Allie Johnson

Thesis Proposal

LMC-4701

Research Spanning Spring 2017-Summer 2017

<u>Effects of Surface Modification on the Osseointegration Properties of Polyetheretherketone</u>

Abstract:

Polyetheretherketone (PEEK) is a thermoplastic polymer with many clinical orthopedic applications. With an elastic modulus similar to bone, PEEK is a preferred implant model due to specific mechanical properties. The limitations of PEEK arise from its poor osseointegration which in a clinical setting may cause implant slippage or dislodgement. Recent methods to improve the osseointegration of PEEK have involved surface modification, including the change of surface structure as well as surface chemistry. The purpose of this study is to characterize various surface structures of PEEK so that their effectiveness at implantation may be evaluated. Surface porous, soda blasted, and smooth injected molded PEEK as well as titanium oxide coated PEEK were evaluated for surface roughness using LEXT imaging. These roughness values will then later be compared with implant integration for each sample. Based on the optimized surface structure of PEEK, future studies will begin to characterize the optimal surface coating or surface chemistry for PEEK implants so that the inert properties of PEEK may be overcome in the clinical setting by surface modification.

Introduction:

Market need

The global demand for orthopedic implants is a billion dollar market that is rapidly increasing. It is expected to reach 6.2 billion dollars in 2024 [1, 2]. The need for orthopedic implants is rising due to a rise in the global geriatric population, of which is at a higher risk for bone disease. Another driver of the market is a dramatic increase in sports and road trauma [2]. In response to this demand, orthopedic research is working to develop the most biocompatible implant for clinical applications by researching implant material and surface structure.

Material Properties

Current orthopedic materials include metals, ceramics, polymers, and thermoplastics [3]. Metal implants have desired strength for biomechanics, can have low toxicity, and low friction resistance. However, these high strength metals have elastic modulus's such that they that do not match those of bone tissues. This often cause stress shielding which leads to absorption of tissues and implant dislodgement. In addition, metals are not radio-opague which limits the medical imaging of patients. Extended exposure to metals can also cause allergic reactions and osteolysis [3]. Metallic oxide and calcium phosphate ceramics are bioactive ceramics that are used for their non-toxic properties, corrosion-resistance, and biocompatibility. However, the current biomechanical applications of ceramics are limited due to their brittleness and high elastic modulus'. With high fracture tendencies, ceramics cannot undergo the cyclic loading of bones [3]. Specific polymers have been designed to heighten bioactivity but are flexible and weak when compared to the mechanical properties of bone. In addition most polymers swell to absorb liquids and then leech out chemicals into the body [3].

Thermoplastics, such as polyetheretherketone (PEEK), are desirable because they can be designed to have an elastic modulus similar to bone with marginal differences of less than 10GPA while maintaining structural integrity [3]. This allows for all the mechanical properties of cortical bone with limited amounts of stress shielding [3-5]. In addition, thermoplastic composites can be designed to degrade at different rates or to maintain integrity for the lifespan of the implant [6]. However, thermoplastics often have hydrophobic surfaces that limit osseointegration and cause fibrous capsule formation around the implant. This capsule formation leads to osteolysis and implant loosening [5].

Current surface modifications to thermoplastic implants include both surface coating and topography [7]. Surface coating with a metal alloy such as a TiO_2 can retain the ideal mechanical and imaging properties that thermoplastics can provide while possibly enhancing osseointegration [4]. Topographical modification of implants, such as pore size, also increases osteodifferentiation involved in integration [7, 8].

An ideal orthopedic implant would have optimal mechanical, imaging, chemical, and topographical properties complete osseointegration. However as previously described, current implant designs often fall short in one of these categories. One method of optimizing implant properties is to combine multiple materials. The first step is to pick an optimized material for mechanical and imaging properties: PEEK. The next step is to surface coat that material with optimized chemical properties for differentiation: TiO2. Implants can then be optimized further by choosing an accepted topography for increased osseointegration: surface porous. While these implant properties have been quantified and tested for osseointegration alone, the purpose of this research quantify the topography of these implant properties when used in combination.

Previous Studies

Previous studies have evaluated both changes in surface structure as well as changes in material. In the Guldberg lab at the Georgia Institute of Technology, it was shown that porous peek increased cell proliferation and bone mineralization *in vitro* when in comparison with smooth injection molded PEEK and a smooth titanium alloy. Mesenchymal stem cells were cultured on three surface sturctures and alkaline phosphatase activity, proliferation, and endothelial growth factor production were assessed. In addition to data supporting increased osseointegration, this study also ran several mechanical tests. Mechanical testing was done for shear stress, tensile stress, and fatigue strength. The study found that porous PEEK should be mechanical favorable in an orthopedic environment. This study also makes the distinction that pore size is a factor for differentiation and states optimal results for pore sizes ranging from 200 nanometers to 500 nanometers.   [7]

In another study performed at the Jagiellonian University in Poland, it was concluded that a porous titanium alloy surface has better osteogenic differentiation than a smooth titanium alloy surface. This study was performed *in vitro* also with mesenchymal stem cells cultured for twenty-one days on the various surface structures of the titanium alloy TiO_2. To approximate osseointegration potential, cell proliferation was tested by an elisa assay. Gene expression for bone formation was tested by assays for alkaline phosphatase, Runx-2 transcription factor, osteocalcin, osterix, bone morphogenetic protein 2, t-box transcription factor, and osteonectin. In addition, bone formation was tested by Alizarin red S staining [9].

Work Plan

Optimal applications for surface modified PEEK are shown through a range of various studies. This thermoplastic is used in orthopedic research for its mechanical and imaging properties and more studies are being gathered for clinical applications. Specifically, surface modifications of porosity and titanium alloy coating have already been tested to be optimal in an in vitro setting. However, porous peek coated with a titanium alloy have not yet been quantified and tested in combination. This is where my proposed work lies.

Materials

Medical grade PEEK Zeniva® 500 was provided by Solvay Specialty Polymers (Alpharetta, GA). Medical grade Ti6Al4V ELI was purchased from Vulcanium (Northbrook, IL) and the surface was fine grit blasted (GB-13 blast media) and anodized according to AMS 2488D Type II by 62 Danco (Arcadia, CA). Sodium chloride was purchased from Sigma (St. Louis, MO).

Sample Preparation

Surface Porous

Surface Porous PEEK was created by extruding PEEK through the open spacing of sodium chloride crystal under heat and pressure. After cooling, embedded sodium chloride crystals were leached in water leaving behind a porous surface layer. To control for pore size, sodium chloride was sieved into #50 U.S. mesh sieves to create pore sizes of 312-425 μm [1].

Injection Molded

Injection molded PEEK samples were created with a smooth non-porous machined surface finish.

ALD Coated

Samples of all three surface structures were sent out for atomic layer deposition of $Al2O2$ and $TiO2$. While $TiO2$ is the compound chemical of interest, $Al2O2$ was deposited as the first layer for increased nucleation on a thermoplastic polymer. $Al2o3$ and $Tio2$ films were deposited using flow type ALD reactors at a range from 80 to 250 degrees celsius with the use of nitrogen as a purging gas [2]. Atomic layer deposition was confirmed with the Oxford EDS detector on the HItachi SU-8230 SEM.

Preparation for Well Plates

All samples were taken from sheet form with a thickness of 2mm+- .5 and punched into 34.8mm diameters using a titanium punch and compress machine. Circumference edges were then sanded down using 3,000 grit sandpaper.

Evaluation of Surface Roughness

Surface roughness values were analyzed on the the Olympus LEXT OLS4000 3D Laser Measuring Microscope. An auto-correlation function was used to evaluate the periodicity of surface roughness in the direction of the plane to eliminate the effects of curved or slanted samples. Additionally a L-filter was used to eliminate undulations and other lateral components from the surface which allows for the extraction of only the roughness components. The L-filter used for this analysis was 100 λ.

Arithmetical mean height (Sa) was taken for a measure of surface roughness for each sample. this parameter is the extension of the arithmetical mean height of a line to a surface. It expresses, as an absolute value, the difference in height of each point compared to the arithmetical mean of the surface. Additionally, root mean square heights (Sq) were taken to represent the root mean square value of ordinate values within the definition area. This is equivalent to the standard deviation of heights [4]. Sa values were analyzed using a one-way ANOVA and Tukey post-hoc analysis (95% confidence interval). Bonferroni comparison test were used to compare each sample group. All data are expressed as mean ± standard error (S.E.).

Results

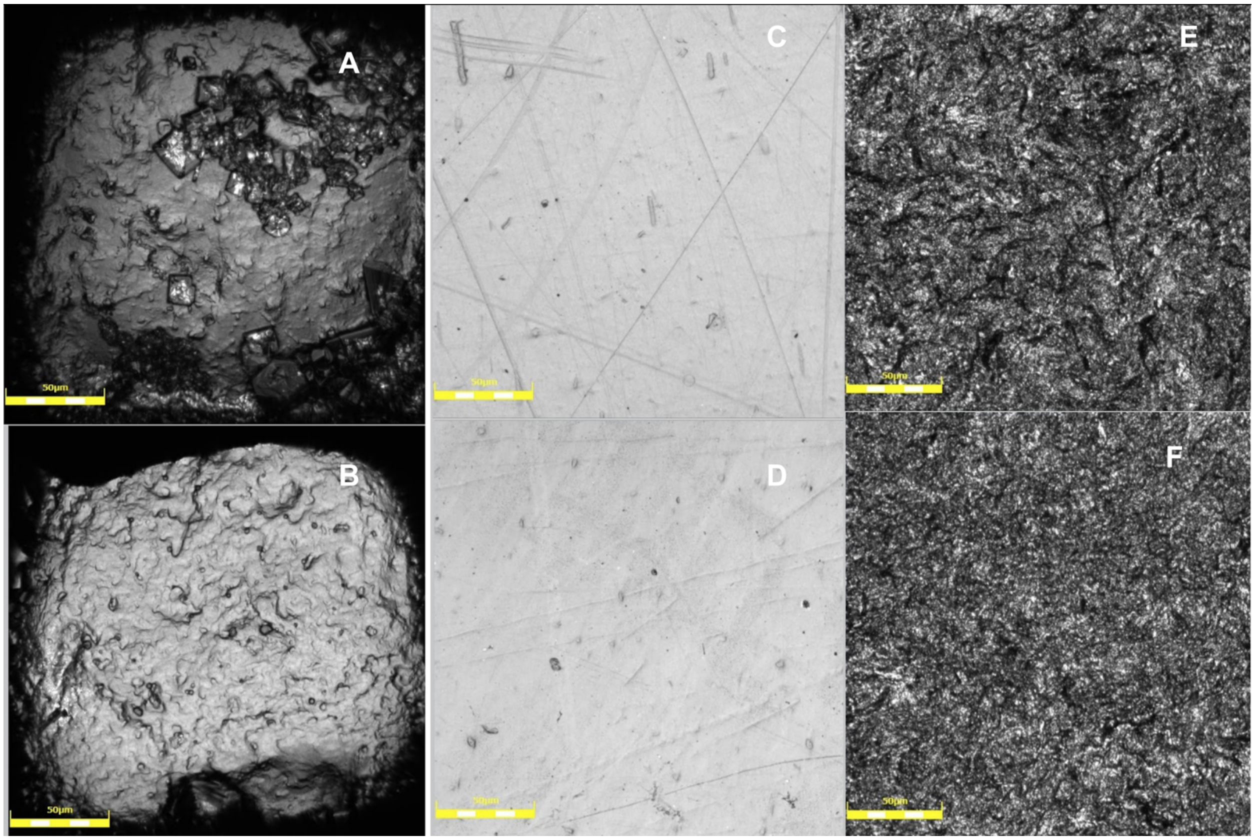

Figure 1: Lext images of PEEK samples before evaluation of surface roughness. **A**. Surface Porous **B**. ALD-Surface Porous **C.** Injection Molded D. ALD-Injection Molded **E.** SodaBlasted **F.** ALD SodaBlasted

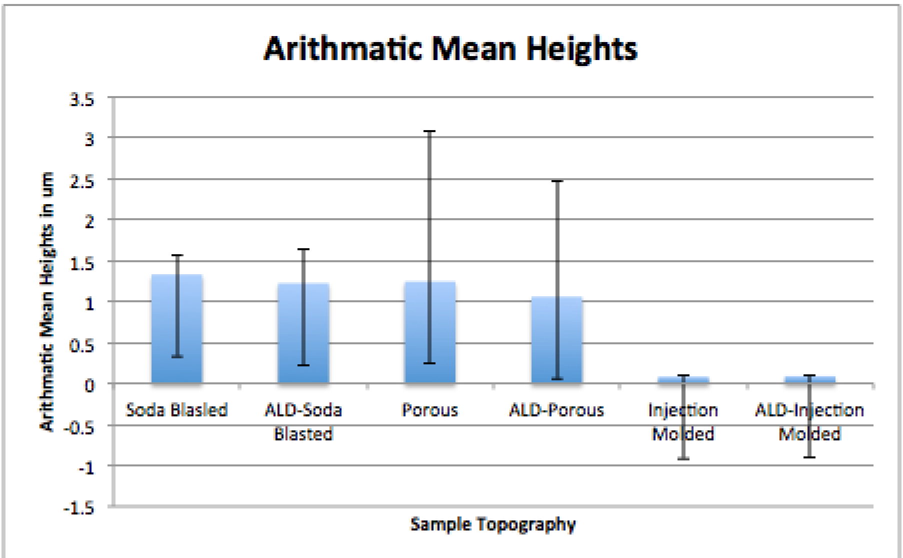

Figure 2: Arithmetic Mean Heights of sample values as a measure of surface roughness.

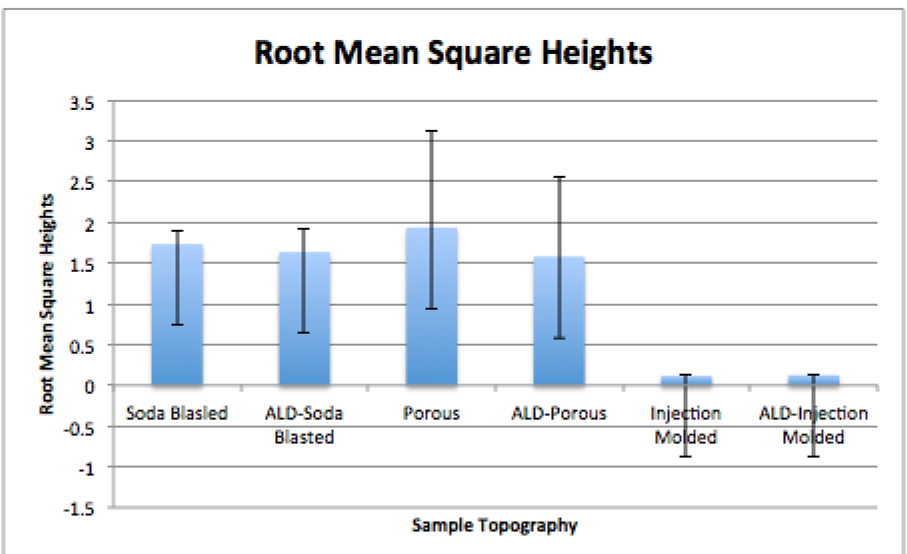

Figure 3 : Root Mean Square Heights for the different PEEK samples.

Surface roughness, evaluated by arithmetic mean height and root mean squared height, were similar in both the samples with and without ALD. However ALD coated samples had higher values of surface roughness than non coated samples. While significance was not found between

ALD and and non-ALD groups of similar topography in a Tukey HSD Post-hoc analysis, significance was found between samples of different topographies.

Conclusion/Discussion

ALD coated samples caused a significant increase in surface roughness of PEEK samples with various surface textures. Also interesting to note is that porous samples and sodablasted samples had similar values of surface roughness. Injection molded samples were thought to have a similar surface roughness to the bottom of the pores in porous samples, however the bottom of the pores of porous samples had an increased surface roughness. Additionally, the standard deviation error for porous samples was greater than expected. This could be because the L-filter was not turned on or the region of interest marked included more than just the bottom surface of the pores.

While previous studies have determined optimal pore size for osseointegration, surface roughness characterisation may give more insight into the topography of porous samples. The purpose of ALD coatings are to preserve the original surface topographies of the implants. These results conclude however that surface roughness, which has been proven to affect osseointegration, is changed after ALD coating. On evaluation of these results it is recommended that surface roughness after ALD coating be taken into account when evaluating topography for orthopedic applications.

<u>Work Plan</u>

Spring 2017 and Fall 2017 semesters

Low Target:

Literature Review and decision matrix on optimization of Methyl Meth-Acrylate (MMA) processing for orthopedic and metal with bone and soft tissue. 2/15/17

Literature Review and decision matrix on optimization of Masson Goldner's Trichrome Staining for MMA sections including bone, metal, and soft tissue. 2/20/17

Literature Review and decision matrix on optimization of Sander's Rapid Bone Stain for MMA sections including bone, metal, and soft tissue. 3/5/17

Literature Review and decision matrix comparing orthopedic bone stains that mark for osseointegration to be used on MMA sections including bone, metal, and soft tissue. 3/15/17

Analysis of osseointegration of smooth versus porous PEEK implants based on an optimized orthopedic bone stain that marks for osseointegration. 4/15/17

Gather image data of osseointegration of smooth versus porous PEEK implants based on an optimized orthopedic bone stain that marks for osseointegration. 4/30/15

Characterize topography of ALD samples using LEXT 11/01/17

Characterize topography of ALD samples using CT 11/10/17

Characterize topography of ALD samples using SEM 11/20/17

Ideal Target:

Literature Review and decision matrix on optimization of Methyl Meth-Acrylate (MMA) processing for orthopedic and metal with bone and soft tissue. 2/15/17

Literature Review and decision matrix on optimization of Masson Goldner's Trichrome Staining for MMA sections including bone, metal, and soft tissue. 2/15/17

Literature Review and decision matrix on optimization of Sander's Rapid Bone Stain for MMA sections including bone, metal, and soft tissue. 2/15/17

Literature Review and decision matrix comparing orthopedic bone stains that mark for osseointegration to be used on MMA sections including bone, metal, and soft tissue. 2/15/17

Analysis of osseointegration of smooth versus porous PEEK implants based on an optimized orthopedic bone stain that marks for osseointegration. 3/30/17

Gather image data of osseointegration of smooth versus porous PEEK implants based on an optimized orthopedic bone stain that marks for osseointegration. 4/15/15

Assist in *in vivo* surgery of ALD coated PEEK implants in a rat model 5/15/17

Collect CT data of ALD coated PEEK implants in a rat model 9/15/17

Characterize topography of ALD samples using CT 8/20/17

Characterize topography of ALD samples using LEXT 8/25/17

Characterize topography of ALD samples using AFM 9/15/17

Characterize topography of ALD samples using SEM 9/20/17

Characterize chemistry of ALD samples using XPS 9/27/17

Characterize topography of titanium samples using CT 10/15/17

Characterize topography of titanium samples using LEXT 10/23/17

Characterize topography of titanium samples using AFM 11/1/17

Characterize topography of titanium samples using SEM 11/15/17

Characterize chemistry of titanium samples using XPS 11/ 25/17

High Target:

Literature Review and decision matrix on optimization of Methyl Meth-Acrylate (MMA) processing for orthopedic and metal with bone and soft tissue. 1/27/17

Literature Review and decision matrix on optimization of Masson Goldner's Trichrome Staining for MMA sections including bone, metal, and soft tissue. 1/27/17

Literature Review and decision matrix on optimization of Sander's Rapid Bone Stain for MMA sections including bone, metal, and soft tissue. 1/27/17

Literature Review and decision matrix comparing orthopedic bone stains that mark for osseointegration to be used on MMA sections including bone, metal, and soft tissue. 1/27/17

Optimization of Methyl Meth-Acrylate (MMA) processing for orthopedic and metal with bone and soft tissue through multiple iterations. 2/26/17

Optimization of an orthopedic bone stain that marks for osseointegration to be used on MMA sections including bone, metal, and soft tissue through multiple iterations. 3/15/17

Analysis of osseointegration of smooth versus porous PEEK implants based on an optimized orthopedic bone stain that marks for osseointegration. 3/15/17

Gather image data of osseointegration of smooth versus porous PEEK implants based on an optimized orthopedic bone stain that marks for osseointegration. 3/17/15

Assist in *in vivo* surgery of ALD coated PEEK implants in a rat model 1/31/17

Collect x-ray data of ALD coated PEEK implants in a rat model 3/30/17

Process and Stain histological slides of ALD coated PEEK implants. 5/15/17

Process and Stain histological slides of porous PEEK implants. 5/15/17

Analysis of osseointegration of ALD coated PEEK implants versus porous PEEK implants based on an optimized orthopedic bone stain that marks for osseointegration. 5/15/17

Gather image data of osseointegration of ALD coated PEEK implants versus porous PEEK implants based on an optimized orthopedic bone stain that marks for osseointegration. 5/17/17

ALD and DNA assay data collection on smooth PEEK 2/15/17

Characterize topography of ALD samples using CT 8/20/17

Characterize topography of ALD samples using LEXT 8/25/17

Characterize topography of ALD samples using AFM 9/15/17

Characterize topography of ALD samples using SEM 9/20/17

Characterize chemistry of ALD samples using XPS 9/27/17

Characterize topography of titanium samples using CT 10/15/17

Characterize topography of titanium samples using LEXT 10/23/17

Characterize topography of titanium samples using AFM 11/1/17

Characterize topography of titanium samples using SEM 11/15/17

Characterize chemistry of titanium samples using XPS 11/ 25/17

References

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