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Anisotropic nonlinear shear elasticity quantification in *ex vivo* muscles

Ha Hien Phuong Ngo¹, Marion Bied¹, Nadia Bahlouli², Ricardo Andrade³,
Antoine Nordez³, Simon Chatelin², Jean-Luc Gennisson¹

¹BioMaps, Université Paris-Saclay, CEA, CNRS, INSERM, Orsay, France,

²ICube, University of Strasbourg, CNRS, Strasbourg, France,

³MIP, University of Nantes, Nantes, France

Abstract — To improve muscle pathology diagnosis or muscle characterization, nonlinear (NL) elasticity assessment could be an essential add-on to better characterize mechanical properties of soft tissues. In ultrasound shear wave elastography, nonlinear elasticity can be evaluated by using the acoustoelasticity (AE) theory. The AE theory was firstly developed and applied to quantify NL elasticity in anisotropic media such as muscles. By carrying out AE experiments on transverse isotropic (TI) Polyvinyl alcohol (PVA) phantom and *ex vivo* muscles, the possibility of estimating TI nonlinear elasticity in biological tissues was demonstrated. In line of this work, a mechanical testing method was used complementary to ultrasound to retrieve the third order NL elastic parameters in *ex vivo* muscles. The mechanical testing method provides the value of Young's modulus parallel to the muscle fibers. Thus, NL elastic coefficients were deduced using the elastodynamic equations and shear moduli retrieved by ultrasound elastography (UE). The results are very repeatable from two *ex vivo* porcine *ilio-psoas* muscles=.

Keywords — *shear wave elastography, nonlinearity, muscles, ultrasound, acoustoelasticity*

I. INTRODUCTION

Investigation of new mechanical parameters is very important to improve medical or physiological diagnosis. In the field of elastography, NL elasticity quantification has become a new complementary measurement to that of shear modulus μ by characterizing tissue linear elasticity. The current technique for NL elasticity quantification relies on acoustoelasticity (AE) theory. First developed for isotropic soft tissues, this technique consists in deducing the NL μ from the evolution of the shear wave (SW) speed in uniaxially stressed media [1]. The implementation of AE in transverse isotropic (TI) soft tissues such as muscles requires refinements to include the specificities of the TI symmetry and implies 9 different configurations where the principal direction of the TI medium, stress, polarization \vec{u} and propagation \vec{k} directions of the SW are either parallel (\parallel) or perpendicular (\perp) to one another [2, 3]. The resulting configurations are dependent on 5 elastic parameters of the second order (μ_{\parallel} , μ_{\perp} , $\mu_{//}$, μ_{\perp} and the Young's modulus $E_{//}$ parallel to the main axis, respectively) and on 3 third order NL elastic parameters (A , H , K). The goal of this work is to quantify $E_{//}$ with mechanical

testing to combine with UE for identifying the third order NL elastic parameters A , H and K .

II. THEORY

In order to calculate the elastic parameters, we solve the internal energy equation by calculating the derivative of the 1st Piola-Kirchhoff stress tensor, which results in 9 elastodynamic configurations (config) and associated equations [2]. On figure 1 is presented the three configurations that were used in this paper, where σ is the uniaxial stress applied. That correspond to three elastodynamic equations (1) to (3) describing the evolution of the shear wave speed as a function of the applied uniaxial stress.

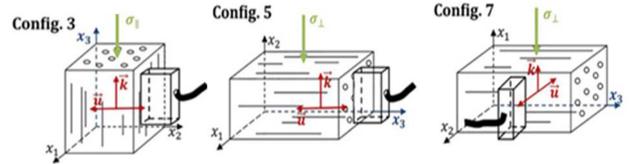


Figure 1: The three AE configurations presented in this work where σ is the uniaxial stress applied, k the shear wave propagation axis, u the shear wave polarization axis.

For config 3:

$$\rho_0 v_s^2 = \mu_{\parallel} - \frac{\sigma}{E_{//}} \left(E_{//} - \mu_{\perp} + \mu_{//} + \frac{A}{4} + \frac{H+2K}{2} \right) \quad (1)$$

For config 5:

$$\rho_0 v_s^2 = \mu_{\parallel} + \frac{\sigma}{2E_{//}} \left[-E_{//} - \mu_{\perp} + \mu_{//} - \frac{\mu_{\parallel} E_{//}}{\mu_{\perp}} + \frac{A}{4} \left(1 - \frac{E_{//}}{\mu_{\perp}} \right) + \frac{H+2K}{2} \right] \quad (2)$$

For config 7:

$$\rho_0 v_s^2 = \mu_{\perp} - \frac{\sigma}{2E_{//}} \left(E_{//} + 3\mu_{\perp} + \frac{A}{2} - K \right) \quad (3)$$

where v_s is the shear wave speed and ρ_0 the density. The other coefficients have been defined above.

From measurement and equations (1) to (3), the 3 NL parameters were deduced from the slope $k_{(i=3,5,7)}$ of each config $v_s(\sigma)$ by the following equations.

$$A = -4(\mu_{\perp}(2 + k_3 + 2k_5) + \mu_{\parallel}) \quad (4)$$

$$K = -(E_{\parallel} + 3\mu_{\perp} + \frac{A}{2} + 2E_{\parallel}k_7) \quad (5)$$

$$H = 2(-k_3E_{\parallel} - E_{\parallel} + \mu_{\perp} - \mu_{\parallel} + \frac{A}{4} - K) \quad (6)$$

III. MATERIAL AND METHODS

A. Materials and method

7 *ex vivo* porcine muscles were excised. To quantify mechanical properties with ultrasound (US) and mechanical tensile tests, a specific setup was built. A linear probe (SL10-2, Hologic, France) driven by an ultrafast US device (Mach 30, Hologic, France) was coupled to a mechanical testing device (Instron 5944, Norwood, MA, USA) in order to catch SW generated during traction (figure 2).



Figure 2: Mechanical testing device (Instron 5944) coupled with an ultrafast ultrasound device (Mach 30) driving a 6 MHz central frequency US linear probe.

For each applied stress, according to each config, SW speed was quantified by a classical elastography sequence: a radiation force is applied to generate SW which are tracked by an ultrafast imaging acquisition [4]. μ_{\parallel} and μ_{\perp} could be first measured at zero strain.

Complementary the parallel Young's modulus was calculated by using the Hooke's law from the slope of the experimental stress-strain curve using a traction device (Instron 5944). In that case the muscle fibers were aligned with the main axis of the traction device.

Stepwise stretches from 0 to 14% nominal strain were induced then by 2% steps. At each 2% strain step, the tensile test was carried out and the US measurements parallel or perpendicular to fibers (depending on the configuration) were performed. From the given stiffness maps of linear elastic regime at each measurement, an averaged stiffness of a defined ROI was found. The ν_s curve as a function of σ (kPa) was then plotted and its slope calculated. Thanks to the 3 equations (3), (5) and (7), the non-linear coefficient A , H and K were then deduced. Each measurement was repeated at least 3 times.

B. Protocols

Each *iliopsoas* muscles from the same pig was sampled into four different pieces: two longitudinal (parallel) and two perpendicular (transverse) to the fibers. Each sample has a similar rectangular form (5x1 cm²) (figure 3). They were fixed to the stretching machine on the two ends by the system of jaws. Three acoustoelastic configs were set up to perform

experiments. For the config 3, the longitudinal samples were used. The stretching stress applied as well as the shear modulus measured are along the fibers. For configs 5 and 7, the transverse samples were used. The stretching stress applied and the shear modulus measured are thus perpendicular to the fibers.



Figure 3: Extracted ilio-psoas muscle and position of the extracted samples (A and B longitudinal samples, C and D transverse samples) used in configurations 3, 5 and 7.

IV. RESULTS

On figure 4 is presented the stress-strain relationship for one muscle sample where the fibers were oriented parallel to the main axis of the mechanical device. The change of slope allowed to define the linear elastic regime and hyperelastic regime. For each step, the slope and the nominal stress values were collected, and the shear wave speed was quantified and a stiffness map as well as the first image of the shear wave movie is presented. It corresponds to the "config 3" of the AE theory. This kind of experiment was repeated for the two others proposed configuration of the AE theory (config 5 and 7).

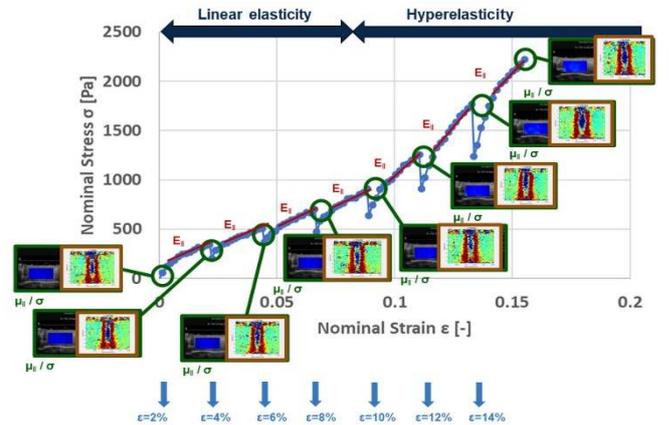


Figure 4: Stress/strain experimental curve obtained on a muscle sample where the fibers were aligned with the main axis of the mechanical device. For each mechanical step the ultrasound acquisition was performed in order to quantify the shear wave speed as a function of the stress applied. This correspond to the "config 3" of the AE theory.

On figure 5 is presented the evolution of the stiffness map as a function of the applied stress obtained for three samples of a same muscle. Each sample was used for one configuration of the AE theory 3, 5 or 7.

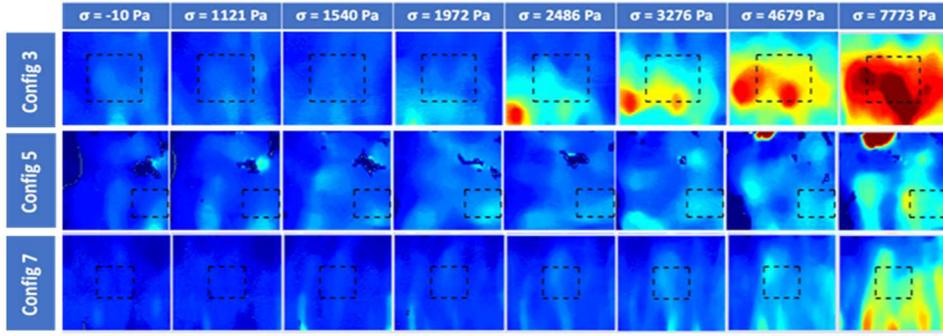


Figure 5: Stiffness maps at different level of tensile stress during stretching by the mechanical device for each of the 3 AE theory configuration.

Figure 6 presents the evolution of the shear elasticity as a function of the applied stress. These curves were fitted in the linear regime to retrieve the nonlinear elastic parameters by using equations (4), (5) and (6).

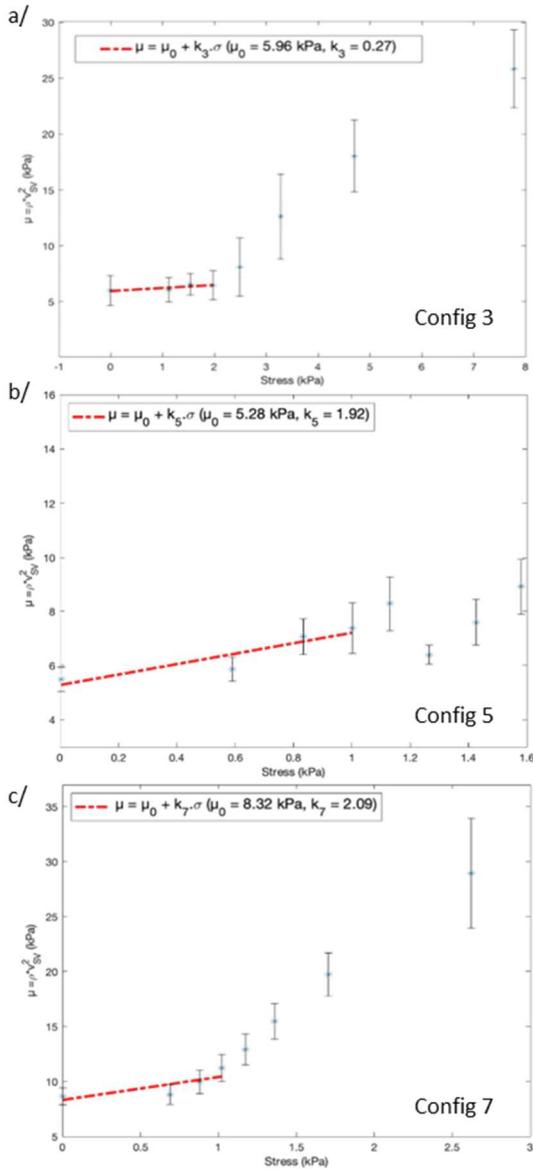


Figure 6: Shear stiffness value in the ROI defined on maps as a function of the stress applied for each configuration of the AE theory: a/config 3, b/config 5, c/ config 7

In table I, mean values of each k_i for 3 repeated experiments are presented for each *ilio-psoas* muscle tested.

Table I: Values of slopes of $v_s(\sigma)$ for each tested muscle.

Sample	k_3	k_5	k_7
Muscle 1	0.27 ± 0.06	1.98 ± 0.58	2.42 ± 0.96
Muscle 2	0.84 ± 0.03	2.8 ± 0.44	2.52 ± 0.55

From equations 4, 5 and 6 the nonlinear elastic parameters were retrieved (Table II).

Table II: Nonlinear elastic coefficients for each tested muscle

Nonlinear elastic parameters (kPa)	Muscle 1	Muscle 2
A	-306.22 ± 12.84	-343.00 ± 8.01
K	-34.06 ± 11.04	-32.66 ± 7.72
H	129.70 ± 33.99	117.61 ± 21.86

V. DISCUSSION

In all samples and for all different configurations, the slope of the apparent $\mu = \rho_0 \cdot v_s^2$ as a function of the propagation direction were retrieved for each applied stress step. As expected by theory and as long as we were in small strain (linear elastic behaviour) apparent μ evolved linearly with stress. A combination of the different configurations (3, 5, 7) coupled with the $E_{//}$ measurement by mechanical tests allowed to quantify the NL parameters.

A good accordance between the results of two muscles was observed (Table II). During experiments, the conservation method of the muscles after sampling could be improved to assure the reproducibility and reduce the margins of error of the results, in particular by ensuring a thermostatic bath regulated at 37°C. The validation of this approach is also considered by other methods, such as numerical simulations or magnetic resonance elastography.

These preliminary results show for the first time that it is possible to get NL shear elasticity in TI tissue such as muscle by coupling mechanical testing and shear wave elastography.

This preliminary proof of concept paves the way for precise and robust NL characterization of muscles *in vivo*.

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REFERENCES

- [1] J.L. Gennisson, M. Rénier, S. Catheline, C. Barrière, J. Bercoff, M. Tanter, M. Fink. “Acoustoelasticity in soft solids: assessment of the nonlinear shear modulus with the acoustic radiation force.”, 2007, *J. Acoust. Soc. Am.*, 122, pp.3211-3219.
- [2] M. Bied and J.-L. Gennisson, “Acoustoelasticity in transversely isotropic soft tissues: Quantification of muscle nonlinear elasticity”, 2021, *J. Acous. Soc. Am.*, vol. 150, pp. 4489–4500, doi: 10.1121/10.0008976.
- [3] J.-P. Remeniéras, M. Bulot, J.-L. Gennisson, F. Patat, M. Destrade, and G. Bacle, “Acoustoelasticity of Transversely Isotropic Incompressible Soft Tissues: Characterization of Skeletal Striated Muscle,” 2021, *Phys. Med. Bio.*, doi: 10.48550/ARXIV.2103.09152.
- [4] J. Bercoff, M. Tanter, M. Fink, “Supersonic shear imaging: a new technique for soft tissue elasticity mapping.”, 2004, *IEEE Ultras. Ferro. Freq. Contr.*, doi: 10.1109/tuffc.2004.1295425.