level of above 4.0 ng/mL, an abnormal DRE finding, or combination of age or family prostate cancer history factors. For 13 of the 21 patient subgroup (PSA levels ranging from 1.0 to 26.7 ng/ml) a biopsy confirmed the presence

of cancerous nodules. The PMI examination confirmed the biopsy results for 10 of the 13 cancer patients while the DRE identified only 6 of the 13. The 8 remaining cases (PSA levels ranging from 4.4 to 13.6 ng/ml) were defined by the TRUS guided biopsy as non-cancerous in the prostate. The PMI System depicted the 8 normal images of the prostate as the DRE detected 7 normal and 1 suspicious reading.

Prostate Imaging

The PMI software provides a real time examination mode and a summary mode. The examination mode was used to guide the operator through the exam and provides 2-D pressure response patterns from both sensor arrays. In the summary mode, an interactive 3-D reconstructed image was presented and measurements of several prostate characteristics were displayed. Figure 3 depicts two characteristic examples of normal and abnormal PMI cases.

Comment

In this study, the first systematic clinical evaluation of the PMI system was conducted. Sufficient quality of the data is necessary for adequate prostate image reconstruction as was demonstrated on models realistically representing a wide range of geometrical and mechanical parameters of normal and diseased prostates²⁶. However, clinical data are highly dependent on a number of factors including prostate mobility, individual anatomical variations in the pelvic region, incorrect manipulation of the probe by an operator, such as stretching the sphincter, and variations in the patient's position. The successful PMI imaging obtained in 84% of the examined cases is substantially high for a first systematic clinical evaluation of a new imaging system. Yet, observed hindrances of an individual's anatomical limitation and an examiner's ability to exert sufficient pressure could be potentially mitigated by certain modifications in the PMI probe design.

The PMI system provides several levels of diagnostic information that include a 3-D reconstruction of the prostate and its internal structures and a series of 2-D tissue hardness images. The system also provides a set of quantitative parameters, such as the prostate size (volume), integral hardness and prostate nodularity, lobular symmetry, mobility, and presence of the medium groove. Among these characteristics, prostate size and nodularity were directly compared to the DRE findings in this study. The PMI size measurements were in close agreement with DRE estimates, indicating the possibility to use the PMI for quantitative assessment of the prostate size. More studies will be needed to determine the accuracy of the PMI provided size measurement.

We found that the PMI sensitivity and specificity for the DRE palpated nodules was 75% and 68%, respectively. These relatively low values could be attributed to a small number of patients with DRE detected nodularity in the prostate and, more importantly, the low sensitivity of manual palpation in detecting hard inclusions²⁰. The comparison between the DRE and PMI in the subset of 21 patients classified as biopsy-defined disease, gave an insight into the potential of the PMI technology. Overall, the PMI System imaged 10 of the 13 malignant nodules and was consistent with all 8 biopsy-negative cases. For the same group, the DRE had identified only 6 of the 13 cancer-positive cases and produced 1 false-positive result in the 8 non-cancerous cases. We found that in each of the three "missed" cancers, an insufficient level of pressure had been exerted by the PMI probe during examination. Another reason for not detecting a nodule could be due to the small size or its location within a gland, since the imaging capability of the PMI device declines with distance from the palpated surface of the prostate.

In light of the mounting evidence of the over-diagnosis and over-treatment of patients with indolent and slow growing prostate cancer, active surveillance emerges as a new pragmatic approach that provides selective intervention based upon an individual's defined need basis

27-30. Since all of the curative treatments are associated with major complications, there is a challenge to differentiate among patients who would benefit from the radical therapy and those who could safely opt to postpone such treatment. Visual and quantitative determination of changes of the mechanical properties of prostate tissue provided by the PMI could augment PSA and biopsy results in the characterization of the biologic phenotype of the cancer that is necessary for the prognosis of the individual disease progression. Thus, application of the PMI imaging for visualization, recording, and tracking of the physical growth of the prostate nodule may significantly add to the technology diagnostic potential.

Conclusion

Results of this clinical study demonstrate that Prostate Mechanical Imaging is an objective and quantitative method for assessment of several mechanical and geometrical parameters of the prostate. The PMI device has the potential to document prostate nodularity by producing three dimensional images of the gland and its internal structures based on their respective hardness. Larger studies will be needed with the TRUS and biopsy controls to reveal full diagnostic potential of the PMI in detection of prostate cancer.

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Figure 1.

The PMI probe is equipped with two pressure sensor arrays installed on the probe head for prostate imaging (1), and on the probe shaft for sphincter imaging and positioning of the probe (2), and (3) an orientation system integrated in the probe handle.

Figure 2.
ROC curve for the PMI detected prostate nodularity vs. abnormal DRE.

Figure 3.

PMI examination results for normal and pathology cases. Each examination window is composed of three panels: 2D orthogonal cross-sections of prostate in frontal (upper left) and transversal images (lower left), and a 3-D reconstruction of the prostate (right panel). Case 1: 63 years old patient, PSA 4.2, DRE normal, PMI image presents a prostate with characteristic symmetrical distribution of hardness in right and left lobes of the gland and with pronounced medium groove. Case 2: 61 years old patient, PSA 6.4, both DRE and PMI detected single nodule in the left lobe. TRUS-guided biopsy identified in left base prostatic adenocarcinoma with Gleason score 6.