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The role of the applied load in bone homeostasis and its implications in implant dentistry: a mini-review

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Abstract. The aim of this work is to carry out a review about the role of applied load on bone development and homeostasis and its implications in dental implantology. The history of theoretical bone physiology has been evaluated in detail. The modern theory of bone physiology is consistent with the integration among regional acceleratory phenomenon, Utah paradigm, and mechanostat hypothesis: bone modelling and remodelling respond to pleiotropic stimuli. To date, several histologic, in silico and in vitro studies in implant dentistry corroborate the theories about bone physiology. However, each evaluation method has pros and cons, providing analytical data that can only be used to esteem the in vivo behaviour of the bone-implant system. There is the need of further research with highly validated methods and improved measurement devices, to better integrate data form different research types. This would progressively lead to more structured comprehension of the in vivo performance of dental implants and their surrounding bone, and hopefully to a clear definition of the impact of loading on implant failure.

Keywords: applied load, bone homeostasis, bone physiology, bone adaptation, dental implants, mechanical factors.

INTRODUCTION

Mainly three kinds of factors control the bone tissue development and morphology: genetic, epigenetic, and environmental factors (Frost 2001). Among the environmental, it has always been studied if the mechanical agents (applied load), could be considered paramount factors affecting the bone homeostasis. In dentistry field, it might be an enormous advantage to predict the bone response and adaptation to the applied load, in both qualitative and quantitative manner. This because of every dentistry procedure is finalized to comply with the occlusal load, most of all in the implantology field, where achieving an adequate osteointegration is mandatory for a successful treatment. The purpose of this mini-review is therefore to outline a historical overview about the role of loading on bone development and homeostasis, to highlight its key implications in implant dentistry and to establish whether the current knowledge is able to predict the bone response to the applied load.

HISTORY AND CURRENT KNOWLEDGE OF BONE HOMEOSTASIS

In 1892, Julius Wolff argued that mathematical laws are the major controllers of the process of bone remodelling, and that it results from mechanical load (Wolff 1892). Beginning in 1930, however, it was argued that osteoblasts and osteoclasts, the effector cells of bone, were responsible for the health or disease of the tissue and that they act under the control of non-mechanical agents. In 1960, all these laws and theories were summoned into the theory of bone physiology called "the paradigm of 1960". The modern theory of bone physiology called "the Utah paradigm" was born. in 1964, during a historic workshop at the University of Utah. A new element in bone physiology was introduced: the biomechanical mechanisms, acting on a tissue level (Frost 2000). It replaced and integrated Wolff's law and the paradigm of 1960. Remodelling, modelling, and repair were identified as biological mechanisms which directly act on bone tissue. The bone acquired a mechanical competence. In 1987, Frost introduced the concept of dynamic interaction between form and function of the bone with the "mechanostatic theory" (Frost 1987). Frost argued that remodelling, modelling and repair determine the structural adaptation of the bone to different demands. This happens in the general context of four levels (windows) of ascending mechanical stress. The transition from one window to another is established threshold values of microstrain. The activation of each adaptive process requires the attainment of a threshold value of microstrain, defined as minimum effective strain (MES) (Figure 1). In association with loading, Frost described the Regional Accelerating Phenomenon (RAP) as a biological local factor for the control of bone adaptation. It is an acceleration of the physiological process of tissue healing (both soft and hard tissues), localized in the site insulted by a micro-damage (Frost 1983).

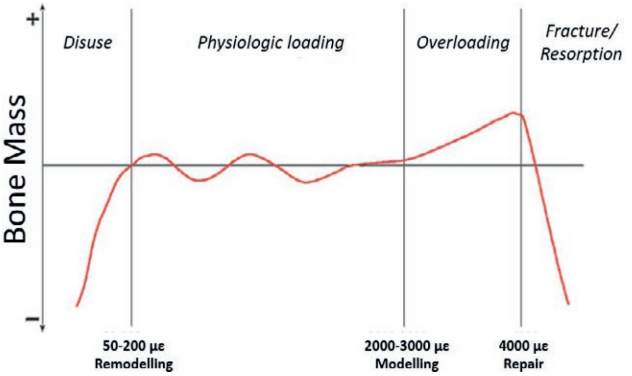

Figure 1. Bone response to applied load following the mechanostat theory. *Window of disuse*: bone exposed to low or without load has very low or zero deformation and undergoes resorption, until reaching a new equilibrium between load and strain. *Window of physiologic load*: the bone exposed to physiologic load presents a continuous remodelling with the achievement of mass balance between resorption and apposition, with a preservation of the bone mass. *Window of overload*: the bone exposed to a load greater than the physiologic limit presents a high deformation and gets a mass gain (corticalization) until reaching a new balance between load and deformation. *Window of fracture*: the bone exposed to a load greater than the limit of the overload fractures and resorbs. Y axis: generic bone mass; x axis: microstrain (ε).

Mechanostatic theory consider load as the main actor on bone adaptation, producing different effects depending on function of the peak level of microstrain. The frequency of load can play an equally important role. The entity of load determines the number of activated cells, while the level of strain is responsible for the strength of osteoblastic activity (Forwood and Turner 1995). After, Turner formulated the following mathematical equation (1):

$$E = K_1 \sum_{i=l}^{n} \varepsilon_i f_i \tag{1}$$

where the strain stimulus E, with a proportionality constant K_1, depends on the entity of the strain and its frequency of the load application f. When the frequency of application of the load is zero ($f = 0$) the stimulus is absent ($E = 0$) (Turner 1998). Figure 2 summarize the current knowledge about bone homeostasis.

APPLIED LOAD ON THE BONE-IMPLANT SYSTEM: HISTOLOGICAL AND MECHANICAL FINDINGS

Dental implants transmit loading forces from the dental arches to the jaw bones. Bone stability around the margins of fixtures is one of the key factors for long-term implant success. However, the biomechanical mechanisms related to implant failure remains unknown (Pesqueira et al. 2014). The main factors that determine the mechanical properties of bone are the collagen fibres orientation (BCFO) and the matrix mineralization

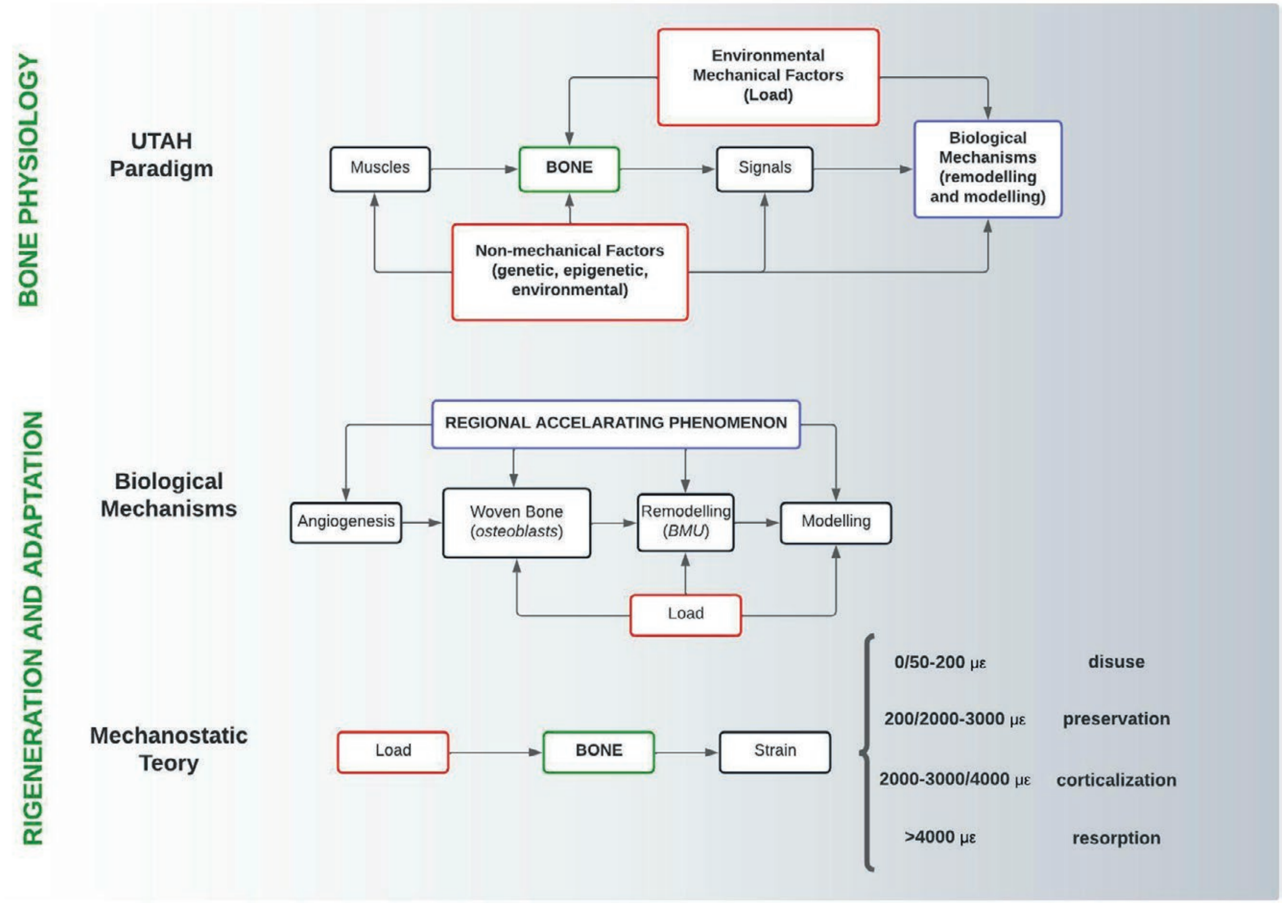

Figure 2. Schematic representation of current knowledge about bone homeostasis. The Utah paradigm gives an important role to both non-mechanical and mechanical factors in determining the balance between bone health and disease with the action of biological mechanisms of modelling and remodelling. This basic mechanism has got continuous feedback modulations. Their maximum expressions are the regenerative and adaptive processes through secondary interactions operated by RAP and mechanisms from mechanostatic theory. RAP: Regional Accelerating Phenomenon; BMU: Bone Multicellular Unit.

degree (Wang et al. 2001). Applied load has a profound effect on BCFO: transversely oriented collagen fibres show the best resistance to compression strength, while longitudinally oriented collagen fibres show the best resistance to shear and traction strengths (Riggs et al. 1993). The predominance of transverse BCFO was noted around an overloaded fractured dental implant after 5 years of function (Traini et al. 2006). In contrast, around unloaded dental implants, there was a predominance of longitudinal BCFO (Traini et al. 2007), along with low mineral density (Traini et al. 2007). These histological findings are consistent with in silico studies (Alemayehu and Jeng 2021). However, high-level validation of Finite Element Analysis using in vivo experiments is still rare in the dental implant field, therefore the precision and accuracy of this kind of studies are still questionable (Chang et al. 2018). In vitro studies concerning the use of strain gauges to evaluate the mechanical stress on bone have been performed. However, when complex geometry is involved in the analysis, it is difficult to determine the analytical solution (Pesqueira et al. 2014). Finally, due to the anisotropic property of the bone, the multitude of factor influencing bone homeostasis, and the inherent limitation of each analysis' method, to date it is difficult to have an in vivo appraisal of the weight of each factor and of the clear impact of masticatory function on periimplant bone adaptation. Further research is needed in this intent.

CONCLUSIONS

The conclusion of this mini-review can be summarized as follows:

1. Applied load is an environmental factor influencing bone homeostasis, in terms of both entity and frequency of application.
2. Experimental findings on bone surrounding dental implants confirms point 1.
3. In dentistry there is lack of findings to clinically predict the periimplant bone adaptation.
4. To date, the major drawback of the in silico, in vitro and in vivo studies available is the difficulty to interconnect their findings for a thorough comprehension of the bone-implant system response to the applied load.
5. Stated the above, it would be highly desirable to have a continuous quantitative control of occlusal loading on dental implants. This would make us able to modulate the mechanical stress in order to build a mechanically competent bone.

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