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● *Review for the Festschrift in honor of Robert C. Waag*

PHYSICAL MODELS OF TISSUE IN SHEAR FIELDS[1]

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Abstract—This review considers three general classes of physical as opposed to phenomenological models of the shear elasticity of tissues. The *first* is simple viscoelasticity. This model has a special role in elastography because it is the language in which experimental and clinical data are communicated. The *second* class of models involves acoustic relaxation, in which the medium contains inner time-dependent systems that are driven through the external bulk medium. Hysteresis, the phenomenon characterizing the *third* class of models, involves losses that are related to strain rather than time rate of change of strain. In contrast to the vast efforts given to tissue characterization through their bulk moduli over the last half-century, similar research using low-frequency shear data is in its infancy. Rather than a neat summary of existing facts, this essay is a framework for hypothesis generation—guessing what physical mechanisms give tissues their shear properties. (E-mail: ecarsten@rochester.rr.com) © 2014 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Shear elasticity, Viscoelasticity, Shear relaxation, Hysteresis, Shear waves, Shear models.**

INTRODUCTION

After it became apparent more than a half century ago that ultrasound had a firm place in both medical diagnosis and therapy, a parallel investigative effort to understand the mechanisms responsible for the acoustic properties of tissues was undertaken. For the irrotational, largely compressional waves employed in most applications of diagnostic ultrasound, the bulk moduli and densities of soft tissues, on which imaging depends, differ from one to another by only a few percent (Goss et al. 1978). Acoustic absorptions in tissues even at megahertz frequencies are modest. Modern diagnostic ultrasound systems have adapted to these properties and produce high-resolution images at large depths of penetration.

The absorptions associated with the propagation of irrotational waves are consistent with models involving acoustic relaxation at the macromolecular level (Duck et al. 1998). Even solutions of a single molecular species such as hemoglobin appear to involve many different relaxation processes with a broad distribution of relaxation times (*e.g.,* Carstensen and Schwan 1959b). Other, largely phenomenological models for tissue properties have been proposed, and research on this subject continues today. However, models based on chemical or structural relaxation at the macromolecular level are consistent with available observations. In fact, because it is possible to invoke arbitrary distributions of relaxation processes to match nearly any observed frequency dependence for the absorption, relaxation models are difficult to disprove. Structure makes a modest contribution to absorption (Carstensen and Schwan 1959a; Pauly and Schwan 1971). Professor Waag has contributed fundamentally to an understanding of ultrasound propagation through macroscopically inhomogeneous tissues (*e.g.,* Mast et al. 1999; Nachman et al. 1990; Salahura et al. 2010).

For years, the use of shear waves in diagnostic medicine languished because of their large absorption coefficients. That changed with the invention of elastography, which uses shear strains and shear waves at extremely low frequencies, where propagation even in soft tissues can extend to useful distances (Parker et al. 2011). Progress in the development of elastography as a diagnostic tool has accelerated over the last two decades, but we have yet to undertake an in-depth study of the mechanisms responsible for the shear properties of tissues.

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[1] This article is dedicated to our friend and colleague, Robert C. Waag.

There are several reasons to believe that such studies will be even more valuable than they have been for compressional wave propagation. First, the shear moduli of soft tissues are five or six orders of magnitude smaller than their bulk moduli (Gao et al. 1996; Sarvazyan et al. 1995). Furthermore, the effective shear viscosities of soft tissues reported at audible frequencies (Boursier et al. 2009; Deffieux et al. 2007; Zhang et al. 2007) are several orders of magnitude greater than they are at megahertz frequencies (Frizzell et al. 1976). Those properties alone suggest that we can expect qualitatively different information about tissues from elastography than we have learned from compressional wave probes of soft tissues. Most important, in contrast to the case for compressional waves, it turns out that the shear moduli of diseased tissues, in many cases, are an order of magnitude or more greater than they are for normal soft tissue, making the value of the shear modulus itself a useful diagnostic datum. Today, we know from many independent studies that there is a rough correlation between shear modulus of liver and its degree of fibrosis as assessed qualitatively through biopsy (Carstensen et al. 2008; Sandrin et al. 2003). Because shear modulus can be measured non-invasively and quantitatively, there is reason to hope that it can eventually provide the diagnostic baseline to which other diagnostic data are referenced in the management of liver disease.

Empirical or phenomenological descriptions of observed data are useful even though they tell us little or nothing about the underlying physical processes. Our purpose in this review, however, is to start first with guesses about what it is in the structure and behavior of tissue that controls its shear properties and, then, to formulate these guesses into models that are sufficiently specific and quantitative that they can be tested experimentally. Of course, all knowledge is faith—guesses or models of the truth that to the best of our experience, directly or indirectly, are consistent with observations of the real world. This essay is more a framework of guesses than a review of tested models. In the long run, however, there is great hope that physically based models will elucidate the diagnostically relevant information that elastography promises.

Our knowledge for shear elasticity as it applies to elastography is at approximately the stage of development that the theory for compressional wave propagation was a half-century ago. And, the opportunities for study are almost completely open to us. There is hope, however, that progress can be more rapid in shear wave studies, in part because of the guidance we may find in the similar effort that has been made over the years in the study of irrotational wave propagation.

The terms *stiffness* and *compliance* are generic descriptors of the difficulty or ease of distorting objects or the materials from which they are made. At one extreme, we might have the stiffness of a coiled spring that could be quantified as a simple 1-D scalar relationship between force applied and its change in length. At the other extreme, to describe the material properties of the steel from which it is made, we need fourth-order stiffness tensors to relate the second-order stresses applied to the material to the second-order strains. Such formulations permit us to deal with materials that are anisotropic. Certain tissues such as muscle are in fact strongly anisotropic. Although this discussion is limited to purely isotropic materials, the need to deal with more complex media in the long run should not be ignored.

The stiffness of an isotropic medium can be characterized by two moduli: the bulk modulus, κ, the ratio of the mean normal stresses on an element of the material to its volume change, and the shear modulus, μ, the ratio of shear stress to shear strain, which characterizes the change in shape of the element. It is the shear modulus of tissue that has been found to change profoundly in certain diseased states; it is the shear modulus that is the focus of elastography, and physical models of the shear modulus are the subject of this discussion. As we illustrate, when stress and strain are purely shear, it is possible to reduce the general tensor equations to simple scalar statements, thus greatly simplifying our presentation. It is possible to design laboratory experiments that involve only shear. All medical applications of elastography involve both shear and bulk strains. However, shear strains in these applications are orders of magnitude greater than bulk strains.

Although no model is ever the full truth, all we ask is that it be "true enough" to be useful. Of the general classes of models for soft tissues (Delingette 1998; Fung 1981; Humphrey 2003), we consider three. The *first* is simple viscoelasticity. It assumes that each element of tissue has shear stiffness and coincident shear viscosity—each quantity independent of time and frequency. It says that shear stress is proportional not only to the strain itself, but also to the time rate of change of strain. Despite its simplicity, this model has a special role in elastography because it is the language in which experimental and clinical data are communicated. In fact, the first generation of clinical elastography systems makes no effort to describe the frequency or rate dependence of shear tissue properties.

As noted earlier, the shear viscosity of soft tissues, as seen through the simple viscoelastic model, is strongly frequency dependent. For the broader picture, therefore, more complex models are required. This *second* class of models involves acoustic relaxation, in which the medium contains inner time-dependent systems that are driven through the external bulk medium. The stress response with relaxation is dependent on both strain

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