

SURFACE MODIFICATION OF POROUS TITANIUM FOR BONE REPAIR: CONTROLLED ETCHING BY CHEMICAL AND ELECTROCHEMICAL TREATMENTS

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ABSTRACT

Stress shielding and osseointegration failures are two important problems that can eventually reduce the reliability of titanium (Ti) implants; they are addressed in this work, in order to improve the whole performance of Ti in biomedical applications. To that end, we fabricated commercially pure Ti (cpTi) porous substrates via space holder technique (50% vol., with three different particle size ranges of NH_4HCO_3 , 800 MPa, by sintering at 1250 °C, 2h in high vacuum, $\sim 10^{-5}$ mbar). Controlled etching of cpTi porous samples and anodizing were performed from previous studies of the authors on bulk Ti: etching solution is a water based one with 2.2 vol.% of HF and a 0.5 ml/L % of an organic inhibitor; temperature was 50°C and immersion times were 0, 5, 25, 125, 625 y 3125 s. Anodizing conditions were: 2 to 10 min, 12, 18 y 40 VDC, 60 g/L H_2SO_4 and 150 g/L H_3PO_4 . Micro-structural, mechanical, and micro-mechanical (*P-h* curves and scratch resistance) characterizations were performed. We measured the roughness of modified samples (inner roughness by confocal laser). Homogeneity, effectiveness and infiltration integrity of the coatings were also evaluated through cracking and adhesion evaluation (SEM, DRX, contact angle) and osteoblasts biological testing.

ANTIBACTERIAL BEHAVIOUR OF POROUS TITANIUM FOR BONE REPAIR

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ABSTRACT

Patients who require bone repair via titanium (Ti) implants still have to suffer the risk of failures. These limitations are normally reflected in facts like failures percentage between 5% and 10%, during the first five years of implantation. Accordingly, we need to solve the stress-shielding problem via development of porous Ti implants, whilst infections and interfacial loosening due to bacteria colonies and proliferation must be reduced. These are events that can be also risky for applications like joints prosthetics and ossteosynthesis. In this work, we fabricated commercially pure Ti (cpTi) porous substrates via space holder technique (50% vol., with three different particle size ranges of NH_4HCO_3 , 800 MPa, by sintering at 1250 °C, 2h in high vacuum, $\sim 10^{-5}$ mbar). These samples exhibit an improved biomechanical balance between stiffness and mechanical strength, as well as a proper stimulation to cells inside the pores due to controlled inner roughness. Specifically in this communication, we are reporting the preliminary antibacterial results of porous Ti samples, after evaluation of contact with a bacterial strain commonly present inside the mouth (*Staphylococcus aureus*), normally introduced via some long term food with *Escherichia coli*. Bacteria growth allowed us to identify some areas with potential beneficial effects.

DESIGN, PROCESSING AND CHARACTERIZATION OF TITANIUM WITH CONTROLLED RADIAL AND LONGITUDINAL POROSITY GRADIENT

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Abstract.

The manufacture of functionally graded materials has gained an enormous interest during last decade due to the diversity of industrial and biological systems that are designed from that criteria; those natural or artificial materials offer multiple possibilities of applications. In this work, a novel uniaxial and sequential compaction device has been successfully designed and fabricated, in order to obtain samples with three different layers; this new device is suitable for both conventional and non-conventional powder metallurgy (PM) techniques. This compaction device is especially powerful to obtain samples with radial graded porosity for biomedical applications (replacement of cortical and trabecular bones involved in different joints and dental restorations). Specifically in this work, Ti cylinders with radial and longitudinal graded porosity were fabricated and their microstructure and mechanical behaviour were characterized. This new device has proved to have unique advantages for solving problems of structural integrity in PM conventional manufacturing in a simple, economic and reproducible way.

COATING OF POROUS TITANIUM WITH BIOACTIVE GLASS TO IMPROVE THE OSSEOINTEGRATION AND REDUCED STRESS SHIELDING

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Abstract.

Titanium osseointegration is a property that can be still improved by reducing fibrous tissue capsule, which usually surrounds Ti implants. One of the routes studied for obtaining a good osseointegration of a bulk titanium implant is by using a coating with a bioactive glass (BG), in a manner that can be ensured strong adhesion. The goal of this work is to study the enameling technique of BG on porous titanium samples in both morphology and properties. Porous titanium samples of cp Ti grade IV have been obtained by space-holder technique (50 vol.% NH₄HCO₃ particles between 100-200 μm, compaction pressure of 800 MPa and sintering temperature of 1250 °C for 2h under high vacuum). The substrates have been coated and infiltrated by using Bioglass® particles via conventional slurring. Once the BG particles are in intimate contact with porous titanium (green samples), they are sintered under high vacuum conditions. Structural characterization (macro-graphics, SEM and roughness) performed on both obtained structures, coated surface and infiltrated pores, showed good adhesion between BG and titanium substrate. The infiltration with bioactive particles exhibited an increased effect of mechanical strength, with a slight increasing of stiffness, which indicates their potential for load bearing implants with improved osseointegration.

Title: μ BRAIN: a dynamic model of the blood-brain barrier

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The blood-brain barrier (BBB) presents a formidable obstacle to the delivery of circulating therapeutic agents to brain tissue. Due to the lack of physiologically accurate models of the BBB (*i.e.* lack of flow), the development of technology and methods for circumventing the BBB depend heavily on expensive and labor-intensive *in vivo* studies. To address this need, we have developed an *in vitro* microfluidics-based dynamic model of the BBB. The microfluidic blood brain barrier with analysis integrated (μ BRAIN) was designed to promote the growth and expression of anatomical and biomolecular components of the BBB, respectively. In static conditions, the μ BRAIN is less permeable than a model BBB cultured in transwell plates. Moreover, the μ BRAIN enables the study of the margination and penetration of biomolecules and drug delivery vehicles across the BBB under flow conditions. Using this platform, we are rationally designing surface-modified colloids for receptor-mediated transcytosis of the BBB.

INFLUENCE OF SURFACE MICRO-MACHINING ON TOPOGRAPHY AND MECHANICAL PROPERTIES OF SOCKETS FOR TRANSFEMORAL AMPUTEES

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Abstract. The topographic properties of sockets in transfemoral amputee's prosthesis have been widely studied due to its importance on the mechanical and tribological properties. These properties are even more critical in countries like Colombia, where most of the sockets are handmade. In this study, we developed two types of surface patterns in polypropylene specimens (handmade grinding and micromachining), in order to analyse the influence on both roughness parameters and mechanical properties. The handmade grinding was performed through a sequence of abrasive papers of SiC, while the micromachining patterns were based in a sinusoidal wave made with a machining center Kern evo of ultra-precision. The results of topographical characterization via roughness measurements have shown the creation of a handmade pattern with reproducible R_a s, approximately of 9.0, 4.0 and 0.75 microns. The micromachining was effective reproducing the sinusoidal wave design with 2 cycles per millimetre, and R_a associated to the micromachining tool of around 10.0 μm . The mechanical uniaxial, micro and nano-mechanical testing have shown an influence with respect to control material (a polished socket). The measurements of micro and nano-indentation have exhibited a bigger effect, compared with uniaxial properties, which could be explained in terms of hardening phenomena's and surface residual stresses.

DIRECTIONAL FREEZE CASTING TO OBTAIN POROUS TITANIUM SCAFFOLDS: INFLUENCE OF PROCESSING CONDITIONS

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ABSTRACT

In this work, a novel device for manufacturing cylindrical porous cp Ti, implementing directional freeze casting has been developed. The influence of the temperature gradient imposed and the diameter of alumina tube used as a mold (8, 15 and 20 mm) has been studied on the directional growth of dendrite ice and titanium powder compaction. A cryogenic salt solution was used to cool the surface of an aluminum cylinder (-15, -10 and -5 °C), on which the mixture (cp Ti, dispersant and water) was poured. The lateral external surface of the ceramic cylinder containing the mixture was thermally insulated, being exposed to room temperature (20 °C) one of its bases. Ice sublimation was performed in a lyophilizer to -50 °C and 0.070 mbar for 24 h. Finally, porous green compacts were sintered at 1250 °C for 5h under high vacuum (~10⁻⁵ mbar). Physical characterization (Archimedes' method), microstructure (optical microscopy and image analysis) and mechanical characterization (ultrasound and uniaxial compression test) include: total and interconnected porosity, equivalent diameter, morphology (aspect ratio), and average size of the pores, dynamic Young's modulus and the yield strength. The results indicate that this device is suitable to obtain cylinders with longitudinal gradient porosity.

DEVELOPMENT OF POROUS TITANIUM REINFORCED WITH CARBON NANOTUBES (CNT's): A BETTER BIOFUNCTIONAL AND BIOMECHANICAL BALANCE

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ABSTRACT

Titanium (Ti) and some of its alloys are widely recognized to be highly successful in clinical applications of bone tissue replacement. However, some important improvements are still required about the desired balance between biological performance (cells and tissue stimulations), mechanical strength, and implant's stiffness. In this work, we developed, fabricated, and characterized a new biocomposite of porous commercially pure Ti grade 4 (cpTi-G4) reinforced with carbon nano-tubes (CNT's); our main hypothesis here is that there must be certain percentages of CNT's reinforcement that can improve all factors involved in the searched balance of properties: bone cells stimulation in contact with a nano-structured surface (CNT's), reduced stiffness, and increased mechanical strength due to the presence of the highly resistant advanced component (CNT's). Characterization results obtained by SEM, XPS and AFM have shown that certain compacting and sintering conditions were effectively able to produce a well dispersed 5% of CNT's with strong attachment to porous cpTi-G4 matrix, which were preferentially located at Ti grain boundaries. These CNT's were associated to a higher twinning within neighbours grains, which was certainly consistent with higher nano-hardness values. Biological evaluation of these samples allowed us to discard, in principle, any doubt about potential cytotoxicity effects.

Joanna Chiu (poster):

Title: Development of a lipid-coated calcium phosphate nanoparticle for oligonucleotide delivery to the brain.

Abstract:

Brain cancer is one of the most difficult cancers to treat, due to the impermeability of the blood brain barrier (BBB) to anti-cancer agents. To overcome this barrier, a ligand-decorated nanoparticle has been developed to facilitate delivery of therapeutic agents across the BBB to malignant cells. The nanoparticle consists of a siRNA-containing calcium phosphate (CaP) core coated with a lipid bilayer. The CaP core facilitates siRNA delivery to the cell cytosol while the lipid shell improves colloid stability and provides a platform for ligand conjugation. In the current work, angiopep was conjugated to the lipid shell, increasing nanoparticle penetration of a model BBB via receptor-mediated transcytosis. Exploration of different calcium to phosphate molar ratios reveals that increasing the ratio inversely reduces particle size, and may also affect siRNA encapsulation and release. Ratios of 50, 100, and 150 resulted in nanoparticle sizes of 244 ± 4.1 nm, 181.0 ± 3.2 nm, and 165.2 ± 2.2 nm respectively. Studies conducted with GFP-expressing breast cancer cells demonstrate successful nanoparticle uptake and up to 67% knockdown of the reporter protein.

Ian Harding:

"The title is "The Effects of Disturbed Flow on Endothelial Glycocalyx and Cancer Cell Attachment" and the abstract is as follows:

The endothelial glycocalyx (EC GCX) is a protein-sugar layer that lines the inside of blood vessels. It supports healthy vasculature by maintaining ideal levels of transvascular transport, facilitating and preventing plasma-endothelial cell interactions, and acting as a mechanotransducer, converting blood flow induced shear stress into biochemical signals. These functions help prevent the development of disease such as atherosclerosis. The goal of this study is to determine the effects of disturbed flow, which is often found in atherosclerosis prone blood vessels, on the endothelial glycocalyx and the subsequent effects on cancer cell attachment in these areas."

ADVANCED PROCESSING OF POROUS TITANIUM FOR BONE TISSUE REPAIR: MULTI-FACTORIAL, MULTI-SCALE AND MULTI-FUNCTIONAL NEW THERAPIES

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ABSTRACT

The tissues of muscle-skeletal system suffer an important degradation, which are mostly associated with aging and diseases that can be consequence of prolonged physical activity, life habits, genetics or traumas. Any proposed use of tissue engineering (TE) and regenerative medicine (RM) with multiple purposes of tissue growth, repair and even regeneration, need rationale approaches from different frameworks. To that end, our highly collaborative work has allowed us to propose a new paradigm for tissue treatment therapies through the development of a bottom-line approach based on both multi-factorial and multi-scale analysis. This new framework will create new therapies by taking advantage of synergistic correlations between advanced bio-inspired hierarchical titanium (Ti) scaffolds, nanotechnology and bio-functionalizing applications for optimized bio-interfaces. The complexity of factors involved has motivate us to develop a new global approach in order to optimize the performance of the implant/tissue systems; with this aim, we decided to emphasize in four factors, which should be studied in order to know their potential synergistic effects: intrinsic properties of Ti, bio-interfaces phenomena, remote and local mechanical stimulation, and health conditions of hosting tissue. Additionally, we modified porous Ti implants from 2nd to 3rd generation by surface nano-structuring with Directed Irradiation Synthesis (DIS).