SITE-SPECIFIC DIFFERENCES IN MOUSE CORTICAL BONE TOUGHNESS ARE UNDER GENETIC CONTROL

Pinaki Bhattacharya[1], An-Katrien Braeken[1], Michaël Laurent[2], Dirk Vanderschueren[2], G. Harry van Lenthe[1]

[1]*Biomechanics Section, KU Leuven, Leuven, Belgium*

[2]*Clinical and Experimental Endocrinology, KU Leuven, Leuven, Belgium*

Introduction

Osteoporosis is a widespread metabolic bone disease which affects the elderly population [Compston, 1998] and is associated with a loss in bone competence leading to fractures [EC Report, 2003]. The loss in bone competence can be attributed to a loss of bone quantity, degradation of bone architecture, and weakening of the bone tissue itself. Anatomical variations in bone tissue quality are not well-documented and their role in affecting bone competence is not well understood. Reference-point indentation (RPI) is a promising new technique that can characterise bone tissue quality in-vivo [Diez-Perez *et al*, 2010]. The aim of this study was to assess the variability of RPI outcomes across anatomical sites. Potential genetic effects were addressed by evaluating two genetically distinct inbred strains of mice that, owing to their genetic similarity with humans, serve as a model in studying bone diseases.

Methods

Left and right tibiae were harvested from five C57BL/6 (B6) and C3H/He (C3H) 12-week old male mice (bred and sacrificed for an unrelated study). The surrounding soft-tissue was removed and bones were stored in PBS at –20º C until mechanical testing. In order to ascertain site-specific differences in bone tissue quality, RPI measurements were taken at five sites on the cortical bone surface using the BioDent (Active Life Scientific, Santa Barbara, USA); specifically, one site distal to the tibia–fibula junction (TFJ), three sites on the anterior ridge and one site on the lateral surface were tested (Figure 1).

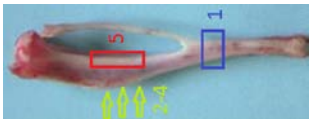

Figure 1: Representative sites at which RPI measurements were taken. Site 1 lies distal to the TFJ, sites 2–4 are located on the anterior ridge, and site 5 is placed on the lateral surface.

For each measurement, 10 cycles were made with a maximum force of 2 N. Total indentation distance (TID) and indentation distance increase (IDI) were quantified. Two-tailed Mann-Whitney U tests were carried out to determine significant differences in the measured parameters.

Results

We found significant site-specific variability for RPI measurements in B6 mice (Table 1). TID and IDI were significantly higher ($P<0.05$) at the lateral surface compared to sites at anterior ridge. On the other hand differences between the distal site and anterior ridge sites were not significant. It is however interesting to note that the standard deviation in both TID and IDI was highest at the lateral surface, intermediate at the distal site and lowest at the anterior ridge sites. Results for C3H mice indicate significant differences between lateral surface and the rest of the sites.

Site	TID [μm]	IDI [μm]
1 (distal to TFJ)	23 (7.1)	3.6 (0.80)
2–4 (ant. ridge)	19 (0.99)	3.1 (0.16)
5 (lateral surf.)	37 (24)	11 (10)

Table 1: Site-specific mean (SD) values of RPI measures obtained from five B6 tibiae.

Discussion

TID and IDI are the two RPI parameters that have been shown to be most strongly correlated with bone toughness [Diez-Perez et al, 2010; Gallant *et al*, 2013]. Site-specificity of TID and IDI reflects the underlying variation in bone-tissue quality.

References

J. E. Compston *et al*, Osteoporosis Int, 8:531–34, 1998.

EU Report, Osteoporosis in the European Community: Action Plan, 2003.

A. Diez-Perez *et al*, J Bone Miner Res, 25:1877–85, 2010.

M. Gallant *et al*, Bone, 53:301–5, 2013.