# Hierarchically Micro- and Nanostructured Surfaces for Dental Implant Abutments

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#### Introduction

Despite the good long-term results of dental implants, the risk of developing peri-implantitis over time is a certain treatment problem. Peri-implantitis is difficult to be treated and often results in the loss of the whole implant. In this work, strategies have been developed and tested to optimize the soft tissue integration on dental implants and dental implat abutments by micro- and nanostructuring in order to reduce the risk of peri-implantitis.

#### Methods

Microgrooves with different lateral widths and different cross-sectional geometries have been fabricated on the material Ti6Al4V ELI by UV-lithographic microfabrication and controlled underetching. In vitro cell tests with human gingival fibroblasts were performed to identify optimal geometric parameters.

In addition to the cell-friendly environment, different mechanisms to reduce bacterial adhesion were evaluated and optimized for the use as dental implant surfaces. For this purpose, different nanostructures were fabricated by various oxidation methods and have been bacteriologically examined.

#### Results

Cell tests revealed optimal geometric parameters where cells maximize alignment, spreading and proliferation. As a result, the cells involved in wound healing align themselves along the grooves, resulting in a faster wound closure.

In addition, nanostructures can be used to realize antiadhesive or even bactericidal properties. Bacterial antiadhesiveness can be associated with the discrete contact area of the nanotopography. The bactericidal effect was found to be related to a certain kind of pyramidal nanostructures and to be gram-stain specific.

### Conclusion

The influence of nano- and microtopography on bacterial adhesion and cell growth offers an enormous potential to reduce the complications related with peri-implantitis. A cell-friendly microstructure can enhance eukaryotic cell aligment, spreading and proliferation and nanostructures can be used to realize antiadhesive or bactericidal properties, slowing down biofilm formation. The combination of the different structures realizes hierarchically micro- and nanostructured implant surfaces with superior properties.

# Investigating dynamic-mechanical properties of multi-layered materials for biomedical applications

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### Introduction

The development and advancement of polymeric implant materials is a frequent focus in current research. The combination of polymeric materials with diverging properties provides a wide range of new materials with innovative characteristics. Medical implant materials technologies that generate multi-layered structures with a thin top layer onto a base material are frequently used in the field of polymeric material development. Established methods for the analysis of coating adhesion are not applicable to examine mechanical properties or durability for polymeric coating layers.

#### Materials and Methods

To examine adhesion and durability of chitosan (CS) coatings on polycarbonateurethane-co-silicone (PCU-co-Si) films, dip-coated films, as well as uncoated reference samples, were tested comparatively under uniaxial quasi-static and dynamic load conditions. Dynamic-mechanical tests were performed under tumescent load conditions for 432,000 load cycles in isotonic saline solution at 37 °C. For further validation of the results gained by dynamic testing scanning electron microscopy (SEM) was used.

#### Results

The CS-coating leads to a increase in mechanical strength compared to uncoated reference samples. Especially an increase regarding Young's modulus can be seen. The curve progression of reference and coated samples is very similar for dynamic load conditions. An exception to this is the stress-offset induced by the coating layer. Hence, the CS-coating on films results in a higher stress under dynamic load conditions. The surface, investigated with SEM-imaging, shows irregularities before and after dynamic-mechanical testing.

#### Conclusion

Combining the results of dynamic-mechanical examinations and SEM-imaging, the general mechanical resistance of CS-coatings on PCU-co-Si films to pulsating stress can be assumed, though crack formation was pbserved before and after dynamic testing. These findings match the results of tensile tests, where a higher Young's modulus and particularly higher tensile strength in lower strain ranges was determined with coated samples. Therefore this study represents a first insight into fatigue testing of multi-layered polymer structures.

# Development of UV-Reactive Electrospinning Method Based on Poly(ethylene glycol) diacrylate Crosslinking

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#### Introduction

In the field of biomaterials, electrospun fibers are favoured because of high surface-to-volume ratio which can be useful for drug loading and release, and because nano-scale fibers mimic native tissue structures, improving cell interactions. However, limitations exist with regards to traditional solvent evaporation-based electrospinning techniques. Reactive electrospinning investigates of methods of electrospinning that rely on in situ crosslinking rather than solvent evaporation to stabilize fibers. Reactive electrospinning could potentially produce more biocompatible materials by avoiding the need for volatile solvents. Here we investigate the development of a UV-reactive electrospinning method based on the in situ crosslinking of poly(ethylene glycol) diacrylate (PEGDA).

#### Methods

FTIR-ATR measurements were performed to compare the crosslinking speeds of various PEGDA solutions mixed with the photoinitiator, Irgacure 2959, when exposed to 365 nm UV light. PEGDA was then mixed with polyvinyl alcohol (PVA) for reactive electrospinning. PEGDA/PVA/Irgacure solutions were electrospun under constant exposure to 365 nm UV light during the fiber time-of-flight. The resulting nonwoven fiber mats were imaged with SEM and assessed for stability in water.

#### Results

PEGDA 700 g/mol crosslinked significantly faster than PEGDA 250 g/mol and was therefore used for all subsequent experiments. PEGDA/PVA solutions were successfully electrospun under constant UV light exposure to initiate the crosslinking of the PEGDA. SEM images showed that reactive electrospun fibers appear more stable immediately after spinning and after washing with water, indicating successful UV crosslinking.

#### Conclusion

In this study, the feasibility of reactive electrospinning of PVA/PEGDA polymer blends based on UV crosslinking was examined. The addition of UV exposure simultaneously with the electrospinning process did not interfere with fiber formation. Reactive electrospun PVA/PEGDA fibers were more stable in water than those created without UV exposure, demonstrating evidence of PEGDA crosslinking. This work establishes a method that can be used for further optimization.

# PEGDA drug delivery scaffolds prepared with UV curing process

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#### Introduction

Individually tailored drug delivery systems (DDSs) are considered one of the most promising therapeutic tools for the creation of safe and effective treatments. Development of particular drug delivery devices require the selection of a suitable scaffold material. Poly(ethylene glycol) diacrylate (PEGDA) according to its properties can be easily used as a DDS resin and shaped into a desired structure with the employment of techniques based on photopolymerization, including some novel 3D printing techniques. As a continuation of our previous works, in this paper drug release studies from conventionally prepared PEGDA scaffolds are presented.

#### Methods

Samples containing different amounts of acetylsalicylic acid (ASS) (20, 10, 5 and 2.5 µg) were prepared from pure PEGDA or 50% v/v PEGDA solutions, diluted in ultrapure water via photopolymerization. The release studies were conducted in 0.9% NaCl solution for 48 h, with complete medium changes at particular time points. Afterwards the complete residual release of ASS was performed in methanol. The released amounts of ASS were determined with an HPLC device.

#### Results

The drug release results for PEGDA pure and PEGDA + 50% H<sub>2</sub>O samples showed the existing differences between these two drug delivery systems for the low molecular model active substance – ASS. The slope of ASS release in PEGDA + H<sub>2</sub>O samples is steeper in comparison with their corresponding PEGDA pure samples and the release is finished rapidly. Therefore we observe a much stronger burst release resulting in an earlier release and a much higher amount of released ASS.

#### Conclusion

We have shown that in PEGDA materials, the release profile of the low molecular weight model drug ASS can be altered by water content. PEGDA as a delivery material should be further investigated to specify its potential as a comonomer and a matrix for pharmaceutical agents.

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# Thickness-reduced pericardial tissue for catheter-based aortic heart valve prostheses

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## Introduction

Aortic stenosis is one of the most common degenerative heart valve defects. When a traditional heart valve surgery cannot be performed, a catheter-based aortic valve implantation (TAVI) represents a modern alternative, provided the patient meets the requirements for that procedure. To make the TAVI implants available to a broader range of patients, the size of the catheter needs to be as small as possible. To achieve this, research is done on reducing the thickness of the pericardial tissue used for leaflets and skirt of the valve prosthesis.

#### **Methods**

The used material is porcine pericardium. Water is extracted from the tissue under controlled conditions to reach a thickness-reduced state. Afterwards, the tissue is fixated with a 0.5% glutaraldehyde solution. During crosslinking, pressure is applied to the tissue, while ensuring a permanent inflow of glutaraldehyde solution.

The thickness and the water content are measured, as well as the mechanical properties using a uniaxial tensile apparatus. The grade of crosslinking is determined by a ninhydrine assay and differential scanning calorimetry. To test the suitability of this material for a valve prosthesis, prototypes were produced and their correct function examined.

## Results

The tissue obtained by the above process has altered properties in comparison to standard pericardium. The tissue is significantly thinner, the appearance becomes transparent and the water content decreases with thickness. The tissue also becomes stiffer and has been shown to be adequately cross-linked for application in medical devices. It has been possible to sew prototype valve prostheses from the thickness-reduced tissue with correct function.

# **Conclusion**

The presented method produces thickness-reduced pericardial tissue in a reliable way. Furthermore, prototype aortic valves were made of thickness-reduced pericardial tissue with correct function. The altered mechanical properties in comparison to standard pericardium need to be further investigated.