Stress relaxation, used as a tool for diagnosis of incompetence of human cervix in terms of a mixture model of tissue

STRESS RELAXATION, USED AS A TOOL FOR DIAGNOSIS OF INCOMPETENCE OF HUMAN CERVIX IN TERMS OF A MIXTURE MODEL OF TISSUE

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1. INTRODUCTION

Cervical incompetence, that is failure of the cervix uteri to remain closed under the load of the developing embryonic sac, is one of the main causes of second-trimester abortion and premature delivery. A cervix known to be incompetent may be treated by suturing it all the way around with a synthetic fibre. However, there is a lack of a reliable technique to assess the diagnosis directly, i.e. based on the determination of the mechanical properties of the cervix. It is known that the mechanical properties change during pregnancy under the influence of hormones. Therefore one may doubt whether measurements done outside pregnancy, which clinically is preferable, is likely to be of value in predicting incompetence. Nevertheless Van Duyl et al. (1) published a retrospective study on non-pregnant women with cervices known to be incompetent and volunteers with normal cervices, that relaxation measurements yield parameters which permit a high level of discrimination between competent and incompetent. The technique is based on observation of stress relaxation after stepwise dilatation of the cervical canal by means of a cylindrical shaped nylon, i.e. almost inelastic, balloon. After insertion into the canal the balloon is inflated by filling it fastly with saline by means of an infusion pump until a reference pressure of 33 kPa is reached. Under these isovolumetric conditions the pressure in the balloon will gradually fall because of stress relaxation in the cervical wall. For clinical convenience we restricted the recording of the pressure to 20 minutes. Within this recording period a static pressure level is almost reached. The pressure decay curves can be fitted by a model consisting of two exponentials and a constant. It has turned out that the values of the time constant of the slower exponential and the value of the constant are negatively correlated and that these parameters have a high discriminatory power for diagnosis of incompetence. A prognostic study is going on to test the predictive value of this new diagnostic technique. Measurements were done also on a group of pregnant women (6-16 weeks) just before they had an artificial abortion for medical or social reasons. These measurements reveal that the parameters are correlated with the duration of pregnancy and tending to values found in cases of incompetence outside pregnancy (2). We postulate that in cases of incompetence the condition is such that an equally directed additive hormone-induced change during pregnancy brings the cervix in a weak condition, which is threatening for gestation.

The clinically observed mechanical characteristics need to be related to basic tissue properties. Histological studies have shown that the cervix owes its competence to the strength of the elastic and collagen tissue of the internal os (3). Stress-strain studies in vitro on strips of tissue taken out of the internal os of fresh human cervix preparations have shown that cervical tissue has viscoelastic properties which phenomenologically

can be presented by a lumped spring-dashpot model (4). Based on known viscoelasticity coefficients and the assumption of tissue-incompressibility one could derive the load-deformation relation of the intact cervix. However, the assumption of tissue incompressibility is not beyond doubt. Like all soft tissues cervical tissue contains interstitial fluid which more or less can be expressed and drained by the lymphatic system. For skin it is known that its water content has a considerable effect on its plasticity (edematous tissue). Uldbjerg et al. (5) reported that during pregnancy the water content of cervical tissue increases. These considerations motivated us to perform compression tests on cervical tissue in a way similar to what has been published for skin by Oomens et al. (6).

2. MATERIALS AND METHODS

A suitable experiment which has been used with success on articular cartilage is a confined compression test (7). Figure 1 shows the apparatus used to perform one-dimensional, confined compression tests*. The load is applied to a tissue sample by means of a cylindrical indentor 2 with a diameter of 7.25 mm. The indentor is attached to a shaft 3 that is guided by means of an air-bearing 4 and attached to a cantilever beam 5. A balance weight 7 keeps the cantilever beam horizontal when unloaded. It can rotate around an air bearing 9. A load of less than 0.01 N is sufficient to overcome the remaining friction and to set it in motion. The load is applied by manually placing a known weight 8 on the cantilever beam. Disk-shaped tissue samples, 7.4 mm diameter and approximately 2 mm thick, were taken out of the wall of the internal os of fresh human cervix preparations by means of a hollow gimlet. A sample is placed in a stainless steel ring of 7.4 mm diameter. This ring is placed on a sintered stainless steel filter, which has a very high permeability for water. The accessory is shown in Fig. 2. A displacement transducer (Sangamo DF/5.0/S) 10 is used to measure the displacement of the shaft as a function of time.

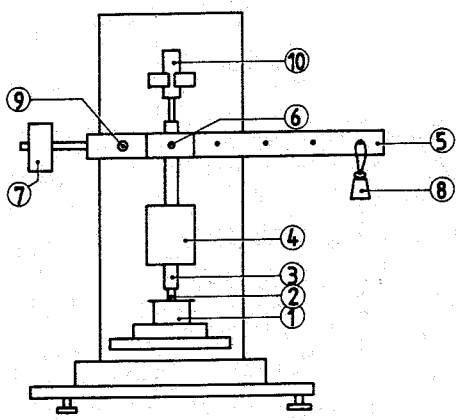

FIGURE 1
Apparatus for finite compression tests

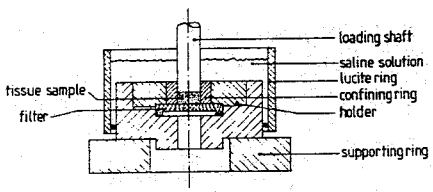

FIGURE 2
Detail of Figure 1

*Placed at our disposal by Twente University of Technology, The Netherlands.

In order to start from standard initial conditions a small pre-load of 0.1 N was applied during about 10 seconds. Then a load of 4.1 N was applied during 20 minutes. This load corresponds to a pressure of approximately 100 kPa, which is three times the pressure initially applied in the in vivo measurements via the balloon. The in vitro measurements have been done at room temperature.

3. RESULTS

Figure 3 is a representative result of 10 confined compression measurements. The initial small decay is caused by the pre-load. The application of the main load is followed almost instantaneously by a relatively large compression. Then compression progresses slowly, which has been recorded during 20 minutes. Semi-logarithmic plots reveal that about one minute after the application of the load the continuing compression follows a mono-exponential function approaching a constant value. To characterize the compression recordings we determined graphically the following parameters (see Fig. 3):

c_t - total compression expressed as a percentage of the thickness of the sample: $c_t = (22 \pm 2)\%$

c_i - instantaneous compression at application of the main load expressed as percentage of the thickness: $c_i = (9.7 \pm 5)\%$

τ - time constant of the mono-exponential compression: $\tau = 11.5 \pm 1.5$ minutes

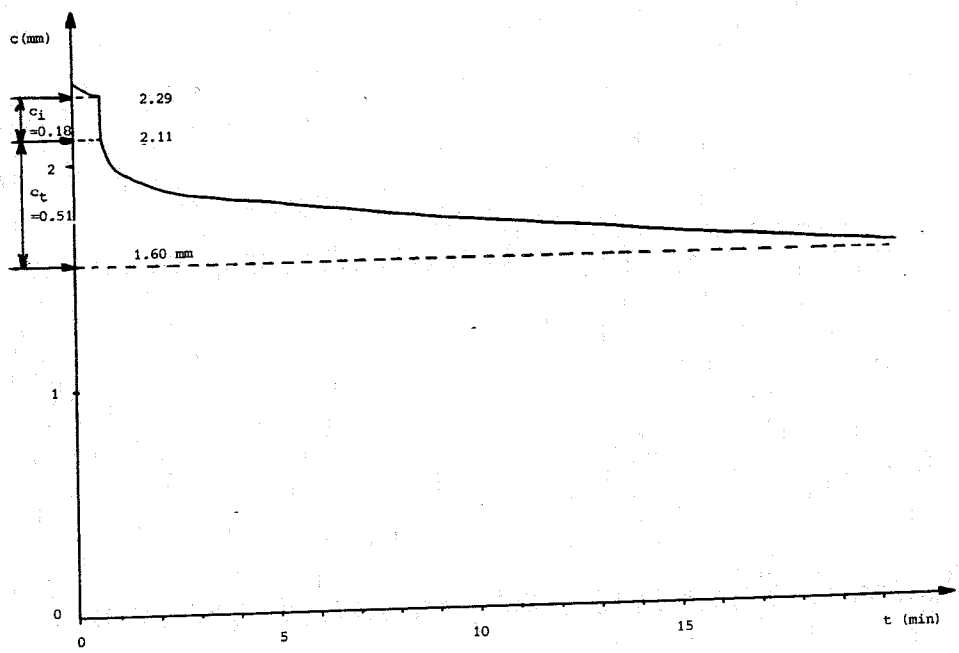

FIGURE 3
Recording of a compression test

4. THEORETICAL CONFINED COMPRESSION MODEL

Results of similar compression measurements on skin have been interpreted in terms of a bi-phasic mixture model consisting of a porous elastic matrix filled with water like a sponge. In this model the compression is governed by the permeability of the matrix for water and the elasticity of the matrix structure via the equations:

$$\frac{\delta\sigma}{\delta y} - \frac{\delta p}{\delta y} = 0 \tag{1}$$

$$\frac{\delta}{\delta y}\left(\frac{\delta v}{\delta t}\right) - \frac{\delta}{\delta y}\left(K\frac{\delta p}{\delta y}\right) = 0 \tag{2}$$

where: y = position variable in the direction of confined compression
σ = normal Cauchy stress on a plane with its normal in the y-direction
p = the hydrodynamic pressure
v = displacement in y-direction
K = permeability in y-direction

For small deformations holds $\sigma = H\varepsilon$, where $\varepsilon = \delta v/\delta y$ is the strain in y-direction and H is the confined compression modulus. For the final equilibrium state of compression, when the hydrodynamic pressure is zero, holds:

$$v(\infty) = \frac{pL}{H} \tag{3}$$

where L is the thickness of the sample.
It has been derived that according to this mixture model the early time response is proportional to $\sqrt{t}$ (8). Oomens (6) applied this result of analysis to experimental compression data of skin and obtained an estimation of the permeability coefficient K. The instantaneous compression c_i, seen at the application of the load, however, cannot be explained with this model. For the measurements on skin Oomens ascribed this phenomenon to an artefact related to consolidation of the sample in the ring. This consolidation probably also affects the initial faster compression part of the curve and consequently reduces the reliability of the values of the parameter obtained by the applied analysis. Now it can be shown theoretically, assuming a constant compression modulus and permeability coefficient, that with increasing time the displacement deviates less from a mono-exponential decay, i.e. less than 8% for $t \geq 0.05\ \tau$ (9), where τ is the time constant:

$$\tau = \frac{4L^2}{\pi^2 HK} \tag{4}$$

Because this theoretical conclusion fits to our experimental results we used this analysis to derive H and K. We found by applying (3) and (4) $H = 0.13\ E + 06\ N/m^2 \pm 20\%$ and $K = 1.89\ E - 14\ m^4/Ns \pm 30\%$. We note that in our approach the likely dependence of H and K on the amount of compression has been ignored.

5. DISCUSSION

The in vitro tests show that samples of cervical tissue are compressible because fluid can be expressed. The compression rate is limited by the permeability of the tissue for the fluid. The time constant of the (isotonic) in vitro compression process appears to be in the order of 11 minutes, which is about twice the value of the larger time constant found in the in vivo (isovolumetric) measurements. The in vitro measurements have been performed on tissue, which has been damaged by excision, and under unphysiological conditions. Consequently the results are not representative for tissue properties in the intact cervix. Even the hypothesis of tissue compressibility needs further verification in in vivo experiments. Because in connection to this hypothesis incompetence is related to fluid content of cervical tissue, such experiments are valuable from a clinical point of view. At this stage of investigation we can refer to observations which are indicative but not decisive for the validity of the mixture model for the cervix. In particular the results of the in vivo relaxation measurements can be explained in terms of the mixture model as follows.

It has been observed by means of marks fixed at a cervix preparation, that at the application of a pressure of 33 kPa by means of the balloon, the radial displacement in the cervical wall predominantly takes place within a layer of 4-5 mm (2). The initial deformation of the cervix at the application of the step in pressure is governed by the incompressibility condition. Subsequently the deformation will change because of viscoelasticity but also because of gradual tissue compression leading to a new state of equilibrium. According to the mixture model the relaxation rate is determined by the rate of drainage of the expressed water instead of viscous slippage of tissue fibers according to the original viscoelastic model. Larger values of the relaxation time constant found in the in vivo measurements in cases of incompetence can be caused by a reduced rate of drainage. In a series of patients we determined the extra volume of saline which need to be infused into the balloon after the 20 minutes relaxation period in order to bring the pressure at the level of 33 kPa again. We take this extra volume as an estimation of the amount of water that has been expressed out of tissue during the relaxation. In the controls we found that 1.1 ± 0.08 mm^3 water is expressed per mm^2 area of the canal exposed by pressure. This amount is comparable to the amount that is expressed out of samples of 4 mm thick in the in vitro compression tests. For incompetent cervices this amount turned out to be about six times larger. This indicates the patho-physiological significance of this parameter.

Aukland (10) describes how local mechanisms are involved for osmotic control of interstitial fluid. We conclude that a further evaluation of the validity of the mixture model, as an alternative for the classical viscoelastic model, to describe the mechanical properties of cervical tissue is both physiologically and clinically relevant because it puts the observations in a new framework of interpretation.

REFERENCES

1. Duyl WA van, Zon ATM van der, Drogendijk AC: Stress relaxation of the human cervix: a new tool for diagnosis of cervical incompetence. Clin. Phys. Physiol. Meas. 5, 207-218, 1984.
2. Zon ATM van der: Cervix insufficientie etiologie en diagnostiek. Thesis Rotterdam, 1982 (in Dutch).
3. Danforth DN: The fibrous nature of the human cervix and its relation to the isthmic segment in gravid and non-gravid uteri. Am. J. Obstet. Gynec. 53, 541-569, 1947.
4. Duyl WA van, Veen BCM in 't, Zon ATM van der, Drogendijk AC: Mechanical properties of the tissue around the internal os of human cervix uter determined in vitro. Submitted, 1986.
5. Uldbjerg N, Ekman G, Malmstrom A, Olson KO, Ulmsten U: Ripening of the human uterine cervix related to changes in collagen, glycosaminoglycans and collagenoolytic activity. Obstet. Gynecol. 147, 662-662, 1983.
6. Oomens CWJ: A mixture approach to the mechanics of skin and subcutis. Thesis Twente, 1985.
7. Mow VC, Holmes MH, Lai WM: Fluid transport and mechanical properties of articular cartilage: a review. J. Biomech. 17, 377-394, 1984.
8. Holmes MH: Comparison theorems and similarity solution approximations for nonlinear diffusion equation arising in the study of soft tissue. SIAM J. Appl. Mat. 44, 545-556, 1984.
9. Duyl WA van: Analysis of confined compression test of cervical tissue. In preparation, 1986.
10. Aukland K: Distribution of body fluid: local mechanisms guarding interstitial fluid volume. J. Physiol., Paris, 79, 395-400, 1984.