ABSTRACT INTRODUCTION
Mechanical loading and systemic intermittent parathyroid hormone (PTH) have been independently shown to stimulate bone formation\(1,2\). Clinical studies indicate PTH acts predominately at the vertebral bodies and at load-bearing sites of the appendicular skeleton\(1\). Studies exploring the relationship of PTH and mechanical loading in exclusively cancellous bone are lacking. We hypothesized mechanical loading combined with the intermittent administration of the systemic agent PTH would have an anabolic bone forming effect on cancellous bone greater than either stimulus delivered alone. We sought to determine if mechanical stimulation and systemic intermittent PTH administration would enhance cancellous bone formation in an in vivo rabbit model of mechanical loading.

METHODS:
One-hundred and four New Zealand White rabbits underwent surgical implantation of a custom loading device on the lateral aspect of the right distal femur. Half of the rabbits underwent sham operation with removal of cortical bone and implantation of a sham loading device on the contralateral left limb. In the remaining half, the left limb acted as a non-operated control. Half of the animals received 20 µg/kg PTH 5 days a week, for 4 weeks following surgery and core bone injury, as occurs at the microscopic level in osteoporosis and at the macroscopic level in cases of bone fracture.

RESULTS:
In placebo treated animals, BV/TV increased with mechanical loading over no-surgery control specimens (p<0.05) (Fig. 2). In the PTH treated animals, significant increases in BV/TV were noted in sham operated limbs and both load magnitudes (p<0.05). Further, the significant increase in BV/TV in sham operated limbs with PTH was not different from loaded limbs with PTH. Of note, no difference was seen in the no-surgery control group with the addition of PTH.

With respect to ultimate strength, in placebo treated animals sham operation and loading failed to induce a change compared to no-surgery controls. However, with the addition of PTH, increases in strength were seen in sham operated limbs and 1.0 MPa loaded limbs (Fig. 3) with the greatest increase seen in the sham group. Despite this trend these differences were not statistically significant (p=0.09). As with BV/TV, PTH did not change ultimate strength in the no-surgery control limbs.

DISCUSSION:
Consistent with Wolff’s Law, mechanical loading alone resulted in increased bone formation. Surprisingly, an anabolic bone response was not seen with PTH alone. However, when PTH was combined with loading a significant increase in bone formation resulted. Interestingly, this enhancement of bone formation was also present in sham operated limbs. Thus, the surgical procedure with removal of cortical bone, as performed on the sham operated and the loaded limbs, may have been the significant event that worked in concert with PTH to augment bone formation. Further, an event such as bone injury that primes the skeleton to PTH may be necessary, and certainly augments, the bone anabolic response to PTH. In our study, we speculate this injury was in the form of cortical bone removal from the distal femur.

These data suggest PTH may act more robustly at sites of bone injury, as occurs at the microscopic level in osteoporosis and at the macroscopic level in cases of bone fracture.

REFERENCES:

ACKNOWLEDGEMENTS
This project was funded by the Orthopaedic Research and Education Foundation Thomas M. Coffman Career Development Award, the Kirby Foundation, and the Lipstock Fellow Research Grant.

Fig. 1 Schematic representation of loading preparation.

Fig. 2 Bone volume fraction with placebo (blue) and PTH (gold).

Fig. 3 Ultimate strength with placebo (blue) and PTH (gold).