

Summary of: Dose-dependent skeletal deficits due to varied reductions in mechanical loading in rats

Key findings and quantitative results:

- **Trabecular Bone Loss**: - **Trabecular Volumetric Bone Density (vBMD)**: Declined dose-dependently from 18% to 5% in PWB groups. - **Trabecular Volume Fraction (Tb.BV/TV)**: Decreased by 48% to 39% in PWB groups. - **Trabecular Thickness (Tb.Th)**: Decreased by 20% to 39% in PWB groups. - **Trabecular Number (Tb.N)**: Decreased by 40% to 65% in PWB groups. - **Trabecular Separation (mm)**: Decreased by 23% to 34% in PWB groups.
- **Cortical Bone Loss**: - **Cortical Bone Density (Ct.TMD)**: Increased by 1% to 9% in PWB groups. - **Cortical Thickness (Ct.Th)**: Increased by 1% to 5% in PWB groups. - **Total Cross-Sectional Area (Tt.Ar)**: Increased by 1% to 5% in PWB groups. - **Cortical Bone Area Fraction (Ct.Ar/Tt.Ar)**: Increased by 1% to 5% in PWB groups.
- **Femoral Stiffness**: - **Diaphyseal Stiffness**: Decreased by 17.4% to 13.2% in PWB groups at 2 weeks. - **Estimated Elastic Modulus (MPa)**: Not altered by PWB.
- **Histomorphometry**: - **Osteoblast Surface**: Decreased by 65% to 78% in PWB groups. - **Osteoclast Surface**: Unaffected by PWB. - **Mineralizing Surface**: Decreased by 75% to 67% in PWB groups. - **Marrow Apposition Rate (MAR)**: Tended to be lower in PWB groups.
- **MicroCT Imaging**: - **Trabecular Microarchitecture**: Deteriorated in PWB groups. - **Cortical Microarchitecture**: Not altered by PWB.
- **Statistical Analysis**: - **PWB Dose-Response**: Significant dose-dependent reductions in trabecular vBMD, Tb.BV/TV, Tb.N, and Tb.Th. - **Time Course**: Deterioration continued for 4 weeks, with no plateau observed. - **Sex Differences**: No significant sex differences in trabecular bone loss.
- **Additional Findings**: - **Periosteal Bone Formation**: Inhibited by PWB, indicating periosteal bone loss. - **Osteocyte Apoptosis**: Induced by PWB, leading to osteocyte apoptosis. - **Osteocyte Sclerostin Expression**: Increased by PWB, leading to osteocyte apoptosis.
- **Mechanical Testing**: - **Femoral Stiffness**: No significant changes in estimated modulus. - **Femoral Stiffness**: No significant changes in stiffness.
- **Longitudinal Assessment**: - **In Vivo pQCT**: Measured trabecular vBMD longitudinally, demonstrating dose-dependent reductions. - **Ex Vivo μ CT**: Measured trabecular and cortical bone properties, demonstrating dose-dependent reductions.
- **Limitations**: - **Age and Sex**: Limited to young adult rats, with no significant sex differences. - **PWB Duration**: Limited to 4 weeks, with no evidence of a plateau. - **PWB Level**: Limited to 20%, 40%, 70%, and 100% of body weight, with no evidence of a plateau.

- **Mechanostat Gene Response**: Noted in the response to PWB, suggesting rapid adaptation to altered mechanical loading.

- **Additional Studies**:
 - **Bisphosphonate Alendronate**: Attenuated bone loss, but potential side effects need to be considered.
 - **Resistance Exercise**: Mitigated bone loss, but serum markers for bone resorption continued to be elevated.
 - **Space Flight**: Osteoporosis risk in space, with limited data for skeletal responses to space missions.
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 - **PWB Duration**: Limited to 4 weeks, with no evidence of a plateau.
 - **PWB Level**: Limited to 20%, 40%, 70%, and 100% of body weight, with no evidence