In vivo mechanical loading induces site-specific, partially reversible tissue adaptation in vertebrae

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Introduction

- Low back pain is associated with mechanical loading, bone adaptation, and degenerative changes in adjacent tissues. [1]
- Previous studies have shown that mechanical stimuli can induce structural adaptations in both the caudal vertebral body and long bones. [2, 3]

Does mechanical loading induce region-specific bone remodeling in the caudal mouse vertebral body, and to what extent is this process reversible?

Material and Methods

- Animal model: Female C57BL/6 mice (n = 18 load, n = 17 sham)
- Loading model: Titanium pins inserted into caudal vertebrae 5 (CV5) and 7 (CV7) to enable axial compression of CV6 (Fig. 1)
- Loading protocol: 10 Hz, 8N, 5 min/session, 3×/week for 4 weeks
- Recovery period: 4 weeks
- Analyses: Longitudinal µCT scans (weekly) assessing bone volume fraction (BV/TV), trabecular thickness (Tb.Th.), formation and resorption rates; histological staining (CD31, EMCN, OSX and VPP3) [4]

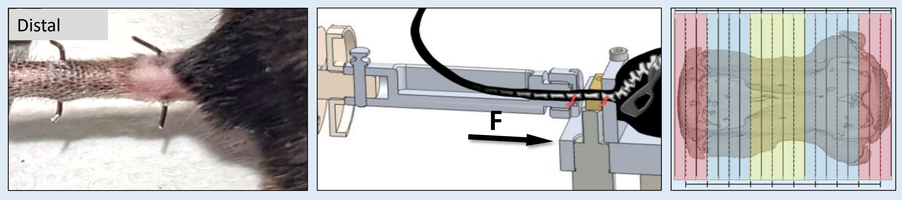


Figure 1. *Experimental setup of the in vivo model. Left: Pinned CV5 and CV7. Middle: Schematic of the loading setup. Right: Loaded CV6 divided into five regions of interest (from left to right): distal (red), distal transition (blue), midshaft (yellow), proximal transition (blue), proximal (red).*

Results

Four weeks of mechanical loading increase BV/TV and Tb.Th. in the vertebral body

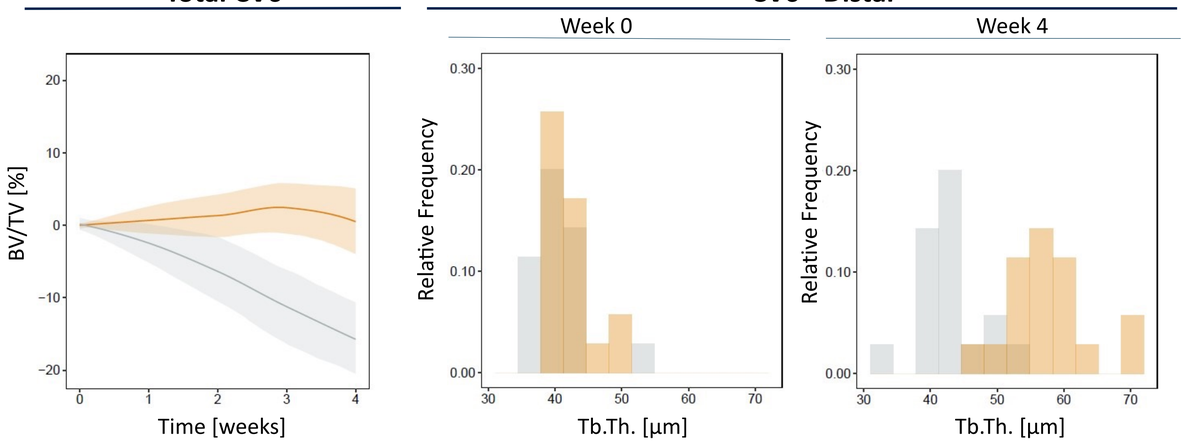


Figure 2. Four weeks of loading increase BV/TV in the entire vertebra and Tb.Th., especially in the distal region.

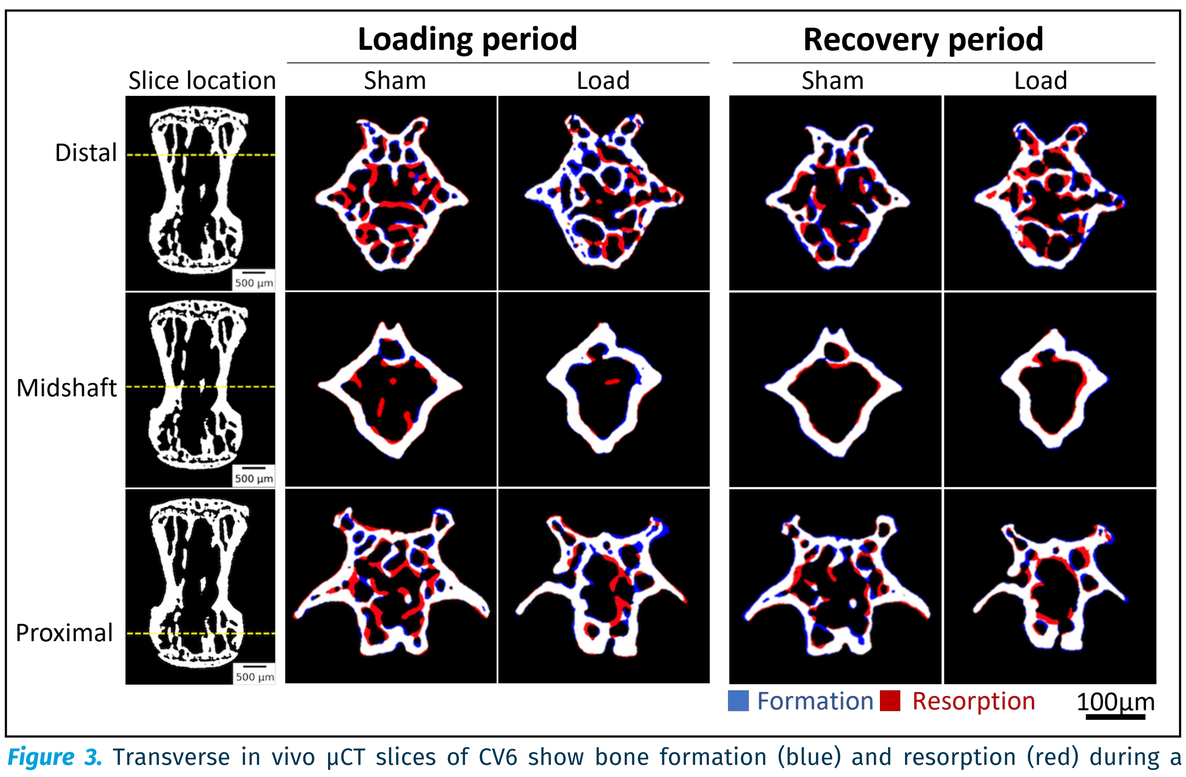


Figure 3. Transverse in vivo µCT slices of CV6 show bone formation (blue) and resorption (red) during a four-week loading period followed by a four-week recovery period.

During the recovery period, load-induced bone formation is partially reversed

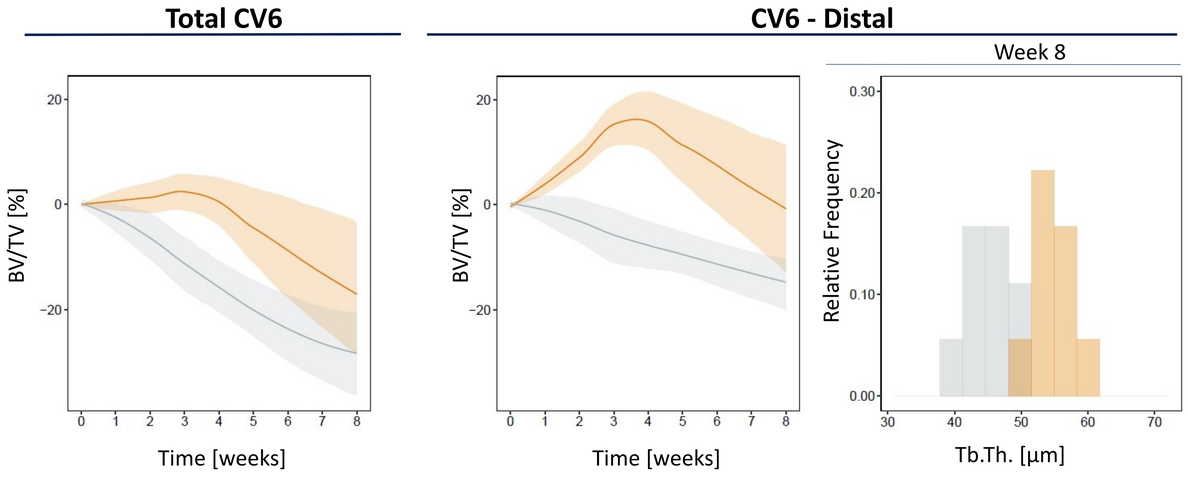


Figure 4. During the recovery period, BV/TV and Tb.Th. decrease but remain above baseline levels.

Mechanical loading shifts the remodeling balance toward bone formation

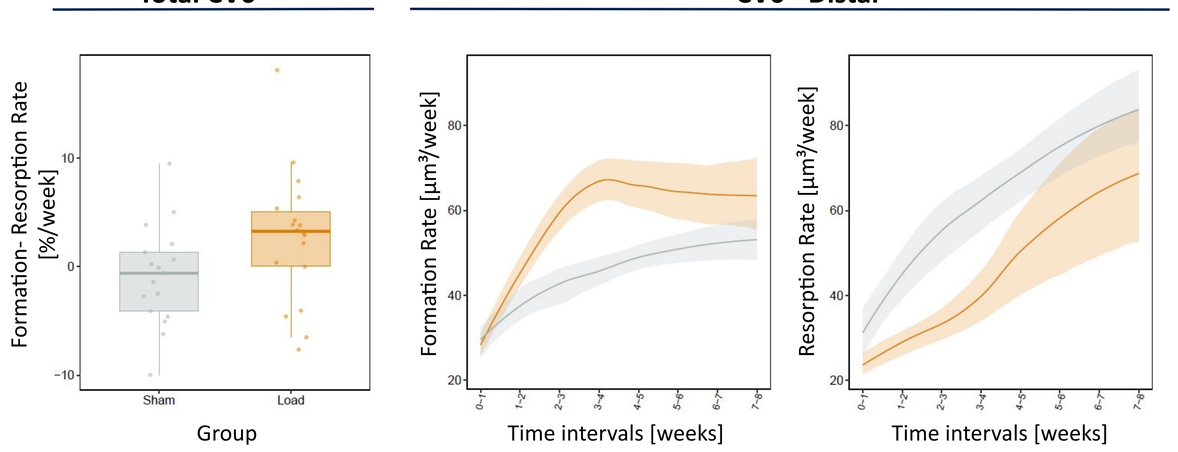


Figure 5. Increased bone formation and reduced resorption rates result in net bone gain during the loading period, particularly in the distal endplate region.

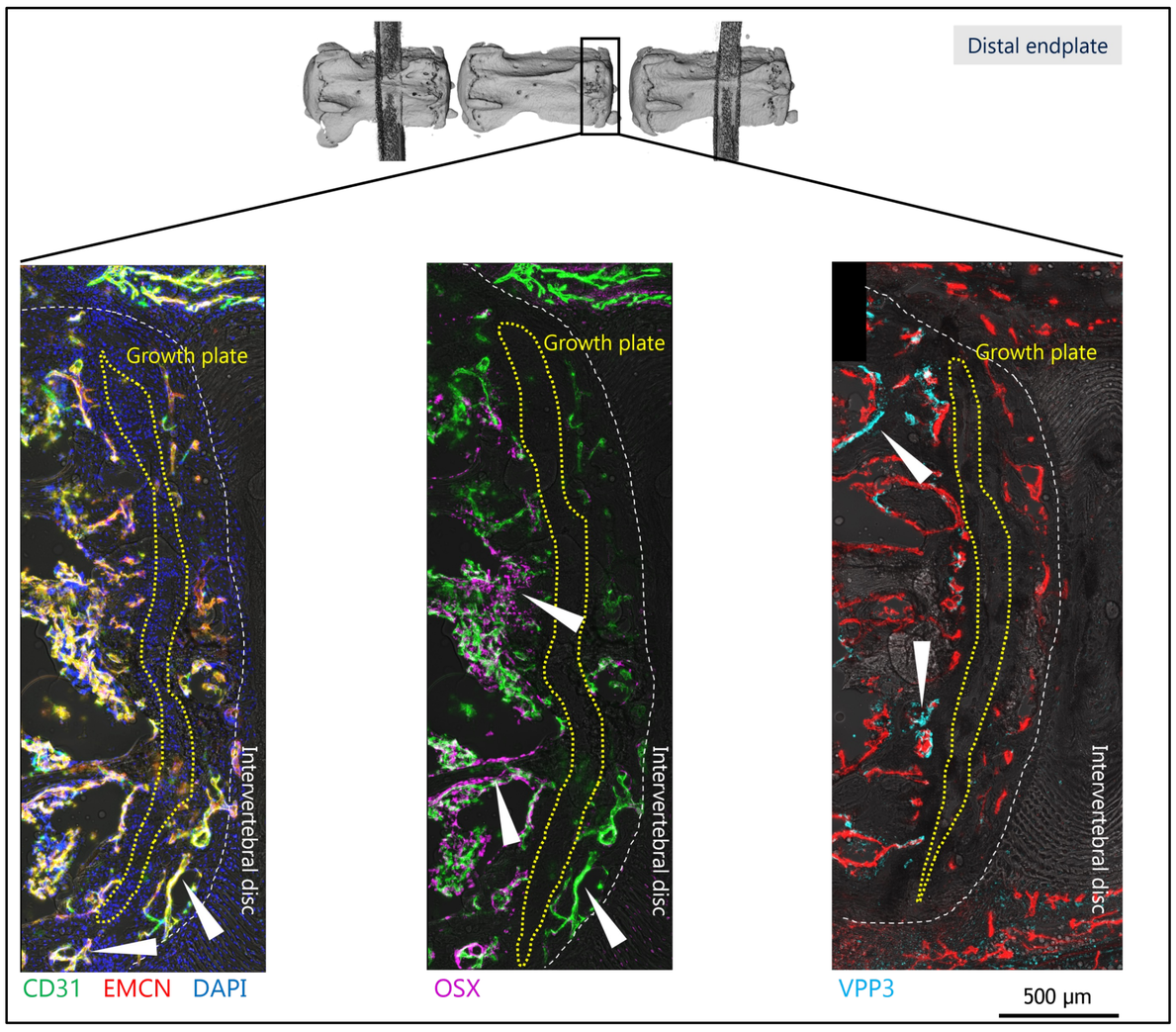


Figure 6. Histological staining of a loaded CV6 identifies the distal endplate region as a active remodeling zone. Vascular invasion (CD31, EMCN) and osteoblast recruitment are observed in the distal endplate and directly below the growth plate. Increased osteoblast presence (OSX) and reduced osteoclast activity (VPP3) are evident.

Sham group Loading group

Discussion and Limitations

Partially reversible bone remodeling in the distal vertebral body induced by mechanical loading:

- Limited duration of the recovery period does not allow conclusions on full reversibility.
- The causal role of vascular invasion in bone remodeling remains unclear.

Conclusion and Outlook

Mechanical loading induces region-specific bone remodeling in the vertebral body that is partially reversible after load cessation and is associated with vascular and osteogenic processes in the endplate regions.

→ Further investigations of vascular processes and mechanical overloading are necessary

LITERATURE

[1] Firouzabadi et. al. (2021), *Front. Bioeng. Biotechnol.* [2] Willie et al. (2013), *Bone.* [3] Lambers et. al. (2011), *Bone.* [4] Kusumbe et. al. (2015), *Nat Protoc.*

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