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QUANTIFICATION OF RATE AND DEPTH OF PITTING IN HUMAN EDEMA USING AN ELECTRONIC TONOMETER

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ABSTRACT

An instrument (tonometer) was developed to measure objectively the rate as well as depth of pitting of edematous limbs under a sudden local load. Displacement versus time curves were obtained in vivo *in postmastectomy edema arms and also* in vitro *(compression of sponges) and were analyzed in terms of spring and dashpot constants.*

There was no significant difference between the quasi-instantaneous indentation of tissue in the edematous and normal arms (median 2.9mm), and the two correlated strongly ($r=0.91$, $p<0.0001$). An exponentially slowing indentation followed. The mean difference between initial and final deformation (X_∞-X_0) was greater in the swollen arms (5.7mm) than in the normal arms (1.3mm, $p<0.01$). The time constant of indentation (τ) was significantly greater in the swollen arms (227s) than in the normal arms (71s). There was no correlation between the duration of the edema and any of the pitting characteristics. There was a significant negative correlation between glycosaminoglycan concentration of interstitial fluid and rate constant $1/\tau$ ($r=-0.9$, $p<0.01$).

The tonometer thus provides an objective way of quantifying the rate and depth of pitting edema.

Normal tissue offers a high resistance to the displacement of interstitial fluid owing to its glycosaminoglycan content (1). Pitting develops when the resistance to interstitial fluid movement is low, which happens when the interstitial fluid volume of the arm has increased to the point where the interstitial gel becomes very diluted and pools of mobile fluid form (2). Pitting thus occurs in edema in conditions such as congestive cardiac failure, nephrotic syndrome and pre-eclampsia. Compression of the tissue with the thumb for one minute leaves a depression, or pit, in the tissue. The clinical assessment of pitting, however, is subjective and qualitative: the pressure applied by the thumb is arbitrary, and the rate of pitting cannot be quantitatively assessed.

Lymphedema, in contrast to the edemas just mentioned, is usually considered "brawny" (hard) i.e. not pitting easily. This is attributed to fibrous or fatty tissue growth. In reality, however, the pitting characteristics vary considerably, from hard truly non-pitting, through soft and deep pitting, to soft but difficult to pit. This aspect has never been properly quantified because there has been no method to record the time course of pitting objectively. Clinical experience suggests that lymphedema starts out as a pitting edema, but becomes hard and brawny over the years (4,5) as the proteins in the tissue stagnate or clot (6,7), or elicit tissue fibrosis and fat deposition (3). It is believed that arms which do not pit respond less well to treatment than those that do (8), and that some pharmaceutical agents can change the pitting characteristics in the arm (9,10).

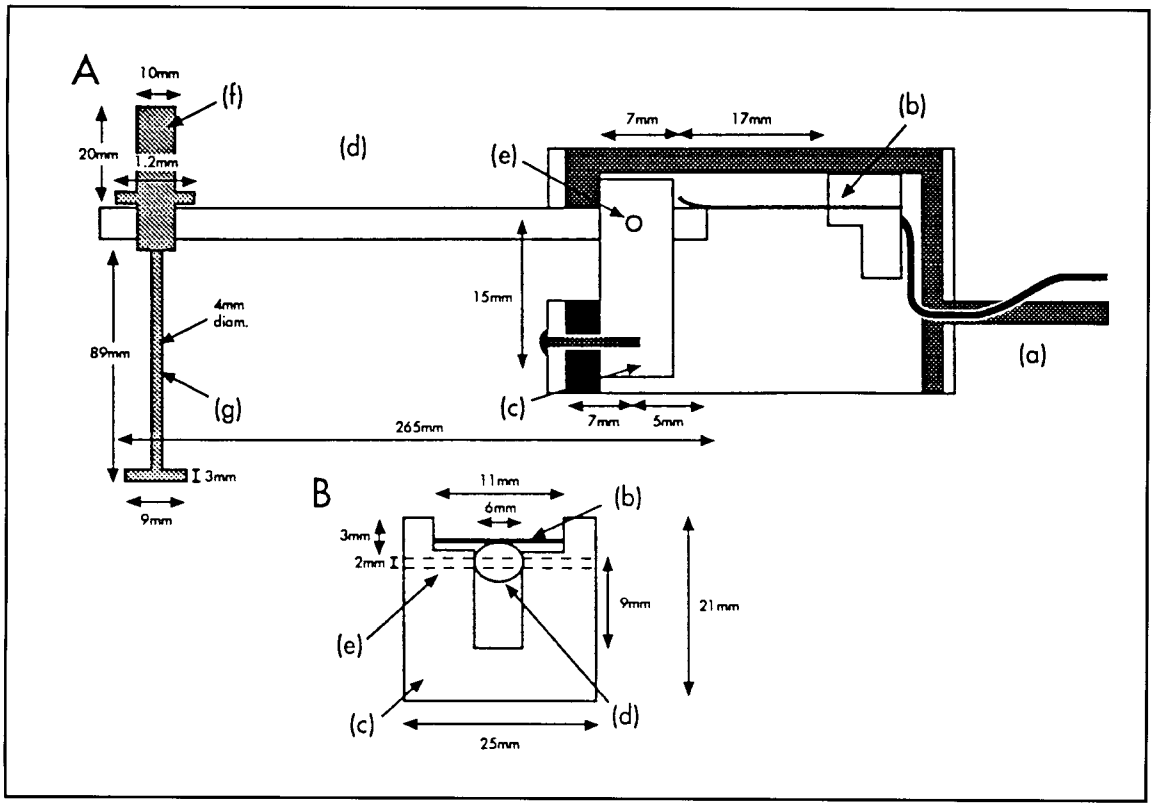

Fig. 1. The tonometer. A. (a) Mounting bar, (b) modified Washington D1 isometric force displacement transducer, (c) aluminium block to provide housing for fulcrum, (d) aluminium bar, (e) pin to act as fulcrum, (f) head of plunger, (g) base of plunger. B. En face view of aluminium mounting block. The block (c) is screwed to the front of the transducer with the strain gauge (b) just overlapping the block. The aluminum bar (d) protrudes through the archway of the block and is held in place by the steel pin (e).

Objective determination of the depth (but not the rate) of pitting in lymphedema was introduced by Clodius, Deak & Piller in 1976 (11). Their "tonometer" was a simple mechanical device that measured the depth of compression of tissue by a mass after a fixed time interval, and was read by eye. The instrument consisted of a plunger connected to a scale. The plunger rested on a base plate on the arm. Weights were added to the plunger and the distance that the plunger moved in a minute was measured. A number of papers have been published using this instrument to quantify edema (12-14). There are two major drawbacks, however, with the instrument. First, it is somewhat unstable and top heavy; addition of weights tends to cause it to fall over. To overcome this, Chen et al (13), fixed the instrument to a movable grip. The second, more important problem is that the instrument measures only the depth of compression, not the rate. Pitting in lymphedema often occurs rather slowly, and therefore the time course of pitting is of considerable interest. The depth of pitting measured by the tonometer of Clodius et al depends on the time allowed (arbitrarily fixed at 1 min), and no information results about the final equilibrium pit depth. The "durometer" (15) is a similar device.

An instrument to record objectively the depth and rate of pitting should therefore be a useful tool for diagnostic, prognostic, and monitoring purposes. Such an instrument is

described here, and a simple analysis of the pitting curves is presented. The instrument was presented at the 1991 World Congress on Lymphology (16), and was demonstrated to the Physiological Society (17).

MATERIALS AND METHODS

The Tonometer

The instrument *(Fig. 1)* was developed from the Clodius et al mechanical tonometer. In outline, a loaded plunger is attached to a lever which deflects a strain gauge. The latter provides a voltage output, which is amplified and recorded on a chart recorder. The free end of the plunger rests on the skin. When a weight is added to a plunger, a continuous record of indentation versus time is obtained.

The tonometer consisted of a modified Washington D1 isometric force displacement transducer (Palmer Bioscience, Kent, UK) *(Fig. 1b)* with the mounting bar still attached *(Fig. 1a)*. The outer casing was removed and a 6mm x 25mm rectangular hole cut out of the front of the transducer. An aluminum block *(Fig. 1c)* was screwed into the front of the casing. An aluminum bar *(Fig. 1d)* with a 2mm hole drilled through it approximately 5mm from the end *(Fig. 1e)* was placed through the hole in the casing and into the arch of the block. A 2mm diameter steel pin was then placed through the hole in the block and the bar, providing a pivot for the bar. The other end of the bar was planed on the anterior surface 30mm from the end to provide a sloping surface. The head of the brass plunger *(Fig. 1f)* (diameter of 10mm with a 12mm diameter "shelf" to support the mass to be placed on it) was pushed onto the bar until it gripped. The base of the plunger *(Fig. 1g)* was then screwed into the head to provide a tight seal. The plate on the end of the plunger that rested on the skin had a diameter of 9mm.

The extra force needed to initiate pitting of the tissue was provided by the addition of three stainless steel discs of diameter 39mm and a combined mass of 152g to the head of the plunger. The discs had a hole 10mm in diameter drilled through the center, and fitted on the "shelf". The mass of the plunger was 32.5g so the pressure applied to the skin by the indented surface prior to the application of the weights was 0.5g/mm^2 (the contact area was 63.6mm^2).

The displacement transducer was a half Wheatstone bridge type. Two 300 ohm resistors were connected to the strain gauge to complete the bridge. The input to the amplifier (Harvard 6101, Palmer BioScience, Kent, UK) depended upon the deflection of the transducer. The amplifier was connected to a Servogor SE120 chart recorder (Belmont, Glasgow, UK).

Calibration

The instrument was calibrated using 6 brass discs of diameter 3.4mm (measured by micrometer). The mounting bar of the tonometer was clamped onto a retort stand. The plunger was placed on the discs and the height of the tonometer adjusted until the bar was level (measured by spirit level). The amplifier was then centered by adjusting the DC level on the amplifier until a change of gain on the chart recorder caused no pen deflection. Removal of a brass disc dropped the plunger by 3.4mm, and the resulting pen deflection was recorded. There was a linear relation between the pen deflection and the distance moved by the plunger (r=0.999, see reference 18).

Testing the Tonometer In Vitro

To test the instrument *in vitro*, the tonometer was applied to a sponge immersed in a viscous medium. The plunger was rested on a natural (open cell) sponge in a glass beaker soaked in various concentrations of glycerol of known viscosity (20). The chart recorder was set running at high speed to record the initial rapid phase of deformation and 152g added to the tonometer. After 1

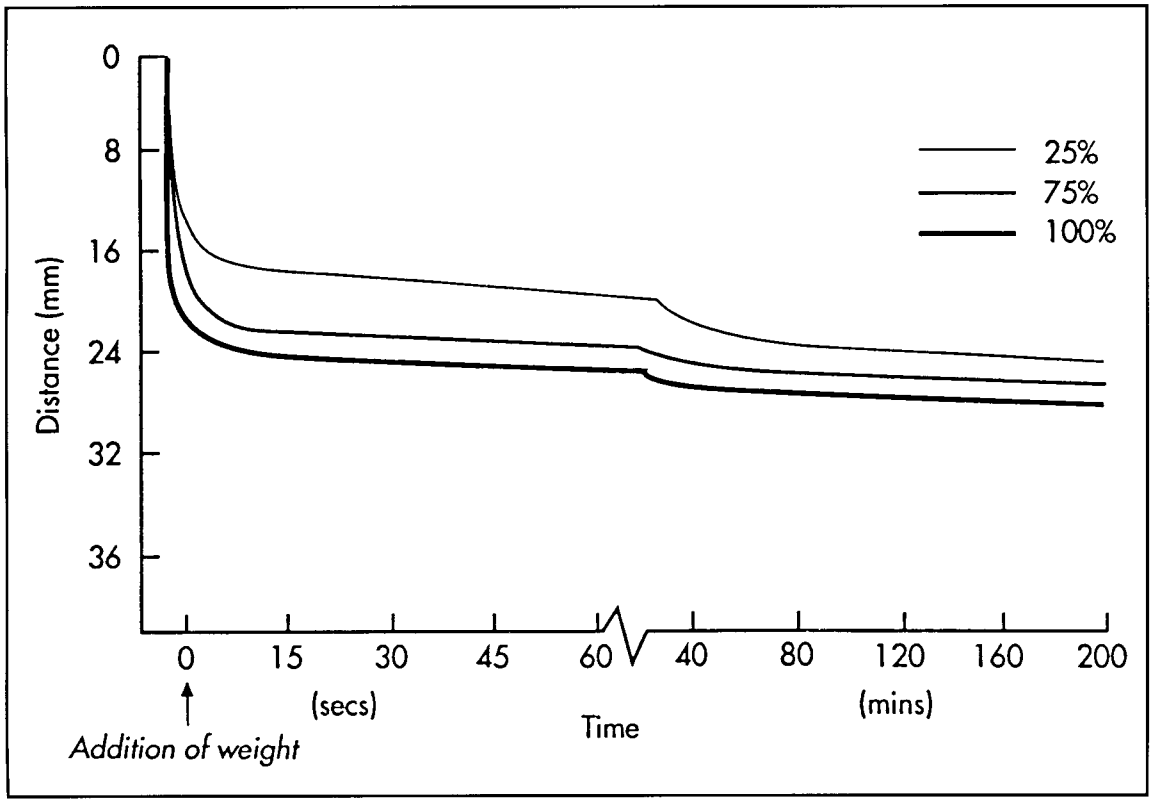

Fig. 2. Pitting curves in vitro. Open cell sponge soaked in a) 25% glycerol, b) 75% glycerol, c) 100% glycerol.

minute the chart recorder was slowed to 3cm per hour and recording was continued for seven hours. Typical traces from sponges are shown in *Fig. 2.*

Measurement of Pitting in Patients with Postmastectomy Arm Edema

With the patient supine and with the arm approximately at heart level, at 45° laterally to the body, flexor surface uppermost and resting on a rigid support, the subject was asked to relax and stay very still. In some cases, the arm was supported on a polythene bag filled with polystyrene beads and evacuated (Orthopaedic Systems, Kent, UK) to enable the patient to lie still for longer periods. The unloaded plunger was rested on the flexor surface of the forearm, 6-12cm below the elbow, avoiding visible veins. The tonometer was adjusted until the bar was horizontal as gauged from the position of the pen compared to the zero calibration position. The chart recorder was run at 3cm per minute for at least 20 seconds with the bar horizontal, and then the 152g mass was placed gently on the head of the plunger. The rate of indentation was recorded on the chart recorder for a varying length of time depending on patient tolerance. Long recordings were needed to resolve the initial part of the curve. Therefore, the recorder was run at 12cm/min for 30-60 seconds immediately after addition of the weights, and then slowed to 0.5cm/min until the reading reached an apparently stable value. This provided better resolution for analysis but made time measurements on the trace troublesome. As a compromise, the

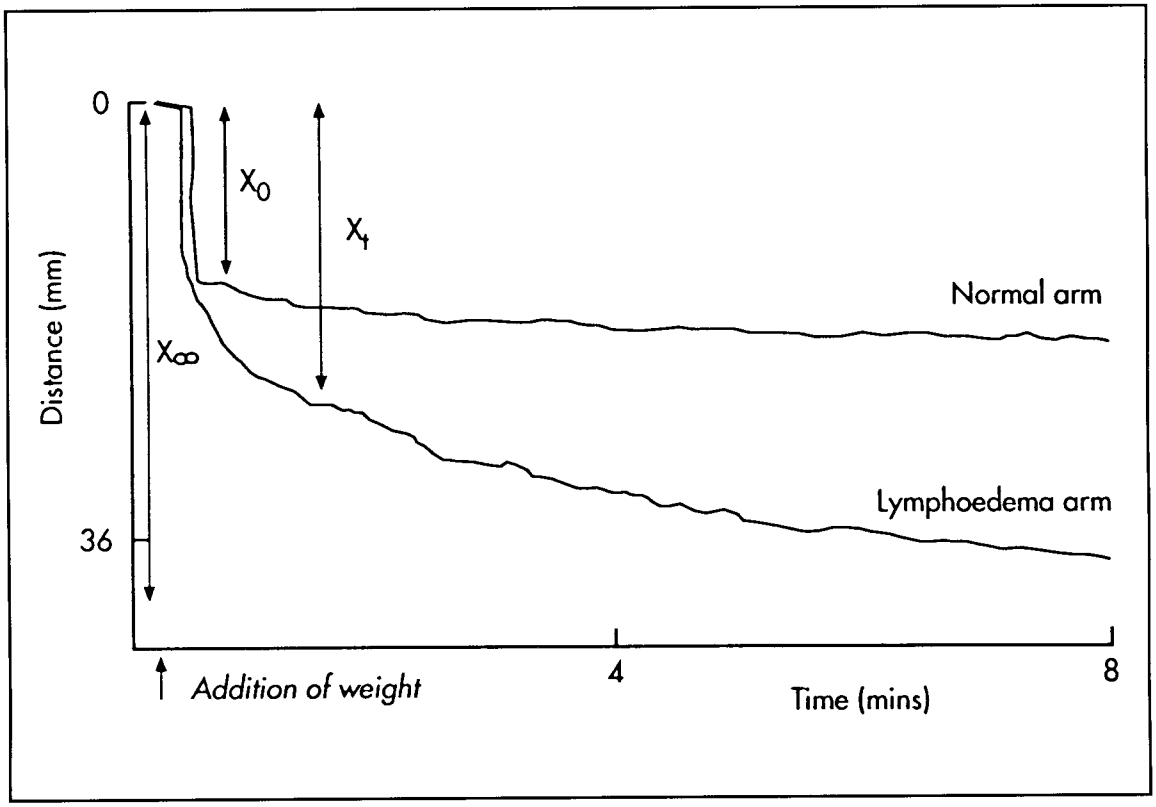

Fig. 3. Typical indentation traces of a) normal arm and b) arms with postmastectomy edema.

tonometer was applied for 8 minutes with the chart recorder running constantly at 3cm/min in many cases. Typical traces of swollen and control arms are shown in *Fig. 3.*

Effect of Venous Obstruction

In order to assess whether vascular compression contributed to the indentation curve, tonometry was carried out on a normal subject with a pneumatic pressure cuff on the upper arm. The subject was female, 40 years of age and premenopausal. Indentation tests were repeated at the same point on the arm with two hours between measurements, with the cuff inflated to 10, 20, 30 or 40 mmHg. The test was begun within one minute of inflation of the cuff to minimize tissue fluid accumulation and was run for 8 minutes. The subject resumed normal activities and returned two hours later for the next test.

Analysis of Pitting Curves

The pitting curves for soaked sponges and the swollen arms were similar *(Figs. 2 and 3).* The curves showed two distinct phases; an initial quasi-instantaneous deformation, followed by a slower indentation at a declining rate. The initial drop represented rapid elastic deformation of the tissue. The exponentially declining creep phase *in vivo* was attributed to fluid flow through the interstitium under the loaded tonometer head, slowly expressing fluid until finally the whole load was borne by "solid" (non flowing) tissue i.e. tissue with a very high resistance to fluid expression.

The Kelvin-Hooke model *(Fig. 4)* is the

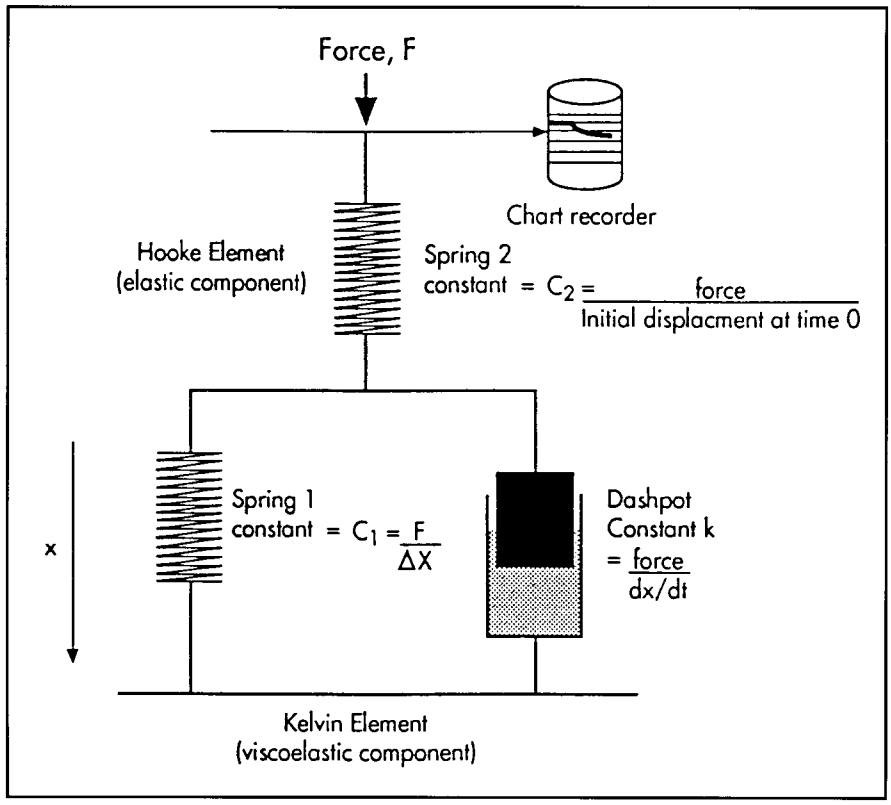

Fig. 4. Spring and dash pot viscoelastic model. Spring 2 provides the initial elastic deformation, and spring 1 in parallel with the dashpot provides the later, viscoelastic component.

simplest mechanical system that generates curves of the form observed, and although it is clearly a simplistic representation for a complex tissue, it proved useful in the numerical analysis of the indentation curves. In the Kelvin-Hooke system the initial rapid deformation depends upon an elastic component or Hooke element (spring 2) in series with a parallel dashpot-spring system (Kelvin element). The latter comprises a dashpot and spring 1 in parallel, and this gives rise to an exponentially decaying creep until finally an elastic equilibrium is reached.

The equation for spring deformation (X) under force F is F=XC, where C is the spring constant. The equation for dashpot deformation rate, dX/dt, is F=k.dX/dt, where k is the dashpot constant. Integration of the expressions for the Kelvin-Hooke array gives the expression for deformation X as a function of time t, equation 1 (19).

$$X_t = a + b\,(1\text{-}e^{-t/\tau}) \qquad \text{eq 1}$$

where X_t is the distance moved at time t, a is force divided by the spring constant of the series Hooke element ($a=F/C_2$), b is force divided by the spring constant of the Kelvin element ($b=F/C_1$), and time constant τ is the ratio of the dashpot constant to the spring constant in the Kelvin element ($\tau=k/C_1$)

Immediately after addition of the weights, the distance travelled (X_0) is:

$$X_0 = a = F/C_2 \qquad \text{eq 2}$$

X_0 can be read from the pitting curve (it is the initial drop) and F is known, so C_2 can be calculated. At infinite time the distance moved (X_∞) is equal to a + b.

$$X_\infty = a+b = X_0 + F/C_1 \qquad \text{eq 3}$$

TABLE 1
Initial (X_0) and Final Deformation (X_∞), and Time Constant (τ) of Tonometer Curves from 5 Natural Sponges, Each Soaked in Four Different Glycerol Solutions

Relative Viscosity	1.086	1.168	1.227	1.263
X_0(mm)*	16.0±0.69	16.8±0.36	15.3±0.67	8.5±0.4^x
X_∞ (mm)$^+$	27.6±7.0	22.6±2.3	25.0±2.2	21.4±1.0
τ(sec)*	61.5±16.5	77.7±14.5	172±45.6†	597±46.4^x
C_1(g/mm)$^+$	9.4±6.7	14.2±5.6	7.6±1.2	5.6±0.52
C_2(g/mm)*	4.5±0.23	4.4±0.09	4.7±0.21	8.5±0.42^x
LC*(g/(mm/s))	645±551	1116±517	1268±137†	3364±276^x

*=p<0.0001, ANOVA. ^{x}=significantly different from 25%, 50% and 75% p<0.001 (paired t tests). †=significantly greater than 25% and 50% p<0.001 (paired t tests). $^+$=p>0.05 ANOVA.

Substituting equations 2 and 3 into 1 gives the relation between distance from final equilibrium (X_∞-X_t), and time -

$$X_\infty - X_t = (X_\infty - X_0)e^{-t/\tau} \qquad \text{eq 4}$$

If X_∞ can be determined then C_1 can be calculated and thence k. From equation 4, a linear expression is obtained by taking the natural logarithm -

$$\ln(X_\infty - X_t) = \ln(X_\infty - X_0) - t/\tau \qquad \text{eq 5}$$

By plotting $\ln(X_\infty - X_t)$ against time a straight line should result, if the model is valid, with an intercept of $\ln(X_\infty - X_0)$ and a gradient of $-1/\tau$ (called the rate constant). Because $\tau = L/C_1$ the dashpot constant (k) can be calculated once C_1 is known. Examples of linearized traces are shown in *Fig. 5*.

X_∞ cannot be measured directly but it was estimated by an iterative procedure. The final recorded X_t was taken as an initial estimate of X_∞. If this value was too small or large, the semi-log plot was non-linear and the correlation coefficient was low. X_∞ was then iteratively increased or decreased until an optimum correlation coefficient (that closest to 1) was found. This was taken as the best estimate of X_∞ and used in the estimation of τ, C_1 and k. A simple computer curve fitting program (18) was designed to find iteratively the best estimate of X_∞.

Glycosaminoglycan and Protein Content of Edema Fluid

Because the time constant might be a function of interstitial fluid viscosity, both the plasma protein concentration and glycosaminoglycan content of samples of the subcutaneous edema fluid in postmastectomy edema were measured. These procedures are described in reference 22.

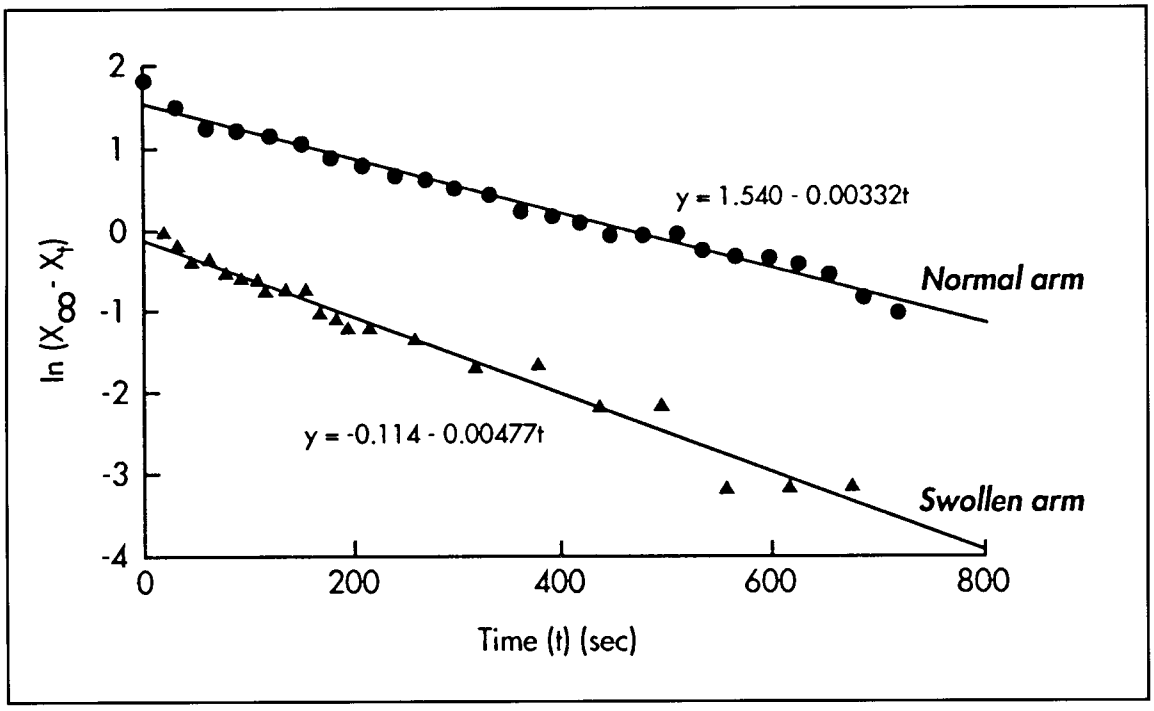

Fig. 5. Linearized indentation curves from normal arm and postmastectomy edema arm. The gradient is -1/τ and the intercept is ln(X_∞-X_0). Regression equations for the two curves are inset.

RESULTS

Tonometer Curves for Sponges In Vitro

The open-cell sponge soaked in liquids of different viscosity was used as a simple *in vitro* tissue to test the applicability of the model. It was predicted that as viscosity was increased, the dashpot constant k should increase, lengthening the time constant τ. This was found to be the case, as shown in *Table 1.* The time constant and dashpot constant increased significantly as glycerol concentration and hence viscosity increased. There was no significant difference between X_0 for the sponge in 25%, 50% or 75% glycerol, though X_0 was significantly less and hence C_2 was significantly greater in 100% glycerol. There was no significant difference between the final compression values (X_∞) in the different glycerol solutions and hence C_1 was not significantly different ($p>0.05$, ANOVA).

Pitting of Swollen and Normal Arms

Tonometry was carried out on 16 patients with swelling of the upper arm following breast cancer treatment. In all cases, tonometry was carried out on both the swollen and contralateral, control arms. The % increase in volume of the swollen arm averaged 40±23%. The mean age of the patients was 62±12 years (mean ± s.d. throughout), the mean time for which they had had a swollen arm was 45 months (median range 6-240), and the time to swelling from cancer treatment was 12 months (median: range 0-144). All the patients had received radiotherapy, 9 had had a wide local excision, and the remainder a simple or radical mastectomy. Other features such as interstitial protein concentration, fluid pressure and limb volume are described in references 21, 22, 23. The values for initial and final deformation, rate constant 1/τ, spring

TABLE 2
Pitting Characteristics of Non-Swollen and Swollen Arms (Median and Range) for 16 Patients with Unilateral Postmastectomy Edema

	X_0 (mm)	X_∞-X_0 (mm)	$-1/\tau \times 10^{-2}$ (sec^{-1})	C_1 (g/mm)	C_2 (g/mm)	k g/(mm/s)
Normal	2.9 (1.4-8.0)	1.3 (0.1-4.0)	1.4 (0.5-50)	115 (37-1500)	51 (22-107)	7568 (600-56818)
Swollen	2.9 (1.4-6.8)	5.7 (0.5-6.4)	0.44 (9.09-1.5)	26.5 (23-250)	52 (19-104)	7922 (1819-45454)
p^+	>0.05	<0.01	<0.01	<0.01	>0.05	>0.05

+Significance of difference between normal and swollen arm (Wilcoxon paired rank test).
1g force under gravity approximates to 0.01 Newtons.

and dashpot constants are shown in *Table 2*. The distributions of τ, X_0 and X_∞ were all skewed and therefore median rather than mean values are given and non-parametric statistics were used.

Initial deformation. There was no significant difference in X_0 or C_2 (initial quasi-instantaneous deformation) between the normal and swollen arms. The correlation between the two sides was high ($r=0.91$, $p<0.001$) with a regression slope not significantly different from 1 (slope 0.88, $p>0.01$).

Slow deformation. The total depth of the second phase of deformation, (X_∞-X_0), was on average over 4 times greater (4.4mm) in the swollen arm than in the normal arm. The calculated spring constant C_1 in the swollen arm was only 23% of that in the normal arm. There was no correlation between depth of pitting in the normal and swollen arms. The value of X_∞-X_0 or C_1 in the swollen arm did not correlate with % increase in arm volume ($r=0.16$, $p>0.05$).

Time course. The time constant (τ) was on average 3 times longer in the swollen arm than in the normal arm, i.e. the rate constant $1/\tau$ was reduced in the edematous arm and the final value X_∞ was approached more slowly. The time constant depends on C_1 and K, and when changes in C_1 were taken into account it emerged that there was no significant difference between the dashpot constant of the swollen and normal arm. In other words, the increase in time constant was entirely due to the decrease in the spring constant C_1, on the current analytical model.

There was a significant negative correlation between the interstitial fluid glycosaminoglycan (GAG) concentration and the rate constant $1/\tau$, in five patients where

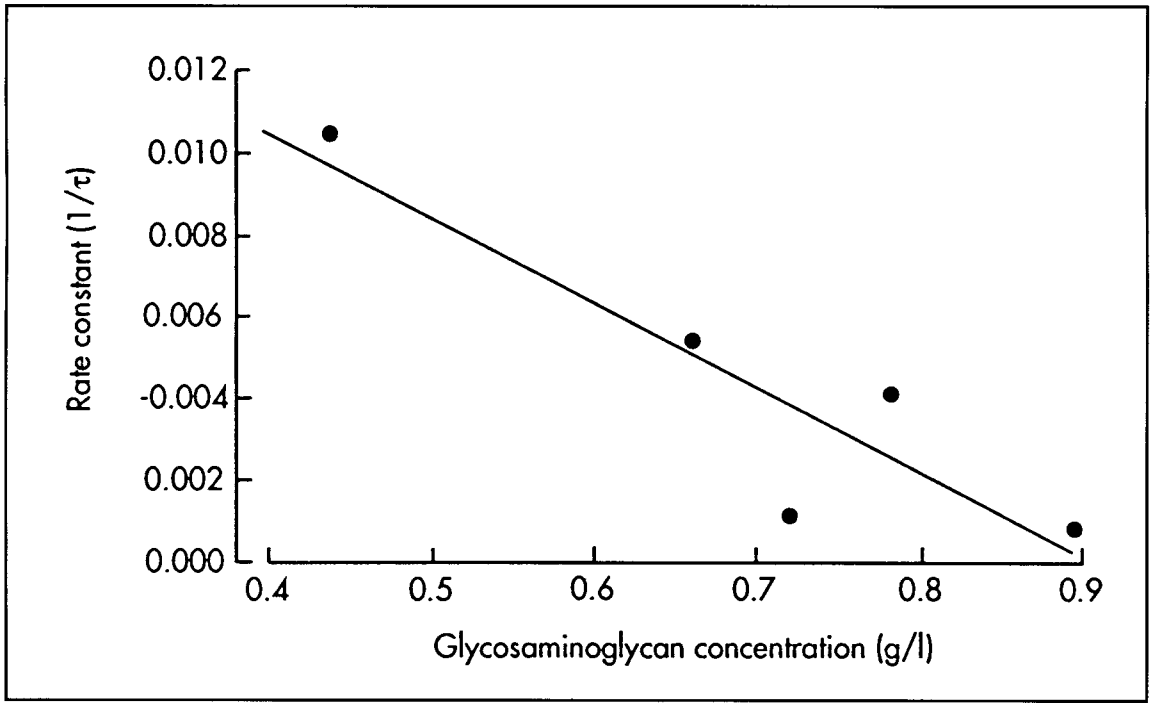

Fig. 6. Rate constant as function of glycosaminoglycan (GAG) concentration (r=0.91, p<0.05).

both were measured, as shown in *Fig. 6*. There was no correlation between the time constant and the duration of swelling, the size of swelling, the time between initial treatment and swelling, the interstitial protein concentration or colloid osmotic pressure, interstitial fluid pressure, albumin concentration or albumin to total protein ratio in the swollen arm.

An attempt was made to see whether the tonometer could distinguish between pitting and brawny edema. A clinician experienced in edema assessment applied the clinical pitting test and classified limbs as "moderate pitting" or "brawny", but found the distinction difficult in these well-controlled cases where truly hard, non-pitting edema was rare. Tonometry revealed a significantly longer time constant in those considered "pitting" (median 250s, range 119-1075s, n=19) than in those considered "brawny" (median 134s, range 75-384s, n=8); $p<0.01$, Mann Whitney U test. Other parameters, such as X_∞-X_0 were not significantly different between the groups.

Venous Obstruction and Pitting

The absence of any apparent reduction in the dashpot constant (k) in postmastectomy edema was surprising because interstitial hydraulic conductivity is greatly increased in edema. We had anticipated that increased ease of fluid dissipation under the tonometer would lower the dashpot constant (force/(dx/dt)). We therefore assessed the possibility that k in the normal arms might provide a misleading comparison if it were influenced by expulsion of blood as well as interstitial fluid. To assess the influence of blood vascular volume, tonometer traces were obtained at several levels of venous congestion in a single patient (same site throughout, normal arm). Cuff pressure had no effect on X_0 or X_∞. There was, however, a significant negative correlation between cuff pressure and time constant and between cuff pressure and the dashpot constant (k) as shown in *Fig. 7*. Thus the value of the time constant and k can be

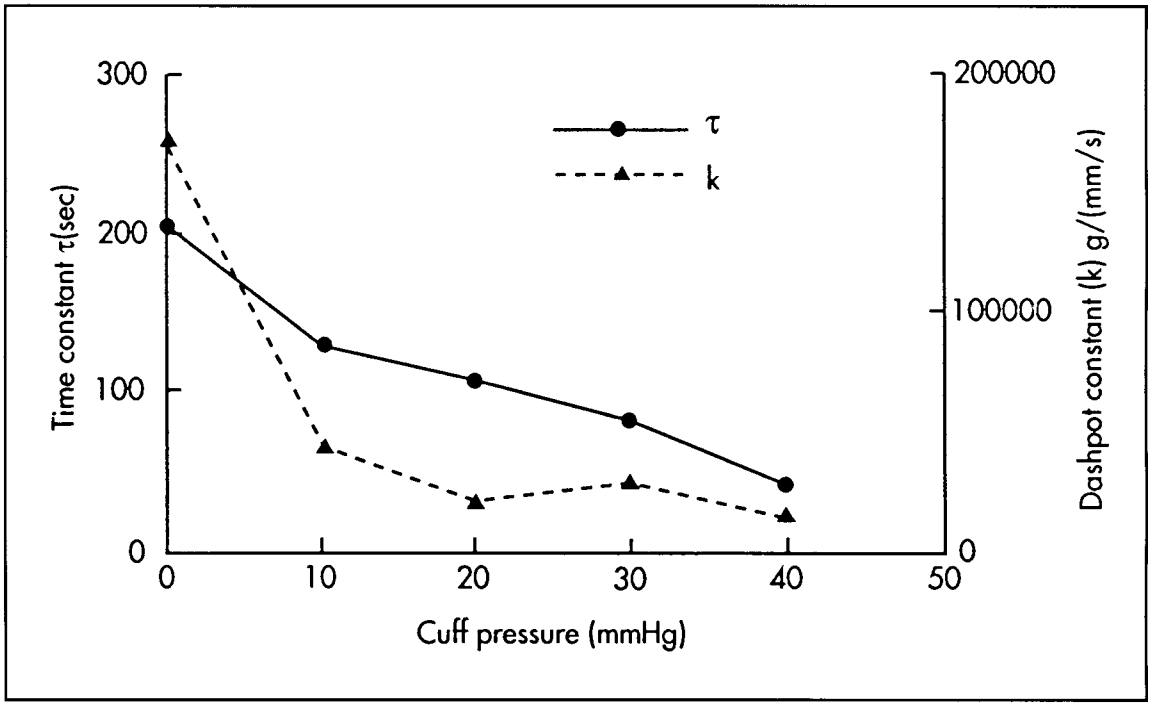

Fig. 7. Time and dashpot constants as function of venous congestion pressure.

affected by blood vascular volume as well as by interstitial mechanics.

DISCUSSION

Pitting in postmastectomy edema was described by Halsted in 1921 (6); "pressure on it [the hand] with the fingers produced deep pits". He also quoted Matas, describing lymphedema as being a "coaguable dropsy, or hard lymph edema". Homans in 1940 described lymphedema as becoming "progressively firmer" (5) and many others have described lymphedema as a hard, non-pitting edema (3,9,24), or edema of variable degrees of pitting (8). The edema was said to become more "brawny", or "woody" over time due to stagnation of interstitial proteins, chronic inflammation and fibrosis (7). The tonometer described here allowed objective permanent-copy assessment of the pitting characteristics.

The Kelvin-Hooke Model and Results In Vitro

The distance against time curve, both *in vitro* and *in vivo*, shows an initial, rapid deformation, and a slow, progressive "creep". Similar curves have been described for excised cartilage on a rigid backplate (25) and shown to be compatible with a complex mathematical model that incorporates non-linear tissue consolidation as interstitial water flows away from the compressed zone (26). Here mechanical conditions were of necessity less tightly controlled, so the curve was described by the simplest model that generates curves of the form observed. The model fitted the results remarkably well. The biological components equivalent to the two elastic and one viscous components are not specified in the Kelvin-Hooke model, but by analogy with other biomechanical work (25,27), the initial elastic deformation might be due to rearrangement of collagen and elastin fibers as the stress of the applied load is taken; and the viscous creep is attributed to the flow of interstitial fluid through the loaded interstitium. The parallel

elastic element C_1 is presumably more elements of the collagen network, coupled perhaps with the increased swelling pressure of the GAG matrix as its water content is reduced. The simplistic nature of the present model and its "constants" is fully recognized and work to develop a more sophisticated analysis of the pressure-flow-time field under the indenter is clearly needed.

The present model yields three coefficients, namely the two elastic spring constants, and the viscous dashpot constant. Their interpretation is considered in more detail below.

C_2 represents the initial ability of the interstitial matrix to undergo elastic deformation without flow. The size of the subsequent deformation X_∞-X_0 for a given load reflects the strength of the in-parallel component, C_1. The rate at which the final value is approached depends both on this and on the resistance of the dashpot. The assumption *a priori*, was that k would depend on the mobility of interstitial fluid, i.e. on interstitial hydraulic resistance; the latter is widely accepted to be reduced in edema.

The above intuitive views were first tested *in vitro* on the sponge-in-glycerol model. From the Kelvin-Hooke analogy the following features were expected. 1. C_2 (or X_0) should depend only on initial elastic compressibility and should not depend on the viscosity of the fluid in the matrix through which it is being forced. This was true, except in 100% glycerol. 2. Total depth of pitting under a given applied force (X_∞) should also depend on C_1, and therefore should not depend on viscosity. This was again true. 3. Time constant, τ, depends on k, and hence on the resistance to flow (as well as C_1), so k should increase with viscosity. Increasing the glycerol viscosity in the sponge did indeed increase the dashpot constant k.

Experiments thus broadly supported the application of a Kelvin Hooke model as a first approximation for a model system *in vitro*, and encouraged its application to similar shaped pitting curves *in vivo*.

Pitting Characteristics in Normal and Swollen Arms

Initial rapid deformation (X_∞ and C_2). The initial deformation and C_2 were essentially the same in the normal and lymphedematous arms, though the *range* of values was very large (40 fold). The variation in C_2 may reflect variation in skin thickness, or skin and subcutaneous fat thickness, or the type of tissue that underlies it, e.g., lean muscle, bone or soft fat. Edema is predominantly restricted to subcutaneous tissue in these patients, and although some skin changes occur in lymphedema of the arm, they do not seem to have a significant effect on the initial compressibility of the tissue. This contrasts with the findings by Kar *et al* (14) using the Clodius tonometer in elephantine filariasis, where more extreme dermatological changes occur.

Depth of pitting (X_∞-X_0) and C_1). The size of the slow deformation was much bigger in swollen than in normal arms, with the corollary that C_1 was much lower in the edematous arms. The increase in X_∞-X_0 was attributed to the increased volume of mobile, displaceable fluid in the subcutis. Dilution of the tissue matrix elements presumably accounts for the weakening of the equivalent spring constant C_1.

Rate of pitting (time constants and dashpot constant). The time constant was longer in the swollen arms than in the normal arms. This was not in itself surprising because τ depends inversely on C_1, which was reduced. When, however, the dashpot constant was evaluated, it was found to be essentially unaltered and this ran counter to expectation based on the Kelvin-Hooke analogy. It was thought that k would be smaller in edema because fluid would escape more easily from the pressurized interstitium than in normal arms. This led us to question whether k might be governed in part by the escape of blood from the pressurized area: such an effect would influence k relatively more in the

normal arm than the edematous arm, where interstitial fluid mobility might dominate. Addition of 150 grams to a plunger with a diameter of 9mm exerts an additional surface pressure of 173 mmHg, i.e., in excess of systolic blood pressure. The fluid movement in the early creep phase might therefore be in part intravascular (vessel compression) rather than interstitial, giving a spuriously low k in normal arms. *Fig. 7* confirms that k is very sensitive to local blood volume in the normal arm. Comparable experiments have yet to be carried out on the edematous arm, but it seems reasonable to expect that interstitial fluid flow will be relatively more important there.

When edematous limbs were classified clinically as brawny or moderately pitting, τ and k were smaller (the latter not significantly) in the brawny limbs. The subjective differences were not very marked, however, and it is considered that a much larger study needs to be done, covering a wider range of soft pitting and hard woody non-pitting edemas. Nevertheless, the development of a machine to quantify pitting is important for the study of mechanisms behind fibrosis in the lymphedematous limb.

The analysis of the tonometer curve is at present very simplified. It should be possible to assess fluid flow through the interstitial matrix from the slow phase of the curve but account needs to be taken of boundary conditions and nonlinear effects such as that of compression on tissue hydration and hydraulic resistance (1). By contrast, hydraulic resistance is assumed to be constant in the Kelvin-Hooke analogy. The effects of blood vascular volume need to be further elucidated, too. Nevertheless, the new instrument seems to offer the opportunity to study human edema in a more objective fashion than heretofore possible.

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