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Mechanical properties of articular cartilage elucidated by osmotic loading and ultrasound

(synovial joint/collagen-proteoglycan matrix/degenerative arthritis/Biot consolidation/cartilage modulus)

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ABSTRACT **The time response of surface displacement and acoustic impedance of *in situ* layers of articular cartilage were measured by using pulse-echo ultrasound. Disturbances were introduced by altering the osmotic pressure. Strongly nonlinear behavior was observed near physiological equilibrium. A model of articular cartilage is proposed which relates our results to cartilage microstructure.**

The superior bearing characteristics of articular cartilage in health and its widespread, painful, and costly deterioration in degenerative arthritis have generated much interest in the mechanical function and constitutive properties of cartilage. Decades of research have not resolved some fundamental issues (1).

As part of an effort to characterize the synovial joint (2), we have developed an experimental approach to investigate the dynamic constitutive properties of articular cartilage. Interpretation of these data illuminates the microstructure of cartilage.

Articular cartilage is composed of a collagen network kept under tension from within by the osmotic pressure of a much finer proteoglycan gel network (3). The dynamic constitutive properties of articular cartilage are determined by the motion of this structure through the surrounding fluid. Under physiologically relevant conditions the gel network appears to remain immobilized relative to the collagen network so an equivalent single network, herein called the "cartilage network," can characterize most cartilage behavior.

Energy is stored in the cartilage network in three forms. An externally applied load is balanced in equilibrium by changes in the elastic (predominantly collagen network), osmotic-ionic, and osmotic-nonionic (predominantly proteoglycan network) potentials of the cartilage network. Equilibrium can be disturbed, or shifted (as is necessary to perform any measurement), by either mechanical loading or by changing the reference level of the osmotic potential. In most biomechanical studies of cartilage (4–6), the former is chosen. Mechanical tests suffer from practical limitations in replicating the *in situ* conditions, especially near equilibrium. Compression specimens, typically plugs excised from the joint, must be preloaded to achieve uniaxial strain conditions, and thin tensile specimens undergo complicating Poisson effects.

Inspired by both the work of Tanaka (7) on the kinetics of gels and by the work of Urban and Maroudas (8, 9) on the osmotic loading of cartilage and proteoglycan gels, we have developed an *in vitro* method to disturb the equilibrium osmotically and, by using ultrasonic techniques, to observe the response of the articular cartilage layer of the human hip joint *in situ*.

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EXPERIMENTAL PROCEDURE

The cartilage is first equilibrated in a controlled-temperature saline bath and then dehydrated by exposure to humid air. The new reference for the osmotic potential of the proteoglycan gel is determined by the partial pressure of the water vapor in the air. The dynamics of dehydration are governed by the rate of evaporation at the surface and by relaxation of the layer. Under conditions of free convection in the surrounding air, the time constant associated with dehydration is 2 orders of magnitude longer than the layer relaxation time constant, so the layer is in quasi-equilibrium throughout the dehydration phase of the experiment. A 10–15% reduction in thickness of the layer provides adequate displacement yet ensures saturation of the layer. The layer is then resubmerged in the saline bath, and the surface displacement during the swelling is measured by using a pulse-echo technique with a focussed ultrasonic transducer. The signals are sampled and digitized at 100 MHz and then processed by using a correlated receiver technique. The resolution of the dynamic distance measurement is <2 μm. In addition to timing (distance) information, the amplitude of the reflection provides a measure of the cartilage/saline acoustic impedance ratio. The reflection amplitude provides a true measure of the impedance ratio only if the ultrasonic transducer is positioned perpendicular to the cartilage surface. We have developed a scanning device which samples the echo as the transducer axis is positioned throughout a solid angle of 8° without changing the location of the focal point.

Under the conditions of uniaxial strain (a reasonable approximation for the thin cartilage layer attached to bone), the motion of an elastic massless network immersed in a fluid is described by a homogeneous diffusion equation (10, 11). The fluid mass content always satisfies a homogeneous diffusion equation. We assume that the constituents are intrinsically incompressible, given the high wave speed (1,760 m/sec) which translates into an apparent bulk modulus of 3.4 GPa at equilibrium; therefore, the surface displacement is proportional to the fluid mass content. If linear constitutive laws with constant network parameters are assumed, the diffusion coefficient D is the product of permeability of the network k and uniaxial stiffness L. After a short time the surface displacement response to a step input is described by a single time constant—i.e., the surface displacement approaches an equilibrium value exponentially. The diffusion coefficient is easily estimated from the slope of the logarithm of the normalized surface displacement with respect to time (12).

RESULTS AND DISCUSSION

The results of a typical experiment are shown in Fig. 1. Near equilibrium the response is significantly different from that predicted by the linear model—note the sharp toe of the sur-

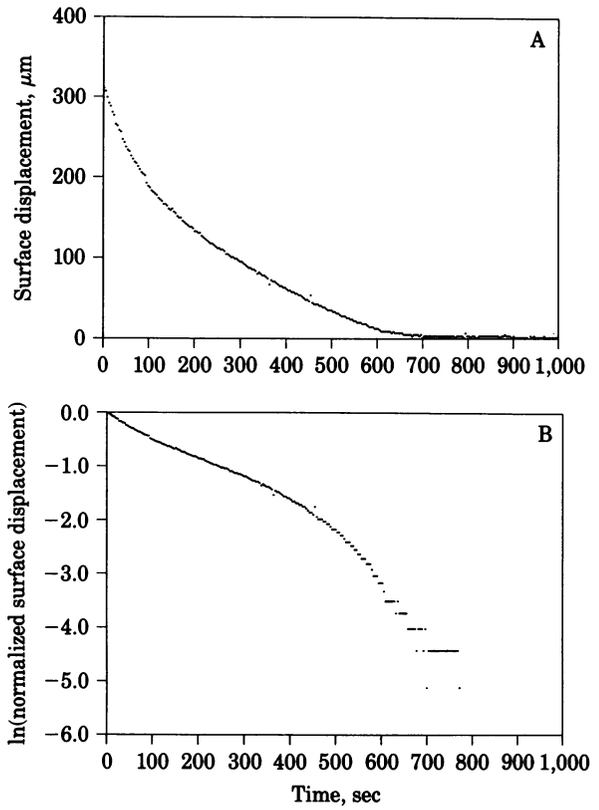

FIG. 1. (*A*) Surface displacement in swelling of human femoral head articular cartilage layer with a local thickness of 1.3 mm. (*B*) Logarithm of the normalized surface displacement.

face displacement (Fig. 1*A*) in the approach to equilibrium at about 600 sec and the corresponding roll-off in the logarithmic plot in Fig. 1*B*. Were the cartilage behaving like the linear simple-time-constant model, the data beyond 600 sec would be a smooth exponential extrapolation that would reach equilibrium at a surface displacement approximately 100 μm above the final level of the experiment. Our experiments suggest that this nonlinearity is caused by the sharply increasing stiffness of the collagen network as it is stretched out by the fluid-absorbing proteoglycans.

The collagen fibers limit the expansion of the proteoglycan gel only near equilibrium—sufficiently far (8) from equilibrium the response is adequately described by the linear model. An additional parameter is necessary for our model—the equilibrium volume of the proteoglycan gel alone. This will be greater than the actual *in situ* volume where the osmotic pressure in the proteoglycan network is balanced by tensile stresses not only in the proteoglycan gel network but also in the collagen fibers. Fig. 2 shows the theoretical response applied to the experimental data shown above. The data were fitted by finding the equilibrium volume of the proteoglycan gel that gave the best linear fit to the logarithm of the displacement relative to the gel equilibrium. The data for short times (<120 sec) and near equilibrium (>600 sec) are omitted; the agreement between theoretical prediction and the experimental results is excellent for all other times.

Additional evidence confirming our description of network nonlinear behavior near equilibrium is derived from the amplitude of the ultrasonic signal reflected from cartilage, which is a measure of the cartilage impedance. The amplitude of the reflected signal is related to the ratio of the acoustical impedances of cartilage and saline—typical ratios are 1.1–1.2. Impedance is the product of wave velocity and medium density. The wave velocity is the square root of the ratio of the restoring pressure per unit displacement to density; so the impedance is the square root of the product of stiffness and density.

Fig. 3 shows the time history of the amplitude relative to its value at equilibrium conditions in the cartilage. The initial few seconds of high impedance may be due to excess dehydration at the collagen-rich surface. The minimum corresponds to the bulk modulus of the gel/collagen mixture because the cartilage has been sufficiently dehydrated to relax the collagen network. This minimum is reached with initial dehydration of about 10% [in good agreement with an earlier estimate (8) of 8%]. The impedance increases as the proteoglycans swell, stretching the collagen and increasing the stiffness. Oscillations occur as the layer of high impedance diffuses toward the bone as reflections from this interface combine with the primary reflection from the cartilage surface.

These results provide an estimate of the stiffness of the collagen network at equilibrium. Typically, the minimum of the amplitude of the reflected signal is about 75% of its equilibrium value. For the range of cartilage-to-saline impedance ratios of 1.1–1.2, this corresponds to a dehydrated impedance ratio of 1.07–1.15. The additional stiffness contributed by the collagen network (under tension) is therefore 160–300 MPa. The decrease in stiffness from equilibrium to the dehydrated state is 4.7–8.7%. Tensile tests of cartilage have measured stiffness in this range (13), confirming our hypothesis that the collagen network is indeed stretched out at equilibrium.

This experimentally verified, rational model of cartilage con-

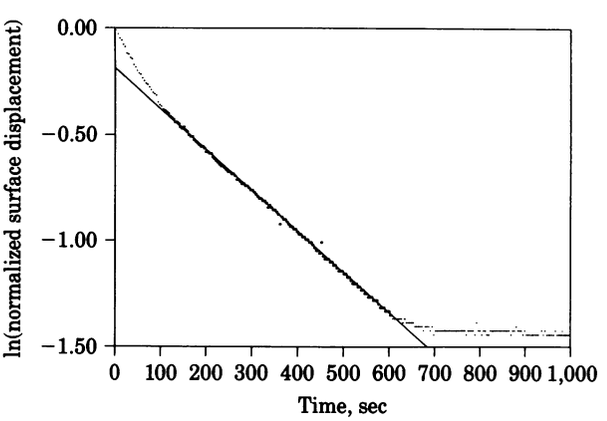

FIG. 2. Theoretical response (solid line) best-fitted to the data between 100 and 600 sec.

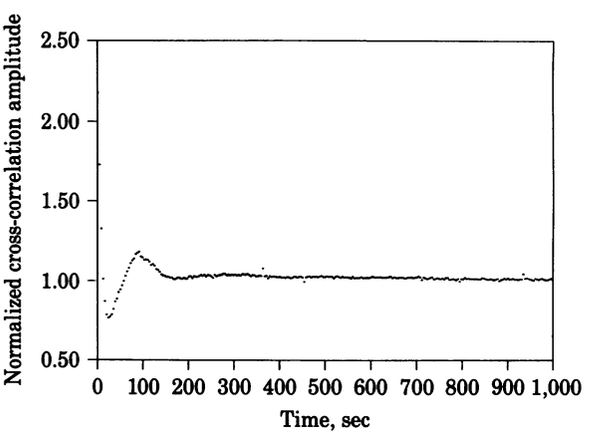

FIG. 3. Normalized cross-correlation amplitude of ultrasonic pulse reflections from the cartilage surface during swelling.

stitutive properties and the *in situ* measurement of their topographical variation in the synovial joint (14), together with detailed geometrical information on the opposing articular layers (15), provide the quantitative data necessary for numerical simulation of the dynamics of the whole synovial joint.

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