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VISCOELASTIC ELASTOGRAPHY BY TORSIONAL WAVES FOR GESTATIONAL DIAGNOSIS

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Resumen
La caracterización ultrasónica y la comprensión de los tejidos blandos se han desarrollado como una herramienta de diagnóstico clínico durante las últimas décadas y han evolucionado a través de diferentes tecnologías. Los recientes avances en las técnicas de sensores de elastografía están permitiendo la cuantificación in vivo y no invasiva de las propiedades mecánicas de los tejidos. Este artículo presenta la base del potencial de los parámetros viscoelásticos como biomarcadores mecánicos de diagnóstico, cubriendo (a) la tecnología de ondas de torsión y sensores para habilitarlos, (b) modelos de propagación de ondas de torsión viscoelásticas y (c) resultados preliminares de pruebas de pacientes.

Palabras clave: elastografía, biomarcadores mecânicos, ondas de torsión, ondas de cizalla.

Abstract
Ultrasonic characterization and understanding of soft tissue have been developed as a clinical diagnostic tool over the last decades and evolved through different technologies. The recent developments in elastography sensor techniques are enabling in vivo and non-invasive quantification of tissues' mechanical properties. This paper presents support of the potential of viscous elastic parameters as diagnostic mechanical biomarkers, covering (a) torsional waves technology, and sensors to enable them, (b) viscoelastic torsional wave propagation models and (c) preliminar patient testing results.

Keywords: elastography, mechanical biomarkers, torsional waves, shear waves.

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1 Introduction

Ultrasonic characterization and understanding of soft tissue have been developed as a clinical diagnostic tool over the last decades and evolved through different technologies: quasi-static, dynamic elastography, based acoustic radiation force: ARFI, vibroacoustography or pSWE, or on direct excitation: sonoelastography and our emerging torsional wave principle. New elastography sensor technologies to characterize soft tissue biomechanics, are bound to endow a new class of biomarkers that quantify the mechanical functionality and abnormalities in the structural architecture of soft tissues are intimately linked to a broad range of pathologies including tumors, atherosclerosis, brain ageing,

gestational disorders, liver fibrosis or osteoarticular syndromes, to name a few. These higher order mechanical parameters may become key discriminating biomarkers since: (1) the physics of wave propagation is explaining how dispersion is a compound expression of the rheological, poroelastic, and microstructural scattering phenomena governed by the complex fibrous multiscale microarchitecture of the stroma, which undergoes characteristic changes during pathologies; and (2) the extreme hyperelasticity that soft tissue exhibits clearly manifests as quantifiable harmonic generation, hypothesized to strongly depend on the unfolding of its collagen fibres, which again controls the tissue's mechanical functionality.

As a practical case study, the WHO estimates that in 2017 approximately 15 million babies will be born preterm, this is, a rate above 1 in 10 newborns [1]. Worldwide, complications of preterm births have supplanted pneumonia as the primary cause of child mortality [1; 2]. While progress is being made in identifying socioeconomic risk factors of preterm birth, the biology of cervical ripening that leads to birth is poorly understood. Currently, there is no clinical tool to quantitatively evaluate the cervical biomechanical state, which in words of Feltovich et al. [3] "…likely contributes to the reason [that] the singleton spontaneous preterm birth rate has not changed appreciably in more than 100 years." Ultrasonic characterization and understanding of soft tissue have been developed as a clinical diagnostic tool over the last two decades [4] and evolved through different elastography technologies.

Towards this problem, we work on enabling new sensor technologies linked to soft tissue dispersive viscoelastic biomechanics, to endow a new class of biomarkers that quantify the mechanical functionality of the cervix, and indeed any soft tissue. Beyond labor disorders, abnormalities in the structural architecture of soft tissues are intimately linked to a broad range of pathologies including tumors, atherosclerosis, liver fibrosis or osteoarticular syndromes.

2 Methods

Existing ultrasonic techniques are restricted to map first order tissue stiffness. In contrast, our recent advances covering (a) torsional waves (shear elastic waves that propagate in quasifluids radially and in depth in a curled geometry), (b) sensors (based on a novel arrangement of concentric sandwiches of piezo- and electro-mechanical elements [5]), (c) propagation models and (d) patient testing, are allowing to quantify the mechanical functionality through relevant parameters beyond linear: dispersive and nonlinear.

Soft tissues are generally assumed to be decomposed into their porous solid phases and their fluid phases. The high fluid content in tissues is combined with the poroelastic structure of the ECM to allow motion between components under load, creating a time delay in the strain and triggering the viscoelastic response. This biphasic nature implies a phase lag between the stress and strain associated with a relaxation time, or in the case of oscillatory mechanical tests, a phase angle. Then it would be advisable to start considering time-dependent effects, since the strain response to load and unload conditions is a function of time, often called the velocity of deformation. During the loading cycle there is dissipation of energy, reflecting the existence of hysteretic effects. At the same time, the strain evolution is slowed to allow the viscous flow to settle. Thus, the duration and rate of loading define the dynamics of the tissue strain. Without this characteristic, the stress during physiological activities would be harmful to the active structure. One of the key features of viscoelastic tissues comes from the physics of wave propagation, where the dispersion is defined as a compound expression of the poroelastic and microstructural media governed by the complex fibrous multiscale microstructure of the stroma [69–72]. It is also known that the amplitude and intensity of waves decays proportionally to the distance traveled. Additionally, in a highly viscous environment, where the microvasculature and hemodynamics

play an important role, it is observed that wave phase velocity changes with frequency, and wave amplitude is affected by geometric factors, such as boundary conditions and the sizes of scattering particles, similar or smaller than the wavelength.

One of the models in the literature most used to fit the parameters is the KV model, due to its simplicity. Other models have been explored, such as Maxwell; fractional derivative versions of the above; and combined models, such as the springpot model. The KV formulation in terms of the stress tensor, assuming constitutive and viscous linearity have been derived with the aim of simplifying equations. Following the references found in the literature,

$$p = 3Kv + 3\eta^{v}\dot{v}$$

$$\tau_{ij} = 2\mu d_{ij} + 2\eta\dot{d}_{ij}$$

where K is the compressional modulus; η and η^{v} are the shear and volumetric viscosities, respectively; and v and d_{ij} are the derivate of the volumetric and deviatoric strains, respectively.

3 Results

The rheological model that best describes the nature of cervical tissue is shown to be the Kelvin Voigt model. The reconstructed viscoelastic parameters, using the selected model are: μepithelial=1.9 kPa, ηepithelial=0.27 Pa s, thepithelial=0.51 mm, μconnective=7.9 kPa, ηconnective=0.13 Pa s. To our knowledge, there are no references to allow comparison with the results obtained in the epithelial and connective layer of cervical tissue. In the literature there is only one reference of the thickness of the vaginal epithelium [6], whose values are close to those inferred in this study.

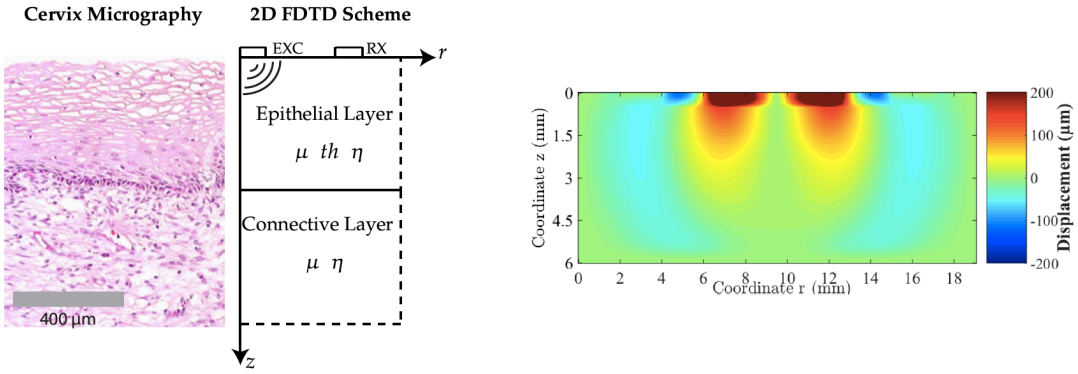

Figure 1: Cervix micrography versus two-dimensional finite difference time domain scheme (left), 2D FDTD model simulation at 1.9 miliseconds using Kelvin-Voigt model (right).

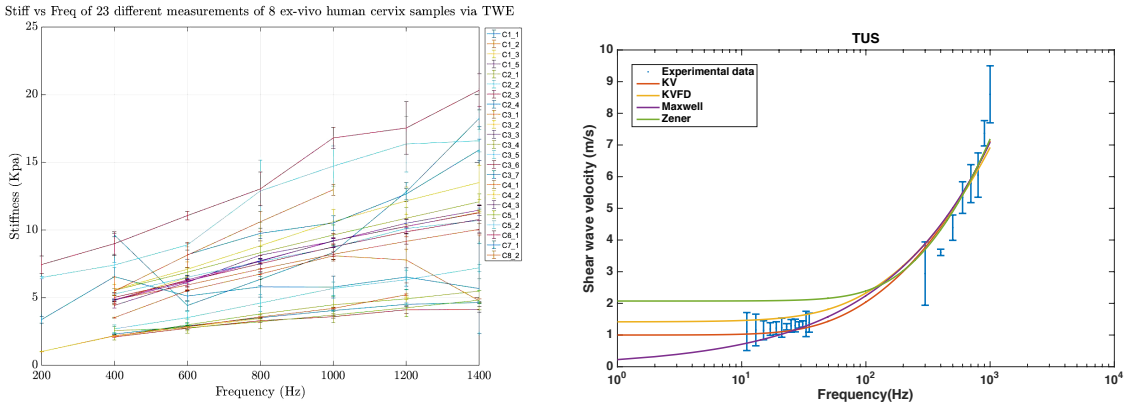

Figure 2: Apparent stiffness dispersion versus frequency for ex-vivo hysterectomy human cervix samples (left), and example of validation of viscoelastic models against rheometry at low frequency (right).

4 Conclusions

New understanding on how structural architecture of soft tissue controls a broad range of pathologies, which underpins the basis for dispersion elastograpghy diagnosis has been presented. New sensor technologies developed ot effectively sense tissue viscoelasticity and yield simple and robust diagnostic tests and instruments are presented. In conclusion, evidence of the diagnostic capability of elastic parameters beyond linear stiffness is gaining momentum as a result of the technological and imaging developments in the field of biomechanics.

Acknowledgements

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