Technical Note

Confined compression of articular cartilage: Linearity in ramp and sinusoidal tests and the importance of interdigitation and incomplete confinement

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Abstract

Experimental and theoretical methods were used to investigate the linearity of the stress response of articular cartilage to ramp and sinusoidal tests in confined compression, as well as the role of cartilage-porous platen and lateral confinement boundary conditions in determining material responses. With respect to linearity, we posed the question as to whether the elicited stress responses to ramp compression, ramp release and sinusoidal tests were similar. With respect to boundary conditions we inquired as to the necessity of specifying a detailed interdigitating contact with the porous filter and of specifying the level of confinement present at the lateral edge of the disk. We found that the stress responses to the three types of tests were dissimilar, with ramp compression the only test exhibiting linear behavior. Ramp release from a static compression offset was non-linear in a manner such that the cartilage maintained a compressive stress higher than expected by a linear theory. Sinusoidal compression also displayed a non-linear response consistent with the presence of a release phase in each cycle. The actual boundary conditions present at the cartilage/porous-filter interface were visualized histologically. Areas (tens of microns) of cartilage in contact with the metal of the filter were interspersed with areas expanded into the pores of the filter. Finite-element analysis incorporating this information suggested that precise specification of this interface and of the level of the extent of lateral confinement would be necessary for the estimation of material properties, such as the hydraulic permeability, from these tests. The trends of the linearity studies did not appear to be significantly affected by the problems posed by these difficult to quantitate boundary conditions. The non-linear cartilage response to release and sinusoidal displacements therefore appear to be physiologically interesting. The maintained, that is higher than would be linear, compressive stress observed during release may be a beneficial adaptation to repeated loading where temporal variations in tissue stresses would be minimized. © 1998 Elsevier Science Ltd. All rights reserved.

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1. Introduction

The mechanisms by which joint cartilage supports physiologically elevated stress while simultaneously reducing friction between articular surfaces have received intense study (Mow et al., 1984). Additionally, the biological mechanisms by which cartilage can respond and adapt to different physical environments have been partially elucidated (Grodzinsky et al., 1996). In both of these cases an understanding of the nature of the cartilage stress response to mechanical stimuli is desired, in the former case to identify physical structures and mechanisms which give rise to the resistance to deformation and which become altered in tissue pathology. In the latter case, understanding of physical events at the spatially resolved level is essential to
correlate spatially specific physical parameters (solid matrix deformation, interstitial fluid flow) with observed cell biological responses (Buschmann et al., 1995; Kim et al., 1994).

The extent of the linearity of stress responses is needed to classify the physical mechanisms resulting in resistance to tissue deformation. Previous studies using the confined compression geometry have partially characterized linearity using one of the several tests: the equilibrium response (Mow and Lai, 1979), transient creep (Hayes and Mockros, 1971), stress–relaxation (Eisenfeld et al., 1978), and dynamic sinusoids (Lee et al., 1981). The diversity of the results, indicating the range from weakening non-linear to linear to stiffening non-linear behavior, was perhaps due to the different test protocols as well as to the different criterion used for judging linearity. Further experimental characterization of the linearity of behavior under these different tests is required.

When used in conjunction with biphasic theory, the confined compression test can be used to estimate material parameters, such as the hydraulic permeability (Armstrong and Mow, 1982; Buschmann et al., 1992). An issue which has arisen in the interpretation of confined compression experiments is the nature of the boundary conditions at the cartilage/porous-platen interface and at the radial-edge/confining-wall interface. At the cartilage/porous-platen interface, the model assumes that the solid is uniformly displaced by the porous platen and that the fluid is uniformly in contact with the fluid of the bath. In reality this interface should contain some areas where the cartilage (solid and fluid) are in contact with the solid parts of the platen and other areas which are in contact with the bathing fluid. The boundary condition imposed at the radial edge of the disk is that solid and fluid displacement are nil. Previous authors have questioned these assumptions (Armstrong and Mow, 1982; Frank and Grodzinsky, 1987; Hori and Mockros, 1976; Lee et al., 1981; Mow et al., 1980), but have not provided experimental evidence of the actual boundary conditions, or theoretical calculations as to the importance of accounting for them.

In this study we had two objectives. Firstly, we wished to determine the linearity or non-linearity of ramp compression, ramp release and sinusoidal tests using the uniform criterion of superposition. Secondly, we wanted to determine whether a detailed specification of boundary conditions would be necessary to derive material parameters from these tests. The results of the linearity measurements demonstrated a previously unobserved and potentially physiologically significant behavior of the stress response to release. The results of the boundary condition investigations suggested prudence in using these tests to quantify intrinsic material parameters.

2. Materials and methods

Cylindrical cartilage disks (8) from the central area of the humeral heads of 1–2 yr old cows (4) were cut using a 6 mm diameter dermal biopsy punch within 24 h of slaughter (Jurvelin et al., 1997). The final disk for testing was punched to 3.6 ± 0.05 mm diameter. Mean individual disk thickness was 1.0–1.22 mm with a variation of ±25 μm within a disk. Disks were stored at 4°C in a humidified chamber for at most 6 h prior to testing.

A custom-built mechanical testing device was used (Jurvelin et al., 1997). Cartilage disks were placed in a 3.78 ± 0.01 mm diameter cylindrical hole of the confined compression chamber containing PBS. A 3.70 ± 0.01 mm diameter stainless-steel porous filter (Meyer Sintermetal AG, Studen Switzerland; ~5 μm pores, 50% porosity, ~15 μm peak–peak surface roughness via TalySurf) was placed on the articular surface. An equilibrium tare load of ~4–7 g was applied. The elastic stiffness of the testing system, 82.7 ± 5.5 g μm⁻¹ (Mean ± S.D. N = 7), was used to correct jaw-to-jaw displacements to obtain specimen surface-to-surface displacements.

Each disk underwent tests during an ~4 h period. The disk was subjected to a sequence of 30–36 ramp compressions of 5 μm amplitude with 1 μm s⁻¹ velocity to a final 15% offset. When the slope during relaxation was less than 0.5 g min⁻¹ the next step was executed. The linear homogeneous isotropic biphasic model (Mow et al., 1980) was fit to each stress relaxation profile of the sequence after transforming the time domain data to the real axis of the Laplace domain (Buschmann, 1996). Best-fit values of the aggregate modulus, $H_\alpha$, and permeability, $k$, were thereby obtained as a function of the compression offset imposed at the beginning of each step. After the 15% offset compression, dynamic sinusoidal tests were performed in the range 0.001–1.0 Hz using a 5, 10 and 15 μm amplitudes. Dynamic stiffness and the total harmonic distortion (THD) were calculated (Frank and Grodzinsky, 1987). The similarity of material behavior for sinusoidal displacements versus compressive ramp displacements was investigated using a numerical technique to convert the last stress relaxation response to a 5 μm ramp displacement at 15% offset to the harmonic response function (Buschmann, 1996). Ramp displacements were applied both in compression and in release from the 15% offset reference using the {amplitude, velocity} pairs {5 μm, 1 μm s⁻¹}, {10 μm, 2 μm s⁻¹}, {15 μm, 3 μm s⁻¹}. Stress relaxation profiles relative to the equilibrium stress and strain at 15% offset were normalized to $H_\alpha e_0$ where $e_0$ was the imposed surface-to-surface strain. Amplitudes, frequencies and velocities were chosen to facilitate linearity assessment since the different signals within one type of test are multiples of the signal with the smallest amplitude.
Interdigitation of the cartilage and the porous filter was examined by fixing disks with glutaraldehyde after a confined static compression of 0, 15 and 30% the original thickness (Buschmann et al., 1996). The influence of observed cartilage–porous platen interdigitation on the stress response in confined compression was investigated using a linear homogeneous axisymmetric poroelastic finite element model. A cartilage disk of 0.90 mm thickness and 0.1 mm radius (to reduce computation time) was subjected to a 4.5 μm (0.5%) ramp in 5 s. Interdigitation was simulated by interleaving boundary conditions of imposed axial strain (contact points of the platen) and zero pore pressure (spaces between contact points). Total contact area was varied from 8 to 90% and the number of contact points from 2 to 10 across the 100 μm radius, chosen to be consistent with histological evidence of interdigitation (Fig. 7) and with surface roughness measurements. Three different levels of mesh refinement were used ensuring convergence and ensuring a minimum of three elements in the porous areas of the upper surface. The effect of unconfinement was also investigated using the classical boundary conditions with no friction and a specimen diameter of 3.6 mm. The ABAQUS software was used.

3. Results

The magnitude of the transient load increased many fold between 0 and 15% compression offset (Fig. 1). The hydraulic permeability obtained using the classical biphasic model decreased substantially with increasing compression (Fig. 2). The amplitude of the dynamic stiffness from the sinusoidal tests was reduced and the THD was increased when the displacement amplitude was increased (Fig. 3).

Normalized compression and release stress–relaxation profiles for 5 μm amplitude displacements were similar (Fig. 4). A gradually increasing asymmetry and non-linearity appeared when increasing the displacement amplitude to 10 μm and to 15 μm, where the decrease in compressive stress for ramp release was smaller than the increase in compressive stress for ramp compression. Normalized compression stress–relaxation profiles demonstrated linear material response while normalized release stress–relaxation profiles demonstrated non-linear behavior (Fig. 5).

The dynamic stiffness obtained from ramp-compression tests was compared with the direct measurement of the dynamic stiffness, made immediately following this last step and to the model calculated using the best-fit values, $H_A = 0.56$ MPa, $k = 1.6 \times 10^{-15}$ m² N⁻¹ s⁻¹, from the ramp response and the root-mean-square thickness of the 8 specimens at 15% compression offset, $l = 0.90$ mm (Fig. 6).

Histological evidence of the static interdigitation between the articular surface and the porous filter was apparent (Fig. 7). These images demonstrated that certain areas of the cartilage surface are in contact with the solid part of the porous filter while others are not. The number of these contact points and their total area appeared to increase with increasing offset compression (Fig. 7, A versus C versus E).

When the observed interdigitating boundary condition (Fig. 7) between the cartilage and the porous platen was included in the finite-element model, the mesh at ramp time demonstrated bulging of the cartilage into the pores of the platen (Fig. 8). The calculated stress responses for different interdigitation boundary conditions revealed a significant effect of classical and the various
interdigitating boundary conditions we examined (Fig. 9). Additionally, the lack of confinement at the lateral edge significantly weakened the simulated stress response to ramp compression (Fig. 9).

4. Discussion

The goals of this study were to evaluate the extent of linearity of ramp and sinusoidal tests and to evaluate the need to specify detailed boundary conditions of the confined compression test in order to estimate material parameters. With respect to the first objective, we discovered several previously uncharacterized linear and non-linear regimes using small 5–15 μm displacement amplitudes which are summarized in the following list (where L# indicates a linear behavior and N# a non-linear behavior).

(L1) Normalized stress response to ramp compression at 15% compression offset was linear when increasing the step amplitude from 5 to 15 μm (Fig. 5).

(N1) Normalized stress response to ramp release at 15% compression offset decreased non-linearly when increasing the step amplitude from 5 to 15 μm (Fig. 5).
Fig. 6. The stress response to 5 \( \mu \)m ramp compression was represented in Fourier domain using a recently developed numerical transform method (Buschmann, 1996) in order to compare, in a model-independent manner, with the stress response to sinusoidal displacements. The best-fit values, \( H_\text{a} = 0.56 \text{ MPa}, k = 1.6 \times 10^{-15} \text{ m}^4 \text{ N}^{-1} \text{ s}, \) from the ramp response were used along with \( l = 0.90 \text{ mm} \) to illustrate the dynamic stiffness and phase of the linear isotropic biphasic model.

(N2) Normalized stress response to sinusoidal compression (dynamic stiffness) decreased non-linearly when increasing the sinusoidal amplitude from 5 to 15 \( \mu \)m (Fig. 3).

(N3) Normalized stress response to ramp compression increased non-linearly with increased compression offset from 0–15% (Figs. 1 and 2).

The stress responses to ramp compression (L1) and ramp release (N1) were different. The non-linear behavior seen in response to release was such that the normalized response became smaller with increasing amplitudes of compression (without any evidence of lift-off). However, this response represents a drop in averaged compressive surface stress so that the lower normalized values therefore represent larger compressive stresses generated by the cartilage, than would be linear. Hence, this previously unobserved non-linear response to release may be characterized as a non-linear maintenance of compressive stress. The weakening non-linear response to dynamic sinusoidal compression (N2) may therefore be the result of the release phase present in each cycle. This result combined with the non-linear maintenance of compressive stress during release suggests a possible

Fig. 7. The interdigitation of the cartilage surface into the pores of the compressing platen was characterized by chemically fixing compressed specimens under free-swelling conditions (A and B), 15% compression (C and D) and 30% compression (E and F). The left panel (A, C, E) shows an intact articular surface free-swelling (A) or in contact with the porous platen (C and E) while the right panel shows a cut surface from the deep radial zone, free-swelling (B) or in contact with the porous platen (D and F). Horizontal arrows indicate an unconstrained free-swelling cartilage surface (A and B). Vertical arrows show regions of the cartilage surface which appear to have been in contact with the solid parts of the porous platen. Arrowheads indicate regions of the cartilage surface which were likely free to expand into the pores of the porous platen. Bar = 10 \( \mu \)m.
Fig. 8. The 100 µm radius finite-element mesh at the ramp time \( t = 5 \) s for the case of four contact points and \( \sim 32\% \) total contact between the cartilage and the solid parts of the porous platen (8 µm per contact). The finite-element formulation allows the incorporation of cartilage/porous-platen interdigitation and transient bulging into the platen pores.

Physiological reason for this behavior, in minimizing temporal variations in tissue stress, potentially to minimize physical factors which could cause cell and tissue damage.

The compression/release asymmetry may be related to the creep/recovery asymmetry (Athanasiou et al., 1991; Mow et al., 1989) except that the latter is complicated by different initial compression offset for release versus creep. Our observed non-linear behavior using dynamic sinusoids is compatible with previous studies where, using harmonic analyses, 2% (20 µm) sinusoidal displacements generated non-linear oscillatory stress responses (Lee et al., 1981) although 0.5% (5 µm) displacements appeared to generate linear responses. In those studies, the weakening nature of the non-linear behavior was not mentioned. Also, the criterion used to judge linearity was that \( \text{THD} < 10\% \). In our study, the dynamic stiffness at 0.1 Hz fell by \( \sim 40\% \) when increasing compression amplitude from 5 to 15 µm, while the THD only increased from 6 to 12% (Fig. 3).

The non-linear stiffening of material behavior (N3) implies that either intrinsic material properties or boundary conditions of the specimen are significantly altered during the sequential imposition of the 15% static compression offset. One explanation suggests that increasing compaction of cartilage matrix leads to reduced hydraulic permeability (Holmes et al., 1985). This explanation does not explain our data since direct permeation experiments (Lai and Mow, 1980; Mansour and Mow, 1976) and hydrodynamic micromodels (Happel and Brenner,
1986) suggest that the change in permeability should be of the order of 2–4 times the bulk dilatation, suggesting 30–60% reduction in permeability due to 15% static offset compression, smaller than our observations (Fig. 2). The depth-dependent material properties of adult articular cartilage (O’Connor et al., 1988; Gore et al., 1983; Schinagl et al., 1996) should only partially account for this large reduction in permeability with compression offset.

Although some change in intrinsic permeability certainly does occur during the sequential imposition of the 15% offset compression, our data and calculations relating to boundary conditions (Figs. 7–9) suggest that these latter effects may predominate in generating the observed stiffening response (Fig. 1 and indirectly Fig. 2). Our data show that interdigitation and incomplete confinement could result in increased transient loads (Fig. 9) with increased compression offset, the former by increasing contact between the solid parts of the porous filter and the articular surface and the latter by improving confinement. The problem of incomplete confinement has been noted previously (Armstrong and Mow, 1982; Hori and Mockros, 1976; Lee et al., 1981; Mow 1980). In our study, the diameter of the confining well was optimized to give a tight fit for the cartilage disk. However, the ability to insert the disk into the confining well demands a certain incomplete confinement. We simulated the error in the hydraulic permeability estimated from curve fits due to uncertain knowledge of the boundary conditions by curve-fitting the finite-element simulations to the classical model. We found that reasonable variations in the interdigitation phenomena (all but the bottom curve in Fig. 9) could produce an error of ~400% while there was essentially no limit to the error introduced by lack of confinement (bottom curve in Fig. 9). Taken together, these data suggest that the discord of actual versus model specimen boundary conditions may lead to erroneous values of hydraulic permeability obtained using curve fits, a problem which may also be present in indentation tests using porous indenters.

Finally, we found (Fig. 6) as have previous investigators (Lee et al., 1981) that the standard implementation of the biphasic model vastly overpredicts stiffness at higher frequencies (>0.1 Hz). Here we add that this disagreement is equally present for stress relaxation tests (Fig. 6). The actual boundary conditions could be responsible for this disagreement since their effects will be accentuated at higher frequencies where fluid pressure increases causing more expansion into the pores of the plate. Our results concerning boundary conditions should not affect the results of our linearity analysis (excluding N3), since the boundary conditions examined still result in a linear model, and since similar trends have been observed in a preliminary series of unconfined compression tests (Fortin et al., 1997), where confinement and interdigitation are not the considerations.

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References


