Corroboration of *in vivo* cartilage pressures with implications for synovial joint tribology and osteoarthritis causation

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Pressures on normal human acetabular cartilage have been collected from two implanted instrumented femoral head hemiprostheses. Despite significant differences in subjects' gender, morphology, mobility, and coordination, *in vivo* pressure measurements from both subjects covered similar ranges, with maximums of 5–6 MPa in gait, and as high as 18 MPa in other movements. Normalized for subject weight and height (nMPa), for free-speed walking the maximum pressure values were 25.2 for the female subject and 24.5 for the male subject. The overall maximum nMPa values were 76.2 for the female subject during rising from a chair at 11 months postoperative and 82.3 for the male subject while descending steps at 9 months postoperative. These unique *in vivo* data are consistent with corresponding cadaver experiments and model analyses. The collective results, *in vitro* data, model studies, and now corroborating *in vivo* data support the self-pressurizing "weeping" theory of synovial joint lubrication and provide unique information to evaluate the influence of *in vivo* pressure regimes on osteoarthritis causation and the efficacy of augmentations to, and substitutions for, natural cartilage.

Osteoarthritis, manifested by cartilage degradation in the major load-bearing joints of the human, is prevalent, debilitating, and costly, affecting over 40 million Americans (1). The etiology of this disease is unknown (2, 3). To quote from the web page of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (3): "The mechanisms responsible for cartilage destruction, however, are not well understood. Current therapeutic modalities provide marginal symptomatic relief and with few exceptions have no effect on the preservation of cartilage or on disease progression."

A decade or more likely passes before cartilage has fissured to the point where bone contact instigates pain, the clinical sign of arthritis. That mechanical factors may contribute to the initiation or progression of cartilage destruction (4, 5) is suggested both by the high loads the joints support and the absence in cartilage of the usual mediators of physiological communication: the tissue is avascular as well as aneural. Again quoting from the web page of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (3): "Mechanical load across joints is critically important for the maintenance of cartilage, and abnormal mechanical loading of joints can lead to pathological conditions."

Thus, cartilage cells (chondrocytes) appear to depend on the mechanical environment to control their function as well as to transport nutrients and metabolites (6–9). The pressures on and in cartilage are the manifestation of the applied load in the environment of the cartilage matrix. Pressure and pressure–time cycling thus appear to be "critically important for the maintenance of cartilage" (3). As a result, the pressure cartilage experiences appears central to the etiology of osteoarthritis, acting either directly, e.g., collagen fiber rupture, or through mechanical/biological coupling, e.g., the influence of the mechanical microenvironment on chondrocyte metabolism. Thus, it is surprising that our project has produced, to our knowledge, the

only experimental *in vivo* mammalian pressures, and these in humans.

Pressure distribution information is also a crucial element in scientific characterization of how, in healthy cartilage, the mechanical and biological properties of cartilage, bone, and synovial fluid synergize locally and globally to achieve high-load-capacity, low-friction, long-wearing skeletal bearings. Normal synovial joints exhibit very little friction (measured coefficients of friction *in vitro* for whole joints range from 0.002 to 0.02), with modest gliding speeds as in gait (0.0–0.3 m/s), even when subjected to high loading; five times body weight has been measured across the human hip joint (10).** To explain this remarkable tribology the mechanisms of human-engineered bearings (hydrodynamic, elastohydrodynamic, boundary, and squeeze-film lubrication) have been invoked, as well as other hypotheses ("weeping" and "boosted"). Over two dozen theories for the extraordinary performance of synovial joints have been proposed (11); however, "although numerous theories have been put forth to attempt to explain joint lubrication, the mechanisms involved are still far from being understood" (12).

Thus, quantifying cartilage pressures and pressure distributions, in actual joints *in vivo* during routine daily activities, appears to be central both to elucidate the pressure regimes that cartilage and its biological components experience and to define the lubrication mechanism of synovial joints. Addressing the *global* synovial joint, uniquely shaped as it has been by evolution and ontogeny, loaded and moving as it does in life, has been the overriding aspect of our research program from its outset.

By contrast, virtually all other cartilage researchers focus their study on small samples of cartilage, excised from joints with or without bone, under uniaxial load with permeable or impermeable platen and/or perimeter restraints (see, for example, ref. 13). This approach poses uncertainties both analytically and experimentally as to the actual boundary conditions on the loaded surfaces and at the perimeter of the sample. The imposed loading and restraint conditions are not those experienced by cartilage in the global joint, either *in vivo* or *in vitro*.

To pursue our "whole joint" approach, we first had to determine whether acquiring *in vivo* pressure data was feasible. We demonstrated a design incorporating pressure transducers and telemetry, based on the standard hemi- or endoprosthesis routinely implanted to replace the defective femoral head (14). Otherwise identical to the standard implant in function and

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**Measured with a force-instrumented total artificial hip joint as compared with the pressure-instrumented partial-joint-replacement prostheses used in this study of cartilage.

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biocompatibility, the instrumented femoral head would bear against the natural cartilage of the acetabulum.

Experiments were conducted on cadaver acetabula to assure future patient safety in the absence of any cartilage pressure data and to establish the calibration range for the transducers. A pseudo hemiprostheses with similar pressure instrumentation, but hard wired, was installed in a custom-designed hip-joint simulator. Theoretical load vectors for human gait, taken from the literature, were applied to acetabula cartilage. These experiments produced direct measurements of local pressures and pressure distribution on cartilage in a synovial joint (15). With the feasibility and safety of the pressure data collection method demonstrated, the research focus shifted to evaluation of the hip-joint environment *in vivo*.

Whereas the nonuniform pressure distributions from our first human subject (16–18) were similar to those measured *in vitro*, the magnitudes of *in vivo* cartilage pressure were considerably higher than the *in vitro* pressure magnitudes. One possibility was that the literature values for forces at the human hip were low. Thus, confirmation of our *de novo in vivo* data required further *in vivo* study. Herein we present pressure data from our second subject, of different gender, morphology, and coordination than our first subject, and compare data from both subjects performing similar activities.

Methods

For both subjects the contact pressures on acetabular cartilage were measured by instrumented endoprostheses (14, 19).^{††} The implants are fabricated of the same cobalt chromium alloy and employ the same geometry as standard endoprostheses of which over 200,000 are implanted annually in the United States (20). The upper hemisphere of the pseudo femoral head, which contacts acetabular cartilage, encloses 14 pressure transducers for the first implant and 13 for the second. Fig. 1 *A* and *B* shows the respective locations of transducers.^{‡‡} The diaphragm of each transducer is integral with the spherical surface of the head and is connected to a silicon cantilever-beam on which is fused a four-arm strain gauge sensor, for an overall sensitivity of 0.28 μm of deflection per MPa applied to the diaphragm. Inside the hermetically sealed head, electronic circuits sequentially sample the transducer outputs and multiplex a frame of 14 pressures at 250 Hz for the first subject and 13 pressures and temperature at 500 Hz for the second subject, transmitted as a radio-telemetry signal in the FM band at 100 MHz. An antenna at the distal end of the stem serves to transmit the data and as a power-receiving antenna from an external 100-kHz source, which is an induction coil garter worn around the thigh during data acquisition.

Our first subject was a 73-year-old female, 1.68 m in height (H) and of body weight (BW) 663 N, with excellent coordination of movement. She fractured her right femoral neck. Our second subject was an 82-year-old male, 1.6 m in H and of BW 565 N, with coordination difficulties. He experienced a left neck fracture. The Institutional Review Board of the Massachusetts Institute of Technology approved the prostheses, and the Institutional Review Board of the Massachusetts General Hospital approved the surgical procedure. Both subjects gave informed consent. By using a gauge to measure the excised natural femoral heads (21), both subjects were implanted with instrumented endoprostheses with 47.5-mm-

Fig. 1. Locations of pressure transducers on pseudo femoral heads of hemiprostheses. (*A* and *B*) Views along the axis of the head through transducer 1. *A* is the implant in the first subject, and *B* is the implant in the second subject. (*C*) Location of central transducer 1.

diameter heads.^{§§} Both subjects' acetabular cartilage was deemed normal by radiographs and, during surgery, by visual observation.

At the Biomotion Laboratory of the Massachusetts General Hospital, pressure data transmission was synchronized with the 3D kinematics of the subject's pelvis, thigh, shank, and foot segments. These data were acquired electro-optically by employing our system called TRACK (22, 23) from arrays of light-emitting diodes (see Fig. 2). Foot-floor forces were measured from two force plates. Because the transducers are in the pseudo femoral head, but we are interested in the locations of the pressure readings on acetabular cartilage on the pelvis, coordinate transformations were performed serially. First a prosthesis coordinate frame fixed the transducer locations with respect to the pseudo femoral head (see Figs. 1 *A* and *B*). Then that frame was referenced to the prosthesis intermedullary stem (see Fig. 1*C*). From surgical and x-ray information the stem coordinate frame was referenced to the femur. TRACK kinematic data provided the relationship between the femur and the pelvis, with

^{††}For illustrations of the pressure-instrumented pseudo femoral head hemisphere, electronics package, and antenna at the end of the intermedullary stem, see figure 1 of ref. 16; and for a frontal plane x-ray of the pelvis–thigh region of the first subject, see figure 2 of ref. 16.

^{‡‡}After experience with a symmetrical location of the transducers on the first implant, transducer locations were slightly changed, and one transducer cavity (T) was used for a temperature sensor.

^{§§}Postmortem measurement of the respective excised pelvis showed that the female's endoprosthesis was 0.6 mm oversized, whereas the male's was 0.7 mm undersized, both within the 1-mm-diameter increment available in commercial endoprostheses.

Fig. 2. Female subject showing garter around right thigh over hip-implanted instrumented-endoprosthesis for powering prosthesis and receiving PAM-FM signal from prosthesis. Light-emitting diode arrays for TRACK kinematic acquisition are attached to the foot, shank, thigh, and pelvis. The cane is also force-instrumented. (Reproduced from ref. 59.)

a final relationship between the pelvis and acetabular coordinates based on x-ray information.

Extensive pressure data were acquired during both subjects' rehabilitation (24–26) and then every several months until their natural demise, 5 years for the female subject and 3 years for the male. Protocols included various exercises, e.g., isometric abduction of the hip muscles, natural or “free-speed” walking, paced walking, negotiating stairs, rising from chairs, and single-leg standing. Here we report representative samples from the extensive data from both subject's prostheses. For details on procedures, see ref. 27; for complete data sets for both subjects, see ref. 28.

Results

The movement studied most extensively was walking, an activity performed routinely during the daily life of each subject, for which kinematic and kinetic data (but not cartilage pressure) are in the literature for comparison. In free-speed gait, the subject was instructed to walk as he or she normally would and to look ahead (rather than down at the ground). Despite significant differences in their morphology and mobility, the maximum pressures from the two subjects during the load bearing, or stance, phase of normal walking was in the 5- to 6-MPa range. Fig. 3 is a plot of the magnitudes of local pressure from all

Fig. 3. Pressure (MPa) measured at transducers in femoral head versus time for the male subject in free-speed gait at 12 months postoperative.

transducers versus time for the male subject during free-speed walking at 12 months postoperative.

The regional pressures on acetabular cartilage for free-speed walking are presented in Fig. 4A for the female at 11 months postoperative, where the maximum pressure was 6.1 MPa, and in Fig. 4B for the male at 1 year postoperative, which shows a maximum pressure of 5.4 MPa. The display of Fig. 4 does not explicitly present temporal information but uses, for the test reported, subject kinematic data to present the locations on acetabular cartilage of pressure measurements from the transducers on the femoral head. The view is into the right hip socket (the male's data are rotated to the right hip) with the subject's anterior toward the right side of the plot. The acetabular cartilage in the socket is regionalized into bins with color-coding

Fig. 4. Maximum pressures in regions of acetabulum. (A and B) Data for free-speed gait. A shows data from the female subject at 11 months postoperative. B shows data from the male subject at 12 months postoperative. (C) Data for the female subject rising from a chair, 11 months postoperative. (D) Data for the male subject descending steps, 12 months postoperative. The views are into the right hip socket (the male's data are rotated to the right hip) with the subject's anterior toward the right side of each plot.

of the maximum pressure recorded in each bin. Regions in which no measurements were made are left blank.

The highest pressures were measured during different activities for the two subjects but were of comparable magnitudes. The maximum pressure measurements occurred during activities undertaken less frequently than walking, rising from a chair and descending stairs. The difference in which activity produced the highest pressures reflects the differing capabilities of the two subjects. In particular, the coordination and balance problems experienced by the second subject were problematic when traversing stairs. In addition, the protocol for rising from a chair was more detailed during tests with the second subject, resulting in different kinematics. However, the most important point is that the overall maximum pressures were of similar magnitude for the two subjects. This was a critical finding because the maximum pressure measurements were surprisingly high.

Data were taken for rising from different height chairs: the lower the chair height, the higher the local pressures. The highest pressure recorded from the female subject, 18 MPa at 11 months postoperative, was while rising from a chair 80% of knee height. Fig. 4C gives the regional maximum pressures for this test for the female subject. In this display, the acetabular surface has been rotated to show the regions of high pressure more clearly. For the male subject, the maximum pressures when rising from a chair were much lower and positioned more anteriorly than were the high pressures for the female subject. However, in stair descent the male subject generally generated higher pressures than did the female, possibly because of balance difficulties since the kinematic data show greater variation and higher frequency components in joint angle measurements. Fig. 4D shows his regional maximum pressures during stair descent with a maximum value of 15.5 MPa. A maximum pressure measurement of 18.2 MPa was made during a similar stair descent test at 9 months postoperative; however, those data could not be displayed in this format because of the absence of synchronized kinematic data.

As mentioned earlier the two subjects had acetabula similar enough to require the same size prosthesis, but the individuals were otherwise quite different morphologically. To account for the different height and weight of each subject the pressure data were normalized and made nondimensional over a range of 0–100 by this equation:

$$yn_i = \frac{y_i}{1,000.0 \left[\frac{BW}{H^2} \right]} \text{ with BW in N and H in mm.}$$

The maximum normalized pressure values (nMPa) for free-speed walking were 25.2 for the female subject at 6 months postoperative and 24.5 for the male subject at 12 months postoperative. The overall maximum nMPa values were 76.2 for the female subject during rising from a chair at 11 months postoperative and 82.3 for the male subject while descending steps at 9 months postoperative.

Discussion

The close correspondence of pressures measured in both subjects is reassuring, especially considering the physical differences between the two subjects. The highest pressures, during chair rise for the woman and during stair descent for the man, and even the 5- to 6-MPa pressures recorded in walking were much higher than our *in vitro* pressure measurements, we believe because of the experienced *in vivo* forces at the hip being higher than those analyzed in the literature. Co-contraction of the musculature about the hip to stabilize the joint by increasing joint stiffness or impedance (29) is likely the source of the higher hip forces. Balanced co-contraction components of forces from opposing muscles, while adding to joint force (and therefore pressures), produce no torque and therefore

no rotation about the joint. As a result, joint force vectors calculated from kinetic and kinematic data using inverse Newtonian analysis as reported in the literature cannot detect the co-contraction components of joint force. The presence of significant co-contraction forces about the hip, even in normal walking, was demonstrated in a study employing acetabular pressure data from the male subject (30). The location of highest pressure on the acetabulum did not correspond, at the same time in the gait cycle, with the location of the force vector at the hip. To measure hip joint force *in vivo* we have in preparation hemiprotheses similar to those used in the study herein but instrumented to measure the components of hip force. Hemiprotheses do not alter the natural femoral head-acetabulum geometry and musculature as do total joint replacement prostheses, where hip-joint geometry and musculature are deliberately altered surgically, as in the case of the instrumented total joint (10).

Whereas the *in vitro* absolute values are lower, as explained above, the nonuniform pressure distributions *in vivo* are similar to those measured *in vitro*. This finding is relevant to characterizing the tribology of the synovial joint, in particular resolving whether, upon loading a synovial joint, interstitial fluid in the cartilage matrix is expressed from the matrix into the interarticular gap, proposed as “weeping” lubrication by McCutchen (31), or from the loaded gap into the matrix, “boosted” lubrication, as proposed by Dowson (32). The *in vivo* local pressures at transducers <10 mm apart vary by megapascals, consistent with our *in vitro* pressure data (15) and therefore our *in vitro* geometric studies of cartilage are germane.

Ultrasonic geometric studies of both components of the same natural hip joint show that the mating surfaces of unloaded acetabular and femoral head cartilage layers are sectors of spheres (33, 34) of virtually the same diameter (35) on which are superimposed undulations of $\approx 75\text{-}\mu\text{m}$ root mean square above and below the mean surface, with wavelengths of millimeter scale. These small variations from sphericity influence the sealing process as Kenyon (36) had shown in an analytic model for surface flow in cartilage. When loaded, the higher ridges contact first, and their patterns of contact comprise the seals, with the resulting valleys forming the passages, accounting for the nonuniform pressure distributions seen both *in vitro* and *in vivo*. Thus, our *in vitro* and *in vivo* pressure data, exhibiting high local maxima, irregular and idiosyncratic isobars, and steep pressure gradients, reflect localized sealing throughout the interarticular gap.

An *in vitro* experiment-based analysis (37), corroborated by and consistent with the *in vivo* pressure data reported herein, used a finite-element-model of the acetabulum cartilage layer, quantified by ultrasonic 3D measurements of surface shape and thickness distribution of the *in situ* layer (33) and ultrasonic determination of the permeabilities and moduli of the tissue (38). Two otherwise identical pseudoprotheses, matched to the acetabulum diameter, one with pressure instrumentation, and the other with an ultrasonic transducer to measure cartilage consolidation, were loaded into the acetabulum. The resulting experimental data were applied as boundary conditions for the finite-element-model analysis. The results show interstitial fluid pressurization in the cartilage layer and in the gap (39) with a fluid pressure distribution in the layer that produced flow from the cartilage thickness into loaded areas of the interarticular gap, and thence through the gap to unloaded, low-pressure regions. A dynamic computer simulation of the natural joint in gait, based on experimental geometric and property data from both components of the hip joint, showed osmotically induced flow (imbibitions) into both acetabular and femoral head cartilage layers occurring only during the unloaded swing phase. During the loaded stance phase of gait, pressurized fluid was expressed from the cartilage layers into the interarticular gap (40).

Thus, our corroborated *in vivo* data are consistent with prior *in vitro* pressure and geometric data and our analytic and computer modeling. All address the natural joint, and all support the 1959

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