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Interspecies Comparisons of In Situ Intrinsic Mechanical Properties of Distal Femoral Cartilage

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Summary: We measured the in situ biomechanical properties of knee joint cartilage from five species (bovine, canine, human, monkey, and rabbit) to examine the biomechanical relevance of animal models of human knee joint injuries and osteoarthritis. In situ biphasic creep indentation experiments were performed to simultaneously determine all three intrinsic material coefficients (aggregate modulus, Poisson's ratio, and permeability) of the cartilage as represented by the linear KLM biphasic model. In addition, we also assessed the effects of load bearing on these intrinsic properties at "high" and "low" weight-bearing regions on the distal femur. Our results indicate that significant differences exist in some of these material properties among species and sites. The aggregate modulus of the anterior patellar groove within each species is the lowest among all sites tested, and the permeability of the patellar groove cartilage is the highest and does not vary among species. Similarly, the Poisson's ratio in the patellar groove is the lowest in all species, except in the rabbit. These results lead to the conclusion that patellar groove cartilage can undergo greater and faster compression. Thus, under high compressive loads, the cartilage of the patellar groove surface can more rapidly compress to create a congruent patellofemoral joint articulation. For any given location, no differences were found in the aggregate modulus among all the species, and no correlation was found between aggregate modulus and thickness at the test site. Thus, in the process of selecting a suitable experimental animal model of human articular cartilage, it is essential to consider the significant interspecies differences of the mechanical properties. **Key Words:** Biomechanical properties—Interspecies comparisons—Knee cartilage—KLM biphasic theory—Creep indentation.

Synovial joints are the functional connections that make possible controlled motion between the bones. The articulating bone ends are covered with a 0.1—5-mm-thick cartilage, depending on species and location in the joint. The main functions of articular cartilage are to decrease the contact stresses in the joint (6,7) and to allow motion of the opposing surfaces with minimum friction and wear (28). The tissue is composed of two phases, an interstitial fluid and a solid matrix. The solid matrix, accounting for 20–30% of the wet weight of the tissue, is composed of collagen fibers (65% of dry weight), proteoglycans (PGs) (25% of dry weight), chondro-

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cytes, and other glycoproteins and lipids (29). The remaining 70–80% of the tissue is water, most of which is freely exchangeable by diffusion with the outside medium (27,39,41).

Experimental studies of early biological changes after joint and ligament injuries and during osteoarthritis (OA) necessarily depend on the use of animal models (4,22,23,25). For example, McDevitt and Muir induced OA in mature dogs of various breeds by using the Pond-Nuki procedure to resect the anterior cruciate ligament (23). They demonstrated that the cartilage of the operated joints was thicker and more hydrated, and that the PGs were more easily extracted than in normal controls. In a later study, McDevitt and co-workers again used the Pond-Nuki procedure in adult dogs of various breeds to induce OA (22). They reported that morphological and biochemical changes in bone, cartilage, synovial membrane, and joint capsule of the operated joints progressed with time and became similar to those in dogs with natural OA. Moskowitz and co-workers studied the size of cartilage PGs extracted from control and OA rabbit knees after partial meniscectomy (25). They noted that in normal control knees approximately 30% of PGs were in aggregate form, whereas no aggregates were found in OA tissue. They correlated the lack of aggregates with "a disorder of link protein, hyaluronic acid, or PG subunit hyaluronic acid binding sites." Altman and co-workers also used the Pond-Nuki procedure in the dog OA model and observed breakdown of collagen network and increased swelling (4). They showed that PG aggregates were reduced in size and that the number of PG subunits was increased.

The utility of the information obtained from these studies depends on the similarities and differences between human and animal articular cartilage biology, biochemistry, and biomechanical properties. Despite the importance of these models and the large variety of animals used to study the OA disease processes, few investigators have attempted to compare the biomechanical properties of human and animal articular cartilage. Simon in 1970 studied the relationship between the thickness of articular cartilage and static compressive stress in six joints of five species (mouse, rat, dog, sheep, and cow), ranging in weight from 0.22 to 2,669 N (35). He concluded that static compressive stresses in the joint cartilage among the various species are within one order of magnitude and are unrelated to the thickness of the cartilage. Furthermore, he attempted to correlate the deformability of articular cartilage with the thickness of the tissue and its "intrinsic elasticity" (36). He used canine, bovine, and human articular cartilage. Even though he could not obtain the Young's modulus, he demonstrated variations in the indentations of cartilage of comparable thickness when subjected to the same compressive stress.

Biochemical studies were performed by Buckwalter and co-workers to determine interspecies differences of articular cartilages from humans, monkeys, and rabbits (8). They measured the PG content, the collagen content, and the collagen cross-linking. They concluded that significant differences exist in the biochemical composition of articular cartilage among the three species despite their anatomic similarity. From these studies, it is unclear if there are significant differences in the intrinsic mechanical properties, as defined by the biphasic theory (aggregate modulus, Poisson's ratio, permeability) of the tissue, among different species.

It is also unclear how functional weight bearing may affect the properties of articular cartilage. It is well known that the biochemical composition of cartilage varies significantly over the joint surface (17,41) and appears to be related to joint loading (9,16,19,32). Many investigators have studied the effects of high and low loading on articular cartilage biochemistry. Caterson and Lowther studied the effect of immobilization and unloading and increased loading on sheep ankle cartilage (9). They found that increased load bearing increases the glycosaminoglycan (GAG) content and vice versa, whereas hydroxyproline content remains unchanged. In addition, non-weight-bearing cartilage shows a decrease in the molecular weight of PGs and a keratan sulfate to chondroitin sulfate ratio of 0.78, compared with 0.38 for the weight-bearing joints. Kiviranta and associates showed that increased weight bearing augments the PG content of the articular cartilage matrix of young beagle dogs, whereas unloading reduces it (17). In general, the hexosamine content decreases as a result of immobilization. In other studies, cartilage PG heterogeneity and aggregating ability were evaluated from high- and low-weight-bearing areas and OA cartilage (19,32). It was found that in low-load-bearing and OA cartilage, a low concentration of the link-glycoprotein or hyaluronate prevents the formation of a larger PG aggregation population. Akizuki and co-workers studied cartilage from regions believed to be high-

and low-weight-bearing areas of human distal femur and reported significant differences in the tensile and kinetic swelling properties (2,3). All of these studies indicate that mechanical factors, such as normal load bearing, play an important role in the maintenance of normal articular cartilage.

Investigations have also shown that the mechanical properties of articular cartilage depend on its biochemical composition (1,3,5,11,15,16). Hirsch in 1944 found that a relationship exists between the magnitude of indentation and the chondroitin sulphate content of human articular cartilage (11). Kempson and co-workers reported that the "creep, or two-second modulus" of cartilage from human femoral head correlates well with the PG content (16). Armstrong and Mow found that the water content of human articular cartilage is highly correlated with the intrinsic equilibrium modulus and permeability; as water content increases, the matrix of the tissue becomes more permeable and softer (5). Akizuki and associates showed that the compressive aggregate modulus of human articular cartilage correlates positively with its PG content (1). In a separate study, Akizuki and co-workers demonstrated a strong correlation between the tensile modulus of the extracellular matrix of human knee cartilage and the collagen/PG ratio (3). Jurvelin and co-workers observed a relationship between the "equilibrium shear modulus" and the PG content of distal femur cartilage in beagles, but could not establish such a correlation in tibial cartilage (15). They also showed that the rate of creep correlates inversely with the PG content (15). Thus, in this study, we examined whether knee joint cartilage biomechanical properties vary intraarticularly in response to weight bearing. Furthermore, we studied whether differences exist in these cartilage properties among species in a consistent pattern.

MATERIALS AND METHODS

We performed in situ biphasic creep indentation experiments in three sites on the distal femoral cartilage of humans (three pairs), bovines (five pairs), cynomolgus monkeys (three pairs), greyhound dogs (three pairs), and New Zealand rabbits (three pairs). Normal human specimens (24, 35, and 43 years old) were obtained from the University of Miami, Tissue Bank, Department of Surgery. The India ink staining technique was used to determine that most of these joint surfaces had no fibrillation (10). All animals were young adults, skeletally mature—as evidenced by their closed physes—and were harvested and frozen within 24 h of slaughter. All specimens were stored at −80°C and underwent only two freeze–thaw cycles before testing. Even though there are conflicting opinions on the effects of freezing on cartilage mechanical properties (13,20), our anecdotal data on testing fresh and then frozen bovine cartilage specimens using the creep indenter

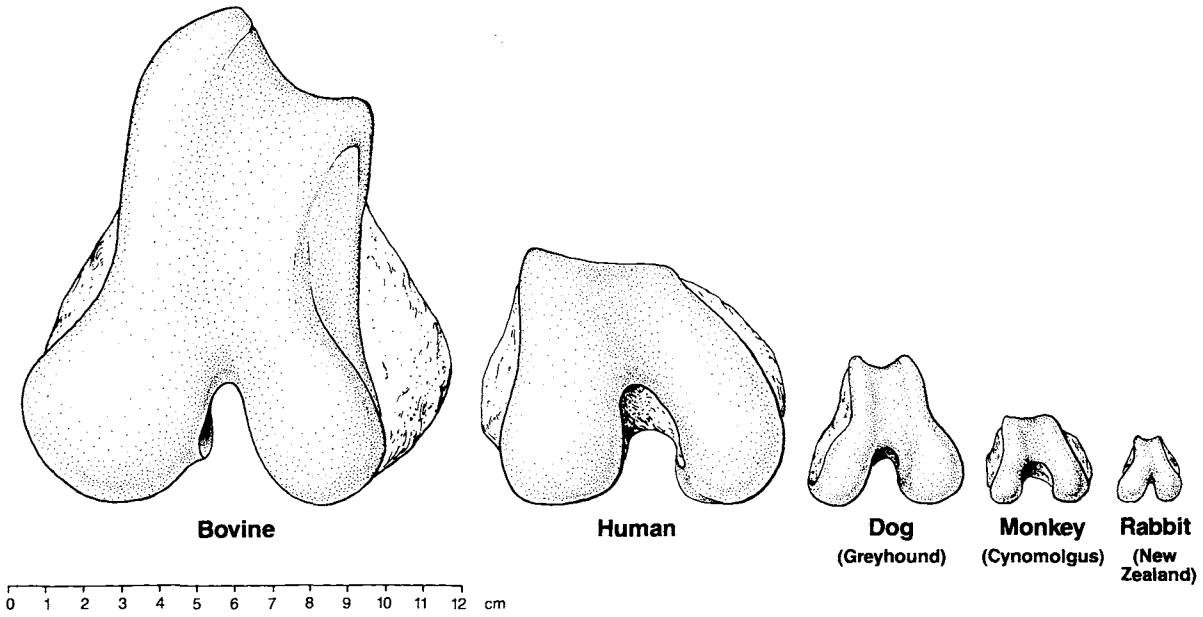

FIG. 1. Schematic comparison of the anatomical differences of the distal femora of the five species tested.

indicate that two freeze–thaw cycles do not affect the material properties of the tissue. Figure 1 depicts the vast variations in size and anatomical contours of the species tested.

We tested the central anterior region of the lateral femoral condyle, the central posterior region of the medial femoral condyle, and the central anterior portion of the patellar groove. The test sites are shown as the shaded areas in Fig. 2. The first two sites are believed to be high-weight-bearing areas, whereas the latter site may be a low or intermittent load-bearing area for human tibiofemoral joints (3,7,34). Even though there is no established evidence that these regions coincide with high or low load areas for all species studied, an attempt was made to be consistent in all species and to test the same sites. In the rabbit, becaue of its normal knee flexion of 135°, it is likely that its patellar groove is habitually highly loaded.

Biomechanical Analysis

The linear KLM biphasic theory, in conjunction with the biphasic indentation creep experiment, provides the means to obtain simultaneously and in situ three intrinsic material coefficients—aggregate modulus (H_A), Poisson's ratio (ν_s), and permeability (k)—of the tissue (18,26). Mak and co-workers presented the theoretical solutions for the biphasic indentation problem of articular cartilage under creep and stress–relaxation conditions (18). Because of the extensive calculations required for this solution, it was necessary to develop an efficient numerical algorithm to curve-fit the indentation data (26). This was done by employing a bicubic spline function representation of the "master solution" of the problem (26). This master solution is provided as a numerical tabulation, and all other solutions may be obtained from the master solution using a similarity principle. It was shown by Mow and co-workers that these solutions can be obtained by simply shifting the master solution along the log–time axis (26). A detailed description of both the theoretical solution and the numerical algorithm using the master solution can be found in references (18,26).

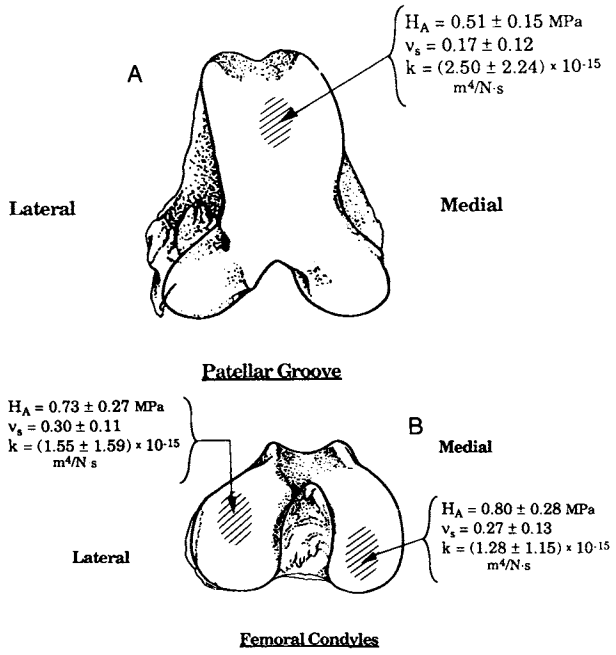

FIG. 2. Average values of the intrinsic material properties for all species combined. Test areas are indicated by shaded regions. **A:** Intermittent or low-weight-bearing areas. **B:** High-weight-bearing areas.

Testing Procedures

A biphasic indenter was used to determine the creep and recovery behavior of articular cartilage in situ (26). This apparatus was specifically designed for accurate and repeatable indentation testing, allowing unimpeded fluid exudation into the indenter tip. Each frozen joint section was thawed for 1 h at room temperature in normal saline solution (0.15 *M* NaCl) containing enzymatic inhibitors (EDTA, 2 m*M;* benzamidine HCl, 5 m*M;* *N*-ethyl malemide, 10 m*M;* and PMSF, 1 m*M*). The osteochondral specimen was mounted in its holder with cyanoacrylate cement and was positioned via the six-degrees-of-freedom assembly, such that the rigid–porous indenter tip was perpendicular to the test site on the articular surface. Correct alignment is usually attained within 1–2 min for the human, bovine, and canine specimens, and up to 5 min for the smaller, more difficult to work with joints (monkeys and rabbits). With the specimen in the aligned position, the test chamber was then filled with the bathing solution. Each specimen was allowed to equilibrate for 15 min to attain swelling equilibrium. In this manner the tissue could regain any fluid loss through evaporation during the specimen-mounting procedure. The porous–permeable indenter tip (1.0 mm in diameter for rabbits, 1.5 mm in diameter for all other species) was ultrasonically cleaned before testing to ensure ease of fluid flow from the specimen into the indenter tip. The permeability of the porous tip, made of sintered steel, was determined to be several orders of magnitude higher than that of

normal articular cartilage and, thus, offered little additional resistance to fluid flow as it passed into the porous tip.

A tare load (0.0343–0.0490 N) was applied, and the tissue was allowed to creep for 15 min prior to application of the actual test load. To ensure that all applied loads were within the linear range of response of articular cartilage, preliminary equilibrium load-deformation tests were performed in all species. Test loads were chosen to be either 0.0980 N for rabbit, monkey, and canine knee joints, or 0.1961 N for human and bovine specimens. The test load was suddenly applied and the osteochondral specimen was allowed to creep to equilibrium. Equilibrium was determined when no variations occurred in the observed value of creep in 20 min. Total creep equilibrium time varied from 3,000 s for rabbits to 10,800 s for humans. After creep equilibrium was achieved, the test site was unloaded and recovery was observed. Subsequently, the surface position of the test site was marked using India ink. The cartilage thickness was then measured at the exact location and orientation of the test site using a penetrating steel needle probe (12,26,38).

Three sites on six human, six cynomolgus monkey, ten bovine, six greyhound dog, and six New Zealand rabbit knee joints were tested for a total of 102 indentation tests.

RESULTS

Figure 3 shows a typical creep-recovery curve of the posterior medial femoral condyle of a human knee joint. Ninety-seven specimens achieved complete recovery after removal of the test load after creep equilibrium. Five slightly fibrillated specimens did not reach complete creep equilibrium under the action of the tare load (15 min) before test load application; as a result, incomplete recovery was observed. Those specimens were not used for calculating material properties. The average amount of recovery obtained for all species and all test sites was 96% of the total creep equilibrium value. Typical creep and recovery indentation curves are significantly different (Fig. 4). Initially, the rate of creep is larger than the rate of recovery. Subsequently, the creep deformation is slower until, finally, the kinetics of the two curves become identical.

By curve-fitting the experimental creep curves with the master solution via a nonlinear regression procedure, the intrinsic material properties of articular cartilage are obtained. A typical curve-fitting result is shown in Fig. 5. This figure is representative of the quality of the vast majority of the curve fits. Table 1 contains the three intrinsic material properties (H_A, ν_s, k) and the thickness (h) at the test site of all five species and three locations. The results shown depict the mean ±SD. Figure 2 contains the mean values of the material properties for all species at each test site.

Statistical Analysis

The material properties of cartilage were obtained from three different sites on the femoral

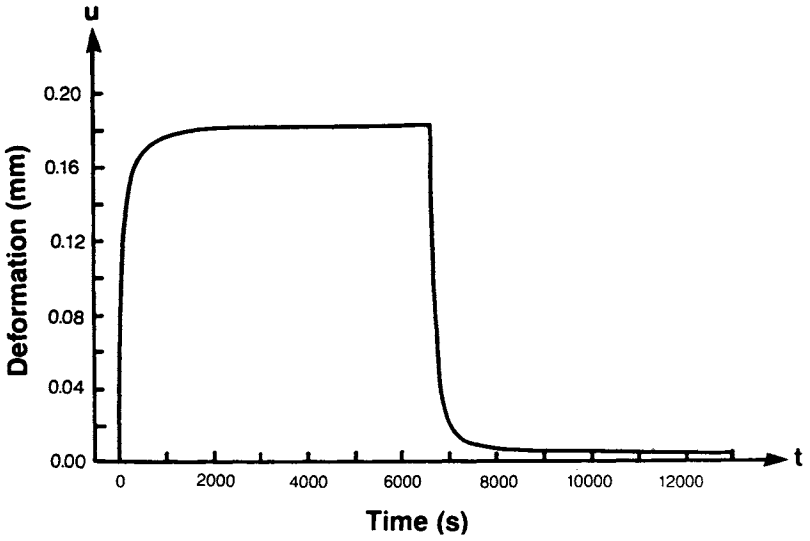

FIG. 3. A typical biphasic creep and recovery curve. Complete recovery is observed.

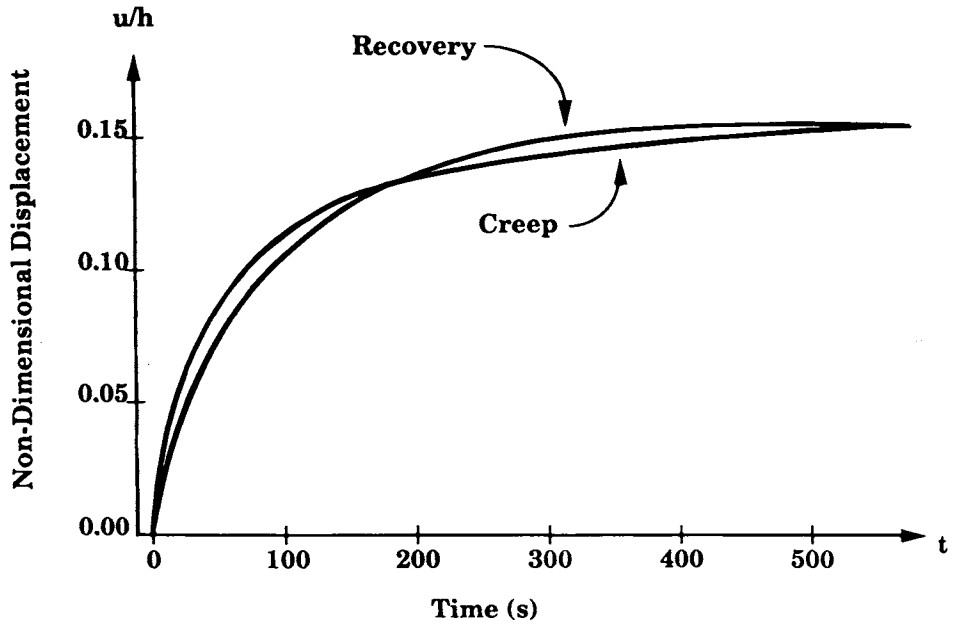

FIG. 4. Significant differences are observed in the rate of creep and rate of recovery in a typical indentation test.

condyles of five species. Thus, there are two independent variables for statistical comparisons: location and species. Because of the heterogeneity of variance and nonnormality of our data, we first rank-transformed the results so that parametric tests could be used. Because bilateral joints were used, the effect of side was first examined by running a measure of rank correlation test (nonparametric Spearman's Rho test) and a factorial analysis of variance (ANOVA) with three independent variables (instead of the actual two): species, location, and side. It was found that the effect of side was not significant. One-way and two-way ANOVA tests were then performed to determine whether there

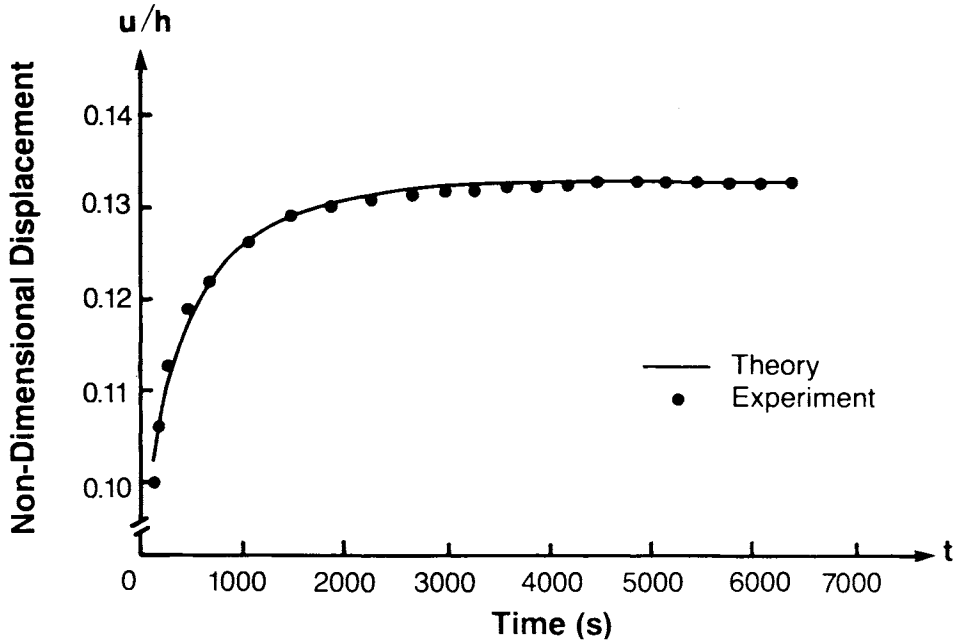

FIG. 5 A typical curve-fit using the time-shift method for the biphasic creep indentation solution, on a linear time scale.

TABLE 1. *Material properties obtained from the nonlinear regression curve fits*

Lateral condyle	ν_s	H_A	k ($m^4/N \cdot s$) $\times 10^{15}$	h (mm)
Human (n = 4)	0.098 ± 0.069	0.701 ± 0.228	1.182 ± 0.207	2.31 ± 0.53
Bovine (n = 10)	0.396 ± 0.023	0.894 ± 0.293	0.426 ± 0.197	0.94 ± 0.17
Dog (n = 6)	0.300 ± 0.075	0.603 ± 0.237	0.774 ± 0.563	0.58 ± 0.20
Monkey (n = 6)	0.236 ± 0.044	0.778 ± 0.176	4.187 ± 1.545	0.57 ± 0.12
Rabbit (n = 6)	0.337 ± 0.092	0.537 ± 0.258	1.806 ± 1.049	0.25 ± 0.06
Medial condyle	ν_s	H_A	k ($m^4/N \cdot s$) $\times 10^{15}$	h (mm)
Human (n = 6)	0.074 ± 0.084	0.588 ± 0.114	1.137 ± 0.160	2.21 ± 0.59
Bovine (n = 10)	0.383 ± 0.047	0.899 ± 0.427	0.455 ± 0.332	1.19 ± 0.24
Dog (n = 5)	0.372 ± 0.050	0.904 ± 0.218	0.804 ± 0.776	0.90 ± 0.15
Monkey (n = 6)	0.236 ± 0.055	0.815 ± 0.180	2.442 ± 1.129	0.72 ± 0.09
Rabbit (n = 6)	0.197 ± 0.094	0.741 ± 0.101	2.019 ± 1.621	0.41 ± 0.10
Patellar groove	ν_s	H_A	k ($m^4/N \cdot s$) $\times 10^{15}$	h (mm)
Human (n = 4)	0.000 ± 0.000	0.530 ± 0.094	2.173 ± 0.730	3.57 ± 1.12
Bovine (n = 10)	0.245 ± 0.065	0.472 ± 0.147	1.422 ± 0.580	1.38 ± 0.19
Dog (n = 6)	0.093 ± 0.067	0.555 ± 0.144	0.927 ± 0.844	0.52 ± 0.12
Monkey (n = 6)	0.197 ± 0.123	0.522 ± 0.159	4.737 ± 2.289	0.41 ± 0.05
Rabbit (n = 6)	0.206 ± 0.126	0.516 ± 0.202	3.842 ± 3.260	0.20 ± 0.04

ν_s, Poisson's ratio; H_A, aggregate modulus; k, permeability; h, tissue thickness at the test site. Numbers indicate mean ± SD.

were any variations in the mechanical properties because of the two variables, location and species. The purpose of the ANOVA tests is to indicate whether any significant differences exist without specifying the exact combination that is statistically different from the others. Using the rank-transformed data in parametric ANOVA tests is tantamount to an approximation of the Kruskal-Wallis ANOVA test in nonparametric statistics.

A Newman-Keuls multiple comparisons test of the means was then performed for an intraspecies analysis with location as the statistical parameter. The mean square error was obtained from the ANOVA test results, and the significance level was chosen to be 0.05. The mean values for the test sites are listed in ascending order in Table 2.

Similarly, a second series of one-way ANOVA tests was performed to determine how species affects the material properties of articular cartilage. This time the material properties were compiled for analysis in three tables representing the three test sites. The ANOVA test indicated that at p = 0.05, ν_s, k, and h for all three test sites do not come from populations with equal means. At the same significance level, the values of H_A for the three sites do not differ significantly from species to species. As

TABLE 2. *Results of the Student-Newman-Keuls multiple comparisons analysis (location as statistical parameter for comparison, p = 0.05)*

Species	ν_s	H_A	k	h
Human	PaG MC LC	PaG MC LC	MC LC PaG	MC LC PaG
Bovine	PaG MC LC	PaG LC MC	LC MC PaG	LC MC PaG
Greyound dog	PaG LC MC	PaG LC MC	LC MC PaG	PaG LC MC
Cynomolgus monkey	PaG MC LC	PaG LC MC	MC LC PaG	PaG LC MC
New Zealand rabbit	MC PaG LC	PaG LC MC	LC MC PaG	PaG LC MC

All material parameters are in ascending order. PaG, anterior patellar groove; MC, posterior medial femoral condyle; LC, anterior lateral femoral condyle. A common underline indicates results with no statistical difference at p = 0.05.

before, the Student-Newman-Keuls test was used to pinpoint the source of variation. The results for the Newman-Keuls tests are given in Table 3.

DISCUSSION AND CONCLUSIONS

The differences in the rates of creep and recovery (Fig. 4) can be explained in terms of the permeability of the tissue or the effects of tare load. When the test load is removed at the beginning of recovery, the tissue is compacted and its permeability is lower; therefore, the rate of deformation is smaller. As the tissue swells through fluid imbibition, both its permeability and rate of deformation increase. A more rigorous model of this phenomenon can be developed incorporating the nonlinear strain-dependent permeability function into the linear biphasic indentation solution (18,26). Another possible mechanism is that the applied tare load may "collapse" the superficial zone and reduce fluid imbibition; as a result the rate of recovery of articular cartilage is significantly decreased (40).

Analysis of the results indicates that major differences exist in the material properties of articular cartilage among species and, furthermore, in different locations within the same joint. To understand the significance of these species differences, it is necessary to appreciate previous work clarifying the relationships between the structure and function of articular cartilage.

High- and Low-Weight-Bearing Articular Cartilage

Our analysis shows that the aggregate modulus is always lower at the patellar groove site for all species tested in this investigation. This site was specifically chosen to represent a low-weight-bearing or intermittent loading region. Low-weight-bearing areas have a higher collagen content and lower PG content, and high-weight-bearing areas have a higher PG content and lower collagen content (9,17,19,32). Furthermore, other studies showed that a high PG content suggests a high compressive modulus (1,11,16). Thus, a low-weight-bearing area is expected to have a compressive modulus that is smaller than that of a high-weight region. Our results, therefore, support our initial assumption that the anterior trochlear groove is a low or intermittent load-bearing region.

All species, except humans, exhibit the highest H_A in articular cartilage from the central posterior region of the medial condyle; the highest modulus of human knee joints is in the central anterior lateral condyle. These results corroborate the idea that these test sites are indeed in the high-weight-bearing regions.

Relation Between Thickness and Compressive Aggregate Modulus

It is usually believed that articular cartilage thickness appears to be related to the compressive stress borne by the joint surface. However, Simon showed that static compressive stresses on joint cartilage are not related to the thickness of the tissue (35,36). Thin cartilage may be indicative of congruent joints, whereas thicker cartilage is needed to distribute high local stresses in incongruent joints. In a later study on canine joints, Simon and co-

TABLE 3. *Student-Newman-Keuls multiple comparisons analysis (species as parameter, p = 0.05)*

Test site	ν_s	H_A	k	h
Lateral condyle	H M D R B	R D H M B	B D H R M	R M D B H
Medial condyle	H R M D B	H R M B D	B D H R M	R M D B H
Patellar groove	H D M R B	B R M H D	D B H R M	R M D B H

All material parameters are in ascending order. H, human; B, bovine; M, cynomolgus monkey; D, greyhound dog; R, New Zealand rabbit. A common underline indicates results with no statistical difference at p = 0.05.

workers proposed a quantitative measure of congruence and showed that cartilage thickness is linearly proportional to incongruency (37). For example, they showed that the congruence ratio of the tibiofemoral joint with menisci included is 92.5%, whereas that of the patellofemoral joint is only 47.2%. Akizuki and co-workers obtained the material properties of human tibial plateau cartilage and concluded that there is no correlation between thickness and aggregate modulus (1). In addition, these investigators observed that cartilage is thicker in the exposed regions not covered by menisci.

In the present study (Table 1), no correlation between aggregate modulus and thickness is observed, in agreement with the work of Simon (35,36) and Akizuki and associates (1). It is of interest to note, however, that there appears to be a repeating pattern in some of the thickness results. If a comparison is made between the test sites in the lateral and medial condyles (Table 1), it can be seen that a larger aggregate modulus corresponds to a higher thickness. This pattern may indicate differences in the functional requirements of the two condylar surfaces.

Interspecies Comparison of Stiffness

A statistical analysis showed that the values of H_A are not significantly different among the tested species when location is the parameter. For example, Fig. 6 depicts that the compressive modulus in the patellar groove does not differ ($p = 0.05$) from species to species. This is not a surprising finding if physiologic compressive stresses are considered to modulate the compressive modulus of the tissue. For example, Simon indicated that static compressive stresses on the articular cartilage of various animals are relatively constant despite the great range of body weight (1:12,000) (35,36).

Congruence and Material Properties

The permeability (k) of articular cartilage in the patellar groove is consistently the highest within the knee joint of all species tested (Table 1) and varies from species to species (Fig. 7). Similarly, the Poisson's ratio (ν_s) in the groove is the lowest in all species, except the rabbit (Table 1), and exhibits interspecies variations (Fig. 8). A small ν_s indicates higher apparent compressibility of the tissue, hence a propensity for more fluid transport, whereas large k indicates greater ease of fluid movement through the solid matrix. Hence, in the patellar groove under compression, these material properties allow greater and faster cartilage compression because greater amounts of interstitial fluid can move through cartilage with greater ease.

Our findings of small ν_s and large k in the patellar groove suggest a different functional requirement for this tissue in terms of congruence. An incongruent joint may require large amounts of fluid exudation to achieve a fast stress distribution under the applied load. A combination of low ν_s and high k means rapid fluid transport under the applied load, which is conducive to greater stress relaxation and better distribution of applied load. This mechanism may provide a better lubrication condition at the patellofemoral joint (28). These results are in agreement with our observations from anatomic dissec-

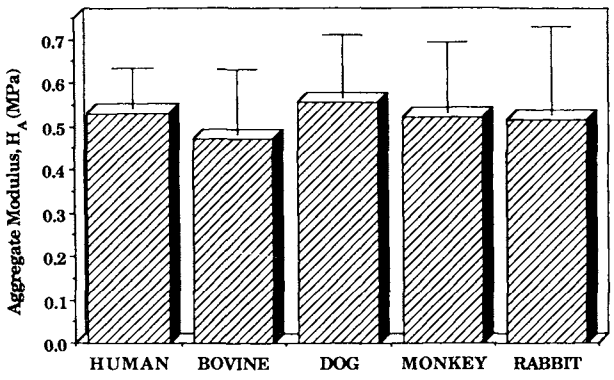

FIG. 6. Species variations of aggregate modulus in the patellar groove. Compressive stiffness does not differ ($p = 0.05$) from species to species.

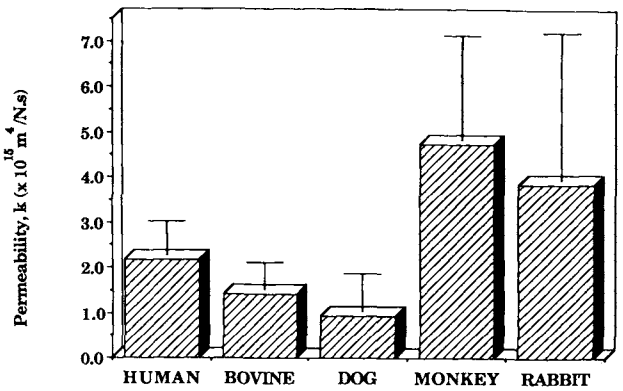

FIG. 7. Species variations of permeability in the patellar groove. The values for humans, bovines, and dogs are significantly different from those for monkeys and rabbits ($p = 0.05$).

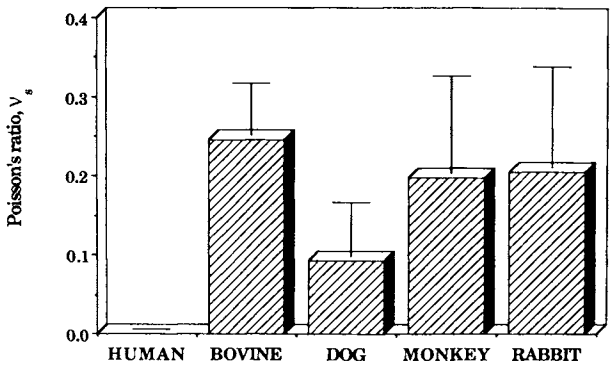

FIG. 8. Species variations of Poisson's ratio in the patellar groove. See Table 3 for statistical significance.

tions, which suggest that overall congruence of the articulation at the lateral and medial femoral condyles is greater than that of the patellar groove for all species, except rabbits.

PG–Collagen Interactions and Poisson's Ratio

In the tissue, the GAG macromolecules interact with collagen to form a strong, cohesive, solid matrix. These interactions may be electrostatic forces between negative charges on the polysaccharide and positive charges on the collagen (21). For example, it is suggested that electrostatic interactions occur between collagen and chondroitin 4-sulfate (31). Obrink and Wasteson found that binding of these macromolecules increases with decreasing pH and ionic strength (31). Obrink reported that these interactions are electrostatic in nature and are abolished with increasing ionic strength (30). Keratan sulfate apparently does not bind to collagen (30). It was concluded that interactions seem to increase with increasing chain length of the polysaccharide and with increasing charge density. Mitchell and Shepard performed morphological examinations of thin tissue sections and produced evidence that PG macromolecules surround and may be attached to collagen fibrils (24). Scott, in studies on rat tail tendon, showed that filamentous PG material is arranged in a regular array around fibrils (33). As Muir proposed, the large PG aggregates are immobilized within the collagen network, enhancing the structural rigidity of the matrix (29). More recently, Hunziker and Schenk developed a procedure of "high pressure freezing, freeze substitution, and low temperature embedding" for preserving the extracellular matrix of epiphyseal cartilage in a state believed to be resembling that of native tissue (14). They observed many contact sites between PGs and collagen fibrils. These points of contact were defined strictly on a structural basis.

As indicated earlier, some mechanical material properties are correlated closely with the biochemical composition and structure of the tissue. For example, the GAG content is directly related to the compressive stiffness. However, the Poisson's ratio, which has a tremendous effect on the creep behavior of articular cartilage, has not been shown to have any correlation with biochemical composition. It is reasonable to hypothesize then, that ν_s depends on the density and strength of the interactions between the PGs and collagen fibers of the solid matrix. A lower ν_s may indicate a weaker PG–collagen interaction and, therefore, a greater apparent compressibility and propensity for fluid flow. Such an interaction may depend on the ratio of keratan sulfate-rich to chondroitin sulfate-rich PGs; the proportions of PGs present as aggregates, and the hydrodynamic size of PGs. Functionally, a tissue with low ν_s exhibits characteristic prolonged creep phenomena, whereas the deformation curve for tissue with $\nu_s \rightarrow 0.5$ reaches equilibrium instantaneously; in such cases, creep does not exist (18,26). A high ν_s means that the solid matrix is loaded quickly without sufficient time for the solid/fluid interactions to occur.

This study shows that despite their superficial similarity, human and animal articular cartilage differ significantly in their material properties. This observation requires further work to validate our hypothesis that, although biochemical composition determines cartilage aggregate modulus and permeability, the number density and strength of PG–collagen interactions determine the Poisson's ratio. How, for example, the density and strength of PG–collagen interactions determine ν_s needs further investigations. Finally, we conclude that if the in situ compressive equilibrium modulus of human knee cartilage needs to be studied, any of the animal models studied in this investigation will suffice. However, if, for example, the Poisson's ratio is to be studied in the anterior patellar groove, then the most appropriate tissue is canine. Thus, care must be exercised to consider the potential differences between human and animal articular cartilage in the development of experimental animal models of cartilage disease or injury.

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REFERENCES

1. Akizuki SA, Mow VC, Lai WM, Pita J, Howell DS: Topographical variations of the biphasic indentation properties of human tibial plateau cartilage. *Trans Orthop Res Soc* 11:406, 1986
2. Akizuki S, Mow VC, Muller F, Pita JC, Howell DS: Tensile properties of human knee joint cartilage: II. Correlations between weight bearing and tissue pathology and the kinetics of swelling. *J Orthop Res* 5:173–186, 1987
3. Akizuki S, Mow VC, Muller F, Pita JC, Howell DS, Manicourt DH: Tensile properties of human knee joint cartilage: I. Influence of ionic conditions, weight, and fibrillation on the tensile modulus. *J Orthop Res* 4:379–392, 1986
4. Altman RD, Tenenbaum J, Latta L, Riskin W, Blanco LN, Howell D: Biomechanical and biochemical properties of dog cartilage in experimentally induced osteoarthritis. *Ann Rheum Dis* 43:83–90, 1984
5. Armstrong CG, Mow VC: Variations in the intrinsic mechanical properties of human articular cartilage with age, degeneration, and water content. *J Bone Joint Surg [Am]* 64:88–94, 1982
6. Askew MJ, Mow VC: The biomechanical function of the collagen ultrastructure of articular cartilage. *J Biomech Eng* 100:105–115, 1978
7. Brown TD, Shaw DT: In vitro contact stress distribution on the femoral condyles. *J Biomech* 2:190–199, 1984
8. Buckwalter JA, Pedrini-Mille A, Dobrowolski AM, Olmstead M, Grood E: Differences in the articular cartilage matrices of humans, monkeys and rabbits. *Trans Orthop Res Soc* 14:155, 1989
9. Caterson B, Lowther DA: Change in the metabolism of proteoglycans from sheep articular cartilage in response to mechanical stress. *Biochim Biophys Acta* 540:412–422, 1978
10. Emery IH, Meachim G: Surface morphology and topography of patello-femoral cartilage fibrillation in Liverpool necropsies. *J Anat* 116:103–120, 1973
11. Hirsch C: The pathogenesis of chondromalacia of the patella. *Acta Chir Scand [Suppl]* 83:1–106, 1944
12. Hoch DH, Grodzinsky AJ, Koob TJ, Albert ML, Eyre DR: Early changes in material properties of rabbit articular cartilage after meniscectomy. *J Orthop Res* 1:4–12, 1983
13. Hori RY, Mockros LF: Indentation tests of human articular cartilage. *J Biomech* 9:259–268, 1976
14. Hunziker EB, Schenk RK: Cartilage ultrastructure after high pressure freezing, freeze substitution, and low temperature embedding. II. Intercellular matrix ultrastructure—preservation of proteoglycans in their native state. *J Cell Biol* 98:277–282, 1984
15. Jurvelin J, Saamanen AM, Arokoski J, Helminen HJ, Kiviranta I, Tammi M: Biomechanical properties of the canine knee articular cartilage as related to matrix proteoglycans and collagen. *Eng Med* 17:157–162, 1988
16. Kempson GE, Muir H, Freeman MAR, Swanson SAV: Correlations between the compressive stiffness and chemical constituents of human articular cartilage. *Biochim Biophys Acta* 215:70, 1970
17. Kiviranta I, Jurvelin J, Tammi M, Saamanen AM, Helminen HJ: Weight bearing controls glycosaminoglycan concentration and articular cartilage thickness in the knee joints of young beagle dogs. *Arthritis Rheum* 30:801–809, 1987
18. Mak AF, Lai WM, Mow VC: Biphasic indentation of articular cartilage—I. Theoretical solution. *J Biomech* 20:703–714, 1987
19. Manicourt DH, Pita JC: Progressive depletion of hyaluronic acid in early experimental osteoarthritis in dogs. *Arthritis Rheum* 31:538–544, 1988
20. Maroudas A: The permeability of articular cartilage. *J Bone Joint Surg [Br]* 50B:166–177, 1968
21. Mathews MB: The interaction of collagen and acid mucopolysaccharides. *Biochem J* 96:710–716, 1965
22. McDevitt C, Gilbertson E, Muir H: An experimental model of osteoarthritis; early morphological and biochemical changes. *J Bone Joint Surg [Br]* 59:24–35, 1977
23. McDevitt C, Muir H: Biochemical changes in the cartilage of the knee in experimental and natural osteoarthritis in the dog. *J Bone Joint Surg [Br]* 58:94–101, 1976
24. Mitchell N, Shepard N: Changes in proteoglycan and collagen in cartilage in rheumatoid arthritis: A study by light and electron microscopy. *J Bone Joint Surg [Am]* 60:349–354, 1978
25. Moskowitz RW, Howell DS, Goldberg VM, Muniz O, Pita JC: Cartilage proteoglycan alterations in an experimentally induced model of rabbit osteoarthritis. *Arthritis Rheum* 22:155–163, 1979
26. Mow VC, Gibbs MC, Lai WM, Zhu WB, Athanasiou KA: Biphasic indentation of articular cartilage—II. A numerical algorithm and an experimental study. *J Biomech* 22:853–861, 1989
27. Mow VC, Kuei SC, Lai WM, Armstrong CG: Biphasic creep and stress relaxation of articular cartilage in compression: Theory and experiments. *J Biomech Eng* 102:73–84, 1980
28. Mow VC, Mak AF: Lubrication of diarthrodial joints. In: *Handbook of Bioengineering*, ed by R Skalak, S Chien, New York, McGraw-Hill, 1987, pp 5.1–5.34
29. Muir H: Proteoglycans as organizers of the extracellular matrix. *Biochem Soc Trans* 11:613–622, 1983
30. Obrink B: A study of the interactions between monomeric tropocollagen and glycosaminoglycans. *Eur J Biochem* 33:387–400, 1973
31. Obrink B, Wasteson A: Nature of the interaction of chrondroitin 4-sulphate and chondroitin sulphate-proteoglycan with collagen. *Biochem J* 121:227–233, 1971
32. Palmoski MJ, Brandt KD: Running inhibits the reversal of atropic changes in canine knee cartilage after removal of leg cast. *Arthritis Rheum* 24:1329–1337, 1981
33. Scott JE: Collagen–proteoglycan interactions: Localization of proteoglycans in tendon by electron microscopy. *Biochem J* 187:887–891, 1980
34. Seedholm BB, Takeda T, Tsubuku M, Wright V: Mechanical factors and patellofemoral osteoarthrosis. *Ann Rheum Dis* 38:307–316, 1979
35. Simon WH: Scale effects in animal joints I. Articular cartilage thickness and compressive stress. *Arthritis Rheum* 13:244–256, 1970
36. Simon WH: Scale effects in animal joints II. Thickness and elasticity in the deformability of articular cartilage. *Arthritis Rheum* 14:493–502, 1971
37. Simon WH, Friedenberg S, Richardson S: Joint congruence. A correlation of joint congruence and thickness of articular cartilage in dogs. *J Bone Joint Surg [Am]* 55:1614–1620, 1973
38. Sokoloff L: Elasticity of aging cartilage. *Proc Fed Am Soc Exp Biol* 25:1089–1095, 1966
39. Torzilli PA: Influence of cartilage deformation on its equilibrium water partition. *J Orthop Res* 3:473–483, 1985
40. Torzilli PA: Effect of articular surface compression on cartilage deformation. *Trans Orthop Res Soc* 15:151, 1990
41. Venn MF, Maroudas A: Chemical composition and swelling of normal and osteoarthrotic femoral head cartilage. I: Chemical composition. *Ann Rheum Dis* 36:399–406, 1977