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Osteophilic properties of bone implant surface modifications in a cassette model on a decorticated goat spinal transverse process

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ABSTRACT

This study comparatively evaluated the osteophilic capacity of 17 different surface modifications (i.e. fourteen different chemical modifications via ceramic coatings and three different physical modifications via surface roughness) for titanium (Ti) surfaces. All surface modifications were subjected to physico-chemical analyses and immersion in simulated body fluid (SBF) for coating stability assessment. Subsequently, a bone conduction chamber cassette model on the goat transverse process was used for comparative *in vivo* analysis based on bone responses to these different surface modifications after twelve weeks. Histological and histomorphometrical analyses in terms of longitudinal bone-to-implant contact percentage (BIC%), relative bone area (BA%) were investigated within each individual channel and maximum bone height (BH). Characterization of the surface modifications showed significant differences in surface chemistry and surface roughness among the surface modifications. Generally, immersion of the coatings in SBF showed net uptake of calcium by thick coatings (>50 μm; plasma-sprayed and biomimetic coatings) and no fluctuations in the SBF for thin coatings (<50 μm). The histomorphometrical data set demonstrated that only plasma-sprayed CaP coatings performed superiorly regarding BIC%, BA% and BH compared to un-coated surfaces, irrespective of surface roughness of the latter. In conclusion, this study demonstrated that the deposition of plasma-sprayed CaP coating with high roughness significantly improves the osteophilic capacity of titanium surfaces in a chamber cassette model.

Statement of Significance

For the bone implant market, a large number of surface modifications are available on different types of (dental and orthopedic) bone implants. As the implant surface provides the interface at which the biomaterial interacts with the surrounding (bone) tissue, it is of utmost importance to know what surface modification has optimal osteophilic properties. In contrast to numerous earlier studies on bone implant surface modifications with limited number of comparison surfaces, the manuscript by van Oirschot et al. describes the data of *in vivo* experiments using a large animal model that allows for direct and simultaneous comparison of a large variety of surface modifications, which included both commercially available and experimental surface modifications for bone implants. These data clearly show the superiority of plasma-sprayed hydroxyapatite coatings regarding bone-to-implant contact, bone amount, and bone height.

1. Introduction

An expanding and aging world population has increased the demand for implantable devices and scaffolds to replace damaged tissues and restore tissue function [1,2]. These implants must be

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designed so they are easy to implant with minimal post-operative complications. Further, these implants must be safe, reliable, and long lasting in patients with varied health status [3,4]. In the field of oral implantology, increasing numbers of dental implants are placed globally to support (complete or partial) prosthetic devices [5]. Long-term implant survival and success rates (up to 90% after 10-years follow-up) have been reported for implants under favorable clinical conditions [6]. Implant failure, however remains significant in patients with chronic medical conditions, impaired bone healing (i.e. osteoporosis), or in anatomical sites with insufficient bone quantity and quality [7,8].

The challenge then is to achieve long term implant success in medically compromised patients. In order to achieve this goal, osteophilic implants i.e. implants that favor bone apposition, are required [9]. Since the implant surface directly interacts with bone tissue, research has focused on modifying the implant surface to improve its osteophilic characteristics with the goal of inducing early peri-implant bone formation [10–12]. These osteophilic implant surface modifications focus on manipulation of physical (roughness) and/or chemical properties of the metallic implant surface (i.e. titanium or titanium-alloy). These modification methods are based on either subtractive (i.e. grit blasting, acid etching) [13] or additive (i.e. coating deposition) procedures [14].

Surface roughening is a popular subtractive modification method because rough surfaces have a larger contact area for interaction with bone tissue in comparison to smooth surfaces [15]. Further, surface roughening creates micro-porosities and small etching grooves that have been hypothesized to enhance protein adhesion and stimulate cell migration on the implant surface facilitating early bone formation [16,17].

Additive techniques utilizing bioactive ceramics (e.g. calcium phosphate, CaP) on implant surfaces have shown superior osteophilicity compared to non coated surfaces [18–21]. It has been hypothesized that this enhanced osteophilicity is related to the (superficial) dissolution of the CaP coating that results in calcium (Ca^{2+}) and phosphate (PO_4^{3-}) ion release in the peri-implant region [22]. Mechanistic studies have shown that Ca^{2+} ions have a positive effect on the differentiation of osteoprogenitor cells [23–25]. Further, both ions enhance the precipitation of a carbonated calcium phosphate layer that has high crystallographic resemblance to natural bone mineral [26,27]. Several studies have shown that the osteophilic properties of the ceramic coating are influenced by the crystal phase, chemical composition and crystallinity of the applied CaP ceramic [28,29]. Hydroxyapatite (HA) [30], tricalcium phosphate (TCP) [31], and octacalcium phosphate (OCP) [32], have been successfully used for the deposition of ceramic-based coatings. In addition to CaP coatings, bioactive silicate-based glass (BG) coatings are thought to demonstrate osteophilic characteristics [33,34]. It has been demonstrated that the formation of a hydrated silica layer and hydroxyl carbonate apatite on the glass surface have an osteopromotive effect on osteoblast proliferation and differentiation [35].

Ceramic-based coatings can be deposited through a variety of techniques, including plasma-spraying, magnetron sputtering, or pulsed laser deposition (PLD) [15,36]. Plasma-spraying is a popular procedure in the field of dentistry and orthopedics for the deposition of CaP-based coatings on metallic bone implants. Numerous *in vivo* studies have been published on the beneficial biological performance of plasma-sprayed CaP surfaces [37–39]. However, clinical use of these coatings is hampered by concerns regarding coating delamination and fragmentation at the implant/coating interface. This delamination and fragmentation jeopardizes the long-term performance of these implants [40]. Magnetron sputtering and pulsed laser deposition can overcome these problems by generating thin, adherent coatings while preserving the osteophilic properties of the CaP ceramic [41,42].

Additionally, wet-chemical coating techniques, such as electrospray deposition (ESD) or coating deposition via biomimetic precipitation, have been used for coating deposition of CaP ceramics under physiological conditions (i.e. low temperature and pressure). Not only do these techniques allow for simultaneous incorporation of organic components and therapeutic agents into CaP ceramic coating [43], but these techniques also make it possible to deposit coatings on scaffolds of complex 3D architectures that are frequently used for regeneration of craniofacial skeletal defects [43]. As these techniques allow for deposition of less stable CaP phases, partial coating dissolution and release of incorporated compound can induce a local anabolic effect, which stimulates the bone remodeling process at the peri-implant interface [44].

All aforementioned surface modifications and coating procedures have shown benefit during the early process of peri-implant bone formation. Straightforward comparison of different *in vitro* and *in vivo* results for each individual study, however, has proven difficult for several reasons. First, there is a lack of suitable models that allow simultaneous evaluation of multiple surface modifications. Second, experiment specific parameters and differences in bone healing in each experimental setup can influence the performance of a coating or surface modification. Third, most of the experimental animal models only allow inclusion of a limited number of experimental groups. In response to these challenges, this study was designed to evaluate the osteophilic capacity of a broad range of seventeen different surface modifications within one *in vivo* experimental setup. For this purpose, a bone conduction chamber cassette model was used on the transverse process of a goat, a common model used for pre-clinical evaluation of bone implant surface modifications. This model allows for simultaneous comparison of different surface modifications, and the effects on bone ingrowth and bone metabolism under unloaded conditions [45,46]. In this study, we compared the osteophilic capacity of different ceramic-based coatings in comparison to different titanium surfaces obtained via subtractive procedures (machined (Ti), grit blasted (GB), grit blasted acid etched (GAE)). Bone response to the different implants was evaluated using histological and histomorphometrical analyses in terms of longitudinal bone-to-implant contact percentage (BIC%), relative bone area (BA %) within each individual channel and maximum bone height (BH).

2. Materials and methods

2.1. Research objectives and experimental study design

This study evaluated the osteophilic capacity of different ceramic-based coatings compared to titanium surfaces obtained through different subtractive procedures within one *in vivo* experimental setup. For this purpose, a previously designed bone conduction chamber model on the goat transverse processes was used [45]. The sample size needed for the study was calculated using online software [61]. An effect size (f) of 0.2, an error probability $\alpha = 0.05$, standard deviation (SD) of 0.1, and a power (P) of 0.85 were assumed. This gave a minimal required sample size per coating type (n) of 10.

2.2. Sample preparation and characterization

Polyacetal chamber cassettes designed for bone conduction evaluation were used [46]. Each cassette contained ten titanium plates that formed five osteoconductive channels that each had a diameter of 0.5 mm in width. After cassette fixation on the transverse processes, the bottom component of the channels was exposed to the underlying bone while the top component was covered by overlying soft tissue.