On the elasticity of transverse isotropic soft tissues (L)

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Quantitative elastography techniques have recently been developed to estimate the shear modulus μ of soft tissues *in vivo*. In the case of isotropic and quasi-incompressible media, the Young's modulus E is close to 3μ, which is not true in transverse anisotropic tissues such as muscles. In this letter, the transverse isotropic model established for hexagonal crystals is revisited in the case of soft solids. Relationships between elastic constants and Young's moduli are derived and validated on experimental data found in the literature. It is shown that $3\mu_\perp \leq E_\perp \leq 4\mu_\perp$ and that $E_{//}$ cannot only be determined from the measurements of $\mu_{//}$ and $\mu_\perp$ *© 2011 Acoustical Society of America*.

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I. INTRODUCTION

It is now well established that anisotropy plays a major role in the mechanical properties of biological media such as muscles,[1] tendons,[2,3] or bones.[4] Linear elastic theory, first developed for crystals,[5] was applied for modeling the propagation of ultrasonic waves in such media. First experimental results were satisfactorily explained by assuming a transverse isotropy around a specific axis of symmetry.[1,3] Elastic constants of the model were determined from the measurement of speed V_L of ultrasound (1–10 MHz) for longitudinal waves propagating in various directions. In these studies, shear elastic constants were neglected or assumed to be zero due to the lack of measurement systems. Some years ago, the transient elastography (TE) technique was applied to measure the speed V_S of low frequency (50–150 Hz) shear waves propagating in soft tissues.[6] Using this technique, local elasticity of soft tissues was obtained from shear velocity measurements and a strong anisotropy was found for shear waves propagating perpendicular or parallel to the muscle fibers.[7] Recently, the supersonic shear imaging (SSI) technique[8] was applied to the measurement of shear wave speed in muscles and confirmed this strong anisotropy.[9] Such experiments allow us to recover the components of the elastic tensor determining the type of anisotropy.

Nevertheless elasticity is most commonly defined in terms of Young's modulus E. In an isotropic elastic soft media (Poisson's ratio $\nu \cong 0.5$), this parameter can be deduced from the shear velocity measurements by the simple relation $E \cong 3\mu = 3\rho V_S^2$, where μ is the shear modulus. In transverse isotropic or hexagonal media, similarly to the other components of the elastic tensor, two Young's moduli are defined. However, the relationship between the Young's modulus and the shear velocity is no more so simple. In this paper, the mechanical behavior of transverse isotropic soft tissues is investigated. Relations between components of the stiffness tensor are established and used to interpret experimental data found in the literature. Finally, the unusual behavior of muscles and tendons, compared with that of hexagonal crystals, is also discussed.

II. ANALYSIS

The propagation of ultrasonic waves is governed by the mechanical properties of the propagating medium.[5] Measurements performed on muscles or tendons have shown that the isotropic model, used for many other biological tissues, is not valid. The transverse isotropic model developed for materials exhibiting at least a hexagonal or an axial symmetry is more appropriated.[1] Given the Cartesian coordinate (x_1, x_2, x_3) with the x_3-axis parallel to the fibers, a muscle or a tendon is isotropic in the (x_1, x_2) plane. In the linear elastic theory, mechanical properties are described by the stiffness tensor c_{ijkl} or the compliance tensor s_{ijkl} (i, j, k, $l = 1$–3). Using the Voigt's notation, they are represented by 6×6 symmetric matrices $c_{\alpha\beta}$ or $s_{\alpha\beta}$ (α, $\beta = 1$–6). For transverse isotropic media, the number of independent elastic constants reduces to five: c_{11}, c_{13}, c_{33}, c_{44}, and c_{66}. Other elastic constants are related to these coefficients or vanish,

$$c_{22} = c_{11}, c_{23} = c_{13}, c_{55} = c_{44}, c_{12} = c_{11} - 2c_{66}. \quad (1)$$

The same features can be established for the components of the compliance matrix $s_{\alpha\beta}$, inverse of the stiffness matrix $c_{\alpha\beta}$.

Stiffness constants c_{11} and c_{33} can be determined from the measurement of longitudinal ultrasound velocities in directions perpendicular (V_{L1}) and parallel (V_{L3}) to the fiber axis x_3,

$$c_{11} = \rho (V_{L1})^2,\ c_{33} = \rho (V_{L3})^2, \quad (2)$$

where ρ is the mass density. The constant c_{13} can be deduced from the velocity of longitudinal waves propagating in a meridian plane such as (x_1, x_3). Other constants can be obtained with TE technique (Fig. 1) from the velocity (V_{S1} or V_{S3}) of shear waves propagating in a direction perpendicular to the

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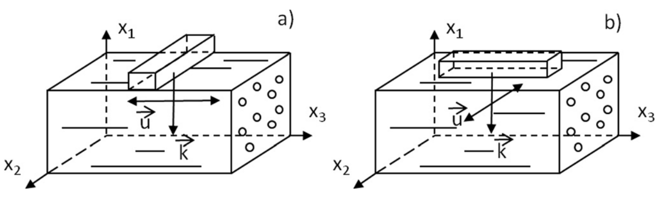

FIG. 1. Schematics of the TE technique where a rod mounted on a vibrator gives a low frequency pulse at the surface of the medium generating shear waves. (a) When the rod is perpendicular to the fibers axis, a shear wave propagates ($\vec{k}$) perpendicularly to the fibers axis with a polarization ($\vec{u}$) parallel to the fibers axis. (b) When the rod is parallel to the fibers axis, a shear wave propagates ($\vec{k}$) perpendicularly to the fibers axis with a polarization ($\vec{u}$) perpendicular to the fibers axis. Such configurations give, respectively, access to the elastic constants c_{44} and c_{66}.

fiber axis with a polarization oriented either parallel to the fibers,

$$c_{44} = \rho (V_{S3})^2, \tag{3}$$

or perpendicular to the fibers,

$$c_{66} = \rho (V_{S1})^2. \tag{4}$$

Regarding SSI technique, as presented in Fig. 2, c_{44} is deduced from the velocity of shear waves propagating along the fiber axis and polarized in any direction perpendicular to the fibers.

In the case of soft tissues, like muscle, the order of magnitude of these constants is very different. Longitudinal wave velocity measured at megahertz frequencies are in the kilometer per second range. With $\rho = 1100\ \mathrm{kg/m^3}$, values of constants c_{11}, c_{33}, and c_{13} were on the order of 3 GPa.[1] Conversely, shear velocities were found to be in 1–10 m/s range.[8] Then, values of constants c_{66} and c_{44} are on the order of 100 kPa, i.e., more than four orders of magnitude lower than the three other constants. These results obtained recently by TE or SSI justifies the hypothesis made by Levinson[1] that the value of the shear constant c_{44} remains equal to zero throughout the iterative process used to determine the elastic constants from the speed of ultrasound. This author approximates the velocity equation by assuming that $c_{13} \approx \sqrt{c_{11}c_{33}}$. Moreover, Levinson notes that this initial estimate meets terminal conditions of the optimization

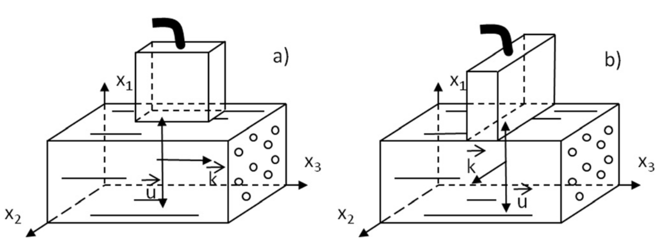

FIG. 2. Schematics of the SSI technique where a radiation force perpendicular to the fibers axis generates shear waves. (a) When the ultrasonic probe is parallel to the fibers axis, a shear wave propagates ($\vec{k}$) parallel to the fibers axis with a polarization ($\vec{u}$) perpendicular to the fibers axis. (b) When the ultrasonic probe is perpendicular to the fibers axis, a shear wave propagates ($\vec{k}$) perpendicularly to the fibers axis with a polarization ($\vec{u}$) perpendicular to the fibers axis. Such configurations give, respectively, access to the elastic constants c_{44} and c_{66}.

algorithm. In the following, this relation is demonstrated and a more general relation between elastic constants is established, which is valid in the case of tendon where the shear stiffness c_{66} cannot be neglected.[3]

Because the stored energy density of any material must be positive, the stiffness matrix is constrained to be definite positive.[5] A transverse isotropic material requires the positivity of c_{44}, c_{66}, and

$$c^2 = c_{33}(c_{11} - c_{66}) - c_{13}^2. \tag{5}$$

Stability constrains imposed a limited range of variations for elastic constants.[10] In Fig. 3, bounds of allowable values of c_{13}^2 are plotted in the dimensionless diagram,

$$b = \frac{2c_{13}^2}{(c_{11} + c_{12})^2} \text{ versus } a = \frac{c_{33}}{c_{11} + c_{12}}. \tag{6}$$

For transverse isotropic materials the stability condition [Eq. (5)] requires that $0 \le b \le a$. Symbols correspond to various crystals (Be, BeO, ZnO, CdS, Ti) of hexagonal symmetry and to soft solids like muscles and tendons. Crystal data are close to the dotted curve $b = 2(1-a)^2$ corresponding to an isotropic material ($c_{33} = c_{11}$, $c_{13} = c_{12}$) of Poisson's ratio $\nu = 1 - a$. With $\nu = 0.5$, a fluid or a soft solid, like isotropic tissues, lies at the intersection with the line $b = a$. Representative points for muscles and tendons are far from the curve of isotropy and border the upper limit of the diagram. This representation exhibits the specific behavior of muscles and tendons as compared with that of transverse isotropic solids and soft isotropic tissues.

Since c^2 vanishes for $b = a$, this quantity plays an important role for characterizing the behavior of a soft material. It intervenes in the Young's modulus, defined as the ratio of the loading stress to the corresponding strain. For a stress parallel to the fiber axis, the Young's modulus $E_{//} = E_{33}$ is equal to,

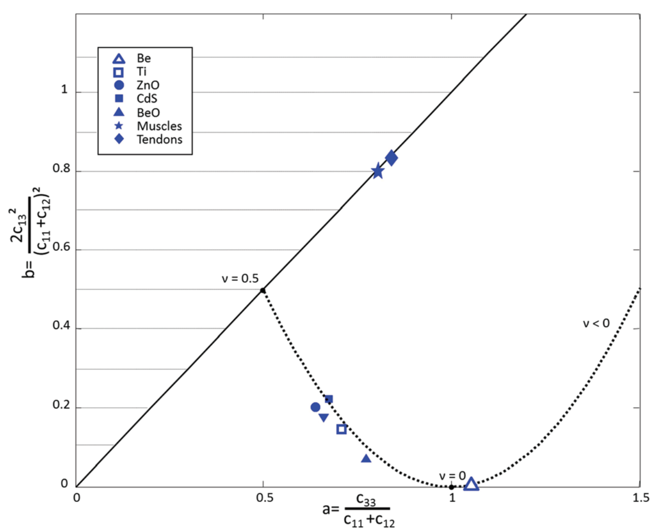

FIG. 3. (Color online) Bounds of allowable values of c_{13}^2 and data plotted for a variety of transverse isotropic crystals: Be (△), BeO (▲), Ti (□), ZnO (●), CdS (■), muscle (⋆), and tendon (◆). a and b are defined from Eq. (6). The dotted curve is for an isotropic medium of Poisson's ratio $\nu = 1 - a$.

$$E_{//} = \frac{1}{s_{33}} = \frac{c^2}{c_{11} - c_{66}}. \tag{7}$$

For a stress perpendicular to the fiber axis, the Young's modulus $E_\perp = E_{11} = E_{22}$ is given by

$$E_\perp = \frac{1}{s_{11}} = \frac{4c_{66}c^2}{c^2 + c_{33}c_{66}}. \tag{8}$$

As pointed out by Hoffmeister, Eqs. (7) and (8) show that parallel and perpendicular Young's modulus do not depend on c_{44}, while variations in c_{66} produce changes in Young's modulus at all angles with respect to the fiber axis.[2]

Experimental values of $E_{//}$ are less than 100 kPa for muscle and less than 1 MPa for tendon.[3] From Eq. (7), the quantity $c^2 = E_{//}(c_{11} - c_{66})$ is of the order of 10^{-3} $(\text{GPa})^2$, i.e., three orders of magnitude lower than each term of the difference in Eq. (5). Then, the equality,

$$c_{13} \cong \sqrt{c_{33}(c_{11} - c_{66})}, \tag{9}$$

is valid with an error less than 0.1%. The determination of c_{13} requires measurements of the phase velocity of longitudinal waves propagating in any direction in a meridian plane such as (x_1, x_3). Equation (9) allows us to calculate c_{13} with stiffness constants deduced from sound velocity measurements only in directions parallel and perpendicular to the fiber axis. We have used results found in the literature for fresh bovine Achilles tendons to check the validity of Eq. (9). The first four columns in Table I list the mean values of stiffness constants obtained by Kuo *et al.* at three strain conditions, 0%, 4.7%, and 9.5%.[3] The last column shows that the values of the constant c_{13} deduced from Eq. (9) are very close to the experimental ones.

Recently, experiments performed *in vivo* with the SSI technique show that shear wave velocities perpendicular to the fiber axis of skeletal muscles are of the order of 10 m/s.[9] Then, the corresponding elastic constants c_{66} and c_{44} are less than 100 kPa and Eq. (9) can be written in a form identical to that postulated by Levinson,

$$c_{13} \cong \sqrt{c_{11}c_{33}}. \tag{10}$$

We have used the experimental results obtained by this author to check the validity of this formula. In Table II, the first three columns list the mean values of stiffness constants obtained for the first specimen in both passive and active phase.[1] The last column shows that the values of the constant c_{13} deduced from Eq. (10) are very close to the experimental ones. The agreement for other specimens is also very satisfactory.

Table 1. Comparison between mean values of stiffness constant c_{13} measured (Ref. 3) and calculated from Eq. (9) (GPa) for bovine Achilles tendons at three strain conditions.

Strain	c_{11}	c_{33}	c_{66}	c_{13} (meas.)	c_{13} [Eq. (9)]
0%	2.93	3.90	0.61	3.00	3.01
4.7%	2.91	3.59	0.25	3.08	3.09
9.5%	2.89	3.32	0.26	2.96	2.95

Table 2. Comparison between average values (GPa) of stiffness constant c_{13} measured (Ref. 1) and calculated from Eq. (10) for a frog sartorius muscle in the passive and active phases.

Phase	c_{11}	c_{33}	c_{13} (meas.)	c_{13} [Eq. (10)]
Active	2.60	4.17	3.29	3.29
Passive	2.60	4.46	3.40	3.41

The main objective of elastographic technique is to estimate the Young's modulus E of soft tissues through measurements of the shear wave velocity V_S. For an isotropic elastic media, this parameter is linked to the Lamé constants λ and μ,

$$E = \frac{\mu(3\lambda + 2\mu)}{\lambda + \mu}. \tag{11}$$

In soft media, λ is 10^5 times larger than μ. Thus such medium are considered as quasi-incompressible and the very good approximation,

$$E \cong 3\mu = 3\rho V_S^2, \tag{12}$$

allows us to determine accurately the elasticity from shear wave velocity measurements.[6]

The elasticity of transverse isotropic media is described by the two Young's modulus $E_{//}$ and $E_\perp$ according to the direction of the applied stress with respect to the fiber axis. Combining Eqs. (7) and (8) leads to

$$E_\perp = \frac{4c_{66}}{E_{//}} + \gamma c_{66}E_{//}, \tag{13}$$

where the coefficient,

$$\gamma = \frac{c_{33}}{c_{11} - c_{66}} = 2a, \tag{14}$$

is equal to unity for a soft isotropic medium ($c_{11} = c_{33} \gg \gamma\, c_{66}$). In this case, $E_{//} = E_\perp = E$ and Eq. (13) gives $E = 3c_{66} = 3\mu$, as expected. For transverse isotropic media such as tendons or muscles, c_{33} is larger than c_{11}. However, values of stiffness constants in Tables I and II and data in Fig. 3 show that $\gamma = 2a$ does not exceed 2. Thus, the perpendicular Young's modulus lies in between $3c_{66}$ and $4c_{66}$. The lower limit corresponds to the isotropic case. The upper limit corresponds to a transverse isotropic soft medium having a longitudinal elasticity $E_{//}$ much larger than the shear elasticity measured by the coefficient $c_{66} = \mu_\perp$,

$$3\mu_\perp \le E_\perp \le 4\mu_\perp. \tag{15}$$

This approximation is valid for muscles, for which $E_{//} \cong 100$ kPa and $c_{66} \le 10$ kPa, with V_{S1} in between 1 and 3 m/s, as measured by Gennisson *et al.*[9] Thus the measurement of the shear elastic constant c_{66} provides a good approximation of the Young's modulus in the direction perpendicular to the fiber axis.

As pointed out by Hoffmeister, the Young's modulus $E_{//}$ cannot be estimated from the shear elastic constant c_{44}. Equation (7) shows that $E_{//}$ is proportional to c^2. For a soft transverse isotropic media, we have shown that this quantity is the difference of two terms, $c_{33}(c_{11} - c_{66})$ and c_{13}^2, that nearly compensate. Taking into account the accuracy of ultrasonic techniques, the relative error on the value of c^2 is very large and the estimation of the Young's modulus parallel to the fiber failed. This remark explains the discrepancy observed by Kuo *et al*. between the experimental and the estimated values of $E_{//}$. For the unstrained tendon (S_0), the measured Young's modulus is one order of magnitude larger than that estimated from elastic constants. This ratio is only twice for the sample with an initial strain state at 9.5%. At a higher strain the tendon becomes harder and the quantity c^2 increases significantly. Thus, the estimation of the Young's modulus becomes more accurate, as noted by Kuo *et al*.

III. DISCUSSION

In this paper, relationships are derived from theoretical considerations and experimental results obtained by TE or SSI techniques applied to transverse isotropic soft tissues. Relationships [Eqs. (9) and (10)] between elastic constants c_{11}, c_{13}, c_{33}, and c_{66} were verified on data reported in the literature for muscles and tendons. Moreover, it is shown that the well-known approximation $E \cong 3\mu = 3\rho {V_S}^2$ is no more valid in the case of transverse isotropic soft tissues. In that way, such medium in TE or SSI techniques must be preferentially defined in terms of shear velocities than in terms of Young's moduli.

A representation in the stability diagram of transverse isotropic media shows that the mechanical behavior of muscles and tendons is very different from that of hexagonal crystals and also from that of isotropic tissues. One reason of this unusual behavior of transverse isotropic tissues is the difference of anisotropy according to the type of elastic waves. Regarding the speed of ultrasound wave, the ratio of anisotropy is quite close to unity for longitudinal waves. The anisotropy of soft tissues is mainly related to the shear parameters governing the speed of slow transverse waves. This explains why the anisotropy was not very well studied in the last decades in ultrasonography. Moreover, expressions of the Young's modulus were derived from the relationship on components of the elastic tensor. Young's modulus perpendicular to the fiber axis was found to be in between $3c_{66}$ and $4c_{66}$. Thus, this parameter can be estimated from the measurement of the speed of the shear wave perpendicular to the axis of symmetry. Conversely, Young's modulus parallel to the fiber axis cannot be expressed in terms of shear wave speed. Moreover the estimation of $E_{//}$ from stiffness constants determined by ultrasonic measurements is very uncertain. Under these conditions, the level of anisotropy defined by the ratio of the shear velocities is a quite good interpretation and Young's moduli are not pertinent parameters. For example, when a muscle is contracting, everybody feels an increase of stiffness. However, as pointed out in Refs. 9 and 11, the shear modulus parallel to the fibers axis (c_{44}) increases much stronger than the shear modulus perpendicular to the fibers axis (c_{66}) with the muscle contraction. The relationship between parallel Young's modulus and transverse stiffness (c_{66}) commonly felt by physicians during palpation remains an open question.

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