

# Method of testing very soft biological tissues in compression

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## Abstract

Mechanical properties of very soft tissues, such as brain, liver, kidney and prostate have recently joined the mainstream research topics in biomechanics. This has happened in spite of the fact that these tissues do not bear mechanical loads. The interest in the biomechanics of very soft tissues has been motivated by the developments in computer-integrated and robot-aided surgery—in particular, the emergence of automatic surgical tools and robots—as well as advances in virtual reality techniques. Mechanical testing of very soft tissues provides a formidable challenge for an experimenter. Very soft tissues are usually tested in compression using an unconfined compression set-up, which requires ascertaining that friction between sample faces and stress-strain machine platens is close to zero. In this paper a more reliable method of testing is proposed. In the proposed method top and bottom faces of a cylindrical specimen with low aspect ratio are rigidly attached to the platens of the stress-strain machine (e.g. using surgical glue). This arrangement allows using a no-slip boundary condition in the analysis of the results. Even though the state of deformation in the sample cannot be treated as orthogonal the relationships between total change of height (measured) and strain are obtained. Two important results are derived: (i) deformed shape of a cylindrical sample subjected to uniaxial compression is independent on the form of constitutive law, (ii) vertical extension in the plane of symmetry  $\lambda_z$  is proportional to the total change of height for strains as large as 30%. The importance and relevance of these results to testing procedures in biomechanics are highlighted.

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**Keywords:** Soft tissue; Mechanical properties; Mathematical modelling; Compression experiment

## 1. Introduction

Mechanical properties of very soft tissues, such as brain, liver, kidney and prostate have recently joined the main directions of research in biomechanics. This has happened in spite of the fact that these tissues do not bear mechanical loads. The interest in the biomechanics of very soft tissues has been motivated by the developments in computer-integrated and robot-aided surgery—in particular, the emergence of automatic surgical tools and robots—as well as advances in virtual reality techniques. Mechanical testing of very soft tissues provides a formidable challenge for an experimenter. Very soft tissues are usually tested in compression using an unconfined compression set-up, Fig. 1 (Estes and McElhaney, 1970; Miller and Chinzei, 1997).

While conducting the experiment care must be taken to minimise friction between the sample and machine platens. Only when friction can be assumed to be zero

can one assume that the sample expands uniformly during the compression and, therefore, that the state of deformation within the sample is orthogonal, Eq. (1).

$$\mathbf{F} = \begin{bmatrix} \lambda_z^{-1/2} & 0 & 0 \\ 0 & \lambda_z^{-1/2} & 0 \\ 0 & 0 & \lambda_z \end{bmatrix}, \quad (1)$$

where  $\mathbf{F}$  is a deformation gradient;  $\lambda_z$  is a stretch in vertical direction. In Eq. (1) incompressibility and isotropy of the sample material are assumed. If the assumption of friction being negligible is violated, Eq. (1) is invalid and measurement results misleading. Current biomechanics literature recognises this problem, and addresses it by proposing reliable (but complicated) ways to ensure the friction is close to zero, see e.g. (Miller and Chinzei, 1997; Nasseri et al., 2003).

To strengthen the argument, I present finite element simulations of unconfined compression experiment with coefficient of friction between the sample and machine platens ranging from 0 to 0.1, conducted using commercial program ABAQUS (ABAQUS, 1998). The

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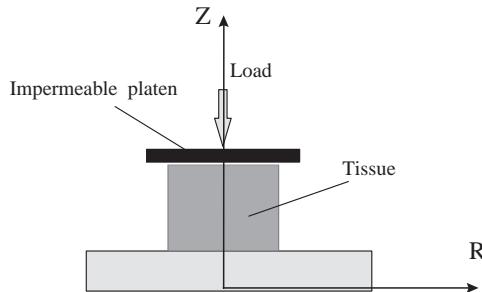


Fig. 1. Layout of unconfined compression experiment set-up with coordinate axes.

Table 1

Reaction force at 20% compression of cylindrical sample (30 mm diameter, 10 mm height) for coefficients of friction between 0 and 0.1

Coefficient of friction	Reaction force (N)
$\mu=0$	0.485
$\mu=0.05$	0.521
$\mu=0.1$	0.563

mesh was taken from (Miller, 1999):  $30 \text{ m} \times 10 \text{ m}^2$  cylinder modelled by 480 CAX4RH four-node, axisymmetric elements. For simplicity, the Mooney–Rivlin material (Mooney, 1940) was chosen, with material constants  $C_1 = C_2 = 200 \text{ Pa}$ . This roughly corresponds to brain mechanical properties at very slow loading. Because of tissue incompressibility the hybrid elements (with pressure as additional variable) were chosen. The compression plates were taken to be circular, 50 mm in diameter (i.e. much larger than specimen), and rigid. The results presented in Table 1 show that even low friction has substantial effect of producing shear stresses, which leads to increasing the measured reaction force, and consequently the overestimation of tissue's stiffness. The numerical result for zero friction agrees exactly with the analytical solution. Analytical solutions for cases with non-zero friction do not exist.

In this paper a more reliable method of testing is considered. In the proposed method top and bottom faces of a cylindrical specimen with low aspect ratio are rigidly attached to the platens of the stress–strain machine (e.g. using surgical glue), Fig. 2.

This arrangement allows using a no-slip boundary condition in the analysis of the results. The no-slip boundary condition set-up has been used previously in my work on soft tissue properties in tension (Miller, 2001; Miller and Chinzei, 2002). It was shown that the no-slip boundary condition, with the application of surgical glue as described in (Miller and Chinzei, 2002) or coarse sand paper as Lynne Bilston used for her shear experiments (Bilston et al., 2001) is reliable. Surgical glues do not infiltrate the tissue. To conduct the experiment is very easy: one prepares a cylindrical sample, applies surgical glue to tissue faces (or attach

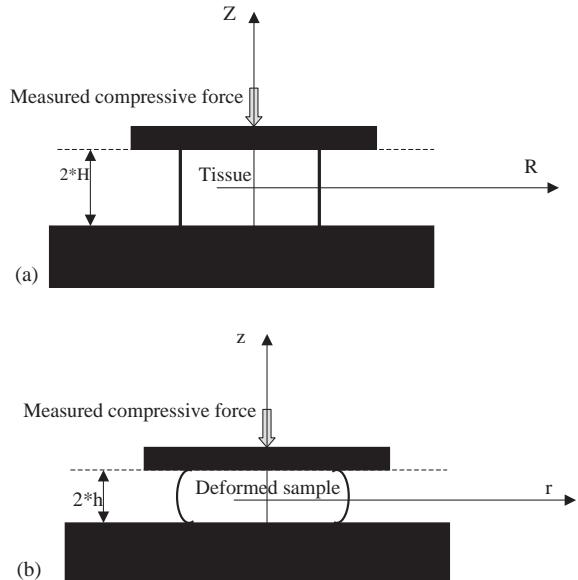


Fig. 2. Sketch of the experimental set-up with no-slip boundary conditions; sample height  $2h$  and vertical force are measured; (a) undeformed sample, (b) deformed sample.

coarse sand paper to machine platens) and conducts the compression. It is the analysis of measurement results that is difficult. The manuscript addresses this problem.

Even though the state of deformation in the sample cannot be treated as orthogonal the relationships between total change of height and strain (needed for the constitutive law identification) are derived below in the way analogous to that used for extension. Two novel (though analogous to similar results for extension) results are obtained:

- (i) The shape of the compressed cylindrical sample of isotropic, incompressible tissue does not depend on the constitutive law describing the properties of the tissue.
- (ii) The vertical extension in the plane of symmetry (middle of the sample height)  $\lambda_z$  is proportional to the total change of height for nominal strains as large as 30%.

It is claimed that these two results allow the analysis of uniaxial compression experiments with no-slip boundary conditions performed on cylindrical samples with low aspect ratio in analogous way to that routinely used in the unconfined compression with no-friction boundary conditions.

## 2. Compression experiment set-up

Typically, in experiments on brain tissue cylindrical samples of diameter  $\sim 30 \text{ mm}$  and height  $\sim 10 \text{ mm}$  are

used (Miller and Chinzei, 1997; Miller and Chinzei, 2002). Steel pipe (30 mm diameter) with sharp edges is used to cut the samples. The faces of the cylindrical brain specimens are smoothed manually, using a surgical scalpel. Uniaxial compression of brain (or other very soft tissue) can be performed in a testing stand sketched in Fig. 2. The testing apparatus should be able to move the machine head within large range of velocities (to simulate strain rates typical to impact, surgical or quasi-static conditions) and measure accurately small (fractions of a Newton) vertical forces.

### 3. Theoretical analysis of compression experiment

In compression experiment described above the kinematics of the deformation is complex, prohibiting the existence of exact analytical relations between the measured force and stress, and between the measured total change of height and strain in the sample for any realistic constitutive law chosen to describe tissue mechanical properties. This, in my opinion, is one of the reasons why such a set-up has not been used before. However, with a few reasonable assumptions an approximate solution can be found.

The mathematical description of the experiment and the analysis of the state of deformation in the sample are similar to those presented for extension in (Miller, 2001). I consider a circular cylinder bonded between two rigid end-plates (Fig. 2). The disc of radius  $R$  and height  $2H$  in undeformed state is compressed to the final height  $2h$  by uniform surface forces applied normal to the end-plates. For the coordinate system in the unstrained state we take Cartesian coordinates  $\{X, Y, Z\}$ . The Cartesian coordinate system  $\{x, y, z\}$  for deformed body is taken to coincide with the system  $\{X, Y, Z\}$ . In the analysis the following assumptions are employed:

#### 3.1. Incompressibility

Very soft tissues are most often assumed to be incompressible (see e.g. Pamidi and Advani, 1978; Walsh and Schettini, 1984; Sahay et al., 1992; Mendis et al., 1995; Miller and Chinzei, 1997; Farshad et al., 1999; Miller, 1999, 2000, 2002).

#### 3.2. Isotropy

Very soft tissues do not bear mechanical loads and do not exhibit directional structure (provided that a large enough sample is considered: for brain we used samples of 30 mm diameter and 10 mm height). Therefore, they may be assumed to be initially isotropic (see e.g. Pamidi and Advani, 1978; Walsh and Schettini, 1984; Sahay et al., 1992; Mendis et al., 1995; Miller and Chinzei,

1997; Farshad et al., 1999; Miller, 1999, 2000; Bilston et al., 2001, Miller and Chinzei, 2002).

Prange and Margulies (2002) report anisotropic properties of brain tissue. However, their sample sizes were 1 mm wide. At such a small length scale a fibrous nature of most tissues will come into play and directional properties will be detected. Experimental technique discussed here aims at identifying “average” properties at the length scale of approx. 1 cm. At such length scales most very soft tissues can be safely assumed not to exhibit directional variation of mechanical properties.

#### 3.3. The planes perpendicular to the direction of the applied force remain plane

From the above assumptions it follows (Miller, 2001) that in the plane of symmetry,  $Z=0$ , off-diagonal components of the deformation gradient vanish. This is a very important observation—the deformation in the plane of symmetry is orthogonal.

$$\mathbf{F}(X, Y, 0) = \begin{bmatrix} \lambda_z^{-1/2} & 0 & 0 \\ 0 & \lambda_z^{-1/2} & 0 \\ 0 & 0 & \lambda_z \end{bmatrix}, \quad (2)$$

where  $\lambda_z$  is a stretch in vertical direction (Fig. 2).

Following the procedure described in detail in Miller (2001), one obtains the following implicit equation for the deformed shape of the compressed sample:

$$z = \frac{\text{Elliptic E} \left[ \arcsin \left[ \frac{f[z]}{f[0]} \right], -\frac{C_2 f[0]^2}{C_1} \right] f[0] \sqrt{\frac{f[0]^2 + f[z]^2}{f[0]^2}}}{\sqrt{\frac{(C_1 + C_2)\text{const } 1(-f[0]^2 + f[z]^2)}{C_1 + C_2 f[z]^2} \sqrt{\frac{C_1 + C_2 f[z]^2}{C_1}}}} \text{const } 2, \quad (3)$$

where  $f(Z) = r/R$  is the shape of the side of the compressed sample.  $C_1$  and  $C_2$  are integration constants. Elliptic E denotes the elliptic integral of the second kind. It is difficult to calculate integration constants and convert Eq. (3) into an explicit formula for  $f(Z)$ . However, one can obtain important relationships for two extremes of the material behaviour:

- Neo-Hookean material  $\Rightarrow W = C_1(I_1 - 3); \mu/2 = C_1$ ;
- Extreme-Mooney material  $\Rightarrow W = C_2(I_2 - 3); \mu/2 = C_2$

where  $W$  is a potential function,  $I_1$  and  $I_2$  are strain invariants and  $C_1$ ,  $C_2$  are material constants. The physical meaning of constants  $C_1$ ,  $C_2$  in the limit of infinitesimal deformation is:  $\mu/2 = C_1 + C_2$ , where  $\mu$  is the shear modulus. It is known that real materials fall somewhere in between these two extremes. These relationships, first obtained by Klingbeil and Shield (1966) are given by Eqs. (4)–(7).

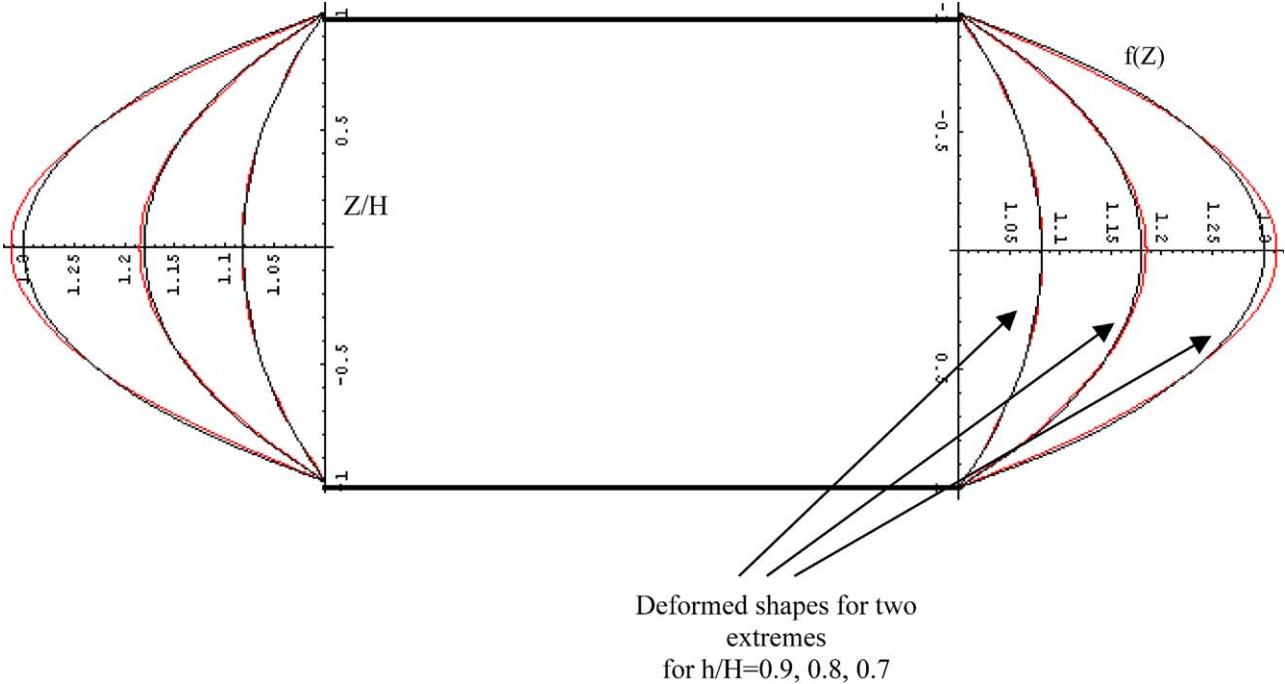


Fig. 3. Deformed shapes of samples made of Neo-Hookean (lighter, exterior curves) and Extreme-Mooney (darker, interior curves) materials for  $h/H=0.9, 0.8$  and  $0.7$ —for practical purposes deformed shapes for the two extreme cases are the same.

For Neo-Hookean material  $\Rightarrow W=C_1(I_1-3); \mu/2=C_1$

$$\frac{h}{H} = \frac{\sqrt{-1 + \lambda_z^2}}{\lambda_z^2 \operatorname{arcsec}(\lambda_z)}, \quad (4)$$

$$f(Z) = \lambda_z \cos\left\{\frac{\operatorname{arcsec}[\lambda_z]}{H} Z\right\} \quad (5)$$

and for Extreme-Mooney material  $\Rightarrow W=C_2(I_2-3); \mu/2=C_2$

$$\frac{h}{H} = \frac{\operatorname{arccosh}(\lambda_z)}{\lambda_z \sqrt{-1 + \lambda_z^2}}, \quad (6)$$

$$f(Z) = \lambda_z \sqrt{1 - \frac{(-1 + \lambda_z^2)Z^2}{H^2 \lambda_z^2}}, \quad (7)$$

where  $\lambda_z$  is a stretch in vertical direction (Fig. 2),  $h$  is half of the current height of the sample (measured),  $H$  is half of the initial height of the sample (known),  $r$  the current radius of the sample at elevation  $Z$ ,  $R$  is the initial radius of the sample (known) and  $f(Z)=r/R$  is the shape of the side of the deformed sample. Eqs. (4)–(7) are different to corresponding equations for extension (Miller, 2001) because the implicit solution (valid for compression) used here, Eq. (3), is different to the one used in the case of extension.

To plot the deformed shapes for both cases for a given displacement of the machine head  $h/H$  one has to compute numerically the vertical stretch in the plane of

symmetry  $\lambda_z$  from Eqs. (4)–(6), and substitute to Eqs. (5) and (7), respectively. Fig. 3 shows the comparison of the deformed shape for different compression levels for these two extreme cases.

It can be seen that despite apparent differences in the form of equations the actual deformed shape is almost the same. The maximum difference in radius for  $h/H=0.7$  does not exceed 1%. From the perspective of testing biological materials, which inherently exhibit large variability of mechanical properties (see e.g. Estes and McElhaney, 1970; Miller and Chinzei, 1997 for brain; Melvin et al., 1973; Farshad et al., 1999, for liver and kidney), this difference in shape, and the resulting difference in the cross-sectional area are negligible. For practical purposes, I conclude that the deformed shape of the cylindrical sample of incompressible biological material is insensitive to the form of the constitutive law defining its mechanical properties.

Fig. 4 presents, for the two extreme cases, the relationship between the vertical stretch in the plane of symmetry  $\lambda_z$  and the displacement of the machine head  $h/H$ , Eqs. (4) and (6).

Even though Eqs. (4) and (6) look complicated they really describe, to high accuracy, the same linear relationship. The vertical stretch in the plane of symmetry is proportional to the change in total height, at least for  $h/H$  between 1 and 0.7.

$$\lambda_z(Z=0) - 1 = K_c \left( \frac{h}{H} - 1 \right); K_c = 1.411. \quad (8)$$

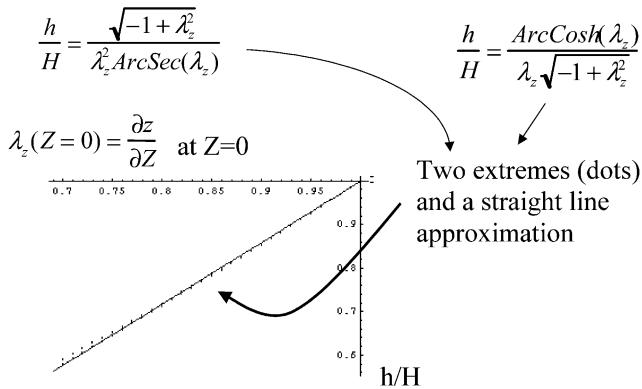


Fig. 4. Linear (for practical purposes) relationship between the measured machine head movement  $h/H$  and the vertical stretch in the plane of symmetry  $\lambda_z(Z=0)$  for samples made of Neo-Hookean and Extreme-Mooney materials.

#### 4. Discussion and conclusions

Two theoretical results presented in this paper have important implications for testing in biomechanics of very soft tissues. As shown above, in the uniaxial compression experiment with no-slip boundary conditions, in the plane of symmetry  $Z=z=0$  (see Fig. 3) the orthogonal state of deformation can be assumed. This state of deformation can be described, as in the case of the unconfined compression experiment with no-friction boundary condition (Miller and Chinzei, 1997), by a diagonal deformation gradient, Eq. (2). Therefore, the results of the uniaxial compression with no-slip boundary conditions of cylindrical biological specimens can be analysed in analogous way to that used in the unconfined compression no-friction boundary conditions:

Unconfined compression with no-friction boundary conditions (see Fig. 1) =>

$$\lambda_z(Z=0) = \frac{h}{H} \quad (9)$$

Uniaxial compression with no-slip boundary condition (see Fig. 2) =>

$$\lambda_z(Z=0) - 1 = K_c \left( \frac{h}{H} - 1 \right); K_c = 1.411. \quad (10)$$

To test how the properties of tissue change with the speed of loading (strain rate) one would like to conduct series of experiments for various, but constant, nominal strain rates. Since  $\lambda_z$  is linearly related to  $h/H$ , constant velocities of the machine head  $h/H = \text{constant}$  translate to constant stretch rates in the plane of symmetry  $\dot{\lambda}_z(Z=0)$ . This is an important feature, which allows equation for stress to be resolved analytically even for complicated forms of energy function  $W$ , used e.g. in quasi-linear, hyper-viscoelastic constitutive laws first proposed for biological tissues by Fung (1981).

The most common of these energy functions are polynomials in strain invariants derived basing on Mooney's theory (Mooney, 1940; Mendis et al., 1995; Miller, 1999, 2000). Another important class is represented by Ogden-type energy functions in the form of powers of principal stretches (Ogden, 1972; Miller and Chinzei, 2002). For both cases if orthogonal state of deformation can be assumed one can compute the only non-zero Lagrange stress component from the simple formula:

$$T_{zz} = \frac{\partial W}{\partial \lambda_z}. \quad (11)$$

This can be done analytically. The explicit formula for stress in case of polynomial energy function is given in (Miller, 1999); and in the case of Ogden-type energy function in (Miller and Chinzei, 2002). These explicit, analytical formulas for stress together with proven orthogonality of the state of deformation in the plane of symmetry of the sample allow analysing measurement results and identifying constitutive models in a straightforward way.

The limitation of the proposed method is that it cannot be used for experiments at very high strains. In such case, at the circumference of the sample face attached to the machine platens high shear stresses would develop. This would result in violation of the assumption (3) that the planes perpendicular to the direction of the applied force remain plane. This limitation does not affect the utility of the method in very soft tissue biomechanics where the most interesting is the material response for strains of a few to about 20%.

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