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Dentin on the nanoscale: Hierarchical organization, mechanical behavior and bioinspired engineering

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ABSTRACT

Objective. Knowledge of the structural organization and mechanical properties of dentin has expanded considerably during the past two decades, especially on a nanometer scale. In this paper, we review the recent literature on the nanostructural and nanomechanical properties of dentin, with special emphasis in its hierarchical organization.

Methods. We give particular attention to the recent literature concerning the structural and mechanical influence of collagen intrafibrillar and extrafibrillar mineral in healthy and remineralized tissues. The multilevel hierarchical structure of collagen, and the participation of non-collagenous proteins and proteoglycans in healthy and diseased dentin are also discussed. Furthermore, we provide a forward-looking perspective of emerging topics in biomaterials sciences, such as bioinspired materials design and fabrication, 3D bioprinting and microfabrication, and briefly discuss recent developments on the emerging field of organs-on-a-chip.

Results. The existing literature suggests that both the inorganic and organic nanostructural components of the dentin matrix play a critical role in various mechanisms that influence tissue properties.

Significance. An in-depth understanding of such nanostructural and nanomechanical mechanisms can have a direct impact in our ability to evaluate and predict the efficacy of dental materials. This knowledge will pave the way for the development of improved dental materials and treatment strategies.

Conclusions. Development of future dental materials should take into consideration the intricate hierarchical organization of dentin, and pay particular attention to their complex interaction with the dentin matrix on a nanometer scale.

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Contents

1. Introduction

The field of restorative dentistry has evolved considerably in the past two decades. New restorative methods have been proposed, the concept of regenerative dentistry has been brought forward, and existing dental materials have increasingly become more biocompatible [1], bioactive [2] and biomimetic [3,4]. Key to such developments has been a profoundly more in-depth understanding of the tissues that compose the tooth at smaller length-scales [5]. This has been made possible by the fast development of characterization tools and techniques that can probe tissue structures at ever-finer scales.

Dentin is the largest structure in the tooth, and is composed of hydroxyapatite mineral crystallites, collagen fibrils (mostly type I) and noncollagenous macromolecules [6]. A great number of current restorative procedures use dentin as a substrate, therefore, the success of restorative dental materials invariably depends on a thorough understanding of the structural and mechanical property relationships that characterize the dentin matrix. Moreover, dentin, together with dental enamel, represents a unique biomaterial in nature, in that it retains outstanding durability despite the life-long cyclic loading imposed onto the tooth, and the absence of cell-regulated mechanisms of remodeling or repair [7] that are common in other tissues. Therefore, dentin offers a classic example of how nature designs stiff and tough natural biomaterials with outstanding longevity, simply by combining soft (proteins) and rigid (mineral) building blocks at precisely organized hierarchical levels [3]. Thus, if from a reverse engineering standpoint the ultimate goal of restorative dental materials is to closely approximate the longevity and properties of the tooth, knowledge of the mechanisms endowing dentin with its outstanding properties is imperative.

In this review we cover recent findings regarding the mechanical and structural relationships of dentin on the nanoscale. We adopt a hierarchical approach to explore aspects that relate to both tissue nano-structure and nano-mechanics, and the relative participation of the inorganic and organic constituents that make up the tissue matrix. Regarding the former, we discus the specific of the intrafibrillar mineral to the mechanical properties of dentin. On the latter, we cover the specific structural and mechanical contributions of collagen and, more in depth, non-collagenous nanoscale components, as determined by various analytical methods. Additionally, we offer specific insights into the challenges and limitations of existing dental materials and treatments (i.e. remineralization and bonding), especially in relation to the complexity of dentin proteins on the nanometer and molecular length scales. Finally, we provide a forward-looking overview of the gradual transition of dentistry into the emerging fields of bioinspired materials engineering and regeneration. We discuss how these emerging topics will influence the development of novel dental materials with properties that more closely approximate those of the natural structures in the tooth, and hence will provide impetus for the shift of clinical dentistry from reparative-based treatment methods to more biologically-assisted regenerative approaches.

2. Dentin inorganic content—extrafibrillar and intrafibrillar mineral

During development, differentiated odontoblasts secrete the dentin matrix in a well orchestrated sequence that is characterized by the release of collagen fibrils with high concentrations of carboxylated non-collagenous proteins [8,9] and proteoglycans [10]. These matrix constituents, respectively, regulate the process of mineral deposition [11,12] and fibrillogenesis [13] during dentin formation. The process of collagen biomineralization has been a topic of much debate in the recent literature. Although it has long been acknowledged that collagen mineralization occurs due to mineral release from vesicles in the extracellular matrix (which have also been called calcospherites early on), it has recently been demonstrated that prior to secretion, the mineral accumulates intracellularly in the mitochondria [14], and travels to the extracellular space where it accumulates calcium while it remains in the form of amourphous calcium phosphate until full release onto the collagenous network [15–18].