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FIBULA: THE FORGOTTEN BONE

May it provide some insight on a wider scope for bone *mechanostat* control?

**Rittweger J^{1,2}, Ireland A³, Lüscher S⁴, Nocciolino LM⁴, Pilot N⁵, Pisani L⁵, Cointry GR⁴,
Ferretti JL⁴, Capozza RF⁴**

¹Division of Space Physiology, Institute of Aerospace Medicine, German Aerospace Center,
Cologne, Germany

²Department of Pediatrics and Adolescent Medicine, University of Cologne, Cologne, Germany

³School of Healthcare Science, Manchester Metropolitan University, Manchester, United
Kingdom

⁴Center of P-Ca Metabolism Studies (CEMFoC) National University of Rosario and Arg NRC
(CONICET), Rosario, Argentina,

⁵Unidad de Estudios Biomecánicos Osteo-musculares (UDEBOM), Instituto Universitario Gran
Rosario (IUGR), Rosario, Argentina.

Corresponding Author: Alex Ireland, Manchester Metropolitan University, John Dalton Building,
Chester Street, Manchester, M1 5GD. a.ireland@mmu.ac.uk. +44 (0)161 247 1987.

Abstract

The human fibula responds to its mechanical environment differently from the tibia accordingly with foot usage. Fibula structure is unaffected by disuse, and is stronger concerning lateral bending in soccer players (who evert and rotate the foot) and weaker in long-distance runners (who jump while running) with respect to untrained controls, along the insertion region of peroneus muscles. These features, strikingly associated to the abilities of the fibulae of predator and prey quadrupeds to manage uneven surfaces and to store elastic energy to jump, respectively, suggest that bone mechanostat would control bone properties with high selective connotations beyond structural strength.

Keywords: pQCT, mechanoadaptation, exercise, disuse

The Utah Paradigm of Skeletal Physiology¹ proposed that bone *mechanostat* dictates the architectural properties of bone cortical shells and trabecular networks tending to adapt bone resistance to fracture by spatially orienting local bone modeling. The directionality of the process would be determined by cell-to-cell mediators delivered by strain-sensitive elements (supposedly osteocytes) according to the direction and magnitude of the tiny deformations of the hard tissue induced by the loads customarily induced by mechanical usage. As a result, the bone's structural stiffness would be directionally adapted to the mode of use of the bone as determined by the amplitude and frequency of the induced modes of deformation². Reasonably, any training activity involving a specific mode of deformation of any mobile bone should reinforce its structure to resist the specific kind of stress involved. Conversely, disuse should weaken bone structure predominantly concerning the directions of the stresses which were seldom supported previously.

In humans, these features and effects have been repeatedly observed in diaphyses of long bones (humerus, radius, femur, tibia). However, in some long bones which work in parallel with others in the limbs, such as the fibula³, and possibly the ulna⁴, this behavior seems to be blunted in some instances by reasons which are not fully understood.

The fibula contributes up to 30% of shank load, with its contribution increasing with load magnitude⁵. Therefore we could expect that in exercise or disuse conditions where load magnitude changes, the relative change in fibular loading would be greater than that in the neighbouring tibia. This contribution does not appear to be trivial, supported by substantial tibia growth following removal of the fibula. Finally, the fibula appears to have mechanoadaptive capacity as evidenced by its dramatic growth when grafted to replace a tibia shaft segment following osteotomy⁶. Thus, we could expect that adaptation of the fibula to exercise and disuse would be at least comparable to that observed in the neighbouring tibia.

We have developed a pQCT scanning protocol that consist in the serial study of the whole length of long bones (scans at every 5% of tibia length throughout the leg)^{3,7}. Using this procedure we have performed a series of observational, cross-sectional studies which have described the whole tibia and fibula structure in otherwise healthy men and women which had been previously subjected to different degrees and types of physical activity^{3,7-10}. These observations showed some striking differences in the behavior of the two bones which seem to describe a 'canonical' response of cortical tibia structure to its mechanical environment concerning the above reference to bone *mechanostat* and a contrasting, 'non-canonical' behavior of that of the fibula of the same individuals. The surprising conclusion from these studies was that the fibula does not adapt, or that it adapts in a peculiar way to loading and unloading stimuli. We will explain and interpret this in the following.

1. Structural aspects of tibia and fibula in healthy, untrained men and women.

Cortical tibia structure seems to reflect the changing pattern of stresses naturally exerted by its mechanical environment⁷. Distally, the bone is chiefly adapted to resist compression, for which only the bone amount present in the cross-section matters, regardless of its distribution.

Cortical mass, thickness, and moments of inertia (MI's) for A-P and lateral bending and torsion are minimal, and cross-sectional circularity is maximal. This is congruent with the need to support the whole body weight at the heel articular surface. Going proximally, cortical mass, thickness and all MI's increase progressively and reach a maximum at about the mid-diaphysis. This is consonant with the need to deal with bending and torsion stresses introduced e.g. by muscle attachments to the bone, which are naturally greatest at mid-shaft and above. Thereon, total bone mass and the MI's show a further increase while cortical thickness is progressively reduced as the amount of trabecular bone increases. This would reflect the need to support the axial load of the whole body weight on each of the two plates at the knee.

Cortical fibula structure shows no less than five different regions with a similar amount of bone mass but changing values of the three MI's³ which is difficult to evaluate following the Theory of Elasticity¹¹. The MI's are maximal at both bone ends and at the mid-shaft and minimal at the middle regions of the proximal and distal halves of the diaphysis, with cortical diameter being minimal and thickness maximal toward the distal end. This suggests a generally minimal compromise with uniaxial load support throughout the bone and, in contrast, a high influence of bending and torsion stresses at the middle of the proximal and distal halves, and an increasing resistance to buckling toward the distal end.

2. Disuse effects on tibia and fibula cortical structure.

The effects of long-term disuse of the lower limbs on tibia¹⁰ and fibula⁸ were examined in nine men with spinal cord injury (SCI) an average of 17.8y (range 9–32y) following injury, and nine age, height and weight-matched men without SCI.

In the tibia, bone mass was 22-51% lower in individuals with SCI than controls with the greatest deficits evident at sites at the proximal and distal ends of the bone. A strong relationship ($R^2=0.98$) was observed between endocortical circumference and BMC deficit at different sites, which may relate to a higher surface:volume ratio for absorption at the endocortical surface which has a high rate of bone turnover. Lower bone mass in SCI was attributable primarily to decreased trabecular bone mineral density (BMD) at distal and proximal sites, whereas deficits in the shaft resulted from a combination of lower cortical BMD and greater endocortical and smaller periosteal circumferences.

In the fibula of the same individuals, there was no difference in bone mass throughout the fibula shaft. Whilst lower bone mass was observed in SCI at the most proximal (5% tibia length) and distal (90%) sites, these deficits were significantly lower than those observed in the neighbouring tibia. In contrast to the tibia, small advantages in cortical thickness at shaft site were evident in SCI in addition to smaller endocortical circumference. Whilst bone geometry explained the majority of site variance in BMC in the tibia, as surface:volume ratio of the fibula was higher than that in the tibia this could not explain dischordant group differences in the two bones.

3. Effects of chronic training on tibia and fibula cortical structure

a. Long-distance running. The effects of chronic training (10 km/wk for >11 years) in long-distance running in young-adult men and women compared with untrained controls were highly diverging between the tibia⁹ and the fibula¹².

In the tibia, as expected, all mass- and geometry-related parameters were positively associated with running training, more evidently in men than in women, with the exception of the cortical vBMD which was decreased (probably because of microdamage-related remodeling).

In the fibula, instead, training had only little effect on cortical area and BMC and, strikingly, it was associated with reductions in the lateral-bending MI (yMI) preserving the A-P bending MI (xMI) with a significant impairment of the 'shape index' (yMI/xMI ratio) at the proximal half of the bone. Also strikingly, at the distal end, training was associated with reduction of all MI's while the buckling ratio was improved¹³.

b. Soccer playing. A cross-sectional study with people who had a history of more than 4 years of competitive soccer training on both bones¹³ yielded much less surprising results than the study in runners.

In the tibia, results largely resembled those observed for long-distance running.

In the fibula, contrasting with the effects of running, soccer training was associated with significant enhancement of all mass- and geometry-related indicators, including all the MI's, especially that for lateral bending (yMI), predominantly at the proximal half of the bone (i.e. coinciding with the insertion area of peroneus longus and brevis which evert and externally rotate the foot and are especially trained in soccer) with respect to untrained controls, in close, region-specific association with the dynamometrically-assessed peak force of foot external rotation. Strikingly, this effect was exerted *beyond* the natural, negative association of the efficiency of distribution of cortical bone (MI, y) and the stiffness of the mineralized tissue (cortical vBMD, x) ('distribution/quality' relationship)¹⁴ which characterizes the outcome of *mechanostat* regulation of bone design.

4. Inferences concerning the bone *mechanostat*.

The effects above, namely that the fibula is less resistant to torsion and bending in runners, but more resistant in soccer players could, at least partly, be explained by self-selection bias, given that the above-cited studies were cross-sectional and that the athletes chose their disciplines by their own volition. However, we argue here that the known effects of mechanical usage on bone are so strong, in particular in the growing skeleton, that therefore bone structure-linked self-selection effects would mostly be explicable through mechanical usage of the fibula at young age, and that therefore the observed group-differences mostly reflect individual-specific adaptations effectuated by *mechanostat* function. In this context, contrasts between the clear divergent traits in the tibia's and fibula's cortical structure are very striking, and they may provide a clue to understand how specific elements of mechanical exposure shape our bones.

a. Running training seems to *weaken* both the *proximal half* (a region which seldom fractures) concerning lateral bending, and the *distal end* (the most prone region to fracture)¹⁵ concerning all kinds of deformation, yet improving distal resistance to buckling (the most common type of fracture). Enabling the fibula to store more muscular energy is favorable to jump higher while running despite the ability of the foot, with little or no effect on fracture rate in the studied conditions, either for the proximal or distal regions^{16,17}.

b. Soccer training, by contrast, seems to *reinforce* cortical structure, perhaps even *beyond the needs* of a bone structure's requirements for preventing fracture, but favorably concerning the achievement of a strong support to the musculature which everts and rotates the foot. This effect is favorable to run on uneven surfaces when the foot is able to manage it¹⁸.

Both kinds of training effects on fibula structure may indeed have a highly selective value, either for prey (a) or predators (b)^{19,20}. To note, a. gazelle's fibula, fused distally to the tibia, departs from it proximally as a thin ribbon of bone, as an ideal arrangement to optimize muscle energy storage^{16,17}, and b. leopard's fibula, totally independent from the tibia, shows a far more robust structure than that of the gazelle's, as an ideal device to provide a strong insertion to peroneus muscles which evert and rotate the clawed foot¹⁸.

This raises questions. Firstly, does the bone *mechanostat* work exclusively to optimize bone strength by ensuring a given safety factor, as currently conceived? Or is there an unrecognized bone adaptive control mechanism that slims structures down to improve elastic energy storage, notably within acceptable strength limits? And if so, then would we humans have the appropriate, ancestral genes to allow for that adaptation to specific kinds of mechanical loads?^{1,2,21-23}.

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