The Mechanical Behavior of Normal and Osteoporotic Canine Femora before and after Hemiarthroplasty

STEPHEN D. COOK, PH.D.*, HARRY B. SKINNER, M.D., PH.D., **
ALLAN M. WEINSTEIN, PH.D., † CARLOS J. LAVERNIA, M.S., ‡
AND RONALD J. MIDGETT, PH.D.§

It is generally agreed that beyond the age of 40 years, a progressive loss of skeletal mass occurs with increasing age.1,2,10,31 This fact has been extensively documented by measurements of bone density in vivo utilizing various radiographic techniques,1,2,10,31 by the analysis of autopsy material,33 and by the measurement of quantitative histologic parameters on bone biopsies.5,15 An increased incidence of vertebral crush fractures and fractures of the long bones has also been noticed with increasing age beyond the age of 40 years.33,42 This age group also represents the population most likely to require prosthetic joint replacement. However, little information exists on the mechanical behavior of osteoporotic bone and its mechanical interaction with a prosthesis.

Numerous numeric finite element analyses and experimental strain gage studies have been performed to determine the stress and strain distribution in bones before and after the insertion of prosthetic devices.2,6,11,12,29,32,36,37,29 It should be noted that these studies have either assumed elastic properties for normal bone tissue (finite element studies) or utilized experimental animals with no reported evidence of osteoporosis (strain gage studies). Thus, these studies fail to address the following questions: What are the possible consequences of inserting a prosthetic device into an osteoporotic bone? What is the prognosis for the success or failure of this procedure based on an analysis of stress or strains present in the femur?

The elastic properties of normal bone tissue have been studied in detail and summarized in numerous review articles.8,10,15,34 The elastic modulus and strength of bone have been shown by Carter and Hayes8,9 and Wright and Hayes14 to be a function of both the apparent density and strain rate. They reported that the strength of bone is proportional to the square of the apparent den-
sity and that the modulus is proportional to the cube of the apparent density. Reilly et al.\textsuperscript{14,25} have reported that cortical bone exhibits mechanical behavior similar to that of engineering materials, with a linear elastic portion followed by a yield point and non-elastic "plastic" deformation. They further showed that cortical bone is anisotropic, the mean value of the elastic modulus being 50% greater in the longitudinal than in the transverse direction.

Although extensive work has been reported on the characterization of the mechanical response of normal bone tissue, the mechanical response of abnormal tissue, \textit{e.g.}, as osteoporotic bone, has not been as widely reported. The data reported to date have been mostly limited to quantitative histomorphometric studies in which osteoporotic bone has been produced by disuse atrophy.\textsuperscript{20,21,26,27,38,40} However, Burstein et al.\textsuperscript{7} have reported the results of tensile tests on specimens from osteoporotic femora. Their study failed to reveal any consistent differences in material properties, but this may have been the result, in part, of a relatively small sample size. In a recent study, Dickenson et al.\textsuperscript{14} reported the results of mechanical tests on specimens of human cortical bone from normal and osteoporotic patients. The osteoporotic bone was found to be less stiff and exhibited less strength when compared with the normal bone tissue.

Nutritional secondary hyperparathyroidism (NSH) has been described as a generalized metabolic bone disease characterized by osteopenia, which may be induced by a diet too low in calcium and/or too high in phosphorus. Krook et al.\textsuperscript{22-24} when using such a diet, determined that early hypocalcemia was caused by low dietary calcium alone, which induced hyperparathyroidism. Isocalcemia was later established, but only at the expense of progressive bone loss. The skeletal osteoporosis resulting from the dietary imbalance was also shown to be reversible by nutritional means. Hendrikson\textsuperscript{18} reported that dietary hyperparathyroidism in animals induced by a diet containing 0.12% calcium and 1.2% phosphorus resulted in generalized skeletal lesions more accentuated in the jaws, especially in the lamina dura. Belanger et al.\textsuperscript{4} have suggested that in horses, osteocytic osteolysis was the primary cause of bone resorption in NSH. Geiger et al.\textsuperscript{16} examined the influence of NSH on the endosteal surface of the human femur using scanning electron microscopy. They noted crater-like formations on the bone surface, indicating osteoclasia.

The above studies indicate that NSH can be induced in laboratory animals through dietary imbalances of calcium and phosphorus and that it results in an osteoporotic-like condition of the bone. NSH, therefore, provides a potential model for studying the effects of osteoporosis on the mechanical behavior of bone. The effect that osteoporosis, induced by NSH, has on the mechanical response of the canine femur and the influence of a stem-type cemented femoral head replacement on the mechanical response of the osteoporotic canine femur were determined.

**MATERIALS AND METHODS**

Twelve adult 1-1½-year-old male beagles were randomly divided into control (6 animals) and experimental (6 animals) groups. The experimental group was fed a diet containing 1.2% phosphorus and 0.12% calcium. The control group was fed the same diet, except that it contained 0.42% phosphorus and 0.54% calcium. The contents of the respective diets are shown in Table 1. These diets were formulated by and obtained from Teklad Mills, Madison, Wisconsin. This dietary calcium-to-phosphorus ratio was identical to that used in the studies of Hendrikson\textsuperscript{18} and Krook et al.\textsuperscript{22-24} The animals were fed their respective diets for a period of 22 weeks. At ten and 20 weeks, blood samples were obtained from each animal, and the immunoreactive parathyroid hormone (i-PTH) levels were determined by performing radioimmunoassays for the C-terminal fragment with a kit from Immuno Nuclear Corporation, Stillwater, Minnesota.

At 22 weeks, eight animals were killed, and the femora in each dog were removed entirely. Two animals from each group were allowed to continue on their respective diets beyond the 22 weeks and
TABLE 1. Dog Diets Containing 0.54% Calcium and 0.42% Phosphorus (Control), and 0.12% Calcium and 1.2% Phosphorus (Experimental)

<table>
<thead>
<tr>
<th></th>
<th>Control (gm/kg)</th>
<th>Experimental (gm/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casein, high protein</td>
<td>230.0</td>
<td>230.0</td>
</tr>
<tr>
<td>Corn starch</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Sucrose</td>
<td>531.9228</td>
<td>517.8099</td>
</tr>
<tr>
<td>Corn oil</td>
<td>60.0</td>
<td>60.0</td>
</tr>
<tr>
<td>Non-nutritive fiber (cellulose)</td>
<td>20.0</td>
<td>20.0</td>
</tr>
<tr>
<td>Vitamin mix, Teklad (Cat. #0060)</td>
<td>10.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Calcium phosphate, dibasic (CaHPO₄)</td>
<td>9.8258</td>
<td>3.9722</td>
</tr>
<tr>
<td>Calcium carbonate (CaCO₃)</td>
<td>6.1830</td>
<td>—</td>
</tr>
<tr>
<td>Sodium phosphate, dibasic (Na₂HPO₄)</td>
<td>1.6182</td>
<td>12.234</td>
</tr>
<tr>
<td>Potassium phosphate, monobasic (KH₂PO₄)</td>
<td>—</td>
<td>29.8621</td>
</tr>
<tr>
<td>Sodium chloride (NaCl)</td>
<td>11.5884</td>
<td>11.5884</td>
</tr>
<tr>
<td>Potassium chloride (KCl)</td>
<td>1.6583</td>
<td>1.6583</td>
</tr>
<tr>
<td>Potassium bicarbonate (KHCO₃)</td>
<td>14.4184</td>
<td>—</td>
</tr>
<tr>
<td>Magnesium sulfate (MgSO₄)</td>
<td>2.3168</td>
<td>2.3168</td>
</tr>
<tr>
<td>Cupric sulfate (CuSO₄)</td>
<td>0.0211</td>
<td>0.0211</td>
</tr>
<tr>
<td>Potassium iodate (KIO₃)</td>
<td>0.003</td>
<td>0.003</td>
</tr>
<tr>
<td>Ferrous sulfate (FeSO₄·7H₂O)</td>
<td>0.3515</td>
<td>0.3515</td>
</tr>
<tr>
<td>Manganese sulfate (MnSO₄·H₂O)</td>
<td>0.0181</td>
<td>0.0181</td>
</tr>
<tr>
<td>Zinc carbonate (ZnCO₃)</td>
<td>0.1046</td>
<td>0.1046</td>
</tr>
</tbody>
</table>

Data Teklad Mills, Madison, Wisconsin.

are not included in the following analyses. The alveolar process from an area mesial to the first molar and distal to the canine tooth was also removed. Electron dispersive radiographic analysis was performed on wet specimens of the area of bone mesial to the second premolars and distal to the canine to obtain the calcium-to-phosphorus ratios in each group. This area contains both cancellous and cortical bone. The analysis was performed on an AMRAY, Inc., scanning electron microscope fitted with a Princeton Gamma Tech energy-dispersion X-ray analyzer. The remaining bone was then ashed and tested for the mineral-to-matrix ratio in the control versus experimental animals by drying approximately 1 g pieces of bone to constant weight and then ashing in a muffle furnace.

The control and experimental femora were cleaned of soft tissue and prepared for mechanical testing. Six Micro-Measurements (CEA-13-0621U-350, Raleigh, North Carolina) uniaxial strain gages (3 medial and 3 lateral) were bonded to each femur as illustrated in Figure 1, using the techniques described by Wright and Hayes. The femora were then mounted in a special fixture, as shown in Figure 2, and oriented in the test machine such that their long axis was 20° from the vertical. Little information has been reported on the normal loading of the canine femur. Therefore, this loading was chosen because it is representative of that present due to joint reaction forces in the one-legged stance in humans. Mechanical testing was performed on a closed-loop hydraulic test machine, operated in stroke control at a constant displacement rate of 0.05 mm/sec. The femora were loaded to 335 N and cycled through five load repetitions. All samples were kept moist with physiologic saline during testing.

Following the mechanical testing of the intact femora, with the strain gages still in place, the
methylmethacrylate. Microradiographs and histologic slides were then prepared from each femoral head using the procedures reported by Jowsey et al.¹⁹ Microradiographs were taken on 100 μm thick sections ground on a precision swivel head grinder and measured to assure uniformity of the section.

A pulsed transmission ultrasound technique was used to determine the stiffness coefficient in the axial (C₁₀₀) direction¹⁴ for specimens of wet cortical bone tissue from the control and experimental groups. Tests were performed at eight standardized locations (45° intervals) on four annular sections of proximal femoral bone obtained from four femora in each group. The phase shift of a continuous sine wave at 2.25 MHz was measured and used to determine the stiffness coefficient. The system utilized and its operation have been described in detail by Van Buskirk et al.¹⁴

RESULTS

The i-PTH levels determined using radioimmunoassay at ten and 20 weeks after initiation of the diets are shown in Table 2. The difference in i-PTH levels between the experimental and control groups was found

<table>
<thead>
<tr>
<th>TABLE 2. Analytic Analyses Comparing Control and Experimental Groups</th>
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<tr>
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<tr>
<td>--------------------------------</td>
</tr>
<tr>
<td>Radioimmunoactive PTH</td>
</tr>
<tr>
<td>(C-terminal assay)</td>
</tr>
<tr>
<td>pg/ml</td>
</tr>
<tr>
<td>Weeks after starting diet</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>20</td>
</tr>
<tr>
<td>Bone ash analysis</td>
</tr>
<tr>
<td>(n = 4)</td>
</tr>
<tr>
<td>Bone ash wt</td>
</tr>
<tr>
<td>Dry bone wt</td>
</tr>
<tr>
<td>EDAX analysis</td>
</tr>
<tr>
<td>Phosphorus</td>
</tr>
<tr>
<td>Calcium</td>
</tr>
<tr>
<td>Ultrasound analysis</td>
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<tr>
<td>Stiffness coefficient (GPa)</td>
</tr>
</tbody>
</table>

n = Number of samples tested.
* = Each sample tested at eight locations.
to be significant, as determined by an unpaired Student's t test at p < 0.05 for both time periods, indicating the experimental group animals were in a hyperparathyroid condition.

The results of the energy dispersive radiographic analysis of calcium-to-phosphorus ratio and the percent of bone ash analysis of mineral-to-matrix ratio for the control and experimental groups are also shown in Table 2. No significant difference was found between the two groups in either analysis, as determined by an unpaired Student's t test. The stiffness coefficient of the control and experimental groups is also shown in Table 2. No significant difference was found between the measurements.

A typical microradiograph and the corresponding histologic section from the femoral head of a control and experimental animal are shown in Figures 3A and 3B. Quantitative optical microscopic analysis using random grid point counting methods of the histologic sections revealed that the experimental group had approximately 25% less volume fraction cancellous bone when compared with the control group. Two sections from each of the eight animals (16 femora) were used in the quantitative analysis. A comparison of cancellous bone in histologic and corresponding microradiographic sections of experimental group animals revealed no abnormally large osteoid seam in the experimental group. Examination of the hist-
TABLE 3. Strain Gage Measurements Along the Medial and Lateral Aspects  
(±Standard Deviation in Microstrain per Newton)

<table>
<thead>
<tr>
<th>Location</th>
<th>Without Device</th>
<th>With Device</th>
<th>% Change (With-Without)</th>
<th>With</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial (compressive)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>4.02 ± 0.54</td>
<td>2.14 ± 0.47</td>
<td>-46.76*</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3.33 ± 0.38</td>
<td>3.24 ± 0.74</td>
<td>-8.21</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2.54 ± 0.38</td>
<td>2.99 ± 0.02</td>
<td>+17.72</td>
<td></td>
</tr>
<tr>
<td>Experimental</td>
<td>5.08 ± 0.27</td>
<td>3.22 ± 0.35</td>
<td>-36.61*</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2.99 ± 0.41</td>
<td>3.22 ± 0.14</td>
<td>+7.69</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.80 ± 0.14</td>
<td>2.16 ± 0.20</td>
<td>+20.00</td>
<td></td>
</tr>
<tr>
<td>% Change (Experimental-Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>+26.36</td>
<td>-50.40*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>-15.30</td>
<td>-0.62</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>-29.13*</td>
<td>-27.76*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lateral (tensile)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1.89 ± 0.14</td>
<td>1.26 ± 0.23</td>
<td>-33.33*</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2.20 ± 0.20</td>
<td>2.25 ± 0.29</td>
<td>+2.27</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.03 ± 0.20</td>
<td>1.01 ± 0.05</td>
<td>-1.94</td>
<td></td>
</tr>
<tr>
<td>Experimental</td>
<td>1.97 ± 0.27</td>
<td>1.19 ± 0.23</td>
<td>-39.59*</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.37 ± 0.52</td>
<td>1.87 ± 0.07</td>
<td>+36.50</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.10 ± 0.79</td>
<td>1.62 ± 0.49</td>
<td>+47.29</td>
<td></td>
</tr>
<tr>
<td>% Change (Experimental-Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>+4.23</td>
<td>-5.55</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>-37.73*</td>
<td>-16.89</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>+6.80</td>
<td>+60.40*</td>
<td></td>
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</table>

* Indicates significant difference (p < 0.05).

tologic sections also revealed increased osteoclastic activity in the experimental group sections. Measurements of the femoral cortex thickness and inner and outer diameters were made for each animal from radiographs obtained after removal of the femora. No significant difference was found between the groups for any of these measurements.

The results of the strain gage measurements at each location on the femur at the positions shown in Figure 1 are presented in Table 3 for the control and experimental groups before and after femoral arthroplasty. The mean of the slopes of the strain-load curve for each group and the standard deviation are presented. The slope of the strain-load curve at each strain gage location was determined using linear regression analysis of the individual strain gage signals coupled with the output of the test machine load cell. A minimum of 12 points on the strain-load curve for each of the five load cycles was obtained for each position from every femur tested. This was used in the linear regression analysis to obtain the best fit line for each specimen at each gage location. The mean slope of the strain-load curve for the data is also presented in graphic form in Figures 4 through 7. These figures are plots of microstrain per unit load versus loc-
Fig. 4. Plot of the mean microstrain per unit load, determined by linear regression analysis from the strain load curves, versus location along the lateral (tension) and medial (compression) femoral shafts for the control and experimental groups without a prosthesis.

Fig. 5. Plot of the mean microstrain per unit load, determined by linear regression analysis from the strain load curves, versus location along the lateral (tension) and medial (compression) femoral shafts for the control and experimental groups after femoral arthroplasty.

Fig. 6. Plot of the mean microstrain per unit load, determined by linear regression analysis from the strain load curves, versus location along the lateral (tension) and medial (compression) femoral shafts for the control group before and after femoral arthroplasty. Again, the locations at which a significant difference occurred on these figures are indicated by asterisks.

DISCUSSION

The results of the histologic and micro-radiographic analysis of the cancellous bone
of the femoral heads revealed increased osteoclastic activity and a decrease in volume fraction cancellous bone in the experimental group as compared with the control group. The quantitative microscopic analysis indicated that the volume fraction bone in the experimental animals had decreased by about 25% in the femoral head. A volume fraction cancellous bone decrease of 78% in the mandibular region has been reported for these animals.30 Insofar as no abnormal osteoid seam was found in the cancellous bone of the experimental animals when compared with the control animals and no significant difference was found in the mineral-to-matrix and phosphorous-to-calcium ratios between the control and experimental groups, the decrease in volume fraction cancellous bone observed in the experimental animals must be considered osteoporotic. This is consistent with the increased i-PTH levels observed in the experimental group. It is apparent from the femoral cortex measurements and the stiffness coefficient of the femoral cortical bone that only trabecular bone was significantly affected by the experimental diet. This may be due to the increased surface area/unit volume available for bone remodeling in cancellous bone compared with cortical bone. It is unknown, however, whether cortical bone tissue would be significantly affected by maintaining the animals on the experimental diet beyond 22 weeks. No data were available for the animals that continued on the diet. However, the cortex measurements were obtained from radiographs and not from histologic sections; histologic sections may reveal significant differences in the cortex thickness and inner and outer diameters.

The results of the strain gage measurements indicate that a substantial reduction and redistribution of proximomedial and lateral strains occurs when a Co-Cr-Mo alloy hip prosthesis is inserted into the femur. These data are consistent with those reported by many investigators utilizing both experimental (strain gage)5,32,36 and analytic (finite element) techniques.3,6,11,12,29,36,37,39 A significant reduction in strains at the most proximal (location 1), medial, and lateral gage positions occurred in both the control (normal) and experimental (osteoporotic) femora (Table 3; Figs. 6 and 7). These strain reductions must be attributed to the stress-shielding effects of the relatively high elastic modulus prosthesis stem. A significant increase in strain at the distal medial gage (location 3) was observed for both the experimental and control groups after placement of the device. No significant difference was found in strain changes at the distal lateral location. This may be attributed to the placement of this gage with respect to the prosthesis tip (Fig. 1). A significant increase in bone strain at a location corresponding to the distal tip of the prosthesis may be expected; however, the placement of the gage was several millimeters proximal to the tip; thus, these gages were not in the position for measuring the strain concentration associated with the tip of the prosthesis.

In addition to the expected difference in strain before and after insertion of the hip prosthesis within the control and experimental groups, a significant difference in strain was observed between the control (normal) and experimental (osteoporotic) femora without a prosthesis (Table 3; Fig. 4). Significantly greater strains were measured at the proximomedial gage locations in the experimental group femora when compared with the control femora, while significantly lower strains were measured at the distal medial and mid-lateral gage locations. Insofar as all of the femora were determined to be approximately equal in size and length, the increase in strains in the experimental group femora must be attributed to the decrease in volume fraction cancellous bone in the femoral head and neck region. A significant difference in strain between the control and experimental group femora with a prosthesis (Table 3; Fig. 5) was also observed for the proximal and distal medial locations and lateral distal location, indicating that the
two groups may remodel differently with time following placement of a prosthetic device.

The data indicate that the femora apparently did not remodel to a constant stress condition for the control and experimental groups, inasmuch as the stiffness coefficients of the two groups were not significantly different. (The stress is directly proportional to the stiffness coefficient and the strain.) It should be noted, however, that although no structural changes of the femoral cortex were noted radiographically, structural changes, such as increasing inner and outer cortical diameters due to periosteal apposition and endosteal resorption characteristic of osteoporosis, may have been present but were not apparent in the radiographs. However, the data do indicate that stress- and strain-induced bone remodeling changes owing to the presence of a prosthetic device may be significantly different in an osteoporotic patient when compared with a patient with normal bone tissue. This may indicate the need to design implants specifically for this group, because in addition to altered stress and strain levels in the osteoporotic bone, stresses and strains may be significantly greater within the prosthetic device.

SUMMARY

Nutritional secondary hyperparathyroidism (NSH) was induced in adult beagle dogs through nutritional control by feeding them a diet containing high phosphorus (1.2%) and low calcium (0.12%). A control group was fed a diet containing 0.42% phosphorus and 0.54% calcium. An osteoporotic condition was produced by NSH, which was verified with histologic, histomorphometric, and biochemical analyses. A significant increase in i-PTH level was measured at both ten and twenty weeks after initiation of the diet in experimental animals when compared with control animals. A 25% reduction in volume fraction cancellous bone and increased osteoclastic activity was found in histologic sections from the femoral heads of the NSH animals when compared with control animals. No abnormally large osteoid seam was found in the cancellous bone of the experimental animals. The results of energy dispersive radiographic analysis and bone ash analysis revealed no significant differences in calcium-to-phosphorus or mineral-to-matrix ratios between the two groups. The results of in vitro mechanical testing indicated significant differences in the strain state for the NSH and control animal femora, with the highest strains being observed in the calcaneal region of the NSH femora. The presence of a Co–Cr–Mo alloy femoral head prosthesis was found to alter the strain distribution significantly in both the control and NSH femora.

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