AGING IMPAIRS TRABECULAR BONE ADAPTATION TO LOADING: A 3D DYNAMIC *IN VIVO* MORPHOMETRY STUDY

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Introduction

The aim of this study was to investigate the trabecular bone (re)modeling response to mechanical loading with increasing age. We hypothesized that mechanical loading would lead to an increase in bone formation and a decrease of bone resorption in young, adult and elderly mice. Additionally, we hypothesized that due to age-related increased bone loss and reduced mechano-responsiveness, the total amount of formed volume, mineralizing surface and velocity of formation would diminish with aging.

Methods

Young, adult und elderly C57Bl/6J mice underwent two weeks of in vivo cyclic loading of the left tibia (n = 216 cycles/day; f = 4 Hz; εmax = 1200 microstrain, based on strain gaging, Fig.1A). The right tibia served as an internal control. In vivo microCT (vivaCT 40, Scanco Medical; isotropic resolution, 10.5µm 55kVp, 145µA, 600ms integration time, no frame averaging) was performed (day 0, 5, 10, 15). The scan region began 50 µm below the growth plate (10% of tibia). First, images were registered onto each other, as described earlier [Birkhold, 2012]. Image segmentation consists of extracting bone region, segmentation to separate trabecular and cortical areas and determination of sites of newly formed, constant and resorbed bones. Normalized newly formed and resorbed bone volume (fBV/tBV, rBV/tBV) surface areas (fSA/tSA, rSA/tSA), and thicknesses (fTh, rTh, Fig. 1B), as well as bone formation and resorption rates (3D-BFR, 3D-BRR) and mineral apposition/resorption rates (3D-MAR, 3D-MRR) were determined.

Results

Age influenced the trabecular bone formation response to loading (Fig.1C, D, E), with differences in fBV/tBV, fSA/tSA, and fTh already at day 5 ($p \leq 0.03$). The influence of age on the bone formation response could also be observed at day 10 (fBV/tBV, fTh, $p<0.0001$) and 15 (fBV/tBV, fSA/tSA, fTh, 3D-MAR, 3D-BFR; $p \leq 0.05$). After 15 days, formation parameters differed between young and adult mice (fBV/tBV, fSA/tSA, fTh, $p \leq 0.003$) and between adult and elderly (fBV/tBV, fTh, 3D-MAR, 3D-BFR; $p \leq 0.018$). Age influenced the bone resorption response to loading at day 5 (rBV/tBV, rSA/tSA, rTh, $p<0.007$), but no differences were measured at later time points, only rBV/tBV approached significance (day 10: $p=0.097$; 15: $p=0.079$). 3D-BRR and 3D-MRR were not affected by aging. The resorptive response changed between young and adult mice (rBV/tBV, rSA/tSA, rTh, 3D-MRR, 3D-BRR; $p \leq 0.045$), only 3D-BRR changed between adult and elderly ($p<0.001$).

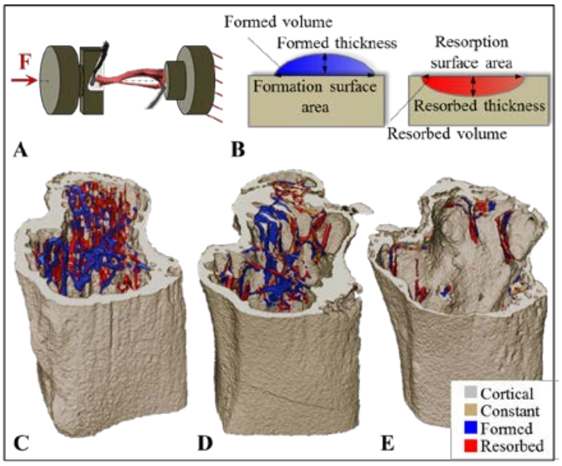

Fig 1: A. In vivo loading. B. Measured (re)modelling parameters. C. Bone (re)modelling after 15 days in young, adult (D), and elderly (E).

Discussion

Our result using the new technique demonstrated that trabecular bone maintains its ability to respond to external loading even into old age, but the amount of the response diminishes with aging. Our findings suggest that mechanical stimulation by e.g. exercise regimes might be an option to maintain trabecular bone mass in the elderly, and these interventions should begin as early as possible.

References

Birkhold *et al*, J Biomech, Suppl.1: S97, 2012.