A feasibility study of novel ultrasonic tissue characterization for prostate-cancer diagnosis: 2D spectrum analysis of *in vivo* data with histology as gold standard

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This study demonstrates the feasibility of using a novel 2D spectrum ultrasonic tissue characterization (UTC) technique for prostate-cancer diagnosis. Normalized 2D spectra are computed by performing Fourier transforms along the range (beam) and the cross-range directions of the digital radio-frequency echo data, then dividing by a reference spectrum. This 2D spectrum method provides axial and lateral information of tissue microstructures, an improvement over the current 1D spectrum analysis which only provides axial information. A pilot study was conducted on four prostate-cancer patients who underwent radical prostatectomies. Cancerous and noncancerous regions of interest, identified through histology, were compared using four 2D spectral parameters: peak value and 3 dB width of the radially integrated spectral power (RISP), slope and intercept of the angularly integrated spectral power (AISP). For noncancerous and cancerous prostatic tissues, respectively, our investigation yielded 23 ± 1 and 26 ± 1 dB for peak value of RISP, $7.8 \pm 0.5^\circ$ and $7.6 \pm 0.6^\circ$ for 3 dB of RISP, -2.1 ± 0.2 and -2.7 ± 0.4 dB/MHz for slope of AISP, and 92 ± 5 and 112 ± 6 dB for intercept of AISP. Preliminary results indicated that 2D spectral UTC has the potential for identifying tumor-bearing regions within the prostate gland. © 2009 American Association of Physicists in Medicine. [DOI: [10.1118/1.3166360](https://doi.org/10.1118/1.3166360)]

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I. INTRODUCTION

Prostate cancer is the most common cancer among American men, second only to skin cancer. The American Cancer Society projected 186 320 new diagnoses of prostate cancer in the United States during 2008.¹ Since conventional imaging modalities such as x-ray, ultrasound, CT, and MRI are unable to reliably distinguish cancerous prostatic tissues from normal tissues, the majority of prostate cancers are diagnosed by transrectal ultrasound-guided prostate biopsies. However, because conventional ultrasound cannot pinpoint the location of the malignant tumors within the prostate gland, these ultrasound-guided biopsies currently have an estimated sensitivity of 50%.² The ability to reliably image cancer-bearing regions within the prostate could increase the success rates of prostate-cancer detection as well as treatment.

In the past decade, major advances have been made in prostate-cancer diagnosis that use advanced imaging techniques such as magnetic resonance spectroscopy (MRS) and ultrasonic tissue characterization (UTC). MRS provides bio-

chemical (metabolic) information of the prostate gland and determines cancerous tissue by identifying regions with an elevated choline/citrate ratio, an indicator of cancer.³⁻⁹ UTC provides physical information of the prostate gland and determines cancerous tissue by evaluating the tissue vasculature as well as their attributes such as size, shape, and compressibility.¹⁰⁻¹³ Due to the safe, cost-effective, and real-time nature of ultrasound imaging, novel ultrasonic techniques are widely pursued to assess the malignancy of prostatic tissues. The following is a brief summary of various ultrasonic approaches in prostate cancer detection.

- (i) *Elasticity approach*: Ultrasound elastography (strain imaging) provides information about tissue elasticity (stiffness). König *et al.* incorporated tissue elasticity as a factor in malignant-tissue detection of the prostate gland, by tissue typing with a trainable classification system.¹⁴ Souchon *et al.* developed an imaging system for prostate elastography *in vivo*, using a transrectal ultrasound probe to guide a high-intensity focused ul-

trasound therapy.¹⁵ Hoyt recently reviewed the use of tissue elasticity properties as biomarkers for prostate cancer.¹⁶ Zhang *et al.* described the viscoelastic properties of the human prostate and correlated them to the inherent elastic contrast produced by cancer.¹⁷

- (ii) *Power Doppler method*: The power Doppler is a 3D vascular-imaging technique that reveals abnormal blood flow. Histological studies have demonstrated increased microvessel density associated with prostate cancer as well as a positive correlation between microvessel density and aggressiveness of disease. Sauvain *et al.* reported that the power Doppler improves detection of abnormal vascular density in isoechoic tumors of the prostate.¹⁸ In addition, the power Doppler can determine the risk of extracapsular involvement, an important prognostic factor, by the presence of vessels perforating the capsule.¹⁸
- (iii) *1D spectrum analysis method*: The most widely investigated UTC technique in prostate-cancer detection, to date, uses the 1D spectrum analysis method. The 1D spectrum method analyzes the radio-frequency (rf) data received at the clinical ultrasound probe and provides quantitative measures of tissue microstructure physical properties. Feleppa *et al.* (Riverside Research Institute) pioneered utilization of 1D spectrum analysis in the early 1990s. In practice, nonlinear classification methods were applied to the spectral parameter values (slope, intercept, and midband value computed from the linear regression of the 1D spectral curve) along with PSA values in order to differentiate cancerous from noncancerous tissues.^{19–21} With a database of over 200 patients, the 1D spectrum technique originally yielded an area under the receiver-operating-characteristic (ROC) curve of 0.80 ± 0.05 .²⁰ More recently, this group reported a ROC curve area of 0.844 ± 0.018 .¹³ Similarly, Scheipers *et al.* described a multifeature tissue characterization including 1D spectral and texture parameters to detect prostate cancer.²² In a study of 100 patients, Scheipers' method yielded a ROC curve area of 0.86 when distinguishing hyper-echoic and hypoechoic tumors from normal tissue, and a ROC curve area of 0.84 when distinguishing isoechoic tumors from healthy tissue. This performance is as good as, if not superior to, current prostate-cancer imaging by MRI/MRS with a mean area under the ROC curve ranging from 0.69 to 0.76.²³

We have developed a novel 2D spectrum technique that extends the analytic concept from one dimension to two dimensions.^{24,25} The theoretical model for our calibrated 2D spectrum analysis method was based on wave propagation in a globally homogeneous medium with randomly distributed local inhomogeneities and is describable by a 3D Gaussian tissue model.^{24,25} 2D spectra are employed by performing two fast-Fourier transform (FFT) operations on windowed rf data obtained from a region of interest (ROI). The rf data along each line were first transformed with respect to time (the range) and the resulting complex spectrum was trans-

FIG. 1. Diagram showing a transducer scanning the prostate, where X is the range direction (beam) and Y is the cross-range direction.

formed with respect to the cross range. This allows both axial and lateral evaluations of physical properties of prostatic tissues, an improvement over the 1D method that only provides axial evaluation. Our 2D method supplies more information regarding tissue microstructures (e.g., morphology), thereby offering more diagnostically relevant information and potentially yielding a greater ROC curve area.

The central premise enabling 2D UTC is that cancerous tissues have different structural features than those of non-cancerous tissues. For example, cancerous tissues are harder than normal prostatic tissues.²⁶ 2D spectra are sensitive to physical properties of tissue microstructures, such as size, shape, and spatial acoustic impedance fluctuation. Even for more challenging cases, such as tumors, which often pose scattering from random (unpredictable) spatial distributions of small scatterers, 2D spectrum analysis has the potential to differentiate malignant from benign prostatic tissues. Thus, the measurements of the 2D ultrasonic spectra could prove to be promising tools for physicians noninvasive prostate-cancer diagnosis.

The purpose of this study was to demonstrate the clinical feasibility of, and lay the groundwork for, using our 2D spectrum technique in prostate-cancer diagnosis. This paper presents the following: (1) a summary of the theory underlying 2D spectrum analysis; (2) the data acquisition system employed in 2D spectrum analysis; (3) data processing procedures of this 2D method in prostate-cancer diagnosis; (4) histology evaluation, which serves as the gold standard for ROI selection in clinical tissue typing; (5) preliminary results of our *in vivo* prostate-cancer study.

II. SCATTERING THEORY UNDERLYING 2D SPECTRUM ANALYSIS

The theory underlying our 2D spectrum analysis method has been discussed in previous reports but is summarized in this section.^{24,25,29} 2D spectrum analyses are performed on the digital rf echo signals gated over a ROI. Radio-frequency data within the ROI undergo the 2D Fourier algorithm along both the range (X, beam propagation) direction and the cross range (Y, scan) direction. Figure 1 is a diagram illustrating the scanning geometry.

Equation (1) is the general equation of the calibrated 2D power spectrum for tissues exhibiting wide-sense stationarity. The equation demonstrates that 2D power spectra of rf signals are determined by three autocorrelation functions (ACFs): R_T , R_D , and R_G . The calibrated 2D power spectrum is a function of temporal frequency f and cross-range spatial frequency ν ,

$$S_{2D}(f, \nu) = \int \int \int [R_T(\Delta x, \Delta y, \Delta z) R_D(\Delta \xi, \Delta z)] \times R_G(\Delta x, \Delta y) e^{j2k\Delta x + j\mu\Delta y - j\mu\Delta \xi} \times d\Delta x d\Delta y d\Delta z d\Delta \xi, \quad (1)$$

where $\xi \equiv y - y_t$, $\xi' \equiv y' - y'_t$, $\Delta \xi = \Delta y - (y'_t - y_t)$, R_T is the tissue acoustic impedance ACF, R_D is a spatial ACF describing the two-way directivity function of the beam,

$$R_D(\Delta \xi, \Delta z) = \int \int D^2(\xi, z) D^2(\xi + \Delta \xi, z + \Delta z) d\xi dz, \quad (2)$$

and R_G is a spatial ACF of the 2D gating function,

$$R_G(\Delta x, \Delta y) = \int \int g_1(x) g_1(x + \Delta x) g_2(y) g_2(y + \Delta y) dx dy. \quad (3)$$

The second degree of freedom in frequency domain allows the exposition of spatial anisotropy and orientation of 3D tissue scatterers, previously unavailable in the 1D spectrum method.

We have solved this equation with a Gaussian approximation for the tissue ACF (R_T). The closed form solution is expressed as

$$S(k, \mu) = \frac{0.24 L_X L_Y C V_s Q^2 k^3 (\alpha \beta \gamma) (a/R)}{\left[1 + 0.22 \left(\frac{ka}{R} \frac{\gamma}{1.17} \right)^2 \right]^{1/2}} \times \exp \left[- \left(k \frac{\alpha}{1.17} \right)^2 - \frac{1}{4} \left(\mu \frac{\beta}{1.17} \right)^2 - \frac{1}{0.88} \left(\frac{\mu R}{ka} \right)^2 \right], \quad (4)$$

where L_X and L_Y are ROI lengths along the range and cross-range directions, respectively, a and R are the aperture and focal length of the transducer, C is the effective volumetric scatterer concentration, Q specifies the relative acoustic impedance difference between the scatterers (with acoustic impedance Z) and the surrounding medium (with average acoustic impedance Z_0), V_s specifies the volume of an average scatterer, and α , β , and γ represent effective scatterer sizes along the X , Y , and Z directions, respectively. The theoretical analysis demonstrates that 2D power spectra are related to tissue properties such as scatterer size and relative acoustic impedance, transducer properties such as aperture and focal length, system properties such as bandwidth and center frequency, and processing properties such as ROI window sizes.

TABLE I. Patient and tumor characteristics.

Patient	Age	PSA	Prostate volume (cm ³)	Gleason score
(1)	61	4.8	18.8	7
(2)	54	5.0	24.2	7
(3)	60	10.7	51.8	7
(4)	56	3.0	26.3	7

Although a Gaussian ACF is used in our theoretical model for randomly distributed scatterers, our 2D spectrum method is not limited to any particular form of ACF. In addition, our 2D spectrum would exhibit distinctive features for deterministic structures. For example, if the structure has well-defined edges, the spectrum will have a peak width that is inversely proportional to the thickness of the structure.

III. MATERIALS AND METHODS

In this feasibility study, we scanned four prostate cancer patients with transrectal ultrasound under an institutional review board-approved protocol at Columbia University Medical Center. The patient selection criterion was prostate-cancer patients undergoing radical prostatectomy who did not receive preoperative hormone or radiation therapy. The patient clinical characteristics are shown in Table I.

The prostate 2D spectrum analysis study consists of the following three elements.

- Acquisition of rf data of the prostate using a clinical ultrasound scanner.
- Ultrasonic data processing through 2D spectrum analysis.
- Validation of the ultrasonic spectral method with pathological findings.

III.A. Ultrasonic imaging and RF data acquisition

Figure 2(a) is a schematic of our ultrasound imaging system. As previously described by Feleppa *et al.*,^{12,21} the data acquisition system has three main components: a clinical ultrasound machine, a custom interface module, and a computer. A B&K Medical System (Marlborough, MA) scanner (model 3535) was employed to transmit and receive ultrasonic signals. The biplane transrectal probe (model 8558) had a nominal center frequency of 7.5 MHz and the convex array transducer had a sector angle of 110°. The rf data (32-bits) was acquired using a 40 MHz sampling frequency. Each scan consisted of 192 scan lines and each scan line consisted of 3000 scan points. For all ultrasound scans, we used fixed scanner settings: 70% overall gain, a single focal zone at 0.5 cm, and the calibrated maximum setting time gain control (TGC). In the future, physicians will be able to adjust the TGC level at their discretion and we will subsequently adjust the spectral normalization to match the corresponding setting.

FIG. 2. (a) Schematic of the ultrasound data acquisition system and (b) photograph of an AccuSeed stepper.

During ultrasound imaging, each patient was scanned with a transrectal ultrasound in the lithotomy position prior to radical prostatectomy. Ultrasound scans were performed along the axial plane of the prostate in 2 mm increments from the base to the apex. An AccuSeed 3D stepper was utilized [Fig. 2(b)] to hold the probe and achieve a 2 mm step size. 3D ultrasound rf data, backscattered from the prostate, was acquired as a set of closely spaced scan planes over the full volume of the gland, and was digitally stored for future processing. 3D data acquisition enables 2D analysis of any ROI within the prostate gland and was further used to ensure accurate correlation with 3D histology images for cancerous/noncancerous ROI identification. For a typical prostate (4–6 cm from base to apex), 20–30 scan planes were required to cover the full gland volume. The duration of an ultrasound examination was between 5 and 10 min.

III.B. 2D spectrum analysis method

We developed MATLAB software for the analysis of the digital rf ultrasound signals backscattered from the prostate gland. 2D spectrum analysis consisted of the following steps.

Step 1: B-model display. 2D spectrum analysis began with a digital computation of B-mode images. An ULTRASONIX® program was used to derive the envelope of stored rf echo signals. The enveloped data were then displayed in a sector format that matched the B-mode image generated by the clinical scanner (Fig. 3). This B-mode image served to identify overall anatomic relationships and acted as the template upon which the ROI was specified.

Step 2: ROI selection. In this pilot study, physicians manually specified the cancerous and noncancerous ROIs within the transducer's focal zone (prostate peripheral zone) based on the corresponding regions from the histology cancer map. The prostate peripheral zone is the posterior portion of the prostate gland, closest to the rectum, where prostate cancers commonly develop. ROIs were positioned and superimposed on the B-mode image, shown in Fig. 3. The ROI specified the region in which spectrum analysis was applied.

Due to the small size of the ROI, we ignored the scan line distance variation of the sector scan through the ROI. The spectrum analysis was applied directly to the rf echo data (not the enveloped data displayed in the B-mode images). There are tradeoffs between the resolution and accuracy in choosing the ROI size.²⁷ For example, a larger ROI results in more statistically accurate parameter estimates, yet simultaneously results in decreased resolution. In consideration of this tradeoff, we employed a ROI size of approximately 4×4 mm. We chose to use a ROI size that is larger (20 wavelengths at center frequency) than that used in 1D UTC studies to ensure a less biased variance. 2D spectral parameters have yet to be evaluated for resolution versus variance; however, the underlying statistical principles are consistent with those developed by Lizzi.²⁷

Step 3: Calibrated spectrum. A calibration procedure was performed to remove the effects of the transducer and system electronic modules. The calibration spectrum was the 1D power spectrum of the echo signal received from an optically flat glass plate, placed perpendicular to the beam axis in the focal zone of the transducer (with a flat TGC). The calibration power spectrum (in dB) was later subtracted from the 2D tissue spectrum along the range direction to compensate for the temporal-frequency transfer function of the beam and receiver. The temporal-frequency range used for 2D spectrum analysis was chosen to ensure an adequate signal-to-

FIG. 3. Conventional B-mode image of the prostate.

FIG. 4. Calibrated 2D power spectrum of the ROI of prostate.

noise ratio. The frequency bandwidth was determined by ensuring the lowest-level echo signal from the prostate parenchyma was at least 6 dB above the noise level of the transducer.²⁸ In this study, no normalization/calibration was performed along the cross-range direction to compensate for the beam-transfer function.

Step 4: Spectrum generation. To compute the 2D spectrum, the 2D rf signals inside the ROI were multiplied by a 2D Hamming function with window lengths L_X and L_Y representing the axial (range) and lateral (cross-range) directions, respectively. A 1D FFT with respect to the axial direction was applied for each scan line. The complex 1D spectrum along each scan line was divided by the 1D calibration spectrum.¹¹ The resulting normalized complex 1D spectrum was then Fourier transformed along the lateral direction to obtain a 2D spectrum. The spectral magnitude was squared to compute a single realization of the 2D power spectrum, shown in Fig. 4. The resulting 2D spectrum was specified in terms of spatial frequencies $k(k=2\pi f/c)$ along the range direction and $\mu(\mu=2\pi\nu/c)$ along the cross-range direction (where c is the speed of sound). In this study, a frequency bandwidth range of 5–8.5 MHz was used for analysis of all patients. The cross-range spatial frequency ranged from -100 to 100 cm^{-1} . The intensity of the 2D spectrum was displayed in color, with red and blue indicating high intensity and low intensity, respectively (Fig. 4). All 2D power spectra reported were calculated in decibel units (dB) as $S_{2D}'(k, \mu) \equiv 10 \log S_{2D}(k, \mu)$.

Step 5: Feature extraction. To quantitatively measure and classify the physical properties of tissue, we defined two spectral functions (Fig. 5) and two 2D spectral parameters from each spectral function. The two spectral functions, radially integrated spectral power (RISP) and angularly integrated spectral power (AISP), are computed from the 2D power spectrum (in dB).²⁹ RISP is defined as an integration of spectral power along each radial line in the 2D spectra, as a function of its angle θ measured from the k -axis. The integration extends over the transducer's bandwidth and the expression for the RISP is

FIG. 5. 2D spectra curves of the prostate tissue analyzed: (a) RISP and (b) AISP.

$$\text{RISP}(\theta) = \frac{\int_{k_1}^{k_2} (S_{2D}'(k, \mu)) dk}{\int_{k_1}^{k_2} dk}, \quad (5)$$

$$\mu = k \cdot \tan(\theta), \quad (6)$$

where k_1 and k_2 are the minimum and maximum spatial frequencies in the bandwidth and θ specifies the angle of the line of integration. Physically, RISP is the distribution of spectral power density for each radial line in the frequency space. AISP is defined as an integration of spectral power over an arc at a specific spatial frequency. AISP measures the spectral power distribution on each arc in the frequency space. The arc is the part of a circle of fixed frequency K within the frequency range of interest. The expression for AISP is

$$\text{AISP}(K) = \frac{\int_{\theta_1}^{\theta_2} (S_{2D}'(k, \mu)) K d\theta}{\int_{\theta_1}^{\theta_2} K d\theta}, \quad (7)$$

$$K = \sqrt{k^2 + \mu^2}, \quad (8)$$

where θ_1 and θ_2 are the minimum and maximum angles within the frequency range of interest and K specifies the frequency of the arc. The four spectral parameters, (1) peak value of RISP, (2) 3 dB width of RISP, (3) slope of AISP, and (4) intercept of AISP, were used to quantitatively evaluate

the physical conditions of tissue microstructures. As described by the 2D model, the slope of AISP and 3 dB width of RISP are predominantly determined by the scatterer size along the axial and lateral dimensions.²⁹ The peak value of RISP and the intercept of AISP are related to the concentration and relative acoustic impedance change of the imaged tissues.

In this study, our 2D UTC method does not treat attenuation directly, as ROIs of the same size and depth within the focal zone of the transducer were used for spectral estimates of the cancerous and noncancerous regions. If 2D spectrum analysis is applied to ROIs of different sizes or depths, or applied to the entire prostate gland (through sliding ROIs), attenuation becomes an important factor. Attenuation can be accounted for using a number of different methods.^{30–32} In previous 1D-spectrum parameter imaging of the entire prostate, a typical rate of 0.5 dB/(MHz cm) was used as the effective intensity attenuation coefficient.³¹ If attenuation scales linearly with frequency, for an intervening tissue depth d (cm) and average attenuation coefficient σ (dB/MHz cm), the attenuation-free slope of AISP is reduced by $2d\sigma$. In this case, the spectral intercept of AISP as well as the peak value and 3 dB width of RISP are not affected by attenuation. For instances in which more complex attenuation compensation is required, Oelze and O'Brian proposed a frequency-dependent attenuation-compensation function to correct for the normalized power spectrum.³²

III.C. Histology as the gold standard

In this study, all prostate-cancer patients underwent a radical prostatectomy. A quarter-mount histology protocol for 3D tissue reconstruction was developed to provide the geometry as well as sizes and spatial locations of the tumors within the prostate gland. The prostate specimens were inked with black and yellow India ink to identify the right and left sides of the prostate, respectively. The specimen was then fixed overnight in 10% neutral-buffered formalin at 4 °C. After fixation, a slicer was utilized to cut thick axial planar sections from base to apex, at approximately 4 mm intervals. Each cross section was cut into four quadrants with ink marking the alignment of sections. Each quadrant was em-

FIG. 6. Histology images of the middle slice of the prostate.

FIG. 7. Microscopic images of malignant and benign areas indicated in Fig. 6.

bedded in paraffin and stained using hematoxylin and eosin. Quarter-mounts were scanned into digital images and whole-mount images were reconstructed.

Figure 6 shows the histology images of the middle slice of the prostate from Fig. 3. The distributions of carcinoma were recorded on the digital images of the cross sections. An experienced pathologist contoured the cancerous regions on the quarter-mounts with a blue/black indelible pen. Figure 7 shows photomicrographs of a tissue slice through a tumor region [Fig. 7(a)] and through a nontumor region [Fig. 7(b)] using a light microscope at low to intermediate power. Histological findings were used as the gold standard to manually identify cancerous and noncancerous ROIs. Parallel and sequential whole-mount digital images served to manually identify cancerous and noncancerous ROIs from the 3D B-mode ultrasound images.

IV. RESULTS

Radio-frequency data from the identified cancerous ROIs as well as data from the noncancerous ROIs were analyzed with our 2D spectrum method. The 2D spectra were radially and angularly integrated to obtain compact RISP and AISP spectral curves. Four spectral parameters were calculated from the spectral curves: slope and intercept of AISP, 3 dB width, and peak value of RISP. In this pilot study of four patients, we analyzed 24 cancerous regions and compared them with 24 noncancerous regions. Each of the four prostates was sampled equally (six cancerous regions and six noncancerous regions per prostate). Each region was approximately $4 \times 4 \text{ mm}^2$ and was selected by a physician based on the histology cancer map (Fig. 6). Significant differences were found in three 2D spectral parameters: peak value of RISP, slope, and intercept of AISP (Table II), but were not found in 3 dB width of RISP.

TABLE II. 2D spectrum results for 24 cancerous vs. 24 noncancerous regions.

2D spectral parameters	Non-CA regions	CA regions
Peak value of RISP (dB)	23 ± 1	26 ± 1
3 dB of RISP (degree)	7.8 ± 0.5	7.6 ± 0.6
Slope of AISP (dB/MHz)	-2.1 ± 0.2	-2.7 ± 0.4
Intercept of AISP (dB)	92 ± 5	112 ± 6

TABLE III. Features of 1D and 2D spectrum analysis for UTC.

1D spectral parameters	2D spectral parameters
Slope	peak value of RISP
Intercept	3 dB of RISP
Midband value	Slope of AISP
	intercept of AISP

V. DISCUSSION

The ultimate goal of the study was to develop a noninvasive and reliable UTC technique to detect prostate cancer. Our investigations were provoked by the high incidence of prostate cancer and inadequacy of conventional medical imaging in prostate-cancer diagnosis. Investigators at Riverside Research Institute used 1D spectral parameters: slope (dB/MHz), intercept (extrapolation to 0 MHz), and midband value (dB value at the center frequency of the linear fit) of the 1D power spectrum linear regression (Table III) as well as PSA to distinguish cancerous from noncancerous prostatic tissues. This technique is a marked improvement over conventional medical imaging but is unable to differentiate asymmetric tissue microstructures such as cylindrical or planar scatterers. Our 2D technique improves upon 1D spectrum analysis by providing lateral properties as well as axial properties of tissue microstructures, thereby supplying more diagnostic information.

We demonstrated the clinical feasibility of our 2D spectrum technique as a tool for prostate-cancer detection and localization. Our clinical study was guided by the 2D spectrum theoretical model and analytical tools described at length in our previous reports as well as summarized above.^{24,25} Four 2D spectral parameters were investigated for quantitative assessment of the prostatic tissue: peak value and 3 dB width of the RISP, slope, and intercept of the AISP. We employed a ROI approach for tissue characterization; each ROI measured $4 \times 4 \text{ mm}^2$ in the axial and lateral dimensions, respectively. 24 cancerous ROIs within the prostate were compared with 24 benign ROIs showing differences in peak value of the RISP, slope of the AISP, and intercept of the AISP. No significant difference, however, was found in the 3 dB width of the RISP.

Despite a small initial patient number, the clinical results are encouraging. With the ability to differentiate asymmetric microstructures, 2D UTC may not only be capable of distinguishing cancerous from noncancerous tissues but also has the potential to distinguish aggressive from slow-growing prostate cancers (cancers of divergent Gleason grades). The four patients enrolled in our preliminary study were all diagnosed with prostate cancer of Gleason grade 7 (Table I). In future population-based studies, we will investigate cancerous prostatic tissues of variant Gleason grades and determine 2D UTC's ability to detect differentiation.

Our 2D spectrum technique was investigated as a noninvasive tool for cancer detection; nevertheless, it has the potential to provide a means of monitoring cancer progress/regression in patients treated for prostate cancer by

nonsurgical means, e.g., radiation therapy.²⁰ In addition, our technique could provide physicians with a manner to assess efficacy of different therapeutic procedures. Ongoing research is focused in the following areas: (1) expanding the patient database, (2) improving calibration to account for the cross-range direction, and (3) determining optimal ultrasound parameters for prostate-cancer diagnosis.

VI. CONCLUSIONS

Advanced ultrasonic tissue characterization techniques have shown promise in prostate-cancer detection. In this study, we explored a novel 2D spectrum analysis method to differentiate benign- from malignant-prostatic tissue. This method provides more information regarding tissue acoustic properties than the current 1D spectrum technique. We demonstrated the potential of 2D spectrum analysis for prostate-cancer diagnosis and its feasibility in the clinic. The ability to noninvasively quantify tumor-bearing regions within the prostate gland will ultimately lead to better evaluation and optimization of prostate-cancer diagnosis and treatment.

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