Good vibrations:
combating bone loss in space

Recent research suggests that bone loss caused by microgravity and old age could be counteracted with daily exposure to low magnitude, high frequency mechanical stimulation. Potentially, this technique could inhibit bone loss during long-duration spaceflight and be an effective treatment for osteoporosis on Earth.

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Humans have been venturing into space for over 40 years. While early concerns regarding breathing, swallowing and the elimination of body waste have now been allayed, moving away from the relative protection of the Earth is inevitably accompanied by a number of physiological complications. These include a redistribution of body fluids, a reduction in cardiac output, the atrophying of muscle, and the demineralisation of bone: the 'price of a ticket into space' (Hawkey, 2003).

Of these, bone loss is commonly regarded as the biggest obstacle to overcome when planning long-duration space missions and is likely to be the principal physiological hurdle to humans' extended presence in space. This article assesses the implications of spaceflight on bone health and how this is mirrored in the ageing process on Earth. It also discusses the effectiveness of current countermeasures in combating bone degradation, and how new research could hold the key both to a successful excursion to Mars and to the suppression of osteoporosis. (Figures 1a and 1b show the dramatic difference between healthy and osteoporotic bone.)

Bone loss

Despite the relatively small number of humans who have flown in space and the limited duration of missions to date, sufficient data have been collected to raise concerns regarding the fracture risk of space crews during skeletal loading on their return to Earth (1g), during activities on the surface of Mars (0.38g) and on the moon (0.16g). During space flights lasting longer than one month, astronauts undergo significant losses of bone mass and 'bone mineral density' (BMD) in the weight-bearing areas of the skeleton, particularly the spine and lower limbs. Quantitative computed tomography (QCT) scans of the spine of one cosmonaut after a 366-day mission showed a 10% loss of bone mass in the first three lumbar vertebrae, while results from dual x-ray absorptiometry (DXA) scans revealed that Russian cosmonauts suffered regional bone loss of up to 1.6% per month during missions lasting from four to 15 months.

The seriousness of the losses in BMD during spaceflight becomes particularly evident when compared with the losses arising from ageing on Earth. On average, the rate of BMD loss for the proximal femur and for the lumbar vertebrae in both men and women over 55 years of age is approximately 0.5-1% per year. The rates of loss from the same skeletal areas during spaceflight are significantly greater, at approximately 1-2% per month. For comparison, while ageing from 50 to 80 years, a woman can expect to lose 20% of BMD from the vulnerable neck of the femur. This degree of loss is likely to result from a single year of spaceflight.

The mechanism by which astronauts lose this bone is poorly understood. It is unclear whether the decrease in bone mass is associated with increased resorption (caused by heightened osteoclast activity: Figure 2), decreased bone formation (caused by a reduction in osteoblast activity), or both. Even though the mechanisms responsible for bone loss in ageing and in spaceflight may well be different, the study of the observed changes in either case may be of benefit to the other. Any countermeasure that is successful in space could significantly benefit the ageing population on Earth.

Active...?

For over 40 years, exercise countermeasures, designed to maintain bone health,

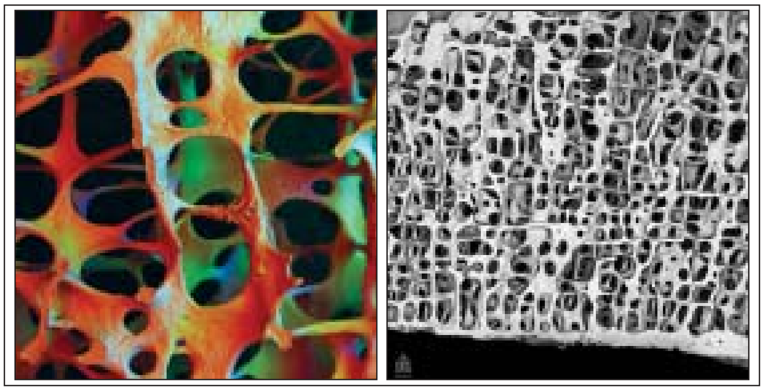


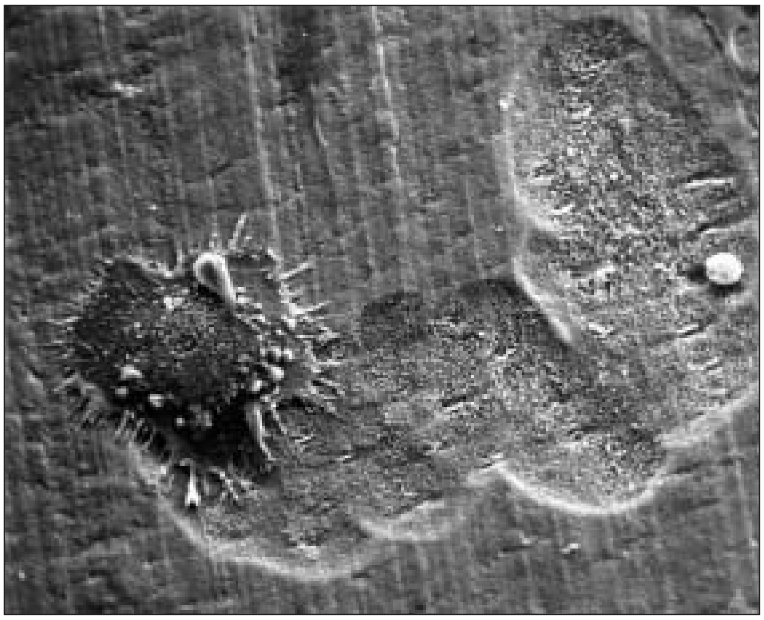
Figure 1a (left). Osteoporotic bone architecture of the 4th lumbar vertebra (Alan Boyde/Bone Research Society). **Figure 1b** (right). Normal bone architecture of the 4th lumbar vertebra (Alan Boyde/Bone Research Society)

have focused on large magnitude forces similar to those we experience on Earth during activities such as running or lifting weights. Although these measures have reduced the amount of bone lost, they have by no means prevented it; the types of load-bearing exercises used have been nowhere near as effective as had been anticipated. Crews on the International Space Station (ISS) currently have 2.5 hours of exercise training incorporated into their daily schedules, utilising a variety of devices:

- Interim Resistive Exercise Device (IRED)
- Treadmill with Vibration and Isolation Stabilisation (TVIS)
- Cycle Ergometer with Vibration and Isolation Stabilisation (CEVIS)

Based on 70-85% of their pre-flight capacity, astronauts undertake a programme that includes 90 minutes of resistive exercise on the IRED (Figure 3) and 60 minutes of aerobic activity on the TVIS (Figure 4).

Figure 2. Osteoclast absorbing bone (Alan Boyde/Bone Research Society).



Information regarding the effectiveness of these devices and training regimes is limited, but it appears from preliminary data collected during expeditions to the ISS that little progress has been made in the prevention of bone loss (Hawkey, 2006). Other studies using force-measuring insoles suggest that neither the load, nor the duration, of treadmill exercise in the current ISS programme is adequate to replace exercise carried out under Earth's gravity.

Bone loss is not only a significant problem for astronauts on missions in microgravity, but also for the ageing population on Earth. Osteoporosis on Earth is associated with a higher rate of fractures, increased pain, and a rise in morbidity and mortality. Load-bearing exercise training on Earth has been used relatively successfully to counter bone loss, with certain activities (such as running, high impact aerobics and weight training) appropriate not only for maintaining bone, but, in some instances, actually increasing BMD. However, for many with a range of medical conditions, and especially for older people, the types of exercise conducive to bone formation can be difficult or even impossible.

… or passive?

With traditional high impact activities being nowhere near as effective as had been anticipated, is it time for a completely new approach? Recent findings, using animal and human subjects, suggest that daily exposure to short periods (<20mins) of extremely low-magnitude (<1g) mechanical signals, at a high frequency (15-35Hz), can maintain bone health in some populations, and actually stimulate bone formation in others. Early studies conducted on ovariectomized rats have demonstrated that vibration stimulation is effective in maintaining BMD six weeks post-ovariectomy. Other animal investigations support this, indicating that vibration therapy is capable of initiating new bone formation, as well as inhibiting the bone loss of disuse, inhibition, or reversal of osteopenia (Rubin *et al*, 2001).

Preliminary findings of studies conducted on humans are also encouraging. High frequency, low-level mechanical signals can be safely and effectively transmitted to the hips and spine. Studies on children with cerebral palsy, on girls with extremely low BMD and on women who have recently undergone menopause, have all indicated that this unique biomechanical intervention may provide a means of successfully treating osteoporosis (Rubin *et al*, 2004).

Other studies appear to show that resistive vibration exercise completely prevents bone loss in healthy humans during prolonged bed-rest (an accepted analogue for spaceflight), with those exposed to the stimulation maintaining their BMD, compared to a 4% loss in control subjects' BMD (Rittweger and Felsenberg, 2004).

The new vibration therapy treatment would have several advantages over existing exercise countermeasures. Current devices are expensive, inherently complicated and difficult to maintain; astronauts find them cumbersome and uncomfortable to use. In contrast, the vibrating platform is a very simple and relatively inexpensive device that can be easily implemented both on Earth (Figure 5) and in space, although cables or bungee cords would be needed to keep the astronaut in contact with the platform. The platform itself occupies a minimal area and can be operated efficiently following only basic training. Capacity and energy requirements would be extremely low and it is possible that the astronaut would be able to perform other duties while receiving treatment. The reduced need for time on the device would also mean that other duties (such as medical or scientific experiments) could be conducted more efficiently.

The future

Future plans for human spaceflight are now primarily centred on a mission to the planet Mars. With a mission duration of at least two years, and no indication that Mars' gravity could aid in the restoration of BMD, a particularly worrying scenario could unfold. A fracture occurring on the planet would have serious consequences both for the individual and for the rest of the crew. As well as the limited availability of medical resources, there is the possible inhibition of fracture repair and of the reduced immune responses associated with weightlessness. There will also be a consequential loss of functionality in terms of the crew member's skills and duties and an increased workload on the remaining crew members.

It is not clear whether current countermeasures would be sufficient to prevent this scenario from occurring. Results from Earth-based studies however, suggest that a new vibration device could be a possible solution. Further research is required in order to confirm and evaluate the efficacy of different vibration regimens and to successfully develop vibrating platforms that are easier to use and more cost-effective. Considering the anabolic potential of these low level signals, and that they can be delivered to sites at greatest risk of fracture, a key step has been made in the development of a non-invasive, non-pharmacological intervention for osteoporosis. If successful, this technique could assist with the management of human conditions of increased bone turnover and bone loss (e.g. postmenopausal and disuse osteoporosis) and could be a possible countermeasure to bone loss during a mission to Mars – and back again.

Figure 3. IRED in use on the ISS (NASA).

Figure 4. TVIS in use on the ISS (NASA).

Figure 5. The vibrating platform in use (Adam Hawkey/University of Wolverhampton).

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