ORIGINAL ARTICLE

Rheological properties of myometrium: Experimental quantification and mathematical modeling

Karel Jelen [1*], František Lopot [1*], Štěpán Budka [1], Vít Nováček [2], Radek Sedláček [3]

1. Charles University, Faculty of Physical Education and Sport, Dept. of anatomy and biomechanics, Laboratory of Biomechanics of Extreme Loading, Prague, Czech Republic
2. University of West Bohemia, Department of Mechanics, Pilsen, Czech Republic
3. Czech Technical University, Faculty of Mechanical Engeneering, Laboratory of Biomedicine, Prague, Czech Republic

**Correspondence to:* Karel Jelen; František Lopot
TEL: +420 603 526 656
E-MAIL: jelen@ftvs.cuni.cz; flopot@seznam.cz

Submitted: 2008-04-10 Accepted: 2008-05-15 Published online: 2008-08-30

Key words: **biomechanics; uterus; rheology; tensile test; creep**

Neuroendocrinol Lett 2008; **29**(4):454–460 **PMID:** 18766144 NEL290408A09

Abstract

This work answers some questions related to detection of rheological properties of soft tissues exemplified in myometrium, stressed by external tensile force.
In the first stage of the experiment the tissue samples were ciclically stressed and response loops were recorded. This test proved severe plastical deformation of samples, which is not usually being stated for living tissues. In addition to course, growth and stabilizing this deformation also energetical losses of individual hysteresis loops of the response were evaluated.
In the second stage of the experiment the tissue samples were exposed to a loading force changed in step-wise manner in four steps. The sample response to each force step was processed and evaluated separately to obtain basic properties of used model. In next step, the changes in model characteristics were obtained and evaluated for each element in subsequent force steps. By reason of following easier interpretation, the quite simple visco-elastic model, defined by differential equation with analytic solution, is used. The results prove necessary to introduce in model both spring and damper constants dependent on the magnitude of the loading force and one damper with even time dependent constant. The interindividual variability of characteristic values of the model elements is surprisingly low. On the other side, they are strongly dependent on load magnitude. Complete mathematical model of uterine wall tissue is obtained by amending the principal equation by formulas describing changes in individual components of the model.

INTRODUCTION AND AIM

The subject to research are visco-elastic properties of myometrium tissue and observation of its transformation from various views. Because the project is still in progress, we do not have any comprehensive results to present and this text is therefore a sort of summary of problems and complications we have faced while processing the data so far and which are to be solved before, during and after every soft tissue testing in general.

Fundamental and irresolvable problem is unability to test samples *in vivo*. This causes some complications that may quite seriously influence results of experimental measurements. Living biological tissues are open systems with constant en-

ergy and mass transformation. Tissue is hence able to change its properties very dynamically, the whole organ can resize etc. As a result especially soft tissues have no unique initial state that can the material return to after the stress releases and it is very difficult and in many cases impossible to define one and only reference system for tension – deformation relation [4, 7]. A specific example are changes of muscular tissue mechanical properties resulting from its nerve control.

This work points out the presence of plastical deformation in the beginning of tested sample response to mechanical stress and evaluates it from the enegetic point of view.

In the actual rheological model of myometrium are used viscous and elastic components with characteristics dependent on stress level as well as time. Use of these components is caused by our struggle to capture the fact that testing is being performed on dead tissue samples.

All tissues can be viewed as visco-elastic materials with strongly non-linear behaviour during the load. How far the non-linearity is expressed, depends on the structure of the investigated material [4, 7]. Uterine wall has a quite complex structure, which changes its mechanical properties very progressively [1, 6]. In principle, there are two possible approaches to assess such complex material structure: First, it is possible to design a simple experiment with continuously changing magnitude of the inlet variable. Material response can be modelled by an equation fitted to the measured values. The equation will actually define numerical solution of a complex differential equations describing power equilibrium on the modelled situation. The second approach needs a more complicated measurement procedure, which however simplifies the calculations. Based on the choice of the controlled variable, i.e. either force or deformation, it is possible to use the creep mode or material relaxation phase. In both cases we observe response of the material caused by its plasticity, which results in gradual decrease of tension in tested sample. Deformation increase is observable during the creep, being a response to stress by constant force. Relaxation shows itself when stressing the sample using constant deformation. Decrease of sample reaction force can be detected.

To detect and analyze progressive change in model characteristics, multiple measurements of the response of the controlled variable are performed under different load. The response is then decsribed by a relatively simple equation, which is in fact an analytically solvable solution of the differential equation of power equilibration of the model structure. Complete mathematical model of the tissue is then created by adding equations describing the recorded behaviour of individual model components.

MATERIAL AND METHOD

Samples characteristics

Samples were taken from different parts of fundum uteri of 32 females (aged 24–65 years) during gynaecological operations and childbearings by sectio caesarea. Before measurement, the samples are conserved in physiological solution at temperatures from 5 to 6 °C not longer than a few days. For easier evaluation of the measured data, the cross sections of the samples are rectangular shaped with dimensions standardised to (20–55)×(3–5)×(3–5) mm. During testing the samples were not moistened.

Measurement procedure, instrumentation

The first experiment took place at the MTS 858 Mini Bionix device following this protocol:

- stress: simple tension
- stress direction: caudal-cranial
- controlled variable:
  deformation (feedback controlled by force from 0 to approx. 4 N (Fig. 1))
- stressing speed: 10 mm / min
- share of liquid in overall sample volume was not monitored before, during and after the test
- the samples were not moistened during the test

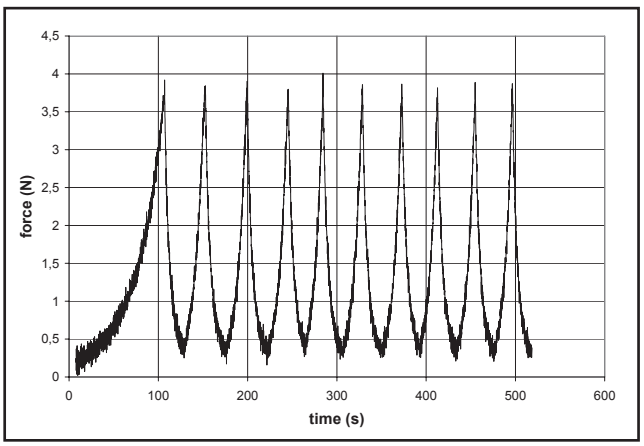

Figure 1: Stressing samples by force 0 - 4 N

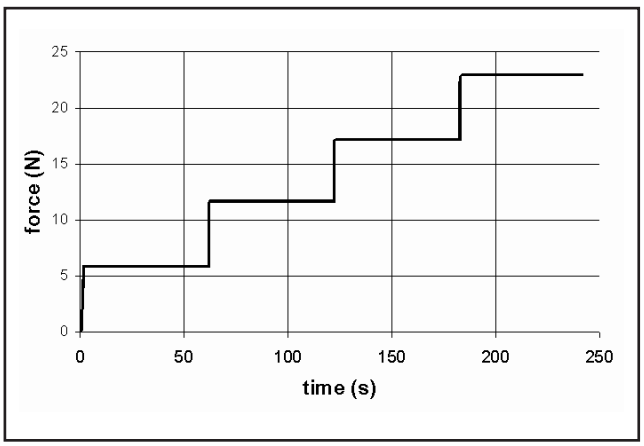

Figure 2: Stressing the sample by step changed force

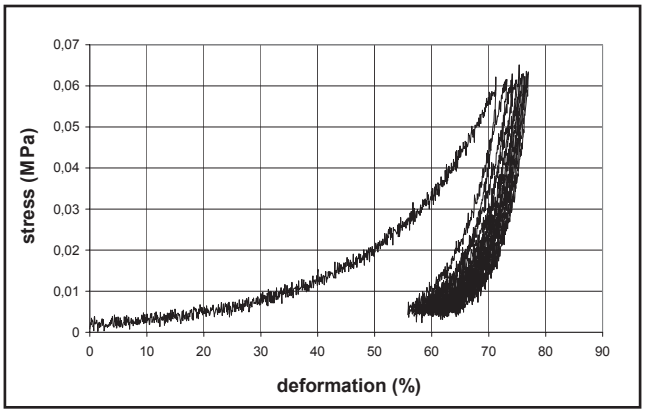

Figure 3: Plastic deformation increase of the sample

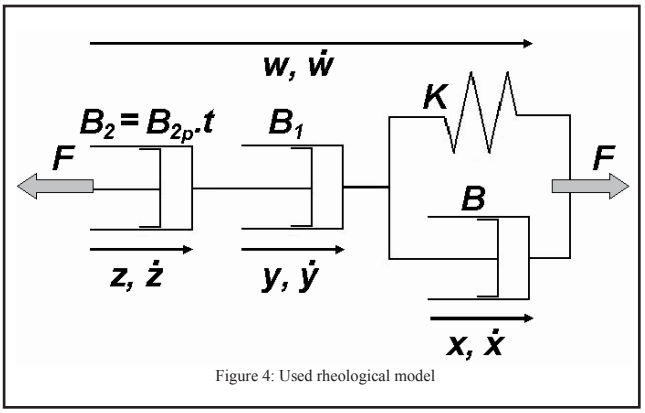

Figure 4: Used rheological model

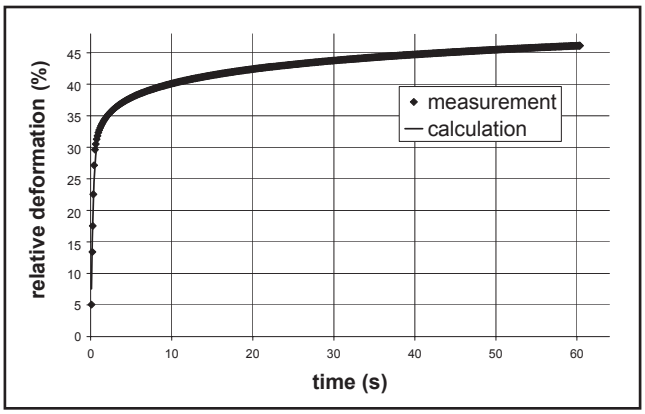

Figure 5: Approximated course of response to the first force step

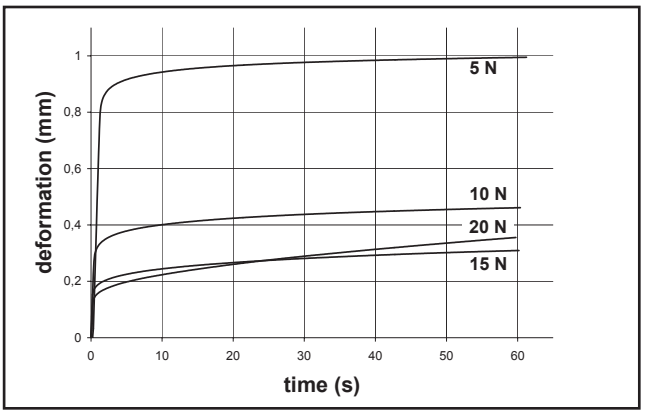

Figure 6: Sample response to individual step changes of stress - creep

For the second experiment we used the Zwick 050 device and following protocol:

- stress: simple tension
- stress direction: various
- controlled variable:
  force changed in step-wise manner (four steps from 0 to cca 20 N in cca 5-N steps; (Fig. 2).
- force change rate: 4,5 N/sec (enables to view the steps as approximately rectangular)
- share of liquid in overall sample volume was not monitored before, during and after the test
- the samples were not moistened during the test

Sample response with sampling frequency of 10 Hz was detected in both experiments. There was constant air humidity of 60–80 % and temperature within 24 to 26 °C in the laboratory.

Data processing and evaluation

Data processing and evaluation is performed in the simplest way possible in order to reach acceptable precision along with objective results interpretation.

Initial plastic deformation

In Fig. 3 is a course of plastic deformation increase of samples during cyclical stress

After the first cycle the relative deformation increased to approx. 56%. In following steps the increase continued to value 63% with gradual decrease of increments in individual cycles.

Evaluation was performed in two steps. In the first stage we smoothened measured curves and evaluated areas of individual hysteresis loops. In the second stage were these values marked in the graph and their change trend was specified.

Rheological model of the tissue

The tissue was modelled as a visco-elastic material using a combination of basic elastic and viscous elements – springs and dampers (Fig. 4).

The results prove necessary to introduce in model both spring and damper constants dependent on the magnitude of the loading force and one damper with even time dependent constant. Force equilibrium is described by the following equation system:

$$F = K.x + B.\frac{dx}{dt};\ F = B_1.\frac{dy}{dt};\ F = B_2.\frac{dz}{dt};$$
$$B_2 = B_{2p}.t;\ w = x + y + z, \qquad (1)$$

Table 1: Results (arithmetic average ± standard deviation)

cycle	area	deformation
	J	–
1	3,913 ± 0,07860	0 ± 0,000
2	0,638 ± 0,02486	0,56 ± 0,014
3	0,498 ± 0,00700	0,57 ± 0,010
4	0,510 ± 0,01551	0,59 ± 0,009
5	0,293 ± 0,00784	0,62 ± 0,009
6	0,299 ± 0,00562	0,61 ± 0,005
7	0,286 ± 0,00481	0,61 ± 0,005
8	0,231 ± 0,00414	0,63 ± 0,009
9	0,194 ± 0,00447	0,62 ± 0,009
10	0,221 ± 0,00291	0,63 ± 0,010

Table 2: Results (arithmetic average ± standard deviation)

Sign	Unit	1. step	2. step	3. step	4. step
K	N /mm	6,85 ± 0,11	18 ± 0,26	29 ± 0,45	38,5 ± 1,02
B	N.s /mm	3,7 ± 0,03	4,5 ± 0,02	4,5 ± 0,03	4,5 ± 0,02
B_1	N.s /mm	178 ± 2,63	200 ± 2,70	220 ± 6,66	235 ± 8,05
B_{2p}	N /mm	$0{,}8.10^6$ ± 0,00*	35000 ± 0,00*	13000 ± 165,7	3100 ± 103,8

* selected values (Displayed values are results of iterative computations rounded to percental units. Due to size of these values and sensitivity of the model to their variation is possible to omit such deviation and consider these values identical in given stress steps for all measurements)

where ***F*** is sample reactive force, ***K, B,*** B_1, B_2 and B_{2p} are characteristics of model components and ***x, y*** and ***z*** are their deformations, ***w*** is overall sample deformation. Fraction ***d.../dt*** is time-based derivation and in this specific case deformation speed.

Fig. 5 displays the nearly perfect fit of the measured and modelled response to the first jump of the loading force. As can be seen from Fig. 6, the increasing load significantly changes the sample response.

As a result a response to each force step was processed and evaluated separately and characterics of each of the model elements were first obtained for each measured tissue sample. Next step was evaluation of the changes in characteristics obtained for each element in subsequent force steps.

RESULTS

Present results show us that interindividual variability of characteristic values of the model elements is surprisingly low not only in case of cyclical stress, but also in case of creep. Cyclical stress was tested on ten samples under stress mode (Fig. 3). We used 32 tissue samples and determined relevant constants ***K, B,*** B_1 ***a*** B_{2p} for construction of rheological model based on Fig. 4.

Initial plastic deformation

Tab. 1 summarizes average values of individual hysteresis loops energies and average relative deformation on every stress cycle end from all ten measurements..

For better clarity the energy data are displayed in graph and interleaved with hyperbolical function (Fig. 7):

$$E = \frac{12000}{(1{,}6.x)^{2{,}5}} + 210\,, \qquad (2)$$

where ***E*** means energy and x is cycle sequence number (counted from 1). Correlation coefficient value R^2 is 0,992.

Rheological model of the tissue

The model used allows very close fitting of curves on measured data. Correlation coefficient R^2 is between 0,978 and 0,996. Mean values of the characteristics of the final model from all 32 measurements are summarised in Tab. 2.

Standard deviations suggest relatively comparable mechanical properties of uteral tissues in different individuals. However, all characteristics exhibited significant changes with increasing load:

1. Spring stifness ***K*** (Fig. 4, eq. 1) increases according to the icreasing loading size steeply (Fig. 8). To describe, a linear function is used:

$$K = 1{,}88.F - 4{,}064\,;\ \mathrm{R}^2 = 0{,}997 \qquad (3)$$

2. Parallel viscosity ***B*** (Fig. 4, eq. 1) changes are very low and the value reaches fastly the equilibrium (Fig. 9). A logarithmic function is applied:

$$B = -32{,}39.e^{-0{,}63.F}\,;\ \mathrm{R}^2 = 0{,}999 \qquad (4)$$

3. Time constant serial viscosity B_1 (Fig. 4, eq. 1) increases according to increasing loading size (Fig. 10). A linear function seems to be well sufficient function for description:

$$B_{1p} = 3{,}39.F + 159{,}28\,;\ \mathrm{R}^2 = 0{,}999 \qquad (5)$$

4. Time variable serial viscosity B_{2p} (Fig. 4, eq. 1) significantly decreases with increasing load (Fig. 11). Its behavior is modeled by a hyperbolic function:

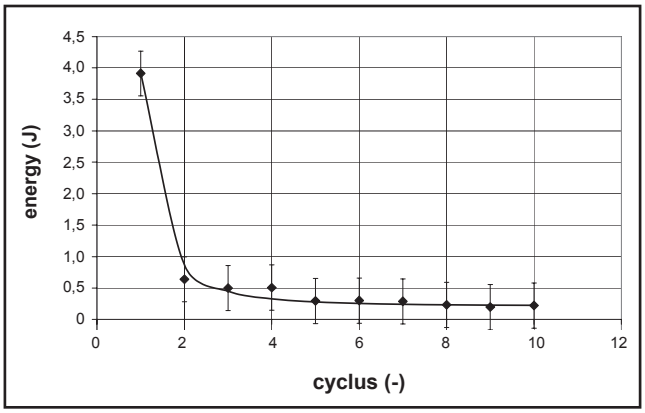

Figure 7: Hysteresis loops energy based on Fig. 3

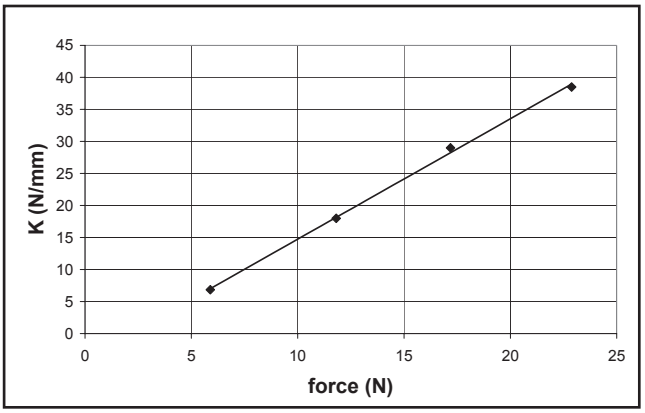

Figure 8: Relation of spring constant ***K*** and tensive force

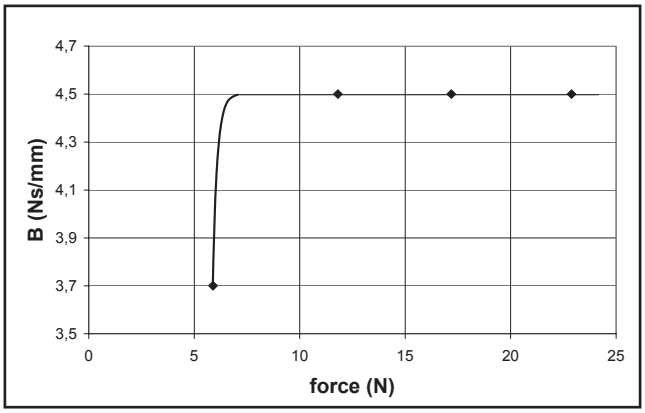

Figure 9: Relation of parallel viscosity ***B*** and tensive force

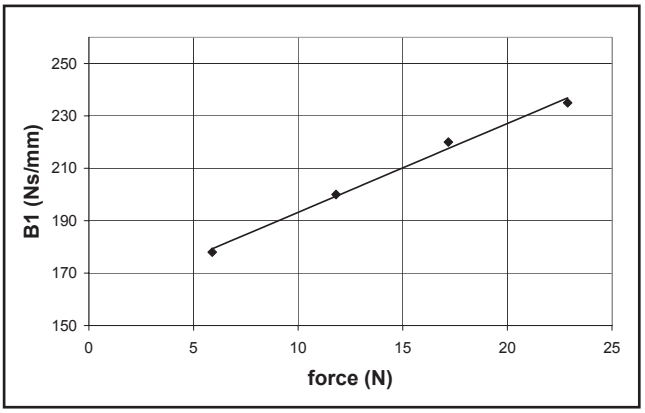

Figure 10: Relation of constant serial viscosity B_1 and tensive force

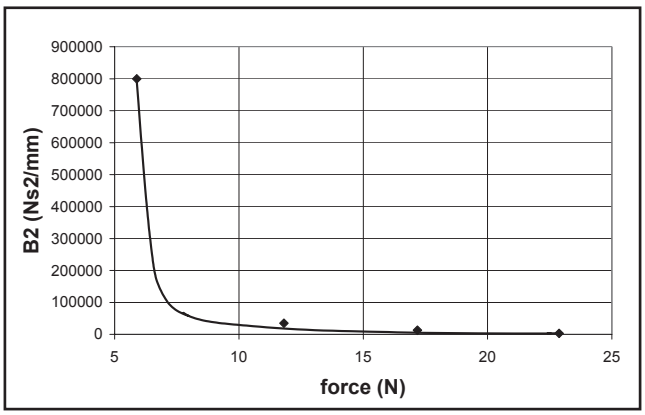

Figure 11: Relation of time-variable serial viscosity B_{2p} and tensive force

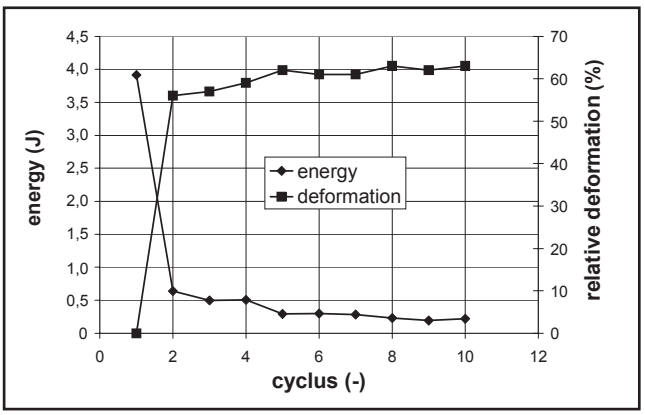

Figure 12: Response hysteresis loops energy and plastic deformation of samples

$$B_2 = B_{2p}.t \qquad (6)$$

$$B_{2p} = \frac{105000}{(0{,}107.F)^{4{,}4}} + 1120\,;\ \mathrm{R}^2 = 0{,}999 \qquad (7)$$

Symbol ***F*** stands for applied force in all equations, the letter ***t*** is used to represent time. By adding these equations (3, 4, 5, 6, 7) to the system (1) have we constructed mathematical model of the myometrium tissue creep.

DISCUSSION

During evaluation of experimental cyclical stressing of samples the offset had been found when comparing energy values of loops and discovered values of plastic deformations. As we can see from tab. 1, significant decrease in plastic deformation growth happened in the fifth stress cycle, while energy value of loop has stopped changing later, approximately from eight cycle (Fig. 12).

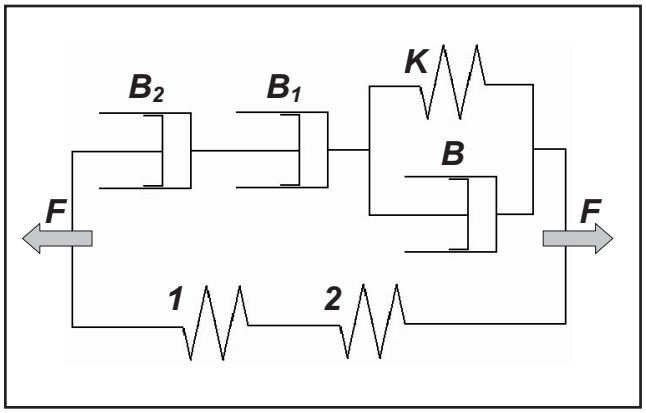

Figure 13: Complete rheological model

This moderate deviation may be caused by limited precision of recording and smoothing of measured loops preceding their area calculation. Due to values we are working with the energy seems to be less demanding for precision and therefore more suitable for consequent processing.

We are able to approximate energy that is consumed in order to transform tissue along with its plastic deformation and also energy, absorbed due to viscosity in given stress rate (Tab. 3). Because the plastic deformation increased as long as to seventh cycle's end, the equation used for computing overall amount of energy consumed in plastic deformation E_{pl} of samples will be as follows:

$$E_{pl} = E_{1-7} - 7.E_v , \qquad (8)$$

where E_{1-7} describes overall energy of the first seven hysteresis loops and E_v is an energy absorbed by viscosity, that is determined by arithmetic average of corresponding values of last three hysteresis loops.

Tab. 3: Distinguishing hysteresis loops energies

E_{1-7}	E_v	E_{pl}
J	J	J
6,4328	0,2156	4,9236

Origin of plastic deformation can be also found in microstructure of the tested tissue. A sample is no longer supplied with energy and chemicals necessary for individual structures since it is gathered. After depleting local energetic resources all processes halt and along with other things the dimensions of sample also remain unchanged. Plastic deformation detected in that case wouldn't be caused by limited mechanical properties of the sample but merely by change of internal tissue structure. Other factors affecting level of plastic deformation are autolytic processes, taking place in the sample after gathering. Because they need energy to keep going, which is not longer being supplied into the sample, their span is also questionable.

Suggested rheological model of myometrium creep fits nicely into experiment restrictions, although better simulation of reality would need some modification based on paralel connection of one or more springs (Fig. 13). To describe passive mechanical properties would suffice connection of spring 1 (pic. 13), that would prevent infinite creep, that exists in current state of the model. According to period in which the samples were stressed by constant force we can suppose that the spring would have really soft characteristic and to succesfully detect this characteristic a long-term stress was necessary. Realization of the experiment wouldn't then be the only question, dehydration of the sample would negatively affect it as well as meaning of this spring's characteristic determination in practical use. In real situations such a long creep is not usually present and in addition to that an adaptive ability of living organism could project itself into sping's characteristic. Determination of the spring's rigidity by testing dead sample would most likely provide very deformed data. For modeling of living tissue it would be necessary to include spring nr. 2 (Fig. 13), which represents contractile units of muscle present.

A viscous damper with time-variable characteristic we have used cannot be implicitly included in description of basic mechanical properties of living tissue. It is a unit used to emphasize the fact that the tissue tested is dead. In living tissue there is metabolism, saturation with liquids keeps approximately constant level and there is no reason for viscosity variations in considered minutes timespan. Completely different situation is when testing dead samples, from which the liquids are visually squeezed out while being stretched. Therefore we have reason to expect changes in viscous characteristic. Such a unit could have found its place in description of living tissue and changes of its properties related to hydration and or age of donors.

CONCLUSION

The performed experiment of cyclic stressing shows very clearly the viscous characteristic of myometrium tissue and allows us to find the number of stress cycles we need to stabilize passive mechanical properties of tested tissue prior to another measurement. The state after cyclic stressing when no more increase in initial plastic deformation occurs can be for many experiments considered a default status for evaluating the relation stress – deformation.

Introduced rheological model of myometrium during creep was created with the clearest later results interpretation possible kept in mind. Suggested way of testing and describing individual model components allows using relatively simple equations for fitting the model on necessary level, speed and time of stressing.

It is an approach that allows finding significant properties with strongest influence on tissue behavior for given stress value when describing mechanical properties of the tissue. As a consequence we can simplify and shorten computations for example in simulation software when solving practical issues.

Acknowledgement:
This project was supported by grant agences GACR – 106/03/0464 and GAUK – 111/C/2006.

REFERENCES

1 Gollnast HK, Dieminger HJ. Quantitative Bestimmung mechanischer Eigenschaften den graviden Uterus. Centralblatt für Gynaekologie; 1982; **104**: 125–128.
2 Moorcroft D, Stitzel J, Duma G, Duma S. Computational Modeling of a Pregnant Occupant. Virginia Tech: Center for Injury Biomechanics; 2001; **217/12:** 1049–1055.
3 Oda K. Study on the bursting test of rabbits viscera and tissues. Kyoto: Med. Univ. Kyoto; 1952.
4 Otáhal S, Tlapáková E. Patobiomechanika a patokinesiologie, kompendium – Biomechanika [(Patobiomechanics and patokinetics, handbook) (In Czech)]. Praha: Katedra anatomie a biomechaniky FTVS UK; 1999. http://biomech.ftvs.cuni.cz/pbpk/kompendium/biomechanika/index.php
5 Pearlman MD, Ashton-Miller JA, Dyer T, Reis P. Data acquisition for development to characterize the uteroplacental interface for the pregnant abdomen. NHTSA; 1999.
6 Pearsall GW, Roberts VL. Passive mechanical properties of uterine muscle (myometrium) tested in vitro. Journal of Biomechanics; 1978; **11**: 167–176.
7 Valenta J. Biomechanika. Praha: Academia; 1985.
8 Yamada H. Strength of biological materials. Evans, editor. Wiliems & Wilkins Co.; 1970.