Endochondral Growth in Growth Plates of Three Species at Two Anatomical Locations Modulated by Mechanical Compression and Tension

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ABSTRACT: Sustained mechanical loading alters longitudinal growth of bones, and this growth sensitivity to load has been implicated in progression of skeletal deformities during growth. The objective of this study was to quantify the relationship between altered growth and different magnitudes of sustained altered stress in a diverse set of nonhuman growth plates. The sensitivity of endochondral growth to differing magnitudes of sustained compression or distraction stress was measured in growth plates of three species of immature animals (rats, rabbits, calves) at two anatomical locations (caudal vertebra and proximal tibia) with two different ages of rats and rabbits. An external loading apparatus was applied for 8 days, and growth was measured as the distance between fluorescent markers administered 24 and 48 h prior to euthanasia. An apparently linear relationship between stress and percentage growth modulation (percent difference between loaded and control growth plates) was found, with distraction accelerating growth and compression slowing growth. The growth-rate sensitivity to stress was between 9.2 and 23.9% per 0.1 MPa for different growth plates and averaged 17.1% per 0.1 MPa. The growth-rate sensitivity to stress differed between vertebrae and the proximal tibia (15 and 18.6% per 0.1 MPa, respectively). The range of control growth rates of different growth plates was large (30 microns/day for rat vertebrae to 366 microns/day for rabbit proximal tibia). The relatively small differences in growth-rate sensitivity to stress for a diverse set of growth plates suggest that these results might be generalized to other growth plates, including human. These data may be applicable to planning the management of progressive deformities in patients having residual growth. J Orthop Res 24:1327–1334, 2006

Keywords: endochondral growth; biomechanics; growth modulation; stress; Hueter-Volkmann law

INTRODUCTION

The progression of postnatal skeletal deformity, such as scoliosis[1,2] and tibia vara (Blount's disease),[3] is associated with mechanically modulated endochondral growth. Angular deformities are believed to produce asymmetrical stress distribution across growth plates, causing asymmetrical growth in a "vicious cycle." It is known that increased compression slows growth, and decreased compression or distraction accelerates it, according to principles attributed to Hueter,[4] Volkmann,[5] and Delpech.[6] However, the relationship between different stresses acting on growth plates and consequential altered growth is not well quantified.

Support for the Hueter-Volkmann principle has been obtained from animal studies,[7–10] and Bonnel et al.[11] reported the amount of growth suppression with four different levels of compressive stress on the rabbit distal femoral growth plate. Staples and other devices are surgically implanted across growth plates to inhibit their growth, and the magnitude of the stress that causes growth arrest has been estimated in human[12,13] and nonhuman[11,14] growth plates. It is unknown how different growth plates respond to differing levels of stress. Growth plates appear to be affected less by cyclic stress than by sustained stress.[8,15,16]

The primary aim of this study was to document the alteration of growth at two different anatomical growth plate locations, for three differing levels of sustained stress, in three different species, and for animals of differing ages. The secondary aim was to identify differences between the growth response to stress between species, anatomical location, and underlying growth rate that might help determine

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the likely growth–stress relationship in human growth plates.

MATERIALS AND METHODS

Growth plates at two anatomical sites (proximal tibia and caudal vertebra) were subjected to sustained compression or distraction stress in three animal species (rat, rabbit, calf) using an external loading apparatus (Fig. 1). The tibial growth plate only was used in rabbits, while both growth plates (tail vertebral and proximal tibial) were used in rats and calves. In rats and rabbits, two ages of animals were studied, with older animals having about 75% of the growth rate of younger animals. The two ages were identified by examining body mass growth curves for each species and assuming that there was a cubic power law relationship between increase in linear dimensions (longitudinal bone growth) and body mass during rapid skeletal growth. Some evidence for this power law for rabbits up to age 24 weeks was obtained by graphing data for tibial length in Masoud et al.[17]

The sustained stress magnitudes applied to each loaded growth plate had target values of either 0.1 MPa (distraction), 0 MPa (sham), −0.1 MPa (compression), or −0.2 MPa (high compression). The contralateral tibia and adjacent unloaded vertebrae provided internal controls for each animal, while the animals that had the apparatus installed, but without spring forces, provided the sham. Provisionally, five animals were used in each loading magnitude group, with some exceptions (three, four, or six animals per group) resulting from technical difficulties that occurred during the experiments. Thus data were included in this study from 41 rats, 39 rabbits, and 18 calves.

Prior to application of loading apparatus, animals were first acclimated to housing in the American Association for Accreditation of Laboratory Animals Care (AAALAC) accredited animal facilities for 6 days. Then pins were inserted under general anesthesia through the diaphysis and epiphysis of the right proximal tibia, and through tail vertebrae adjacent to the loaded tail vertebra (rats and calves only). The pins transfixed the tail or limb (except in the case of calf tibiae where bicortical threaded bone screws were used), and were attached to external loading plates that were linked by passing threaded rods through holes in the loading plates. Calibrated springs on these rods were tightened to a desired force level to achieve the desired stress magnitudes.

Each animal's body mass and spring lengths were measured and adjusted on days 2, 4, and 7. Animals were housed in individual cages provided with standard laboratory animal food and water ad libitum. Penicillin G (50 kU/kg) was administered prophylactically to rabbits and calves, starting on the day of surgery. Animals were euthanized 8 days after the installation of the loading apparatus. All live animal procedures were reviewed and preapproved by the University of Vermont Animal Care and Use Committee. After euthanasia, the loaded and within-animal control growth plates were excised, and blocks about 4-mm cube were cut from several representative regions of each growth plate.

Sprague-Dawley male rats were purchased from a single approved breeder. The loading apparatus[18] was installed at postnatal age 38 days (younger group) or at age 58 days (older group). The older animals had provisionally 75% of the growth rate of the younger animals. The apparatus was installed under general anesthesia (Ketamine 80 mg/kg and Xylazine 10 mg/kg) with postoperative pain control (Buprenorphine 0.05 mg/kg). The tail loading apparatus was attached via two percutaneously inserted 0.55-mm diameter stainless steel insect mounting pins to each of the Cd6 and Cd8 tail vertebrae, with both growth plates of the Cd7

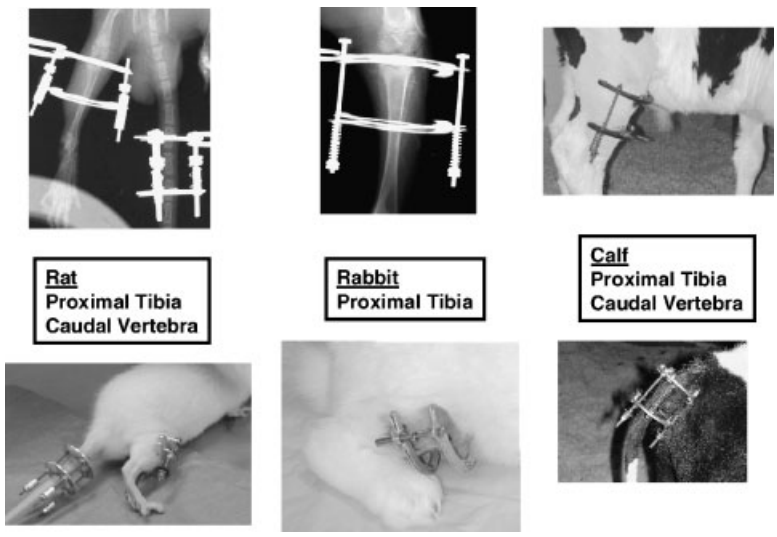

Figure 1. Photographs and radiographs of growth plate loading apparatus. Left: rat tibia and tail vertebrae; center: rabbit tibia; right: calf tibia and tail.

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vertebra considered as the loaded ones and the within-animal control growth plates were the caudal and cephalad growth plates of Cd5 and Cd9, respectively. Two 0.35-mm diameter pins (younger animals) or 0.45-mm diameter pins (older animals) were inserted into the proximal tibial epiphysis at approximately 45 degrees to the sagittal plane under direct visualization by surgical exposure of the ventral aspect of the tibia with a midline skin incision. Two diaphyseal pins were inserted percutaneously parallel to the epiphyseal pins at approximately one third of the tibial length from the tibiofemoral joint. Pins were presharpened to a three faced pyramid cutting point and inserted by hand using a "Starrett" chuck (Athol, MA) with a counterrotating action to avoid binding soft tissue structures. The pins were attached with cyanoacrylic glue (Loctite 4471) to aluminum loading plates. These plates were ring-shaped (tail apparatus) and horseshoe-shaped (tibial apparatus).

White New Zealand male rabbits were purchased from a single breeder. The loading apparatus was installed at the proximal tibia at age 41 days (younger group) or at age 62 days (older group). The apparatus was installed under general anesthesia (Ketamine 80 mg/kg, Xylazine 10 mg/kg, and Acepromazine 1 mg/kg) with postoperative pain control (Buprenorphine 0.05 mg/kg). The pins were 0.75-mm diameter 17-7PH annealed stainless steel installed by the same procedure as for rats. Pairs of horseshoe-shaped aluminum loading plates were clamped over the pins with screws, and the gaps were filled with cyanoacylic glue.

Male Holstein calves were obtained from a research dairy farm. At age 24 days, animals were given Xylazine 0.1 mg/kg and Ketamine 80 mg/kg, and intubated for Halothane gas anesthesia. They were supported in a canvas sling while under anesthesia. The tail apparatus was connected by two 1.5-mm Kirschner wires drilled percutaneously through each vertebra of the Cd4 and Cd6 vertebrae;[19] thus, the growth plates of the Cd5 vertebra were considered as the loaded ones, and the third and seventh as controls. The wires were then tensioned and clamped to 60-mm diameter Ilizarov rings (Richards, Memphis TN). For the tibia apparatus, taper threaded bone pins of 6-mm diameter (EBI, Parsippany NJ) were screwed percutaneously into the epiphysis (two pins) and diaphysis (two pins) after provisional pin insertion points and trajectories had been verified in intraoperative lateral radiographs. Pins were inserted into the anteromedial and anterolateral aspects after predrilling the bone and advanced until they emerged from the opposite cortex. Each pin was attached by a single clamp (EBI, Parsippany NJ) to the horseshoe-shaped external loading plate.

The spring lengths were adjusted to apply forces whose magnitude, divided by the estimated area, produced the desired stress of nominally 0.1, 0, −0.1, −0.2 MPa. The areas were not measured until the end of the experiments, so prior to initiating the experiments for each species an approximate relationship for estimating the area A for each animal was established by using the presumed power-law relationships: $A_t = A_{0t} * (W/W_0)^{2/3}$; and $A_v = A_{0v} * (W/W_0)^{2/3}$, where A_t represents tibial growth plate area, A_v the vertebral growth plate area, W represents the body mass of the animal, and A_{0t} and A_{0v} the mean areas measured directly from tibiae and vertebrae, respectively, removed previously from animals of each species and similar age, having an average mass of W_0. The 2/3 power-law was based on presumed geometrical similarity of each species during its postnatal growth. At the end of each experiment, when loaded and control bones were excised, the dimensions of each growth plate were measured directly by use of a vernier caliper. For caudal vertebrae, the transverse and dorsal–ventral diameters were measured and averaged. Area was then calculated as πr^2, where r was half of the average diameter. For tibiae, the area was estimated as half of the product of the transverse and dorsal–ventral dimensions (i.e., assuming a triangular shape). The mean measured growth plate areas of each species were used to estimate the actual average stress acting on the growth plates in each of the nominal stress groups. The preliminary estimated areas and the actual values for animals in these series are given in Table 1.

The fluorochromes Calcein (15 mg/kg) and Xylenol Orange (90 mg/kg) were administered systemically 48 and 24 h prior to death, respectively, to label the ossifying front under the growth plates. All live animal procedures were conducted at approximately the same time of day.

Blocks of tissue containing approximately 4×4 mm of growth plate were taken for growth measurement. Blocks were selected from the central, dorsal, ventral, right, and left regions of the vertebral growth plates and from the central, dorsal, ventral, medial and lateral regions of the tibial growth plates. In rats (because of the smaller size), the medial and lateral sides of vertebral growth plates only were sampled. In older rats, three sections (lateral, central, and medial) of tibial growth plates were sampled, whereas in the younger rats only medial and lateral tibial samples were selected. Each block was fixed,[20] dehydrated first in serial alcohols and then in propylene oxide, and embedded in Epon-812 Araldite (Electron Microscopy Sciences, Hatfield, PA) using serial dilutions in propylene oxide and vacuum.

Table 1. Tibial (A_t) and Vertebral (A_v) Growth Plate Area Values in mm^2 for Rats, Rabbits, and Calves Having Body Weight 125 g, 1250 g, and 45 kg, Respectively

	Initial Estimate		Final Value	
	A_t	A_v	A_t	A_v
Rat	17.3	9.9	19.0	9.0
Rabbit	100.6	—	110	—
Calf	3670	118	2600	115

These values were used to convert "nominal" to "actual" stresses according to the ratio between the initial estimates available at the beginning of the experiment, and the final values obtained from experimental animals at the time of dissection. Because the actual areas were not known until the end of the experiments, the spring forces for each animal was set to an expected "nominal" value (see Equation 1).

Growth measurements were made from mounted 1.5-micron thick sections (rats, rabbits) or from the cut surfaces of the blocks (for calves) that had been trimmed using a diamond faced wafering saw (Buehler Isomet, Buehler Ltd, Chicago, IL). In both cases, epifluorescent images were obtained at 1300×1030 pixel resolution using a Zeiss "Axioskop" microscope with $10\times$ lens. The microscope stage was rotated to align the presumed growth direction with the image frame. Images were captured with filtration for each of the two fluorescent labels, and the two images were subsequently "merged" digitally. These images were displayed using custom software on a computer screen, and measurements of the images were then made by "clicking" on boundaries of the fluorescent labeled bone with a computer "mouse." The coordinates of approximately 25 points in each label boundary were recorded, and a cubic spline function was fitted through these selected points. Twenty-four-hour growth (expressed as microns/day) was measured as the average separation of curved lines converted to microns by dividing by the image magnification (pixels per micron).

Sections were cut from the embedded blocks at depths separated by 100 microns, and typically two fields were selected from each section to provide growth measurements at several spatially separated locations, from which averages of the growth measurements were obtained. Based on initial variance estimates, provisionally 12 measurements of each growth plate from different locations were measured and averaged.

Statistical Methods

For group-wise comparisons, the growth of loaded and internal control growth plates for each animal were differenced and expressed as a percentage of the corresponding internal control value; thus, 100% indicated unaltered growth relative to the control. These percentage values were then averaged for each species, age group, and anatomical location (provisionally five animals per group). For each loaded group, these mean values were then expressed as a difference from the mean value obtained in the respective sham group to measure the degree of growth modulation in each group. Differences between the stress/growth-rate modulation relationships for groups of growth plates were examined by analysis of covariance. In these analyses the factors were: anatomical location (vertebra or proximal tibia); and species (rat, rabbit, calf); age (younger versus older animals), with stress (corrected values based on measured growth plate values) included as the covariate. Linear regression analyses were used to obtain overall relationships between growth modulation and applied stress. Statistical observations having a probability <0.05 were considered significant.

RESULTS

A wide range in the rates of measured growth was found in the growth plates, with averages ranging from 30 microns/day for older rat vertebrae to 366 microns/day for younger rabbit proximal tibiae (Table 2). However, across species relatively little variation in growth occurred at each anatomical site (tibiae and vertebrae) compared to the difference in size of the animals. In all cases the mean growth rate of compressed growth plates was decreased relative to the internal controls (Table 3). In most cases the growth plates under tensile stress had increased growth relative to controls (the two younger rats' growth plates were the exception), but this finding was complicated by the "sham" effect (altered growth associated with application of the loading apparatus, but without loads applied). Generally, the sham-loaded growth plates were observed to have lesser growth rates than their controls (Table 3). After compensating for the "sham" effect by subtracting the mean value from each of the corresponding values for loaded growth plates, growth decreased on average between -2 and 38% in the nominally -0.1 MPa compression groups, and decreased between 19 and 61% in the nominally -0.2 MPa compression groups. It was increased by 2 to 36% for distracted growth plates (Fig. 2).

After subtracting the sham effect, the regression relationship between proportional modulation of growth and actual stress (growth-rate sensitivity to stress, as listed in Table 4) did not differ by species and age of animal, but was significantly greater in tibiae than vertebrae; 18.6 and 15% per 0.1 MPa, respectively. Overall (for all animals and anatomical locations) the growth-rate sensitivity to stress averaged 17.1% per 0.1 MPa:

$$\beta = 1.71\ \text{MPa}^{-1} \text{ in a linear formulation}$$
$$G = G_m[1 + \beta(\sigma - \sigma_m)]$$

where G is the actual growth, G_m is the mean baseline growth (unaltered stress), σ is the actual stress on growth plate (compression negative), and σ_m is the mean prevailing (baseline) stress on growth plate.

Table 2. Mean Growth Rates (and SD) for Control Growth Plates, Measured in μm per day

	Younger Animals	Older Animals
Rat vertebra	45 (8) [$N = 24$]	30 (8) [$N = 17$]
Rat Tibia	251 (29) [$N = 19$]	206 (51) [$N = 16$]
Rabbit Tibia	366 (42) [$N = 19$]	257 (42) [$N = 20$]
Bovine vertebra	38 (13) [$N = 18$]	—
Bovine Tibia	179 (37) [$N = 18$]	—

N = provisionally 20.

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Table 3. Mean Growth Rate of Loaded and Control Growth Plates (μm per day, with Values of the Standard Deviation in Parentheses)

		Nominal Stress Group							
		0.1 MPa		0 MPa		−0.1 MPa		−0.2 MPa	
	Species (Age)	C	L	C	L	C	L	C	L
Vertebrae	rat (45 days)	46.7 (4.9) [*N* = 7]	46.3 (11) [*N* = 7]	46.6 (8) [*N* = 5]	44.5 (6) [*N* = 5]	39.5 (9) [*N* = 4]	32.1 (8) [*N* = 4]	44.0 (10) [*N* = 8]	24.3 (4) [*N* = 8]
	rat (65 days)	22.5 (1.9) [*N* = 3]	26.4 (1) [*N* = 3]	28.8 (3) [*N* = 5]	27.3 (5) [*N* = 5]	33.4 (10) [*N* = 5]	28.5 (13) [*N* = 5]	31.1 (10) [*N* = 4]	20.8 (5) [*N* = 4]
	calf (55 days)	28.4 (7.2) [*N* = 5]	30.1 (9) [*N* = 5]	37.8 (7) [*N* = 4]	32.8 (7) [*N* = 4]	47.2 (15) [*N* = 5]	35.4 (6) [*N* = 5]	37.4 (14) [*N* = 4]	18.1 (10) [*N* = 4]
Tibiae	rat (45 days)	244 (13) [*N* = 4]	226 (12) [*N* = 4]	256 (22) [*N* = 5]	231 (22) [*N* = 5]	236 (40) [*N* = 4]	162 (41) [*N* = 4]	261 (38) [*N* = 6]	187 (44) [*N* = 6]
	rat (65 days)	177 (12) [*N* = 3]	178 (13) [*N* = 3]	198 (12) [*N* = 5]	181 (5) [*N* = 5]	195 (35) [*N* = 4]	162 (37) [*N* = 4]	249 (90) [*N* = 4]	147 (51) [*N* = 4]
	rabbit (48 days)	355 (33) [*N* = 6]	426 (16) [*N* = 6]	385 (34) [*N* = 4]	426 (33) [*N* = 4]	366 (56) [*N* = 5]	329 (77) [*N* = 5]	362 (52) [*N* = 4]	298 (25) [*N* = 4]
	rabbit (69 days)	228 (15) [*N* = 5]	284 (51) [*N* = 5]	255 (55) [*N* = 5]	285 (68) [*N* = 5]	267 (35) [*N* = 5]	261 (25) [*N* = 5]	278 (48) [*N* = 5]	190 (48) [*N* = 5]
	calf (55 days)	169 (33) [*N* = 5]	256 (57) [*N* = 5]	185 (42) [*N* = 4]	182 (44) [*N* = 4]	156 (37) [*N* = 5]	105 (36) [*N* = 5]	206 (24) [*N* = 5]	102 (17) [*N* = 5]

The age is that of the animals at the time of growth measurement after administration of the second fluorochrome, that is 7 days after installation of the loading apparatus. Group size was nominally five animals.

Negative stress = compression; 0 MPa = sham; L = loaded growth plates; C = internal control growth plates.

DISCUSSION

The relationship between actual stress and percentage growth modulation (percent difference between loaded and control growth plates) appeared to be linear, and quantitatively similar relationships were found for all three species, for different ages of animals, and at both anatomical locations, although a significant difference between tibiae and vertebrae was found. All groups had a significant correlation between growth alteration and stress. As expected, distraction accelerated growth and compression slowed growth. Doubling the compressive stress approximately doubled the proportional reduction in growth rate. These findings were consistent over a substantial range in the measured growth rates of control growth plates that averaged from 30 microns/day (older rat vertebrae) to 366 microns/day (younger rabbit proximal tibia). More variation was evident between species in the growth modulation produced by distraction than by compression (Fig. 2); the reasons for this are unknown. Thus, extrapolation from these findings to humans may be more reliable for growth plate compression than for distraction.

Extrapolation from the average rate of growth suppression of 17.1% per 0.1 MPa stress suggests that a sustained compressive stress of 0.6 MPa would result in a 100% reduction in growth rate, that is, arrested growth, providing the stress–growth relationship follows the same linear relationship for higher compressive stresses. Studies directly addressing the stress required to arrest growth indicate values of 0.5[10] and 1 MPa,[12] more than 0.3 MPa,[11] more than 0.5[13] and 0.15 MPa[14] (the last may be underestimated by bending of the pins used for loading).

It is generally accepted that the progression of scoliosis deformity and of tibia vara during growth is in part mechanically mediated by asymmetrical loading of growth plates. "Overgrowth" of immature limb bones after a fracture might result from the unloading associated with pain and the favoring of that limb. Although usually attributed to vascular changes, clinical observations suggested that these are not necessarily a consistent explanation of the overgrowth phenomenon.[21]

In these experiments the loading was constant (sustained over time). A much smaller effect on growth occurs with cyclic loading.[8,15,16] Recent evidence[22] suggests that endochondral growth varies acutely and correlates inversely with activity level, but that over time the growth is relatively insensitive to cyclic loading. This differs from the

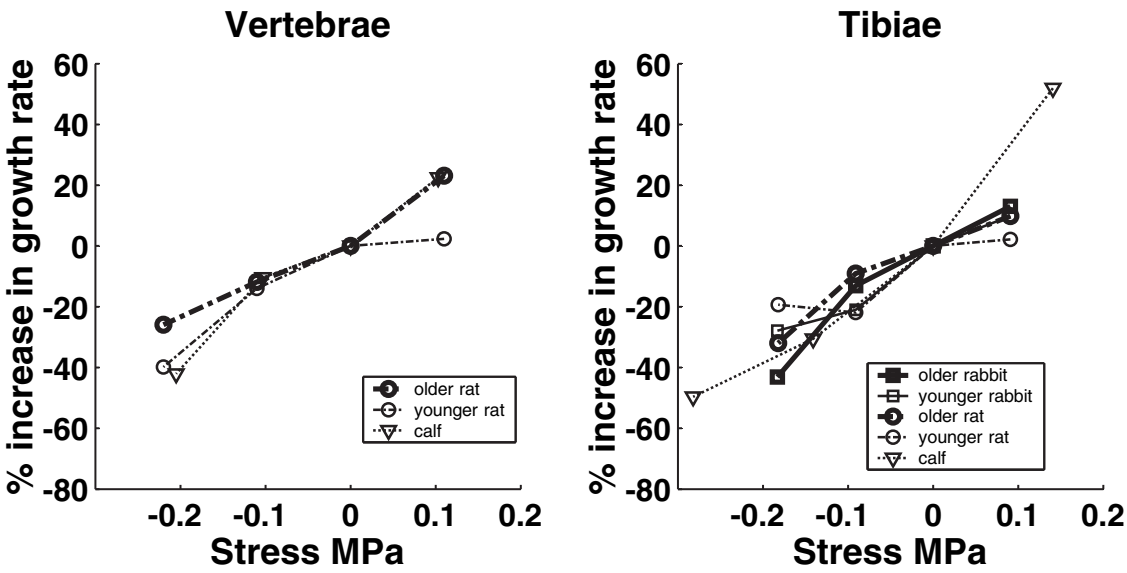

Figure 2. Relationship between applied stress and the percentage alteration in growth (relative to control) for the growth plates at two anatomical sites. The mean values from provisionally five animals are plotted. In each case, the mean values obtained from sham animals were subtracted (hence, all mean values at 0 MPa are zero).

mechanical stimulus required for bone remodeling (Wolff's law), where the cyclic loading is thought to provide the mechanical stimulus.[23]

The rate of endochondral growth in different growth plates has been found to depend on a combination of differing number and rate of proliferation of proliferative-zone cells and differing amount of cell enlargement and matrix synthesis in the hypertrophic zone.[24–26] Sustained mechanical loading in this rat model (both vertebral and tibial growth plates) altered these parameters of growth plate activity,[18] but the exact mechanisms of growth regulation and its mechanical modulation are unknown.

The magnitude of the sustained stress imposed in these experiments (up to nominally 0.2 MPa of compression) was comparable with the alterations in the stresses acting on human growth plates in deformities such as scoliosis and tibia vara. Estimates of the normal physiological stresses acting on human vertebral end plates[27] are in the range 0.8 to 0.9 MPa, with differential compressive stress associated with the scoliosis curvature on the order of $\pm 10\%$ of the total stress,[28] that is, about 0.1 MPa. Cook et al.[3] estimated that tibia vara increases the stress on the medial side of the tibia by up to 5 MPa, but this is likely an overestimate because of many simplifying assumptions about

Table 4. Growth-Rate Sensitivity to Stress (the Gradient of the Growth–Stress Relationships as Shown in Fig. 2) in Each Group of Growth Plates

Species	Growth Plate	Gradient (Percent per 0.1 MPa)	SE of Gradient Estimate
Calf	tail vertebra	19.7	4.8
Younger rat	tail vertebra	13.0	1.9
Older rat	tail vertebra	14.1	3.0
Calf	proximal tibia	23.9	2.6
Younger rat	proximal tibia	9.2	2.0
Older rat	proximal tibia	15.1	1.9
Younger rabbit	proximal tibia	14.7	2.6
Older rabbit	proximal tibia	19.9	2.9

The gradients were significantly different between anatomical locations (vertebrae vs. proximal tibiae), but within each location gradients were not different between species, or for younger vs. older animals).

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muscular activity. The compression forces acting on the rabbit knee have been estimated to be about three times bodyweight when hopping,[29] implying a stress at the growth plate of about 0.5 MPa. The mean ultimate tensile stress of 5-month-old bovine growth plates was reported as 1.4 MPa.[30]

In these animal studies, we initially assumed that the experimentally imposed forces were superimposed on (and did not alter) the prevailing physiological forces. The observed sham effect, which was significant, implied that the application of the apparatus alone did alter the underlying growth. This sham effect may have been due to altered loading of the growth plate associated with altered activity levels, altered blood flow, or other consequences of the surgical insult. The sham effect had to be taken into account in the analysis of the growth-modulation effect. In most cases sham-operated growth plates had decreased growth, with rabbit proximal tibiae being the exception. The duration of the experiments was 1 week, with this time frame based on known rates of chondrocyte turnover.[26] However, it may have exaggerated sham effects that might have been reduced after longer duration of postoperative healing. We assumed no alteration of the loading of control growth plates. In the tibiae, some gait or other activity changes and limited use of the tail might have occurred, confounding this assumption. The only subjective observations of such altered behavior were a "circumduction" gait in the rats and some limping in the calves.

For vertebral and tibial growth plates we relied on the stiffness of epiphyseal and diaphyseal bone to redistribute the forces applied through the transecting pins. Also, the apparatus was installed to distribute the loading springs as equally as possible around the growth plate.

The growth rates in our experiments ranged from 30 to 366 microns per day in species that complete skeletal growth more rapidly than humans. Spinal growth in children is approximately 10 mm per year or 13 microns per day for the entire spine (about 1 micron per day for each of 34 thoracic and lumbar growth plates),[31] with higher values expected during growth spurts. Spinal growth was estimated to be about 20 microns per day at age 8 and 16 microns per day at age 13.[32] For the human proximal tibia, the growth averages about 10 mm per year or 27 microns per day.[31] Therefore, these experiments in young, rapidly growing animals correspond to generally higher growth rates than those seen in postnatal human growth. Skeletal maturation takes longer in humans relative to all three animal species, for example, by a factor of about 20 in rabbits.[33]

The rationale for conservative management of progressive deformities during skeletal growth assumes a biomechanical mode of deformity progression (Hueter-Volkmann principle).[1–3] The present study provides a quantitative basis for understanding the mechanisms underlying the natural history and management of these conditions. Based on the consistency of the growth modulation effect measured in nonhuman species, our findings can be applied to estimate the expected response of any human growth plate to a specific stress level.

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