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In vitro evidence of the structural optimization of the human skeletal bones

Luca Cristofolini *

Department of Industrial Engineering, School of Engineering and Architecture, University of Bologna, Viale Risorgimento 2, 40136 Bologna, Italy

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ABSTRACT

Optimization can be seen in a number of human skeletal bones. While there is strong evidence concerning the mechanism at the tissue-level for bone adaptation to the applied loads, the structural optimization at the organ-level is somewhat less clear. This paper reviews the evidence, mainly based on *in vitro* testing, but also from anatomical and biomechanical considerations, concerning the shape-function relationship in some exemplar cases. The proximal femur is robustly optimized to resist a force applied in a range of directions during daily life, but also to absorb a large amount of energy if an impact is delivered on the greater trochanter during a sideways fall. The diaphysis of the tibia is shaped so as to act as a uniform-stress structure (*i.e.* structurally efficient) when loaded by a bending moment in the sagittal plane, such as during locomotion. The body of the thoraco-lumbar vertebrae is optimized to resist to a load applied strictly in an axial direction. The result of this review suggests that the structure of bones derives from a combination of local stimulus-driven tissue-level adaptation within the subject, and organ-level generational evolution.

1. Introduction

The structure of skeletal bones has called the attention of scientist for centuries. In the nineteenth century, anatomy studies combined with modern mechanics provided the first evidence that the arrangement of the trabeculae of cancellous bone is strongly related to the biomechanical function. In 1856 Swiss engineer Karl Culmann remarked the similarity of the trabecular arrangement in the proximal femur, and that of the "Culmann crane" he had recently designed (Crystal, 1998). Few decades later Wolff (1892) gave the first formal description of the optimization principle underlying the structure of bones. While Wolff focussed on the mechanical description of such an optimized design, it was Roux (1881) who first introduced the concept of a quantitative self-regulatory mechanism as an explanation for such an optimal structure. Shortly later, Koch (1917) provided a thorough theoretical analysis of the stress distribution in the proximal human femur, including a first estimate of the safety factor for the femoral neck (5.7, both for the maximum tensile and compressive stress). With the advent of contemporary biology, a hundred years later it became possible to describe a cellular mechanism capable of managing bone adaptation (Carter, 1984; Roesler, 1987). Although the concepts of bone adaptation (misleadingly known as "Wolff's law") have often been put under discussion (Bertram and Swartz, 1991; Huiskes, 1995), its general principles remain valid, and are the backbone of modern bone biomechanics (Cowin, 2001; Currey, 1982; Fung, 1980; Roesler, 1987).

It was Carter (1984) who provided a first description of the bone apposition/resorption balance in response to cyclic loading, in the form of an algorithm, which was soon converted into numerical models based on finite element (FE) analysis (Huiskes et al., 1987). The principles of bone adaptation were incorporated in FE models initially to predict adaptation of bone to the presence of an implant (*e.g.* Huiskes et al., 1989, 1992). With the advancement of the understanding on the control mechanism of bone cells, FE models became capable of predicting trabecular morphology (*i.e.* sizes and branching of struts) in relation to the local loads (Huiskes et al., 2000; Mullender et al., 1994; Ruimerman et al., 2005b). Predictions of bone adaptation based on such local optimization criteria have been validated qualitatively (Huiskes, 1993). More recently, quantitative validation has become possible thanks to the advancement of high-resolution *in vivo* imaging (Lambers et al., 2011).

While local adaptation has extensively been explored at the tissue-level, its up-scaling to the organ-level has only partially been accomplished (*e.g.* Kuiper et al., 1991). Optimization of the shape of bones to achieve the maximum resistance with the minimum amount of material has been for long hypothesized (Roux, 1881). It has recently been stated that measuring bone strains can improve the understanding of bone shape-function relationships (Demes, 2007). Several studies suggest that bone geometry and density are adjusted by bone remodelling so as to attain a constant level of

* Corresponding author. Tel.: +39 051 2093266; fax: +39 051 2093412.
E-mail address: luca.cristofolini@unibo.it

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stress/strain (*e.g.* Lanyon, 1980). A recent study when contralateral bones of the human lower limbs were compared (Cristofolini et al., 2014) showed that the differences in stiffness observed at the whole-bone level are mainly explained by bone segment geometry (*i.e.* global anatomical adaptation), rather than by differences in bone tissue properties (*i.e.* tissue-quality adaptation). A structure that is optimized for a given loading condition presents a uniform state of stress: this corresponds at the same time to a minimum amount of material (which translates into a minimal metabolic energy expenditure, both during growth and during locomotion), and a minimum risk of damage (Beer et al., 2011). However, the link between different dimensional scales (from tissue-scale local adaptation to organ-level optimal structure) is far from understood.

The problem should then be considered at different dimensional scales. Rather than sticking to the classic reductionist strategy, an integrative approach has recently been proposed, which is capable to provide a deeper understanding (Noble, 2006). It has been demonstrated that a synergic use of numerical models and *in vitro* simulations (Cristofolini et al., 2010b) can provide the most reliable and extensive understanding for such multiscale problems (Cristofolini et al., 2008; McDonald et al., 2010; Webster and Muller, 2011).

This paper will review the evidence coming from *in vitro* testing concerning the following questions:

- Are bones optimized in their multiscale structure?
- How does the structure of bones respond to the different “design specifications”?

2. “If bone is the answer, then what is the question?” (Huiskes, 2000)

Prof. Rik Huiskes certainly knew how to be provocative, and probably he actually enjoyed fierce debates with colleagues, both at conferences and in scientific papers (Huiskes 1995, 2000). Myself, like many others who work in bone biomechanics, was inspired by the work of prof. Huiskes, and, like him, tried to understand better how and why bone adapts itself. Most of the work of prof. Huiskes and his co-workers in the Eighties and Nineties concentrated on total hip replacement, rather than focusing directly on bone. I suspect that he saw hip stems as a tool to “interrogate” the bone by modifying the loading imposed to the proximal femur, so that the laws of bone adaptation could be investigated. In fact, in the last decade his activity was more characterized by investigation on the bone in itself, including ageing, osteoporosis, fatigue (Isaksson et al., 2006, 2008; Ruimerman et al., 2005a; van Oers et al., 2008, 2011), and more in general on the mechano-biology of bone adaptation (van der Meulen and Huiskes, 2002).

3. Optimization of the proximal human femur

3.1. Design requirements”

One frequently addressed example of structural optimization is the proximal human femur. If one had to describe it in engineering design terms, these are the main mechanical requirements:

- Provide a rigid structure for the attachment of muscles, ligaments and tendons, which enables enable body movements.
- Effectively respond to physiological loads: daily loads applied to the femoral head are cyclic by nature, and vary in direction (Bergmann, 2013). To resist them effectively, a combination of cortical and trabecular bone is arranged so as to provide the maximal fracture load with a minimal (but optimally arranged) amount of bone material. No sort of failure (other than bone-adaptation-inducing microcracks Martin and Burr, 1982; Taylor and Prendergast, 1997) is acceptable, due to the cyclic nature of such loads. The concept here is similar to the one that structural engineers apply to the design of strenuously loaded mechanical components such as a crankshaft.
- Safely resist to occasional trauma: a sideways fall is a common challenge to the proximal femur (Grisso et al., 1991; Hwang et al., 2011; Michelson et al., 1995; WHO, 1994, 2007). In this perspective, what really matters is toughness, *i.e.* the amount of energy absorbed prior to catastrophic failure. Sub-critical structural damage (partial bone fracture) is not desirable, but acceptable under these special circumstances. The concept here is similar to the principle that engineers apply to the design of car safety components such as the bumpers.
- Meet the requirements above with a minimal mass.

3.2. Response to loading in a physiological direction

As far as physiological loading of the femur is concerned, most of the published *in vitro* studies focussed on the effect of hip stems (Cristofolini, 1997). Failure of the proximal femoral metaphysis has often been investigated *in vitro* (*e.g.* Cristofolini et al., 2007; Lochmüller et al., 2002; Yang et al., 1996), but the strain distribution has seldom been assessed. A theoretical study has shown that the shape and anteversion of the femoral neck provides an optimal response to physiological loads (Fabeck et al., 2002). The strain

Table 1
Strain values measured *in vitro* when physiological motor tasks are simulated. When available, forces are expressed in Body weight (BW).

Reference	Motor task	Measured strain (microstrain)	Note
In vitro experiment			
Field and Rushton (1989)	$F=1500$ N at 16° in the frontal plane	Range: −1800 to +1200	Peak value out of 17 uniaxial strain gauges
Cristofolini et al. (2009)	Single leg stance, walk ($F=2.5$ BW)	Max tensile: +735, Max compressive: −1029	Average of 12 locations, 24 femurs
	Stumbling ($F=8.7$ BW)	Max tensile: +5760 to 8468 Max compression: −11850	Local peak
In vivo measurements			
Aamodt et al. (1997)	One-leg stance	Range: −435 to +1463	One strain triaxial strain gauge on the lateral proximal part of the femur
	Walking	Range: −393 to +1198	
	Stair climbing	Range: −948 to +1454	
Physiological ranges			
Lanyon (1980)	Bone resorption/formation	Approximately 1000	
Bayraktar et al. (2004)	Bone tissue fracture	Tensile: +7300, Compressive: −10000	