Noninvasive Measurement of Elastic Properties of Living Tissue

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The new approach builds upon the theory, that the elasticity of a sample is dependent on the velocity of sound waves propagating in the material. In technical mechanics, this relationship is well known. A model, describing the mechanical behaviour of biological tissue is developed. It takes non-linear mechanical tissue properties into account. The quantification of a relation, appropriate for the determination of the elastic material properties by non-invasive measurements of the sound speed is discussed on the basis of the experimentally derived data and the biophysical considerations.

1 INTRODUCTION

For the purpose of education and training in the field of minimally invasive surgery, a system has been developed prototypically at Forschungszentrum Karlsruhe [1] [2], simulating the interactions between surgical instruments and biological tissue graphically. The physician uses “real” instruments, which are located in an input box, while the virtual operation scenario is shown on a screen. According to the movements of the instruments, the deformation and movement of the organs is simulated in the way the scenario would behave in a real operation. The simulated bladder tissue has elastic behaviour and is deformable in real-time. For a realistic representation and modelling of the elastodynamic behaviour of biological tissue the coefficients of stiffness (Young's modulus, shear modulus, bulk modulus, viscosity) have to be known. Especially if force feedback is added to the simulation, the intuitive impression strongly depends on the model used and its elastodynamic parameters. Previously, elastic soft tissue parameters have been estimated, because there was no testing method available to measure the quantities non-invasively. Elastic properties of biological tissue are leading values in medical diagnosis, too. The physician palpates hard and soft regions with means of his sense of touch and he evaluates pathology using his experience. This kind of diagnosis allows only qualitative statements, which depend on the subjective feeling of the physician.

If mechanical means for classical elasticity determination (tension or compression tests) are used, only body regions near the surface are taken into account, or invasive incisions have to be made. Gauging tissue, that is removed from the body and is cut from innervation and blood supply, yields incorrect values [3]. State of the art methods determine the elastic material properties of living tissue by means of stimulating the test item with vibrations at low frequencies. They conclude elasticity parameters from tissue behaviour at only one kind of sinusoidal strain. Further, they only estimate the amount of the stress amplitude inside the body [4], [5],

[6], [7]. As a result, present methods of elasticity testing are unreliable due to stress amplitude changes, which are not measured, and due to the retroactive testing principle.

There are several radiological imaging methods for the non-destructive testing of biological bodies (Ultrasound, X-ray- and magnetic resonance technique). They are capable of registering regions lying deep inside the body non-invasively. However, only a small selection of material properties can be determined by such means. In order to develop a new method to measure the coefficients of stiffness of living tissue non-invasively (in-situ), an investigation is carried out on a transformation of the technical laws being applicable to the mechanical and acoustical properties of biological living tissue.

2 THEORETICAL BACKGROUND

Typically, the elastodynamical properties of biological tissue are more complex than those of technical materials. In terms of mechanical features, organic tissues are mostly non-linear, anisotropic, non-homogeneous viscoelastic and viscoplastic media. In this work, we restrict the subject to the local determination of mechanical properties. In Figure 1 a typical stress-strain-diagram recorded from tension and compression tests on soft biological materials is shown.

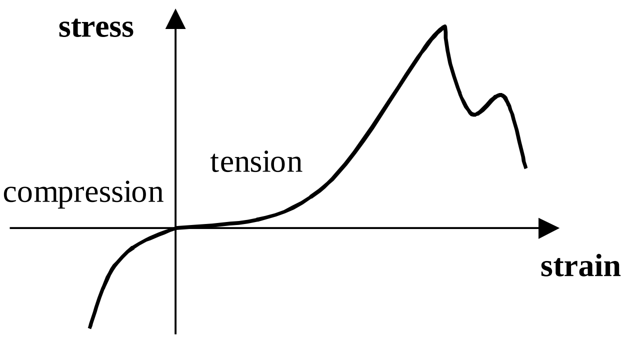

Figure 1: typical stress-strain-diagram for biological media

Combining Hooke's Law with Newton's second law of motion, and including the description of a propagating planar wave, the *Christoffel equation*

$$(\boldsymbol{C}_{ijkm}\mathbf{n}_j\mathbf{n}_m - r\ c^2_{sound} \cdot d_{ik})\mathbf{U}_k = 0 \tag{1}$$

is derived. ($\boldsymbol{C}_{ijkm}$: adiabatic anisotropic tensor of elasticity, **n**: unit vectors of the direction of propagation, r: tissue density, c_{sound}: sound wave velocity, δ_{ik}: Kronecker symbol and $\mathbf{U}_k$: vector of particle displacement)

The Christoffel equation states that the elasticity tensor of a material is related to the propagation velocity of a planar mechanical wave. Therefore, a connection between the coefficients of stiffness, in the linear case they are named Young's modulus, shear modulus and Lamé constants respectively, and the velocity of sound is stated by theoretical foundations.

A general phenomenological model is proposed, which is shown in the following equation:

$$s = f(e, c_{sound}, \vec{\mathrm{v}}_{load}, T, \text{material}) \tag{2}$$

(σ: compressive stress, f: general function, ε: compressive strain, c_{sound}: sound speed, $\vec{\mathrm{v}}_{load}$: deformation speed and direction, T: temperature)

The results of the experimental series will show, to which extent anisotropy and the viscous material properties have to be taken into account for the construction of a theoretical model. Afterwards it is to decide, whether the complexity of the model can be reduced by assuming linear or time-independent material behaviour.

3 NONINVASIVE MEASUREMENT

In order to carry out the non-invasive measurement, a method is proposed to determine the speed of ultrasound waves propagating in living organs in situ using diagnostic imaging systems. Two images have to be recorded, one of which providing the ultrasound echo time information, the other one showing the topological data.
In order to apply the non-invasive method to living tissue the sample has to meet the following conditions:

- To determine the sound velocity in a body region, always both, the transfer time and the spatial sound path length, must be measurable by means of non-invasive testing.
- The sound velocities of the sample and the surrounding parts must be different from each other. In this case, refraction phenomena occur at the boundary, which result in reverse propagating sound waves. By measuring the time difference of the echo signals arriving at the receiver, the transfer time is given.
- An unambiguous relation between an echo and a boundary must be established to reconstruct the path of the sound beam.

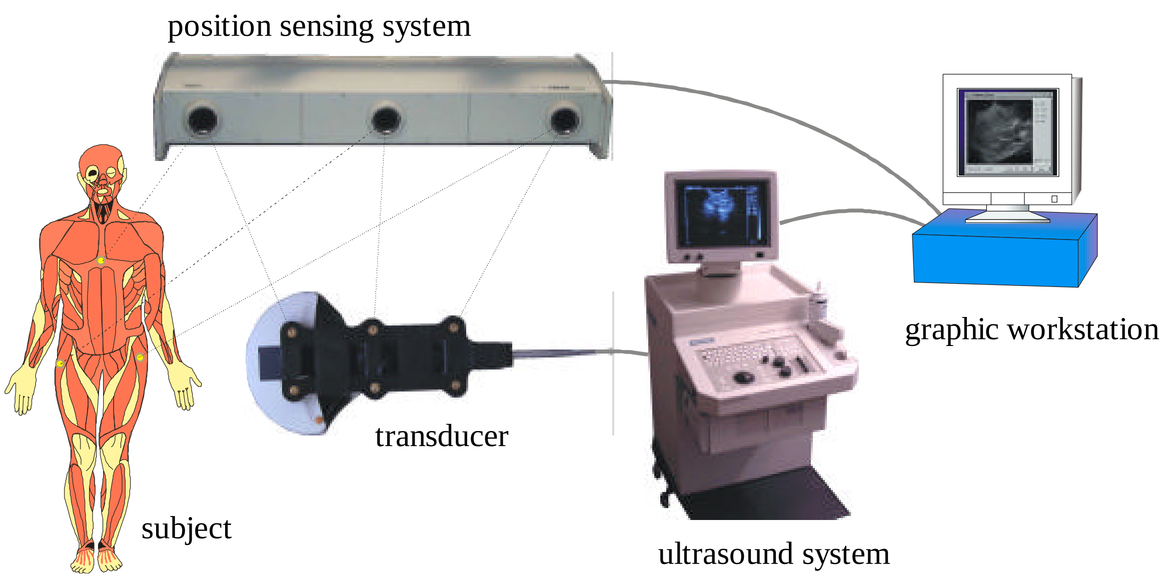

Figure 2: arrangement for the non-invasive sound speed measurement

In Figure 2 the arrangement being used for the measurement of the sound speed is shown. The non-invasive determination of the sound speed has been performed for living kidney and liver. The obtained velocity values are similar to those given in literature [8]. The error caused by the non-invasive measurement does not exceed 1%. Performing the measurement the user has to choose two targets. Both targets have to be taken by the imaging system twice, using two different gauging directions. Subsequently, one image has to be distorted in order to match the other. The sound speed results from the scalefactor of the echographic image which does the best match.

The propagation behaviour of mechanical waves at ultrasound frequencies was studied in a simulation. A computer calculates a resulting ultrasound image from materials' topological and acoustical properties. The calculations show the problems, that occur if considerable acoustic impedance differences or high values of acoustical damping are present.

4 EXPERIMENTS AND RESULTS

A large series of practical experiments was conducted. In a first step, the elastic tension behaviour of biological tissue was investigated by means of uniaxial tension tests of bovine tissue. Tissue samples of freshly slaughtered animals were fixed in a tension test machine and stress-strain curves were recorded at different strain dynamics. The test showed that the mechanical tension properties are non-linear, viscoelastic and strongly dependent on the sample type. In a second step, stress-compression diagrams and the sound velocity were recorded at the same time. A uniaxial compression test was combined with sound transfer time measurements along the compression axis. In order to quantify the phenomenological model a mobile testing machine was designed, providing means for the simultaneous measurement of the compression modulus and the sound velocity.

If mechanical strain is applied to living cell tissue, the stress quantities result from coupled longitudinal and transversal stiffness. The stiffness of individual cell membranes combines with the incompressibility of intra- and extracellular water [9]. The acoustic properties are mainly affected by the chemical material composition and the temperature, which is actively held constant in living organisms. Average sound speed and stress are being measured using the testing device. Figure 3 shows the comparison between sound speed- and origin tangential modulus ranges for each inner organ tested.

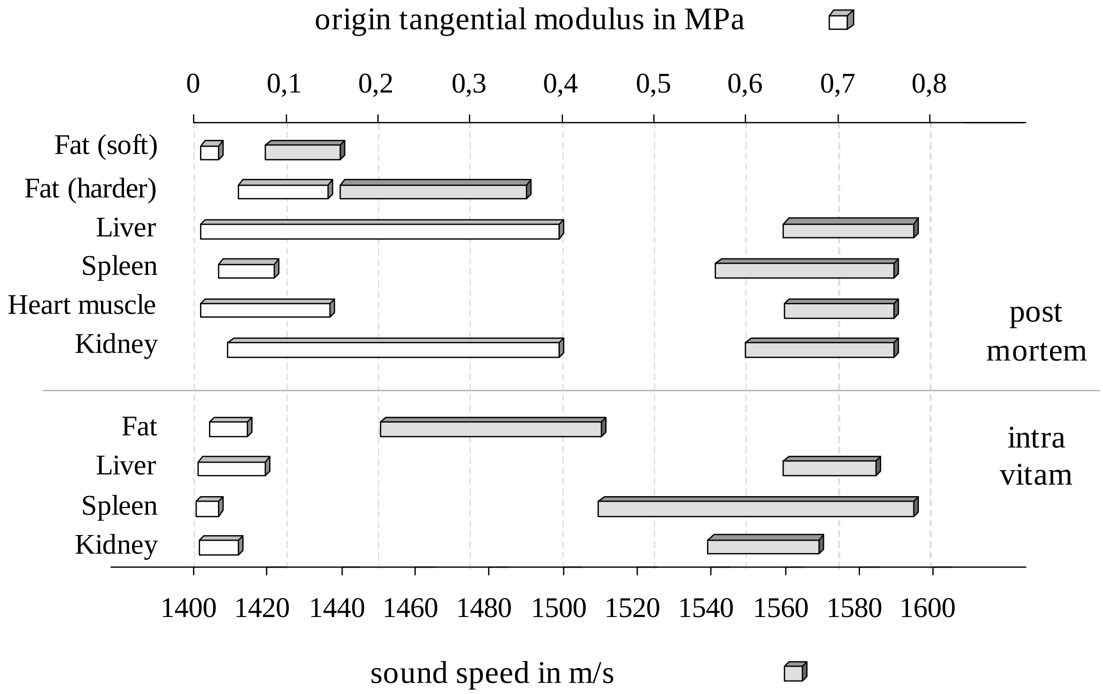

Figure 3: sound speed and origin tangential modulus

Experiments were performed on excised tissue from freshly slaughtered pigs and cows. Further, inner organs of living pigs, which can be strained in compression, were tested in vivo and post mortem and the results were compared with each other.

The stress-strain diagrams were approached by linear and polynomial regression analysis. Consequently, the resulting coefficients were compared with the speed of sound and the compression velocity by correlation methods.

The non-linear shape of the stress-strain curves was quantified by an approach using a 3rd degree polynomial curve. The polynomial was splitted in a scaling part (scaling value *E*) and a shape part, described by the shape factors P_1 and P_2 as shown in the equation

$$s = E \cdot e \cdot (1 + P_1 \cdot e + P_2 \cdot e^2) \tag{3}$$

(σ: compressive stress, ε: compressive strain, E: scaling value, P_1, P_2: non-linear shape factors)

Important results from the experiments are:

- Fat can be differentiated from the other materials by measurements of the speed of sound.
- The detailed results showed no correlation between mechanical compression behaviour and sound velocity.
- Considerable changes in the mechanical properties have been observed between samples tested in vivo and post mortem.
- The non-linear shape of the stress-strain curves was organ specific.
- There was a linear slope in the stress-compression relationships in the range between 0% and 15% compressive strain.
- No dependence could be observed between compression velocity and mechanical behaviour in the range of rather slow deformations.

5 CONCLUSIONS

The new aspects of the proposed method for measuring stiffness coefficients are the evaluation of a correlation between mechanical properties and sound speed of soft biological tissue and the non-invasive multimodal measurement using medical diagnostic imaging systems. Only the quantities that can be determined non-invasively were taken into account. All testing devices provided sufficient accuracy and sensitivity. Further, enough tests have been carried out to give generalised statements.

The mechanical properties of biological tissue depend on further quantities. For example, it has been observed that blood perfusion is of fundamental importance. The experiments, performed on samples in vivo, resulted in lower elastic values, while higher elastic quantities were derived from the same objects tested post mortem. In comparison, the sound speed showed no change. Also, the organ shape and location in the mechanical system has a leading influence on the elastodynamical material behaviour. On the other hand, the sound speed mainly depends on the chemical composition of the sample.

In this work squeeze-tests are being performed. This kind of method is not known in technical material testing. It was found to be the only practicable way to apply mechanical and acoustical testing simultaneously to biological media in situ. Shear forces that occur at the boundaries of the piston may affect the measured stress values.

Combined experiments, including tension tests and sound speed measurements, have not been carried out in this work. In literature, almost all given values refer to tension tests. But the results are not comparable with each other, because the cross-section of a biological soft tissue can not be held constant during tension tests. Further, it is not well documented, which part of the stress strain curve was taken into account for the calculation of the stated Young's modulus.

The non-invasive determination of the sound speed can be used for the differentiation between fat and other soft materials or the evaluation of the fat proportion in biological tissue.

For the construction of a general acoustomechanical model according to this work quantities have to be considered, which cannot be determined non-invasively using currently available medical diagnostic systems [10].

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