Anisotropic nonlinear shear elasticity quantification in *ex vivo* muscles

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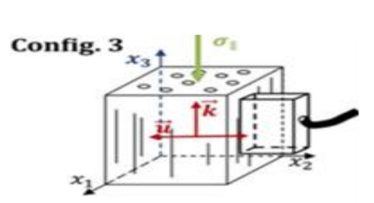
Introduction

Quantification of new mechanical parameters is quite important to improve medical or physiological diagnosis. In the field of elastography, nonlinear (NL) elasticity quantification has become a new complementary measurement to that of shear modulus (SM) μ characterizing tissue linear elasticity. The current technique for NL elasticity quantification relies on acoustoelasticity (AE). First developed for isotropic soft tissues, this technique consists in deducing the NL SM from the evolution of the shear wave (SW) speed in uniaxially stressed media [1,2]. 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 (//) or perpendicular (⊥) to one another [2]. The resulting configurations are dependent on 3 elastic parameters of the second order ($\mu_{//}$, $\mu_{\perp}$ and $E_{//}$, $SM_{//,\perp}$ and the Young's modulus // 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 retrieve the third order NL elastic parameters.

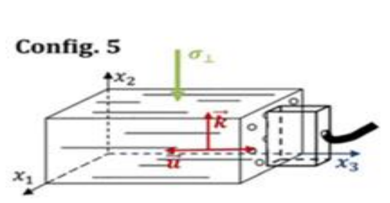
Methods

7 *ex vivo* pork muscles were excised by 10 years old experienced surgeon. To quantify mechanical properties with ultrasound (US) or mechanical testing a specific setup was built. Two US probes (6 MHz) driven by an ultrafast US device (Mach 30) were coupled to a mechanical testing device (Instron 5944) in order to catch SW generated during traction. Their speed was measured based on the supersonic shear imaging technique during applied stress in muscles during traction. For each applied stress, the US probe was rotated using an automated motor by 90° to get to different configurations at each step. Complementary $E_{//}$ was measured by stress/strain relationship measured using a bi-column traction) machine (Instron 5944) with a thermal bath.

- Configuration 3: muscle longitudinal samples were used. During tensile tests, the stretching stress applied and the shear modulus were measured along the fibers. $E_{\parallel}$ and $\mu_{\parallel}$ were found.
- Configurations 5 and 7: muscle transverse samples were used. During tensile tests, $\mu_{\perp}$ was found, the stretching stress applied and the shear modulus were measured perpendicularly to the fibers.



$$k_3 = -\frac{E_{\parallel} - \mu_{\perp} + \mu_{\parallel} + \frac{A}{4} + \frac{H+2K}{2}}{E_{\parallel}}$$

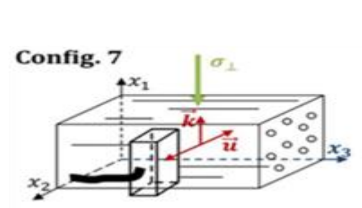


$$k_5 = \frac{-E_{\parallel} - \mu_{\perp} + \mu_{\parallel} - \frac{\mu_{\parallel} E_{\parallel}}{\mu_{\perp}} + \frac{A}{4}\left(1 - \frac{E_{\parallel}}{\mu_{\perp}}\right) + \frac{H+2K}{2}}{2E_{\parallel}}$$

$$\Rightarrow k_3 + 2\,k_5 = \frac{-2E_{\parallel} - \frac{\mu_{\parallel} E_{\parallel}}{\mu_{\perp}} - \frac{A}{4}\frac{E_{\parallel}}{\mu_{\perp}}}{E_{\parallel}}$$

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

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



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

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

$$\Rightarrow H = 2 * (-k_3 * E_{\parallel} - E_{\parallel} + \mu_{\perp} - \mu_{\parallel} - \frac{A}{4} - K)$$

k_3, k_5, k_7 are the slopes of three curves ρv_S^2 as a function of the applied stress σ (kPa) corresponding to three configurations 3, 5 and 7. Using equations 3, 5 and 7, A, H and K were found

Theory

Expressing the speed of SH (Shear Horizontal) mode elastic shear waves in an uniaxially stressed (along $\overrightarrow{x_1}$) TI quasi-incompressible solid.

Strain energy e:

$$e = \mu_{\perp} I_2 + \left(\frac{E_{\parallel}}{2} - \frac{3\mu_{\perp}}{2}\right)\varepsilon_{33}^2 + 2(\mu_{\parallel} - \mu_{\perp})(\varepsilon_{13}^2 + \varepsilon_{23}^2) + \frac{A}{3} I_3 + (G + H + K)\varepsilon_{33}^3 + (H + 2K)\varepsilon_{33}(\varepsilon_{13}^2 + \varepsilon_{23}^2) + K\varepsilon_{33}(\varepsilon_{11}^2 + \varepsilon_{22}^2 + 2\varepsilon_{12}^2)$$

(with ε the Green-Lagrange strain tensor, $I_2 = \mathrm{Tr}\,\varepsilon^2$, $I_3 = \mathrm{Tr}\,\varepsilon^3$)

1st Piola-Kirchhoff stress tensor: $P_{ik} = \frac{\partial e}{\partial \left(\frac{\partial u_i}{\partial a_k}\right)}$ → Particle motion equation: $\rho_0 \ddot{u}_i = \frac{\partial P_{ik}}{\partial a_k}$ (with $\vec{u} = \overrightarrow{u^D} + \overrightarrow{u^S}$) → Wave equation → Hooke's law for static strain expression

Config #:

#3 $\rho_0 v_s^2 = \mu_{\parallel} - \frac{\sigma}{E_{\parallel}}(E_{\parallel} - \mu_{\perp} + \mu_{\parallel} + \frac{A}{4} + \frac{H+2K}{2})$

#5 $\rho_0 v_s^2 = \mu_{\parallel} + \frac{\sigma}{2E_{\parallel}}(-E_{\parallel} - \mu_{\perp} + \mu_{\parallel} - \frac{\mu_{\parallel} E_{\parallel}}{\mu_{\perp}} + \frac{A}{4}(1 - \frac{E_{\parallel}}{\mu_{\perp}}) + \frac{H+2K}{2})$

#7 $\rho_0 v_s^2 = \mu_{\perp} - \frac{\sigma}{2E_{\parallel}}(E_{\parallel} + 3\mu_{\perp} + \frac{A}{2} - K)$

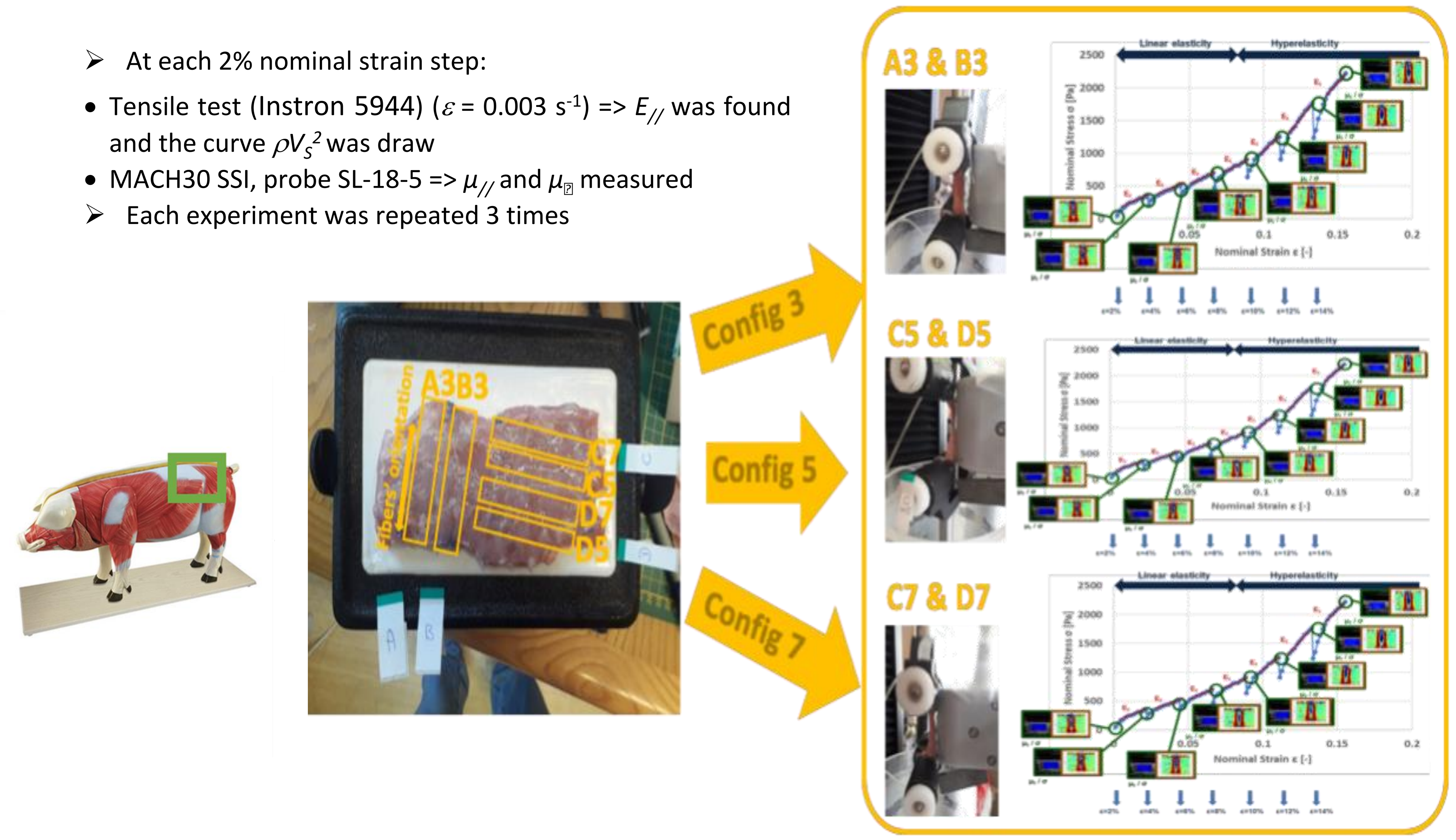
Among nine possible elastodynamic configurations, only three are necessary to retrieve the three nonlinear coefficients A, H and K.
Three configurations 3, 5 and 7, were thus carried out to calculate A, H and K

Where $\vec{u}, \overrightarrow{u^S}, \overrightarrow{u^D}$ are the total, static (due to static stress), and dynamic (due to the shear wave) displacement vectors, respectively. $\vec{a}$ the position in Lagrangian coordinates, $\vec{k}$ the propagation vector, ($\mu_{//}$, $\mu_{\perp}$, $E_{//}$) the linear elastic coefficients, (*A*, *G*, *H*, *J*) the third order elastic coefficients, (I_2, I_3) invariant of the strain tensor and ρ_0 the density.

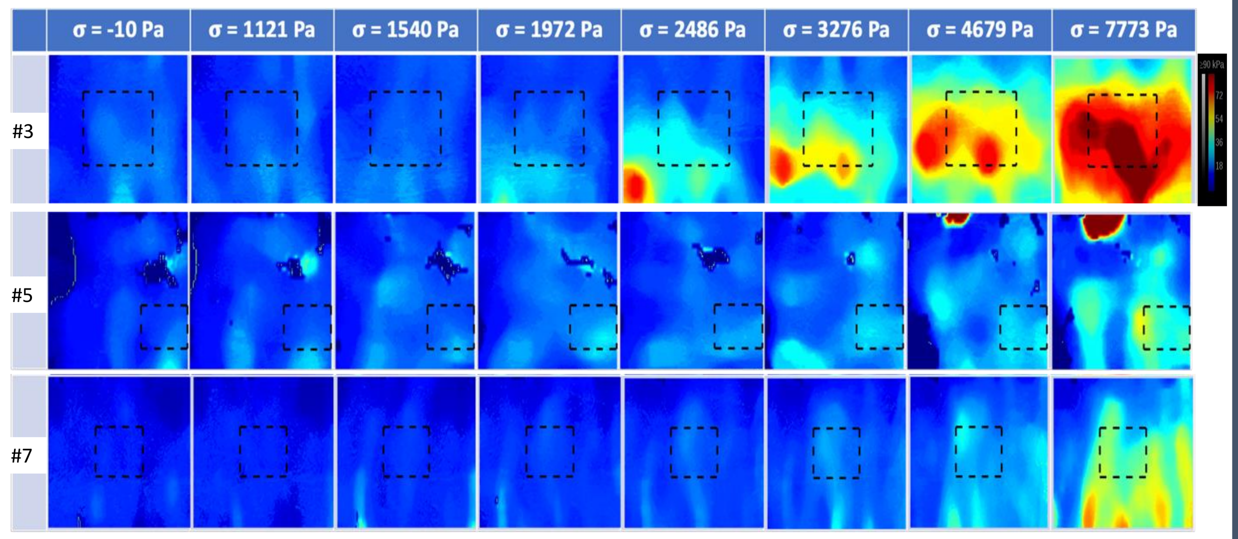
Results

- At each 2% nominal strain step:
  - Tensile test (Instron 5944) (ε = 0.003 s^{-1}) => $E_{//}$ was found and the curve ρV_S^2 was draw
  - MACH30 SSI, probe SL-18-5 => $\mu_{//}$ and $\mu_{\perp}$ measured
- Each experiment was repeated 3 times

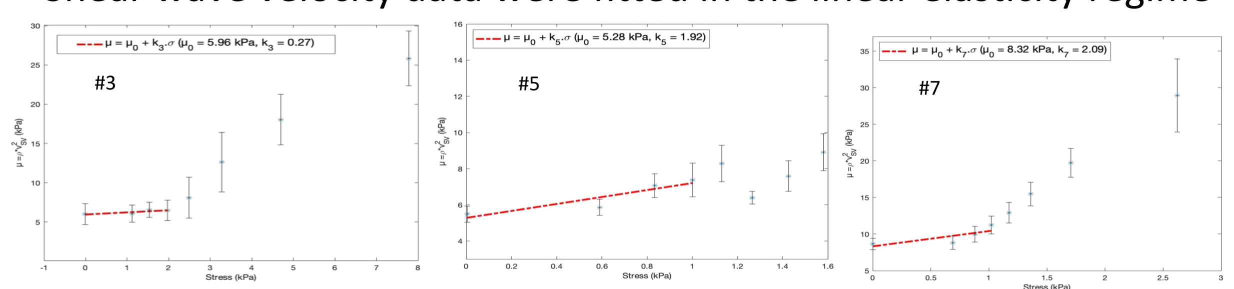
Tensile tests and Stress-Strain curves



Shear wave velocity mapping for each configuration #3,5,7



Shear wave velocity data were fitted in the linear elasticity regime



$k_3 = 0.27 \pm 0.06$ $k_5 = 2.21 \pm 0.32$ $k_7 = 1.97 \pm 0.24$

Coefficients (kPa)	Sample 1	Sample 2
A	-306.22	-343
H	-34.06	-32.66
K	129.7	117,61

Discussion

In all samples and for different configurations the local extrema of the apparent μ as a function of the propagation direction were retrieved for each applied stress step. As expected in theory, apparent μ evolved linearly with stress. At zero stress, $\mu_{//}$ and $\mu_{\perp}$ were measured in standard elastography mode with the ultrafast ultrasound device (Mach30). A combination of the different configurations (3, 5, 7) coupled with the $E_{//}$ measurement allowed to quantify the NL parameters. These preliminary results show for the first time that it is possible to get NL shear elasticity by coupling mechanical testing and shear wave elastography. It gives a proof of concept that paves the way for precise and robust NL characterization of muscles *in vivo*.

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1/ Bied, JASA, 2021; 2/ Remenieras, PMB, 2021