BONE LOSS AND HUMAN ADAPTATION TO LUNAR GRAVITY

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Long-duration space missions and establishment of permanently manned bases on the Moon and Mars are currently being planned. The weightless environment of space and the low-gravity environments of the Moon and Mars pose an unknown challenge to human habitability and survivability. Of particular concern in the medical research community today is the effect of less than Earth gravity on the human skeleton, since the limits, if any, of human endurance in low-gravity environments are unknown. This paper provides theoretical predictions on bone loss and skeletal adaptation to lunar and other nonterrestrial-gravity environments based upon the experimentally derived relationship, density $\approx$ *(mass* $\times$ *gravity)*$^{1/8}$. *The predictions are compared to skeletal changes reported during bed rest, immobilization, centrifugation, and spaceflight. Countermeasures to reduce bone losses in fractional gravity are also discussed.*

INTRODUCTION

Since the founding of the National Aeronautics and Space Administration (NASA) in 1958, manned spaceflight has been one of our nation's priorities. The scientific and engineering accomplishments by NASA over the past three decades represent some of the greatest technological achievements in human history. Throughout the course of development of manned spaceflight, one of the chief concerns of physicians and life scientists practicing space medicine has been to assure the health and well-being of astronauts and people who will live and work in space and other non-Earth environments.

After 25 years of U.S. and Soviet manned spaceflight experience, a wealth of physiological data has been gathered and studied. Research conducted on animals and humans exposed to the microgravity (as low as 10^{-6}) or "weightless" state in space has provided a better understanding of the physiological changes resulting from weightlessness. Exposure to the space environment has been found to produce changes in nearly every physiological system, but, in general, humans can acclimate well to weightlessness. Several biomedical problems have been identified, however, that may lead to potentially progressive pathophysiological deterioration, including alterations in vestibular function, cardiovascular deconditioning, hematological imbalances, and bone and mineral imbalances.

Among the most striking findings from space missions and Earth-based simulations of weightlessness is the rapid and continuous loss of bone mineral (*Nicogossian and Parker,* 1982), and alterations in skeletal mass are thought by many scientists to be one of the most serious physiological hazards associated with long-term spaceflight. The major health hazards associated with skeletal bone loss are toxic accumulations of excess mineral in tissues such as the kidney, increased risk of fracture, and potentially irreversible damage to the skeleton. For these reasons, numerous Earth-based and space-based studies are currently being directed toward two complementary goals: (1) elucidating the fundamental mechanisms of skeletal adaptation in altered gravity (or stress) environments and (2) developing practical countermeasures to preserve normal skeletal structure and function.

One often-asked question remains unanswered: How long should an astronaut remain in space? This paper presents theoretical predictions on skeletal adaptation in response to chronic altered weight bearing in a lunar gravity environment. Data from spaceflight, Earth analogs of weightlessness, and centrifugation are compared to theoretically derived predictions. The gravity field question is addressed with the principal aim to define an optimal gravity environment that preserves physiological function and ensures survival.

REVIEW AND THEORY

Spaceflight

In the last two decades, manned space programs conducted by the U.S. and the U.S.S.R. have successfully placed over 319 men and women into near-Earth orbit. Since Soviet cosmonaut Lt. Uri Gagarin's historic single orbit of the Earth lasting 108 minutes (Vostok 1), over 160,000 man hours have been logged in space (as of 1987). Following the first successful Moon landing on July 16, 1969, a total of 600 man hours were logged by U.S. astronauts on the lunar surface, including a record stay of 75 hours on the lunar surface by astronauts Cernan and Schmitt during the Apollo 17 mission (December 7-19, 1972). Shortly thereafter, astronauts Carr, Gibson, and Pogue spent a record-setting 84 days in a milligravity to microgravity environment aboard the Skylab 4 orbital workstation.

Since Skylab, the longest U.S. space mission has been 248 hours aboard the space shuttle STS-9 (Space Transportation System). The Soviets, however, have continued to extend their presence in space and have accumulated 117,000 man hours during 35 Soyuz missions aboard the Salyut and Mir space stations. The Mir station has been constantly manned since February 8, 1987, and on December 29, 1987, 43-year-old Soviet cosmonaut Col. Yuri Romanenko established an Earth-orbit endurance record of 326 days aboard the Mir space station, surpassing the previous Soviet endurance record by 90 days. Col. Romanenko's 11-month experience attests to the remarkable adaptability of the human body and should provide answers to key questions as well as provide fresh insight into the planning of future spaceflights of even longer duration.

The primary effect of microgravity is the elimination of deformations and mechanical stresses on body tissues that are normally present on the Earth due to its gravitational field. This results in a disordered interaction of afferent mechanoreceptors and the development of sensory conflicts. The major immediate manifestations of microgravity are twofold: a headward redistribution of body fluids and underloading of the musculoskeletal system. The former shifts the center of mass of the body toward the head, triggering nervous, reflex, and hormonal mechanisms of adaptive reactions in order to restore hemodynamic homeostasis. The latter produces changes in movement, coordination, neuromuscular function, metabolic requirements, and intrinsic musculoskeletal structure function relationships, and may reduce the role of the muscular system in hemodynamics as a whole. Exposure to the space environment has been found to produce adaptations in nearly every human physiological system. Some of these adaptations such as motion sickness are self-limiting; others produce progressive changes in different body systems. Among the most striking findings from long-term Skylab and Soyuz Earth-orbit space missions is the rapid and continuous loss of bone mineral, particularly cancellous bone losses, which have been reported to be as high as 0.5% per week in the human calcaneus.

Earth Analogs of Weightlessness

Skylab, Salyut, and Mir Earth-orbit space stations have enabled man to live and work for extended periods in a weightless environment. The long-term physiological effects of spaceflight were originally hypothesized to be similar to the deleterious physiological changes associated with chronic inactivity and immobilization. Consequently, in order to ensure the safety and survivability of the space station crew, ground-based methods were sought that could be used to predict physiological responses to weightlessness and to test and evaluate effective countermeasures to physiological deconditioning. The methods used to simulate weightlessness on Earth have included water immersion, hyperbaric environments, immobilization and restraint of animals, and bed rest, all of which were found to simulate, to a certain degree, some of the many physiological changes associated with spaceflight.

Of the Earth-based techniques, bed rest and immersion techniques result in physiological adaptations closest to the low gravity state. Water immersion produces rapid body fluid redistributions similar to weightlessness, making this method an ideal short-term analog of spaceflight. However, most subjects cannot tolerate long-term exposure to water. As a result, Soviet scientists have developed a "head-out dry immersion" technique, in which subjects are protected from water contact, making prolonged immersion more practical (*Gogolev et al.,* 1986). Bed rest, however, is the most commonly used method to simulate weightlessness. Studies of this type were found to be the most endurable method for chronic exposure (*Sandler and Vernikos,* 1986). Numerous horizontal and "head-down" simulations lasting over six months have also been reported. Head-down or "antiorthostatic" bed rest produces more rapid and pronounced fluid shifts than horizontal bed rest, and more closely reproduces the early physiological effects (orthostatic intolerance) and sensory symptoms (vertigo, nausea, nasal congestion) of weightlessness.

In general, chronic immobilization (bed rest and paralysis) results in a 1% to 2% per week loss in calcaneous cancellous bone mineral content (*Donaldson et al.,* 1970; *Hantman et al.,* 1973; *Hulley et al.,* 1971; *Krolner and Toft,* 1983; *Krolner et al.,* 1983; *Lockwood et al.,* 1973; *Minaire et al.,* 1974, 1981; *Schneider and McDonald,* 1984; *Vignon et al.,* 1970; *Vogel,* 1971). The magnitude of bone loss appears to be unrelated to the underlying course of inactivity (*Arnaud et al.,* 1986). Maximum cancellous bone losses occur after 6-9 months (30-40% loss) and appear to be self-limiting (*Minaire et al.,* 1984). The point at which bone losses become self-limiting will henceforth be referred to as the (Earth) "genetic baseline." The effects of immobilization on cortical bone are much less pronounced, ranging from 0.1% per week (dog humerus) to 0.3% per week (dog radius, ulna) (*Jaworski et al.,* 1980). Differences between cortical and cancellous bone losses have been attributed to the greater surface area of cancellous bone (*Krolner and Toft,* 1983; *Krolner et al.,* 1983), but other factors such as functional differences in weight bearing may also be important. For example, bed-rest studies in which patients have been allowed to ambulate (stand, walk, or cycle) for several hours per day have been effective in reducing cancellous bone losses (*Issekutz et al.,* 1966). Thus, functional weight bearing and postural shifts appear to be important conditioning factors affecting subsequent skeletal reactions.

Adaptation to Increased Activity

In contrast to the hypofunctional skeletal loading conditions of immobilization and spaceflight, hyperfunctional loading conditions in humans have been reported to result in a net increase in bone mass. Clinical studies examining the bone mineral content (BMC) of the playing arm of professional tennis players report increased radial and humeral cortical bone density ranging from 16% (*Jacobson et al.,* 1984) to greater than 30% in comparison to the contralateral arm (*Dalen et al.,* 1985; *Jones et al.,* 1977). Changes in the BMC of top-ranked athletes participating in weight training programs are even more dramatic. *Nilsson and Westlin* (1971) reported an average 50% increase in distal femur BMC in Olympic-class athletes vs. age-matched controls. More recently *Granbed et al.* (1987) reported an average 36% increase (in comparison to age- and weight-matched normal men) in the BMC of the L3 vertebrae of power lifters participating in the 1983 Power Lifting World Championship. They also noted that there was a significant relationship between the total annual weight lifted and the BMC within this group of athletes. Increases in cancellous BMC in distance runner (*Dalen and Olsson,* 1974) and infantry recruits (*Margulies et al.,* 1986) are much less marked, ranging from 5% to 20%.

Several animal experimental strategies have been employed to study the "adaptive" behavior of bone including hypergravitational studies using centrifuges (*Amtmann and Oyama,* 1973, 1976; *Jaekel et al.,* 1977; *Jankovich,* 1971; *Kimura et al.,* 1979; *Smith,* 1977; *Wunder et al.,* 1979), mechanical overloading of limbs by surgical resection (*Carter et al.,* 1980; *Chamay and Tschantz,* 1972; *Goodship et al.,* 1979; *Saville and Smith,* 1966), and externally applied loading techniques (*Burr et al.,* 1984; *Churches and Howlett,* 1982; *Lanyon et al.,* 1982; *O'Connor et al.,* 1987; *Rubin and Lanyon,* 1984, 1985, 1987). These studies have, in general, produced pronounced cortical hypertrophy and increased breaking strength of the same magnitude as those obtained in the clinical studies. Consistent with the moderate changes in BMC associated with distance running, the results of involuntary exercise in rats (*Adams,* 1966; *Donaldson,* 1935; *Kato and*

Ishiko, 1966; *Keller and Spengler,* 1989; *Kiiskinen,* 1977; *Lamb et al.,* 1969; *Saville and Whyte,* 1969; *Steinhaus,* 1933; *Tipton et al.,* 1972) have been much less conclusive and significant than the aforementioned adaptational strategies.

Differences in the results of these studies might be the result of differences in the mechanical stimuli (loading type, period, intensity) or to species-specific factors such as animal age, sex, diet, and genetics. In a review article, *Carter* (1982) speculated that, in addition to the above, differences in the results of exercise, hypergravitational, and hyperfunctional studies might be attributed to strain magnitudes, and he hypothesized that the "hypertrophic response to increased bone strain levels is a nonlinear response in mature bone." Subsequent experimental studies demonstrated that mechanical stimuli such as strain rate and strain distribution were critical to the osteoregulatory processes of the skeleton (*Lanyon et al.,* 1982; *O'Connor et al.,* 1982).

More recently *Rubin and Lanyon* (1984, 1985, 1987) and *Lanyon and Rubin* (1984) examined the magnitudes and distributions of surface cortical bone strains required to elicit an osteogenic response using a functionally isolated turkey ulna model. They concluded that the osteoregulatory response of the skeleton was most significant when the mechanical stimuli were dynamic in nature and above or below an "optimal strain environment," increased strains resulting in a positive response, while decreased strains resulted in a negative response. Their results suggest that, regardless of the number of cycles (≥ 20), cortical bone strain magnitudes of 400-1500 microstrain will not result in any net significant change in bone geometry or density (Fig. 1). Activities that exceed the 1500 microstrain threshold will initiate a positive adaptive or "osteogenic" response, whereas prolonged inactivity below 400 microstrain will induce a negative response; the former is analogous to intensive physical activity (i.e., sprinting, weight lifting) and the latter is analogous to sedentary activity (bed rest, paralysis, immobilization). In space and nonterrestrial environments such as the Moon and Mars, gravitational forces and forces due to muscle activity are decreased, and both may reduce the subsequent musculoskeletal stimuli below the functional level of strain required to maintain bone mass under normal terrestrial conditions.

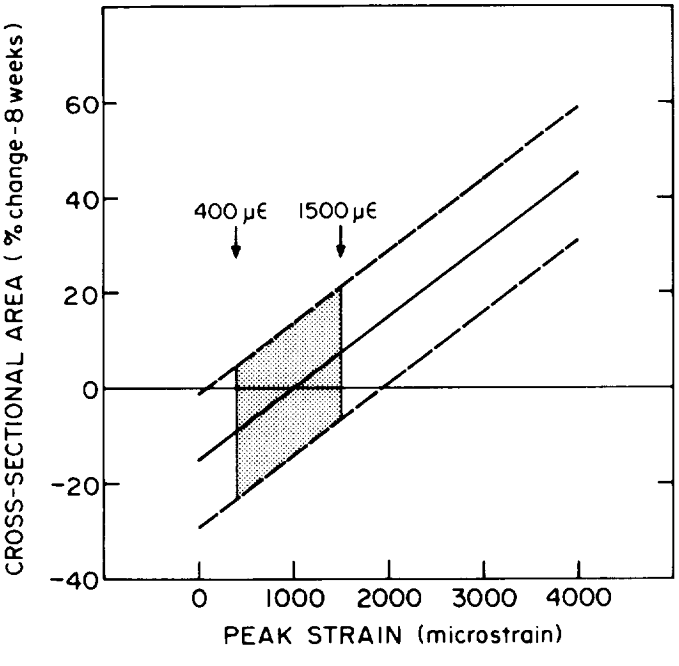

Fig. 1. Adaptational response of the functionally isolated turkey ulna following eight weeks of cyclic loading (100 cycles/day) at peak strains ranging from 0 to 4000 microstrain. Based on data from *Rubin and Lanyon* (1985).

Modeling of Skeletal Adaptation

The role of gravity in regulating the functional requirements of the human and animal body has been studied for over a century. *Thompson* (1942) pointed out that "the forms and actions of our bodies are entirely conditioned by the strength of gravity upon this globe.... Gravity not only controls the actions but also influences the forms of all save the least of organisms." Mathematical formulations that characterize the "stress-adaptive" behavior of the skeleton in a feasible manner have yet to be determined. Establishment of permanent Moon and Mars bases and future space exploration, however, necessitate the development of practical empirical solutions concerning skeletal demineralization and effective countermeasures that ensure an adequate level of human performance and, more importantly, survivability in these less-than-Earth-normal gravity environments. In the argument that follows we will describe an experimentally based mathematical formulation that can be used to estimate, in the absence of prophylactic countermeasures, the alterations in skeletal mass associated with microgravity ($10^{-6}g$), lunar gravity ($1/6\,g$), and other nonterrestrial environments. The mathematical formulation is based upon the results of dual photon absorptiometry (DPA) measures of lumbar vertebral BMC in a group of world-class power lifters, and the formulation has been generalized to include gravity (g) as a variable. Details of the experimental methods have been previously published by *Granhed et al.* (1987), but a brief description follows.

Eight Swedish world-class power lifters participating in the 1983 World Power Lifting Championships in Göteborg, Sweden, volunteered for the study. Age, height, weight, and L3 vertebral BMC were obtained from each power lifter and from 39 age- and weight-matched "normal" healthy men who served as controls. Dual photon absorptiometry was used to assess the BMC. Detailed weight-training records were obtained from each athlete (including maximum weight lifted and annual weight lifted) and pictures of the athletes during their ground lifts were taken with a high-speed camera. Figure 2 illustrates the way in which the ground lift was performed.

Estimates of the loads on L3 in different positions of the ground lift were calculated using the kinematic model developed by *Schultz and Andersson* (1981) and the ultimate strength of the L3 vertebrae was estimated using experimentally determined relationships for cancellous bone strength vs. density (*Hansson et al.,* 1980, 1987).

The mean BMC value of the power lifters (7.06 ± 0.87 g/cm) was 36% greater than that of the age- and weight-matched controls (5.18 ± 0.88 g/cm). Estimates of the ultimate strength of the L3 vertebrae were 4.1 times greater than the estimated peak L3 loads during the ground lift maneuver. The ratio of ultimate strength *in vivo* load is defined as the safety factor (SF). Long bone SFs have been experimentally determined to lie in the range three to five (*Biewener,* 1982, 1983; *Keller and Spengler,* 1988; *Rubin and Lanyon,* 1982), which is consistent with the mean value of 4.1 obtained for the power lifters.

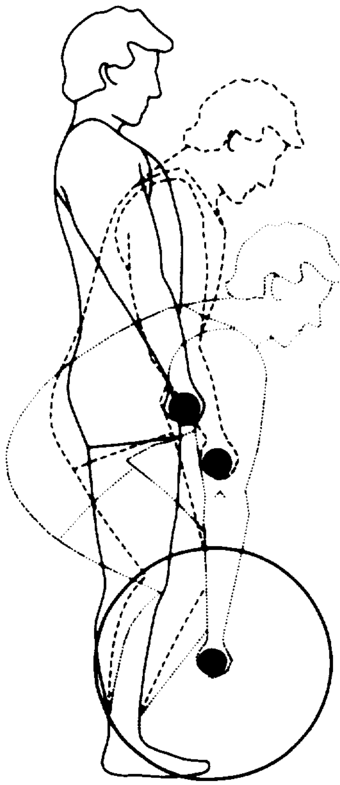

Fig. 2. Schematic representation of the ground lift maneuver. Reprinted from *Granhed et al.* (1987).

Table 1 summarizes the results of the analysis of the forces required to elicit an increase in BMC by increments of 10%. As indicated in Table 1, the change in BMC is highly nonlinear in terms of the mechanical stimulus: More than a thirtyfold increase in total force was required to elicit a 50% increase in BMC. The data can be represented mathematically as

$$\mathrm{BMC} \propto [\Sigma \mathrm{F}]^{1/8} \qquad (1)$$

where ΣF is the total force experienced during weight training by the L3 vertebrae in a one-year period.

Manned spaceflights, missions to the Moon and Mars, and the establishment of lunar and martian bases will take place in gravitational environments where the weight, defined as the force of terrestrial gravitation, experienced by the human or animal body will be reduced. A body of mass m on the Earth (of mass M and radius R_0) experiences a weight

$$F_g = M(GM/R_0^2) = mg \qquad (2)$$

where G is a universal constant and g is a constant equal to the acceleration due to the Earth's force of gravity. Simple substitution of equation (2) into equation (1) yields

$$\mathrm{BMC} \propto [\Sigma \mathrm{mg}]^{1/8} \qquad (3)$$

Assuming that bone adapts to reduced forces in a similar manner as increased forces, then one can predict the changes in L3 BMC during, for example, Moon life ($GM/R_0^2 = 1/6\,g$), in terms of

$$\mathrm{BMC} \propto 0.799\ [\Sigma \mathrm{mg}]^{1/8} \qquad (4)$$

where 0.799 represents the BMC fraction retained annually. Similar predictions can be obtained for other non-Earth environments by substituting the appropriate Earth gravity ratio ($GM/R_0^2)/g$. The exponent in equation (3) can also be verified analytically using a "dimensional analysis" (see Appendix).

TABLE 1. Lumbar bone mineral content changes due to hyperactivity.

BMC (g/cm)	Increase (%)	ΣF (kg/yr × 10^6)
5.2	0	1.5
5.7	10	2.9
6.3	20	6.1
6.9	30	12.0
7.6	40	24.7
8.4	50	52.4

Based on the data of *Granhed et al.* (1987).

RESULTS AND DISCUSSION

The effects of adaptation to altered gravitation environments are predicted in Table 2. Equation (4) predicts that under normal activity conditions, a person will experience a 21.1% reduction in L3 BMC per year, or an average weekly loss of 0.41% in a lunar gravity field. In terms of bone strength, this represents a reduction of 0.7% per week (*Hansson et al.*, 1980, 1987). Skeletal adaptation to the lunar gravity field would require roughly 120 weeks for lunar homeostatis (83% strength reduction). Assuming an optimal safety factor for bone of 3 (*Alexander*, 1984), the longest Moon mission for a safe return to Earth would be about 96 weeks (66.6 strength reduction). By Earth standards, microgravity ($\leq 10^{-6}\,g$) would require approximately 5-6 months for skeletal homeostatis (30-40% bone loss), and the skeleton would be at risk for fracture after 35 weeks. In terms of homeostatis in fractional and microgravity environments, it is not known whether these effects would be self-limiting as they appear to be for immobilized patients on Earth. Furthermore, bone losses in cosmonauts exposed to chronic periods of weightlessness (0.5% per week) are much less dramatic than the model predictions, reflecting the fact that cosmonauts generally exercise 2-4 hours per day and wear elastic-corded "penguin" suits up to 16 hours/day. Using a value of -0.5% BMC per week, the model predicts that the longest safe space mission would be about 60 weeks,

TABLE 2. Predicted BMC and strength changes due to altered gravity field.

	Environment g	BMC (%/week)	Strength (%/week)	Stasis (weeks)	SF = 1 (weeks)
Space	$<10^{-6}$	-1.58	-1.86	54	36
Moon	0.17	-0.39	-0.69	120	96
Mars	0.4	-0.22	-0.42	153	159
Earth	1.0	0	0	0	0
Jupiter	2.7	0.25	0.54	314	—

which is slightly greater than the current microgravity endurance record (47 weeks).

The effects of fractional gravity and hypergravity presented in Table 2 are depicted graphically in Fig. 3. Based on ranges of immobilization data (*Donaldson et al.,* 1970; *Hantmann et al.,* 1973; *Hulley et al.,* 1971; *Krolner and Toft,* 1983; *Krolner et al.,* 1983; *Lockwood et al.,* 1973; *Minaire et al.,* 1974, 1981; *Schneider and McDonald,* 1984; *Vignon et al.,* 1970; *Vogel,* 1971) and spaceflight data (*Gazenko et al.,* 1982; *Rambaut and Johnson,* 1979; *Stupakov et al.,* 1984) obtained from the literature, the "1/8 Power Law" of equation (3) suggests that immobilization and spaceflight are comparable to a 10^{-2} to 10^{-3} gravity environment and Moon-Mars gravity environment, respectively. Centrifuge data obtained from dogs exposed to chronic accelerations of 2.5 g (*Oyama,* 1975) are in close agreement with the model predictions, but the data obtained from rats (*Amtmann et al.,* 1979; *Oyama and Zeitman,* 1967; *Wunder et al.,* 1979) are more scattered and deviate considerably from the model predictions. The latter may reflect the fact that adult rats do not experience bone internal remodeling. Dog and human bones model and remodel and achieve skeletal adaptations through changes in surface geometry and internal architecture.

The temporal changes in cancellous BMC and strength associated with bed rest and spaceflight along with model predictions for space, Moon, and Mars environments are illustrated in Fig. 4. The model predicts that microgravity and lunar and martian gravitational environments will result in a net 1.6% per week, 0.7% per week, and 0.4% per week loss in BMC, respectively, in the absence of prophylactic measures. Changes in BMC associated with bed rest and immobilization are in close agreement with the predicted losses accompanying microgravity ($\leq 10^{-6} g$). As described earlier, the experimentally measured changes in BMC associated with spaceflight are much less dramatic than the bedrest data and fall in the range of 0.4% per week to 0.7% per week losses in BMC. The horizontal dashed line corresponding to losses in bone strength of 66.6% in Fig. 4 represents the genetic baseline at which point no further bone loss will occur (Earth-gravity standard). This point (66.6%) also corresponds to the clinical horizon or point at which the skeleton is at an increased risk for fracture (no margin for safety). Note that in a microgravity or fractional-gravity environment, the genetic baseline may not be the same as that for Earth.

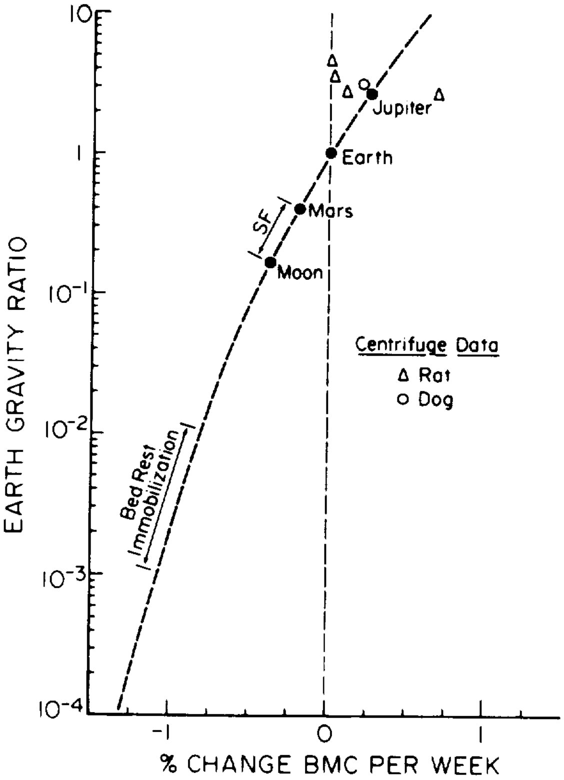

Fig. 3. Log-linear plot of the effects of fractional gravity and hypergravity on the change in BMC based upon the "1/8 Power Law" of equation (3).

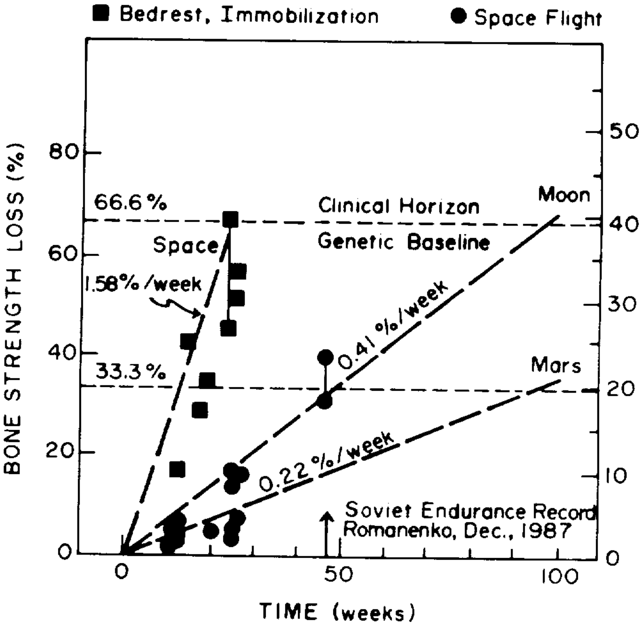

Fig. 4. Temporal changes in bone strength (left ordinate) and bone mineral content (right ordinate) as a function of time (weeks). Experimental data from bed rest (solid squares) and spaceflight (solid circles) are shown (see text for literature citation). The data points connected by bars represent data ranges for which exact values were not available from the literature citation.

In the absence of countermeasures, the results presented in Table 2 and Figs. 3 and 4 provide a preliminary estimate of the long-term effects of microgravity and fractional gravity on the human cancellous skeleton. Although these results are based upon clinical observations of bone changes in lumbar vertebrae, reasonable estimates of the changes in other skeletal sites, such as cortical and cancellous bone in the appendicular skeleton, can be obtained provided suitable adjustments are made. For example, our results would overestimate (nearly threefold) changes in diaphyseal regions of long bones where the rate of bone loss appears to be the lowest in the skeleton. Additional factors such as histories of activity, age, and body weight may also affect the precision of these estimates.

Application of the empirical formulae presented in this paper makes an important, but currently inadequately supported, assumption that results obtained for an osteogenic or positive skeletal adaptive response can be extrapolated to negative skeletal adaptations associated with disuse and fractional-gravity environments. Preliminary support for the assumption has been provided, however, by the experimental studies of *Rubin and Lanyon*

(1984, 1985, 1987), which suggest that the adaptive behavior of bone corresponding to hypo- and hyperactivity are linear functions of bone strain. Data obtained from future fractional-gravity experiments may provide additional support for this assumption.

The theoretical results presented in this paper provide insight into the limits (if any) of human performance and survivability in non-Earth environments. This is an issue of major importance in terms of extended human presence in future orbiting space stations, during long-term space exploration, and on permanently manned Moon and Mars bases. In a lunar gravitational environment (1/6 *g*), bone strength losses of 0.7% per week would limit human presence on the Moon to about 100 weeks, at which point a weakened skeletal structure could create serious hazards to crew health during the stresses of reentry and return to terrestrial gravitation. Similarly, more than three years could be spent in Mars environment (3/8 *g*) before a weakened skeleton would be health threatening. This would be equivalent to a period of about 35 weeks in a microgravity environment (10^{-6} *g*). The latter is consistent with the results of bed-rest and immobilization data but appears to be grossly underestimated in terms of data obtained from astronauts and cosmonauts chronically exposed to microgravity. Physiological manifestations intrinsic to the absence of a gravitation field such as nervous, hormonal, and hemodynamic factors and/or countermeasures employed during space missions may be responsible for this apparent inconsistency.

On the basis of changes in skeletal mass observed during increased activity, and in lieu of the recent 11-month endurance record established by Soviet cosmonaut Romanenko, we might predict that humans can function and survive indefinitely in a microgravity or fractional-gravity environment provided that adequate countermeasures are taken. Preliminary reports by Soviet space officials that appears in the December 29, 1987, issue of the New York *Times* indicate that Col. Romanenko was in good health following his return to Earth. In addition to a rigorous work schedule, Soviet cosmonauts exercise two hours a day on a stationary bicyle and a treadmill, and they wear suits fitted with elastic bands ("penguin" suits) that provide resistance to movement and thus aid muscular conditioning. While countermeasures of this nature appear adequate for relatively long space missions, the results of this study suggest that more time- and energy-effective exercise measures might include, for example, anaerobic weight lifting.

Alternatively, artificial gravity may be sufficient to preserve musculoskeletal conditioning within safe limits. Our results suggest that a 3/8-*g* field should preserve skeletal strength above the fracture risk level for over three years. One scenario for a manned mission to Mars being considered by NASA is an "all-up" type of mission, which would require a 36-month round trip. In this type of mission the crew, equipment, and supplies are transported together in one vehicle. Such a mission would be nearly three times as long as the current human microgravity endurance record. An artificial gravity field of 3/8 *g* should be sufficient to preserve muscoloskeletal integrity for the round trip to Mars and, in addition, would enable the crew to acclimate to the martian gravitational field. Artificial gravity, however, may not be the most effective solution as problems associated with gravity gradients, vehicle design, and energy expenditure may be prohibitive. Exercise in conjunction with other countermeasures, such as as osteogenic drug therapy, may be more practical. In addition, problems associated with breakdown of the immune and cardiovascular systems must also be considered.

CONCLUSION

This study's finding of a close correlation between skeletal adaptation and activity provides the framework for the development of future studies that will address the question of human survival and habitability in space and on the Moon or Mars. Our results predict that, in the absence of suitable countermeasures, there are limits to the ability of humans to function in space for extended periods and then return to Earth-normal gravity. Based upon the results of previous clinical investigations of the osteogenic response of bone during increased activity, we believe that rigorous activity such as weight training and sprinting are more effective than more sedentary and less intensive activities such as bicycling and running exercises. In addition, a 3/8-*g* artifical gravity environment should sustain skeletal function in space at a level suitable for a return to Earth for periods of greater than three years. Fractional-gravity studies and studies of osteogenic-inducing agents also deserve attention.

APPENDIX

Dimensional Analysis

Consider the parameters mass (M), gravity (g), density (ρ), and modulus (E), which, with the exception of E, are representative of the measured quantities comprising the power lifters data. The above parameters are related to the fundamental quantities mass (M), length (L), and time (T) as follows (*Keller,* 1988)

	(k_1) ρ	(k_2) M	(k_3) g	(k_4) E
M	1	1	0	1
L	-3	0	1	-1
T	0	0	-2	-2

The power coefficients (k_i) are thus related by the following equations

$$k_1 + k_2 + k_3 = 0 \tag{A1}$$

$$-3k_1 + k_3 - k_1 = 0 \tag{A2}$$

$$-2k_3 - 2k_4 = 0 \tag{A3}$$

Note that the number of dimensionless groups (DG) equals the number of parameters minus the matrix rank, namely DG = 4 - 3 = 1. There are three equations and four unknowns. If, however, we arbitrarily assign a power coefficient of 1 to the coefficient k_1, one can show that the coefficients k_2, k_3, and k_4 become

	(k_1) ρ	(k_2) M	(k_3) g	(k_4) E
π	1	-1/2	-1/3	-3/2

where the K_i represent power coefficients in the dimensionless expression

$$\pi = \rho[M^{1/2}E^{3/2}g^{3/2}] \quad (A4)$$

In the case of the power lifters, E is an experimentally indeterminant quantity, but is related to bone density as $E \propto \rho^3$ (*Carter and Hayes,* 1976). Substituting the above into equation (A4) and simplifying yields

$$\rho \propto M^{1/7}g^{3/7} \quad (A5)$$

$$\rho \propto (Mg^3)^{1/7} \quad (A6)$$

On Earth g is a constant, and equation (6) reduces to

$$\rho \propto M^{1/7} \quad (A7)$$

The exponent 1/7 in equation (A7) was found experimentally to be 1/8 using the density and weight-lifted data obtained for the power lifters.

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REFERENCES

Adams J. E. (1966) Little league shoulder. Osteochondrosis of the proximal humeral epiphysis in boy baseball pitchers. *Calif. Med., 105,* 22-25.

Alexander R. McN. (1984) Optimum strengths for bones liable to fatigue and accidental fracture. *J. Theor. Biol., 109,* 621-636.

Amtmann E. and Oyama J. (1973) Changes in functional construction of bone in rats under conditions of simulated increased gravity. *Anat. Entwicklungsgesch., 139,* 307-318.

Amtmann E. and Oyama J. (1976) Effects of chronic centrifugation on the structural development of the musculo-skeletal system of the rat. *Anat. Embryol., 149,* 47-70.

Amtmann E., Kimura T., Oyama J., Doden E., and Potulski M. (1979) Maximum likelihood factor analysis of the effects of chronic centrifugation on the structural development of the musculoskeletal system of the rat. *Anat. Embryol., 156,* 89-101.

Arnaud S. B., Schneider V. S., and Morey-Holton E. (1986) Effects of inactivity on bone and calcium metabolism. In *Inactivity: Physiological Effects* (H. Sandler and J. Vernikos, eds.), pp. 49-76. Academic, Orlando.

Biewener A. A. (1982) Bone strength in small mammals and bipedal birds: Do safety factors change with body size? *J. Exp. Biol., 98,* 289-301.

Biewener A. A. (1983) Locomotory stresses in the limb bones of two small mammals: The ground squirrel and chipmunk. *J. Exp. Biol., 103,* 131-154.

Burr D. B., Martin R. B., and Lefever S. (1984) The prevention of disuse osteoporosis in sedentary rabbits. *Trans. ORS, 9,* 146.

Carter D. R. (1982) The relationship between *in vivo* strains and cortical bone remodeling. *Crit. Rev. Biomed. Eng., 8,* 1-28.

Carter D. R. and Hayes W. C. (1976) Bone compressive strength: The influence of density and strain rate. *Science, 194,* 1174-1176.

Carter D. R., Smith D. J., Spengler D. M., Daly C. H., and Frankel V. H. (1980) Measurement and analysis of *in vivo* bone strains on the canine radius and ulna. *J. Biomechanics, 13,* 27-38.

Chamay A. and Tschantz P. (1972) Mechanical influences in bone remodeling. Experimental research on Wolff's law. *J. Biomechanics, 5,* 173-180.

Churches A. E. and Howlett C. R. (1982) Functional adaptation of bone in response to sinusoidally varying controlled compressive loading of the ovine metacarpus. *Clin. Orthop. Relat. Res., 168,* 265-280.

Dalen N. and Olsson K. E. (1974) Bone mineral content and physical activity. *Acta Orthop. Scand., 45,* 170-174.

Dalen N., Laftman P., Ohlsen H., and Stromberg L. (1985) The effect of athletic activity on the bone mass in human diaphyseal bone. *Orthopedics, 8,* 1139-1141.

Donaldson C. L., Hulley S. B., Vogel J. M., Hattner R. S., Bayers J. H., and McMillan D. E. (1970) Effect of prolonged bed rest on bone mineral. *Metabolism, 19,* 1071-1084.

Donaldson H. H. (1935) Summary of data for the effects of exercise on the organ weights of the albino rat: Comparison with similar data from the dog. *Am. J. Anat., 56,* 57-70.

Gazenko O. G., Genin A. M., and Egoro A. D. (1982) Major medical results of the Salyut-6-Soyuz 185-day space flight. In *Space: Mankind's Fourth Environment XXXII International Astronautical Congress, Rome 1981,* pp. 275-293. Pergamon, Oxford.

Gogolev K. I., Aleksandrova Ye. A., and Shul'zhenko Ye. B. (1980) Comparative evaluation of changes in the human body during orthostatic (head down) hypokinesia and immersion. *Fiziol. Chel., 6,* 978-983.

Goodship A. E., Lanyon L. E., and McFie H. (1979) Functional adaptation of bone to increases stress. *J. Bone Joint Surg., 61A,* 539-546.

Granhed H., Jonson R., and Hansson T. (1987) The loads on the lumbar spine during extreme weight lifting. *Spine, 12,* 246-249.

Hansson T., Roos B., and Nachemson A. (1980) The bone mineral content and ultimate compressive strength of lumbar vertebrae. *Spine, 5,* 46-55.

Hansson T. H., Keller T. S., and M. M. Panjabi (1987) A study of the compressive properties of lumbar vertebral trabeculae: Effects of tissue characteristics. *Spine, 12,* 56-62.

Hantmann D. A., Vogel J. M., Donaldson C. L., Friedman R., Goldsmith R. S., and Hulley S. B. (1973) Attempts to prevent disuse osteoporosis by treatment with calcitonin, longitudinal compression and supplementary calcium and phosphate. *J. Clin. Endocrin. Metab., 36,* 845-858.

Hulley S. B., Vogel J. M., Donaldson C. L., Bayers J. H., Friedman R. J., and Rosen S. N. (1971) The effect of supplemental oral phosphate on the bone mineral changes during prolonged bed rest. *J. Clin. Invest., 50,* 2506-2518.

Issekutz B., Blizzard J., Birkhead N., and Rodahl K. (1966) Effect of prolonged bed rest on urinary calcium output. *J. Appl. Physiol., 21,* 1013-1020.

Jacobson P. C., Beaver W., Grubb S. A., Taft T. N., and Talmage R. V. (1984) Bone density in women: College athletes and older athletic women. *J. Orthop. Res., 2,* 328-332.

Jaekel E., Amtmann E., and Oyama J. (1977) Effect of chronic centrifugation on bone density of the rat. *Anat. Embryol., 151,* 223-232.

Jankovich J. P. (1971) *Structural Development of Bone in the Rat Under Earth Gravity, Simulated Weightlessness, Hypergravity and Mechanical Vibration.* NASA CR-1823. 140 pp.

Jaworski Z. F. G., Liskova-Kiar M., and Uhthoff H. K. (1980) Effects of long-term immobilisation on the pattern of bone loss in older dogs. *J. Bone Joint Surg., 62B,* 104-110.

Jones H. H., Priest J. D., Hayes W. C., Tichenor C. C., and Nagel D. A. (1977) Humeral hypertrophy in response to exercise. *J. Bone Joint Surg., 59A,* 204-208.

Kato S. and Ishiko T. (1966) Obstructed growth in children's bones due to excessive labor in remote corners. *Proc. Int. Congr. Sport Sci.,* p. 476.

Keller T. S. (1988) *Functional Adaptation of Bone During Growth and Altered Activity.* Ph.D. thesis, Vanderbilt Univ., Nashville, Tennessee. 435 pp.

Keller T. S. and Spengler D. M. (1989) Regulation of bone stress and strain in the immature and mature rat femur. *J. Biomechanics, 22,* 1115-1127.

Kiiskinen A. (1977) Physical training and connective tissue in young mice—Physical properties of Achilles tendons and long bones. *Growth, 41,* 123-137.

Kimura T., Amtmann E., Doden E., and Oyama J. (1979) Compressive strength of the rat femur as influenced by hypergravity. *J. Biomechanics, 12,* 361-365.

Krolner B. and Toft B. (1983) Vertebral bone loss: An unheeded side effect of therapeutic bed rest. *Clin. Sci., 64,* 537-540.

Krolner B., Toft B., Nielsen S. P., and Tondevold E. (1983) Physical exercise as prophylaxis against involutional vertebral bone loss: A controlled trial. *Clin. Sci., 64,* 541-546.

Lamb D. R., Van Huss W. D., Carrow R. E., Heusner W. W., Weber J. C., and Kertzer R. (1969) Effects of prepubertal physical training on growth, voluntary exercise, cholesterol and basal metabolism in rats. *Res. Q., 40,* 123-133.

Lanyon L. E. and Rubin C. T. (1984) Static vs. dynamic loads as an influence on bone remodeling. *J. Biomechanics, 17,* 897-905.

Lanyon L. E., Goodship A. E., Pye C. J., and MacFie J. H. (1982) Mechanically adaptive bone remodeling. *J. Biomechanics, 15,* 141-154.

Lockwood D. R., Lammert J. E., Vogel J. M., and Hulley S. B. (1973) Bone mineral loss during bed rest. In *Clinical Aspects of Metabolic Bone Disease* (B. Frame, A. M. Parfitt, and H. Duncan, eds.), pp. 261-265. Excerpta Medica, Amsterdam.

Margulies J. Y., Simkin A., Leichter I., Bivas A., Steinberg R., Giladi M., Stein M., Kashtan H., and Milgrom C. (1986) Effect of intense physical activity on the bone-mineral content in the lower limbs of young adults. *J. Bone Joint Surg., 68A,* 1090-1093.

Minaire P., Berard E., Meunier P. J., Edouard C., Goedert G., and Pilonchery G. (1981) Effects of disodium dichloromethylene diphosphanate on bone loss in paraplegic patients. *J. Clin. Invest., 68,* 1086-1092.

Minaire P., Edouard C., Arlot M., and Meunier P. J. (1984) Marrow changes in paraplegic patients. *Calcif. Tiss. Int., 36,* 338-340.

Minaire P., Meunier P., Edouard C., Bernard J., Courpron P., and Bourret J. (1974) Quantitative histological data on disuse osteoporosis. Comparison with biological data. *Calc. Tiss. Res., 17,* 57-73.

Nilsson B. E. and Westlin N. E. (1971) Bone density in athletes. *Clin. Orthop. Relat. Res., 77,* 179-182.

Nocogossian A. E. and Parker J. F. Jr. (1982) *Space Physiology and Medicine.* U.S. Govt. Printing Office, Washington, DC. 324 pp.

O'Connor J. A., Lanyon L. E., and MacFie H. (1982) The influence of strain rate on adaptive bone remodeling. *J. Biomechanics, 15,* 767-781.

Oyama J. (1975) Response and adaptation of beagle dogs to hyperactivity. In *COSPAR: Life Sciences and Space Research XIII* (P. H. A. Sneath, ed.), pp. 2-17. Akademie-Verlag, Berlin.

Oyama J. and Zeitman B. (1967) Tissue composition of rats exposed to chronic centrifugation. *Am. J. Physiol., 213,* 1305-1310.

Rambaut P. C. and Johnson R. S. (1979) Prolonged weightlessness and calcium loss in man. *Acta Astronaut., 6,* 1113-1122.

Rubin C. T. and Lanyon L. E. (1982) Limb mechanics as a function of speed and gait: A study of functional strains in the radius and tibia of horse and dog. *J. Exp. Biol., 101,* 187-211.

Rubin C. T. and Lanyon L. E. (1984) Regulation of bone formation by applied dynamic loads. *J. Bone Joint Surg., 66A,* 397-402.

Rubin C. T. and Lanyon L. E. (1985) Regulation of bone mass by mechanical strain magnitude. *Calcif. Tiss. Int., 37,* 411-417.

Rubin C. T. and Lanyon L. E. (1987) Osteoregulatory nature of mechanical stimuli: Function as a determinant for adaptive remodeling in bone. *J. Orthop. Res., 5,* 300-310.

Sandler H. and Vernikos J., eds. (1986) *Inactivity: Physiological Effects.* Academic, Orlando. 205 pp.

Saville P. D. and Smith R. (1966) Bone density, breaking force and leg muscle mass as functions of weight in bipedal rats. *Am. J. Phys. Anthropol., 25,* 35-40.

Saville P. D. and Whyte M. P. (1969) Muscle and bone hypertrophy. Positive effect of running exercise in the rat. *Clin. Orthop. Relat. Res., 65,* 81-88.

Schneider V. S. and McDonald J. (1984) Skeletal calcium homeostatis and countermeasures to prevent disuse osteoporosis. *Calcif. Tiss. Int., 36,* S151-S154.

Schultz A. B. and Anderson G. B. J. (1981) Analysis of loads on the lumbar spine. *Spine, 6,* 76-82.

Smith S. D. (1977) Femoral development in chronically centrifuged rats. *Aviat. Space Environ. Med., 48,* 828-835.

Steinhaus A. H. (1933) Chronic effects of exercise. *Physiol. Rev., 13,* 103-147.

Stupakov G. P., Kazeykin V. S., Koslovskiy A. P., and Korolev V. V. (1984) Evaluation of changes in human axial skeletal bone structures during long-term spaceflights. *Space Biol. Aerospace Med., 18,* 42-47.

Thompson D'Arcy W. (1942) *On Growth and Form.* Cambridge Univ., New York. 1116 pp.

Tipton C. M., Mathes R. D., and Maynard J. A. (1972) Influence of chronic exercise on rat bones. *Med. Sci. Sports, 4,* 55.

Vignon G., Meunier P., Pansu D., Bernard J., Chapuy P., Edouard C., and Courpron P. (1970) Enquet clinique et anatomique sur l'etiopathogenie de l'osteoporose senile. *Rev. Rhum. Mal. Osteo-Articulaires, 37,* 615-627.

Vogel J. M. (1971) Changes in bone mineral content of the Os Calcis induced by prolonged bed rest. In *Hypogravic and Hypodynamic Environments* (R. H. Murray and M. McCally, eds.), pp. 261-269. NASA Scientific and Technical Information Office, Washington, DC.

Wunder C. C., Welch R. C., and Cook K. M. (1979) Femur strength as influenced by growth, bone-length and gravity with the male rat. *J. Biomechanics, 12,* 501-507.