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Research Paper

Numerical identification method for the non-linear viscoelastic compressible behavior of soft tissue using uniaxial tensile tests and image registration – Application to rat lung parenchyma

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ABSTRACT

This paper presents an improved identification method of the constitutive properties of lung parenchyma. We aim to determine the non-linear viscoelastic behavior of lung parenchyma with a particular focus on the compressible properties - *i.e.* the ability to change volume. Uniaxial tensile tests are performed on living precision-cut rat lung slices. Image registration is used to compute the displacement field at the surface of the sample. The constitutive model consists of a hyperelastic potential split into volumetric and isochoric contributions and a viscous contribution. This allows for the description of the experimentally observed hysteresis loop. The identification is performed numerically: each test is simulated using the realistic geometry of the sample; the difference between the measured and computed displacements is minimized with an optimization algorithm. We compare several hyperelastic potentials and we can determine the most suitable law for rat lung parenchyma. An exponential potential or a polynomial potential with a first order term and a third or higher order term give similarly satisfactory results. The identified parameters are: for the volumetric contribution: κ=7.25e4 Pa, for the exponential form: k_1=4.34e3 Pa, k_2=5.92, for the polynomial form: C_1=2.87e3 Pa, C_3=3.83e4 Pa. The identification of the time parameter for the viscous contribution shows that it depends on the loading frequency (0.2 Hz: τ=0.257 s, 0.4 Hz: τ=0.123 s, 0.8 Hz: τ=0.050 s). Adding a viscous contribution significantly increases the accuracy of the identification.

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1. Introduction

Characterizing the mechanical behavior of lung tissues has been the subject of several scientific studies as it is required to model the global and local behavior of the lung. A computational model of the whole lung could help understanding several phenomena related to lung diseases. For instance, acute respiratory distress syndrome (ARDS) is a disease that alters the mechanical behavior of lung parenchyma (Kallet and Katz, 2003). When a patient suffering from ARDS is mechanically ventilated to help him breathe, healthy and diseased areas are deformed but the compliance difference of these two tissues can lead to local overstretching in the parenchyma. A lung model including mechanical properties of both healthy and diseased parenchyma could help locating and quantifying the possible overstretching occurring within the parenchyma; treatment strategies could therefore be adjusted to avoid this phenomenon. A comprehensive model of the lung is currently developed in our group including among others, structure and fluid phenomena (Wall et al., 2010).

Lung parenchyma consists of alveolar tissue, including respiratory bronchioles, alveolar ducts and terminal bronchioles, as well as surfactant. At the macroscale (organ scale, *i.e.* a few cm for rat lung), it can be considered as homogeneous but at the microscale (alveolar scale, *i.e.*50–100 μm for rat lung), it exhibits a foam-like structure due to the alveoli, which are inflated with air during breathing. Therefore, unlike most of the soft tissues commonly studied (*e.g.* abdominal organs, skin, aorta), it cannot be considered as incompressible at the macroscale as its main function is to be inflated. Most of the previous studies to characterize the lung parenchyma have investigated its non-linear elasticity and viscoelasticity but the compressible properties – *i.e.* the ability to change volume – have not been characterized sufficiently so far.

To characterize lung parenchyma, the few available previous studies describe mostly uniaxial tensile tests on tissue slices. Briefly, in terms of elasticity, either an exponential potential (Navajas et al., 1995) or a polynomial potential (Rausch et al., 2011) describes rather accurately the uniaxial behavior of the lung parenchyma. Gao et al. performed biaxial tensile tests and concluded that an exponential law was the best fit for the tissue behavior (Gao et al., 2006). A volumetric component of the constitutive law is only assessed in Rausch et al. (2011); however, the method to identify the volumetric parameters of the constitutive law only relied on the displacement of a single location in the sample and the measurement of this displacement was done by hand.

In terms of viscoelasticity, uniaxial tensile tests were used to characterize the dynamic response of the tissue. Different frameworks helped quantifying the tissue viscosity, the most common (Mijailovich et al., 1994; Navajas et al., 1995; Romero et al., 2011; Pinart et al., 2011; Yuan et al., 1997) being quasilinear viscoelasticity proposed by Fung that decouples the elastic and viscous phenomena and allows accounting for elastic non-linearities (Fung, 1993). In these studies, harmonic distortion, loss and storage moduli as well as elastance, resistance and hysteresivity of the tissue were computed with the help of a Fourier transform. These parameters allow for the investigation of the influence of loading factors – like stress amplitude, strain amplitude, frequency – or pathologies – like fibrosis (Dolhnikoff et al., 1999), acute lung injury (Ingenito et al., 1994; Rocco et al., 2001) – on the material parameters. A review of the elastic and viscous characterization of lung tissue, in particular using tests on excised samples, is given in Suki and Bates (2011). Another framework is proposed by Holzapfel and Gasser (2001) to account for the three-dimensional non-linear viscoelasticity of fiber-reinforced composites: the hyperelastic potential associated with the elastic behavior of the tissue is modified by a viscous contribution. This framework is particularly suited for a direct use in non-linear continuum mechanics based simulations, this is why this approach is chosen in the present paper.

The aim of this paper is to determine a non-linear viscoelastic constitutive model for lung parenchyma employing novel experimental and identification methods. As our complete lung model describes explicitly the surfactant, it requires the characterization of the tissue itself without surfactant – which induces further viscoelasticity. This characterization is done in the present paper.

The paper is divided into five parts: the first part covers the description of the experimental methods, particularly the optical method to measure the displacement field on the sample. In the second part, the numerical model and the constitutive law proposed for the lung parenchyma are detailed. The third, fourth and fifth parts are focused on the identification method, the results and the discussion respectively. The sixth part gives some limitations to the present work.

2. Uniaxial tensile tests on living PCLS

Since the preparation of the samples and the experimental setup are described in a previous paper (Rausch et al., 2011), only the main features are recalled here.

2.1. *Preparation of the samples*

The Precision-Cut Lung Slices (PCLS) are prepared from three isolated rat lungs as previously described in Martin et al. (1996). The lungs are dissected from the animal, filled with an agarose solution (1.5%) via the trachea and put on ice to allow the agarose to cool down and solidify. The lung lobes are separated and cut into tissue cylinders using a coring tool. The obtained cylinders have a diameter of 14 mm; they are then cut into slices using a Krumdieck tissue slicer (Alabama Research and Development, Munford, AL). The thickness is set to 500 μm. The two sides of the round slices are trimmed with two parallel razor blades giving the tissue strip a width of 7.0 mm. The obtained strips are therefore $7 \times 12 \times \simeq 0.5\ \mathrm{mm}^3$ (Rausch et al., 2011).

The strips are incubated in minimal essential medium (MEM) and the agarose is washed out by frequently changing the medium within the first 4 h and completing an overnight incubation. As shown in Martin et al. (1996), the obtained PCLS are viable for three days. In this protocol, the rat samples are tested within 48 h after death, which guarantees that the tissue is still living while being tested (Martin et al., 1996; Ressmeyer et al., 2006); preliminary studies showed that the mechanical properties are not changing within 3 days