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Hydroxyapatite coating on PEEK implants: Biomechanical and histological study in a rabbit model

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ABSTRACT

A bioactive two-layer coating consisting of hydroxyapatite (HA) and yttria-stabilized zirconia (YSZ) was investigated on cylindrical polyetheretherketone (PEEK) implants using ion beam assisted deposition (IBAD). Post-deposition heat treatments via variable frequency microwave annealing with and without subsequent autoclaving were used to crystallize the as-deposited amorphous HA layer. Microstructural analysis, performed by TEM and EDS, showed that these methods were capable of crystallizing HA coating on PEEK. The in vivo response to cylindrical PEEK samples with and without coating was studied by implanting uncoated PEEK and coated PEEK implants in the lateral femoral condyle of 18 rabbits. Animals were studied in two groups of 9 for observation at 6 or 18 weeks post surgery. Micro-CT analysis, histology, and mechanical pull-out tests were performed to determine the effect of the coating on osseointegration. The heat-treated HA/YSZ coatings showed improved implant fixation as well as higher bone regeneration and bone-implant contact area compared to uncoated PEEK. The study offers a novel method to coat PEEK implants with improved osseointegration.

1. Introduction

Biomedical implants for orthopedic and dental applications are designed to replace damaged internal tissues with the goal of restoring normal biomechanical activity for the patient. In designing these implants, various engineering materials are employed to match the implant device with the surrounding tissue to achieve successful outcomes, a difficult challenge considering the complexity of biological systems. Stress shielding due to improper mechanical matching, and lack of bone apposition due to interfacial chemical interactions are two major concerns stemming from the implant design. Additional surgical intervention is necessary to address complications caused by these issues [1], increasing overall procedural costs and recovery time for the patient. It is expected that engineered materials that exhibit mechanical and surface chemical properties similar to bone tissue will result in reduced occurrences of revision procedures and improved clinical outcomes.

Polyetheretherketone (PEEK), a thermoplastic polymer, has an elastic modulus that falls between that of cancellous and cortical bone. The reduced mechanical mismatch with bone tissue compared to that of metallic implants can reduce stress shielding and has made PEEK popular in a number of clinical applications [2,3]. The inert chemical structure and high heat resistance of this material make it suitable for a wide range of sterilization techniques such as ethylene oxide, gamma irradiation or autoclave [4]. PEEK is also radiolucent, facilitating effective observation of peri-implant tissue healing.

However, the bioinert chemical properties of PEEK do not promote bone apposition once implanted [5]. Bioactive calcium phosphate coatings such as hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$), or HA, have been applied to metallic implant surfaces to improve osseointegration with promising results [6–8]. Coating processing techniques often involve high temperatures to produce the desired crystalline phase of HA, which has much lower dissolution rates in vivo than amorphous HA, an important consideration for bioresorbable coatings [9,10]. Despite the heat resistance of PEEK with respect to polymers (T_{glass} = 150 °C; T_{melt} = 350 °C), it is not sufficient to withstand the high temperatures needed to crystallize HA, and can be damaged during coating deposition or heat treatment. This has driven recent research in developing a method for modifying the surface of PEEK to improve bioactivity. Three main categories of PEEK modification have been investigated for bioactivity in the literature: i) surface physical and chemical treatments such as various plasma exposures [11,12], surface functionalization [13], and sulfonation [14], ii) composite HA/PEEK materials [15,16], and iii) alternative HA coating methods such as spin-coating [17], aerosol deposition [18], cold spraying [19], and radiofrequency magnetron sputtering [20]. HA-coated implants offer strong bioactive potential; however, achieving an adequate bond between a ceramic HA coating and a polymer

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(PEEK) is not trivial and is an important factor in determining success in implantable applications.

Studies recently reported the deposition of a two-layer bioactive coating on PEEK using an ion beam assisted deposition (IBAD) technique [21]. IBAD has proven to be an effective method to increase coating adhesion due to atomic mixing at the film-substrate interface [22,23]. The coating consists of yttria-stabilized zirconia (YSZ) as a heat protection layer over the PEEK substrate and an HA top layer for improved bioactivity. Subsequent heat treatment via microwave processing followed by autoclaving resulted in crystallization of the HA layer without causing damage to the underlying PEEK. YSZ is used as a thermal barrier coating in high temperature applications and its columnar grain structure helps mediate residual film stresses caused by heat treatment. Recent studies have shown these coatings to exhibit high adhesion strength to PEEK substrates, indicating potential for a robust method for implant surface preparation [24]. In addition, an in vitro study using MC3T3 cells showed promising bone growth on coated samples that underwent post-deposition heat treatments [21]. For the in vivo study described herein, uncoated control PEEK implants were compared with coated implants that underwent subsequent heat treatment in order to determine if the HA/YSZ coating deposited by IBAD could improve the osseointegration of PEEK implants.

2. Materials and methods

2.1. Implants

2.1.1. Sample preparation

PEEK (PEEK-OPTIMA®, Invibio, Lancashire, UK) rods measuring 5 mm in diameter and 9 mm long were used as the implant substrates for coating deposition. The bulk, extruded rod was machined down to achieve the desired implant diameter and length using a lathe. A 1-mm axial through-hole was drilled while mounted to the lathe to aid in implant placement and fixation onto the IBAD substrate holder. Substrates were ground sequentially against 600 and 800-grit silicon carbide paper (Buehler, Lake Bluff, IL, USA) using an automated grinding technique designed to allow for equal material removal in the radial and axial directions by rotational symmetry. The substrate surfaces were rinsed with deionized water between grinding steps to avoid particle contamination. The cylindrical rods were then submerged and ultrasonically cleaned for 10 min in acetone, isopropanol, and deionized water, respectively. The substrates were dried via compressed air and stored in sterile tissue culture plates prior to vacuum deposition.

2.1.2. Surface activation

The PEEK substrate surfaces underwent a brief surface treatment via O_2 plasma prior to deposition using a radio-frequency plasma barrel reactor (model PM-600, March Instruments, Concord, CA, USA) for 10 min. This method has been described in greater detail in previous studies [20,21]. Substrate rods were then mounted on 1 mm titanium rods before being transferred to the IBAD system vacuum chamber for deposition.

2.1.3. Coating deposition

Deposition of the HA/YSZ coatings was achieved by way of a custom rotational substrate fixture and an IBAD system (Univex 600, Oerlikon Leybold Vacuum, Export, PA, USA). The deposition system is composed of 8-in. HA and YSZ sputtering targets (Plasmaterials, Inc., Livermore, CA, USA) with 16-cm primary and 12-cm secondary ion sources outfitted with argon process gas. A custom substrate fixture developed for cylindrical PEEK substrates fixed on rotating titanium rods was used to ensure even coating during deposition. Adjustable-speed simultaneous rotation was achieved by way of a water-cooled gearbox and an external feed-through stepper motor. The ion source deposition parameters were optimized for film thickness and density. The base vacuum achieved before deposition was approximately 5×10^{-7} Torr and the deposition pressure varied from 3×10^{-4} to 5×10^{-4} Torr depending on primary and secondary ion source parameters. The temperatures near the deposition area were monitored during deposition and maintained below the glass transition temperature of PEEK to avoid damage to the polymer substrate. The deposition chamber was vented to atmospheric conditions between the YSZ and HA layer deposition in order to perform the target exchange.

2.1.4. Post-deposition heat treatment

The HA/YSZ coatings on PEEK were processed via two heat treatment methods following deposition: i) microwave processing (AD + MW), and ii) microwave plus autoclave processing (AD + MW + AC). For microwave processing, selective heating of the HA coating layer was achieved with the use of a variable frequency microwave oven (Microcure, Lambda Technologies, Morrisville, NC, USA) in order to aid in crystallization of the HA layer without damaging the PEEK substrate. The microwave treatment conditions were administered in accordance with the methods described in patent US8323722 [25]. Subsequent autoclave processing was applied to the coated implants using a commercial sterilization unit (Prevac Steam Sterilizer, Steris, Mentor, OH, USA). The temperature-programmable autoclave was adjusted to apply a saturated steam cycle of 136 °C for 8 h.

Prior to surgical placement, all implants (coated and uncoated PEEK) were sterilized by ethylene oxide and allowed a three-day de-gassing period to ensure no residuals remained on the surface.

2.2. Coating analysis

2.2.1. Microstructural analysis

A Transmission Electron Microscope (TEM) (2100F, Jeol, Huntington Beach, CA, USA) was used to observe coating microstructure, interfacial zones, and to quantify the layer thickness with the use of image analysis software (ImageJ, National Institutes of Health, Bethesda, MD, USA). High-resolution TEM was used to examine the crystallized regions formed within the HA layer by heat-treatment processes. Samples were prepared using focused ion beam (FIB) milling and lift-out. A thin layer of gold (Au) was sputter-deposited on the surface to protect the sample from excessive damage during ion beam thinning and removal.

2.2.2. Compositional analysis

A Scanning Tunneling Electron Microscope (STEM) (Titan, FEI, Hillsboro, OR, USA) equipped with Energy Dispersive Spectroscopy (EDS) was used to determine the atomic percentage of the elements present in the HA coating layer. This data was then used to quantify the Ca/P ratio and compared to stoichiometric HA present in the sputtering target. Two cross-sectional coating regions, approximately 400 nm × 400 nm in size, were used to determine averages for each sample.

2.3. Animal study

2.3.1. Surgical procedure

This study was used to evaluate HA-coated PEEK implants in 18 skeletally mature male New Zealand White rabbits (3.5–4.5 kg). The following surgical protocol was approved and performed within the guidelines of the local Institutional Animal Care and Use Committee (IACUC) facility; NIH guidelines for the care and use of laboratory animals (NIH Publication #85-23 Rev. 1985) have been observed. The rabbits were randomly allocated to one of two time points for observation after either 6 weeks (N = 9 animals) or 18 weeks (N = 9 animals). Within each time point, the 9 animals yielded 18 implants (N = 6 implants of each of the three candidate surface treatments). The rabbits were weighed and administered glycopyrrolate (0.1 mg/kg body weight) subcutaneously to reduce salivation during the procedure. Animals were sedated with xylazine (5 mg/kg IM) and anesthetized with