Mechanical Characterization of the Liver Capsule and Parenchyma

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Abstract. Internal organs are heterogeneous structures, both on the macro- and on the micro-scale. However, they are often modeled as homogeneous solids with uniform material properties. In this light, this work investigates the impact of the liver capsule on the integral behavior of the organ by means of in vitro tests and computer simulations. The stiffness of bovine liver obtained in tissue aspiration experiments differed by a factor of 2 to 3 when the capsule was removed. As a first step, the capsule was implemented as separate structure in a finite element model of the organ undergoing tissue aspiration. The finite element simulations are in good agreement with the experimental results.

1 Introduction

The identification of the mechanical properties of soft biological tissues is essential to the understanding of their functions, and therefore to a number of medical applications such as diagnosis, surgery planning and training of surgical procedures with virtual reality-based simulators (Picinbono et al. [1], Snedeker et al. [2] and Szekely [3]). Several experimental methodologies have been proposed for the mechanical testing of soft tissues (Brown et al. [4], Kalanovic et al. [5], Nava et al. [6], Nava et al. [7], Ottensmeyer [8] and Snedeker et al. [9]), but only few quantitative data are available for the in vivo behavior of human organs (Kauer et al. [10], Mazza et al. [11], Nava et al. [12] and Carter et al. [13]). Current methodologies describe the entire organ complex as a homogeneous material, neglecting the individual component tissues.

Internal organs essentially consist of a functional vascularized internal part (parenchyma), and an external capsule (stroma). The capsule is a thin but tough fibrous supporting connective framework of densely interwoven collagen fibers. The capsule primarily serves the structural integrity of the organ. Previous studies investigated the histology and quasi-static properties of the renal capsule (Yamada [14], Herbert et al. [15] and Farshad et al. [16]) and parenchyma (Yamada [14], Melvin et al. [17] and Farshad et al. [16]). Recently, Snedeker et al. [9] investigated the dynamic properties of the renal capsule at strain rates associated with blunt abdominal trauma. However, little data exist on the mechanical properties of the liver capsule (Yamada [14] and Arnold et al. [18]).

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The preliminary study presented in this paper has been undertaken in order to quantify the influence of the capsule on the mechanical behavior of internal organs. For this purpose, capsule and parenchyma of a bovine liver have been characterized individually and compared with their integral "parenchyma-capsule" response. These investigations are for example essential for the interpretation of in vivo aspiration experiments performed during open surgery (Mazza et al. [11], Mazza et al. [19] and Nava et al. [12]).

The capsule was tested in quasi-static uniaxial tension, whereas aspiration experiments were used to characterize the intact organ and the parenchyma. Constitutive equations were derived for implementation in numerical simulations. Finite element (FE) simulations of the liver undergoing aspiration, treating the capsule and parenchyma as separate structures, are presented.

2 Methods

The importance of the capsule in modeling the mechanical behavior of internal organs has been investigated using the example of a bovine liver. All experiments were conducted ex vivo and were performed in accordance with Swiss federal ethical research standards.

An intact bovine liver was obtained from the slaughterhouse immediately following animal euthanasia. The liver was transported on ice and kept moist wrapped in a physiological saline soaked surgical cloth at 4°C until the samples were prepared. The samples were tested within 8 hours of animal euthanization.

2.1 Uniaxial Tensile Testing of the Liver Capsule

For the specific characterization of the liver capsule, samples were extracted and tested in a standard uniaxial tensile test setup. The load-displacement diagrams were recorded with a Zwick 1456 universal uniaxial test machine (Zwick Inc., Ulm, Germany). A custom-made bio-chamber was used to simulate "in vivo" conditions. The vertical test setup is shown in Fig. 1A.

The capsule samples were prepared according to a method similar to Herbert et al. [15] and Snedeker et al. [9]. Samples were delicately excised using a surgical scalpel and a thin copper sheet template. The samples were approximately 15 mm in width and 50 mm in length. After incision, the trace of the scalpel in the underlying liver cortex was measured to verify a uniform sample width. The sample thickness was assumed equal within the same sample, and was assessed by averaging three measurements taken at random locations using a micrometer caliper. The capsule samples were then gently peeled off from the liver cortex using the fingers and surgical forceps. To facilitate the handling of the liberated samples, they were carefully placed and spread with the fingers on a sheet of ordinary paper, yielding a membrane sample with paper backing. The capsule tissue adheres to the paper due to surface tension. Once on the paper, the underside of the capsule was cleansed thoroughly of the parenchymal remainders by softly applying a gauze. Finally, the samples were immersed in physiological saline at room temperature until testing. The time between sample preparation and mechanical test never exceeded 1 hour.

For testing, the paper-backed samples were comfortably fixed outside the test setup on clamps equipped with sandpaper, leaving an initial gage length of at least 40 mm. The paper-backing was then carefully removed over the gage length with forceps. The integrity of the clamp interfaces, i.e. slip-free condition, was verified by Snedeker et al. [9] using video data. Immediately after clamping, the capsule samples were introduced into the bio-chamber. During testing, the samples remained entirely immersed in the physiological saline. A heating plate in combination with a thermocouple controlled the solution temperature of 37°C (bovine body temperature). The tensile force was measured with a 50 N load cell at a specified accuracy of ±0.25% of the effective force. The specified positioning accuracy of the clamps is ±3 μm. A xy-bench was installed on the load cell to align and prevent from shearing the sample during testing. A preload of 0.2 N was applied at the beginning of the test. Tests were carried out under displacement-controlled conditions, with a strain rate of 0.5% per second. In order to obtain a "preconditioned" state of the tissue samples, i.e. stable response to several loading-unloading cycles, the samples were cycled 10 times between 0 and 15% nominal strain prior to ultimate loading until tissue rupture.

In the present work, test results are reported as nominal stress and nominal strain, whereas the nominal stress is reported as the axial force divided by the original cross-sectional area of the undeformed sample (i.e. the undeformed sample width before extraction multiplied by the average thickness measured), and the nominal strain was calculated using measurements of the clamp displacement. Ideally the nominal quantities would be specified according to the "in vivo" condition of the tissue. This is assumed in this study, but was not verified.

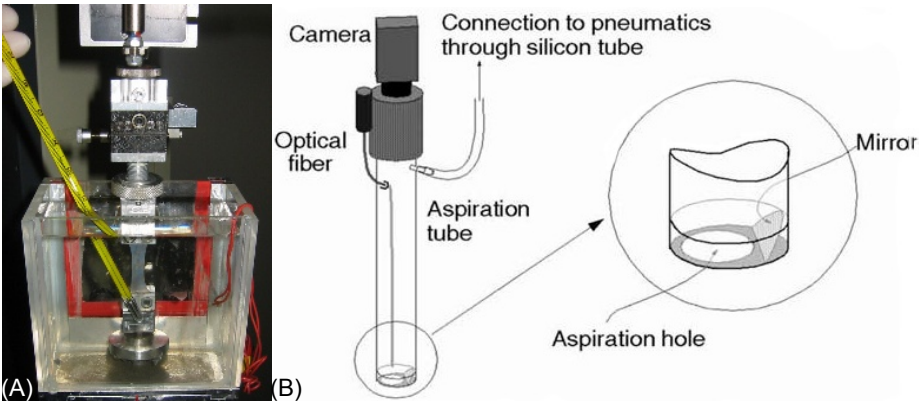

Fig. 1. (A) Capsule membrane sample exposed to uniaxial tensile testing inside the bio-chamber, and (B) aspiration device and principle of working

2.2 Constitutive Equations for the Capsule

With the simplifying assumptions of incompressibility, isotropy and non-dissipative behavior, the material response is characterized here by the so called reduced polynomial formulation of the strain energy potential U, shown in Eq. 1 (Yeoh [20]). The resulting relation between nominal uniaxial stress σ and stretch λ is given in Eq. 2.

$$U = \sum_{i=1}^{N} C_{i0} \left(\bar{I}_1 - 3 \right)^i \tag{1}$$

$$\sigma = 2\left(\lambda - \lambda^{-2} \right) \sum_{i=1}^{N} i C_{i0} \left(\lambda^2 + 2\lambda^{-1} - 3 \right)^{i-1} \tag{2}$$

C_{i0} are the material parameters and N is the order of the polynomial fit. $\bar{I}_1$ is the first deviatoric strain invariant. The parameters of the reduced polynomial form were determined for $N = 5$. Fitting was carried out with respect to the "preconditioned" final loading cycle. Constitutive equation parameters were defined after averaging of all data sets.

2.3 Aspiration Device

2.3.1 Setup and Experiments

The aspiration device shown in Fig. 1B has been developed by Vuskovic [21] and recently improved for new experiments, see Mazza et al. [11] and Nava et al. [6]. The device has been designed for in vivo applications. It consists of a tube in which the internal pressure can be controlled according to a desired pressure law. The experiment is performed by (i) gently pushing the tube against the tissue to ensure a good initial contact, and (ii) creating a time variable vacuum inside the tube so that the tissue is sucked in through the aspiration hole (diameter of 10 mm).

A complete description of the deformed tissue can be given by simply monitoring the side-view profile of the tissue during its deformation. The images of the side-view are reflected by a mirror and are captured by a digital camera. Time histories of measured pressure and deformation profiles are the input data used to evaluate the mechanical properties and to determine the constitutive model.

Two different sets of experiments were performed on the same bovine liver by applying the identical pressure history: (i) 4 experiments on different locations on the surface of the intact organ (in presence of the capsule), and (ii) 4 experiments on different locations after removal of the capsule. The organ was not perfused. The mechanical parameters were extracted from average displacement curves.

2.3.2 Mechanical Modeling

A phenomenological model is determined based on three-dimensional continuum mechanics analysis. The material is modeled as an incompressible, isotropic continuum with so called quasi-linear viscoelastic equations (Fung [22]). Viscoelasticity is taken into account by applying relaxation coefficients to the constants that define the energy function, Eq. 3. As for the capsule, the reduced polynomial form has been chosen for the strain energy potential U, Eq. 1.

$$C_{n0}(t) = C_{n0}^{\infty} \frac{\left(1 - \sum_{k=1}^{K} \bar{g}_k^P \left(1 - e^{-t/\tau_k} \right) \right)}{\sum_{k=1}^{K} \bar{g}_k^P} \tag{3}$$

In Eq. 3 the long term elastic module C_{n0}^{∞}, $\bar{g}_k^P$ and τ_k are material parameters to be determined from the experimental data. In the current implementation the second order

of the series expansion for the strain energy potential ($N = 2$) and at the second order for the Prony series ($K = 2$) are used.

The finite element method is applied to solve the so called ”inverse problem”: the experiment is simulated by a FE-model in which the time dependent aspiration pressure is imposed as kinetic boundary condition; the material constants are determined iteratively from the comparison of calculated and measured soft tissue deformation.

In order to evaluate the influence of the capsule on the mechanical behavior, two different models were applied: (i) a homogeneous model (Model A), and (ii) a bilayer model (Model B, see Fig. 4A), including as its top layer the organ capsule (thickness of 80 μm) and as the underlying layer the “homogeneous” parenchyma. Model A was used to analyze (i) the experimental curves of liver with capsule, and (ii) the data without capsule. The material parameters of the parenchyma were determined from (ii). Validation of the parameters (for capsule and parenchyma) is performed by simulating the aspiration experiment with Model B and comparing the displacement history to the experimental findings for liver with capsule.

3 Results and Discussion

The capsule samples were extracted from random locations of one bovine liver. A total of 5 samples were tested, and nominal stress-stretch data are reported for the preconditioned state of each sample. These preliminary results are not sufficient for proper statistical analysis, but allow a first insight on the mechanical properties of the liver capsule.

The tests yielded approximately bilinear nominal stress-stretch characteristics, Fig. 2. The curves are characterized by a relatively low initial stiffness, with a nearly linear stress-strain curve up to 3% strain. Considerable stiffening occurs between 5 and 10% strain, an effect typically attributed to the progressive fiber recruitment. Once a majority of fibers is engaged, the curves become nearly linear again, almost until tissue rupture.

The bilinear nature of the response is characterized with four scalar quantities: the low-strain elastic modulus E_1 and the high-strain elastic modulus E_2, the ultimate stress and strain denoted by σ_{max} and ε_{max}, respectively. A summary of the values is presented in Table 1.

Table 1. Results of the bovine liver capsule in tension (average and standard deviation are indicated)

Thickness [μm]	93 ± 6
E_1 [MPa]	1.1 ± 0.2
E_2 [MPa]	38.5 ± 4.9
σ_{max} [MPa]	9.2 ± 0.7
ε_{max} [%]	35.6 ± 5.2

The transition from low to high stiffness is quite consistent between samples, with the transition point, i.e. "locking stretch", occurring around 8% strain. The data show good repeatability. The evaluated low-strain elastic modulus E_1 varied less than 6.5% and the high-strain modulus E_2 less than 8%. The high-strain modulus agrees to a great extent with the published data of Snedeker et al. [9] and Yamada [14] for the similar tissue kidney capsule: Snedeker reported corresponding values of 41.5 MPa for human and 35.9 MPa for porcine kidney capsule, whilst Yamada obtained 38 MPa for cadaveric human kidney capsule. The average failure stress was calculated as 9.2 ± 0.7 MPa, which is in good agreement with findings of Snedeker, who reported a value of 9.0 ± 2.9 MPa. The measured thickness of the liver capsule samples varied as much as 5% within a given sample, and as much as 10% within the given liver, with an average value of 93 μm, what is almost double the values presented by Snedeker for the kidney capsule thickness.

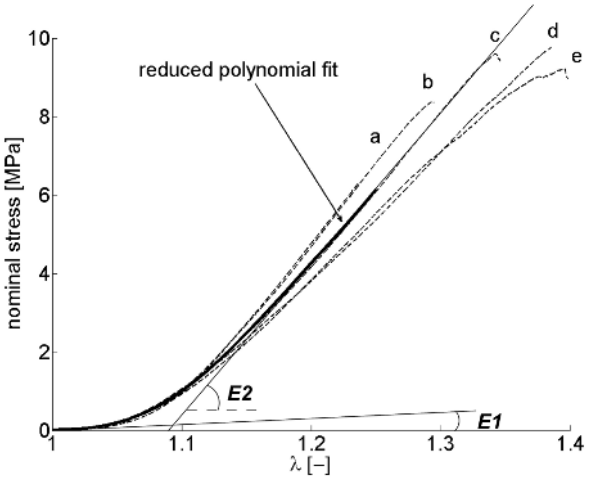

Fig. 2. Bovine liver capsule in uniaxial tension: the five samples *a* through *e* (*dashed*) and the resultant fit of a reduced polynomial hyperelastic material (*continuous bold*). The capsule exhibits a bilinear characteristic. E_1 was calculated as the slope of the best linear fit between 0 and 5% of the ultimate strain, and similarly E_2 was calculated between 60 and 80% of the ultimate strain. The parameters used in the reduced polynomial fit are [MPa]: C_{10} = 0.21, C_{20} = 33.7, C_{30} = -125.6, C_{40} = 235.6 and C_{50} = -58.2.

Through the inverse FE-characterization process of the aspiration tests, the mechanical parameters of the parenchyma and of the homogenized liver tissue (capsule and parenchyma considered as a single homogeneous tissue) were extracted. Fig. 3A shows the correspondence between simulated and measured displacement history in the aspiration test on the intact organ and the parenchyma. Fig. 3B shows the comparison of the corresponding uniaxial responses. Due to the influence of the capsule (with 3 orders of magnitude higher stiffness) the evaluation of the liver as homogenized tissue leads to an overestimation of the properties of the parenchyma by a factor of 2 to 3.

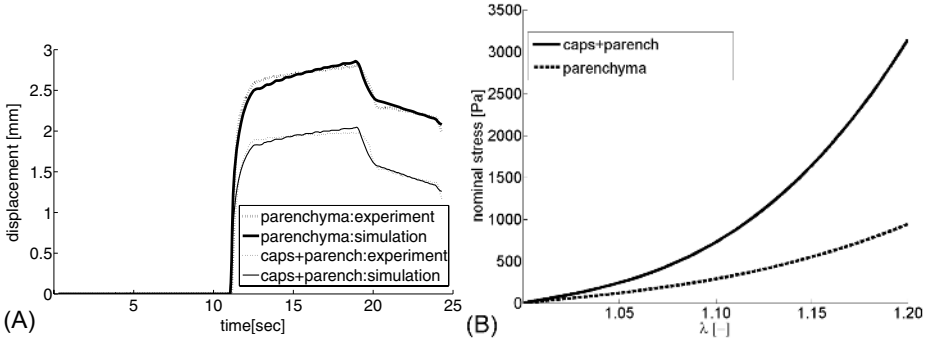

Fig. 3. Aspiration experiment on intact organ and parenchyma: (A) Inverse FE-characterization: simulation and experiments. (B) Corresponding uniaxial stress-strain behavior.

As a validation of the proposed models, the aspiration test on the intact liver has been simulated with the bilayer model. Fig. 4B shows the simulated and measured displacement history. The curve agrees to a good extent with the corresponding experimental data. The observed discrepancy might be related to the neglected time dependence of the mechanical response of the capsule.

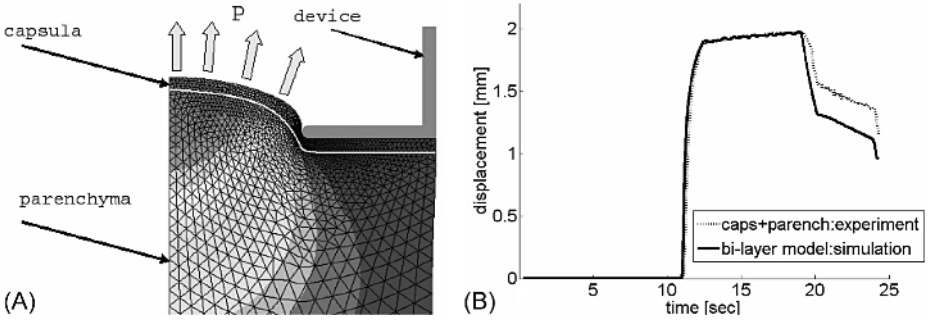

Fig. 4. (A) Bilayer FE-model. In the figure, the thickness of the capsule has been magnified by a factor of 10 to graphically better represent the model. (B) Comparison between the bilayer FE-simulation and the experiments.

4 Conclusions

The bovine liver capsule has been mechanically characterized in vitro in uniaxial tension in preconditioned state until tissue rupture. Findings agree well with published data for the human and the porcine kidney capsule (Snedeker et al. [9], Yamada [14]). The good repeatability of the tests confirms the suitability of the testing protocol and evaluation procedure. Accurate characterization of the "in vivo" loading conditions of the capsule and implementation of these as initial experimental condition in tensile tests will improve the reliability of the corresponding constitutive equations. In

addition, experiments with different loading rates will allow time dependence of the capsule response to be characterized.

Aspiration experiments were carried out on the intact organ and, having removed the capsule, on the parenchyma. The results show considerable differences in the corresponding mechanical response, and neglecting the influence of the capsule leads to a significant overestimation of the parenchymal properties. This demonstrates the importance of correct modeling of the capsule for (i) simulation of organ behavior, and (ii) interpretation of experimental data for diagnostic purposes.

To this end, a bilayer model of the organ has been implemented in the inverse FE-characterization process of the aspiration experiment. Using constitutive equations extracted from the individual measurements of capsule and parenchyma, FE-simulations yield good agreement with respect to the experimental displacement curves.

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