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Characterizing the stiffness of Human Prostates using Acoustic Radiation Force

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Abstract

Acoustic Radiation Force Impulse (ARFI) imaging has been previously reported to portray normal anatomic structures and pathologies in *ex vivo* human prostates with good contrast and resolution. These findings were based on comparison with histological slides and McNeal's zonal anatomy. In ARFI images, the central zone (CZ) appears darker (smaller displacement) than other anatomic zones, and prostate cancer (PCa) is darker than normal tissue in the peripheral zone (PZ). Since displacement amplitudes in ARFI images are determined by both the underlying tissue stiffness and the amplitude of acoustic radiation force which varies with acoustic attenuation, one question that arises is: how are the relative displacements in prostate ARFI images related to the underlying prostatic tissue stiffness? In linear, isotropic elastic materials and in tissues that are relatively uniform in acoustic attenuation (e.g. liver), relative displacement in ARFI images has been shown to be correlated with underlying tissue stiffness. However, the prostate is known to be heterogeneous. Variations in acoustic attenuation of prostatic structures could confound the interpretation of ARFI images due to the associated variations in the applied acoustic radiation force. Therefore, in this study, co-registered three-dimensional (3D) ARFI datasets and quantitative shear wave elasticity imaging (SWEI) datasets were acquired in freshly excised human prostates to investigate the relationship between displacement amplitudes in ARFI prostate images and the matched reconstructed shear moduli. The lateral time-to-peak (LTTP) algorithm was applied to the SWEI data to compute the shear wave speed and reconstruct the shear moduli. Five types of prostatic tissue (PZ, CZ, transition zone (TZ) and benign prostatic hyperplasia (BPH), PCa, and atrophy) were identified, whose shear moduli were quantified to be 4.1 ± 0.8 kPa, 9.9 ± 0.9 kPa, 4.8 ± 0.6 kPa, 10.0 ± 1.0 kPa and 8.0 kPa, respectively. Linear regression was performed to compare ARFI displacement amplitudes and the inverse of the corresponding reconstructed shear moduli at multiple depths. The results indicate an inverse relation between ARFI displacement amplitude and reconstructed shear modulus at all depths. These findings support the conclusion that ARFI prostate images portray underlying tissue stiffness variations.

Keywords

Acoustic radiation force; Ultrasound; Tissue elasticity; Shear wave; Prostate

INTRODUCTION

Prostate cancer (PCa) is the most common non-cutaneous cancer and second leading cause of cancer death in men in the United States. Current diagnostic procedures use screening methods including digital rectal examination (DRE) and prostate-specific antigen (PSA) analysis, which are not specific to PCa. When suspicion arises through these mechanisms, prostate needle biopsies are performed for the final diagnosis of PCa, which depends upon the presence of adenocarcinoma in the biopsy cores. Although the needle biopsy is typically guided with transrectal ultrasound (TRUS), PCa does not, in general, have unique characteristics in B-mode images that distinguish PCa from other prostatic diseases such as benign prostatic hyperplasia (BPH) and prostatitis. This fact leads to random or systematic sampling of 6 – 12 cores in the prostate without targeting needles to suspicious regions.^{1–3} With only a small amount of prostatic tissue sampled, PCa detection rates on first-time biopsies are as low as 25–36% in over 1,000,000 prostate biopsies performed annually, and are 10–35% on repeat biopsies (cases with negative first biopsies).^{4, 5} Therefore, new imaging techniques capable of visualizing suspicious PCa regions are urgently needed to increase the diagnostic accuracy of prostate biopsy.

Pathological processes change the mechanical properties of prostatic tissue, which provides opportunities for elasticity imaging techniques to image abnormal tissue in the prostate. Several recent reports support the feasibility of using elasticity imaging methods to visualize PCa.^{6–10} Acoustic radiation force impulse (ARFI) imaging is an elasticity imaging technique, which uses remotely generated, focused acoustic beams to excite tissue and produces images of the tissue displacement response.^{11, 12} ARFI imaging has been developed to visualize pathological or thermal lesions in various organs.^{13–17} In a recent study, ARFI imaging was implemented to image excised human prostates.¹⁰ Various prostatic zonal structures and pathologies (i.e. BPH, PCa, calcification and atrophy) were clearly portrayed in ARFI images. ARFI images are made by monitoring the displacement within the region of excitation (ROE) from multiple excitations and synthesizing an image from all the locations at a given time after the push. The central zone (CZ), PCa and atrophy exhibited smaller displacement than the normal tissue in the peripheral zone (PZ) and transitional zone (TZ). In all these ARFI imaging applications, relative stiffness among different tissues was assessed based on the assumption that displacement amplitudes in ARFI images are inversely related to underlying tissue stiffness at a given acoustic radiation force (i.e. displacement = K/G, G is the shear modulus, K is a constant determined by the applied acoustic radiation force). This assumption was validated in finite element method (FEM) models that assume uniform acoustic attenuation and isotropic linear elastic media.¹⁸

Acoustic radiation force is a common phenomenon when acoustic wave propagates in attenuating media, whose amplitude is determined by the local acoustic intensity (I), acoustic attenuation (α) and speed of sound (c),¹⁹ as is shown below:

$$F = \frac{2\alpha I}{c} \quad (1)$$

In ARFI images, the applied acoustic radiation force is typically assumed to be constant at a given depth, so that the relative tissue stiffness can be evaluated. This assumption is true in relatively homogeneous organs (e.g. liver). However, with multiple anatomic zones and pathological structures, the human prostate is a complex, heterogeneous organ. Variations of acoustic attenuation in these structures can cause significant changes in the distribution of applied acoustic radiation force, and can potentially confound the interpretation of relative stiffness of structures in the ARFI images. Thus, the relationship between ARFI displacement amplitude and the underlying tissue stiffness needs to be investigated. The

mechanical properties of prostatic tissue have been characterized by multiple groups;^{20–25} yet, large discrepancies exist in the reported stiffness values. Therefore, in this paper, we are interested in answering two questions: 1) what is the stiffness of various prostatic structures as determined by radiation force methods? and 2) how are the displacement amplitudes in prostate ARFI images correlated with the underlying prostatic tissue stiffness?

There are two general approaches to quantifying tissue stiffness: static or quasi-static mechanical tests such as uni-axial compression and indentation,^{21, 26} and dynamic methods that monitor shear wave propagation.^{27–31} The first approach is impacted greatly by boundary conditions and generally cannot be used to quantify the stiffness of organs or structures inside the human body.^{21, 25, 32, 33} In the second approach, some researchers have used external vibrators to introduce shear waves into tissue.^{29, 30} However, this method is challenged by the difficulties of coupling shear excitation into deep lying organs under clinical situations. Alternatively, impulse acoustic radiation force methods overcome these problems by using remotely generated, focused acoustic beams to excite tissue; the resultant tissue displacement response creates shear waves propagating away from the ROE, which can be ultrasonically monitored to quantify the tissue stiffness. This concept, shear wave elasticity imaging (SWEI), was originally introduced by Sarvazyan,²⁷ and successfully implemented by several groups to quantify soft tissue stiffness *in vivo*.^{28, 31, 34} The similarities in implementation techniques between SWEI and ARFI imaging allow co-registered ARFI and SWEI datasets to be acquired using the same experimental setup.

In this study, matched ARFI and SWEI datasets were acquired on excised human prostates to correlate relative stiffness portrayed by displacement in ARFI prostate images with quantitative stiffness estimates. The shear moduli of the prostate tissues were reconstructed using the lateral time-to-peak (LTP) algorithm.³⁴ Five types of prostatic tissues were determined by McNeal's zonal anatomy and histology, whose shear moduli were reconstructed and compared to those reported in literature. Then, the shear moduli computed from the SWEI data were correlated with ARFI displacement in the registered regions to determine ARFI displacement is correlated with underlying tissue stiffness in the heterogeneous prostate.

METHODS

Data acquisition

This study was approved by the institutional review board (IRB) of the Duke University Medical Center. Informed patient consent was waived by the IRB as imaging was performed post-resection. A modified Siemens SONOLINE AntaresTM ultrasound scanner and a VF10–5 linear array (Siemens Healthcare, Ultrasound Business Unit, Issaquah, WA, USA) were used to acquire imaging data. The array contains 192 elements, whose dimensions are 5 mm in height and 0.2 mm in width. The lateral beam spacing is 0.15 mm. Custom ARFI and SWEI sequences were implemented, with detailed imaging parameters provided in Table 1. 4:1 parallel receive sequencing techniques were used to decrease the total number of push pulses.³⁵ In a given imaging plane, an ARFI imaging dataset (lateral span 26 mm) was acquired, followed by four adjacent SWEI datasets (lateral span 6.5 mm × 4). The relative positions of ARFI and SWEI data are shown in Figure 1b. In the SWEI sequence, the excitation pulses were placed at the right edge of the interrogated field, and the resultant shear waves propagating to the left were monitored.

Six freshly excised specimens (A – F) were collected and imaged immediately after radical prostatectomy. Figure 1a illustrates the experimental set up. During imaging, the specimen was held by a custom prostate holder and placed in an isotonic saline bath at the room temperature (24 °C). The ultrasound probe was connected to a translation stage and

positioned over the specimen. The imaging data were acquired from the posterior side of the prostate. By mechanically translating the probe in the elevational direction, co-registered three-dimensional (3D) ARFI and SWEI datasets of the prostate were acquired. The spacing between two adjacent imaging planes was 1 mm. Depending on the size of each specimen, a total of 35–50 imaging planes were acquired to interrogate the entire volume of each prostate specimen. In-phase/Quadrature (IQ) data were saved and processed offline. Since the lateral dimension of the prostate specimens was usually larger than 26 mm (the lateral field of view of ARFI images), the left and right half volumes were acquired separately, then registered and stitched together in post-processing. The entire data acquisition took 20 – 30 minutes per specimen depending on its size.

After the completion of imaging, prostate specimens were returned to the surgical pathology lab for regular histological analysis. Histological sections were cut along either the lateral-axial (axial view) or lateral-elevational (coronal view) imaging plane every 3 mm, and then were sliced (5 μm thick) to mount on microscope slides. The location of each section was recorded to facilitate correlation with imaging data. During histological analysis, anatomic landmarks (e.g. urethra and ejaculatory ducts) and pathologies (i.e. PCa, BPH and atrophy) were identified and outlined in all histological slides by a pathologist who was blinded to the ARFI images.

Data processing

Displacements were estimated using Loupas' algorithm from the IQ data.³⁶ In the ARFI data, the earliest tracked displacements (0.23 ms) from within each ROE after each ARFI push pulse were used to form ARFI images. ARFI displacement data were normalized using a depth-dependent gain (DDG) algorithm to compensate for the displacement variation due to the spatial distribution of the applied acoustic radiation force.¹⁰ Linear interpolation was performed to achieve a uniform spacing of 0.1 mm in all three dimensions in the 3D ARFI data. In the SWEI data, the LTTP algorithm³⁴ was used to reconstruct the shear moduli of prostatic tissues. The LTTP algorithm is a time-of-flight method, which computes the shear wave propagation velocity (c_T) by tracking the arrival time of wave peaks at a series of lateral locations that are increasingly laterally offset from the ROE. Assuming a linear, isotropic and elastic medium, the shear modulus (G) can be reconstructed by:

$$G = \rho c_T^2 \quad (2)$$

in which ρ is the tissue density and was assumed to be 10^3 kg/m^3 throughout this study. The LTTP algorithm estimates the average propagation velocity over the lateral extent of estimation, which was 6.5mm in this study.

To reconstruct the shear moduli, it is assumed in the LTTP algorithm that the shear wave propagates exclusively in the lateral direction. This assumption limits stiffness reconstruction to the depth of field (DOF) of the excitation beams.³⁴ Outside the DOF where this assumption is not valid, the shear moduli estimated by the LTTP algorithm can be biased due to the non-lateral wave propagation. However, in this study, prostate tissues beyond the DOF (12.6mm – 17.4mm) were also of interest. To determine the bias factors for axial depths beyond the DOF when applying the LTTP algorithm, a study on a homogeneous tissue mimicking zerdine phantom (CIRS Inc., Norfolk VA, $G=1.5 \text{ kPa}$) was performed. Using the parameters shown in Table 1, 12 independent SWEI datasets were acquired at different locations in the phantom. The LTTP algorithm was applied to reconstruct the shear modulus every 0.5 mm axially $\times$ 6.5 mm laterally for each SWEI dataset without considering the lateral propagation assumption. The reconstructed shear modulus as a function of depth normalized by the known phantom stiffness is shown in Figure 2. This curve demonstrates the expected bias in the reconstructed shear modulus

with depth when using the LTTP algorithm and neglecting the propagation direction for the SWEI sequence used in this study. As shown in Figure 2, the deviation of the reconstructed shear moduli from the material stiffness is less than 3% within the DOF, and increases outside the DOF. Considering the large variations of the reconstructed values in the near field, the axial range of 7.2 mm to 20.9 mm where the reconstructed values were within $\pm 20\%$ deviation from the material stiffness were used to process the prostate data. In this region, the shear moduli of prostate tissue were reconstructed using the LTTP algorithm with the bias corrected as determined from Figure 2. Each reconstruction region has a dimension of 6.5 mm (lateral) $\times$ 0.5 mm (axial) $\times$ 1 mm (elevational). A reconstructed shear modulus was considered a valid estimate when the linear regression goodness-of-fit metric exceeded 0.8.³⁴

Five types of prostatic tissue (PZ, CZ, TZ/BPH, PCa and atrophy) were identified in the 3D ARFI datasets based on the McNeal zonal anatomy and histological results as previously reported by Zhai et al.¹⁰ Based on the anatomical landmarks and notes taken during the pathological sectioning, histological slides were registered with ARFI images. The mismatch between ARFI images and histological slides were within 3 mm. Anatomic zones were determined by comparing ARFI images with McNeal zonal anatomy; pathologies such as BPH, PCa and atrophy were determined from registered histological slides. Then, coronal ARFI images were subdivided into rectangular blocks (6.5 mm (lateral) $\times$ 3 mm (elevation)) at 0.5 mm depth spacing. Each block was identified as a particular tissue type if 70% of its area was inside that tissue based upon the histological and anatomic analysis. The mean shear modulus of each block was reconstructed from the corresponding SWEI data to represent its stiffness.

The mean ARFI displacement was computed for each region (6.5mm $\times$ 0.5mm $\times$ 1mm) where a valid stiffness estimate was obtained to investigate the relationship between ARFI displacement and the reconstructed shear moduli. For each specimen, linear regression between ARFI displacement and the inverse of the reconstructed shear moduli was performed for data in each coronal plane.

RESULTS

Figure 3a shows a coronal ARFI image (Specimen B, axial depth 11.5 mm) with the matched reconstructed shear moduli from the SWEI data overlaid on this ARFI image shown in Figure 3b. The symmetric stiff structures at the top of the image are the slightly distorted CZ (circled in blue dashed lines). The remaining regions are predominantly the PZ. The rectangular regions have dimensions of 3 mm (elevational) by 6.5 mm (lateral), where the numbers represent the mean estimated shear moduli in those blocks. The reconstructed shear moduli demonstrate the CZ is stiffer than the PZ, while the ARFI image portrays smaller displacement in the CZ.

Figure 4 shows ARFI images and matched histology slides from Specimen D where both PCa and BPH were identified in the histological analysis. In Figure 4a, different types of tissues (i.e. CZ, PZ, TZ/BPH and PCa) are circled or labeled in the coronal ARFI image. In Figure 4b, the mean reconstructed shear modulus of each rectangular block (3 mm (elevational) $\times$ 6.5 mm (lateral)) is overlaid on the coronal ARFI image. Figures 4c and 4d are an axial ARFI image from the elevation position at 15 mm and the corresponding histological slide. In the histological slide, anatomic structures and pathologies were identified by the pathologist: PCa is masked in red; BPH nodules are circled with dashed blue lines; and the urethra is colored green. In the ARFI images, the PCa is circled with red dashed lines and anatomic zones are labeled.

Figure 5 summarizes the reconstructed shear moduli for five types of prostatic tissue (PZ, TZ, CZ, PCa and atrophy) in all six prostate specimens. A total of 2,107 independent blocks were characterized and included in the analysis. Each group of bars represents the results from one specimen. The error bars represent standard deviations of the reconstructed shear moduli for each type of tissue. The number of blocks of each tissue type in each specimen is shown above each error bar. The TZ represents the entire TZ tissue including regions of BPH. Focal PCas were identified in four specimens (B, C, D and E). In specimen A, cancerous cells were diffusely distributed in the PZ without any isolated cancerous lesion; the reconstructed shear modulus represents the stiffness of the entire PZ region. In specimens B-F, only blocks of healthy tissue in the PZ were included to represent the PZ stiffness. Compared to PZs in other specimens, the reconstructed PZ stiffness is higher in specimen A. A non-parametric, Wilcoxon rank test between the estimated stiffness of the PZ in specimen A and other specimens gives a p-value less than 0.001, and demonstrates the stiffness increase in the PZ of specimen A is statistically significant. Overall, the CZ and PCa demonstrate similar stiffness and are stiffer than the PZ and TZ.

Taking the mean estimated stiffness of each tissue type from all specimens, the reconstructed shear moduli of the five types of prostatic tissue are summarized in Table 2, in which the stiffness estimates of the PZ in specimen A were not included due to the presence of diffusely distributed PCa in the specimen. The PZ and the TZ comprise around 80% prostate volume in young men and this percentage increases in older men.³⁷ Considering the normal tissue to be the PZ and TZ, the stiffness ratio of PCa-to-normal was computed to be 2.2 from these data.

Figure 6 shows a scatter plot of mean ARFI displacement amplitudes vs. the inverse of the reconstructed shear moduli from the data shown in Figure 3. This plot reveals an inverse relationship between the ARFI displacement and underlying tissue stiffness ($\text{displacement} \propto 1/G$). The solid line (forced to pass through the origin) represents the linear regression of these points (slope $k = 60 \mu\text{m} \cdot \text{kPa}$). This positive slope indicates larger ARFI displacement amplitudes are associated with more compliant tissue in this plane. The correlation coefficient between ARFI displacement and $1/G$ was computed to be 0.72. Similar trends were observed for all coronal planes in all specimens, although the slope varied as a function of depth. Figure 7 summarizes the regression slopes at different axial depths, in which error bars were computed from all six specimens. The plot demonstrates the largest linear coefficient (the slope) occurs around 13–15 mm, where the highest amplitude of acoustic radiation force is expected for the ARFI push pulses (focused at 15 mm) used in this study.

DISCUSSION

The stiffness contrast among prostatic tissues forms the physical basis for elasticity imaging methods to visualize the internal structures and differentiate pathologies from normal tissue. In past studies, elastography has been reported to improve the PCa detection rate,^{6–9} and ARFI imaging has been used to visualize prostate zonal anatomy as well as PCa and BPH.¹⁰ Yet, these methods (strain imaging and ARFI) image prostatic structures based on their relative stiffness. The contrast shown in the images can be impacted by either boundary conditions and applied stress (elastography), or variations in applied acoustic radiation force (ARFI). The mechanical properties of prostatic tissue have also been reported by several research groups.^{20–25} However, large discrepancies exist in the reported shear moduli of prostatic tissues, which is likely due to different experimental conditions such as compression rates, temperature, boundary conditions, sample variation and choice of different mechanical models for reconstructing the tissue stiffness.

In this study, acoustic radiation force methods were used both to image prostatic structures (ARFI) and to quantify the tissue stiffness (SWEI). To our knowledge, this is the first study reporting acoustic radiation force based quantification of prostatic shear moduli. The relative stiffness among prostatic tissues derived from this study is in good agreement with the literature. Despite large differences in the reported absolute reconstructed shear moduli, all groups reported a PCa-to-normal stiffness ratio between 1.5 and 2.6 as compared to our result of 2.2. As demonstrated in Figure 5 and Table 2, the large stiffness contrast between PCa and normal PZ and TZ tissues suggest great potential for elasticity imaging methods to identify PCa in these zones. The CZ was found to be much stiffer than the TZ and PZ, which is consistent with results reported in a magnetic resonance elastography (MRE) study.²² Although PCa rarely develops in the CZ, based on these findings, low contrast would be expected in prostate elasticity images when PCa develops adjacent to or within the CZ in the basal area due to their similar stiffness. This fact may explain the lower cancer detection rates in the basal regions that have been reported for elastography.^{7, 9, 8} In specimen A, where PCa had developed diffusely in the PZ, no obvious discrete regions of suspicion were identified in ARFI images. However, the reconstructed shear stiffness is significantly higher than the PZ tissue in other specimens. This suggests that diffusely distributed cancerous cells can stiffen the prostate tissue independent of the morphology.

This study was designed to address the fundamental question: in the heterogeneous prostate, does relative ARFI displacement portray the underlying tissue stiffness? In ARFI images, tissue stiffness differences are inferred by the relative displacement amplitudes based on the assumption of uniform force at a given depth. Variations in acoustic attenuation properties can change the distribution of the applied force field, thus potentially introducing bias in ARFI image interpretation. SWEI quantifies tissue stiffness through a different mechanism (i.e. shear wave speed), which is not dependent upon the applied acoustic radiation force amplitude. Thus, co-registered ARFI and SWEI data can be used to investigate the origin of displacement variations in ARFI images. To our knowledge, this is the first study that correlates relative ARFI displacement amplitudes with independent quantitative stiffness measurements within a heterogeneous organ. As shown in Figure 6, displacement amplitudes at a given depth in ARFI images are inversely related to the reconstructed tissue stiffness. Although the high correlation (0.72) between ARFI displacement and $1/G$ does not directly quantify the impact of variable acoustic attenuation, it does suggest that the underlying tissue stiffness is a primary factor in determining the displacement amplitudes in coronal prostate ARFI images.

The absolute slope between ARFI displacement amplitudes and $1/G$ is determined by the applied acoustic radiation force. At different depths, acoustic radiation force amplitudes vary due to acoustic focal gain effect and energy loss, which contributes to the different slopes shown in Figure 7. The different slopes mean that tissues with the same stiffness exhibited different ARFI displacement amplitude at different depths. When evaluating tissue at different depths, this effect can confound the interpretation of relative stiffness based on displacement amplitudes.³⁸ This plot also implies that relative ARFI displacement amplitude alone cannot be used to quantify underlying tissue stiffness.

A limitation of this study was the low spatial resolution of the stiffness quantification method. The LTP algorithm used a lateral range of 6.5 mm, in which tissue structures can introduce variations in the reconstructed shear modulus. In addition, a number of factors such as patient age, Gleason pattern of PCa and presence of prostatitis were not considered. These factors will likely impact the prostatic tissue stiffness. Delineating the impact of these factors on tissue stiffness would require a large number of prostate specimens, and is beyond the scope of this study.

CONCLUSION

In this study, prostatic tissue stiffness was quantified using acoustic radiation force methods. Five types of prostatic tissue were identified from six excised human prostates and their shear moduli were reconstructed: PZ (4.1 ± 0.8 kPa), CZ (9.9 ± 0.9 kPa), TZ/BPH (4.8 ± 0.6 kPa), PCa (10.0 ± 1.0 kPa) and atrophy (8.0 kPa). The stiffness ratio of PCa-to-normal tissue was computed to be 2.2, which is in good agreement with the literature. Co-registered ARFI and SWEI prostate datasets were acquired to investigate the correlation between ARFI displacement amplitude and underlying tissue stiffness in human prostates. The results reveal an inverse relationship between ARFI displacement amplitude and the reconstructed tissue stiffness, which suggests the contrast seen in coronal prostate ARFI images is determined mainly by the underlying tissue stiffness, and variations in acoustic attenuation do not introduce a significant bias in the ARFI displacement data.

Acknowledgments

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(a)

An ARFI imaging plane

(b)

Figure 1.

Diagrams of experimental setup. (a) the prostate specimen was stabilized in a custom specimen holder submerged in isotonic saline. The transducer imaged the specimen through its posterior side. A series of 2D planes were imaged through mechanical translation of the probe to acquire 3D imaging datasets. (b) In a single ARFI imaging plane, four independent SWEI datasets were acquired. The dashed lines indicate the lateral range of each SWEI dataset.

Figure 2.

Normalized reconstructed shear moduli of a homogeneous tissue mimicking phantom as a function of axial depth using the LTTP algorithm. All the points were normalized by the manufacturer calibrated material shear stiffness of 1.5 kPa. Each point represents the mean and standard derivation of 12 repeated data acquisitions. The DOF (12.6mm – 17.4mm) of the ARFI push beams is indicated by the dashed lines. The axial range within 20% deviation (7.2 mm and 20.9 mm) from the phantom shear stiffness is indicated by the dot-dashed lines. These data were used to compensate for the bias in this region.

Figure 3.

(a) coronal ARFI image of an *ex vivo* human prostate. The displacement amplitudes in the ARFI image were normalized. Two anatomical zones CZ and PZ are identified in this image. The reconstructed shear moduli from the matched SWEI datasets are overlaid on the corresponding regions in (b). Each number represents the mean reconstructed shear modulus (unit: kPa) of each rectangular area (3 mm (elevational) $\times$ 6.5 mm (lateral)). The middle two columns have an overlapped region of 2 mm.

Figure 4.

ARFI images with the co-registered reconstructed shear moduli and histological slides. CZ, TZ/BPH and PCa are circled in blue, green and red dashed lines in the ARFI images, respectively. The urethra is indicated by the green arrow. (a) A coronal ARFI image with zonal anatomy, PCa and BPH indicated; (b) the coronal ARFI image with co-registered reconstructed shear moduli; (c) An axial ARFI image with zonal anatomy, PCa and BPH indicated; (d) Co-registered histological slide of the axial ARFI image, in which PCa is masked in red and BPH is circled in black. (a) and (c) are perpendicular to each other and intersect at the dashed lines.

Figure 5.

Summary of reconstructed shear moduli of prostatic tissue. Five types of prostatic tissue (PZ, TZ, CZ, PCa and Atrophy) were characterized. Each group of bars represents the data from a single specimen. The number above each error bar represents the number of ROIs used for calculating the tissue stiffness. The empty column represents absence of the tissue type.

Figure 6.

ARFI displacement amplitudes vs. the inverse of the reconstructed shear moduli at a given depth (11.5 mm). Data were taken from specimen B. The positive slope ($k = 60\mu\text{m} \cdot \text{kPa}$) of the regression line indicates that more compliant tissue is associated with larger displacement amplitude in ARFI prostate images.

Figure 7.

The regressed linear coefficient between the inverse of the reconstructed shear moduli and ARFI displacement amplitudes vs. axial depth. The error bars were computed over data acquired from all six specimens.

TABLE I**ARFI AND SWEI SEQUENCING PARAMETERS**

	ARFI	SWEI
Excitation beam		
F#	1.5	1.5
Center frequency (MHz)	5.7	5.7
Lateral focal depth (mm)	15	15
Insonification duration (μ s)	53	53
Number of insonifications	44	11X4
Track beam		
PRF of track lines (kHz)	9.2	9.2
Lateral beam spacing (mm)	0.15	0.15
Lateral tracking range (mm)	26	6.5X4

TABLE II

MEAN AND STANDARD DEVIATION OF RECONSTRUCTED SHEAR MODULI OF DIFFERENT PROSTATIC TISSUE FROM SIX EXCISED SPECIMENS

Tissue type	PZ	TZ	CZ	PCa	Atrophy
Shear moduli (kPa)	4.1±0.8	4.8±0.6	9.9±0.9	10.0±1.0	8.0
Number of specimens	5	6	5	4	1