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134.1 Authors

Rubin CT, Lanyon LE.

134.2 Reference

J Bone Joint Surg Am. 1984;66:397–402.

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134.4 Abstract

In vivo external loads were applied to a functionally isolated avian-bone preparation to evaluate the following data

1. Removal of load-bearing resulted in substantial endosteally bone remodelling, intracortically, and, to a lesser extent, periosteally. The balance of this remodelling was negative – bone mass declined. This suggests that functional load-bearing prevents a remodelling process that would lead to disuse osteoporosis.
2. Four consecutive cycles a day of an externally applied load that prevented physiological strain magnitudes but allowed an altered strain distribution prevented remodelling and was associated with no change in bone mass. A small exposure to, or the first effect of, a suitable dynamic strain regimen appears to be sufficient to prevent

the negatively balanced remodelling that is responsible for disuse osteoporosis.

3. Thirty-six 0.5-Hz cycles per day of the same load routine also prevented intracortical resorption but was associated with substantial periosteal and endosteal new-bone formation. Over a 6 week period, bone mineral content increased to between 133 and 143 % of the original value. Physiological levels of strain applied with an abnormal strain distribution can produce an osteogenic stimulus that is able to increase bone mass. Neither the size nor the nature of the bone changes that were observed were affected by any additional increase in the number of load cycles from 36 to 1,800.

The sensitivity of bone remodelling in this model to prevailing mechanical circumstances is apparent. Functional levels of bone mass in patients may only be maintained under the effects of continued load-bearing. The osteogenic effect of an unusual strain distribution suggests that a varied exercise program may provoke a greater hypertrophic response than an exercise program that is restricted. A substantial osteogenic response may be achieved after remarkably few cycles of loading.

134.5 Summary

Rubin and Lanyon confirmed that bone remodelling was responsive to dynamic strains within the matrix with experiments showing a progressively increasing osteogenic response to progressively increasing loads. In these experiments a bone was deprived of its normal loading in vivo and the subsequent disuse interrupted by daily intermittent loading. Strains of less than 1,000 microstrain were associated with loss of bone, whereas higher strains resulted in a proportional increase in bone area.

The beneficial effect of external loading on the ulna of roosters were assessed by measuring strains across the osteotomy and amount of bone formation by histology, microradiography and photo-densitometry.

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134.6 Citations

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134.7 Related References

1. Turner CH, Owan I, Takano Y. Mechanotransduction in bone: role of strain rate. *Am J Physiol*. 1995;269(3):E438–42.
2. Lanyon LE. Functional strain as a determinant for bone remodeling. *Calcif Tissue Int*. 1984;36(1):S56–61.
3. Turner CH. Three rules for bone adaptation to mechanical stimuli. *Bone*. 1998;23(5):399–407.

134.8 Key Message

This study showed the effects of varied loads on bone formation and evidence for the need for loading to maintain bone mass. It was the first study of its kind showing that isolated specific loading of a diaphysis *in vivo*, is related to the amount of healing and remodelling.

134.9 Why Is It Important

In 1964, Frost showed that not only was mechanical strain the principal determinant of bone adaptation, but that a “minimum effective strain” threshold must be surpassed before bone adaptation would occur [1]. In 1971 Hert and coworkers showed that dynamic, but not static, strains increased bone formation in rabbits. Dynamic strains thus appeared to be the primary stimulus of bone adaptation.

This article published in 1984 by Rubin and Lanyon was important as it confirmed Liskova and Hert’s [2] finding using an isolated avian ulna model. These investigators also demonstrated that bone adaptation in the isolated avian ulna model was directly proportional to the peak applied strain.

Rubin and McLeod went on to demonstrate that low magnitude mechanical stimuli was incapable of maintaining bone mass at 1 Hz but can induce significant new bone formation when loading was applied at 20 Hz [3].

Lanyon and Rubin’s experimental evidence established the “rules” of bone mechanosensitivity. The beneficial effects of intermittent loading of bone over short periods of time was clearly demonstrated by the authors.

134.10 Strengths

This project was an *in vivo* study with clear protocols to identify the effects of measured external loading for short periods of time on bone healing and remodelling. Strains

through each bone were measured and correlated with amount of bone formation with histology, microradiography and photo-absorption densitometry.

134.11 Weaknesses

This study is an animal model on the effects of loading on only two roosters. A limitation of this model is that it was surgically invasive, and thus may have introduced unintended side effects related to inflammation and soft tissue damage.

This model has been criticized because it causes woven bone formation, which is often considered to be a pathological response [4, 5].

134.12 Relevance

Functional bone adaptation, the relationship linking mechanical loading and bone structure, was recognized by Roux and Wolff well over a century ago [6–8]. However, only since the 1960s have advances in animal models and strain measurement techniques allowed researchers to explore this relationship with a controlled experimental approach [9].

A series of now-classic papers from the 1960s through the 1980s appeared to provide clear evidence for bone functional adaptation to mechanical loading and unloading using various experimental animal models.

A number of seminal studies from Lanyon and Rubin led to the overarching paradigms of cortical bone mechanoresponsiveness [10, 11]. The following “rules” relating mechanical loading and cortical bone formation are widely accepted.

1. Bone adaptation is driven by dynamic, rather than static, loading
2. There exists a minimum strain threshold. Applied loads that produce strains below this threshold induce no change in bone formation while loads above this threshold increase bone formation in a dose-dependent manner. The exact magnitude of the threshold is context dependent and may vary based on factors like species, age, sex, and loading model.
3. Third, the anabolic effects of adaptive loading, plateau after a relatively low number of cycles (<100 cycles per day)
4. Only a short duration of mechanical loading is necessary to initiate an adaptive response. Extending the loading duration has a diminishing effect on further bone adaptation.
5. Bone cells accommodate to a customary mechanical loading environment, making them less responsive to routine loading signals

The clinical relevance of this study is that short periods of bone loading is sufficient to promote bone healing and bone formation. Further similar studies have confirmed the beneficial effects of intermittent loading which confirms that there is no necessity for long time periods of repetitive loading [12, 13].

Bone cells must be in a receptive state to detect a stimulus. Bone cells desensitize rapidly to mechanical stimuli, to the point where subsequent mechanical signals that would otherwise be osteogenic are largely ignored by the cell. Animal limb bones loaded in vivo exhibit a large gain in bone mass when administered relatively few (10–50) load cycles per day, but as that number is increased beyond 50 cycles/day, very little additional bone is formed [14]. These data suggest that the cells are receptive to the first 50 or so load cycles (first few minutes of loading), but as the loading bout is continued uninterrupted the cellular response is greatly diminished.

Pead et al. [15] demonstrated the direct transformation of normal, quiescent, adult periosteum to active bone formation with a single period of dynamic loading.

References

1. Turner CH. Three rules for bone adaptation to mechanical stimuli. *Bone*. 1998;23(5):399–407; Frost HM. The laws of bone structure. Springfield: Thomas; 1964.
2. Liskova M, Hert J. Reaction of bone to mechanical stimuli. 2. Periosteal and endosteal reaction of tibial diaphysis in rabbit to intermittent loading. *Folia morphologica*. 1971;19(3):301.
3. Hsieh YF, Turner CH. Effects of loading frequency on mechanically induced bone formation. *J Bone Miner Res*. 2001;16(5):918–24.
4. Forwood MR, Turner CH. The response of rat tibiae to incremental bouts of mechanical loading: a quantum concept for bone formation. *Bone*. 2003;15(6):603–9.
5. Turner CH, Forwood MR, Rho JY, Yoshikawa T. Mechanical loading thresholds for lamellar and woven bone formation. *J Bone Miner Res*. 1994;9(1):87–97.
6. Frost HM. Skeletal structural adaptations to mechanical usage (SATMU): 1. Redefining Wolff's law: the bone modeling problem. *Anat Rec*. 2004;226(4):403–13.
7. Frost HM. Skeletal structural adaptations to mechanical usage (SATMU): 2. Redefining Wolff's law: the remodeling problem. *Anat Rec*. 2004;226(4):414–22.
8. Ruff C, Holt B, Trinkaus E. Who's Afraid of the big bad Wolff?: 'Wolff's law' and bone functional adaptation. *Am J Phys Anthropol*. 2006;129(4):484–98.
9. Turner CH, Owan I, Takano Y. Mechanotransduction in bone: role of strain rate. *Am J Physiol*. 1995;269(3):E438–42.
10. McBride SH, Silva MJ. Adaptive and injury response of bone to mechanical loading. *Bonekey Osteovision*. 2012;1:192.
11. Turner CH. Three rules for bone adaptation to mechanical stimuli. *Bone*. 1998;23(5):399–407.
12. Judex S, Gross TS, Zernicke RF. Strain gradients correlate with sites of exercise-induced bone-forming surfaces in the adult skeleton. *J Bone Miner Res*. 1997;12(10):1737–45.
13. Lanyon LE. Control of bone architecture by functional load bearing. *J Bone Miner Res*. 1992;7 Suppl 2:S369–75.
14. Robling AG, Hinant FM, Burr DB, Turner CH. Improved bone structure and strength after long-term mechanical loading is greatest if loading is separated into short bouts. *J Bone Miner Res*. 2002;17(8):1545–54.
15. Pead MJ, Skerry TM, Lanyon LE. Direct transformation from quiescence to bone formation in the adult periosteum following a single brief period of bone loading. *J Bone Miner Res*. 1988;3(6):647–56.