

## A Little Shake Up for Healthy Bones

*Using a vibrating platform and a NASA-developed technique to simulate the effects of microgravity on the musculoskeletal system in the rat, Clinton Rubin and Stefan Judex have shown that the bone loss caused by unloading can be counteracted by ten minutes of low magnitude, high frequency mechanical stimulation per day. This approach shows strong potential for inhibiting space flight-related bone loss and treating osteoporosis.*

**B**one loss is a serious problem both in space and on the ground. In microgravity, astronauts can lose bone mass at rates of up to 1.6 percent per month, even with the drug and exercise countermeasures tried to date. While it is not known whether deterioration of weight-bearing bone continues indefinitely at these high rates, this risk to crew health and well-being has led the Space Studies Board at the National Research Council to identify microgravity-induced bone loss as the primary physiological obstacle to long-duration space travel.

Back on Earth, bone loss has a number of causes. Osteoporosis is generally associated with aging or menopause but it can also arise under other conditions such as prolonged bed rest, lack of using the musculoskeletal system such as occurs in a sedentary life style, steroid use, or malnutrition. The number of sufferers is in the tens of millions in the United States alone, which costs our health services over 20 billion dollars each year. So, it is not surprising that Clinton Rubin's recent findings have drawn a good deal of attention. His NASA-funded research has shown that placing rats on a vibrating platform for 10 minutes per day can mitigate the bone loss resulting from unloading of the musculoskeletal system.

### Is Frequency More Important Than Force?

Bone is dynamic tissue. It is continually broken down and rebuilt in a cycle of two separate processes known as resorption and formation. Normally, these processes are closely linked, but conditions such as aging, bed rest, and space flight can throw the cycle out of balance. Resorption gets the upper hand and bone loss results.

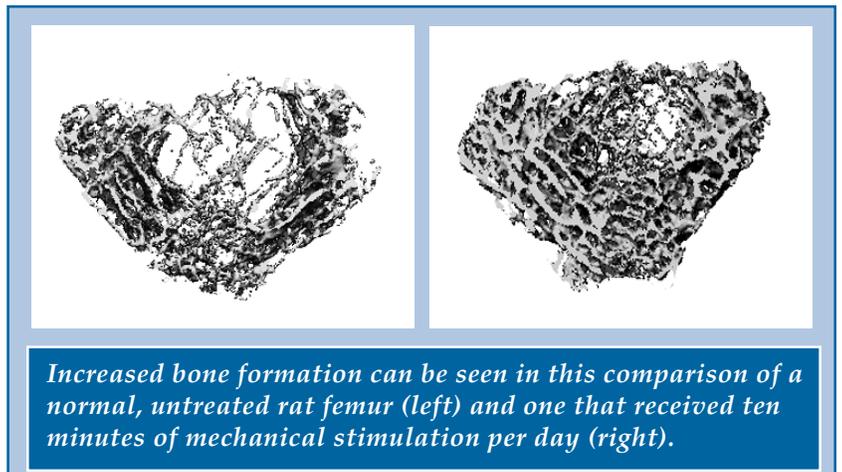
The standard view has been that large magnitude forces like those we experience while running or lifting weights are the best way to maintain healthy bones or counteract conditions that result in bone loss. It is becoming clear, however, that under space flight conditions, the kinds of load-bearing exercise employed to date are not as effective a countermeasure as had been anticipated.

Rubin and Judex, based at the State University of New York at Stony Brook, have taken a different approach. They believe that as important as the high magnitude, low frequency forces of exercise are the low magnitude, high frequency forces that our bones experience continually under more "omnipresent" conditions such as standing. Our muscles generate these forces when we sit, stand, and walk in order to coordinate movement and to maintain balance and posture. In a study funded through the NASA Biomedical Research and Countermeasures program, the Stony Brook researchers used rats to determine whether these stimuli could counteract reduced bone formation levels resulting from disuse. Their results show that they can.

### Proving the Point in Rats

The study used five groups of rats. The control group was allowed to move freely about and provided a baseline for normal bone formation rates. A second group was also allowed normal activity but experienced ten minutes per day of low magnitude, high frequency forces. The mechanical stimulation was delivered by placing the rats in a standard cage with a vibrating floor. The magnitude of this stimulus was such that a human would hardly notice it.

The remaining experimental groups all underwent variations on an unloading regimen. This was accomplished using a hindlimb tail suspension technique



developed by Emily Morey-Holton at the NASA Ames Research Center to mimic microgravity effects on the musculoskeletal system. With this technique, rodents can move about their cages, but only their forelimbs can touch the ground, thus reducing weight bearing on the hindlimbs. The unloaded group received continuous hindlimb suspension for the duration of the four-week study as a measure of total unloading. The unloaded plus weight-bearing group received continuous hindlimb suspension interrupted by ten minutes of normal weight-bearing per day. The unloaded plus mechanical stimulation group received continuous hindlimb suspension interrupted by ten minutes of low magnitude, high frequency stimulation per day (during stimulation, the animals were also free to roam their cage).

These investigators found that unloading plus ten minutes of daily weight-bearing resulted in bone formation rates only marginally better than total unloading. On the other hand, unloading plus mechanical stimulation resulted in bone formation rates roughly equivalent to normal activity. Coupling normal activity with mechanical stimulation resulted in rates nearly double those of the baseline control group.

These results clearly indicate that low magnitude, high frequency forces foster bone formation and have the potential to counteract the bone loss associated with microgravity, unloading, and osteoporosis. Additional animal studies with sheep, mice, and turkeys, as well as pilot studies with humans, support this conclusion.

### Advantages Over Existing Countermeasures

Osteoporosis is an insidious disease that—on Earth—takes several decades to become symptomatic, while in space the bone loss is so severe that a flight to Mars may be hampered due to skeletal distress. If these findings do translate to humans, this form of therapy might have several advantages over existing countermeasures, namely load-bearing exercise and pharmaceuticals. As already mentioned, exercise countermeasures employed to date have shown only limited effectiveness in space. In addition, it occupies valuable crew time and astronauts find the equipment cumbersome. For many on Earth, regular exercise appropriate for bone formation can be difficult or impossible due to medical conditions.

Drug-based countermeasures tend to focus on reducing bone loss by inhibiting resorption rather than stimulating bone formation. While this helps to conserve overall bone mass, bone quality can be compromised since it is the cycle of resorption and formation that maintains the health and strength of bones. Drugs also do nothing to specifically target the

weight-bearing bones that are most affected by disuse. “Another potential advantage of standing on this device,” says Rubin, is that, like exercise, “it is self-targeted to the areas that need it most—weight-bearing bones.” In addition, the device has no apparent side effects or drug interaction issues.

The vibration countermeasure would be easy to implement in space or on Earth. The device which generates the stimulus looks, as Rubin says, like a pizza box. A person simply stands on this inexpensive vibrating box for

several minutes each day to inhibit bone loss. In microgravity, something would be needed to hold the astronaut against the device,

but space and energy requirements would be extremely low, and the astronaut could perform other duties while receiving treatment. The challenge will be to effectively administer the vibration therapy to the entire musculoskeletal system in the absence of gravity.



*The current exercise countermeasures being performed in space could be supplemented by administering vibration therapy to the body to help counteract bone loss. Kenneth Bowersox exercises on ISS (NASA photo ISS006-E-11016).*

Rubin has a full research slate ahead. He has just begun working with NASA on plans to test this intervention on astronauts in the International Space Station. With upcoming studies funded by NASA and the National Space Biomedical Research Institute, these researchers along with their colleague Michael Hadjiargyrou hope to explain why some individuals are more susceptible to bone loss than others by using mice to explore the genetic mechanisms at work and to map the active genes. In addition, these investigators are working with the National Institutes of Health to investigate patient compliance, and subsequently set up a Phase 3 clinical trial with post-menopausal women to demonstrate the therapeutic value of low magnitude, high frequency forces for the treatment of osteoporosis.

### References

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