Application of vibro-acoustography in prostate tissue imaging

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Purpose: To evaluate the potential of the imaging modality vibro-acoustography (VA) for imaging of the prostate.

Methods: Excised cadaver prostate specimens were embedded in tissue mimicking gel to simulate the properties of surrounding soft tissues. The samples were imaged at various depths using a laboratory prototyped VA imaging system. The recorded signals were used for offline processing and image reconstruction. In a selected subgroup of tissue samples, conventional ultrasound (B-mode) and x-ray imaging were performed for further analysis, evaluation, and validation of the VA images.

Results: The imaging results of prostate tissue samples indicate the capability of VA imaging to detect prostatic nodules and lesions. In the prostate sample with an adenocarcinoma, the lesion appears with a clear contrast with respect to its surrounding tissue. The VA images could also identify the presence of calcifications deep inside the prostate tissue. Further, quantifications of the imaging results demonstrate that VA imaging has higher sensitivity to detect the calcifications compared to conventional ultrasound imaging. VA is also capable of visualizing prostatic tissue structures and in some cases can identify the anatomical zones. More specifically, the observed higher texture level in peripheral zones demonstrates the ability of VA to differentiate between prostatic anatomical zones.

Conclusions: Imaging results of *ex vivo* prostate tissues, reveals the potency of VA as a promising tool to detect abnormalities, delineate tissue structures and anatomical zones, and locate calcifications. The results of this pilot study suggest that *in vivo* VA imaging of the prostate may be of clinical utility.

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I. INTRODUCTION

Prostate cancer imaging is the focus of intense research with increasing clinical interest. The main reason for this growing interest is the increasing incidence of prostate cancer in industrialized countries, although mortality rates from prostate cancer are declining in those countries.¹⁻⁴ Currently, prostate cancer is the second most common cause of cancer-related death in men in the United States.⁵ The anatomical distribution of prostatic diseases plays an important role in their clinical evaluation and, thus, method of treatment.⁶⁻¹⁰ Therefore, an ideal diagnostic tool must provide clinicians with anatomical distribution of prostatic diseases through enhanced imaging of the prostate and periprostatic structures.⁷

The optimal imaging approach in prostate cancer diagnosis continues to evolve.¹¹⁻¹³ Recent advances in ultrasound (US), computed tomography (CT), and magnetic resonance (MR) imaging technologies have led to a growing interest in enhancing these modalities for prostate imaging.^{12,13} However, CT scans deal with issues related to radiation and its dose and MR imaging is associated with significant cost.¹⁴ These imaging modalities are not frequently used for prostate cancer screening, but are frequently used in prostate cancer staging, including identification of regional disease and in staging locally invasive prostate cancers.¹⁵⁻¹⁸ Transrectal ultrasound (TRUS)-guided prostate biopsy is the preferred method for prostate cancer diagnosis, particularly as a means of image guidance for biopsy. However, major limitations of TRUS are

its low sensitivity (60%–85%) and even lower specificity for prostate cancer detection, mostly because of the insufficient and inconsistent contrast between echogenicity of cancerous and benign prostate lesions.^{4,19}

For the past two decades, imaging tissue stiffness has been an area of active investigation in prostate imaging.^{20,21} US elastography^{22–26} and magnetic resonance elastography^{27–29} are examples of such efforts. It is generally believed that the pathological changes in biological tissues are highly correlated with the change in tissue stiffness.^{30,31} Therefore, elastography techniques have been widely studied for cancer detection³¹ including prostate cancer.²⁸ US elastography^{31,32} has been studied for prostate cancer diagnosis.^{33,34} However, considerable false positive and false negative results^{34,35} have been reported for US elastography of the prostate.^{36,37}

Current limitations of existing prostate imaging modalities for prostate disease diagnosis justify further investigation and development of a suitable imaging technique. Ideally, an improved method must have the following characteristics: capable of detecting and characterizing lesions with high sensitivity and specificity, provide anatomical information of different prostatic zones, be noninvasive, and cost effective.

Vibro-acoustography (VA) has been introduced as a novel imaging technique, based on the dynamic radiation force of ultrasound.^{38,39} Unlike other radiation force techniques, VA imaging utilizes two confocal ultrasound beams at slightly different frequencies in the form of relatively long tone bursts in order to generate an amplitude-modulated ultrasound field at the focal region. This modulated ultrasound radiation force oscillates at a low frequency equal to the difference between the two primary ultrasound frequencies, which vibrates a highly localized region of tissue.^{38,39} As a result, the excited region of tissue generates an acoustic field (acoustic emissions) at the vibration frequency. These acoustic waves can be detected by a sensitive hydrophone and then used to reconstruct the VA images. As a result, VA images can provide not only information about ultrasound properties of the object but also indicate the dynamic behavior of the object at low frequencies, which means that VA offers information that is not available through conventional US imaging.³⁹

The potential abilities of VA have been demonstrated in various diagnostic applications, including detection of calcium deposits on heart valves,⁴⁰ imaging human vessels,⁴¹ *in vivo* imaging of animal arteries,⁴² imaging breast tissue,^{39,43,44} liver tissue,⁴⁵ bone,⁴⁶ and more recently, *in vivo* imaging of human breast.^{47,48} We have recently evaluated the application of VA imaging to identify prostate brachytherapy seeds⁴⁹ and to monitor prostate cryotherapy.⁵⁰ A review of VA and its potential applications can be found in Ref. 51. In this study, we evaluate the capabilities of VA imaging to detect prostatic lesions and calcifications, as well as to provide high contrast images of different anatomical structures within excised human prostate tissue samples.

II. MATERIALS AND METHODS

A custom-built VA system was developed to image excised cadaver prostate samples. The VA images were reconstructed

FIG. 1. (a) Diagram of the prototype VA system for prostate imaging. The dual-beam probe is connected to a motorized 3D scanning axes system (not shown in this diagram) in order to image different planes (X-Y plane) at different focal depths (Z). The hydrophone signal is filtered with a bandpass filter (typically 40–60 kHz) and stored by a computer (not shown in this diagram) for postprocessing and image reconstructions. (b) Photographs of the experimental setup where the excised prostate tissue embedded in a gel block are indicated by (G). The hydrophone and the confocal transducer are indicated by (H) and (T), respectively.

and analyzed through postprocessing procedures. The tissue samples were also imaged using x-ray and B-Mode US imaging systems (GE Vivid7, equipped with a 7L probe operating at 7 MHz center frequency) for comparison and validation purposes.

II.A. VA system

Figure 1 represents the block diagram and a photograph of the experimental VA prototype system used in our *ex vivo* prostate imaging studies. A dual-element ultrasound probe was used to perform dual frequency, confocal ultrasound excitation. The details of the custom-built VA excitation probe utilized in this study are described in Refs. 38 and 39. Briefly, the dual-element confocal ultrasound transducer consisted of a center disk surrounded by a ring shaped piezoelectric such that both elements have identical focal lengths. The focal length and aperture size of the confocal transducer are 7 and 4.5 cm, respectively. The confocal transducer elements were driven using two function generators operating at 3 MHz (center element) and $(3 + \Delta f)$ MHz (outer ring element), where Δf ranged from 40 to 60 kHz. At the focal zone, the two beams mix and generate a radiation force oscillating at the

difference frequency— $\Delta f = |f_1 - f_2|$ —to locally vibrate the tissue. The duration of ultrasound excitation at each point was set to be 100–200 μs . The acoustic emission due to the tissue vibrations was detected by a preamplified hydrophone (ITC-6050 C; ITC, Santa Barbara, CA) placed approximately 5 cm directly behind the left edge of the gel block containing the prostate tissue. The hydrophone was outside the path of ultrasound beams because if the beams impinge directly on the hydrophone surface they can cause mixing which produces an artificial acoustic signal unrelated to the object acoustic emission. The detected signal represents the object's localized dynamic response to the force exerted at the focal point.³⁹ The VA probe was mechanically scanned across the object by using computer-controlled motorized linear axes with the step size of 200 μm in both transverse (X and Y) directions (Fig. 1). In most cases, a region of interest (ROI), measured as a $5 \times 5\text{-cm}^2$ area, was scanned. Another motorized axis was utilized to precisely control the distance between the VA transducer and the object in order to change the depth of the focal plane within the object. The VA images were acquired at multiple equally distanced parallel imaging planes separated by 5 mm. All experiments were performed within a tank of degassed water. The hydrophone signal was digitized using a 12 bit digitizer, sampling analog signal at 500 kS/s and the digitized signal was stored in a computer for image reconstruction and further postprocessing purposes. Although the image is reconstructed from a low-frequency signal (at Δf), the spatial resolution of the image is determined by the focal spot size, typically in submillimeter to millimeter range, which is suitable for clinical diagnosis.

II.B. Tissue samples preparation

Seventeen whole prostate specimens were excised from human cadavers and were used to perform imaging studies under a protocol approved by the institutional review board (IRB). The first seven specimens were used to optimize the VA imaging system. These optimizations include casting samples in tissue mimicking gel blocks, adjusting Δf , scanning step size, and hydrophone location.⁵² After optimizing the system, ten tissue samples were divided into subgroups and imaged consistently to evaluate the abilities of VA in detecting prostatic lesions, calcifications, and identifying anatomical zones. Amongst these ten tissue samples, one of them had a malignant lesion. Another tissue sample contained a nodule of benign prostatic hypertrophy (or adenofibromatous hyperplasia) and the location of the lesion was marked by implanting a gold marker. These two tissue samples were imaged to evaluate the ability of VA to identify prostatic lesions. To evaluate the ability of VA to identify tissue structures and zonal anatomy of prostate tissues, three tissue samples were imaged over transverse planes. These prostate samples contained benign prostatic hyperplasia (BPH) nodules. In one of these cases the presence of a large BPH nodule, compressed the peripheral zone and made it difficult to locate it. Identified tissue structures and anatomical zones were confirmed upon histological examination by experienced urologists and

pathologists. Six tissue samples were used for evaluating the ability of VA to detect calcifications. These specimens were imaged with VA, US, and x-ray consistently. Tissue samples were fixed in 10% formaldehyde for 1 h to prevent potential contamination. Although fixing with formaldehyde may alter the stiffness of the prostate tissue,^{53–55} such changes affect both healthy and diseased areas. Hence, tissue fixation should not have a major effect on the capability of VA imaging to detect contrast between normal and diseased tissue.^{45,56} The prostate tissues were embedded in tissue mimicking gel (10% v/v, gelatin from porcine skin, 300 bloom) to simulate the *in vivo* situation where the prostate is surrounded by soft tissues. In most cases, the specimen was oriented such that the entrance of the urethra into the prostate (bladder side) was oriented superiorly and the exit of the urethra was oriented inferiorly, oriented in a roughly vertical line cranial to caudad (top to bottom). The blocks of gel in which the prostates were embedded were placed in the water tank for scanning as shown in Fig. 1. In most cases the imaging was performed on transverse planes. However, in a few cases and in order to visualize specific features (such as the results represented in Fig. 3), VA images were obtained over sagittal planes.

II.C. Histology

Upon completion of VA scanning, histological assessment was performed on a selected subgroup of tissue samples. The formaldehyde-fixed specimens were oriented for apex-to-base, anterior-to-posterior, and left-to-right microscopic evaluation. The prostate specimens were fixed in formalin for paraffin-embedding and hematoxylin-eosin slide production. The cassettes were oversized and had a thickness of 5 mm. Thus, the prostate was cut in 5-mm sections and placed into the cassettes for processing. Once a paraffin block was generated, a microtome was used to generate 4- μm -thick sections for hematoxylin-eosin staining and microscopic analysis. The hematoxylin-eosin slides were evaluated microscopically to determine the presence of prostatic tumors and other pathologies of interest, including adenofibromatous hyperplasia (benign prostatic hyperplasia), atrophy, inflammation, calcifications, and infarction.

II.D. Image reconstruction, postprocessing, and analysis

The amplitude of the recorded acoustic signal was used to reconstruct the VA images. A bandpass filter (SR650, Stanford Research Systems, Sunnyvale, CA), centered at Δf and with a bandwidth of 10 kHz was applied on recorded signals to reject the noise that might have been mixed with the acoustic emission signals. To analyze the VA images, further processing including image segmentation to identify lesion and quantitative evaluation of VA in detecting calcifications, were performed. A threshold-based segmentation procedure was utilized to demonstrate the ability of VA to identify prostatic lesions and calcifications. The potential of VA in identifying tissue structures and anatomical zones within prostate tissue was evaluated by subjective analysis of obtained VA images

FIG. 2. (a) Gray-scale VA image of the axial section of an excised prostate. The VA image clearly shows the prostate anatomy, including the urethra (arrow) and a malignant lesion with bright and coarse texture in the peripheral zone (dashed circle). (b) The colored VA image and the selected ROI for classification process. (c) The selected ROI after threshold based processing and boundary removal that identifies the lesion.

by experienced urologists and pathologists. Also, the clear appearance of tissue structures, such as the urethra, was used as a landmark to identify the anatomical structure of prostate tissues. The histology of tissue samples was also used to confirm the identified structures and anatomical zones in VA images. The textural difference between the peripheral zone and BPH nodule (in central and transitional zone) suggests the ability of VA in differentiating anatomical zones in prostate tissue. To quantitatively demonstrate the contrast in texture level of these two anatomical zones, spatial standard deviation (std) in selected ROIs within the PZ and BPH nodules were calculated and presented. All data processing codes were written in a MATLAB (Mathworks®, Natick, MA) environment.

III. RESULTS AND DISCUSSIONS

The amplitude of the signal detected by hydrophone, which corresponds to the response at each excited point, was utilized to reconstruct the VA images. Reconstructed VA images revealed several characteristics of prostatic tissues as discussed below.

III.A. Detecting prostatic lesions by VA

The VA image of a prostate specimen is shown in Fig. 2(a). While the image shows the anatomical details such as pro-

static zones and the urethra (yellow arrow), a mass lesion within the peripheral zone (red dashed circle) was clearly identified. The detected contrast is based on different mechanical properties of the lesion compared to its surrounding tissue. The pathological analysis of the tissue sample classified the lesion as a prostatic adenocarcinoma. The speckle-free appearance of the VA image makes it easier to observe the abnormalities as compared to typical conventional B-mode image. To further demonstrate the ability of the VA image to identify the lesion and its borders, an amplitude-based classifier was applied to the image. A threshold value was selected by selecting a ROI around the lesion and analyzing the distribution of amplitudes of every pixel (i.e., histogram) of the image within the selected ROI. The contrast between the lesion and surrounding tissue in the VA image appears as a distinct peak in the histogram at higher intensities belonging to the pixels associated with the lesion. The choice of an optimum threshold varies in different images depending on the contrast between the lesion and the surrounding background and also the dynamic range of the image within the selected ROI. The lesion can be clearly identified by its higher amplitude within its surrounding uniform, lower amplitude background [Fig. 2(a)]. Upon performing a threshold-based classification, both lesion and bright areas within the peripheral zone and the prostate tissue boundary were identified. Later, the tissue

FIG. 3. (a) Sagittal plane microscopic image of the whole-mount prostate (hematoxylin-eosin, $1 \times$ magnification) with a nodule from a benign prostatic hypertrophy (marked with a black ellipse). (b) and (c) The matching VA images, respectively, at 25 and 30 mm depth [field of view (FOV) = $54 \times 62 \text{ mm}^2$], detect the pathology (marked with white ellipses). The VA images were obtained on sagittal plane and the base of the prostate appears on the left and the apex appears on the right side of VA images. The FOV for VA images measures as $54 \times 62 \text{ mm}^2$. The histology image confirms the presence of the detected lesion in VA images.

boundaries, which possess high amplitude as in lesion area, were identified through a customized boundary detection algorithm (based on Prewitt's operator)⁵⁷ and separated from the areas associated with the lesion. As a result, the prostatic lesion was identified with a clear contrast compared to its surrounding tissue [Fig. 2(c)]. The values shown on colorbars indicate the amplitude of the VA signal (arbitrary unit).

Figure 3 shows the VA images [3(b) and 3(c)] of a post-mortem excised prostate. The tissue sample was excised from a patient with previous radiotherapy for prostate cancer. The VA images were obtained from two different depths of 25 and 30 mm from the tissue surface. A benign prostatic hypertrophy nodule (seen as an elongated region) was identified within the central zone with a clear contrast to its surrounding tissue. The whole-mount histology analysis of the matching section validates the detected lesion by VA images [Fig. 3(a)]. A gold marker was implanted as a landmark to indicate the lesion location. This marker appears on VA images as a bright short line, marked with an arrow in Fig. 3(b). The location of the marker can be also identified in the histology image [marked with a black arrow in Fig. 3(a)]

III.B. VA imaging to identify prostate tissue structures and anatomical zones

The internal structure of the prostate gland includes the central zone (CZ), peripheral zone (PZ), and transitional zones (TZ).^{9,58} Figure 4 depicts the VA images of two prostate tissue samples and the whole-mount radical retropubic prostatectomy by H&E microscopy of approximately the same planes. The tissue structures, such as BPH nodules, urethra, peripheral zones, and periprostatic tissue, are marked in each set of images (VA and histology). The subjective anatomical

assessment was performed by experienced pathologists and other clinicians of our team. Although matching histologic images with the VA images is associated with limitations such as the difference between the orientation of the VA imaging plane and the sectioned tissue caused by tissue deformation, a good agreement was found between VA and histological images. All VA images display the tissue structures including urethral slit and BPH nodules. The boundary between the peripheral zone and the BPH nodule could be clearly identified by VA images. The peripheral zone appears with coarse rough texture in VA images and can be differentiated from the BPH and used to define the BPH nodule boundaries. This difference in texture level is not very clear in the first tissue sample due to the presence of large calcifications (bright regions within the BPH nodule in Fig. 4(a) which affected the contrast in the VA image. However, the clear difference between the peripheral zone with coarse texture and fine texture structure of the BPH nodule can be observed in Fig. 4(c). This latter observation suggests that the VA images have the potential of delineating anatomical zones in prostate tissue.

To further demonstrate the difference between the texture of the peripheral zone and the BPH, two similar sized ROIs were selected within the peripheral zone and the BPH nodule in the VA image obtained at 20 mm depth [Fig. 4(b)]. The ROIs were selected adjacent to each other to better demonstrate the contrast in tissue structure visualized by VA. The image of the selected ROIs within the BPH and PZ are shown in Figs. 5(b) and 5(c), respectively. The ROI selected from the peripheral zone exhibits larger standard deviation corresponding to the coarse texture of the peripheral zone than that of the BPH.

It must be noted that the presence of large BPH nodules, in some sections appears to compress the peripheral. However, the clear appearance of tissue structures such as the urethra, periprostatic tissue, and tissue borders in VA images, can be useful for clinicians in the subjective assessment of anatomical zones in the prostate.

III.C. VA for detection and localization of calcifications within prostate tissue

Figure 6 shows the x-ray, B-mode US, and VA images of a prostate specimen. The x-ray image [Fig. 6(a)] indicates the presence of a round-shaped calcified lesion (yellow arrow), a large calcification (red arrow), and a cluster of microcalcifications (green arrow). The gray-scale B-mode US image can visualize the calcifications to some extent, as their greater backscattering leads to brighter visualization of calcified regions. However, the VA image [Fig. 6(c), obtained at 15 mm depth] clearly identifies the same calcified regions with a superior contrast.

To better demonstrate the capability of VA imaging in detecting and localizing calcified regions within the prostate tissue, corresponding ROIs were selected within x-ray, VA, and US images. As the calcified regions are shown with higher amplitudes in all three images, a histogram thresholding⁵⁹ was applied to all three ROIs to identify the calcifications. Similar to the threshold-based segmentation to identify the

FIG. 4. (a) and (b) Plain VA images of two prostate tissue samples, imaged over transverse planes, (c) and (d) VA images with identified tissue structures and anatomical zones landmarks, (e) and (f) matching transverse plane of sections evaluation whole-mount radical retropubic prostatectomy by H&E microscopy. The matching tissue structures and anatomy is marked in VA and histology images showing a good agreement between VA and histology images. Both VA images were acquired at the depth of 20 mm. The FOV was $50 \times 44 \text{ mm}^2$ in (a) and $50 \times 37.6 \text{ mm}^2$ in (b).

lesion in Sec. III.A, the threshold values (for each image) were selected according to an analysis of the image histogram within the selected ROI and thus can be different in different images. The postprocessed masked ROIs are shown in Figs. 6(d)–6(f). Figure 6(d) represents the calcification regions identified from the x-ray image. The amplitude-based

filtered image of the US ROI is shown in Fig. 6(e). Although the large calcified regions could be identified to some extent in this image, the cluster of microcalcifications was not detectable. Suboptimal performance of US in detecting calcification may be attributed to the presence of speckle that lowers image contrast and masks small-size calcifications.

FIG. 5. (a) VA image of a prostate sample at 15 mm depth ($\text{FOV} = 50 \times 37.6 \text{ mm}^2$); (b) and (c) Enlarged demonstration of ROIs within PZ and BPH nodule ($\text{FOV} = 6.6 \times 5.5 \text{ mm}^2$). A coarse texture structure within the PZ is clearly demonstrated. The standard deviation values for the regions within PZ and BPH nodule were calculated as 31.08 and 14.81, respectively.

Figure 6(f) represents the processed ROI within the VA image, which can identify and localize all three types of calcifications with a superior clarity compared to the US image [Fig. 6(e)] and comparable to the x-ray image [Fig. 6(d)].

To further quantify the comparison between conventional US and VA imaging in their capabilities of detecting calcifications within the prostate tissue, the imaging results (x-ray, US, and VA) for another three prostate tissue samples with calcified regions were further analyzed. All x-ray (gold-standard), US, and VA images were resized to an identical size using a cubic regression.⁶⁰ Three ROIs of identical sizes were selected around the locations where calcifications were known to be present (according to the x-ray image) and an amplitude-based thresholding technique was used to identify the calcifications in both US and VA images. The contrast-to-noise ratio (CNR) for both US and VA images was calculated through the following definition:

$$\text{CNR} = \frac{\mu_{\text{signal}} - \mu_{\text{background}}}{1/2(\mu_{\text{signal}} + \mu_{\text{background}})}, \quad (1)$$

where μ_{signal} was defined as $\frac{\sum \text{signal}}{\text{No. of signal points}}$, and “signal” represents the values for each pixel identified as calcification. The number of signal points was determined by the x-ray images. The parameter $\mu_{\text{background}} = \frac{\sum \text{background}}{\text{No. of background points}}$ was defined to represent the mean value of the signal detected in noncalcified regions within the ROI.

The detectability rate (DTR) parameter was defined to describe the detection rate of the technique in comparison to x-ray imaging, as defined by the following equation:

$$\text{DTR} = \frac{\text{No. of pixels in the image classified as “calcifications”}}{\text{No. of pixels in the “x - ray image” classified as “calcifications”}}. \quad (2)$$

FIG. 6. (a) X-ray, (b) B-mode US, and (c) VA image of the prostate tissue sample on matching imaging planes ($\text{FOV} = 40 \times 40 \text{ mm}^2$). (d)–(f) Postprocessed ROIs ($\text{FOV} = 16.5 \times 17.1 \text{ mm}^2$) within x-ray, US, and VA images, respectively, which demonstrate the superior sensitivity of VA imaging in identifying calcified lesions and microcalcifications.

FIG. 7. Comparison of CNR and DTR values for detection of calcification in VA and US imaging in six prostate tissue samples. (a) CNR and (b) DTR.

Figure 7 represents the quantified comparison between VA and US imaging modalities to identify the calcifications within the prostatic tissues. The CNR and DTR of both VA and US imaging are calculated for six prostate tissue samples, then are normalized to each parameter's maximum value, as shown in Figs. 7(a) and 7(b), respectively. The average CNR for VA and US was calculated as 0.74 and 0.24, respectively, and the average DTR for VA and US was calculated as 0.69 and 0.18, respectively. As expected, comparing the CNR and DTR parameters confirm the superiority of VA over US in detection of prostatic calcifications. US imaging does not demonstrate the ability to identify calcified regions based on the changes in the echogenicity of the calcified areas in all prostate tissue specimens.

All tissue samples utilized in this study were fixed in formaldehyde for 1 h. Although the short fixation time may lead to less tissue stiffening and thus makes our findings more realistic, it can affect our measurements. It is generally accepted that tissue fixation increases its stiffness as a result of the reaction of formaldehyde on proteins. This reaction can decrease the contrast between the lesion and stiffer regions such as calcifications and their surrounding medium. Therefore, it is reasonable to expect improved contrast in fresh tissue and for *in vivo* imaging. We speculate that tissue stiffening does not have a significant effect on the texture level of different anatomical zones. Therefore, VA can potentially identify zonal anatomy *in vivo*.

The VA signal depends on several parameters including the mechanical properties of the object. However, other parameters such as the propagation medium transfer function are also

involved in VA signal. Therefore, it cannot be readily established that the lesions always appear with larger amplitude than normal adjacent tissues. This observation is similar to findings from one of our prior studies.³⁹ However, VA is capable of visualizing the lesions through enhanced border contrast because the change in mechanical properties of the tissue at the lesion border is solely a function of the mechanical properties of the object.

We have implemented VA on a customized ultrasound scanner equipped with a transrectal ultrasound probe. We have previously reported implementation of VA on a clinical ultrasound scanner equipped with a linear array probe.⁶¹ The same system can be equipped with a transrectal probe for *in vivo* imaging of prostate tissue. The challenge for *in vivo* studies is the signal detection as the acoustic emission must pass through various intervening tissue layers and be detected by the hydrophone coupled to the perineum with ultrasound gel. However, we believe that further modifications of the system will enable VA to be utilized as a clinical tool in prostate imaging. The key advantage of this technique is that it can be implemented in a clinical ultrasound scanner without complex hardware modifications. Therefore, it can be combined with TRUS and provide more information for clinicians.

IV. SUMMARY AND CONCLUSIONS

We have investigated applications of VA in prostate imaging. These investigations are designed to specifically identify prostatic lesions, prostate tissue structures and anatomical zones, and calcified regions within the excised human prostate. Although fixing in formalin changes the mechanical properties of the excised tissue compared to *in vivo* cases, this mechanical change takes place in the entire tissue including both normal and abnormal portions. Therefore, it is reasonable to expect that the CNR of *ex vivo* samples correlates with that of *in vivo* tissue. The textural differences between the peripheral zone and the BPH nodule (in central and transitional zones), as well as the distinct appearance of calcification with respect to the surrounding tissue, are features that are expected to be similar during *in vivo* VA. Although prostatic calcifications, in the form of large calcium buildups, or microcalcifications, do not generally have clinical significance as they do in other tissues such as breast, the anatomical distribution of calcifications are clinically important. The calcifications within the transitional zone are mostly associated with benign prostatic hyperplasia. However, peripheral zone calcifications and intraluminal microcalcifications are associated with prostate carcinoma.⁶²⁻⁶⁴ Nevertheless, it should be noted that large calcifications can block ultrasound beams and thus affect the ability of VA to image deeper lesions and tissue structures behind the calcified regions.

The ability of VA to identify lesions, tissue structures, and anatomical zones can be clinically important because the types of proliferative prostatic lesions frequently differ by anatomical region.^{6,8,9} Most cancers derive from the PZ, where the greatest density of glandular structures per unit area resides. Therefore, further development of *in vivo* clinical VA

can lead to a unique and effective tool in the diagnosis of prostate diseases. The results of this study reveal the ability of VA imaging for prostate imaging and can pave the way for future studies of *in vivo* prostate imaging by VA.

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