# Bone strength loss during long-term bed rest is related to bone loading history

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**INTRODUCTION**

Bed rest studies are an accepted model for simulating bone loss due to microgravity during space flights. In a previous 60 days bed rest study, we investigated the loss of bone mass and the microstructural degeneration at the distal radius and tibia using a high-resolution (HR) pQCT device[1]. In combination with micro-finite element (micro-FE) analyses, it was possible to also quantify the loss of strength during bed rest[2]. In that study large variations in loss of bone strength were found between subjects. For some subjects no loss of strength was found whereas for others strength was reduced by 6.5%. Although these values are small and thus may not increase the risk of fracture, it may cause premature age-related osteoporosis and understanding the fundamental nature of the skeletal response to unloading is of great interest to develop countermeasures for overcoming the adverse effects of microgravity during spaceflights.

In this study we investigate if the variation in loss of bone strength between subjects as observed in the earlier bed rest study could be related to their activity level prior to the bed rest. Since we expect that subjects that were more active would be more affected by the disuse, we hypothesized that the loss of bone strength is positively correlated to the physical activity of the subjects.

As the activity level of the subjects prior to the bed rest study was not known, we used a recently developed method to estimate the bone loading history based on the bone architecture and correlated that with the loss in bone strength measured in the bed rest study to test our hypothesis.

**MATERIALS AND METHODS**

HR-pQCT *in vivo* measurements from a long-term bed rest study as part of the Women International Space for Exploration (WISE-2005) project were used. In this project, healthy women ($n$ = 8) aged 25 to 40 years underwent 6° head-down tilt bed rest for 60 days. Distal tibia was scanned at the beginning and the end of this period with an isotropic resolution of 82 µm. Bone strength was calculated using micro-FE and a failure criterion where failure is expected if 2% of bone is strained beyond 7000 µstrain. Since the reproducibility of this approach is around 1.7%[3] we only considered subjects for which the loss of strength exceeded this value for the correlation.

To estimate the loading history, a previously developed bone loading estimation algorithm was used that is based on the hypothesis that bone strives for uniform tissue loading. In a first step, micro-FE models of the distal tibia were generated based on the HR-pQCT images to calculate the actual tissue loading, quantified as strain energy density (SED), for unit load cases representing compression ($F_z$), shear ($F_{zx}$, $F_{zy}$), torsion ($M_z$), and bending ($M_{zx}$, $M_{zy}$) (Figure 1). Then, in a second step, an optimization method was used to calculate the magnitude for each load case such that a bone tissue SED closest to a target value of 0.02 MPa was obtained when the results for all scaled load cases were combined to represent a loading history.

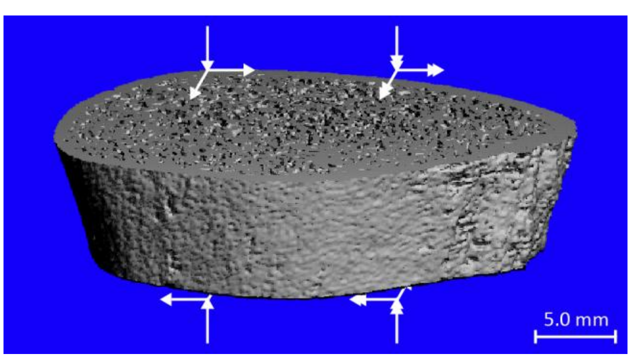


*Figure 1: Micro-FE model and boundary conditions (unit load cases) of the distal tibia.*

**RESULTS**

The bone loading estimation algorithm, applied to the data set of the beginning of the bed rest determined a loading history with a compressive force ranging from $F_z$ = 2017 to 3031 N and shear forces ranging from $F_{zx}$ = 1043 to 1546 N and $F_{zy}$ = 966 to 1464 N. Zero values for torsion and bending moments were predicted for all subjects.

A weak correlation between the loss of bone strength and the estimated loading history was found, both when considering the compressive force as well as when considering the shear forces (Table 1). If, however, only subjects were included with loss of bone strength beyond the reproducibility limit of 1.7%, a strong linear correlation was found between loss of strength and predicted loading history.

| Correlation coefficient $r$ | $F_z$ | $F_{zx}$ | $F_{zy}$ |
|---|---|---|---|
| All subjects ($n$ = 8) | -0.483 | -0.598 | -0.553 |
| Strength loss > 1.7% ($n$ = 4) | -0.887 | -0.839 | -0.933 |

*Table 1: Correlation coefficients of the change in bone strength over 60 days of bed rest and the estimated bone loading history.*

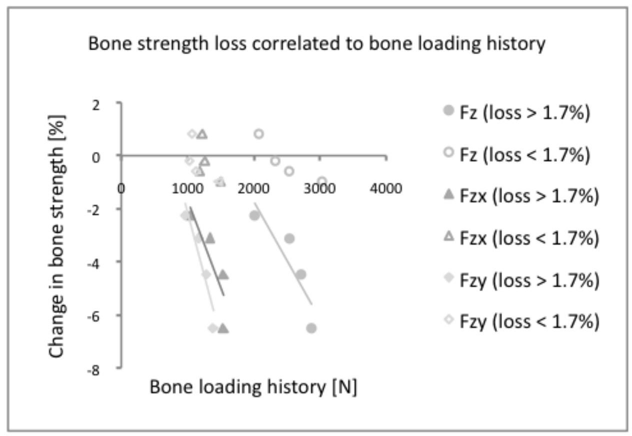


*Figure 2: Correlation of the change in bone strength over 60 days of bed rest and the estimated bone loading history.*

**DISCUSSION**

In the present study, a weak correlation between the loss of bone strength over 60 days of bed rest and the loading history estimated at the beginning of the bed rest period was found when considering all subjects. A strong correlation, however, was found if considering only subjects with a bone strength loss beyond the reproducibility limit of 1.7%.

This indicates that *if* a subject responds to the disuse by a loss of strength beyond this reproducibility limit, then the loss of strength can be well predicted from the bone loading history. For several subjects, however, no clear loss of strength was found in response to disuse, which could relate to genetic factors or compliance to the bed rest.

We therefore conclude that loss of bone strength indeed is related to the bone loading history, but that other factors might determine the risk that a subject responds to bone disuse.

**ACKNOWLEDGEMENTS**

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