Tribocorrosion Studies of Dental Materials,

and the Clinical Implications

ΒY

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#### THESIS

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GDM

#### PREFACE

This work is divided into two parts, the prophylactic treatment of dental implants by thermal oxidation, and the tribocorrosive role of nicotine in dental implant failure. The reader should take care to read the introduction of this thesis as it gives an introductory understanding of dental implants and their limitations. There is simply no substitute to oral hygiene and the preservation of one's natural dentition. Though implants have tremendous functional and esthetic value, dentist should view them as a last resort. There is a trend amongst young dentist to undervalue procedures such as the root canal or traditional periodontal treatments. The trend is fed by the expedient nature of dental implants in an economical sense, and not at all backed up by preventive health studies that show the value of traditional and conservative treatment planning. Dental implants are a wonder of modern society and appropriate for numerous patients, however respect for this technology is necessary. Too much hype, and the presentation of false success rates in the private sector make the failures that due occur all the worse. We should be humbled by the success of the dental implant and recognize the value of conservative treatment planning in dentistry, particularly preventive.

#### **CONTRIBUTION OF AUTHORS**

This thesis reflects a group effort at all phases. The thermal oxidation experiments were primarily conducted by Newton Lucchiari, however Arman Butt prepared the samples and performed the thermal annealing. The nicotine tribocorrosion experiments were primarily conducted by Dmitry Royhman. For both sets of experiments, Dr. Mathew Mathew performed the imaging, and oversaw each step of the laboratory experiments. The author of this thesis conducted data analysis, including statistical studies, created figures and is responsible for greater than 90% of the written work presented here and for publication. Presentations of the thermal oxidation work exist in a second thesis by Newton Lucchiari in Portuguese and English, however that material consists of different interpretations, statistical analysis, figures, tables, results, discussion and conclusions. The major overlap between these two works lies in the introduction to thermal oxidation, in this work it is presented as Chapter 2 Section 1, and the work by the coauthor can be viewed in the Appendix. The reader will immediately note the similarities as the newer version presented in this thesis is an adaptation of the prior work, and 10% of the previous iteration remains. It was necessary to re-present the thermal oxidation work again, because of differences in interpretations, statistical analysis, and conclusions between the coauthors, however the influence of the previous iteration is greatly appreciated and acknowledged.

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## LIST OF ABBREVIATIONS

ANOVA	Analysis of Variance
ASTM	American Society for Testing of Materials
C3b	Complement Factor 3b
CI	Confidence Interval
CPE	Constant Phase Element
CPE <sub>film</sub>	Constant Phase Element of Film
CPE <sub>ox</sub>	Constant Phase Element of Oxide
E <sub>corr</sub>	Corrosion Potential of the Metal (Alloy)
EDS	Energy Dispersive Spectroscopy
EIS	Electrochemical Impedance Spectroscopy
FDA	Food and Drug Administration
FTIR	Fourier Transform Infrared Spectroscopy
I <sub>corr</sub>	Corrosion Current Density or Rate
I <sub>pass</sub>	Current of Passivation
ISO	International Organization for Standardization
K <sub>c</sub>	Total Weight Loss due to Corrosion
K <sub>w</sub>	Total Weight Loss due to Mechanical Wear
K <sub>wc</sub>	Combined Weight Loss due to Corrosion and Wear
mg	Milligram
OCP	Open Circuit Potential
PEEK	Polyether ether ketone

## LIST OF ABBREVIATIONS

Ra	Roughness Average
R <sub>film</sub>	Polarization Resistance of Film
RMS	Root Mean Square
R <sub>ox</sub>	Polarization Resistance of Oxide
R <sub>p</sub>	Polarization Resistance
Rs	Resistance of Solution
SEM	Scanning Electron Microscopy

#### DENTAL TERMINOLOGY

**Abutment** is a part of an implant that acts as the intermediary between the final restoration (crown) and the body of the implant, oftentimes a screw.

Edentulous refers to missing or lacking teeth.

Endosseous refers to "within bone."

**Implantitis** is a site-specific inflammatory process in soft tissues and bone immediately surrounding a dental implant. Often times this can be due to an infectious disease and lead to bone loss, destabilizing the osseointegration of the implant

**Occlusal loading** is when a dental implant has been restored (crowned) and is feeling the mechanical load of mastication from a proper bite.

**Osseointegrates** or **osseointegration** is the morphological connection of bone to implant, not a covalent interaction or direct connection.

Osteoclastogenesis is the creation of new osteoclastic, or bone breakdown, cells.

**Osteolysis** is bone breakdown due to cell mediated response.

Peri-implant refers to "immediately around or adjacent to the implant."

**Wolff's law** states that bone in a healthy person or animal will adapt to the loads under which it is placed, for example, if load increases the bone will remodel itself overtime to become stronger.

#### SUMMARY

The questions this study seeks to answer are i) whether nicotine leads to greater tribocorrosion in titanium alloy, thus invoking a non-biological implant centered failure mechanism in dental implants, and ii) whether a processing technique such as thermal oxidation can reduce the corrosion and increase the longevity of dental implants in smokers. The methods used to evaluate these questions are electrochemical impedance spectroscopy, potentiodynamic testing, white light interferometry, and scanning electron microscopy. A tribocorrosion apparatus simulating the oral environment was used under both free potential and potentiostatic mode to study the effect of nicotine on titanium alloy. Using Faraday's law the potentiostatic mode allows us to calculate weight loss due to corrosion, and wear separately as well as classify the material breakdown on a spectrum of both. For the tribocorrosive studies of nicotine, different doses, 0, 1, 5, and 20 mg in artificial saliva were used to mimic smoking habits in patients, as well as an acidic and resting oral pH to mimic the effects of food. For the thermal oxidation studies, different temperatures 200, 400, and 700 °C were used as well as both acidic and neutral pH to mimic food, and different annealing times of 1, 3, and 6 hours. The major findings for the thermal oxidation study were: (1) temperature dependence of corrosion properties that at first improve with temperature and then reverse as higher temperatures display inhomogeneity and cracking, (2) time independence of the effect of thermal oxidation on the corrosion properties, and (3) reduction in the effect of acidic medium on the corrosion properties. The major findings for the tribocorrosion study of nicotine were: (1) a dose dependence of nicotine with a protective effect at low doses and a detrimental one at high doses, (2) a pH reversal of the protection of nicotine due to its effect on polarization resistance, (3) synergism between wear and corrosion, and (4) a three-body mechanism of degradation. Overall, the results of this study indicate that thermal oxidation is an effective prophylaxis for implant centered failure and that smoking habits in patients determine failure risks.

Tribocorrosion Studies of Dental Materials,

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# INTRODUCTION

(Chapter One)

#### 1.1 Themes Behind Implant Science

Endosseous dental implants are a proven method for replacement of teeth in fully or partially edentulous patients. In the United States alone, nearly 300,000 patients receive one or more implants a year, for single tooth or full arch rehabilitation.[1] Survival of dental implants is genuinely good, however, there are cases where the rate of failure is significant. The variation in survival is dependent on both lifestyle, anatomy and design. For example, smokers are more than twice as likely to experience a failure than nonsmokers.[2] The success rates of implants placed in the posterior region of both the mandible and maxilla are less than those placed in the anterior segments, where load is less.[3] And, the mechanical properties of the system are determined by the design, for example an external abutment connection was determined to have higher fatigue and fracture resistance compared to an internal design.[4] Material selection complicates matters further, as numerous dental implant materials exist, the most popular being the titanium alloy (Ti-6Al-4V), but ceramics and other metals are becoming more common.

Dental implant diversity is a necessity to the diversity of needs underlying the unique biology of the patient. Different implants have advantages over one another considering their placement brought on by design and surgical choice. As dental implant failure is common with only 91.9% success rate after 5 years for any single tooth replacement, and 87.6% for those in the molar region, clinicians need to better understand the implant itself and its interaction with the patient to make informed decisions on which to use, where and when.[5] The "one implant, one life" goal is one that will come from a plethora of choices and the knowledge of where each is applicable

through longitudinal studies of design, biocompatibility and outcomes. Understanding failure is the first step in choosing an implant.

Failure is a phenomenon that lies on a spectrum between failures of the device, the surrounding biology, and those of a mixed etiology or response of the biology to the device. A failure of the device such as a fracture can occur at any point in the life of a dental implant, design and materials determine this outcome. Biological failure occurs when an implant does not achieve secondary stability, or osseointegrates into the underlying bone. The final failure route is dynamic and occurs after an extended period as particles or metal debris are shed from the implant the surrounding biology recedes and produces a foreign-body response to the implant eventually leading to loosening. In all cases, implant failure is defined by the compromise of osseointegration.

Osseointegration was first described by Per-Ingvar Branemark in 1952.[6] At the time it was thought of as the process by which living remodeling bone would heal around an implant to make a direct connection without any intermediate soft tissue component, providing direct transfer of loads to anchoring bone.[7] In essence, osseointegration is the morphological connection of bone to implant, not a covalent interaction or direct connection. Since that time osseointegration has come to be considered an immune mediated inflammatory process, or a relative response to the implant that shifts the surrounding environment from bone building to bone resorbing processes. This foreign body equilibrium compromises the secondary stability of a dental implant and is therefore responsible for overall longevity. Deeper understanding of this response has the potential to guide choices in material to have a more lasting and predictable clinical outcome. To get there, one must recognize the complexity of the immune response.

After the initial placement of an implant proteins adsorb to the surface of the implant activating an innate immune response through the coagulation and complement system. In vitro experiments with titanium, aluminum, and silicon in blood plasma show increased surface binding of complement factor 3b (C3b) and degradation products.[8] This activation of the intrinsic pathway on the surfaces of implants is assumed to activate numerous inflammatory and immune cells with receptors to C3b. Macrophages differentiate from circulating monocytes and bone cells originate from Mesenchymal stem cells. In the right balance, bone formation, including extracellular matrix formation, angiogenesis, and hydroxyl apatite precipitation occur leading to direct transfer of loads as bone-implant contact ensues, or osseointegration.

Events such as overloading, cement remnants, or systemic disturbances affecting the immune system disrupt the immunological balance. The deposition of proteins to the surface of the device leads to further complement binding proteins, such products has been known for some time to recruit mononuclear osteoclast precursors to the surface of bones, or in this case the bone-implant contact surface.[9] Further, titanium particles at low concentrations have been shown to enhance osteoclastic activity.[10] The reactivation of macrophages leads to increasing numbers of foreign body giant cells, and osteoclastogenesis. Eventually, the mucosal coronal seal is disturbed leading to a secondary infection by bacteria and further peri-implant bone resorption.[11]

There is much debate on whether infection is the primary cause of peri-implant bone loss or a secondary result. This author believes that both possibilities are true, and patient specific. However, it is more likely that the shift is initiated by a change in implant loading, such as the loss of an adjacent tooth, systemic disease in the patient, or cement

particles. This change in stress shielding has been studied in numerous animal models showing histological changes adjacent to implants where load has been altered.[12, 13] It is important for the modern clinician to recognize that initial marginal bone loss represents a reaction to the treatment, and is not a disease process, such as periodontitis. Indeed, there is no evidence that bacteria cause the initial osseoseperation, and numerous authors point this out in the literature.[14-17]

Bone remodeling occurs in a specialized vascular entity known as the bone remodeling compartment, providing the structural basis for coupling and regulating cellular activity.[18] Specifically, it is here that the interplay between local factors, osteoclasts and osteoblasts determine whether bone will be built or resorbed. In essence anabolism and catabolism is coupled, occurring hand in hand, with one dominating the other governed only by local factors. This is true for the bone-implant contact region as well.

In orthopedics, prosthesis undergo a process known as aseptic loosening, in which a foreign body response causes local resorption of bone.[19] Similar findings, of inflammatory markers, have been found in dental implants and are responsible for periimplant bone resorption.[20] The best dental implant is therefore the one with the least interaction with the local environment, those that do not corrode, release particles, or have direct contact without an intermediary such as a biological coating. The design of such implants is however impractical as the majority of such devices are designed from metals and coatings having a tendency to be displaced over time. The relative biocompatibility of the material determines its longevity.

Unfortunately, biocompatibility is a difficult topic to address as no material is truly inert within the body. There are extreme cases such as unsuitable materials like copper, whose ions result in a prolonged inflammatory reaction, and increased foreign body response with a thicker fibrous capsule, mononuclear and giant cells, and blood vessels when compared to titanium.[21] These materials are often rejected in favor of titanium for its strength, low weight, corrosion resistance, and biological inertness. However, metals have a large elastic modulus relative to surrounding bone leading to poor loading of periimplant bone.[22] According to Wolff's law this leads to resorption of bone in the surrounding area and further stress shielding. Coupled with the foreign body response to the corrosion particles and metal surface, it is a matter of time before any metallic dental implant is rejected. From the standpoint of patients, however, a metal based implant may have a lifetime of use, and therefore the continued research and use of such devices is practical.

A new material to enter the dental implant market is polyether ether ketone (PEEK). PEEK has substantial corrosion properties and is very inert, but its major improvement is its mechanical and physical properties, namely an elastic modulus that is close to bone and insures adequate load transfers without stress shielding.[23] The major challenge to PEEK is increasing its bioactivity or natural osseointegration properties without altering its mechanical properties. Plasma spraying of calcium hydroxyapatite or titanium has been used to modify PEEK for better osseointegration.[23] The disadvantage here is the highly rough surface ( $R_a \sim 7$  um) can delaminate, and the high temperatures of plasma spraying can damage the PEEK structure which has a melting point of 340 °C.[23] Another approach, spin coating has also been used to apply

hydroxyapatite without the drawbacks of degradation and animal studies have shown higher bone-implant contact when compared to uncoated PEEK.[23]

The highly inert nature of PEEK, and its mechanical properties similar to bone make it a long-term prospect to push titanium out of the dental implant industry. Major concerns however are its biocompatibility or ability to osseointegrate. Though biological coatings are a possible correction for PEEKs biocompatibility it is clear from titanium and other materials to which coatings have been applied that there are limitations, namely application can adversely affect the underlying material or can delaminate in vivo causing pain and reversing the biocompatibility. Only time will tell if PEEK becomes a dominate player, and much like titanium there are numerous designs currently marketed to dentist.

Dental implants come in three basic designs: cylinders, screws and blades. Each of these designs has a patient specific use. The design of an implant must conform to the anatomy of a patient as this will determine the mechanical stress and osseointegration of the prosthesis. The first dental implants where in fact of the blade design, however, early on they were criticized for reacting adversely to loading and poor osseointegration.[11] The blade implant was originally designed due to the need to address anatomy with very shallow ridges, or low bone stock. Decades out it is apparent that the blade implant does osseointegrate, with good bone-to-implant contact.[24] However the initial blade were not two stage, allowing for healing, and had the disadvantage of snapping at the neck leading to burial of the blade and adverse outcomes for the patients oral rehabilitation.[25]



Figure 1: Astra Tech Implant with micro and macro threads.[26]

Going further there are substructure elements of design that also matter. The most popular dental implant is an endosseous cylinder with a thread. However, not all threads are the same. Astra Tech has an implant with a microthread and macrothread on the surface (Figure 1). In comparison to the popular Branemark and ITI implants with a single thread type, the Astra Tech combination reduces the peak tensile stress on the bone.[26] Additionally the switch between thread types while maintaining the diameter increases axial stiffness and reduces peak bone stress.[26]



Figure 2: Flat-to-flat implant-abutment interface, and conical interface.[26]

Astra Tech doesn't stop there with a conical abutment interface they reduce peak bone stress at the marginal bone (Figure 2).[26] This directly addresses peri-implant bone resorption at the marginal tissue.



Figure 3: Implant with a vent on the left, and implant with trabecular metal on the right.

Other substructures exist in implant design. A vent design is an obvious macro element (Figure 3), in that it allows for bone in growth or anchoring to the peri-implant tissue. Other elements include trabecular metal, that allow bone in growth to the implant. All substructure design elements are used for a single purpose—to influence osseointegration. Osseointegration is the purpose of both design and material selection in dental implants. These design elements are either geared towards inducing bone ingrowth or preventing stresses that would lead to osteolysis in the adjacent bone structure.

Finally, dentistry still needs to embrace the concept of "one implant, one life." To do this a recognition of design attributes must be considered, including chemical, mechanical, and biological. Dental implants are not inert and osseointegration is in fact a chronic inflammatory process that must be considered in the context of the material and environmental characteristics of the patient. Over the long term, implants need to interact in a manner that promotes bone formation without inducing a foreign body response. To do this the material must be inert and have good corrosive properties, additionally its surface must favor morphological connection and bone building, without design elements that generate osteolytic stress in the peri-implant region. In the end, it is the responsibility of the clinician to know which implant is best for the specific patient, their anatomy, and their biology. This is an overwhelming task that requires significant investiture in the literature and design of numerous implants. To that end this thesis, beyond this introduction to the important themes behind implants, will investigate the leading cause of implant failure, smoking, and seek to investigate a prophylactic surface treatment to implant-centered failure.

#### 1.2 Smoking a Contraindication for Dental Implants

Today tobacco is a known killer, as the established leading cause of preventable death in the world, accounting for nearly six million deaths worldwide and almost half-amillion in the United States per year.[27, 28] Understandably the prevalence of smoking is declining in the United States, from 42.4% of adults in 1965 to 16.8% of adults in 2014, however, the same cannot be said of smoking habits worldwide.[29, 30] Tobacco is a huge burden in developing nations where health awareness of smoking is low, such as Asian markets, where half or more of male adults smoke.[31-34] Given such prevalence, the cost of tobacco use is far reaching. In the United States tobacco use costs nearly 300 billion dollars per year, including 132.5 to 175.9 billion in healthcare costs and 151 billion in productivity losses.[27] Loses worldwide are expected to be far greater as the majority of the world smokers are in developing nations. How much of these loses are attributable to oral health is yet unclear, though the central role of nicotine is becoming more evident.

Despite thousands of constituents in cigarette smoke, the addictive nature is imparted by nicotine, which along with the carcinogenic tar and carbon monoxide are the only agents produced in milligram quantities per cigarette.[35] In Massachusetts where machine testing of nicotine is required for the commercial sale, measured nicotine yield has been on the rise from 1.65 mg per cigarette in 1999 to 1.89 mg per cigarette in 2011.[36] It is clear that big tobacco understands its product, and given the prevalence of smoking and dose of principle components, the effect on health due to nicotine exposure is a consummate concern to clinicians.

Where smoking is associated with numerous health risks such as cancer and ischemic heart disease, its principle components must be investigated independently, as their isolated role is not predictable. Studies of smokeless tobacco use, or vaporized nicotine, for example have shown no increase in relative risk for users vs. non-users in the development of acute myocardial infarction.[37] Interestingly the biological effects of nicotine can be dose dependent. At very low doses nicotine has been shown to accelerate angiogenesis and promote wound healing with less contraction in a rabbit model.[38] Contrarily, wound healing is impaired at higher doses, with delayed wound contraction, reduced inflammatory cell infiltration, and lower expression of growth factors in a mouse model, as well as reduced fibroblast migration in vitro.[39] The effects of nicotine are most notable in osteoporosis, bone fracture and healing. Nicotine has been shown to delay fracture healing and reduce mechanical strength of healed fractures in animal models.[40, 41] These effects could be due to the dose dependent effects of nicotine on bone metabolism-associated genes, such as osteocalcin, type 1 collagen and alkaline phosphatase, or on the dose-dependent effects on proliferation and differentiation of osteoblasts.[42-44] Extracellular matrix components are also affected as nicotine has been shown to suppress bone sialoprotein, and reduce both bone density and mineral content.[45, 46] The extent to which nicotine effects overall biological health is documented, but its local effect at the site of contact with the body, the oral cavity, is no less profound.

In the oral cavity, nicotine has been shown to affect matrix metalloproteinases in teeth, and dental pulp cells.[47] Further, nicotine has been shown to reduce alveolar bone regeneration following tooth extraction in a rat model, impairing osteoneogenesis in a

dose dependent manner.[48, 49] Additionally, it has been shown to reduce bone growth, vascularity, and bone lengthening in a mandibular distraction osteogenesis model.[50] Finally, in the past decade investigations have begun to unravel the role of nicotine in implant failure.

The care for such implants is lifelong, as one large 29 year follow-up study of patients showed relative survival rates of 86% for prostheses, and 92% of patients showed no failure whatsoever.[51] Implant success is dependent on the process of osseointegration, or the direct connection of the implant to living remodeling bone without any intermediate soft tissue component, providing direct transfer of loads to anchoring alveolar bone.[7] Given nicotine impairment of healing, bone growth and mineralization, its effect on osseointegration is expected to be negative. Unsurprisingly smokers exhibit greater implant failure both early, before abutment placement, and late, after occlusal loading of a prosthesis.[2, 52, 53] Early failure is due to impaired wound healing leading to poor osseointegration or bone-implant contact. Even those patients with good initial bone quality exhibit a 31% early failure rate if smokers compared to 4% if non-smokers.[52] Failure of dental implants are divided into biologic and prosthetic failures, nicotine's impact on the former has been the subject of numerous studies.

Many of the initial studies that assessed the effect of nicotine on osseointegration of titanium implants found no significant difference between animals with or without exposure.[54-56] Despite this, further histological studies of bone density showed that nicotine impacts cancellous bone resulting in lower bone-to-implant contact and less bone area within the threads of an implant.[57, 58] The quality or strength of such bone to withstand load was further called into question by push-in biomechanical testing of

titanium implants in animal models when exposed to nicotine.[59] The effect of nicotine on the quality of the peri-implant bone was investigated, and gene expression for bone markers were found to be down-regulated.[60] It is clear that the initial opinion on nicotine's role in implant failure is being overturned, but what is not clear is whether the argument is purely biological, prosthetic or mixed. Failure of an implant lies on a spectrum between failures of the device, the surrounding biology, and those of a mixed etiology, or response of the biology to the device. The biological argument is clear, what is unclear is if there is an implant centered failure mechanism, and are there ways to prevent such failure?

#### 1.3 Implant Centered Failure, and the Studies to Follow

It appears that only two works exist in the literature directly addressing the effect of nicotine on titanium alloy.[61, 62] The first of these studies to identify nicotine's effect on the suprastructure of the implant showed that moderate concentrations of nicotine reduces corrosion, impressing a possible protective role given local microenvironment concentrations at the implant in vivo.[62] However, all concentrations of nicotine also reduced the passive film formation on the surface of the implant.[62] Given the context of intermittent motion of the implant during mastication it is unclear if the smaller passive film layer will reform in clinical context. In essence, the initial data does not give a clear answer on whether nicotine reduces or increases corrosion or wear loss of material. As such loss breaks the continuity of the bone-implant contact region exposing the implant surface to the immune system it exacerbates long-term failure due to a mixed etiology, that is, the chronic foreign body response. It is important to understand if nicotine exacerbates failure from both a biological and implant centered pathway, as it can lead to innovation in implant design to reduce such failure.

Such implant design changes to reduce the impact of nicotine on implant centered failure can be simple. For example, recent literature has shown that thermal oxidation, or the heating of titanium alloy typically to temperatures ranging from 200 °C to 1000 °C causes an increase in the titanium dioxide TiO<sub>2</sub> layer and a change in structure to a harder, rougher, thicker and crystallized layer, called a rutile.[43, 63] Several studies have shown that the process of thermal oxidation changes the surface of TiO<sub>2</sub> layer by increasing the thickness, corrosion resistance, surface topography, roughness, surface

energy, and improving the biological and mechanical properties of titanium.[43, 63, 64] The clinical implications of thermal oxidation had been that the more vigorous treatment corresponded to the more biocompatible product. This is because alkaline phosphatase activity has been shown to be higher in samples of titanium treated with high temperature thermal oxidation, corresponding to greater surface roughness.[43] Alkaline phosphatase is a general biomarker for osteoblastic activity and can mediate bone mineralization.

These results are important because the three factors influencing a clinician's decision in material selection of an implant are: (i) cost, (ii) physical properties of the alloys, and (iii) biocompatibility. It is evident that the rationale for implant component (metal or polymer) selection should be biological safety and satisfactory functionality of the device rather than cost consideration. The use of thermal oxidation as a processing technique to improve the corrosion properties of titanium does not sacrifice the choice of metal and is also cost effective, whilst improving biocompatibility.

Therefore, thermal oxidation should be investigated as a prophylactic to implant centered failure mechanisms stemming from corrosion and wear, and nicotine, the primary component of smoking, should be investigated as an inducer of implant centered failure from such mechanisms. The current paradigm that smoking is a contraindication primarily for biological reasons, that is, impaired osteoneogenesis and wound healing is important, but may in fact be half the story.[48, 49] Moreover, the biological response only explains primary failure of a dental implant, that is, a failure to achieve secondary stability through a period of osseointegration, it doesn't explain the majority of failures occurring at later periods. As smokers exhibit greater implant failure both early, before abutment

placement, and late, after occlusal loading of a prosthesis it is imperative to discover both the etiology of such failures and potential prophylactic methods.[2, 52, 53]

Late failure occurs after osseointegration has occurred and secondary stability is achieved through a period of healing in the dental implant placement protocol. Late failure, or loss of secondary stability of a dental implant, is due to the foreign body response that defines the dynamic process that is in fact osseointegration. Osseointegration is therefore responsible for overall longevity and is more than the initial bone to implant contact but the continuity of an immune mediated inflammatory process at this junction over time. What is unknown is if nicotine impacts osseointegration by reducing the continuity of the bone implant contact region through a corrosion and wear mechanism, and whether or not simple processing techniques can prevent such failure routes. As prosthetic failure is a concern best addressed in the design and choice of the implant before surgery, the body of this thesis will focus on these questions through novel experimental design, and testing apparatus.

#### 1.4 Organization of this Thesis

This thesis is divided into five sections. The first section serves as an introduction to implant science, the effect of smoking on dental implants, and to the significance of the studies to follow on the effects of nicotine and thermal oxidation on dental implants. After this introduction two body sections, chapters two and three, deal with the effects of thermal oxidation on titanium alloy and with the effects of nicotine on the tribocorrosive properties of titanium, respectively. The body sections represent stand-alone publications with separate introductions, methods, results, discussions and conclusions. A cohesive discussion (chapter four), and conclusions section (chapter five), follow the two body chapters. Those sections bookending the body of work are meant to deal with the two articles as they relate to one another and implant science, the theme of which is the effect of nicotine and the prophylaxis of thermal oxidation. Clinical observations with respect to dental implants are made throughout the thesis, but can primarily be found in the discussion section.

Tribocorrosion Studies of Dental Materials,

& the Clinical Implications

# THERMALLY OXIDIZED TITANIUM, AN ELECTROCHEMICAL INVESTIGATION

(Chapter Two)

#### 2.1 Introduction

Titanium and its alloy have been used as a material in the dental implant industry due to present biocompatibility, corrosion resistance, and good mechanical strength.[65-67] However, several studies reported that titanium is passive to corrosion and degradation when exposed to certain chemical components in acidic medium or even wrapped in saliva.[68-71] When titanium and oxygen interact, a dense layer of titanium dioxide (TiO<sub>2</sub>) between 1.5 to 10 nm in thickness spontaneously forms on its surface, this passivation layer is responsible for an increase in corrosion resistance.[72] Unfortunately, when titanium dioxide layer is compromised, and corrosion often takes place.[68, 71] Such corrosion is exasperated by electrolytes in saliva itself which can cause metal ion loss from the titanium surface.[68] This environmental effect can damage the function and biocompatibility of dental implants, which over time may cause the implants to fail in the oral cavity.

Exasperating all of this is the fact that dental implants are continuously exposed to adverse factors that can contribute to titanium degradation, such as masticatory forces, changes in peri-implant oxygenation, variation in temperature and changes caused by food and salivary composition.[73] Possibly most important of all is the variation in salivary pH a phenomenon common to the vary function of the mouth, the ingestion of food. Certain foods such as nuts, milk, and those that are calcium-fortified can alter the saliva to a more alkaline environment.[74] On the other hand, infections, sugary foods, fruits,
juices and soft drinks produce an acidic environment dropping the pH to between 2.5 and 3.5.[74-76] In general, smoking, medications, chronic and systemic diseases can all contribute to lowering the pH of saliva and therefore influencing the corrosion of dental implants.[68, 69, 71] Both titanium and titanium alloys suffer more intense corrosion in acidic environments compared to basic conditions, with increased corrosion rates for both pure titanium and its common alloy Ti-6AI-4V.[77]

In addition to the chemical process of corrosion, mechanical forces on dental implants are a concern, exerting compression and causing wear across the titanium dioxide layer, a tribocorrosion mechanism.[63] The mechanical properties of the native form of TiO<sub>2</sub> are so fragile that low shear stress, such as rubbing against soft tissue can lead to the dissolution of this layer. Thermal oxidation, or the heating of the metal typically to temperatures ranging from 200 °C to 1000 °C cause an increase in the titanium dioxide TiO<sub>2</sub> layer and a change in structure to a harder, rougher, thicker and crystallized layer, called a rutile.[43, 63] Several studies have shown that the process of thermal oxidation changes the surface of TiO<sub>2</sub> layer by increasing the thickness, corrosion resistance, surface topography, roughness, surface energy, and improving the biological and mechanical properties of titanium.[43, 63, 64, 78]

To date no study extensively explores the effect of thermal oxidation on titanium surfaces as a function of temperature and duration. To better understand these relationships this study investigated the phenomenon of artificial saliva at pH 3 and 6.5 with respect to the corrosion process of titanium alloy treated by thermal oxidation at various temperatures and durations (Figure 4). The aim of this study is to understand the

impact of thermal oxidation on the corrosion of titanium alloy surfaces under acidic and physiological conditions similar to those in the oral cavity using electrochemical impedance spectroscopy and evaluation of the potentiodynamic polarization tests. It is our belief that if Ti-6AI-4V is treated by thermal oxidation, then those samples exposed to higher temperatures and longer durations of treatment will experience superior corrosion characteristics compared to those with shorter and lower temperature exposures and a control group with no thermal oxidation.

	Thermal Oxidation Temp/Time	Control	200ºC, 1hr	200ºC, 3hr	200ºC, 6hr	400ºC, 1hr	400ºC, 3hr	400ºC, 6hr	700ºC, 1hr	700ºC, 3hr	700ºC, 6hr
N=60	рН 3.0	N=3									
	pH 6.5	N=3									

Figure 4: Schematic diagram of the design of experiment and sample groups.

The work in section 2.1 of this thesis is 10% identical to a previous iteration by the coauthor Newton Lucchiari, which can be viewed in the Appendix.

## 2.2 Materials and Methods

## 2.2.1 Study design

Sixty Ti-6Al-4V alloy disks with 15 mm in diameter and 1mm thickness were milled from Ti-6Al-4V rods (Mc-Master Carr, Elmhurst, IL, USA). The chemical composition of Ti-6Al-4V (in % of weight) was 89.62 Ti, 6.1 Al, 4 V, 0.004 C, 0.16 Fe, 0.106 O<sub>2</sub>, 0.008 N<sub>2</sub>, and 0.0022 H<sub>2</sub>, characterizing Ti grade 5. The samples were divided into twenty groups (n=3) as a function of pH of artificial saliva, both 3.0 and 6.5, (2 conditions) annealing treatment temperature, 200 °C, 400 °C, and 700 °C (3 conditions) and duration of treatment, 1 hour, 3 hours, and 6 hours (3 conditions), as well as two sets of controls at each pH without thermal oxidation treatment (Figure 4).

#### 2.2.2 Preparation of Ti-6AI-4V Disks

Initially, the disks were polished with sequential grades of sandpaper (#320, #400, #600, 3800) (Carbimet 2, Buehler, Lake Bluff, IL, USA) and polishing cloth (TextMet Polishing Cloth, Buehler), with 9-µm diamond paste (MetaDi, Buehler), and lubricant (MetaDiFluid, Bueheler). Final polishing with a cloth (Chemomet I, Buehler) with colloidal silica polishing suspension (MasterMed, Buehler) was performed to obtain Ti-6Al-4V disks with mirror surfaces with a standardized surface roughness average of 20nm. Samples were ultrasonically cleaned (FS 20, Fisher Scientific Inc., Pittsburg, PA, USA) with deionized water (10 min), then 70% propanol (10 min), and finally dried using nitrogen, N<sub>2</sub>, gas.

## 2.2.3 Thermal Oxidation

Thermal oxidation was carried out in a Lindberg furnace (S# 54032, 120/240 Volts,  $T_{max} = 1200^{\circ}$ C, 50/60 Hz, 960 W). A k-type thermocouple was placed at the center of the quartz tube, 35 cm from opening, and connected to a temperature controller (JLD-612) to maintain working temperatures of 200°C, 400°C, or 700°C for 1, 3 or 6 hours. The samples were loaded into the quartz tube to the center of the furnace at a gradual insertion rate of 5 cm every 5 minutes to prevent thermal shock and micro-crack formation. After samples had been exposed to the desired temperature for the appropriate time frame they were gradually extracted again at a rate of 5 cm every 5 minutes to prevent micro-cracks from abrupt cooling.



Figure 5: On the left, a schematic diagram of electrochemical setup of corrosion experiment, and on the right, an actual image from the Wimmer laboratory.

## 2.2.4 Electrochemical Tests

A custom made acrylic electrochemical cell was used to conduct corrosion experiments (Figure 5). All measurements were conducted through a standardized method with three electrode cells according to the instructions of the American Society for Testing of Materials (ASTM) (G61 and G31-72). A saturated calomel electrode (SCE) was used as the reference electrode, a graphite rod as the counter-electrode (auxiliary), and the exposed surface of the Ti-6AI-4V disks as the working electrode (exposed area of the polished Ti =  $1.77 \text{ cm}^2$ ). A potentiostat (G300, Gamry Inc., Warminster, PA, USA) connected to a computer was used to acquire the data and perform the corrosion measurements. A total of 10 mL of electrolyte (artificial saliva) was used for each corrosion experiment. The composition of artificial saliva (in g/L) was KCI (0.4), NaCI (0.4), CaCl<sub>2</sub>• 2H<sub>2</sub>O (0.906), NaH<sub>2</sub>PO<sub>4</sub>•2H<sub>2</sub>O (0.005), and urea (1).[79] Artificial saliva pH values of 3.0 and 6.5 were achieved by adding lactic acid or basic sodium hydroxide to the artificial saliva and evaluated using a pH meter (Accumet AB15, Fisher Scientific Inc.). After mounting the sample into the cell, electrochemical stabilization of the system was achieved in 4 hours. The temperature of the test solution was maintained at 37 ± 1°C to duplicate the oral environment.

The open circuit potential (OCP) was monitored for 3600 s to evaluate the material potential in the solution and stabilize the system. Electrochemical impedance spectroscopy (EIS) was conducted to investigate the electrochemical formation of oxide layer on Ti-6AI-4V surface and film properties (corrosion kinetics). Through EIS, the electrochemical process could be represented by an equivalent electrical circuit and the oxide film properties (capacitance and resistance) were quantified to determine the corrosion process. The EIS measurements were performed in the frequency range from 100 KHz to 5 MHz, with the AC curve at  $\pm$  10 mV amplitude applied to the electrode in its corrosion potential ( $E_{corr}$ ). The values were used to determine the real (Z') and imaginary (Z'') components in which the Nyquist plot or total impedance (|Z|), and phase angle were

plotted. The EIS results were used to model the corrosion process (corrosion kinetics) and elucidate the properties of the Ti-6AI-4V oxide layer, using a simple equivalent circuit (Randle's circuit). A specific software, Zview2 (Scribner Associates Inc., Southern Pines, NC, USA) was used to simulate the EIS data (Capacitance of double layer—CPE<sub>film</sub> & CPE<sub>ox</sub>, and polarization resistance—R<sub>film</sub> & R<sub>ox</sub>). The reported values of resistance and capacitance were derived from a Randle's circuit with a CPE element in parallel with R<sub>p</sub>.

Finally, the samples were cyclically polarized from 0.8 V to 1.8 V and from 1.8 V to -0.8 V at a scan rate of 2 mV/s. The electrochemical parameters were obtained by potentiodynamic polarization curves. An electrochemical software (Echem Analyst Software, Gamry) was used to estimate the corrosion rate, corrosion current density ( $I_{corr}$ ), and corrosion potential ( $E_{corr}$ ) of Ti-6AI-4V by Tafel extrapolation method. Passivation current density ( $I_{pass}$ ) was also extrapolated from said curves.  $I_{corr}$  corresponds to corrosion rate of the Ti-6AI-4V surface and  $I_{pass}$  corresponds to the current value of the transition from the active region to the passive state of the Ti-6AI-4V surface.

#### 2.2.5 Surface Characterization

The evaluation of corroded and worn surfaces plays an essential role on understanding the mechanisms of material degradation. A white light interferometry (WLI) microscope (Zygo New View 6300, Zygo Corporation, Middlefield, CT, USA) was used to capture three-dimensional changes on Ti-6AI-4V surfaces with different thermal oxidation parameters and pH solution exposures. Surface roughness (R<sub>a</sub>—arithmetic mean value, and R<sub>rms</sub>—root mean squared value) was also measured before (baseline) and after corrosion using a WLI microscope. A scanning electron microscope (SEM) (Joel JSM-

6490 LV, Oxford Instruments, Oxford, UK) was used for characterization of surface morphology. Finally, energy dispersive spectroscopy (EDS) evaluated the formation and composition of the oxide layer on the Ti-6AI-4V surface.

### 2.2.6 Statistical Analysis

All statistical analyses were performed using Statistical Package for the Social Sciences (Version 24; SPSS Inc, Chicago, IL, USA). Corrosion was assessed based on the parameters of the standard electrochemical tests (Icorr, Ecorr, Ipass, Rox, Rfilm, CPEox, and  $CPE_{film}$ ) and from white-light interferometry surface roughness measurements ( $R_a$ and rms). To interpret the effects of thermal oxidation temperature and thermal oxidation duration on the corrosive behavior of Ti alloy electrochemical corrosion test and surface roughness, parameters were tested separately using one-way ANOVA, comparing groups with the other independent variables, pH, etc. as consistent between groups. Outliers in the data, were assessed by inspection of boxplots. Normality of distribution for each group was assessed by Shapiro-Wilk test (p > 0.05), and homogeneity of variances was assessed by Levene's test of homogeneity of variances (p > 0.05). If homogeneity of variances was found to exist post hoc analysis (Tukey) was used for pairwise comparisons within groups. If however, homogeneity of variance was violated, a Welch one-way ANOVA followed by a different post hoc analysis (Games-Howell) was pursued. For the electrochemical parameters, a two-sample independent t-test was performed in order to compare the differences between pH levels for groups with consistent thermal oxidation temperature and duration, with a critical value of p = 0.05. Similarly, surface roughness parameters (R<sub>a</sub> and rms) were evaluated using a two-sample independent ttest in order to compare the surface roughness values before and after corrosion, and also to determine the effect of pH, again a critical value p=0.05 was used. Outliers in the data, were assessed by inspection of boxplots. Normality of distribution for each group was assessed by Shapiro-Wilk test (p > 0.05), and homogeneity of variances was assessed by Levene's test of homogeneity of variances (p > 0.05).

# 2.3 Results

## 2.3.1 EIS data

During a corrosion process the Nyquist (Figure 6) and Bode (Figure 7) plots provide the variation of impedance as a function of the frequency of the electrochemical double layer formed at the interface of titanium and the solution. The Nyquist plot represents the electrochemical resistance of the sample surface, with better resistance represented by higher  $Z_{img}/Z_{real}$  values. As in similar studies, acidic pH decreased the semicircular diameter of capacitance loop, meaning lower corrosion resistance.[77] All groups regardless of thermal oxidation temperature or time displayed higher corrosion rates at lower pH. Those samples thermally oxidized at 200°C, and 400°C achieved the best results for the Nyquist regardless of pH. The protective capacity of the surface treatment is exemplified by the impedance results of the 200°C sample at acidic pH, which is so large as to drown out the control sample at near neutral pH.



Figure 6: Nyquist plot from EIS recorded for Ti-6AI-4V alloy treated and untreated with

thermal oxidation in artificial saliva of varying pH.

The Bode plot (Figure 7) displays two time constants, a low constant for the high 700°C, pH 6.5, and 400°C, pH 3.0, and a different constant for all other groups. The lower time constant is evidence of non-uniform surface layer formation on the samples oxidized at 700°C, pH 6.5, and 400°C, pH 3.0. Contrary to this, are the samples oxidized at lower temperatures which display graphs that are constant and uniform, indicating an oxide film that is homogenous, compact, and resistant to corrosion. At high frequency, both the phase angle and impedance were low. As frequency was lowered, both impedance and phase angle steadily rise. At low frequencies impedance stabilizes, and the samples thermally oxidized at 700°C, pH 6.5, and 400°C, pH 6.5, and 400°C, pH 3.0, exhibit the lowest phase angle values, a characteristic of poor corrosion resistance.



Figure 7: Bode plots from EIS recorded for Ti-6AI-4V alloy treated and untreated with thermal oxidation in artificial saliva of varying pH.

The impedance values for the untreated alloy Ti-6AI-4V were obtained using a simple Randle's circuit (Figure 8A), where  $R_s$  is the resistance of the solution, CPE<sub>film</sub> is

the capacitance of the double layer at the working electrode-electrolyte interface and  $R_{film}$  resistance of the charge transfer at the passive layer. For analysis of samples treated by thermal oxidation a complex Randle's circuit (Figure 8B) was used. This modified circuit consists of two new corrections, CPE<sub>ox</sub> and R<sub>ox</sub>, which allow for an electrical equivalent circuit to the electrochemical reactions at the metal-solution interface. These new units revealed the existence of two time constants to control the corrosion mechanism. Due to surface layer imperfections, inhomogeneity, the capacitance is represented by a constant-phase element (CPE) as an alternative to an ideal capacitance element.[80] The impedance data were compared to an ideal capacitor model, fitting line analysis by chi-square error (<0.001). The EIS results are shown in Table 1 and Figure 9, where low capacitor values, CPE<sub>ox</sub> and CPE<sub>film</sub>, and high resistor values, R<sub>ox</sub> and R<sub>film</sub>, indicate higher corrosion resistance.



Figure 8: (A) Simple Randle's circuit and (B) a complex Randle's circuit.

EIS Results										
		R film (Ω)		R oxio	de (Ω)	CPE fi	lm (μF)	CPE oxide (µF)		
	Sample	Average	Std. Dev.	Average	Std. Dev.	Average	Std. Dev.	Average	Std. Dev.	
	Control	6.46E+06	4.74E+06	6.46E+06	4.74E+06	21.50	2.20	21.50	2.20	
	200°C 1h	2.57E+07	1.49E+07	8.24E+02	6.95E+02	1.59	1.39	10.35	1.40	
	200°C 3h	1.61E+07	8.11E+06	1.52E+03	1.23E+03	1.14	0.99	10.63	1.16	
	200°C 6h	3.08E+07	1.27E+07	7.46E+02	6.39E+02	1.75	0.77	10.61	1.51	
pH 6.5	400°C 1h	3.09E+07	4.10E+07	4.75E+05	7.46E+05	5.34	5.41	16.17	2.13	
	400°C 3h	2.72E+10	4.70E+10	4.22E+04	2.77E+04	11.16	4.07	22.83	4.70	
	400°C 6h	1.65E+10	1.77E+10	3.90E+04	5.42E+03	15.13	6.17	30.20	6.23	
	700°C 1h	8.45E+05	2.11E+05	1.04E+03	9.98E+02	56.11	27.36	29.66	4.68	
	700°C 3h	3.60E+05	3.18E+04	2.02E+02	3.62E+01	120.60	4.24	35.76	9.14	
	700°C 6h	3.92E+05	8.29E+04	1.07E+03	1.48E+01	30.88	0.38	9.87	0.41	
	Control	9.28E+05	4.94E+05	9.28E+05	4.94E+05	20.34	0.29	20.34	0.29	
	200°C 1h	6.47E+06	2.22E+05	1.48E+04	8.40E+03	0.004	0.01	15.61	0.07	
	200°C 3h	7.33E+06	1.48E+06	8.65E+02	3.23E+02	2.38	0.11	13.51	0.60	
	200°C 6h	6.55E+06	1.47E+06	1.11E+03	5.66E+02	1.19	1.19	14.86	1.86	
pH 3.0	400°C 1h	1.37E+06	1.82E+05	6.38E+03	5.62E+03	1.12	0.81	19.99	0.53	
	400°C 3h	3.02E+06	1.50E+06	2.83E+04	1.09E+04	5.64	2.28	22.10	0.73	
	400°C 6h	4.65E+06	1.82E+06	1.20E+04	1.19E+03	6.37	1.34	21.02	1.47	
	700°C 1h	4.92E+05	1.73E+05	4.07E+02	5.46E+01	79.56	11.20	13.03	3.54	
	700°C 3h	4.18E+05	8.31E+04	4.04E+02	7.65E+01	82.00	23.05	27.02	11.42	
	700°C 6h	1.51E+06	1.96E+06	3.04E+02	1.86E+02	172.10	36.35	56.01	31.89	

Table 1: EIS Results.



Figure 9: Polarization resistance ( $R_{ox}$  and  $R_{film}$ ) and capacitance ( $CPE_{ox}$  and  $CPE_{film}$ ) for oxide layer and oxide film.

The effect of thermal oxidation duration on the EIS parameters,  $R_{ox}$ ,  $R_{film}$ ,  $CPE_{ox}$ , and  $CPE_{film}$ , was assessed through a series of one-way ANOVA tests for each possible combination of constant pH and thermal oxidation temperature. For the most part, the effect of thermal oxidation duration was not statistically significant (p > 0.05) for all four EIS parameters at each combination of pH and thermal oxidation temperature. Exceptions to this were as follows:  $R_{film}$  at pH 6.5 and 700°C showed significant differences (p=0.006) for 1 hour vs. 3 hours (p=0.008; Tukey test), and 1 hour vs. 6 hours (p=0.011; Tukey test).  $CPE_{ox}$  at pH 6.5 at 400°C showed significant differences (p=0.029) for 1 hour vs. 6 hours (p=0.024; Tukey test), and also at 700°C (p=0.001) for 1 hour vs. 6 hours (p=0.005; Tukey test) and 3 hour vs. 6 hours (p=0.001; Tukey test). CPE<sub>ox</sub> also showed significant differences at pH 3.0 and 700°C (p=0.030) for 1 hour vs. 6 hours (p=0.027; Tukey test). CPE<sub>film</sub> at pH 6.5 at 700°C showed significant differences (p=0.001) for 1 hour vs. 3 hours (p=0.006; Tukey test), and 3 hours vs. 6 hours (p=0.001; Tukey test). CPE<sub>film</sub> also showed significant differences at pH 3.0 and 200°C (p=0.016) for 1 hour vs. 3 hours (p=0.013; Tukey test), at 400°C (p=0.014) for 1 hour vs. 3 hours (p=0.031; Tukey test), and 1 hour vs. 6 hours (p=0.016; Tukey test), and finally at 700°C for 1 hour vs. 6 hours (p=0.004; Tukey test), and 3 hours vs. 6 hours (p=0.005; Tukey test). It is interesting to observe that duration appears to be least significant at lower thermal oxidation temperatures, and significantly more important at 400°C and 700°C.

This was followed by a series of one-way ANOVA experiments on the EIS parameters,  $R_{ox}$ ,  $R_{film}$ ,  $CPE_{ox}$ , and  $CPE_{film}$ , for each combination of constant pH and thermal oxidation duration to assess the effects of thermal oxidation temperature. For the most part, the effect of thermal oxidation temperature was statistically significant (p < 0.05) for all temperatures at each combination of pH and thermal oxidation duration. The specifics are as follows:  $R_{ox}$  at pH 6.5 showed significant differences at a 3 hour duration (p=0.030) for 200°C vs. 400°C (p=0.047; Tukey test), and 400°C vs 700°C (p=0.042; Tukey test), and again at 6 hour duration (p<0.0005) for 200°C vs. 400°C (p<0.0005; Tukey test).  $R_{ox}$  at pH 3.0 showed significant differences at a 3 hour duration (p=0.002) for 200°C vs. 400°C (p=0.004; Tukey test), and 400°C vs 700°C (p=0.002) for 200°C vs. 400°C (p=0.005) for 200°C vs. 400°C (p=0.002) for 200°C vs. 400°C (p=0.005) for 200°C vs. 400°C (p=0.0005; Tukey test).  $R_{ox}$  at pH 3.0 showed significant differences at a 3 hour duration (p=0.002) for 200°C vs. 400°C (p=0.005) for 200°C vs. 400°C (p=0.004; Tukey test), and 400°C vs 700°C (p=0.005; Tukey test).  $R_{ox}$  at pH 3.0 showed significant differences at a 3 hour duration (p=0.002) for 200°C vs. 400°C (p=0.005) for 200°C vs. 400°C (p=0.004; Tukey test), and 400°C vs 700°C (p=0.004; Tukey test), and 400°C vs 700°C (p=0.005; Tukey test).  $R_{film}$  at pH 6.5 showed significant differences at a 6 hour duration (p=0.002; Welch ANOVA) for

400°C vs 700°C (p=0.005; Games-Howell test). R<sub>film</sub> at pH 3.0 showed significant differences at each duration, first at 1 hour (p<0.0005) for 200°C vs. 400°C (p<0.0005; Tukey test), for 400°C vs 700°C (p=0.003; Tukey test), and for 200°C vs 700°C (p<0.0005; Tukey test), then at 3 hours (p=0.001) for 200°C vs. 400°C (p=0.012; Tukey test) and for 200°C vs 700°C (p=0.001; Tukey test), and lastly at 6 hours (p=0.021) for 200°C vs 700°C (p=0.018; Tukey test). CPE<sub>ox</sub> at pH 6.5 showed significant differences at each duration, first at 1 hour (p=0.001) for 200°C vs. 700°C (p=0.001; Tukey test), and for 400°C vs 700°C (p=0.004; Tukey test), then at 3 hours (p=0.002) for 200°C vs. 400°C (p=0.042; Tukey test), for 200°C vs 700°C (p=0.001; Tukey test), and for 400°C vs. 700°C (p=0.034; Tukey test), and lastly at 6 hours duration (p=0.039; Welch ANOVA) for 200°C vs. 400°C (p=0.050; Games-Howell test). CPE<sub>ox</sub> at pH 3.0 showed significant differences at each duration, first at 1 hour (p=0.004; Welch ANOVA) for 200°C vs. 400°C (p=0.008; Games-Howell test), then at 3 hours (p=0.001; Welch ANOVA) for 200°C vs. 400°C (p=0.001; Games-Howell test), and lastly at 6 hours (p=0.017) for 200°C vs. 700°C (p=0.020; Tukey test), and for 400°C vs. 700°C (p=0.039; Tukey test). CPE<sub>film</sub> at pH 6.5 showed significant differences at each duration, first at 1 hour (p=0.010) for 200°C vs. 700°C (p=0.014; Tukey test), and for 400°C vs. 700°C (p=0.020; Tukey test), then at 3 hours (p<0.0005) for 200°C vs. 400°C (p=0.015; Tukey test), for 200°C vs. 700°C (p<0.0005; Tukey test), and for 400°C vs. 700°C (p<0.0005; Tukey test), finally at 6 hours (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test). CPE<sub>film</sub> at pH 3.0 showed significant differences at each duration, first at 1 hour (p=0.006; Welch ANOVA) for 200°C vs. 700°C (p=0.012; Games-Howell test), and for 400°C vs. 700°C (p=0.012; Games-Howell test), then at 3 hours (p=0.031; Welch ANOVA) for 200°C vs.

700°C (*p*=0.049; Games-Howell test), and lastly at 6 hours (*p*<0.0005) for 200°C vs. 700°C (*p*<0.0005; Tukey test), and for 400°C vs. 700°C (*p*<0.0005; Tukey test).

Finally, independent t-tests were conducted to compare the EIS parameters,  $R_{ox}$ ,  $R_{film}$ ,  $CPE_{ox}$ , and  $CPE_{film}$ , for the effect of pH, at constant combinations of thermal oxidation temperature and duration. pH was found to be sporadically significant for the EIS parameters, specifically:  $R_{ox}$  showed significance between pH levels at 200°C and 1 hour of thermal oxidation (*p*=0.045), at 400°C and 6 hours of thermal oxidation (*p*=0.001), at 700°C for both 3 hours of thermal oxidation (*p*=0.044) and 6 hours (*p*=0.029).  $R_{film}$  only showed significance between pH levels at 200°C at 1 hour (*p*=0.030).  $CPE_{ox}$  showed significance between pH levels at 200°C at 1 hour (*p*=0.003), 3 hours (*p*=0.020), and 6 hours (*p*=0.038) of annealing, again at 400°C at 1 hour (*p*=0.039) annealing, and finally at 700°C at 1 hour (*p*=0.008) annealing. Finally,  $CPE_{film}$  showed significance between pH levels at 700°C for 1 hour (*p*=0.032) of thermal oxidation.

To interpret the significance of these results Figure 9 shows the EIS parameters for the individual groups. It is clear that the 700°C thermally oxidized group had the worst results in both pH settings, that is, poor corrosion with high capacitance and low resistance relative to other groups at the same pH and time of oxidation. It is also clear that samples annealed at 200°C had excellent corrosion results with significant reductions in capacitance and strong resistance values. What is less clear is the samples at 400°C which show the highest resistance values but similar to the samples at 700°C begin to show elevations in capacitance. Meanwhile, acidic pH tended to increase the corrosion properties with thermal oxidation at lower temperatures appearing to be least effected, in

contrast to those samples oxidized at 700°C which show markedly higher capacitance values in acidic medium.

## 2.3.2 Data of cyclic polarization

The cyclic polarization curves for titanium alloys treated by thermal oxidation show differences in behavior based on temperature (Figure 10). In the anodic region of the graph a clear transition from the active to the passive region occurs in the artificial saliva. Though no pitting corrosion was observed by imaging for the samples, the greatest tendency for pitting corrosion was observed in the samples thermally oxidized to 200°C, and the potential for pitting is greater in the thermally oxidized groups than the control group. All samples passivate, as observed in the cyclic polarization curve.





with thermal oxidation in artificial saliva of varying pH.

Based on these curves, electrochemical parameters such as  $E_{corr}$ ,  $I_{corr}$ , and  $I_{pass}$ were obtained and are presented in Table 2. E<sub>corr</sub> is the corrosion potential of the alloy, while I<sub>corr</sub> expresses the corrosion rate and I<sub>pass</sub> the current at which passivation occurs. The more positive the Ecorr value, the less tendency the alloy has to corrode, whereas the higher the values of  $I_{corr}$  and  $I_{pass}$ , the higher the corrosion rate. To analyze the effect of thermal oxidation duration on the potentiodynamic curve parameters, E<sub>corr</sub>, I<sub>corr</sub>, and I<sub>pass</sub>, a series of one-way ANOVA tests for each possible combination of constant pH and thermal oxidation temperature were conducted. For the most part, the effect of thermal oxidation duration was not statistically significant (p > 0.05) for all three parameters at each combination of pH and thermal oxidation temperature. The specifics are as follows: E<sub>corr</sub> showed significance for duration at 700°C and pH 6.5 (p=0.001) for 1 hour vs. 6 hours (p=0.002; Tukey test) and 3 hours vs 6 hours (p=0.003; Tukey test), and again at 200°C and pH 3.0 (p=0.011) for 1 hour vs. 6 hours (p=0.011; Tukey test) and 3 hours vs 6 hours (p=0.033; Tukey test). I<sub>corr</sub> showed significance for duration at 400°C and pH 6.5 (p=0.002) for 1 hour vs. 3 hours (p=0.003); Tukey test) and 1 hour vs 6 hours (p=0.003); Tukey test), and again at 700°C and pH 6.5 (p<0.0005) for 1 hour vs. 3 hours (p<0.0005; Tukey test) and 1 hour vs 6 hours (p<0.0005; Tukey test). I<sub>pass</sub> showed significance for duration at 700°C and pH 6.5 (p=0.002) for 1 hour vs. 3 hours (p=0.002; Tukey test) and 3 hours vs 6 hours (p=0.006; Tukey test).

Potentiodynamic Results										
		Ecorr (m	V vs SCE)	lcorr (r	nA/cm2)	lpass (µA/cm2)				
	Sample	Average	Std. Dev.	Average	Std. Dev.	Average	Std. Dev.			
	Control	-670.0	23.1	16.1	2.2	13.47	0.31			
	200°C 1h	-365.0	75.6	13.1	3.5	0.06	0.00			
	200°C 3h	-221.0	42.1	13.1	3.6	0.14	0.16			
	200°C 6h	-343.0	99.3	18.7	13.5	0.18	0.20			
pH 6.5	400°C 1h	-359.0	109.1	29.2	5.7	0.23	0.20			
	400°C 3h	-521.0	139.6	74.8	29.6	0.49	0.15			
	400°C 6h	-604.0	132.8	57.6	10.6	0.56	0.14			
	700°C 1h	-439.0	43.0	401.0	84.3	3.33	0.53			
	700°C 3h	-413.0	5.7	704.0	82.5	7.14	0.68			
	700°C 6h	-294.0	25.5	289.0	34.9	4.13	0.95			
	Control	-238.0	83.8	156.0	75.6	14.70	0.30			
	200°C 1h	-138.0	25.7	23.8	6.0	0.84	1.10			
	200°C 3h	-111.0	15.0	20.6	5.8	0.19	0.04			
	200°C 6h	-52.0	12.3	24.4	3.0	0.25	0.14			
pH 3.0	400°C 1h	-34.3	27.4	58.4	12.1	1.40	1.44			
	400°C 3h	-112.0	32.5	48.4	18.7	0.97	0.50			
	400°C 6h	-77.0	30.8	46.0	15.6	0.43	0.15			
	700°C 1h	-285.0	29.5	406.0	37.1	5.13	0.76			
	700°C 3h	-242.0	31.2	449.0	22.8	5.23	1.23			
	700°C 6h	-283.0	18.4	759.0	218.3	11.00	0.58			

Table 2: Potentiodynamic Data.

This was followed by a series of one-way ANOVA experiments on the potentiodynamic curve parameters,  $E_{corr}$ ,  $I_{corr}$ , and  $I_{pass}$ , for each combination of constant pH and thermal oxidation duration to assess the effects of thermal oxidation temperature. For the most part, the effect of thermal oxidation temperature was statistically significant (p < 0.05) for all three temperatures at each combination of pH and thermal oxidation duration. The details are as follows:  $E_{corr}$  showed significance for temperature at pH 6.5 and 3 hours of thermal oxidation (p=0.016; Welch ANOVA) for 200°C vs 700°C (p=0.022; Games-Howell test), and again at 6 hours of annealing (p=0.010), for 200°C vs 400°C

(p=0.024; Tukey test) and for 400°C vs 700°C (p=0.011; Tukey test). E<sub>corr</sub> showed significance for temperature at pH 3.0 and 1 hour annealing (p<0.0005) for 200°C vs 400°C (p=0.013; Tukey test), for 200°C vs 700°C (p=0.002; Tukey test), and for 400°C vs 700°C (p<0.0005; Tukey test), again at 3 hours annealing (p=0.001) for 200°C vs 700°C (p=0.002; Tukey test), and for 400°C vs 700°C (p=0.001; Tukey test), and finally at 6 hours annealing (p<0.0005) for 200°C vs 700°C (p<0.0005; Tukey test), and for 400°C vs 700°C (p<0.0005; Tukey test). I<sub>corr</sub> showed significance for temperature at pH 6.5 and 1 hour annealing (p<0.0005) for 200°C vs 700°C (p<0.0005; Tukey test), and for 400°C vs 700°C (p<0.0005; Tukey test). I<sub>corr</sub> showed significance for temperature at pH 3.0 for 3 hours of annealing (p<0.0005) for 200°C vs 700°C (p=0.001; Tukey test), and for 400°C vs 700°C (p=0.001; Tukey test). I<sub>pass</sub> showed significance for temperature at pH 6.5 and each duration, first at 1 hour annealing (p=0.009; Welch ANOVA) for 200°C vs 700°C (p=0.016; Games-Howell test), and for 400°C vs 700°C (p=0.009; Games-Howell test), then at 3 hours annealing (p < 0.0005) for 200°C vs 700°C (p < 0.0005; Tukey test), and for 400°C vs 700°C (p<0.0005; Tukey test), and finally for 6 hours annealing (p<0.0005) for 200°C vs 700°C (p<0.0005; Tukey test), and for 400°C vs 700°C (p=0.001; Tukey test). I<sub>pass</sub> showed significance for temperature at pH 3.0 at 1 hour annealing (p=0.007) for 200°C vs 700°C (p=0.009; Tukey test), and for 400°C vs 700°C (p=0.016; Tukey test), and also for 3 hours annealing (p=0.020; Welch ANOVA) for 200°C vs 700°C (p=0.035; Games-Howell test), and for 400°C vs 700°C (p=0.031; Games-Howell test).

Finally, independent t-tests were conducted to compare the potentiodynamic curve parameters,  $E_{corr}$ ,  $I_{corr}$ , and  $I_{pass}$ , for the effect of pH, at constant combinations of thermal oxidation temperature and duration. Each parameter showed varying degrees of

statistical significance (p<0.05) for the groups analyzed, in particular E<sub>corr</sub> was almost always influenced by pH, I<sub>corr</sub> sporadically influenced, and I<sub>pass</sub> almost never so. The specifics are as follows: E<sub>corr</sub> showed significance for pH at 200°C and 1 hour annealing (p=0.014), 200°C and 3 hours annealing (p=0.031), 200°C and 6 hours annealing (p=0.009), 400°C and 1 hour annealing (p=0.008), 400°C and 3 hours annealing (p=0.008), 400°C and 6 hours annealing (p=0.002), 700°C and 1 hour annealing (p=0.009), and finally at 700°C and 3 hours annealing (p=0.001). I<sub>corr</sub> showed significance for pH at 200°C and 1 hour annealing (p=0.021), 200°C and 3 hours annealing (p=0.035), 400°C and 1 hour annealing (p=0.009), 700°C and 1 hour annealing (p=0.001). I<sub>corr</sub> showed significance for pH at 200°C and 1 hour annealing (p=0.021), 200°C and 3 hours annealing (p=0.035), 400°C and 1 hour annealing (p=0.009), 700°C and 1 hour annealing (p=0.001), and 700°C and 6 hours annealing (p<0.0005). I<sub>pass</sub> showed significance for pH at 700°C and 1 hour annealing (p=0.029).

The potentiodynamic curve parameters can be generalized as follows: At the pH of saliva, 6.5,  $E_{corr}$  values (Figure 11) for the samples thermally oxidized were more resistant to corrosion as compared to control group, with more positive and significant results. Those samples oxidized at 200°C appear to present the best  $E_{corr}$  values and corrosion resistance at pH 6.5. At acidic pH, 3.0, the thermally oxidized groups again appear to be less prone to corrosion, but samples at 400°C appear best despite strong performance at 200°C. As for  $I_{corr}$ , those samples thermally oxidized at 700°C had higher corrosion rate as compared to the control group at both pH values, and samples oxidized at 400°C displayed higher values as compared to control at neutral salivary pH. As for the corrosion current of the other thermally oxidized samples, substantial reductions in  $I_{corr}$  were apparent as compared to control for samples thermally oxidized at 200°C. For acidic pH, the  $I_{corr}$  for those samples oxidized at 200°C had much smaller corrosion rates,

relative to the elevated rates seen between control samples for the switch to acidic medium. Finally, the  $I_{pass}$  for all groups treated by thermal oxidation had better results than the control groups for both pH 3.0 and 6.5, displaying superior passivation in the corrosion process, particularly samples oxidized at 200°C. To summarize, for all electrochemical parameters the thermally oxidized groups at 200°C displayed better corrosion outcomes for both pH 3.0 and 6.5 as compared to control. The samples oxidized at 400°C display the best  $E_{corr}$  values at pH 3.0 but also worse  $I_{corr}$  values at pH 6.5 as compared to control samples for both pH 3.0 and 6.5, the exceptions being the  $I_{pass}$  values which were better for all oxidized samples and  $E_{corr}$  values at pH 6.5.



Figure 11: Electrochemical parameters, E<sub>corr</sub>, I<sub>corr</sub>, and I<sub>pass</sub> for Ti-6AI-4V alloy treated and untreated with thermal oxidation in artificial saliva of varying pH.

#### 2.3.3 Surface Topography

The surface analysis of samples (Table 3, Figure 12) was conducted by white light interferometry. Observed difference in surface roughness between samples before and after corrosion was sporadic, with significance validated via an independent t-test (p < 0.05) for measures of samples at the same pH, thermal oxidation temperature, and duration. The control samples at pH 6.5 showed significance for both the RMS value (p=0.009) and the R<sub>a</sub> value (p=0.006) for samples before and after corrosion. Similarly the control samples at pH 3.0 showed significance for both the RMS value (p=0.005) and the  $R_a$  value (p=0.001) for samples before and after corrosion. Other samples that showed significant differences between roughness values before and after corrosion are as follows: Samples at 200°C, pH 6.5 and 6 hours of annealing displayed significance for both RMS (p<0.0005) and R<sub>a</sub> (p=0.001). Samples at 400°C, pH 6.5 and 3 hours of annealing displayed significance for both RMS (p=0.020) and R<sub>a</sub> (p<0.0005). Samples at 700°C, pH 6.5 and 3 hours of annealing displayed significance for  $R_a$  (p=0.022). Samples at 700°C, pH 6.5 and 6 hours of annealing displayed significance for both RMS (p=0.037) and R<sub>a</sub> (p=0.002). Samples at 200°C, pH 3.0 and 1 hour of annealing displayed significance for R<sub>a</sub> (p=0.009). Samples at 400°C, pH 3.0 and 1 hour of annealing displayed significance for both RMS (p=0.013) and R<sub>a</sub> (p=0.016). Samples at 400°C, pH 3.0 and 3 hours of annealing displayed significance for  $R_a$  (p=0.007). Samples at 400°C, pH 3.0 and 6 hours of annealing displayed significance for R<sub>a</sub> (p=0.032). Samples at 700°C, pH 3.0 and 6 hours of annealing displayed significance for both RMS (p=0.039) and R<sub>a</sub> (p=0.016).

	<b>Rms Before Corrosion (nm)</b>		Rms After Corrosion (nm)		Ra Before Corrosion (nm)		Ra After Corrosion (nm)		
	Sample	Average	Std. Dev.	Average	Std. Dev.	Average	Std. Dev.	Average	Std. Dev.
	Control	12.969	4.513	18.722	7.132	9.093	2.492	12.730	4.313
	200°C 1h	24.586	3.245	24.990	5.221	18.467	2.282	19.208	4.178
	200°C 3h	24.786	8.387	22.032	5.241	16.007	2.549	16.891	4.151
	200°C 6h	28.360	3.188	36.890	7.524	19.462	2.376	26.143	7.306
pH 6.5	400°C 1h	28.723	5.917	31.544	8.688	21.376	5.088	23.517	5.551
	400°C 3h	27.420	7.732	33.085	6.153	17.804	2.852	25.454	4.702
	400°C 6h	30.617	4.178	30.123	7.254	21.642	2.183	23.291	6.287
	700°C 1h	229.369	35.536	234.236	31.287	101.072	12.110	107.656	11.790
	700°C 3h	250.883	20.641	253.827	18.497	160.492	11.316	170.325	13.205
	700°C 6h	310.326	30.861	332.627	30.619	198.303	12.908	211.597	10.707
	Control	12.969	4.513	17.385	3.646	9.093	2.492	12.651	2.994
	200°C 1h	28.620	5.003	30.767	5.322	19.490	3.003	22.319	3.161
	200°C 3h	32.051	18.936	28.486	11.879	18.847	2.176	18.987	2.049
	200°C 6h	26.322	3.782	25.566	4.289	17.882	2.098	17.494	1.965
pH 3.0	400°C 1h	27.410	2.394	31.258	5.788	20.092	2.230	23.343	4.953
	400°C 3h	29.891	5.923	31.581	3.891	21.315	3.368	24.557	3.407
	400°C 6h	27.257	5.139	28.244	3.521	18.285	2.438	20.029	2.229
	700°C 1h	206.946	26.316	199.283	18.498	97.837	7.800	96.794	6.296
	700°C 3h	265.242	69.022	262.466	82.490	134.048	31.070	135.457	34.718
	700°C 6h	531 996	119 896	617 884	120 617	288 620	55 378	339 686	65 041

Table 3: Mean value for surface roughness (RMS and Ra) in nm as a function of corrosion process for Ti-6AI-4V alloy treated and untreated with thermal oxidation in artificial saliva of varying pH.

The effect of pH on samples exposed to media through the corrosion process was assessed via an independent t-test (p<0.05) for measures of samples at the same thermal oxidation temperature, and duration. The effect of pH did not appear significant for the control samples for either the RMS value (p>0.05) or the R<sub>a</sub> value (p>0.05). Other samples that showed significant differences between roughness values due to pH are as follows: Samples at 200°C and 1 hour annealing duration display significance for both RMS (p=0.002) and R<sub>a</sub> (p=0.017). Samples at 200°C and 3 hours annealing duration display significance for RMS (p=0.042). Samples at 200°C and 6 hours annealing duration display significance for both RMS (p<0.0005) and R<sub>a</sub> (p<0.0005). Samples at 400°C and 6 hours annealing duration display significance for both RMS (p=0.046). Samples at 400°C and 6 hours annealing duration display significance for RMS (p=0.046). Samples at

700°C and 1 hour annealing duration display significance for both RMS (p<0.0005) and R<sub>a</sub> (p=0.002). Samples at 700°C and 3 hours annealing duration display significance for R<sub>a</sub> (p<0.0005). Samples at 700°C and 6 hours annealing duration display significance for both RMS (p<0.0005) and R<sub>a</sub> (p<0.0005).



Figure 12: Surface roughness (Rms and Ra) of Ti-6AI-4V alloy treated with thermal oxidation before and after corrosion in artificial saliva of varying pH.

A series of one-way ANOVA was used to measure the effect of duration on the roughness values for fixed temperature, pH, and corrosion exposure. Overall duration was found to be a significant (p<0.05) variable on the roughness values. The specifics

are as follows: Before corrosion at 200°C and pH 6.5 duration was found to be significant for RMS (p=0.005; Welch ANOVA) for 1 hour vs. 6 hours annealing (p=0.004; Games-Howell test), and for  $R_a$  (p<0.0005) for 1 hour vs. 3 hours annealing (p=0.010; Tukey test), and 3 hours vs. 6 hours annealing (p < 0.0005; Tukey test). After corrosion at 200°C and pH 6.5 duration was found to be significant for RMS (p<0.0005) for 1 hour vs. 6 hours annealing (p<0.0005; Tukey test) and 3 hours vs. 6 hours annealing (p<0.0005; Tukey test), and for  $R_a$  (*p*<0.0005; Welch ANOVA) for 1 hour vs. 6 hour annealing (*p*=0.005; Games-Howell test), and 3 hours vs. 6 hours annealing (p<0.0005; Games-Howell test). Before corrosion at 400°C and pH 6.5 duration was found to be significant for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 1 hour vs. 3 hours annealing (p=0.039; Games-Howell test), and for 3 hours vs. 6 hours annealing (p<0.0005; Games-Howell test). Before corrosion at 700°C and pH 6.5 duration was found to be significant for RMS (p<0.0005) for 1 hour vs. 6 hours annealing (p<0.0005; Tukey test) and for 3 hours vs. 6 hours annealing (p < 0.0005; Tukey test), and for R<sub>a</sub> (p < 0.0005) for 1 hour vs. 3 hours annealing (p<0.0005; Tukey test), 3 hours vs. 6 hours annealing (p<0.0005; Tukey test), and for 1 hour vs. 6 hours annealing (p<0.0005; Tukey test). After corrosion at 700°C and pH 6.5 duration was found to be significant for RMS (p < 0.0005) for 1 hour vs. 6 hours annealing (p<0.0005; Tukey test) and for 3 hours vs. 6 hours annealing (p<0.0005; Tukey test), and for  $R_a$  (p<0.0005) for 1 hour vs. 3 hours annealing (p<0.0005; Tukey test), 3 hours vs. 6 hours annealing (p<0.0005; Tukey test), and for 1 hour vs. 6 hours annealing (p<0.0005; Tukey test). After corrosion at 200°C and pH 3.0 duration was found to be significant for R<sub>a</sub> (p<0.0005; Welch ANOVA), for 1 hour vs. 3 hours annealing (p=0.002; Games-Howell test) and for 1 hour vs. 6 hours annealing (p < 0.0005; Games-Howell test). Before corrosion at 400°C and pH 3.0 duration was significant for R<sub>a</sub> (p=0.006) for 3 hours vs. 6 hours annealing (p=0.004; Tukey test). After corrosion at 400°C and pH 3.0 duration was significant for RMS (p=0.026; Welch ANOVA) for 3 hours vs. 6 hours annealing (p=0.028; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 1 hour vs. 6 hours (p=0.041; Games-Howell test) and for 3 hours vs. 6 hours (p<0.0005; Games-Howell test). Before corrosion at 700°C and pH 3.0 duration was significant for RMS (p<0.0005; Welch ANOVA) for 1 hour vs. 3 hours annealing (p=0.008; Games-Howell test), for 1 hour vs. 6 hours annealing (p<0.0005; Games-Howell test), and for 3 hours vs. 6 hours annealing (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 1 hour vs. 3 hours (p<0.0005; Games-Howell test), for 1 hour vs. 6 hours (p<0.0005; Games-Howell test), and for 3 hours vs. 6 hours annealing (p<0.0005; Games-Howell test). After corrosion at 700°C and pH 3.0 duration was significant for RMS (p<0.0005; Welch ANOVA) for 1 hour vs. 3 hours annealing (p=0.013; Games-Howell test), for 1 hour vs. 6 hours annealing (p<0.0005; Games-Howell test), and for 3 hours vs. 6 hours annealing (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 1 hour vs. 3 hours (p=0.001; Games-Howell test), for 1 hour vs. 6 hours (p<0.0005; Games-Howell test), and for 3 hours vs. 6 hours annealing (p < 0.0005; Games-Howell test).

A series of one-way ANOVA was used to measure the effect of temperature on the roughness values for fixed duration, pH, and corrosion exposure. Overall temperature was found to be a significant (p<0.05) variable on the roughness values. A notable exception to significance was occasionally found between samples annealed at 200°C and 400°C, all other factors being equivalent. The specifics are as follows: Before corrosion, with 1 hour annealing duration and pH 6.5, temperature was found to be

significant for RMS (p<0.0005; Welch ANOVA) for 200°C vs. 400°C (p=0.039; Games-Howell test), for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test). After corrosion, with 1 hour annealing duration and pH 6.5, temperature was found to be significant for RMS (p<0.0005; Welch ANOVA) for 200°C vs. 400°C (p=0.028; Games-Howell test), for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 200°C vs. 400°C (p=0.034; Games-Howell test), for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test). Before corrosion, with 3 hours annealing duration and pH 6.5, temperature was found to be significant for RMS (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p < 0.0005; Games-Howell test). After corrosion, with 3 hours annealing duration and pH 6.5, temperature was found to be significant for RMS (p<0.0005; Welch ANOVA) for 200°C vs. 400°C (p<0.0005; Games-Howell test), for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 200°C vs. 400°C (p<0.0005; Games-Howell test), for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test). Before corrosion, with 6 hours annealing duration and pH 6.5, temperature was found to be significant for RMS (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-

Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 200°C vs. 400°C (p=0.019; Games-Howell test), for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test). After corrosion, with 6 hours annealing duration and pH 6.5, temperature was found to be significant for RMS (p<0.0005; Welch ANOVA) for 200°C vs. 400°C (p=0.025; Games-Howell test), for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test). Before corrosion, with 1 hours annealing duration and pH 3.0, temperature was found to be significant for RMS (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test). After corrosion, with 1 hours annealing duration and pH 3.0, temperature was found to be significant for RMS (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005) for 200°C vs. 700°C (p<0.0005; Tukey test), and for 400°C vs. 700°C (p<0.0005; Tukey test). Before corrosion, with 3 hours annealing duration and pH 3.0, temperature was found to be significant for RMS (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 200°C vs. 400°C (p=0.037; Games-Howell test), for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test). After corrosion, with 3 hours annealing duration and pH 3.0, temperature was found to be significant for RMS (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 200°C vs. 400°C (p<0.0005; Games-Howell test), for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test). Before corrosion, with 6 hours annealing duration and pH 3.0, temperature was found to be significant for RMS (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for R<sub>a</sub> (p<0.0005; Welch ANOVA) for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test), and for 400°C vs. 700°C (p<0.0005; Games-Howell test), and for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 200°C vs. 700°C (p<0.0005; Games-Howell test), and for 200°C vs. 700°C (p<0.0005; Games-Howell test), for 200°C vs. 700°C (p<0.0005; Games-Howell test), for 200°C vs. 700°C (p<0.0005; Games-Howell test), for 200°C vs. 700°C (p<0.0005; Games-Howell test).

To generalize the findings, the roughness averages and standard deviations for both RMS and R<sub>a</sub> were for the most part similar being within an order of magnitude of one another, the exception being samples thermally oxidized at 700°C. There is a visible and significant difference in the roughness of the samples thermally oxidized at 700°C compared to the other groups for both before and after corrosion at either pH level. Those samples thermally oxidized at 700°C presented a noticeable roughness to the naked eye, and a darker gray appearance in comparison to other samples. The mean roughness values for samples thermally oxidized at 700°C are an order of magnitude greater than either control and samples oxidized at lower temperatures (Table 3).

The SEM images show the differences in surface roughness more clearly, as Figure 13 clearly shows a rough appearance for samples oxidized at 700°C. Cracks are also noticeable in this figure for a sample undergoing corrosion at pH 6.5, but not found in samples at lower oxidation temperatures. No pitting corrosion was observed in any of the samples after potentiodynamic tests. Infrared spectroscopy (FTIR) shows the evolution of the increase of the titanium dioxide layer by thermal oxidation, and shows that the oxide layer increases with temperature during thermal oxidation (Figure 14). Further impurities are seen in the sample at 700°C, as opposed to lower temperatures.



Figure 13: SEM images of Ti-6Al-4V alloy treated with thermal oxidation after corrosion in artificial saliva at pH 6.5 (Left) and pH 3.0 (Right), cracks are visible as well as a rough surface pattern at higher thermal oxidation temperatures.



Figure 14: Representative FTIR spectra of thermal oxidation of Ti-6AI-4V alloy.

# 2.4 Discussion

The study hypothesis that titanium alloy treated by thermal oxidation exhibits better corrosion resistance compared to untreated titanium alloy was partially accepted. The treatment of the surface positively affected the electrochemical stability of the alloy with greater corrosion stability as shown for samples annealed at 200°C, but not at higher temperatures. There are several findings, first the protective effects of thermal oxidation do not improve with duration of annealing, though different parameters showed significant differences from one another based on annealing duration, there was no consistent trend, either negative or positive, seen for such parameters with increasing time. Second, the protective effects of thermal oxidation are temperature dependent, and that there is a reversal of this protection with increasing temperature leading to non-homogenous oxide films, prone to cracking, that are more corrosive. Finally, the results reveal that the corrosion process of Ti-6AI-4V alloy and its thermally oxidized variants is increased in acidic medium.

The time independent finding is not shown by a lack of statistical significance with respect to corrosion parameters, on the contrary groups differing by duration are shown to be significantly different from one another. Instead time independence is seen in the lack of consistent trends, either positive or negative, with respect to duration and the varying parameters, and a lack of consistency of significance existing between subgroups upon posthoc analysis. To what then was the occasional significance due to duration attributed to? It is important to note the sample size, and to place doubt on whether consistent trends would have been seen if the number of samples were to increase.

Additionally, inhomogeneity of thermal oxide layers based on EIS spectroscopy and cracking on images may have led to some of the significance found between samples due to duration. In fact, for the corrosion parameters presented in this paper, duration tended to be significant for parameters at higher temperatures which displayed the inhomogeneity and cracking. Further experiments with larger sample sizes are needed to totally dismiss the idea that duration matters, and a more gradual annealing process to prevent crack formation and reduce inhomogeneity are needed, but it is safe to say that this article raises doubts on the relevance of duration to effect corrosion properties.

This considered, the finding is interesting because previous studies showed that thermal oxidation duration determines the thickness of the oxide layer, with longer durations leading to thicker oxide layers.[81] It is apparent from our study that duration did not affect the corrosion properties of titanium dioxide despite its effect on the thickness of this layer. For this reason, it is believed that some other structural property, not thickness of oxide layers grown under thermal oxidation, is responsible for enhanced corrosion properties. What this other property may be, is not immediately obvious but the authors believe it is the change to a rutile packing structure, which is more common after high temperature thermal annealing.[82] This simple change in packing structure will alter the diffusion processes underlying corrosion at the junction between the oxide layer and underlying non-corroded metal.

The temperature dependence finding is first observed through electrochemical impedance spectroscopy. Impedance spectroscopy was used because it has been effective in other studies of corrosion testing of titanium and its alloys.[77, 83, 84] In the Nyquist plot (Figure 6) we see higher values for the ratio of impedance Z<sub>img</sub>/Z<sub>real</sub> at lower
thermal oxidation values, but values significantly lower than control samples for those samples oxidized at 700°C. Higher Z<sub>img</sub>/Z<sub>real</sub> is indicative of better corrosion properties, meaning higher oxidation temperature is more corrosive. Next the Bode plot (Figure 7) displays two time constants, one for control samples and those oxidized at lower temperatures, and another lower time constant for samples oxidized at 700°C and 400°C. This second time constant represents a non-uniform surface layer, which is also verified by cracks upon SEM imaging (Figure 13). Furthermore, at lower frequencies impedance and phase angle should stabilize to higher values on the Bode plot, but the samples at 700°C and 400°C do not, a characteristic of poor corrosion resistance. Finally, the impedance values obtained using models of simple and complex Randle's circuits show that thermally oxidized samples had high resistance values and lower capacitance values relative to control, with the exception being the samples at 700°C and in some cases those at 400°C. These values listed in Table 1 represent good corrosion character when resistance values are high, and capacitance values are low in the model. This is markedly different from previous studies that suggest a temperature dependence to corrosion protection that is not reversible, utilizing the same complex Randle circuit as the one in this study on similar titanium alloys.[78]

The findings that thermal oxidation improves corrosion resistance extend to the electrochemical parameters for the cyclic polarization data. The potentiodynamic data in Table 2 and Figure 11 show that the thermally oxidized groups at 200°C show higher  $E_{corr}$ , and the lowest  $I_{corr}$  and  $I_{pass}$  values as compared to control samples, consistent with better corrosion character. This contrasts with samples at higher thermal oxidation temperature, which show higher  $I_{corr}$  and  $I_{pass}$  values, or worsening corrosion

characteristics with respect to controls. Ashrafizadeh et al. used potentiodynamic curves to show that thermally oxidized grade 5 titanium alloy had better corrosion characteristics than untreated.[85] It is important to note that Ashrafizadeh et al. studied a narrower range of temperatures, 500 to 800°C, and heated there samples differently, possibly explaining the results. The samples in this study at similar temperatures did retain some improved corrosion parameters, namely  $E_{corr}$ , but were compromised by their corrosion current density and EIS outcomes. It is possible that the heating methods of Ashrafizadeh et al. allowed for a more homogenous oxide layer at higher temperatures, a factor critically lacking in our own samples at such temperatures, as displayed by cracks on SEM imaging.

Notably a search of the literature does suggest a reversal of corrosion improvement with increasing temperature, as de-bonding is noted for commercially pure titanium that is thermally oxidized.[86] Based on the potentiodynamic data in Table 2 the corrosion increases with treatment temperature for thermally oxidized samples as the corrosion current density values increase with temperature relative to control. This can be attributed to the porosity of the oxide layer and irregularities in the formation at the junction between oxide layer and titanium, manifesting as cracks on the surface. Another principle to consider is the one of thermal expansion coefficients, which given the process of heating and cooling are not constant or necessarily linear, leading to non-uniform surfaces as different crystals in the metal surface expand and shrink separately of one another. This expansion and contraction can lead to thermal shock and micro-crack formation. Interestingly surface topography studies, such as white light interferometry pick up the non-uniformity of the surfaces at higher temperature, with increased roughness values

noted in Table 3 and visible on SEM imaging, as well as to the naked eye as darker grey. It is likely that the sample processing for our experiments is to blame for inhomogeneity of the oxide layer at higher temperatures, and that the reversal of corrosion resistance with temperature seen in our studies is simply an artifact. Only further studies will identify if the reversal of temperature dependence holds up.

Next, the use of thermal oxidation influenced the corrosion tolerance of titanium exposed to acidic medium, as demonstrated by the significant changes in the model values of the complex Randle circuit for the electrochemical impedance spectroscopy experiments. Acidic medium accelerated the ion exchange between Ti and saliva, and reduced the opposition of Ti surfaces to corrode as evidenced by the capacitance and resistance results of the Randle models. As compared to samples that had not undergone thermal oxidation, there was a significant improvement in the electrochemical parameters and Randle model components for exposure to acidic medium for samples annealed at 200°C. For samples annealed at this low temperature resistance values were notably increased and capacitance values decreased, the effect extended to samples at low pH relative to control. The acidic environment was expected to increase the exchange of ions between artificial saliva and Ti-6AI-4V alloy, decreasing corrosion resistance but to a lesser extent in samples thermally oxidized. This was expected because the increased titanium oxide layer should prevent the electrochemical exchange of electrons present in saliva with underlying metallic ions of the titanium surface. Indeed, Barao and Souza found low corrosion resistance in acidic pH for titanium alloys, each using artificial saliva and Ringer solution respectively.[77, 87] Though the samples annealed at 200°C performed as expected, the same cannot be said of higher temperatures with respect to

acidic pH. Unfortunately, samples at higher temperature, in particular those at 700°C, show increased corrosion relative to control at acidic pH, noting significantly higher capacitance values and reduced resistance (Figure 9). These results with pH extend to the potentiodynamic data where low thermal oxidation temperatures display low corrosion current relative to control at acidic pH, but higher corrosion current at higher thermal oxidation temperatures relative to control samples at acidic pH. Again the inhomogeneity of the oxide layer is blamed for these poor results with respect to pH performance. This inhomogeneity is evidenced by multiple time constants on the Bode plot, and SEM imaging showing cracks (Figure 13).

Finally, the clinical implications of thermal oxidation had been that the more vigorous treatment corresponded to the more biocompatible product. This is because alkaline phosphatase activity has been shown to be higher in samples of titanium treated with high temperature thermal oxidation, similar in surface topography and roughness to our own samples treated at 700°C.[43] Alkaline phosphatase is a general biomarker for osteoblastic activity and can mediate bone mineralization. It is unfortunate that the most biocompatible thermal oxidation group is also the least durable in the sense of corrosion. What is unknown is whether the thick rutile will survive the life of an implant after insertion, as the limitation of this study was the lack of masticatory loading, that is, wear. Surface roughness appears to be stable after corrosion despite pH and treatment temperature indicating that the oxide layer may be thick enough to survive corrosion alone, especially considering that in vivo the metal oxide surface may be contiguous with bone and not exposed to the media. Whether the oxide film survives a tribocorrosion experiment would determine the impact of thermal oxidation from a clinically useful sense. Though the

higher thermal oxidation temperature experiences increased corrosion, it may be more stable if it maintains a continuity with bone, preventing exposure to the fluid media and subsequent corrosion. This enhanced osseointegration would mean better performance, but more realistic testing must be done. For instance, tribocorrosion testing of the thermally oxidized samples will most likely show that those samples annealed at higher temperatures are the most resistant to wear and perhaps the most stable for integration into bone. This is expected because Kumar et al. found the hardness of the titanium alloy was directly proportional to temperature and duration.[82] As it is well known that the amount of wear that a surface undergoes is determined by the Archard wear equation

$$Q = \frac{KWL}{H},\tag{1}$$

where, Q is the total wear volume produced, W is the total normal load, H is the hardness of the softest contacting surfaces, K is a constant and L is the sliding distance of the interacting bodies, one would expect reduce wear with increased hardness.[88] Thus, the samples that are most biocompatible are also most likely to survive mechanical stresses in the mouth. Not surprisingly thermal oxidation of grade 5 titanium dental implants has been tested in animal models after annealing at 700°C for 1 hour, showing improved early bone formation.[89] The limitation of these studies is the short time of testing and lack of functional loading. Further studies both in vitro and in vivo need to explore the longevity of the thermal oxide layer with respect to wear and corrosion simultaneously to explore if the most biocompatible film is robust enough to survive in vivo for the life of an implant.

## 2.5 Conclusion

The corrosion properties of titanium treated with thermal oxidation, as measured by potentiodynamic polarization testing and electrochemical impedance spectroscopy, improve with temperature initially, but are far worse than control above a certain threshold, in this case 700°C. There is clearly a temperature dependence to the improvement of the corrosion properties that is reversible after a certain point, and this is believed to be due to the inhomogeneity of the surface oxide with higher thermal oxidation. This failure at higher temperatures maybe an artifact of the heating methods used in this study. Additionally, the improvement of the corrosive properties by thermal oxidation are time independent, as increasing time did not appear to change results. Moreover, acidic media accelerates corrosion independent of thermal oxidation, though for samples thermally oxidized at lower temperatures with homogenous surfaces the corrosion properties are superior to non-treatment. Finally, only an electrochemical evaluation of the titanium was performed in the present study, without considering masticatory forces. Further studies evaluating the behavior of the rutile under wear are necessary to determine if thermal oxidation is a cost effective processing technique to improve the outcomes of dental implants for patients.

Tribocorrosion Studies of Dental Materials,

& the Clinical Implications

# INFLUENCE OF NICOTINE ON THE TRIBOCORROSION BEHAVIOR OF Ti-6AI-4V

## ALLOY IN ARTIFICIAL SALIVA

(Chapter Three)

## 3.1 Introduction

Today tobacco is a known killer, as the established leading cause of preventable death in the world, accounting for nearly six million deaths worldwide and almost half-amillion in the United States per year.[27, 28] Understandably the prevalence of smoking is declining in the United States, from 42.4% of adults in 1965 to 16.8% of adults in 2014, however, the same cannot be said of smoking habits worldwide.[29, 30] Tobacco is a huge burden in developing nations where health awareness of smoking is low, such as Asian markets, where half or more of male adults smoke.[31-34]

Despite thousands of constituents in cigarette smoke, the addictive nature is imparted by nicotine, which along with the carcinogenic tar and carbon monoxide are the only agents produced in milligram quantities per cigarette.[35] In commercial sale, measured nicotine yield has been on the rise from 1.65 mg per cigarette in 1999 to 1.89 mg per cigarette in 2011.[36] It is clear that big tobacco understands its product, and given the prevalence of smoking and dose of principle components, the effect on health due to nicotine exposure is a consummate concern to clinicians.

The extent to which nicotine effects overall biological health is very well documented. At very low doses nicotine has been shown to accelerate angiogenesis and promote wound healing with less contraction.[38] Contrarily, wound healing is impaired at higher doses, with delayed wound contraction, reduced inflammatory cell infiltration, and lower expression of growth factors, as well as reduced fibroblast migration in vitro.[39] Further, nicotine has been shown to delay bone fracture healing and reduce mechanical strength of healed fractures in animal models.[40, 41]

In the oral cavity, nicotine has been shown to affect matrix metalloproteinases in teeth, and dental pulp cells.[47] Further, nicotine has been shown to reduce alveolar bone regeneration following tooth extraction in a rat model, impairing osteoneogenesis in a dose dependent manner. [48, 49] Additionally, it has been shown to reduce bone growth, vascularity, and bone lengthening in a mandibular distraction osteogenesis model.[50] Given nicotine impairment of healing, bone growth and mineralization, its effect on osseointegration is expected to be negative. Unsurprisingly smokers exhibit greater implant failure both early, before abutment placement, and late, after occlusal loading of a prosthesis. [2, 52, 53] Early failure is due to impaired wound healing leading to poor osseointegration or bone-implant contact. Even those patients with good initial bone quality exhibit a 31% early failure rate if smokers compared to 4% if non-smokers.[52] In animal model, histological studies of bone density showed that nicotine impacts cancellous bone resulting in lower bone-to-implant contact and less bone area within the threads of an implant.[57, 58] Nicotine also negatively effects the guality of the periimplant bone, displaying down-regulation of gene expression for bone markers.[60]

In dental implants, titanium and its alloy are chosen for their good strength, corrosion resistance and biocompatibility.[77, 90-92] Nonetheless, the saliva, acid, fluoride, and bacteria present in the oral cavity as well as the physical load of mastication can damage dental implants and reduce their longeivity.[77, 93, 94] The milieu of saliva, or the ambience of its relative components, react electrochemically with dental implants leading to corrosion and the release of metal ions into the surrounding environment.[95, 96] Substances encountered in the mouth, such as fluoride in toothpaste, lipopolysaccharides from gram negative bacteria, and mouthwash have been

investigated for their effects on the corrosion behavior of titanium.[62, 72, 90, 97, 98] Recent studies showed the negative effects of nicotine on the corrosion behavior of titanium.[61, 62] Barao et al. showed that nicotine increased the biofilm of titanium, increasing the risk of peri-implantitis.[61] Whereas, Royhman et al. showed that the effects of nicotine on the suprastructure of the implant reduces corrosion at moderate concentrations, impressing a possible protective role given local microenvironment concentrations at the implant in vivo.[62] However, all concentrations of nicotine also reduced the passive film formation on the surface of the implant.[62] Given the context of intermittent motion of the implant during mastication it is unclear if the smaller passive film layer will reform in clinical context. Though the corrosion tendancy of the material is increased, its rate maybe significant in the presence of motion given the lack of a passive film layer, to understand the effects of nicotine on the tribocorrosion of dental implants a tribocorrosion study is necessary.

The objective of this study was to test the effects of increased concentrations of nicotine in artificial saliva on the tribo-corrosive behavior of titanium alloy (Ti-6Al-4V). Variable concentrations of nicotine were used in order to simulate the amount that an individual would absorb from smoking one cigarette (1 mg), five cigarettes (5 mg), and 20 cigarettes (20 mg). Furthermore, artificial saliva with different levels of pH was used in order to simulate the transient oral environment. An alumina pin was allowed to make contact and move across the surface of a Ti-6Al-4V disc. The results of this study describes the tribo-corrosion effects of nicotine on Ti-6Al-4V.



Figure 15: Schematic diagram of the experimental design.

## 3.2 Materials and Methods

#### **3.2.1** Sample Preparation

Titanium alloy (Ti6Al4V) rods (Mac-Mater Carr, Elmhurst IL, USA) were milled into thirty-six discs (Diameter=15mm, height=3mm). The elemental composition of the alloy in wt% is: Ti 88.18 - 90.70%, AI 5.50 - 6.75%, V 3.50 - 4.50%, Fe 0.30% max, C 0.08%, other 0.0-0.27%. The discs were divided into twelve groups in order to study the effects of nicotine concentration (0mg/ml [Control], 1mg/ml, 5mg/ml, and 20mg/ml) and pH levels (pH 3.0 and pH 6.5) on the tribocorrosion behavior of Ti6Al4V in artificial saliva. The experimental design is shown in Figure 1. Prior to testing, the discs were systematically brought to a mirror finish by first wet-grinding with a series of SiC grinding papers, up to 800 grit (Carbimet 2, Buehler, Lake Bluff, IL, USA), followed by polishing with 9µm diamond paste (MetaDi 9-micron, Beuhler, Lake Bluff, IL, USA) suspended in MetaDi Fluid (Beuhler, Lake Bluff, IL, USA), and finally brought to a mirror finish using a colloidal silica suspension (MasterMed, Beuler, Lake Bluff, IL, USA). Before testing, the samples were ultrasonically cleaned (FS 20, Fisher Scientific Inc., Pittsburg, Pa, USA) with 70% isopropanol (15 min), followed by rinsing with deionized water (10 min), and finally dried with hot air (250°C). The surface roughness was measured using a white light interferometer (Zygo Corp). The resultant final roughness ( $R_a$ ) of the surfaces was approximately 20nm.

#### **3.2.2** Electrochemical Parameters

All electrochemical measurements were made with a Gamry G700 Potenitostat with a 3-electrode configuration. A Saturated Calomel Electrode (SCE) was used as the reference electrode, a graphite rod was used as a counter-electrode, the Ti alloy (exposed surface = 0.38 cm<sup>2</sup>) served as working electrode. The tribocorrosion experiments were run under both free potential and potentiostatic conditions. As suggested by Liu et al., artificial saliva was used to mimic the chemical nature of natural saliva. For each trial, 120ml of artificial saliva served as the electrolyte fluid. The artificial saliva contained the following chemical composition: KCL (0.4g/L), NaCl (0.4g/L), CaCl<sub>2</sub>·2H<sub>2</sub>O (0.906g/L), NaH<sub>2</sub>PO<sub>4</sub>·2H<sub>2</sub>0 (0.690g/L), Na<sub>2</sub>S·9H<sub>2</sub>0 (0.005g/L), and Urea (1.0 g/L). Once the stock solutions of the artificial saliva were prepared, the pH values were adjusted by adding lactic acid to lower pH to the two stock electrolyte solutions (pH 6.5 and pH 3.9). All pH values were evaluated using a pH meter (Accumet AB15, Fisher Scientific Inc.). Nicotine extract was added directly to the stock solutions to achieve the preselected nicotine concentrations (0mg/ml, 1mg/ml, 5mg/ml, and 20mg/ml). The Ti6Al4V samples were then mounted in the tribocorrosion cell which maintained an electrolyte temperature of 37±2°C using an externally fixed water jacket mechanism.

The sequence of tests included: OCP (Open Circuit Potential), EIS (Electrochemical Impedance Spectroscopy), followed by tribocorrosion tests under free potential and potentiostatic conditions, and finally concluded with a second EIS test to measure the changes in corrosion kinetics as a function of mechanical stimulation. OCP was initially run for a period of 3600 seconds in order to let the system reach steady state, and was run as a final test under static conditions to stabilize the system. Potentiostatic

tests were performed at -300mV (V vs SCE). EIS measurements were performed in the frequency range from 100 KHz to 5 MHz, with AC sine wave amplitude of 10 mV applied to the electrode at its corrosion potential (V vs SCE). EIS test were used to evaluate the passive layer formation at the Ti alloy/electrolyte interface (corrosion kinetics). The EIS results were then used to model an equivalent electrical circuit in order to quantify the corrosion process. The modeling was done with EC-Lab v. 10.23 (Bio-Logic, Claix, France). A simple model of this circuit is presented in Figure 20, which consists of solution resistance ( $R_s$ ), polarization resistance ( $R_p$ ), and a constant phase element (CPE). Validity of impedance data was evaluated using the Kramers-Kronig transformations and the regression method of Dominguez-Benetton et al.[99] The reported values of resistance and capacitance were derived from a Randle's circuit (Figure 20) with a CPE element in parallel with  $R_p$ .



Figure 16: Schematic diagram of the experimental apparatus.

#### **3.2.3** Tribocorrosion Tests

A custom-built Tribocorrosion testing apparatus, described by Butt et al., was used for all testing procedures in this study (Figure 16) [100] The testing apparatus, schematically shown in Figure 16, featured a pin-on-disk design in which a zirconia pin/counter-body (contacting surface area of 0.071 mm<sup>2</sup>) articulated against the Ti alloy samples in a reciprocating, linear motion at a frequency of 1Hz for 1800 cycles. The zirconia counter-body was selected for this study due its high resistance to wear and its chemically inert nature, allowing for reproducible wear results and noninterference in the electrochemical measurements. With the exception of the working electrode (Ti alloy pins) and the counter electrode (graphite rod), all components of the electrochemical cells were made of chemically inert, nonconductive materials in order to isolate the electrochemical measurements to the Ti alloy discs. The counter-body was routinely inspected, cleansed, and replaced as needed. A normal load of 1.7N was applied from the counter-body onto the Ti alloy pin. This translated to approximately a 24MPa of Hertzian contact pressure, which is in the range of the expected physiological contact pressure based on the current literature.

### 3.2.4 Surface Characterization

A white-light interferometry microscope was used to obtain three-dimensional images of the titanium surfaces (Zygo New View 6300, Zygo Corporation, Middlefield, CT, USA). Six measurements were taken for each sample. Images were taken before and after tribocorrosion tests for each sample in order to quantify the loss of material due to wear, as well as the changes in roughness (R<sub>a</sub>) to the Ti alloy surface. Additional

surface morphology characterization was performed using a SEM (scanning electron microscope) (Joel JSM-6490 LV, Oxford Instruments, Oxford, UK) to examine pitting and fretting behavior of the metal surfaces.

#### **3.2.5** Total Weight Loss Measurements

The synergistic relationship under the potentiostatic conditions, as proposed by Stack and Abdulrahman was studied using the following equation.[101]

$$K_{wc} = K_w + K_c , \qquad (2)$$

where  $K_w$  is the total weight loss due to mechanical wear,  $K_c$  is the total weight loss due to corrosion and  $K_{wc}$  is the total weight loss due to the combined interaction of chemical and mechanical degradation.

 $K_{wc}$  can be determined using the following equation:

$$K_{wc} = V \times D , \qquad (3)$$

where *V* is the total volume of material loss during mechanical and chemical degradation process (obtained by using white-light interferometric microscopy, NewView 6300, Zygo Corporation, Middletown, PA) and *D* is the density of material.

 $K_c$  can be calculated using Faraday's equation:

$$K_c = \frac{M \times Q}{n \times F} \tag{4}$$

and

$$Q = i \times t , \tag{5}$$

where *M* is the atomic mass of the metal alloy, *Q* is the charge passing through the working electrode in coulombs. The value for *Q* can be broken down into equation (5) where *i* is the total current density in A cm<sup>-2</sup> and *t* is the total duration of the test. *n* is the number of electrons involved in the corrosion process (n = 2) and *F* is Faraday's constant (96,500 C mol<sup>-1</sup>). It is important to note that the actual number of electrons can vary with each reaction. For example *n* can equal +2 or +3; however, for purpose of simplicity, we assumed that n = 2.

Once  $K_c$  is calculated using equation (4) and  $K_{wc}$  is calculated using equation (3), the relationship in equation (2) can be modified to calculate  $K_w$ .

$$K_w = K_{wc} - K_c \,. \tag{6}$$

Based on the criteria proposed by Stack and Abdulrahman, the ration of weight loss due to corrosion  $K_c$  and wear  $K_w$  ( $K_c/K_w$ ) was used in order to classify the involved wear and corrosion mechanisms. The criteria for classification are as follows:

 $K_c/K_w < 0.1 \qquad \qquad Wear \qquad (7)$ 

 $0.1 < K_c/K_w < 1.0$  Wear – Corrosion (8)

 $1.0 < K_c/K_w < 10$  Corrosion – Wear (9)

$$10 < K_c/K_w$$
 Corrosion (10)

#### 3.2.6 Statistical Analysis

All statistical analyses were performed using Statistical Package for the Social Sciences (Version 24; SPSS Inc, Chicago, IL, USA). Corrosion behavior was evaluated based on three parameters from electrochemical impedance spectroscopy (CPE, Rs, and  $R_{p}$ ) both before and after tribocorrosion sliding test, and two parameters from white-light interferometry surface roughness measurements (Ra and rms). A three-way mixed ANOVA was performed on the electrochemical impedance spectroscopy parameters to determine the effects of nicotine, pH and sliding under free potential conditions. The between-samples factors were pH (two levels), and nicotine concentration (two levels), while the within-samples factor was sliding (two levels; pre and post). All EIS parameters were normally distributed, as assessed by Shapiro-Wilk's test (p > 0.05), and there were no outliers in the data, as assessed by inspection of a boxplot. There was homogeneity of variances for both pre sliding (p > 0.05) and post sliding (p > 0.05), for all EIS parameters, as assessed by Levene's test for equality of variances. Surface roughness parameters (Ra and rms) were evaluated using a two-sample independent t-test in order to compare the surface roughness values before and after corrosion. For potentiostatic conditions a two-way ANOVA was used to determine the effects of nicotine concentration (four levels) and pH (two levels) on the ratio of mass loss due to corrosion to mass loss due to wear  $K_0/K_w$ , total weight loss  $K_{wc}$ , weight loss due to corrosion  $K_c$ , and weight loss due to wear  $K_{w}$ . For free potential conditions a two-way ANOVA was used to determine the effects of nicotine concentration (four levels) and pH (two levels) on the total weight loss  $K_{wc}$ . Residual analysis was performed to test for the assumptions of the two-way ANOVA. For all two-way ANOVAs there were no outliers, as assessed by inspection of a

boxplot, data was normally distributed as assessed by Shapiro-Wilk's test (p > 0.05), and there was homogeneity of variances, as assessed by Levene's test for equality of variances, p > 0.05. All pairwise comparisons were run to a 95% confidence interval, and p-values were Bonferroni-adjusted.

## 3.3 Results

#### 3.3.1 Changes in Corrosion Mechanism

Free-potential tests were used to study the pure tribological behavior of titanium alloy at different pH (3.0 and 6.5) and nicotine concentration (0mg/ml, 5 mg/ml). Figure 17 shows the dropping curve of potential in response to the sliding. This potential change was expected due to the removal of passive film, which caused the exposure of bare metal to the electrolytic environment. In this figure, it is clear that acidic pH has a smaller magnitude of potential decrease, and nicotine has a much larger magnitude potential change.



Figure 17: Change in potential in response to the sliding process in Ti alloy as a function of pH and nicotine concentration.

The evolution of current density throughout the entire experiment is pictured in Figure 18. There is a clear increase in current density during sliding for titanium alloy with higher and more consistent density at pH 3.0 and for larger concentrations of nicotine.



Figure 18: Evolution of the current density for titanium alloy during the tribocorrosion process at pH 3.0 (top) and pH 6.5 (bottom) for varying concentrations of nicotine.

Weight loss calculations.								
Potentiostatic weight loss (µg)								
Kc	Kw	Kc/Kw						
1.7 ± 0.1	11.6 ± 0.9	0.15						
1.5 ± 0.2	10.5 ± 1.8	0.15						
1.5 ± 0.1	10.7 ±0.9	0.14						
$2.3 \pm 0.2$	14.1 ± 1.5	0.16						
1.5 ± 0.1	11.9 ± 1.5	0.13						
1.4 ± 0.3	10.2 ± 2.4	0.14						
1.7 ± 0.3	11.1 ± 2.0	0.16						
$2.2 \pm 0.3$	13.6 ± 1.5	0.16						
		Kc Kw $1.7 \pm 0.1$ $11.6 \pm 0.9$ $1.5 \pm 0.2$ $10.5 \pm 1.8$ $1.5 \pm 0.1$ $10.7 \pm 0.9$ $2.3 \pm 0.2$ $14.1 \pm 1.5$ $1.5 \pm 0.1$ $11.9 \pm 1.5$ $1.4 \pm 0.3$ $10.2 \pm 2.4$ $1.7 \pm 0.3$ $11.1 \pm 2.0$ $2.2 \pm 0.3$ $13.6 \pm 1.5$						

Table 4: Weight loss calculations.

The individual contributions of total weight loss and their mechanisms were calculated as explained in section 2.4. The results of these calculations are listed in table 4. The effects of nicotine concentration and pH on the total weight loss  $K_{wc}$ , under free potential conditions (Figure 19), were compared using a two-way ANOVA. There was a statistically significant interaction between nicotine and pH for the total weight loss  $K_{wc}$  under free potential conditions, F(1, 8) = 6.219, p = 0.037, partial  $\eta^2 = 0.437$ . There were no statistically significant (p < 0.05) simple main effects, for either independent variable where the other is fixed.



Figure 19: Total weight loss  $K_{wc}$ , under free potential conditions as a function of pH and nicotine concentrations.

The effects of nicotine concentration and pH, under potentiostatic conditions, on the overall degradation of Ti alloy were compared using a two-way ANOVA for the ratio of mass loss due to corrosion to mass loss due to wear,  $K_o/K_w$  (Figure 20). There was no statistically significant interaction between pH and nicotine concentration for the  $K_o/K_w$ ratio, F(3,16) = 1.047, p = 0.399, partial  $\eta^2 = 0.164$ . Additionally, there was no statistically significant main effect of pH on  $K_o/K_w$  ratio, F(1, 16) = 0.037, p = 0.850, partial  $\eta^2 = 0.002$ . Also, there was no statistically significant main effect of nicotine concentration on  $K_o/K_w$ ratio, F(3, 16) = 1.726, p = 0.202, partial  $\eta^2 = 0.245$ . As there are no statistically significant main effects, no pairwise comparisons, either Tukey or Bonferroni are reported.





A two-way ANOVA was used to compare the effect of nicotine and pH, under potentiostatic conditions, on the total weight loss  $K_{wc}$  (Figure 21). There was no statistically significant interaction between nicotine and pH for the total weight loss  $K_{wc}$ , under potentiostatic conditions, F(3, 16) = 0.175, p = 0.912, partial  $\eta^2 = 0.032$ . There was no statistically significant main effect of pH on total weight loss  $K_{wc}$  under potentiostatic conditions, F(1, 16) = 0.175, p = 0.007, partial  $\eta^2 = 0.000$ . However, there was a statistically significant main effect for nicotine on total weight loss  $K_{wc}$  under potentiostatic conditions, F(3, 16) = 6.984, p = 0.003, partial  $\eta^2 = 0.567$ . Examination of pairwise comparisons showed that 20mg nicotine was significantly different (p < 0.05) in comparison to all other nicotine concentrations. However, 0, 1, and 5mg concentrations showed no significant (p > 0.05) differences with each other.





The effect of nicotine and pH on the weight loss due to corrosion  $K_c$  (Figure 23), under potentiostatic conditions, were compared using a two-way ANOVA. There was no statistically significant interaction between nicotine and pH for the weight loss due to corrosion  $K_c$  under potentiostatic conditions, F(3, 16) = 1.324, p = 0.301, partial  $\eta^2 =$ 0.199. There was no statistically significant main effect of pH on the weight loss due to corrosion  $K_c$  under potentiostatic conditions, F(1, 16) = 0.238, p = 0.633, partial  $\eta^2 =$ 0.015. However, there was a statistically significant main effect for nicotine on the weight loss due to corrosion  $K_c$  under potentiostatic conditions, F(3, 16) = 17.143, p < 0.005, partial  $\eta^2 = 0.763$ . Examination of pairwise comparisons showed that 20mg nicotine was significantly different (p < 0.05) in comparison to all other nicotine concentrations. However, 0, 1, and 5mg concentrations showed no significant (p > 0.05) differences with each other. The effect of nicotine and pH on the weight loss due to wear  $K_w$  (Figure 23), under potentiostatic conditions were compared using a two-way ANOVA. There was no statistically significant interaction between nicotine and pH for the weight loss due to wear  $K_w$  under potentiostatic conditions, F(3, 16) = 0.119, p = 0.947, partial  $\eta^2 = 0.022$ . There was no statistically significant main effect of pH on the weight loss due to wear  $K_w$  under potentiostatic conditions, F(1, 16) = 0.001, p = 0.977, partial  $\eta^2 < 0.005$ . However, there was a statistically significant main effect for nicotine on the weight loss due to wear  $K_w$ under potentiostatic conditions, F(3, 16) = 5.358, p = 0.010, partial  $\eta^2 = 0.501$ . Examination of pairwise comparisons showed that 20mg nicotine was significantly different (p < 0.05) in comparison to 1mg and 5mg nicotine, but not to control. However, 0, 1, and 5mg concentrations showed no significant (p > 0.05) differences with each other.

### **3.3.2** EIS Measurements

The Nyquist and Bode plots (Figure 22) provide the variation of impedance as a function of frequency for the electrochemical double layer formed at the Ti-solution interface during active corrosion. The Nyquist plots demonstrate the electrochemical resistance of the alloy surface. For all groups the Bode plots phase angle (Figure 22) displays a single time constant. At high frequency, both the phase angle and impedance were low. As frequency decreases, the impedance and phase angle increase, though samples at low pH or containing nicotine tended to have their phase angle peak and decrease again at lower frequencies (Figure 22 A1, B1, & C1).



Figure 22: Electrochemical impedance spectroscopy Bode plots (A1, B1, & C1) and corresponding Nyquist plots (A2, B2, & C2)) for titanium alloy under free potential conditions at different pH values before and after sliding (A1 & A2), at pH 3 with and without Nicotine before and after sliding (B1 & B2), and at pH 6.5 with and without Nicotine before and after sliding (C1 & C2).

#### 3.3.3 EIS Models

A simple equivalent circuit (Randle's circuit) (Figure 23) comprising the resistance of solution ( $R_s$ ) in series with the polarization resistance ( $R_p$ ), in parallel with the capacitance of double layer, was used for the EIS model. This model represents an equivalent circuit to the electrochemical reactions at the metal-solution interface.  $R_s$  is the uncompensated resistance of the electrolyte between the working and reference electrode.  $R_p$  is the polarization resistance or the charge transfer resistance at the working electrode-electrolyte interface. Due to the inhomogeneous passive layer at the material surface, the capacitance is represented by a constant-phase element (CPE) as an alternative to an ideal capacitance element, embodying a specific double-layer capacitance at the working electrode/electrolyte interface. Impedance experimental data were fitted with chi square error <0.001.[102] Table 5 display the evolution of  $R_s$ ,  $R_p$ , and CPE as a function of pH and nicotine concentration both before and after the tribocorrosion experiments in free potential conditions. Lower CPE and higher  $R_p$  values indicate higher corrosion resistance.



Figure 23: Equivalent Randle's circuit depicting the corrosion model.

EIS Model Parameters Under Free Potential Conditions								
		Nicotine Concentration						
		Control		5 mg/mL				
Parameter		pH 3.0	pH 6.5	pH 3.0	pH 6.5			
R <sub>s</sub> (Ω)	Before	240 (6)	320 (9)	237 (11)	312 (9)			
	After	231 (1)	300 (4)	232 (1)	298 (2)			
CPE (μF <sup>(α-1)</sup> )	Before	46.1 (0.82)	32.1 (0.83)	32.2 (3.5)	28.7 (1.1)			
	After	41.4 (0.14)	29.3 (1.8)	30.8 (3.5)	25.6 (0.24)			
$\alpha$ (dimensionless)	Before	0.9500	0.9245	0.9216	0.9227			
	After	0.9323	0.9124	0.9170	0.8689			
$R_{p}$ (M $\Omega$ )	Before	2.58 (0.31)	5.71 (0.54)	2.27 (0.65)	2.19 (0.22)			
<u> </u>	After	0.256 (0.012)	0.781 (0.19)	0.246 (0.0023)	0.391 (0.011)			

Table 5: EIS Model Parameters Under Free Potential Conditions.

A three-way mixed ANOVA was used to determine the effects of nicotine, pH, and sliding on EIS parameters under free potential conditions. The between-samples factors were pH (two levels), and nicotine concentration (two levels), while the within-samples factor was sliding (two levels; pre and post). Significance of results were unique at the three-way, and two-way level as follows.

There was a statistically insignificant three-way interaction between sliding, nicotine and pH for R<sub>s</sub>, F(1, 8) = 0.081, p = 0.783, partial  $\eta^2 = 0.010$ . The two-way interactions between sliding and nicotine F(1, 8) = 0.818, p = 0.392, partial  $\eta^2 = 0.093$ , was insignificant. Likewise the two way interactions between sliding and pH, F(1, 8) = 4.071, p = 0.078, partial  $\eta^2 = 0.337$ , and between pH and nicotine, F(1, 8) = 0.471, p = 0.512, partial  $\eta^2 = 0.056$ , were also insignificant for R<sub>s</sub>. R<sub>s</sub> values are presented in Figure 24 as a function of pH, nicotine, and sliding.



Figure 24: R<sub>s</sub> values as a function of pH, nicotine, and sliding under free potential conditions.

For R<sub>p</sub> there was a statistically significant three-way interaction between sliding, pH and nicotine F(1, 8) = 40.121, p < 0.05, partial  $\eta^2 = 0.834$ . Statistical significance of a simple two-way interaction was accepted at a Bonferroni-adjusted alpha level of 0.025. For R<sub>p</sub> there was a statistically significant simple two-way interaction for pH and Nicotine before sliding, F(1, 8) = 42.964, p < 0.0005, and after sliding F(1, 8) = 11.680, p = 0.009. Statistical significance of a simple main effect was accepted at a Bonferroni-adjusted alpha level of 0.025. For R<sub>p</sub> there was a statistically significant simple main effect of pH for samples without nicotine before sliding, F(1, 8) = 81.827, p < 0.0005, but not for samples with 5mg of nicotine before sliding, F(1, 8) = 0.050, p = 0.828. There was a statistically significant simple main effect of nicotine for samples at pH 6.5 before sliding, F(1, 8) = 103.450, p < 0.0005, but not for samples at pH 3.0 before sliding, F(1, 8) = 0.812, p = 0.394. There was a statistically significant simple main effect of pH for samples without

nicotine after sliding, F(1, 8) = 44.598, p < 0.0005, but not for samples with 5mg of nicotine after sliding, F(1, 8) = 3.404, p = 0.102. There was a statistically significant simple main effect of nicotine for samples at pH 6.5 after sliding, F(1, 8) = 24.583, p = 0.001, but not for samples at pH 3.0 after sliding, F(1, 8) = 0.016, p = 0.904. Data are mean ± standard deviations unless otherwise stated. All pairwise comparisons were performed for statistically significant simple main effects. Bonferroni corrections were made with comparisons within each simple main effect considered a family of comparisons. Adjusted *p*-values are reported. Before sliding, in the absence of nicotine, mean R<sub>p</sub> values was higher for samples at pH 6.5 (5.71  $\pm$  0.54 M $\Omega$ ) than those at pH 3.0 (2.58  $\pm$  0.31 M $\Omega$ ), a mean difference of 3.13 M $\Omega$  (95% CI, 2.3 to 3.9), p < 0.0005. Before sliding, at pH 6.5, the mean  $R_p$  values was higher for samples without nicotine (5.71 ± 0.54 M $\Omega$ ) than those with 5mg of nicotine (2.19  $\pm$  0.22 M $\Omega$ ), a mean difference of 3.52 M $\Omega$  (95% CI, 2.7 to 4.3), p < 0.0005. After sliding, in the absence of nicotine, mean R<sub>p</sub> values was higher for samples at pH 6.5 (0.781  $\pm$  0.19 M $\Omega$ ) than those at pH 3.0 (0.256  $\pm$  0.012 M $\Omega$ ), a mean difference of 0.525 M $\Omega$  (95% CI, 0.343 to 0.705), *p* < 0.0005. After sliding, at pH 6.5, the mean  $R_p$  values was higher for samples without nicotine (0.781  $\pm$  0.19  $M\Omega)$  than those samples with 5mg of nicotine (0.391  $\pm$  0.011 M $\Omega$ ), a mean difference of 0.39 M $\Omega$  (95%) CI, 0.208 to 0.570), p = 0.001. R<sub>p</sub> values are presented in Figure 25 as a function of pH, nicotine, and sliding.





For CPE there was a statistically significant three-way interaction between sliding, pH and nicotine F(1, 8) = 8.302, p = 0.020, partial  $\eta^2 = 0.509$ . Statistical significance of a simple two-way interaction was accepted at a Bonferroni-adjusted alpha level of 0.025. There was a statistically significant simple two-way interaction for pH and nicotine before sliding, F(1, 8) = 22.259, p = 0.002, and after sliding F(1, 8) = 9.251, p = 0.016. Statistical significance of a simple main effect was accepted at a Bonferroni-adjusted alpha level of 0.025. There was a statistically significant simple main effect of pH for samples without nicotine before sliding, F(1, 8) = 78.508, p < 0.0005, but not for samples with 5mg of nicotine before sliding, F(1, 8) = 4.789, p = 0.060. There was a statistically significant simple main effect of nicotine for samples at pH 3.0 before sliding, F(1, 8) = 76.730, p <0.0005, but not for samples at pH 6.5 before sliding, F(1, 8) = 4.357, p = 0.070. There was a statistically significant simple main effect of pH for samples without nicotine after sliding, F(1, 8) = 56.514, p < 0.0005, and for samples with 5mg of nicotine after sliding, F(1, 8) = 10.344, p = 0.012. There was a statistically significant simple main effect of nicotine for samples at pH 3.0 after sliding, F(1, 8) = 43.153, p < 0.0005, but not for samples at pH 6.5 after sliding, F(1, 8) = 5.142, p = 0.053. Data are mean  $\pm$  standard deviations unless otherwise stated. All pairwise comparisons were performed for statistically significant simple main effects. Bonferroni corrections were made with comparisons within each simple simple main effect considered a family of comparisons. Adjusted p-values are reported. Before sliding, in the absence of nicotine, mean CPE values were lower for samples at pH 6.5 (32.1  $\pm$  0.83  $\mu$ F) than those at pH 3.0 (46.1  $\pm$ 0.82  $\mu$ F), a mean difference of 14  $\mu$ F (95% CI, 10.4 to 17.7  $\mu$ F), p < 0.0005. Before sliding, at pH 3.0, the mean CPE values were higher for samples without nicotine (46.1 ± 0.82  $\mu$ F) than those with 5mg of nicotine (32.2 ± 3.5  $\mu$ F), a mean difference of 13.9  $\mu$ F (95%) CI, 10.2 to 17.6), p < 0.0005. After sliding, in the absence of nicotine, mean CPE values were lower for samples at pH 6.5 (29.3  $\pm$  1.8  $\mu$ F) than those at pH 3.0 (41.4  $\pm$  0.14  $\mu$ F), a mean difference of 12.1  $\mu$ F (95% CI, 8.39 to 15.81  $\mu$ F), p < 0.0005. After sliding, in the presence of 5mg nicotine, mean CPE values were lower for samples at pH 6.5 (25.6 ± 0.24  $\mu$ F) than those at pH 3.0 (30.8 ± 3.5  $\mu$ F), a mean difference of 5.2  $\mu$ F (95% CI, 1.47 to 8.89  $\mu$ F), p = 0.012. After sliding, at pH 3.0, the mean CPE values were higher for samples without nicotine (41.4  $\pm$  0.14  $\mu$ F) than those samples with 5mg of nicotine (30.8 ± 3.5  $\mu$ F), a mean difference of 10.6  $\mu$ F (95% CI, 6.86 to 14.28  $\mu$ F), p < 0.0005. CPE values are presented in Figure 26 as a function of pH, nicotine, and sliding.





## 3.3.4 Surface Characterization

The exposed surfaces were characterized by both SEM and optical white-light microscopy (Zygo). The surface roughness parameters ( $R_a$  and rms values) before and after corrosion are presented in table 6. These values where evaluated using an independent t-test and the effect of corrosion was found to be insignificant (p > 0.05). The SEM images are presented in Figure 27. Generally there was an increase in surface damage observed as nicotine content increased, particularly at pH 6.5 which showed a high amount of surface damage. Furthermore, trapped particles were observed in the wear-scar region.

Roughness Parameters								
		Nicotine Concentration						
		Control		5 mg/mL				
Parameter	Before Corrosion	pH 3.0	pH 6.5	pH 3.0	pH 6.5			
rms	19 (2.6)	23 (3.5)	22 (2.3)	20 (3.7)	21 (3.1)			
Ra	14 (2.3)	17 (2.4)	17 (1.6)	15 (3.1)	16 (2.2)			

 Table 6: Roughness Parameters



Figure 27: SEM images of the worn surface of Ti alloy after tribocorrosion exposure. At

60x the wear scare is visible, at 1000x pitting corrosion is seen, and at 3000x a trapped

wear particle is shown within the scar region.

#### 3.4 Discussion

The objective of this study was to test the effects of increased concentrations of nicotine in artificial saliva on the tribo-corrosive behavior of titanium alloy (Ti-6AI-4V). There are several conclusions from this work. Firstly, the effect of nicotine on the tribocorrosive behavior of titanium is dependent on the dose, with lower doses potentially protective and higher doses augmenting tribocorrosive loss. Secondly, the effect of low dose nicotine may vary with pH, being protective at the near neutral resting pH of the oral cavity, and possibly ineffective at lower pH. Next, the effect of sliding or wear is synergistic with corrosion, increasing the corrosion properties of titanium, however, wear is the major dominant degradation method of titanium. Finally, particulate debris is found in the wear scar, implicating a three-body tribocorrosive mechanism.

Regardless of pH and nicotine concentration, upon rubbing titanium experiences an instantaneous potential drop, indicating an instant removal of the passive layer. Larger potential drops signify a decrease in protection from the passive layer. Previous studies found that nicotine reduced the polarization resistance of titanium signifying a reduction in passive film formation, explaining the large potential drops in Figure 17 for samples exposed to nicotine.[62] This may explain the protective effect of nicotine that is seen for overall loss (Figure 21) at low doses. If there is less passive film formation, then there will be less to rub off under wear at each cycle, leading to a compound reduction in loss. This may also explain why there is less current density in Figure 18 for low doses of nicotine, as it represents the removal of the passive film.[103-105] This is an easier and more homogenous process at acidic pH and with high concentrations of nicotine, meaning both
compromise the protective oxide film. This is seen in the appearance of the lines on Figure 18, at pH 3.0 the flat appearance represents the constant and complete delamination of the oxide film, where the jagged appearance at pH 6.5 represents the resilience of the oxide film to reform and resist delamination. It is interesting that low concentrations of nicotine appear to reduce the current density relative to control in Figure 18, implicating less corrosion with low doses of nicotine. Overall, low doses of nicotine are seen to reduce total loss under free potential conditions at pH 6.5 (Figure 19), and for both loss due to corrosion, and wear under potentiostatic conditions (Figure 21). It is important to note that loss due to low doses of nicotine under potentiostatic conditions were not seen to be significant upon two-way ANOVA testing, meaning the protective effect is suspected to be there based on the previously noted trends alone. High doses of nicotine did show significance to control and low doses for having a detrimental effect on loss, that is most notable by an increase in corrosion current density, this represents a new finding as previous studies found that nicotine reduces current density, independent of dose.[62] It is possible that this is due to the synergism of wear, as no other reasonable explanation is apparent at this time for the effect of high doses. Dose dependence and the reversal of the effect of nicotine was not expected, and is not in the literature.

There was a statistically significant interaction effect between nicotine and pH for the total weight loss  $K_{wc}$  under free potential conditions. This interaction appears to be different based on pH and is notable in Figure 18 where low doses of nicotine lead to inconsistent current density at pH 6.5 appearing as a jagged line, but consistent current density at pH 3.0 appearing as an elevated plateau. The line or current density is generated by the delamination of the oxide film, a more consistent process at acidic pH,

and a tougher proposal at near neutral pH. The potentiostatic data foreshadows the result of the free potential weight loss (Figure 19) where nicotine reduces total weight loss at pH 6.5 but increases weight loss at pH 3.0. The reversible nature was seen in the Bode and Nyquist plots under free potential (Figure 22) where upon sliding nicotine is seen as protective at pH 6.5 displaying higher phase angles on the Bode plot and increased Z<sub>img</sub>/Z<sub>real</sub> values on the Nyquist plot relative to samples without nicotine, and the reverse at pH 3.0 for samples with and without nicotine after sliding. This effect of low doses of nicotine is not expected, as previous studies indicated that nicotine reduces current density, a protective effect, but also reduces passivation, a detrimental one, at both pH 6.5 and 3.0.[62] The previous study did not consider wear, and with sliding the reduced ability to form a passive layer may be beneficial to a surface undergoing constant repetitive delamination of the oxide film, presenting gaps in the current density in Figure 18 at pH 6.5. Therefore, the reduced loses may in fact be due to both a reduction in current density and ability to form a passive layer. Interestingly the polarization resistance is found to be significantly altered after sliding at pH 6.5 with or without nicotine (Figure 25), seeing a significant decrease in the ability to form a passive layer at pH 6.5 with nicotine. After sliding at pH 3.0 the effect of nicotine on the polarization resistance is not significant. Similarly, the capacitance was found to be significant for pH after sliding both with and without nicotine, in each case capacitance was elevated for pH 3.0, a sign of worsened corrosion, but reduced for pH 6.5, a sign of improved corrosion character. It is believed that the effect on polarization resistance at pH 6.5 leads nicotine to be protective at this pH, but ineffective at a lower pH under sliding conditions or detrimental as seen by the elevation in capacitance. The reversal of the effect was not seen under potentiostatic

conditions for total weight loss (Figure 21) where all low doses of nicotine showed less loss compared to control, though no significance was noted on ANOVA.

Given that the  $K_c/K_w$  ratio signifies a mechanically dominate system, the result that neither pH nor nicotine, or the combination of the two has a significant effect on the systems performance is expected. Had the system been corrosion dominated, then the effect of pH and nicotine would be expected to influence the ratio. As the system is wear dominated, the Archard wear equation

$$Q = \frac{KWL}{H} , \qquad (1)$$

where, *Q* is the total wear volume produced, *W* is the total normal load, *H* is the hardness of the softest contacting surfaces, *K* is a constant and *L* is the sliding distance, provides the governing principles to the observed weight loss.[88] Titanium alloy was previously found to be a wear dominated system, so it is easy to accept that the extrinsic variables represented in the equation above are not influenced by solubilized materials in the media.[88] Though the direction of degradation mechanism appears unchanged, it is important to note that the magnitude of the results is influenced by nicotine, which appears to be protective at low doses and detrimental at high doses. Additionally, it is interesting corrosion properties of titanium. Both before and after sliding the Bode plots (Figure 22) display a single time constant, indicative of the presence of a compact, homogenous, and protective passive film. However, the exhibition of low phase angles at low frequencies characterizes poor corrosion resistance for both samples exposed to wear testing. Upon

sliding the Nyquist plot displays lower  $Z_{img}/Z_{real}$  values, again indicative of increased corrosion susceptibility. Furthermore, the polarization resistance,  $R_p$ , was found to be significantly influenced by sliding as a three-way interaction was found, in all cases sliding reduced the resistance of the passive film to prevent charge transfer, indicative again of poor corrosion. What's more, Figure 18 clearly indicates that the passive film is not effective in protecting the surface under sliding motion, and that this film is less stable in acidic medium and with high doses of nicotine.

Finally, the presence of wear particles in the wear region changes the wear mechanism to a three-body mechanism from a two-body mechanism, leading to accelerated degradation and loss. The presence of particles may explain why the  $K_o/K_w$  ratio fits into the synergistic range where 'Wear' dominates a still present 'Corrosion' according to Stack's criteria.[101] The 'Wear' dominant mechanism could be due to the high loading forces leading to wear particles being enveloped into the wear region during tribological contact. A three-body degradation mechanism in which particles are entrapped in the wear scar substantially changes the wear process. It is highly likely that due to viscosity of the solution particles accumulate within the wear scar.

#### 3.5 Conclusion

The tribocorrosive properties of titanium alloy (Ti-6AI-4V) treated with increasing doses of nicotine in artificial saliva at a resting oral pH and an acidic one as measured by electrochemical impedance spectroscopy, current density profiles, and various weight loss measures and ratios shows that the effect of nicotine is dose dependent and pH reversible. There is a clear dose dependence, with lower doses being protective with reduced corrosion and wear loss under both free potential and potentiostatic conditions, but higher doses displaying significantly higher loses to both control and low doses. A clear pH reversal of the protection of low doses is evident under free potential conditions for tribocorrosive loss, and is due to the significant reduction low dose nicotine has on the polarization resistance of titanium alloy at the resting oral pH but lack of an effect at acidic pH. This is due to compound and instantaneous loss of the passive film upon rubbing, a process greatly reduced when the polarization resistance is diminished by nicotine. No immediate explanation is available for the effect of high doses of nicotine, or why it is so detrimental to titanium alloy leading to increases in total weight loss  $K_{wc}$ , and those due to wear  $K_{w}$ , and corrosion  $K_{c}$ . Synergism between wear and corrosion was found in the EIS plots as wear significantly lowered impedance at low frequencies on the Bode plot, and reduced the relative impedance ratio of the Nyquist. The  $K_{\alpha}/K_{w}$  ratio reveals that titanium is a wear centered mechanism, and nicotine does not affect the degradation route though it does appear to affect the magnitude. Finally, particulate debris was found in the wear scar implying increased wear degradation from a three-body mechanism.

Tribocorrosion Studies of Dental Materials,

& the Clinical Implications

DISCUSSION

(Chapter Four)

### 4.1 A Review of Findings

Dental implant failure is common with a 9% failure rate after 5 years for any single tooth replacement, and a 12% failure rate for teeth in the molar region.[5] As such, to achieve the "one implant, one life" goal, clinicians need to better understand the implant and its interaction with the surrounding tissues so that they can guide the patient in making better informed decisions. Given that nearly 300,000 patients in the United States alone receive one or more implants in a given year, and an additional 5 million worldwide, the problems stemming from failure will only worsen with time.[1, 106] Since the effects of implant failure can be devastating from a functional and psychological perspective, it is important to understand the mechanisms of failure, e.g.: corrosion, delamination, cracking, immune system rejection, and environmental factors. In this thesis, we have used mechanical, electrical and chemical tests to monitor changes in the implant under controlled conditions to establish material biocompatibility and to guide the design of improved implants.

Longitudinal failure of a dental implant is brought on by a foreign body immune response that compromises osseointegration (Section 1.1). The etiology of which is due to the exposure of the implant surface to the immune system and aggravated by particle release. The release of particles has been shown to cause inflammation-induced osteolysis and this is believed to lead to implant failure.[106] The stability of the boneimplant contact region is most essential to long-term survival of a dental implant. For this reason, the corrosion and tribocorrosion properties of implant materials are studied greatly, with 1,410 articles listed on PubMed since 1990 for "corrosion implants."

(https://www.ncbi.nlm.nih.gov/pubmed/) In the research conducted as part of this thesis, we—and our colleagues—used a prophylactic method, thermal oxidation, to combat corrosion and also we sought to elucidate the role of nicotine on the tribocorrosion properties of titanium. The studies revealed new knowledge about the processes, but also raised significant clinical questions that we will here address.

There are three factors that influence the clinician's decision on the selection of the material: (1) cost, (2) physical properties of the alloys, and (3) biocompatibility. It is evident that the rationale for implant component (metal or polymer) selection should be biological safety and satisfactory functionality of the device rather than cost considerations. The use of thermal oxidation as a processing technique to improve the corrosion properties of titanium does not sacrifice the choice of material, has been shown to improve biocompatibility, and increases hardness.[43, 82] Increased hardness, would naturally lead to a more wear resistant surface according to the Archard wear equation

$$Q = \frac{KWL}{H},\tag{1}$$

where, *Q* is the total wear volume produced, *W* is the total normal load, *H* is the hardness of the softest contacting surfaces, *K* is a constant and *L* is the sliding distance of the interacting bodies, thus one would expect reduced wear with increased hardness.[88] Thermal oxidation improves the latter two selection factors through a cost effective and facile modification of the thermal oxide layer to a rutile atomic configuration. For this reason it's corrosive properties were studied, as a potential prophylactic measure to corrosion mitigated failure. Such failure was implied by an early study of the effect of nicotine on titanium alloy through the reduction of the polarization resistance.[62] Since 2015 a corrosion study had been available for the effect of nicotine on titanium alloy, so

a wear study of the effect was the natural next step in our investigation. Nicotine was studied because smoking is a leading cause of implant failure, and its implications are centered on its effect on the surrounding biology, with little known of its effect on the implant itself.

In brief, we hypothesized that nicotine will have a negative tribocorrosive effect on the dental implant, leading to an implant centered failure in addition to the well documented biological effects, and believe that thermally oxidized titanium may improve the long-term stability of dental implants to such failure modes. To study these two scenarios titanium alloy discs (Ti-6AI-4V) were used to model a dental implant. This metal alloy was used as it is the predominate material in the dental implant market. To study the effects of corrosion, standard corrosion testing was pursued, namely potentiodynamic curve estimates and electrochemical impedance spectroscopy. Additionally, surface topography was measured by white light interferometry and analyzed by SEM imaging. For the nicotine analysis a custom built tribocorrosion testing apparatus, described by Butt et al (Figure 16) was used. [100] The apparatus allows the user to draw conclusions on synergistic interactions between wear and corrosion for nicotine's effect on titanium alloy in a single setup simultaneously by controlling the mechanical interaction of a pinon-disc setup in electrolytic fluid. The wear experiments were done under both a free potential condition and a potentiostatic condition, the latter allowed for the use of Faraday's law (Outlined in Section 3.2.5) to delineate total losses due to corrosion and wear separately, and classify the materials tribocorrosive mechanism according to Stack's criteria.[101]

For electrochemical impedance spectroscopy (EIS) a voltage of fixed frequency is applied and the current response measured to indirectly compute impedance which serves as a transfer function between electrical signals. This then is repeated at each frequency. For EIS measurements to be valid they must be linear, stabile, and causal. The electrical response is then analyzed using the appropriate reaction theory to determine the time-varying concentrations of oxidized and reduced species. The electrical behavior of the system reflects the charging and discharging events at the electrodeelectrolyte interface, providing information about the underlying reactions. For a small amplitude sinusoidal excitation, the electrical impedance of the working electrode, in this case the titanium discs, can be represented by the Randle's equivalent circuit (Figure 8A or Figure 23). The network is named after J.E.B. Randles, who first proposed its use for electrochemistry in 1947.[107] The circuit includes a resistor, Rp or Rfilm in this work, which represents the resistance of charge transfer at the passive layer or resistance to the Faraday reaction, placed in parallel with a capacitor, in this work a constant phase element CPE<sub>film</sub> is used to model the simple Randle circuit, which represents the capacitance of double layer formed at the electrode-electrolyte interface. The constant phase element occurs in situations where diffusion plays a dominant role in the charge transfer, in electrochemical studies it is often expressed as the Warburg impedance.[108, 109] Corrosion involving an oxide film is a diffusion limited process as the film provides a barrier that must be overcome by either the underlying metal ions or oxygen in the electrolytic fluid. Finally these parallel reactive elements are placed in series with a resistor, R<sub>s</sub> in this work, representing Ohmic losses in the electrolyte. The governing equation for impedance for the Randle circuit when a constant phase element is

substituted for the capacitor is given by equation (11) where  $0 < \alpha < 1$  and  $C^{\alpha}$  has units of F/(sec)<sup>1-  $\alpha$ </sup> and standard SI units for all other variables.

$$Z = R_s + \frac{R_p}{1 + (j\omega)^{\alpha} C^{\alpha} R_p}$$
(11)

EIS is an excellent method of determining the corrosion properties of a material because it is non-destructive, and provides a great deal of information about the variation of impedance as a function of frequency of the electrochemical double layer formed at the titanium solution interface. Often, this information is represented as Bode and Nyquist plots. The Bode plot is a combination of two graphs, one the magnitude of response as a function of frequency, and the other, the phase shift of the response. In the Bode plot individual charge transfer processes are resolvable, frequency is explicit, and small impedances in the presence of large impedances can be identified. Often, a single time constant should be seen on the Bode plot for the corrosion of a metal forming an oxide film, as multiple time constants will represent inhomogeneity of films between samples of the same metal. Additionally, the impedance of a capacitor is inversely proportional to the frequency as seen in equation (12), so current flowing through the representative Randle circuit will represent the solution resistance at high frequencies, and the resistance to charge transfer at low frequencies.

$$Z = \frac{-1}{j\omega C} \tag{12}$$

Excellent corrosion resistance is represented on a Bode plot by a large phase angle, and high resistance at low frequencies. In the Nyquist plot individual charge transfer processes are resolvable, but the frequency is not explicit, and small impedances are hidden by large ones. The steeper the line on the Nyquist, or the higher  $Z_{img}/Z_{real}$  values,

correspond to improved corrosion resistance as this indicates high complex resistance at all frequencies. The frequency ( $\omega$ ) dependence of the impedance of a Randle circuit can be seen in equation (11). Finally, a model Randle's circuit that is established by curve fitting the actual data should show high polarization resistance and low capacitance to represent strong corrosion resistance.

Since corrosion is an equilibrium process between opposing electrochemical reactions, potentiodynamic curves can be used to extrapolate several corrosion parameters. As in any equilibrium process two or more reactions occur, the first is the anodic reaction in which a metal is oxidized, releasing an electron, and the second is the cathodic reaction in which a solution species, often oxygen, is reduced removing electrons from the metal. In the case of titanium, a passive layer of titanium dioxide forms creating a diffusion barrier that if insurmountable prevents further corrosion. When these two reactions are in equilibrium the flow of electrons is balanced, and no net electrical current occurs. The potentiodynamic curves shown in Figure 10 illustrates this process, the vertical axis is potential and the horizontal axis is the logarithm of absolute current, with each curved line representing the total current for a sample, or both the sum of the anodic and cathodic currents. For the potentiodynamic curve to be generated we measure the total current as we sweep the potential of the working electrode, or the titanium discs. The current from each half reaction depends directly on the electrochemical potential of the metal, it is thus explicit that the higher the equilibrium potential the less anodic current tendency the metal experiences. The equilibrium potential is represented by the sharp points in the curves where the current changes from anodic to cathodic, displaying zero absolute current. This point known as E<sub>corr</sub>, or the corrosion potential of the alloy, is thus

reflective of corrosion tendency. Similarly, classic Tafel analysis is performed by extrapolating the linear portions of the log of current versus potential plot back to their intersections where we can find both  $E_{corr}$  and a corresponding  $I_{corr}$  value, on the graph.[110] The  $I_{corr}$  value represents the corrosion current density or rate, and the lower this value the less corrosion tendency the metal has. Finally, the passivation current,  $I_{pass}$ , is also seen in these graphs by an inflection in potential towards infinity, with lower values representative of improved corrosion tendency.

Using these methods, we observed that the corrosion properties of titanium treated with thermal oxidation improved with temperature initially, but were far worse than control above a certain threshold. At relatively low temperatures (such as 200°C) the EIS and potentiodynamic parameters were favorable, but as temperature increases to 700°C we see poor corrosion performance, inhomogeneity, and cracked oxide layers on imaging as well as orders of magnitude increases in roughness. There is a clear temperature dependence to the improvement of the corrosion properties that is reversible after a certain point, and it is unclear if other heating methods would provide a more homogenous rutile layer. What is clear is the time independence of the improvement in the corrosion properties, implying the diffusion barrier of the passive layer is due to the rutile atomic confirmation and not the thickness of oxide film. As expected, acidic media accelerates corrosion independent of thermal oxidation, though for samples thermally oxidized at lower temperatures with homogenous surfaces the corrosion properties are superior to non-treatment. The limitation of this work was the thermal cracking and inhomogeneity seen on imaging for samples heated at higher temperatures. A program controlled heating may improve outcomes by slowly raising and lowering the temperature during

annealing, preventing thermal shock. However, it should be noted that de-bonding of the surface layer is a common phenomenon of thermal oxidation of titanium, though generally at much higher temperatures than seen in this work.[86] The key result of the thermal oxidation study is that this cost-effective prophylaxis may prevent an implant-centered failure through short cycling of the implant at low temperatures.

Finally, these methods further revealed that the tribocorrosive properties of titanium alloy (Ti-6AI-4V) treated with increasing doses of nicotine in artificial saliva at a resting oral pH and an acidic one is dose dependent and pH reversible. Lower doses showed reduced corrosion and wear loss, being protective, while higher doses showed significant losses, being detrimental. A clear pH reversal of the protection of low doses is evident under free potential conditions for tribocorrosive loss, and is due to the significant reduction on the polarization resistance of titanium alloy at the resting oral pH but lack of an effect at acidic pH. This is due to compound and instantaneous loss of the passive film upon rubbing, a process greatly reduced when the polarization resistance is diminished by nicotine. There are several possible explanations as to why the effect of high doses of nicotine were so detrimental, leading to increases in total weight loss  $K_{wc}$ , and those due to wear  $K_{\rm w}$ , and corrosion  $K_{\rm c}$ . Most likely high doses of nicotine lead to reduced passivation and the bare metal was rubbed off directly instead of a sacrificial oxide film. Synergism between wear and corrosion was found in the EIS plots as wear significantly lowered impedance at low frequencies on the Bode plot, and reduced the relative impedance ratio of the Nyquist. The  $K_0/K_w$  ratio reveals that titanium is a wear centered mechanism, and nicotine does not affect the degradation route though it does appear to affect the magnitude. Finally, particulate debris was found in the wear scar implying

increased wear degradation from a three-body mechanism. The key result of the nicotine study is that this chemical alters the implant environment in a dose dependent manner, which will reduce the lifetime of the material dependent on the smoking habits of the patient with increased failure rate seen for those reporting high pack years.

### 4.2 Clinical Implications and Future Work

Dentists need to better understand the implant and its interaction with the patient in order to make informed decisions on which to use, where and when. Ideally, there should be a concerted effort to study implant design and interaction with host, in order to make better treatment decisions for individuals. The biocompatibility, strength and corrosion resistance of titanium make it the material of choice for dental implants.[111] Nevertheless, there are several drawbacks to its use and maintenance in-vivo. This viewpoint of understanding the material and design is starting to gain ground, as common surgical methods and materials are being scrutinized, as well as treatments to maintain implants once in place. For example, a common treatment for peri-implantitis, ultrasonic scaling, has been found to release titanium particles inducing the inflammation and osteolysis it was intended to prevent.[106] Even the surface preparation, in this case sandblasting, can drastically increase the release of particles in this circumstance intensifying the osteoclastogenesis and macrophage drastically inflammatory response.[106] Going further other studies revealed external influences on the performance of dental implants related to the final restorations.[111] For example, dental cement used to place the final crown has been cited as a source of inflammation, and peri-implantitis.[111] Indeed cements have been found to significantly lower polarization resistance values, similar to nicotine in this work, and experience higher corrosion rates.[111] In the future it may become common practice for dental practitioners to use cementless restorations and or stop scaling placed implants that present with implantitis.

The common concept that ties these scientific observations to clinical decision making is the secondary stability of a dental implant, which is responsible for overall longevity, and directly determined by the foreign body equilibrium (See Section 1.1). This foreign body equilibrium can maintain the bone-implant contact region (1) when the implant is not exposed to the immune system, and (2) when the implant is not producing particulate debris to induce an immune response. There are two sides to this argument, one that is implant centered and another that is host or biological, centered. The biological response or bone ingrowth can be negatively affected by smoking, and positively affected by biocompatibility of the material, such as thermal annealing leading to increased osteoblastic activity as measured by alkaline phosphatase.[43, 48-50] The implant centered response is due to corrosion, wear, and the immunological response to surfaces not morphologically connected to bone and to particles release from the implant through the first two processes. In this thesis, we sought to make scientific observations with respect to implant centered failure mechanisms, first by investigating the effect of thermal oxidation on the corrosion properties of titanium alloy, and second by investigating the effect of nicotine on the tribocorrosion properties of titanium alloy.

There are several clinical implications of the results of this study. First, the use of thermal oxidation is a cost effective and facile means to improve both the biocompatibility of an implant and the survival through implant-centered failure mechanisms.[43] The alternative that thermal oxidation may not be a positive feature under all circumstances also needs to be addressed. Sandblasting has been used for some time in implants to improve biocompatibility, but when an implant is cleaned it has been shown to induce increased osteolysis and peri-implantitis.[106] Under all clinical scenarios thermal

oxidation may simply not stand up as a positive feature, and dentist need to be prepared for such a circumstance, only further testing and time will tell. However, thermal oxidation was found to improve the corrosion properties of titanium alloy, and future work needs to address its mechanical suitability. Thermal oxidation has been shown to increase the hardness of the material, and according to the Archard equation (1) should reduce the wear of the implant.[82] This is important as the implant will be placed under mechanical load through mastication, as well as the shear force of insertion. Delamination of implant surfaces is a common problem that must be considered before thermal oxidation is adopted as a clinical standard.[112] In order to investigate surface failures fatigue testing of dental implants can be pursued, commonly using ISO 14801, however other alternatives have been proposed.[113] The testing can be coating specific, as the Food and Drug Administration (FDA) recommends ASTM F1160-98 for calcium phosphate and metallic coatings but ASTM F1501-95 for ceramic coatings. Delamination of a surface coating can cause loss of mechanical integrity and peri-implantitis.[114] Additionally, the poor corrosion resistance and cracking seen on imaging for higher temperatures has the alternative explanation of rapid heating and cooling with uneven thermal expansion and shrinking. This could potentially be alleviated by programmed thermal oxidation, replacing the manual insertion of the samples with an oven that slowly reaches a desired temperature and then slowly cools down. It should be noted, that some de-bonding of the surface oxide layer has been noted with higher temperature thermal annealing, and it may not be possible to improve results at higher temperature.[86] De-bonding in the literature is seen at much higher temperatures than what was seen in this study, so it is possible that successful thermal annealing will be seen above 200°C. Lastly, only an

electrochemical evaluation of the titanium was performed in the present study, without considering masticatory forces. Further studies evaluating the behavior of the rutile under wear are necessary to determine if thermal oxidation is a cost-effective processing technique to improve the outcomes of dental implants for patients. Such studies should include surface based spectroscopy, such as Rutherford backscattering spectrometry, X-ray photoelectron spectroscopy, and grazing incidence X-ray diffraction. These techniques will allow us to quantitatively assess the oxide films composition and differentiate both impurities and homogeneity between samples based on temperature, to determine the samples with the most rutile character.

The clinical implications of the tribocorrosion testing of nicotine are even more significant. The biological response of an implant to smoking only explains primary failure of a dental implant, that is, a failure to achieve secondary stability through a period of osseointegration, it doesn't explain the majority of failures occurring at later periods which are of a mixed etiology. As smokers exhibit greater implant failure both early, before abutment placement, and late, after occlusal loading of a prosthesis it is imperative to discover both the etiology of such failures and potential prophylactic methods.[2, 52, 53] This work elaborated the role of nicotine in implant centered failure, as it proved that not all smokers are affected equally. Overall, heavy smokers should show significant increases in released particles which may worsen osseointegration.[106] Though it is clear a biological failure exists in smokers, it appears that implant centered failures are dose dependent meaning that heavy smokers or those using chewing tobacco may be more likely to have dental implant failure. Indeed initial clinical studies have found that the amount of smoking expressed as pack years has a valid influence on implant survivability.

with increasing failure related to dose.[115] What has not been reported in the literature is a protective effect of light smoking or nicotine exposure on dental implant survival, and the alternative that the biological effect of smoking is more significant than the implant centered failure needs to be considered given the large influence that smoking has on biological processes. Nicotine's influence on the polarization resistance of the alloy is not a new phenomenon and has been seen for example in bone cement used to place the abutment.[111] However, the protective effect this has depends on the mechanism of degradation and whether it is wear centered or corrosion centered. For the latter, the decrease in passivation would imply increase loss due to corrosion, but in a wear centered failure the passive layer is rubbed off leading to reductions in loss with a decrease in polarization resistance. This effect is reversible with pH as the polarization resistance is naturally suppressed in acidic medium. All things considered, the effect of this pH reversible protection in a wear domain is not clinically relevant at this time because the forces on a dental implant in-vivo have never been modeled so it is hard to know if wear dominates corrosion under natural conditions. This study used a tribological system with a pin-on-disc configuration, however, the in-vivo environment is very complex. Variations in load and stress conditions, through mathematical modelling and simulations need to be considered in future studies.

Further, does nicotine effect other metals and materials similarly to titanium to induce an implant centered failure, or are other implants superior in this regard such as ceramics? The use of ceramics as the primary material for dental implants is a relatively new phenomenon, and though the literature supports increased failure for smokers a comparative analysis of failure based on the primary material does not exist in the

literature at this time. All things biological being equal, implant centered failure and overall failure may differ among smokers based on the primary material used, and further studies are needed now. It is unfortunate, but true of society that a financial incentive leads to results. The FDA classifies endosseous dental implants as a class II special controls device under title 21 of the code of federal regulations in section 872.3640. They further award indications for dental implants such as immediate loading, which can then give a device manufacturer or provider a marketing advantage to a subset of patients. Awarding of an indication for smokers would be a means to incentivize the development of implants for this population. Unfortunately, such an indication is unlikely to be rewarded through a 510k process, making the guidance documents published and the listed ISO and ASTM standards for aspects such as biocompatibility, fatigue testing, static strength, etc. inadequate for FDA evaluation of said indication. Simply put a new standard must be developed to measure a materials susceptibility to the tribocorrosive effects of nicotine in order to develop an implant for smokers.

Additionally, there are several shortcomings to these studies that require follow-up experiments. Primarily from the in vitro perspective the exclusion of proteins significantly limits the strength of drawing conclusions upon this work. That is because proteins absorb to the surface of an implant immediately and are responsible for the foreign body immune response that leads to failure. The importance of proteins is not merely one of the biological mediated failure but also one of the implant centered category. One study found that proteins play a significant role in the repassivation kinetics, and that under sliding conditions the pitting potential is lowered significantly.[116] Previous work has shown that the formation of a protein biofilm on alloy surfaces can increase corrosion rate.[117]

Proteins can directly interact with the metal to influence local corrosion, and may indirectly influence corrosion by interrupting the passive film formation by disrupting electrochemical reactions.[118, 119] This leads to delayed formation of the oxide film, preventing passivation. Some metals form a tribolayer, a mixture of organo-metallic complexes, that protect the surface, this is most commonly observed in cobalt-chrome-molybdenum alloys.[120] Finally it has been proposed that a layer of adsorbed organic molecules on the metal surface hinders the charge transfer involved in passive film dissolution.[121] The studies composed in this thesis need to be extended to include protein in the solution to provide a more realistic model of the role of titanium in vivo.

Tribocorrosion Studies of Dental Materials,

& the Clinical Implications

# CONCLUSSIONS

(Chapter Five)

The overall objective of these studies was to identify the effects of nicotine on dental implant corrosion undergoing wear and to investigate thermal oxidation as a prophylactic measure to mediate implant centered failure.

Firstly, the corrosion properties of titanium treated with thermal oxidation, as measured by potentiodynamic polarization testing and electrochemical impedance spectroscopy, improves with temperature initially, but then yields results far worse than control above a certain threshold. A reversible temperature dependence was found that gave improvements in corrosion properties up to 400°C, at which point inhomogeneities in the surface oxide lead to poor corrosion resistance. However, the failure at higher temperatures could be an artifact of the heating methods, and future studies using a programmed ascent and descent in temperature to prevent thermal shock are necessary to confirm our finding. Interestingly the improvement in corrosion properties is time independent implying that the thickness of the oxide film is not relevant but a change in the diffusion with the rutile phase is responsible. Additionally, thermal oxidation improves the corrosion properties in acidic medium which is a natural consequence of chewing food in the mouth where a pH of 3 to 5 is common. Though thermal oxidation may reduce corrosion, like other surface modifications it could prove detrimental in clinical scenarios, such as implant scaling as has been seen for sandblasted surfaces. [106] Additionally, only an electrochemical evaluation of the titanium was performed in the present study, without considering masticatory forces. Further work evaluating the behavior of the rutile under wear are necessary to determine if thermal oxidation is a cost-effective processing technique to improve the outcomes of dental implants for patients. Such studies, including those already undertaken in this work, should also be repeated in the presence of

proteins, which are known to play an important role in the failure of implants and in the kinetics of passivation of metal surfaces.[116] In addition, quantitative analysis of the surface layers' atomic configuration, homogeneity, and thickness by surface based spectroscopic techniques such as Rutherford backscattering spectrometry, X-ray photoelectron spectroscopy, and grazing incidence X-ray diffraction should be pursued in the future. Nonetheless, these results are very consistent with previous studies and suggest that thermal oxidation could be used as a cost-effective clinical method for improving the biocompatibility of dental implants.

Next, the effect of nicotine on the tribocorrosive properties of titanium alloy (Ti-6AI-4V), when measured using electrochemical impedance spectroscopy, current density profiles, and weight loss, all show reduced material degradation at low doses compared to control, but significantly higher loses at high doses. This dose dependence was coincidental with a pH reversible phenomenon, were loss was reduced at the normal oral pH of 6.5 for the low doses examined in comparison to acidic medium. This is due to a significant reduction in the polarization resistance for low dose nicotine at the resting oral pH (but the lack of an effect at acidic pH). Reductions in polarization resistance with nicotine reduces passive film formation leading to a reduction in compound and instantaneous wear of material upon rubbing of the pin-on-disc. No immediate explanation is available for the effect of high doses of nicotine, which is detrimental to the titanium alloy leading to significant increases in total weight loss  $K_{wc}$ , wear  $K_{w}$ , and corrosion  $K_{\rm c}$ . It is suspected that the high doses of nicotine lowered the polarization resistance to an extent where passivation was not possible allowing for continuous corrosion and direct wear of the bare metal. This is one possible explanation, but further

experiments to measure polarization resistance at this dose are necessary. Synergism between wear and corrosion was also found in the EIS plots as wear significantly lowered impedance at low frequencies as shone in the Bode plot, and reduced the relative impedance ratio on the Nyquist plot. The  $K_o/K_w$  ratio indicates that titanium is a wear centered degradation mechanism, and nicotine does not affect the degradation route, although it does appear to affect the magnitude. Also, particulate debris was found in the wear scar implying increased wear degradation from a three-body mechanism. Additionally, these studies should also be repeated in the presence of proteins, as they mediate the immune response that is implant failure and effect the corrosion rate of the metal.[117] Lastly, the clinical implications of this work are clear. Smoking has a dose dependent effect on implant centered failure. The tribocorrosive studies are backed up by clinical results which show that pack years predicts implant failure.[115] The fact that smoking habits correlate with the failure of dental implants is an obvious trend throughout this study, where dose dependence was seen to be significant.

Finally, dental materials are of high importance to modern society. Their safety, utility, and effectiveness must be placed under constant scrutiny because of the role they play in improving the lives of patients. The variety of dental materials extends across the field of materials science from metal alloys to polymers. Each material fits the needs of a different dental specialty and addresses problems arising from underlying pathologies of patients. Materials must fit, form, function, and meet specific patient concerns. Since the discovery of osseointegration by Per-Ingvar Branemark in 1952, dental implants have proliferated.[6] The use and need for these materials is extraordinary, such that, the American College of Prosthodontists estimates 35 million Americans are fully edentulous,

and 178 million, or 56% of Americans are missing at least one tooth. Understandably, the use of dental implants is now routine for replacement of missing teeth. In the United States alone, nearly 300,000 patients receive one or more implants in a year.[1] Globally, it has been estimated that approximately 12 million oral implants are placed per annum.[17] In dental implants, titanium and its alloy are chosen for their strength, corrosion resistance and biocompatibility.[77, 90-92] Nonetheless, the saliva, acid, fluoride, and bacteria present in the oral cavity as well as the physical loads of mastication damage dental implants and reduce their longevity.[77, 93, 94] The milieu of saliva, reacts electrochemically with dental implants leading to corrosion and the release of metal ions into the surrounding environment.[95, 96] The surface of implants and degradation products are known to increase surface binding of complement factor and other innate immune responders.[8] This process produces a foreign body response that eventually leads to implant loosening and failure.[11, 17] A leading cause of failure and the major contraindication to dental implants is smoking.[122] Smokers exhibit greater implant failure both early, before abutment placement, and late, after occlusal loading of a prosthesis.[2, 52, 53] The biological implications for smoking's effect on osseointegration is prevalent in the literature. The fact that smoking causes an implant centered failure and that processing techniques may mitigate such failure were shown by this study. However, now that this is known further studies are needed to determine if the effect of nicotine is the same on other materials. Most recently ceramics have been adopted as a material for dental implants, gaining in popularity. What remains to be seen is whether implant failure for smokers is higher or lower for patients with ceramic implants versus titanium alloy. Further studies need to focus on other materials to determine if tribocorrosive loss is

significant with nicotine *in vitro*, and at the same time clinical studies of smoking determining if the failure rate of the dental implant varies based on the material of choice needs to be conducted. It may become apparent through such studies that there is an implant of choice for smokers, and that perhaps the current trend towards ceramics or processing techniques such as thermal oxidation of titanium alloy will improve outcomes for such patients.

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APPENDIX

## INTRODUÇÃO

O titânio e as suas ligas são utilizados nos implantes dentários por apresentarem as propriedades de biocompatibilidade, resistência à corrosão, boa resistência mecânica, etc. No entanto, vários estudos relatam que o titânio é passível de degradação e corrosão quando exposto a certos componentes químicos no meio ácido ou mesmo em contato com a saliva<sup>1,2,3,4</sup>. O contato do titânio com o oxigênio forma espontaneamente uma densa camada de dióxido de titânio (TiO2) em sua superfície, de espessura entre 1,5 a 10 mm.

Essa camada faz com que ocorra um aumento na resistência à corrosão do titânio<sup>5</sup>. Porém, quando o titânio é envolto por um meio ácido, saliva ou outros componentes, o efeito protetor da camada de dióxido de titânio pode ser afetado, iniciando o processo de corrosão<sup>1,3</sup>. Esse processo pode influenciar a função e a biocompatibilidade dos implantes dentários, podendo gerar a perda desses implantes na cavidade oral<sup>1</sup>.

Os implantes dentários são continuamente expostos a fatores adversos, tais como forças mastigatórias, alteração da composição química no meio em que estão expostos, o que pode influenciar na degradação do titânio, níveis alterados de oxigênio ao seu redor, variação de temperatura, alterações causadas pelos alimentos e mudança na composição salivar<sup>6</sup>. Entretanto, os eletrólitos presentes na saliva, podem induzir à perda de íons metálicos da superfície do titânio pelo processo de corrosão<sup>1</sup>. A variação no pH da saliva ao redor dos implantes dentários é um

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fenômeno comum de acontecer<sup>7</sup>. O titânio e as ligas de titânio em meio ácido sofrem corrosão muito mais intensa se comparado a uma condição de ambiente básico, onde o pH geralmente apresenta-se com valor de 6.0<sup>7</sup>. Certos alimentos como nozes, leite e alimentos ricos em cálcio podem tornar a saliva mais alcalina<sup>8</sup>; já por outro lado, existem alguns fatores que podem interferir tornando o meio salivar mais ácido. Elementos como infecções, alimentos açucarados, frutas, sucos e refrigerantes geralmente tornam o meio ácido, baixando o pH para valores entre 2,5 a 3,5<sup>8,9,10</sup>. O fumo, uso contínuo de medicamentos, doenças crônicas e sistêmicas também podem contribuir para a saliva apresentar uma concentração ácida e influenciar no processo de corrosão dos implantes dentários<sup>1,2,3</sup>. Como consequência do processo de corrosão, há o aumento da produção de mediadores inflamatórios pelos macrófagos, o que contribui para que ocorra perda do tecido ósseo na área afetada<sup>11</sup>.

Além do processo químico e biológico, existe também a preocupação com as forças mecânicas sobre os implantes dentários, as quais causam desgaste e exercem compressão sobre o material, o que faz com que a camada de dióxido de titânio seja alterada, causando danos e, em casos mais extremos, podem até mesmo causar a perda dos implantes<sup>12</sup>. A oxidação térmica (OT) (processo de aquecimento a elevadas temperaturas variando de 200°C a 1000°C) do titânio promove um aumento da camada de TiO2 e também uma alteração em sua estrutura, fazendo com que a superfície do titânio apresente uma camada mais dura, rugosa, espessa e cristalizada, chamada de camada rutile<sup>12,13</sup>. Vários estudos demonstram que o processo de oxidação térmica altera a camada superfícial de TiO2, aumentando a espessura, a

resistência à corrosão e melhora as propriedades biológicas e mecânicas do titânio<sup>12,13,14</sup>. Esse tratamento faz com que ocorra uma mudança na topografia superficial, rugosidade e aumento da energia de superfície<sup>15</sup>, melhora a adesão plaquetária e acelera a formação da rede de fibrinas sobre a superfície dos implantes<sup>13</sup>.

O comportamento da oxidação térmica sobre a superfície do titânio, em relação a sua temperatura e duração de exposição, ainda não foi explorado de forma satisfatória.

Para melhor compreender essa reação, este trabalho investigou a relação do meio oral com diferentes pHs (3 e 6.5) no processo de corrosão na liga de titânio tratada por oxidação térmica com variações de temperaturas e duração em seu tratamento. O objetivo deste estudo é compreender o processo de corrosão sobre a superfície termo oxidada, utilizando um teste de espectroscopia de impedância eletroquímica (EIS) e testes básicos de corrosão. A hipótese deste trabalho é que a liga de titânio (Ti-6AI-4V) tratada por oxidação térmica apresenta melhor resistência à corrosão comparada à liga de titânio (Ti-6AI-4V) não tratada.

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## INTRODUCTION

Titanium and its alloy have been used as a material in the dental implant industry due to present biocompatibility, corrosion resistance, good mechanical strength, etc. However, several studies reported that titanium is passive to corrosion and degradation when exposed to certain chemical components in acidic medium or even wrapped in saliva<sup>1,2,3,4</sup>. When the interaction between titanium and oxygen, spontaneously forms a dense layer of titanium dioxide (TiO2) on its surface of thickness around 1.5 to 10 nm, this layer is responsible to an increase in corrosion resistance (Huang 2003). Moreover, when titanium is surrounded by an acidic environment, saliva or other component may affected the protectiveness effect of the titanium dioxide layer and corrosion process can take place<sup>1,2</sup>. These processes can damage the function and biocompatibility of dental implants, which may cause the implants failure in oral cavity<sup>1</sup>.

Dental implants are continuously exposed to adverse factors such as masticatory forces, changing in chemical composition at the medium they are exposed and that can contribute to titanium degradation, oxygen levels changed around him, variation of temperature and changes caused by food and salivary composition<sup>5</sup>. In addition, the electrolytes present in saliva can cause the metal ions loss from the titanium surface by the corrosion process<sup>1</sup>. The saliva pH variation around dental implants is a common phenomenon to happen. Both titanium and titanium alloys suffer more intense corrosion in acid environment compared to a basic condition where the

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pH usually is  $6.0^{6}$ . Certain foods such as nuts, milk and calcium-fortified foods can alter the saliva to a more alkaline environment<sup>7</sup>, on the other hand some factors can acidify the saliva pH. Factors such as infections, sugary foods, fruits, juices and soft drinks generally can make the medium acid, dropping pH to  $2.5 - 3.5^{7,8,9}$ . In general, smoking, medication, chronic and systemic diseases can also contribute to acidified saliva concentration and influence the corrosion process of dental implants<sup>1,2,3</sup>. As a result of the corrosion process, the increases of inflammatory mediators as a product from macrophages, contributes to occur bone loss in the affected area<sup>10</sup>.

Besides the chemical and biological process there is also a concern with mechanical forces on dental implants, causing wear and exerting compression on the material, thereby causing changes at the titanium dioxide layer, resulting in damage or in extreme situation may cause failure<sup>11</sup>. The thermal oxidation (TO) (heating process at elevated temperatures ranging from 200 ° C to 1000 ° C) causes an increase of titanium in TiO<sub>2</sub> layer and also a change in structure, making the surface of the titanium present a harder, rougher, thicker and crystallized layer, called as rutile<sup>11,12</sup>. Several studies have shown that the process of thermal oxidation changes the surface of TiO<sub>2</sub> layer by increasing the thickness, corrosion resistance and improves the biological and mechanical properties of titanium<sup>11,12,13</sup>. This treatment causes a change in the surface topography, roughness and increased surface energy<sup>14</sup>, improves the platelet adhesion and accelerates the formation of fibrin mesh over the implant surface<sup>12</sup>.

The behavior of the thermal oxidation on the titanium surface as a function of temperature and duration has not been explored satisfactorily. To better understand

those relationship this study investigated the phenomenon of artificial saliva at different pH (6.5 and 3) and the corrosion process on titanium alloy treated by thermal oxidation with variations in temperature and duration during treatment. The aim of this study is to comprehend the corrosion process on the thermal oxidized surface using a test of electrochemical impedance spectroscopy (EIS) and basic corrosion tests. The hypothesis is titanium alloy (Ti-6AI-4V) treated by thermal oxidation exhibits better corrosion resistance compared to untreated titanium alloy (Ti-6AI-4V).

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