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Two dimensional penile ultrasound vibro-elastography for measuring penile tissue viscoelasticity: A pilot patient study and its correlation with penile ultrasonography

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ABSTRACT

The purpose of this research is to demonstrate the feasibility of a 2 dimensional (2D) penile ultrasound vibro-elastography (PUVE) technique for measuring the shear wave speed map over an area of regional of interest (ROI) in the penis. In PUVE, a 0.1 s harmonic vibration at a low frequency is generated on the surface of the penis using a handheld vibrator. An ultrasound probe is used to measure the resulting shear wave propagation in the penis. The shear wave speed is analyzed in the ROI of corpus cavernosum from both sides of penis using a 2D wave speed analysis technique. The shear wave speed of the penis is measured at three excitation frequencies of 100 Hz, 150 Hz, and 200 Hz. The viscoelasticity of penis is analyzed based on the wave speed dispersion with frequency. A pilot study was performed in men with ED and/or PD. It is found that both elasticity and viscosity of corpus cavernosa positively correlate with the peak systolic velocity (PSV) from penile ultrasonography. Both elasticity and viscosity of corpus cavernosa negatively correlate with the cardiovascular (CV) risk for patients with ED and/or PD. These results suggest that PUVE may provide a noninvasive and painless technique for assessing patients with ED/PD and their future CV risk. We will further evaluate PUVE in a large cohort of patients with ED/PD.

1. Introduction

Erectile dysfunction (ED) is recognized as an important marker of overall health, as it is commonly associated with medical comorbidities, including cardiovascular disease, and diabetes mellitus, among others (Rosenet al., 2004). ED is estimated to occur in 52% of men aged 40–70 years (Feldman et al., 1994). The pathogenesis of ED is often multifactorial, and it commonly results from changes in penile corporal smooth muscle and endothelial cells. The ratio of collagen to smooth muscle often increases in men with ED, resulting in corporal fibrosis, and eventual veno-occlusive dysfunction (Mulhallet al., 2002). Peyronie's disease (PD) represents another condition associated with penile fibrosis that occurs in 0.4–13% of men (Dibenedetti et al., 2011; Lindsay et al., 1991). PD is associated with fibrotic plaque formation in the tunica albuginea of the penis resulting in penile morphologic changes, including curvature, indentation, hourglass deformities, or other similar findings (Kadioglu et al., 2002; Rhoden et al., 2010; Chung et al., 2012).

Penile ultrasonography provides objective, minimally invasive, and relative inexpensive assessments of penile characteristics, including vascular parameters and structural abnormalities (Smithet al., 2009). During the procedure, an artificial erection is typically induced using a vasoactive medication, such as prostaglandin. Penile ultrasonography is then used to identify areas of arterial obstruction or venous leak (Lewis, 1988). Penile ultrasonography provides broad assessments of penile vascular state, however, unable to provide measurement of penile tissue stiffness.

We have developed a novel penile ultrasound vibro-elastography (PUVE) technique for noninvasively measuring viscoelasticity of the corpus cavernosum of the penis (CCP) (Zhang et al., 2018a). In PUVW, a 0.1-s harmonic vibration was generated on the penis using a handheld shaker. An ultrasound probe was used to measure the resulting shear wave propagation in the penis. The shear wave speed was measured over a length of about 8 mm. It was found that both elasticity and viscosity moduli were significant higher at the erectile state after erectogenic

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injection than those at the baseline state before injection. Baseline viscoelasticity measures also significantly correlated with the volume of erectogenic medication required to achieve an erection. As erectogenic medications likely represent the most accurate measure of erectile function, these findings suggest a potential role for PUVE as a viable diagnostic modality for ED.

The purpose of this research was to measure the shear wave speed map over an area of regional of interest (ROI) in the penis. The shear wave speed is analyzed in the ROI of corpus cavernosum of penis using a 2D wave speed analysis technique. The viscoelasticity of penis is analyzed based on the wave speed dispersion with frequency. The correlation of PUVE measurements including elasticity and viscosity with penile ultrasonography measurements was analyzed. In addition, the correlation of PUVE measurements with cardiovascular (CV) risk was analyzed.

2. Material and method

Following approval by the Mayo Clinic Institutional Review Board (IRB), ten men were recruited from a sexual medicine clinic in the Department of Urology. All patients had previously been selected to undergo a penile ultrasound based on clinical assessment for suspected end-stage erectile dysfunction or Peyronie's disease. Once informed consent was obtained, the participant was placed on an examination bed in the supine position. At this point, PUVE was performed on each side of the penis, with three assessments each obtained on the right and left corpora cavernosa. Assessments were specifically obtained of the corporal tissue and not of the tunica albuginea. Following baseline assessments, men underwent repeated intracavernosal injections with a vasoactive compound (alprostadil 10 μg/ml, papaverine 30 mg/ml, phentolamine 1 mg/ml) until a fully rigid erection was achieved or a maximum of 1 ml administered. At that point, repeat PUVE assessments were performed in a similar manner to the baseline testing, and then a traditional penile ultrasound was conducted.

A 0.1-s harmonic vibration was generated on the penis using a small indenter of the handheld shaker (Model: FG-142, Labworks Inc., Costa Mesa, CA, USA) (Zhou et al., 2017a; Zhang et al., 2018b; Zhanget al., 2017; Zhou et al., 2019a). The indenter of shaker is only used for generating wave propagation. We keep the duration of excitation 0.1 s for all frequencies. For example, a 0.1 s 100 Hz signal of 10 cycles generates and measures wave speed at 100 Hz. A high pulse repetition rate of 2000 frame/s was used to detect tissue motion in response to the vibration excitation at 100, 150 and 200 Hz. Therefore, we measured 200 frames (0.1 s) wave propagation for each frequency.

The indenter was located at a region away from any penile plaques (if present) on the lateral aspect of the penis and aiming to the contralateral side. The excitation force from the indenter of the shaker was much less than 1 N and the subject only felt a small vibration on his penis. Since the force is very gentle, it should not affect the results. One of the advantages is that we do not need to quantify the excitation force. The wave speed measurement is independent of excitation or location of excitation. The wave speed is dependent of local tissue elastic properties. This in contrast of other techniques, such as durometer (Kissinet al., 2006; Merkelet al., 2008), the measurements are typically dependent on probe size and interaction of probe and skin.

An ultrasound probe was positioned about 5 mm away from the indenter to measure the resulting shear wave propagation in the penis. In this research, 3 exciting frequencies were used to measure the shear waves at 100, 150 and 200 Hz. The excitation signal at a frequency was amplified by an audio amplifier (Model D150A, Crown Audio Inc., Elkhart, IN, USA). The handheld shaker applies a local excitation on the penis through an indenter with 3 mm diameter (Kuboet al., 2018a). A Verasonics ultrasound system (Verasonics V1, Verasonics, Inc., Kirkland, WA, USA) with an ultrasound probe of L11-4 with a central frequency of 6.4 MHz was used. The Verasonics ultrasound system can collect up to a few thousand imaging frames per second by using a plane-wave pulse transmission method (Chenget al., 2018/06; Kuboet al., 2018b), (Zhou et al., 2019b). The measurement of shear wave speed in the penis was independent of the location and amplitude of excitation. A small tissue motion in tens of μm was enough for sensitive ultrasound detection of the generated tissue motion. The tissue motion velocity was in response of the external vibration excitation induced by the handheld vibrator.

The radio-frequency (RF) data of ultrasound echo from the tissues are obtained. By demodulation of the RF data using quadrature detection, the in-phase/quadrature (IQ) data of ultrasound signals are processed. The IQ data consist of 2D intensity information for the duration of the vibration excitation. Particle velocity in the axial direction (V) caused by wave propagation is used for wave speed estimation. V is calculated from IQ data of consecutive frames using a one-dimensional autocorrelation method (Zhang et al., 2018a; Kasai et al., 1985).

Wave speed measurement is performed by cross-correlating two particle velocities from two imaging pixels (denoted by $v\left(m-\frac{w}{2},n,t\right)$ and $v\left(m+\frac{w}{2},n,t\right)$), where m is the lateral dimension, n is the axial dimension, t is the slow time dimension, and w is the window size that are a fixed distance apart which is equal to window size w, to estimate the wave speed of the pixel at location (m, n) (Tanteret al., 2008). The normalized cross-correlation coefficient of each pixel in the lateral direction (CC_x) is calculated by (Pinton et al., 2006),

$$CC_x(j)=\frac{\sum_{i=-M/2}^{M/2}\left[v\left(m-\frac{w}{2},n,i\right)-\bar{v}\left(m-\frac{w}{2},n\right)\right]\left[v\left(m+\frac{w}{2},n,i+j\right)-\bar{v}\left(m+\frac{w}{2},n\right)\right]}{\sqrt{\sum_{i=-M/2}^{M/2}\left[v\left(m-\frac{w}{2},n,i\right)-\bar{v}\left(m-\frac{w}{2},n\right)\right]^2\sum_{i=-M/2}^{M/2}\left[v\left(m+\frac{w}{2},n,i+j\right)-\bar{v}\left(m+\frac{w}{2},n\right)\right]^2}} \quad (1)$$

where M is number of wave signal data points along slow time direction. A directional filter in the lateral direction is then applied upon the correlation coefficient field to extract the correlation coefficient peak. Temporal delay (Δt) between the two pixel velocities in the lateral direction is then given by, $\Delta t=\left[\frac{arg_j maxCC(j)}{PRF}\right]$, where PRF is the pulse repetition frequency. PRF is 2000 in our study. Local wave speed of the center pixel at location (m, n) is given by,

$$c_x(m,n)=\frac{w\cdot\Delta x}{\Delta t} \quad (2)$$

where $\Delta x=\frac{c}{f}$ is the spatial resolution of the imaging pixels. Same technique is used to calculate correlation coefficient ($CC_z(m,n)$) and wave speed of each pixel in the axial direction ($c_z(m,n)$).

In order to increase the robustness of the 2D wave speed calculation while preserving the spatial resolution of the wave speed map, a 2D processing window technique is used (Anderssen and Hegland, 1999; Song et al., 2014). In the 2D window processing technique, all pixels within the 2D window are used to estimate wave speeds along the axial and lateral directions, respectively. A sliding patch of size p that is

smaller than the window size w is used to calculate normalized cross-correlations between each pair of wave signals at spatial locations that are p pixels apart. A window size of 12 and patch size of 9 are used throughout this study. The 2D wave speed c at the center pixel (m,n) can be calculated by,

$$c = \frac{c_X c_Z}{\sqrt{c_X^2 + c_Z^2}} \tag{3}$$

The correlation coefficient of the center pixel *CC* (m,n) is calculated by the minimum of CC_x and CC_z, where CC_x and CC_z are the average of all normalized correlation coefficients along the lateral and axial directions. Via iterating the calculations through all imaging pixels, a 2D wave speed map and correlation-coefficient map can be obtained.

The measurement of wave speeds at multiple frequencies enables calculation of both elasticity μ_1 and viscosity μ_2 using the Voigt model (Zhang et al., 2018a), (Zhang and Greenleaf, 2007; ZhangOsborn et al., 2011),

$$c = \sqrt{\frac{2(\mu_1^2 + \omega^2\mu_2^2)}{\rho\left(\mu_1 + \sqrt{\mu_1^2 + \omega^2\mu_2^2}\right)}}, \tag{4}$$

where ω is the angular frequency, μ_1 is shear elasticity and μ_2 is viscosity. The shear wave speeds are typically measured in a frequency band between 100 Hz and 200 Hz according to our experience in various tissue applications. The 100 Hz wave motion is stronger than the wave motion of higher frequency waves. The higher frequency waves have smaller wave length but decay rapidly over distance than the lower frequency waves. The frequency ranges chosen in this study consider the wave motion amplitude, spatial resolution and wave attenuation. By measuring the wave speeds at three frequencies, μ_1 and μ_2 are estimated from Eq. (4) with a nonlinear least-squares fitting technique (ZhangOsborn et al., 2011).

Statistical analyses included matched pairs analysis, linear regression, and logistic regression where appropriate. Statistical significance was set at 0.05, and tests were two-sided where appropriate.

3. Results

Fig. 1 shows the shear wave speed imaging at 100 Hz overlaid the ultrasound B-mode imaging. A region of interest (ROI) of 5 mm × 15 mm was selected to analyzed the shear wave speed in the corpus cavernosum. Three measurements were made for each frequency and at each location. The penis was measured on both the left and right sides. A comparison of wave speeds for ten patients with ED or PD before and after the injection is shown in Fig. 2 for both sides of penis at 100 Hz, 150 Hz, and 200 Hz. One patient did not undergo testing pre-injection and only had post-injection data available. An unpaired, two-tailed *t*-test between the baseline (before) and after injections was conducted to compare the sample means. Differences in mean values were considered significant when $p < 0.05$. The p-values for the *t*-test were less than 0.05 for both sides of the penis and three frequencies.

Fig. 3 shows the comparison of elasticity and viscosity for 10 patients before and after the injections. The p-values for the *t*-test were less than 0.05 for both sides of penis. Therefore, the magnitudes of both elasticity and viscosity of patients were statistically higher after the injection than the baseline.

After the injection of medicine and at the erectile state, Fig. 4 shows a measurement of an in-plane cavernosal artery. The peak systolic velocity (PSV) is 62.3 cm/s (normal >25–30), end-diastolic velocity (EDV) is -13.0 cm/s (normal <5), and resistive index (RI) is 1.21 (normal >0.8). Table 1 shows the correlation coefficients between elasticity μ1, viscosity μ2, wave speeds at 100 Hz, 150 Hz, 200 Hz with PSV, EDV, and RI for both the right and left sides of penile measurements in the erect state. Fig. 5 show the linear correlation of μ1and viscosity μ2 with PSV, EDV, and RI in the erect state.

Erectile dysfunction (ED) and cardiovascular (CV) disease share many risk factors, and their pathophysiology is mediated through endothelial dysfunction. Cardiovascular disease is the cause of ED in many men. Also, men who present with ED are at higher risk for subsequent development of cardiovascular events. Endothelial dysfunction, an early predictor of atherosclerosis, plays a major role in ED causation. While it is rare for man with ED to have penile artery atherosclerosis, penile artery endothelial dysfunction is common and when present, is a significant risk factor for the onset of symptomatic cardiovascular disease events. In addition, lifestyle changes aimed at improving cardiovascular risk have also been shown to reduce ED (Gupta et al., 2011). The cardiovascular (CV) risk is assessed for these ED patients according to the consensus in (Nehraet al., 2012). Table 2 shows the correlation coefficients between elasticity μ1, viscosity μ2, and wave speeds at 100 Hz, 150 Hz, 200 Hz with cardiovascular (CV) risk after injection (erect state) and before injection (baseline), respectively. Fig. 6 shows the correlation of elasticity μ1 (a) and viscosity μ2 (b) with CV risk before injection (baseline). A negative correlation between μ1and viscosity μ2 with CV risk is noted in both the flaccid (baseline) and erect states. One potential clinical utility of this information is the ability to assess CV risk

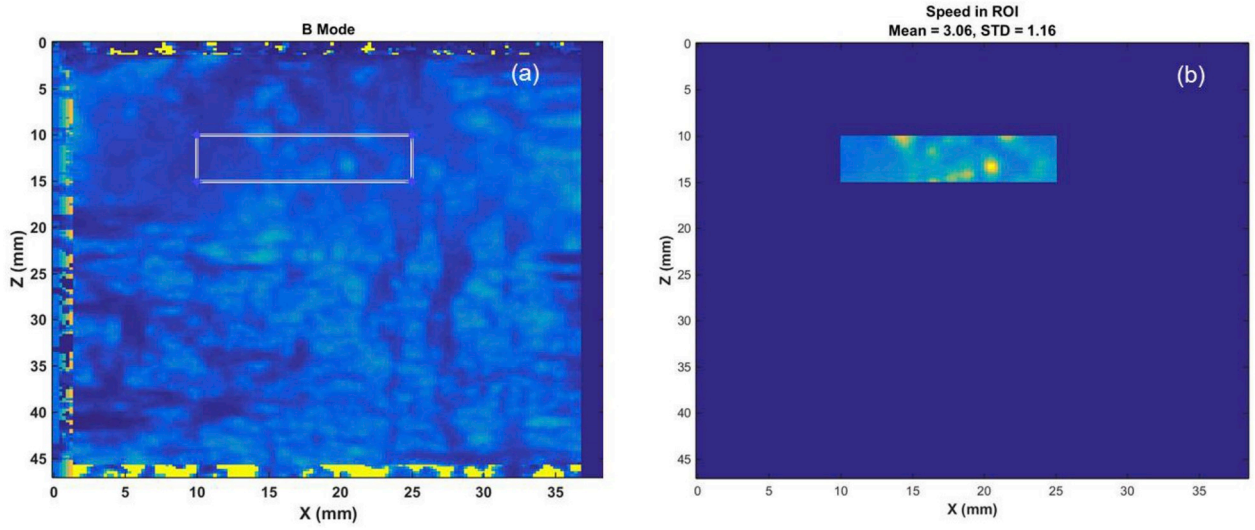

Fig. 1. (a) The shear wave speed imaging at 100 Hz overlaid the ultrasound B-mode imaging. A region of interest (ROI) of 5 mm × 15 mm is selected to analyzed the shear wave speed in the penis; (b) The corresponding shear wave speed imaging in the ROI.

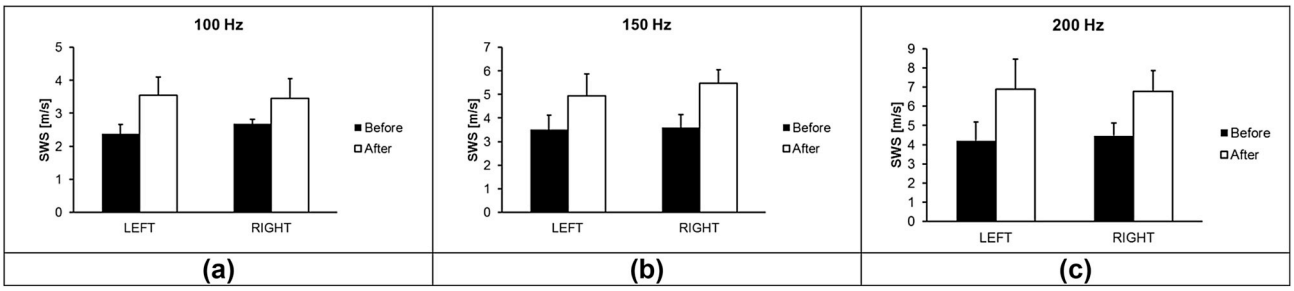

Fig. 2. Comparison of wave speeds for patients before and after injections at both sides of penis. Wave speeds at (a) 100 Hz, (b) 150 Hz, (c) 200 Hz.

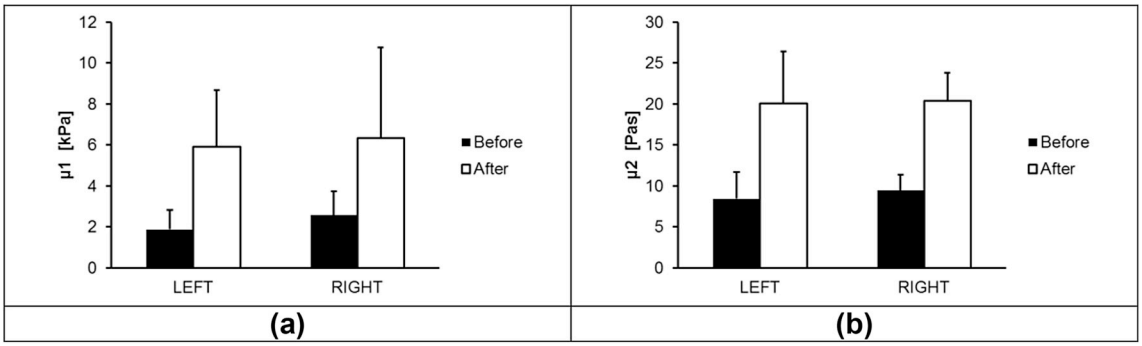

Fig. 3. Comparison of elasticity μ1 (a) and viscosity μ2 (b) before and after injection at both sides of penis.

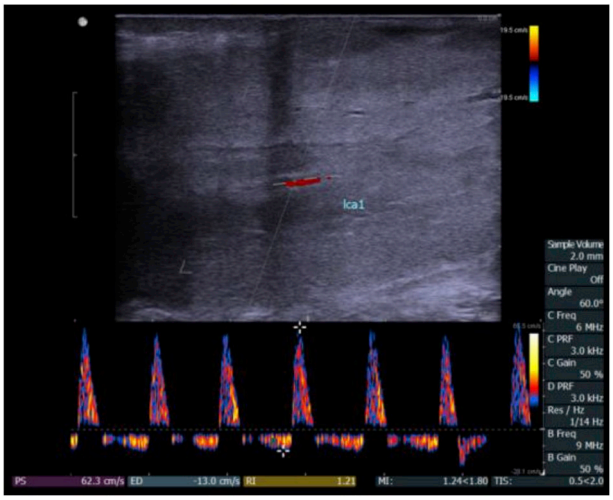

Fig. 4. Penile ultrasound measurement of an in-plane cavernosal artery. PSV is 62.3 cm/s, the ED is -13.0 cm/s, and the RI is 1.21.

Table 1
Correlation coefficients between elasticity μ1, viscosity μ2, and wave speeds at 100 Hz, 150 Hz, 200 Hz and PSV, EDV, and RI bilaterally in the erect state.

Right penis		PS	ED	RI
	u1	0.72	-0.05	0.14
	u2	0.42	-0.24	0.31
	Wave speed at 100 Hz	0.65	-0.08	0.11
	Wave speed at 150 Hz	0.56	0.29	-0.23
	Wave speed at 200 Hz	0.66	-0.10	0.24
Left penis		PS	ED	RI
	u1	0.86	0.87	-0.90
	u2	0.44	0.47	-0.48
	Wave speed at 100 Hz	0.80	0.41	-0.47
	Wave speed at 150 Hz	0.84	0.66	-0.67
	Wave speed at 200 Hz	0.66	0.33	-0.36

without need for erectogenic medication administration.

4. Discussion

The current study validates the potential role for a novel PUVE method. The obtained results in our study showed positive correlation between viscoelasticity, wave speeds with PSV on penile ultrasonography. Doppler sonography with clinically accepted parameters in terms of peak-systolic and end-diastolic velocities and resistance index, provide data of vascular state (Gillon and Barnea, 2002; Borowitz and Barnea, 2000). Evaluation of erectile dysfunction using both strain elastography and Doppler sonography has been conducted (Jain et al., 2015). PD was diagnosed using ultrasound shear wave elastography (SWE) by Richards (Richards et al., 2014). In this study, the results demonstrated that sonoelastography is useful when palpation and B-mode ultrasonography are unable to show a plaque and patient benefit from the local injections made to the lesion region. The relationship between corpus cavernosum rigidity obtained using shear wave elastography and age has also been investigated (Inci et al., 2017; Zhanget al., 2015). They used Young's modulus to characterize the penile stiffness and showed contradictive results in the relationship between SWE and age. In our study, we use both elasticity and viscosity to characterize the elastic properties of penile tissue, providing more measures for evaluating the corpus cavernosum rigidity.

Shear wave elastography (SWE) use ultrasound radiation force (URF) to generate tissue motion. URF is a physical phenomenon resulting from the interaction of an acoustic wave with an obstacle placed along its path. URF may be generated by the interaction of ultrasound waves, for example, using two focused ultrasound beams with a lightly two different frequencies (Zhang et al., 2005). To generate sufficient tissue motion using URF, a high-intensity ultrasound field is needed. Although URF has been widely used in many organs—including the liver, URF should not be applied to some vulnerable organs such as lung and eye. For example, the relatively high-intensity ultrasound field can cause alveolar hemorrhage or injury (Zachary et al., 2006). Because the eye is vulnerable to thermal and mechanical damage from excessive ultrasonic

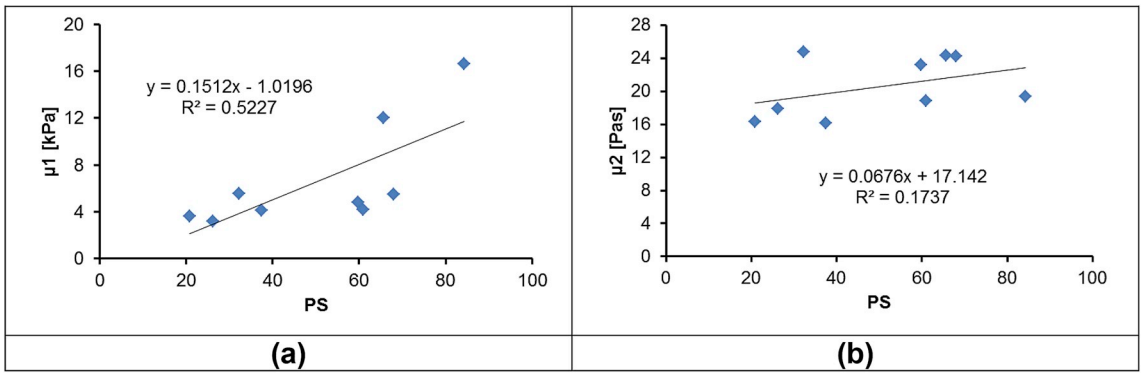

Fig. 5. Correlation of elasticity μ1 (a) and viscosity μ2 (b) with the peak systolic velocity (PSV).

Table 2
Correlation coefficients between elasticity μ1, viscosity μ2, wave speeds at 100 Hz, 150 Hz, 200 Hz and cardiovascular disease risk after injection (erect state) and before injection (flaccid - baseline).

Erect state	CV Risk	Baseline	CV Risk
u1	-0.56	u1	-0.01
u2	-0.53	u2	0.01
Wave speed at 100 Hz	-0.47	Wave speed at 100 Hz	0.21
Wave speed at 150 Hz	-0.39	Wave speed at 150 Hz	-0.11
Wave speed at 200 Hz	-0.25	Wave speed at 200 Hz	0.07

energy, the FDA and World Federation for Ultrasound in Medicine and Biology (WFUMB) have imposed strict thermal (TI) and mechanical index (MI) limits for ocular application (TI < 1.0, MI < 0.23) (Barnett et al., 2000). In addition, long periods of ultrasound pulses with relatively high-intensity ultrasound energy may damage the ultrasound system, e.g., probe element damage.

In PUVE, wave generation is safely produced using a gentle mechanical vibration on the skin. Diagnostic ultrasound is only used for detection of wave propagation. Therefore, PUVE is safe and can be used for the lung (Zhanget al., 2017) and eye (Zhou et al., 2017b). PUVE can easily and safely generate large tissue wave propagation in a large area of the penis than URF. PUVE in this study, however, was performed by safely generating a local mechanical vibration on the penile tissue while diagnostic ultrasound was only used to detect wave propagation of the penile tissue. Hence, PUVE represents a potentially safer option for screening erectile function.

PUVE provides accurate measurement of wave speed at each frequency. For example, a 0.1 s 100 Hz signal of 10 cycles generates and measures wave speed at 100 Hz. PUVE provides much higher signal to noise ratios (SNRs) for wave speed measurement compared with SWE, which uses a short pulse of ultrasound push for generating the shear wave in the tissue. PUVE provides much stronger wave generation than SWE, but the mechanical generation is safe and simple. In PUVE, we measure surface wave speeds at 100 Hz, 150 Hz, and 200 Hz. We can estimate tissue elasticity and viscosity. PUVE may be used to study both surface tissue such as skin (Zhang et al., 2018c)and lung surface and inside tissue such cornea in the eye (Sit et al., 2017). The surface wave is used to study the surface tissue, and the shear wave is used to study the internal tissue.

The current study has several notable limitations. The sample size is small and represents pilot data only. These patients with ED and/or PD are clinically confirmed with a comprehensive sexual, medical and psychosocial history, validated sexual function questionnaires, and a thorough physical examination. Penile ultrasonography is an additional test that is often performed in select cases of ED or PD. Physicians look at parameters such as the peak systolic velocity (PSV), end-diastolic velocity (EDV), and resistive index (RI) to see if penile ultrasonography provide useful information. In this pilot study, we can only see positive correlations between elasticity and viscosity with the PSV. Further study is needed for a large number of patients. As such, all findings require further study and validation prior to acceptance and routine implementation. The population assessed is also very heterogeneous, as penile ultrasounds are only recommended in our practice in certain clinical scenarios (i.e. PD, severe ED, or if the patient specifically requests). As PD and ED represent very distinct conditions, these differences in our study cohort may have impacted outcomes. Despite these limitations, the current study demonstrates several potential strengths. This is the first study to specifically correlate penile tissue viscoelasticity with penile ultrasonography measurements. It was demonstrated that both elasticity μ1 and viscosity μ2 increase with the peak systolic velocity (PSV). Additionally, it is the first to correlate elasticity μ1 and viscosity μ2 with the CV risk at the baseline and erect states. This is important because we may evaluate the CV risk for patients with ED/PD non-invasively and painless (at baseline state) and no erectile medicine is

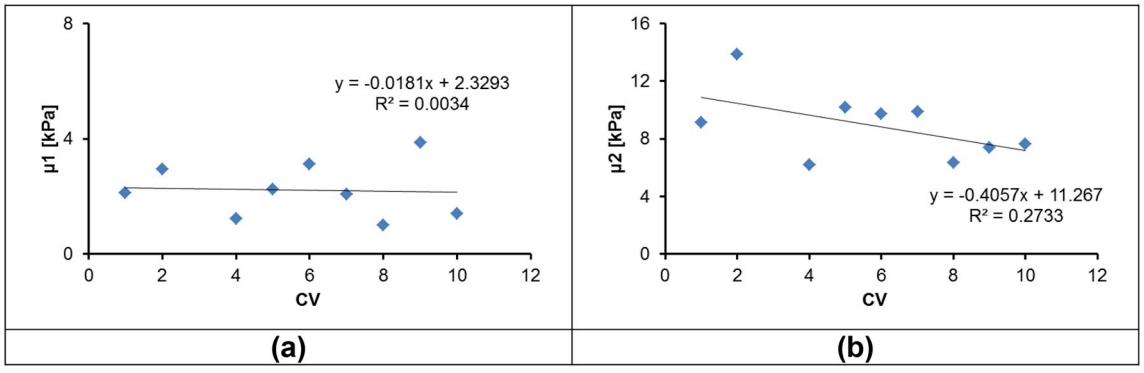

Fig. 6. Correlation of elasticity μ1 (a) and viscosity μ2 (b) with cardiovascular disease risk before injection (flaccid - baseline).

needed. We will further study these correlations by studying a large cohort of patients.

5. Conclusions

The purpose of this research is to demonstrate the feasibility of a 2D penile ultrasound vibro-elastography (PUVE) technique for assessing patients with ED/PD. It is found that both elasticity and viscosity positively correlate with the peak systolic velocity (PSV) from penile ultrasonography. Both elasticity and viscosity negatively correlate with the CV risk. These results suggest that PUVE may provide a noninvasive and painless technique for assessing patients with ED/PD and their future CV risks. We will further evaluate TUVE in a large cohort of patients with ED/PD.

Declaration of competing interest

There are no conflicts of interest.

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References

Anderssen, R., Hegland, M., 1999. For numerical differentiation, dimensionality can be a blessing! Math. Comput. Am. Math. Soc. 68 (227), 1121–1141.
Barnett, S.B., Ter Haar, G.R., Ziskin, M.C., Rott, H.D., Duck, F.A., Maeda, K., Mar 2000. International recommendations and guidelines for the safe use of diagnostic ultrasound in medicine. Ultrasound Med. Biol. 26 (3), 355–366.
Borowitz, E., Barnea, O., 2000. Hemodynamic mechanisms of penile erection. IEEE Trans. Biomed. Eng. 47 (3), 319–326.
Cheng, Y.-S., et al., 2018/06/06/2018. Comparison of two ways of altering carpal tunnel pressure with ultrasound surface wave elastography. J. Biomech. 74, 197–201.
Chung, E., Yan, H., De Young, L., Brock, G.B., Oct 2012. Penile Doppler sonographic and clinical characteristics in Peyronie's disease and/or erectile dysfunction: an analysis of 1500 men with male sexual dysfunction. BJU Int. 110 (8), 1201–1205.
Dibenedetti, D.B., Nguyen, D., Zografos, L., Ziemiecki, R., Zhou, X., 2011. A population-based study of Peyronie's disease: prevalence and treatment patterns in the United States. Adv. Urol. 2011, 282503 (in eng).
Feldman, H.A., Goldstein, I., Hatzichristou, D.G., Krane, R.J., McKinlay, J.B., Jan 1994. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. J. Urol. 151 (1), 54–61.
Gillon, G., Barnea, O., 2002. Erection mechanism of the penis: a model based analysis. J. Urol. 168 (6), 2711–2715.
Gupta, B.P., Murad, M.H., Clifton, M.M., Prokop, L., Nehra, A., Kopecky, S.L., Nov 14 2011. The effect of lifestyle modification and cardiovascular risk factor reduction on erectile dysfunction: a systematic review and meta-analysis. Arch. Intern. Med. 171 (20), 1797–1803.
Inci, E., Turkay, R., Nalbant, M.O., Yenice, M.G., Tugcu, V., 2017. The value of shear wave elastography in the quantification of corpus cavernosum penis rigidity and its alteration with age. Eur. J. Radiol. 89, 106–110.
Jain, V., Yadav, S., Jaipal, U., Tomar, V., 2015. Role of elastography in evaluation of erectile dysfunction and its comparison with colour Doppler-pilot study. Int. J. Sci. Res. 4 (11), 402–405.
Kadioglu, A., Tefekli, A., Erol, B., Oktar, T., Tunc, M., Tellaloglu, S., Sep 2002. A retrospective review of 307 men with Peyronie's disease. J. Urol. 168 (3), 1075–1079 (in eng).
Kasai, C., Namekawa, K., Koyano, A., Omoto, R., 1985. Real-time two-dimensional blood flow imaging using an autocorrelation technique. IEEE Trans. Son. Ultrason. 32 (3), 458–464.
Kissin, E.Y., et al., Aug 15 2006. Durometry for the assessment of skin disease in systemic sclerosis. Arthritis Rheum. 55 (4), 603–609.
Kubo, K., et al., Jan 2018. Ultrasound elastography for carpal tunnel pressure measurement: a cadaveric validation study. J. Orthop. Res. : Off. Publ. Orthop. Res. Soc. 36 (1), 477–483 (in eng).
Kubo, K., et al., Jan 3 2018. The quantitative evaluation of the relationship between the forces applied to the palm and carpal tunnel pressure. J. Biomech. 66, 170–174.
Lewis, R.W., Feb 1988. Venous surgery for impotence. Urol. Clin. N. Am. 15 (1), 115–121.
Lindsay, M.B., Schain, D.M., Grambsch, P., Benson, R.C., Beard, C.M., Kurland, L.T., Oct 1991. The incidence of Peyronie's disease in Rochester, Minnesota, 1950 through 1984. J. Urol. 146 (4), 1007–1009 (in eng).
Merkel, P.A., et al., May 15 2008. Validity, reliability, and feasibility of durometer measurements of scleroderma skin disease in a multicenter treatment trial. Arthritis Rheum. 59 (5), 699–705.
Mulhall, J.P., et al., Mar 2002. Erectile dysfunction after radical prostatectomy: hemodynamic profiles and their correlation with the recovery of erectile function. J. Urol. 167 (3), 1371–1375 (in eng).
Nehra, A., et al., Aug 2012. The Princeton III Consensus recommendations for the management of erectile dysfunction and cardiovascular disease. Mayo Clin. Proc. 87 (8), 766–778.
Pinton, G.F., Dahl, J.J., Trahey, G.E., 2006. Rapid tracking of small displacements with ultrasound. IEEE Trans. Ultrason. Ferroelectr. Freq. Control 53 (6), 1103–1117.
Rhoden, E.L., Riedner, C.E., Fuchs, S.C., Ribeiro, E.P., Halmenschlager, G., Apr 2010. A cross-sectional study for the analysis of clinical, sexual and laboratory conditions associated to Peyronie's disease. J. Sex. Med. 7 (4 Pt 1), 1529–1537 (in eng).
Richards, G., Goldenberg, E., Pek, H., Gilbert, B.R., 2014. Penile sonoelastography for the localization of a non-palpable, non-sonographically visualized lesion in a patient with penile curvature from P eyronie's disease. J. Sex. Med. 11 (2), 516–520.
Rosen, R.C., et al., May 2004. The multinational Men's Attitudes to Life Events and Sexuality (MALES) study: I. Prevalence of erectile dysfunction and related health concerns in the general population. Curr. Med. Res. Opin. 20 (5), 607–617.
Sit, A.J., Lin, S.C., Kazemi, A., McLaren, J.W., Pruet, C.M., Zhang, X., Aug 28 2017. In vivo non-invasive measurement of Young's modulus of elasticity in human eyes: a feasibility study. J. Glaucoma 26 (11), 967–973.
Smith, J.F., et al., Oct 2009. Penile sonographic and clinical characteristics in men with Peyronie's disease. J. Sex. Med. 6 (10), 2858–2867.
Song, P., Manduca, A., Zhao, H., Urban, M.W., Greenleaf, J.F., Chen, S., Jun 2014. Fast shear compounding using robust 2-D shear wave speed calculation and multi-directional filtering. Ultrasound Med. Biol. 40 (6), 1343–1355.
Tanter, M., et al., 2008. Quantitative assessment of breast lesion viscoelasticity: initial clinical results using supersonic shear imaging. Ultrasound Med. Biol. 34 (9), 1373–1386.
Zachary, J.F., Blue Jr., J.P., Miller, R.J., Ricconi, B.J., Eden, J.G., O'Brien Jr., W.D., Nov 2006. Lesions of ultrasound-induced lung hemorrhage are not consistent with thermal injury. Ultrasound Med. Biol. 32 (11), 1763–1770 (in eng).
Zhang, X., Greenleaf, J.F., Nov 2007. Estimation of tissue's elasticity with surface wave speed. J. Acoust. Soc. Am. 122 (5), 2522–2525.
Zhang, X., Kinnick, R.R., Fatemi, M., Greenleaf, J.F., Apr 2005. Noninvasive method for estimation of complex elastic modulus of arterial vessels. IEEE Trans. Ultrason. Ferroelectr. Freq. Control 52 (4), 642–652.
Zhang, X., Zhou, B., Miranda, A.F., Trost, L.W., Jun 2018. A novel noninvasive ultrasound vibro-elastography technique for assessing patients with erectile dysfunction and Peyronie disease. Urology 116, 99–105.
Zhang, X., Zhou, B., Kalra, S., Bartholmai, B., Greenleaf, J., Osborn, T., Feb 2018. An ultrasound surface wave technique for assessing skin and lung diseases. Ultrasound Med. Biol. 44 (2), 321–331.
Zhang, J., et al., 2015. A new method of measuring the stiffness of corpus cavernosum penis with ShearWave™ Elastography. Br. J. Radiol. 88 (1048), 20140671.
Zhang, X., et al., Sep 2017. Lung ultrasound surface wave elastography: a pilot clinical study. IEEE Trans. Ultrason. Ferroelectr. Freq. Control 64 (9), 1298–1304.
Zhang, X., Osborn, T.G., Pittelkow, M.R., Qiang, Kinnick, R.R., Greenleaf, J.F., 2011. Quantitative assessment of scleroderma by surface wave technique. Med. Eng. Phys. 33, 31–37.
Zhou, B., Sit, A.J., Zhang, X., 2017. Noninvasive measurement of wave speed of porcine cornea in ex vivo porcine eyes for various intraocular pressures. Ultrasonics 81 (Suppl. C), 86–92, 2017/11/01/.
Zhou, B., Sit, A.J., Zhang, X., Nov 2017. Noninvasive measurement of wave speed of porcine cornea in ex vivo porcine eyes for various intraocular pressures. Ultrasonics 81, 86–92.
Zhang, X., Zhou, B., Osborn, T., Bartholmai, B., Kalra, S., Oct 1 2018. Lung ultrasound surface wave elastography for assessing interstitial lung disease. IEEE Trans. Biomed. Eng. 66 (5), 1346–1352.
Zhou, B., Bartholmai, B.J., Kalra, S., Osborn, T.G., Zhang, X., Mar 5 2019. Lung US surface wave elastography in interstitial lung disease staging. Radiology 181729.
Zhou, B., Bartholmai, B.J., Kalra, S., Osborn, T.G., Zhang, X., May 2019. Lung US surface wave elastography in interstitial lung disease staging. Radiology 291 (2), 479–484.