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Invited Review Paper
Dental Implants

Mineralization at the interface of implants

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Abstract. Osseointegration of implants is crucial for the long-term success of oral implants. Mineralization of the bone's extracellular matrix as the ultimate step of a mature bone formation is closely related to implant osseointegration. Osteogenesis at oral implants is a complex process, driven by cellular and acellular phenomena. The biological process of the maintenance and emergence of minerals in the vicinity of oral implants is influenced to a great extent by biophysical parameters. Implant-related structural and functional factors, as well as patient-specific factors, govern the features of osteogenesis. To understand the influence of these factors in peri-implant bone mineralization, it is important to consider the basic biological processes. Biological and crystallographic investigations have to be applied to evaluate mineralization at implant surfaces at the different hierarchical levels of analysis. This review gives insight into the complex theme of mineral formation around implants. Special focus is given to new developments in implant design and loading protocols aimed at accelerating osseointegration of dental implants.

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The establishment of dental implants in clinical routine has profoundly changed the possibilities of oral rehabilitation[1]. The long-term success of bone-interfacing implants requires rigid fixation of the implant within the host bone site. This condition, known as functional osseointegration, is achieved in various implant systems by an interlock between the surface features of the implant (threaded, porous or textured surfaces) and the bone tissue. Clinical and experimental studies demonstrate that osseointegration can be achieved when implants are placed under distinct circumstances in bone of different quantity and quality[63]. It was shown that implants cannot only become stable in bone of compromised size and structure but also have the ability to remain stable when implants are loaded[7]. Recent research indicates that an undisturbed osseointegration can be achieved even when healing under load is present[70]. In contrast, evidence from a multitude of clinical and experimental studies reveals that implant failures do also occur[46]. The failure of osseointegrated implants in the treatment of completely and partially edentulous patients with a sufficient amount and quality of bone has been well documented in the literature[1]. Various studies indicated a higher rate of long-term implant loss in the maxilla in comparison to the mandible. It has been suggested that the amount and quality of maxillary bone is responsible for the higher rate of implant failure in this area[2]. A failure of osseointegration or a disintegration of a formerly stable anchored implant can be conceptualized as a failure of the mineralized extracellular matrix directly attached to the artificial surface, since a mechanically competent implant/bone bond is dependent on an intact mineralized interface structure. Understanding of the maintenance and emergence of mineralized bone tissue is, therefore, fundamental to gaining an insight into implant/bone interface reactions[92].

The structural and functional tissue properties adjacent to the implant surface can be related to the interaction between an artificial material (e.g. titanium, calcium phosphates) and the microenvironment at the host site. The dynamic interaction between artificial materials and bone are inter-related as one object affects the other. The interaction is different in the sub-areas of the bony host site, since the cellular as well as the biophysical microenvironment between, for example the cortical and spongiosal layer, and even within such a layer is different. Therefore, various attempts have been made to improve bone formation around implants by influencing implant-specific or bone-specific aspects. Most notably, implant surface characteristics[23,48,61,66] (material, surface topography, surface chemistry) and implant geometries were altered to improve osseointegration[42,70].

It is important to note in this respect that osseointegration of implants, a term that was initially defined by Branemark et al.[13] as a direct bone-to-implant contact and later on defined on a more functional basis as a direct bone-to-implant contact under load, is not definitively determined in its details. Specifically, the dynamic cellular and acellular processes at the interface at a micro- and nanoscale level are not fully elucidated. Additionally, early aspects of the bone/biomaterial interaction in terms of seconds and minutes are not well known in the *in vivo* environment. Recent knowledge in both aspects of implant osseointegration is even more limited when the process of biomineral formation is under consideration. To gain insight into the state of mineralization at implant interfaces, the various levels of bone structure and physiology are considered and evaluated in light of the recent knowledge on implant osseointegration.

Influence of bone properties on osseointegration

The properties of bone are directly related to the features of the mineralized extracellular matrix adjacent to implants in 2 ways. First, the macroscopic and microscopic implant geometry and the insertion approach (as characterized by the preparation of the implant bed) determine the principal bone–implant relation. Second, the properties of bone have a major impact on the load-related characteristics of the microenvironment adjacent to implants.

Bone is defined as a bone-specific mineralized hard tissue[3]. Mineralization is therefore not only the defining feature of bone presence or formation, it is also the fundamental aspect that enables implants to remain stable in place even when forcibly loaded. Bone can be considered on a basic level as a compound material (a soft tissue network that is reinforced by minerals), possessing rigid as well as elastic properties[54]. It is composed of a variety of cell types and an organic matrix that is strengthened by matrix-associated calcium minerals (primarily calcium and phosphate in the form of hydroxyapatite). Cells, matrix and minerals are connected in a special way to give bone its unique biophysical and biological properties[55]. Morphologically there are 2 forms of bone that impose different structural and functional features: cortical and cancellous bone. Both types of bone tissue interact differently with implants[38]. The structure of the cortical layer and the trabecular system is optimised to transfer the loads through the bone by a dynamic feedback between load perception of cells and their subsequent cellular reaction. The differences in the histological and ultrastructural appearance of the 2 tissue types are related to some extent to their functions: the cortical part of bone provides the mechanical and protective functions, whereas cancellous bone is also involved in metabolic functions (e.g. calcium homeostasis). Both aspects (structural and metabolic) are closely related to the features of the mineralized extracellular matrix at implant surfaces.

One guiding principle in implant bone interaction is that the fixture design should be coincident with primary stability. A second emerging principle is that the implant must allow the transmission of forces without threading the biomechanical competence of the bone's material properties, leading to microfractures of the mineralized matrix. Third, implants should have an intimate contact with the bone directly after insertion. All 3 prerequisites, interacting mainly with the bone considered as a compound material and leaving behind the biological reactivity of bone, are closely related with the shape of implants.

With dental implants, where axial symmetry is possible, symmetrical implant forms have proved effective for achieving secure implant fixation within bone[1]. During the development of implant dentistry, root-form implants of screw, coated cylinder and, to a minor extent, hollow-basket geometries, were introduced in clinical treatment protocols[29,94]. In the past decade, a convergence to threaded screw designs has been observed[81]. More recently, parabolic 'root'-shaped implants have been demonstrated to possess advantages in respect to the biomechanical features of load transfer from implants to bone[70,73].

The threads of implants are representative of macroscopic surface features that allow mechanical interlocking of implant within bone[18]. Thread-containing implants can be inserted in bone by a self-cutting procedure or by preparation of the implant bed through a thread cutter. Histological analysis of probes indicates that self-cutting screws are associated with a generally higher bone-to-implant contact pronounced at the crestal part, when compared to preparation of the bony implantation bed[17]. The results of various experimental studies suggest that the quality of the primary implant stability is dependent to a large extent on the geometric relation between implant shape and the surgically created host side. The reason that an intimate contact between implants and bone directly after insertion can be achieved is based on the fact that cortical bone has an elasticity of up to 5% (with cancellous bone having an even higher elasticity). If the implant insertion is not accompanied by an extension of the cortical layer over this threshold, a direct contact between the implant and the present mineralized matrix can be assured. The core diameter of the implant bed should therefore be adjusted to the core implant diameter. By a slight expansion of fully mineralized bone, a direct contact can be achieved over large areas. Therefore, bone remodelling more then new bone formation (modelling) would take place. Experimental studies reveal that implant systems having a conceptual geometric approach of insertion may, therefore, affect the tissue response in a positive way. A histological evaluation of screw-shaped parabolic implant systems revealed a high congruency between the implant and the surrounding bone tissue[67]. A direct contact between implants and bone was achieved over large surface areas directly after insertion when parabolic implant systems were used. Cylindrical implant systems, in contrast, possess the disadvantage of a crestally pronounced incongruency[17]. Excellent adaptation of the host bone to titanium surfaces was observed on an ultrastructural level in a comparable manner after insertion of self-tapping screws in calvaria bone by Sowden & Schmitz[96]. Several studies demonstrated that when self-tapping parabolic-shaped screws were placed in loading or non-loading positions, the long-term histology showed that the bone tissue around the implants was maintained in both situations[31].