ENDOCHONDRAL GROWTH IN GROWTH PLATES OF THREE SPECIES AT TWO ANATOMICAL LOCATIONS MODULATED BY MECHANICAL COMPRESSION AND DISTRACTION

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INTRODUCTION:

Progression of post-natal skeletal deformity such as scoliosis during growth is often attributed to the 'Hueter-Volkmann Law' of mechanically modulated endochondral growth. However, the mechanically altered bone growth and disc remodeling are not well quantified. The aim of this study was to document the alteration of growth in growth plates for differing levels of sustained stress, different species and age of animals, and anatomical location. The long-term objective is to develop regression relationships, including histological measures of numbers of chondrocytes, their rate of proliferation and hypertrophic enlargement, that would permit extrapolation to any human growth plate.

MATERIALS AND METHODS:

Growth plates of three animal species (rat rabbit, calf) were subjected to sustained compression or distraction stress. The animals had pins inserted under general anesthesia through the diaphysis and epiphysis of the right proximal tibia, and (rats and calves) through tail vertebrae adjacent to a desired experimental (loaded) level. External plates were attached to the pins. Springs on rods connecting the plates were tightened to a desired force level to achieve stress magnitudes of -0.1 MPa (distraction), 0 MPa (Sham), or 0.1 or 0.2 MPa compression for different groups of animals. The contra-lateral tibia and the adjacent vertebrae served as internal controls for each animal. All live animal procedures were reviewed and approved by the University of Vermont Animal Care and Use Committee. After one week the animals were euthanized. Calcein and Xylenol Orange fluorochromes were administered systemically 48 and 24 hours prior to death to label the ossifying front under the growth plates. Sections of each growth plate were examined under fluorescent light, and 24-hour growth was measured as the separation of the two fluorescent labels.

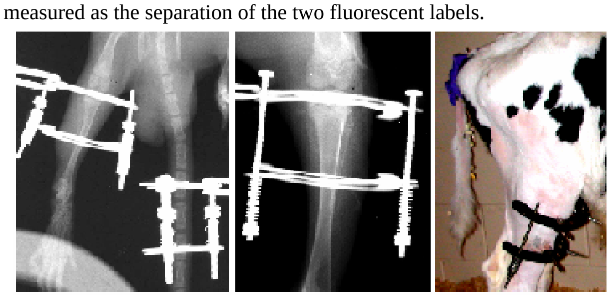

Figure 1: Growth plate loading apparatus. Left: radiograph of rat tibia and tail vertebrae; Center: radiograph of rabbit tibia ; Right: photograph, calf tail and tibia

RESULTS:

The mean values in Table 1 indicate that across both species and anatomical sites, and for animals of differing ages (growing at differing rates), the mechanical loading altered the rate of longitudinal growth by a similar proportional amount. Doubling the compressive stress approximately doubled the proportional reduction in growth rate. However, these results were complicated by a 'sham' effect (altered growth associated with application of the loading apparatus, but without loads applied). After compensating for the 'sham' effect by subtracting its value from each of the corresponding values for loaded growth plates, growth was found to be reduced by between 9 and 28 percent at 0.1 MPa compression, and by between 18 and 48 percent at 0.2 MPa compression (values in square brackets in Table 1). Because there was relatively little systematic difference between the proportional modulation of growth by anatomical site, species and age, the data were pooled to obtain a measure of growth modulation. Overall, the growth modulation due to altered stress averaged 18.7% per 0.1 MPa. i.e. $ß=1.87\ MPa^{-1}$ in a linear formulation $G = G_m(1-ß(s - s_m))$ where: G = actual growth; G_m = mean baseline growth (unaltered stress); s = stress on growth plate; s_m = mean prevailing (baseline) stress on growth plate.

DISCUSSION:

The rationale for conservative management of progressive deformities during skeletal growth assumes a biomechanical mode of deformity progression (Hueter-Volkmann principle). The present study provides a quantitative basis for these approaches. The mechanical influence on endochondral growth is very different from the remodeling effect (Wolff's law) where cyclic loading provides the mechanical stimulus [1]

Estimates of the stresses acting on vertebral growth plates [2] are in the range 0.8 to 0.9 MPa, with differential compressive stress associated with the scoliosis curvature was on the order of +/- 10% of the total stress, i.e. about 0.1 MPa. This was the magnitude of sustained stress used in the animal studies, indicating that the animal study data were in the appropriate range of loading relative to the stresses acting on human growth plates in deformities such as scoliosis.

In these animal studies it was 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 was probably due to altered mechanics, altered blood flow or other consequences of the surgical insult, and it had to be taken into account in the analysis of the growth-modulation effect.

Several novel treatment approaches (such as memory alloy stapling, innovative bracing concepts and muscle strengthening or temporary denervation) that presume the biomechanical mode of progression are available, or under development. Such improved treatments generally imply early interventions that are less destructive than multi-level spinal arthrodesis, so the ability to improve prognosis of progressive curves is key to their introduction, to avoid treating non-progressive curves.

Table 1. Mean growth of loaded growth plates expressed as a percentage of internal control [differences relative to sham values]. Group size was nominally 5 animals.
Negative stress = distraction; 0 MPa=sham

	Species (age)	-0.1 MPa	0 MPa	0.2 MPa	0.2 MPa
Vertebrae	rat (5 weeks)	96 [-4]	100	82 [-18]	56 [-44]
	rat (9 weeks)	114 [19]	95	86 [-9]	62 [-33]
	calf (6 weeks)	130 [43]	87	72 [-15]	48 [-39]
Tibiae	rat (5 weeks)	93 [4]	89	70 [-19]	71 [-18]
	rat (9 weeks)	101 [9]	92	82 [-9]	63 [-29]
	rabbit (6 weeks)	121 [10]	111	90 [-21]	79 [-32]
	rabbit (8 weeks)	125 [14]	111	100 [-11]	63 [-48]
	calf (6 weeks)	166 [71]	95	67 [-28]	48 [-47]

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[1] Rubin CT, Lanyon LE. Osteoregulatory nature of mechanical stimuli: Function as a determinant for adaptive remodeling in bone. J. Orthop Res. 1987; 5:300-310.
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