SBIR PHASE I PROPOSAL COVER SHEET

Topic Number PHS 2021-1	SubTopic Letter (if any) N/A	Topic Title SBIR Phase 1
Proposal Title Development of a PEKK/tantalum/eADF4(C16) bone substitute with enhanced antibacterial and osseointegration capabilities		
Company Name: North Point University, Applied Biomaterials Laboratory		Employer Identification Number (EIN) or Taxpayer Identification Number (TIN) 12-3847978
Name of any Affiliated Companies (Parent, Subsidiary, Predecessor) N/A		
Address (including address of Company Headquarters and zip code plus four digit extension) North Point University 90 State Street Boston, MA 02109-2202		
Requested Amount $2,652,500	Proposed Duration 18 months	Period of Performance October 1 2021 – March 31 2023

THE SMALL BUSINESS CONCERN CERTIFIES THAT:	**Y/N**
1. It is a small business as defined.	N
2. It qualifies as a socially and economically disadvantaged business as defined. (FOR STATISTICAL PURPOSES ONLY)	N
3. It qualifies as a women-owned business as defined. (FOR STATISTICAL PURPOSES ONLY)	N
4. It has submitted an equivalent proposal to another Federal agency. If YES, provide required information as outlined in the solicitation.	N
5. A minimum of two-thirds of the research will be performed by this firm in Phase I.	Y
6. It will permit the government to disclose the title and technical abstract page, plus the name, address and telephone number of a corporate official, if the proposal does not result in an award, to parties that may be interested in further information or possible investment.	Y
7. It will comply with the provisions of the Civil Rights Act of 1964 (P. L. 88-352) and the regulations pursuant thereto.	Y

PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR	
Name Dr. Catherine Trojanowski	Title Associate Professor
Social Security No. 143-23-9687	Telephone Number 617-555-1246
E-Mail Address ctrojanowski@northpoint.edu	Fax Number 617-555-1200

COMPANY OFFICER (FOR BUSINESS AND FINANCIAL MATTERS)		
Name Dr. Kevin Johnson	Title Dean of Engineering	Telephone Number 617-555-3386

OTHER INFORMATION		
President's Name N/A	Year Firm Founded N/A	Number of Employees (Parent Co.) Average Previous 12 Mo.: N/A Currently: N/A

PROPRIETARY NOTICE: See instructions concerning proprietary information.
Check here [X] if proposal contains proprietary information.
NOTE: The signed Certification Page **must** be included immediately following this Cover Page with the original copy of the proposal only.

CERTIFICATION PAGE

Certification for Principal Investigators

I certify to the best of my knowledge that:

(1) the statements herein (excluding scientific hypotheses and scientific opinions) are true and complete, and

(2) the text and graphics herein are as well as any accompanying publications or other documents, unless otherwise indicated, are the original work of the signatories or individuals working under their supervision. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if an award is made as a result of this application.

I understand that the willful provision of false information or concealing a material fact in this proposal or any other communication submitted to NSF is a criminal offense (U.S. Code, Title 18, Section 1001).

Name (Typed)	Signature	Date
PI/PD Dr. Catherine Trojanowski	*CTrojanowski*	08/24/2021

Certification for Authorized Organizational Representative or Individual Applicant

By signing and submitting this proposal, the individual applicant or the authorized official of the applicant institution is: (1) certifying that statements made herein are true and complete to the best of his/her knowledge; and (2) agreeing to accept the obligation to comply with NSF award terms and conditions if an award is made as a result of this application. Further, the applicant is hereby providing certification regarding Federal debt status, debarment and suspension, drugfree workplace, and lobbying activities (see below), as set forth in the *Grant Proposal Guide (GPG)*, NSF 99-2. Willful provision of false information in this application and its supporting documents or in reports required under an ensuing award is a criminal offense (U.S. Code, Title 18, Section 1001).

In addition, if the applicant institution employs more than fifty persons, the authorized official of the applicant institution is certifying that the institution has implemented a written and enforced conflict of interest policy that is consistent with the provisions of *Grant Policy Manual,* Section 510; that to the best of his/her knowledge, all financial disclosures required by that conflict of interest policy have been made; and that all identified conflicts of interest will have been satisfactorily managed, reduced or eliminated prior to the institution's expenditure of any funds under the award, in accordance with the institution's conflict of interest policy. Conflicts which cannot be satisfactorily managed, reduced or eliminated must be disclosed to NSF.

Debt and Debarment Certifications (If answer "yes" to either, please provide explanation.)

Is organization delinquent on any Federal debt?	YES	☐	NO	☒
Is the organization or its principals presently debarred, suspended, proposed for debarment, declared ineligible, or voluntarily excluded from covered transactions by a Federal Department or agency?	YES	☐	NO	☒

Certification Regarding Lobbying

This certification is required for an award of a Federal contract, grant or cooperative agreement exceeding $100,000 and for an award of a Federal loan or a commitment providing for the United States to insure or guarantee a loan exceeding $150,000.

Certification for Contracts, Grants, Loans and Cooperative Agreements

The undersigned certifies, to the best of his or her knowledge and belief, that:

(1) No Federal appropriated funds have been paid or will be paid, by or on behalf of the undersigned, to any person for influencing or attempting to influence an officer of employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a member of Congress in connection with the awarding of any federal contract, the making of any Federal grant, the making of any Federal loan, the entering into of any cooperative agreement, and the extension, continuation, renewal, amendment, or modification of any Federal Contract, grant, loan, or cooperative agreement.

(2) If any funds other than Federal appropriated funds have been paid or will be paid to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, and officer or employee of Congress, or an employee of a Member of Congress in connection with this Federal contract, grant, loan, or cooperative agreement, the undersigned shall complete and submit Standard Form-LLL, "Disclosure of Lobbying Activities," in accordance with its instructions.

(3) The undersigned shall require that the language of this certification be included in the award documents for all subawards at all tiers including subcontracts, subgrants, and contracts under grants, loans, and cooperative agreements and that all subrecipients shall certify and disclose accordingly.

This certification is a material representation of fact upon which reliance was placed when this transaction was made or entered into. Submission of this certification is a prerequisite for making or entering into this transaction imposed by section 1352, title 31, U.S. Code. Any person who fails to file the required certification shall be subject to a civil penalty of not less than $10,000 and not more than $100,000 for each such failure.

Authorized Company Officer	Signature	Date
Name /Title (Typed) Dr. Kevin Johnson, Dean of Engineering	*KJohnson*	08/24/2021

Telephone Number	Electronic Mail Address	Fax Number
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2.0 Table of Contents

3.0 Identification and Significance of the Problem or Opportunity

Bone grafting is a surgical procedure that replaces missing bone with transplanted bone or a bone substitute [1]. Every year, more than 2 million bone grafting procedures are performed worldwide, including 500,000 procedures in the United States [2]. Bone grafting using autografts is the current gold standard, however donor site morbidity is a concern. Allografts are another common surgical option, although there is a risk of infection and limited donor availability. Bone substitutes are synthetic or biologically derived products which can be inserted for the treatment of a bone defect instead of autogenous or allogenous bone [2], [3]. They are increasingly being used in various surgical fields, including oncologic surgery, traumatology, revision prosthetic surgery, and spine surgery [2].

Unfortunately, many current bone substitutes lack mechanical strength which limits their application [3]. Furthermore, most of the commercial products available are incapable of inhibiting bacterial colonization, which can cause pain, infection, implant failure, and even death [4], [5]. Initial bacterial colonization on implants can eventually lead to the formation of biofilms which are very resistant against antibacterial attacks. Thus, bone substitutes that possess adequate antibacterial properties are required to ensure implant success [5]. In addition to achieving desired mechanical and antibacterial characteristics, bone substitutes should allow for osseointegration to ensure implant stability [6].

The development of a bone substitute that encompasses the aforementioned properties is the focus of this research proposal. **The proposed solution will give patients another surgical option for bone replacement that overcomes the drawbacks associated with current bone substitutes. Due to its enhanced mechanical strength, antibacterial properties, and osseointegration capabilities, the proposed solution should result in a lower incidence of post-surgical complications and a quicker patient recovery time.** This project will provide further insight into the design and manufacture of composite biomaterials and will advance an understanding of the effectiveness of composites as bone substitutes. If the bone substitute is successful, the engineering methodology can potentially be applied to other biomaterials and promote the innovation of additional solutions. So far, an ideal bone substitute material has not been discovered, making the development of alternative strategies a critical research endeavor.

4.0 Background, Technical Approach and Anticipated Benefits

4.1 Overall Background

Bone is a part of the vertebrate skeleton that is involved in structural support, organ protection, mineral storage, and blood cell production. Bone comprises an inner and outer layer, each containing various cell types, matrix-deposited inorganic minerals, and a nonmineral proteinaceous matrix. The outer layer of bone is called cortical bone and it is tough and strong. In contrast, the inner layer is called trabecular bone and it is lighter and less dense [7].

When a bone is fractured, the healing process begins and involves 3 stages: inflammation, bone production, and bone remodeling. Bone fracture leads to an inflammatory response that lasts for several days. The blood from the torn blood vessels starts to clot and provides the structural

framework for new bone production. The clotted blood is first replaced with fibrous tissue and cartilage and then with hard bone. Bone continues to form during bone remodeling and becomes compact [8].

In cases where a fracture results in a large loss of bone, bone grafting may be necessary [9]. Bone grafting is a surgical procedure that replaces missing bone with transplanted bone or a bone substitute [1]. In addition to promoting bone healing and growth after trauma, bone grafts can be used to restore bone defects resulting from infection, disease, surgery, or congenital etiology [3], [9].

Bone grafting using autografts is the current gold standard as it meets the necessary mechanical criteria, is nonimmunogenic, and does not pose a risk for disease transmission. However, donor site morbidity and associated complications have resulted in alternative techniques being used such as allografts [3]. Allografts are associated with other disadvantages such as disease transmission, limited donor availability, and high cost due to the required treatment and sterilization procedures [2], [3]. Xenografts can also be used, but they carry a risk of immunogenicity and disease transmission and may not be accepted by patients due to their beliefs [3]. To overcome these limitations, many bone substitutes have been proposed. Bone substitutes are synthetic or biologically derived products which can be inserted for the treatment of a bone defect instead of autogenous or allogenous bone [2], [3]. They are increasingly being used in various surgical fields, including oncologic surgery, traumatology, revision prosthetic surgery, and spine surgery [2].

Synthetic bone substitutes include calcium sulfate, calcium phosphate, bioactive glass, and polymer-based substitutes. Calcium sulfate is osteoconductive, inexpensive, and available in various forms. However, it resorbs more quickly than the rate of bone deposition and is not osteoinductive or osteogenic. There are many forms of calcium phosphate being used for bone substitutes such as calcium phosphate cements, β-tricalcium phosphate ceramics, and biphasic calcium phosphates. These materials are osteoconductive, bioresorbable and biocompatible, but have poor mechanical properties. Bioglasses possess similar advantages and disadvantages to calcium phosphates for use as a bone substitute [3]. Lastly, polymer-based bone substitutes can be easily manipulated, but lack adhesion to living tissues [10].

Bone substitutes derived from biological products include demineralized bone matrix (DMB), platelet-rich plasma, bone morphogenetic proteins (BMPs), hydroxyapatite (HA), and coral. DMB is derived from human bone and is not associated with immunological rejection. However, DMB lacks mechanical strength and much of bone's osteogenic capacity is lost during processing. Similarly, platelet-rich plasma shows limited mechanical resistance and is thus used as a supplement rather than a stand-alone bone substitute. BMPs are osteoinductive growth factors which require carriers to deliver and maintain them at the target site. However, their high cost and risk of complications limit their application. HA is the primary mineral component of bones and is thus very biocompatible. While HA is porous and allows for bone ingrowth, its brittleness makes it unsuitable for load-bearing applications [3]. Lastly, bone substitutes derived from the exoskeleton of marine corals can act as a carrier for growth factors and have

been shown to be safe, biocompatible, and osteoconductive. However, the use of coral bone grafts may be limited due to their inherent mechanical weakness [11].

4.2 Related Research

There have been various studies examining novel biomaterials for use as bone substitutes. For instance, the incorporation of tantalum into polyaryletherketone polymers such as polyetheretherketone (PEEK) and polyetherketoneketone (PEKK) has yielded mechanically robust materials capable of osseointegration [12]–[14]. Recently, a microporous PEKK surface containing Si_3N_4/tantalum microparticles has been developed to yield a mechanically robust material capable of both osseointegration and antibacterial activity. Tantalum was found to improve osseointegration more than Si_3N_4 while Si_3N_4 exhibited superior antibacterial activity [14]. **The proposed solution aims to improve upon previous approaches by maximizing both osseointegration and antibacterial properties.**

4.3 Technical Approach

The bone substitute suggested in this proposal is a polymer-metal composite made from PEKK, tantalum, and engineered spider silk. The porous PEKK implant will contain tantalum microparticles and will be coated with a biodegradable and antibacterial silk coating. PEKK is a promising biomaterial for long-term orthopedic applications due to its excellent biocompatibility, acceptable wear resistance, and high strength. Additionally, it possesses an elastic modulus comparable to that of bone which reduces stress shielding [15]. However, PEKK is bioinert and cannot integrate with the host bone. Instead, a fibrous tissue encapsulates the material which causes implant loosening and eventual failure. Osseointegration can be achieved using tantalum, a biocompatible and corrosion resistant metal. Unfortunately, bulk tantalum implants are ineffective as bone substitutes due to their high elastic modulus and density [12]. Thus, a PEKK implant containing tantalum microparticles will possess an appropriate elastic modulus and high strength while simultaneously achieving osseointegration. In addition to these properties, bone substitutes should also possess antibacterial capabilities to prevent bacterial colonization, which can lead to pain, infection, implant failure, and even death [4], [5]. The rate of infection associated with the use of bone substitute materials is reported to be approximately 12% [16]. The engineered silk protein eADF4(C16) can be processed into a film for coating applications and has been shown to be effective in preventing adhesion of *Staphylococcus aureus* (*S. aureus*), which is a common bacterium causing implant related infections [17], [18].

4.4 Innovativeness and Originality of the Proposed Research

Most of the commercial bone substitutes available lack mechanical strength and are incapable of inhibiting bacterial colonization which limits their application [3]–[5]. While there has been progress in developing a bone substitute which is strong, has antibacterial characteristics, and is capable of osseointegration, there is potential to improve upon previous approaches. Recently, a microporous PEKK surface containing Si_3N_4/tantalum microparticles has been developed to yield a mechanically robust material capable of both osseointegration and antibacterial activity. The researchers found that PEKK surfaces solely containing tantalum microparticles were more effective in inducing cellular response *in vitro* and improving osseointegration *in vivo* compared

to PEKK modified with Si_3N_4. The results also showed that PEKK modified with Si_3N_4 exhibited a 99.23% percent reduction of *S. aureus in vivo* compared to less than 60% reduction observed for PEKK modified with tantalum. Thus, the research provides evidence that tantalum is more effective than Si_3N_4 in promoting osseointegration while Si_3N_4 exhibits superior antibacterial activity [14].

To maximize osseointegration and antibacterial properties, a porous PEKK implant containing tantalum microparticles will be engineered and coated with biodegradable eADF4(C16). Since implanted-associated infections occur when bacteria adhere to a surface and form a biofilm, it is essential to prevent the initial bacterial attachment [5], [19]. **An antibacterial coating such as eADF4(C16) can inhibit this initial colonization and degrade when it is no longer required. This approach enables more tantalum particles to be embedded within the PEKK implant in an effort to achieve improved strength and osseointegration, while maintaining antibacterial activity for an adequate timeframe.**

4.5 Anticipated Results and Commercial Applications of Research

As part of the research, the following materials will be tested: PEKK, PEKK/tantalum composite, PEKK/eADF4(C16) composite, and PEKK/tantalum/eADF4(C16) composite. It is anticipated that PEKK will enable significant microbial attachment and exhibit no osseointegration capability, whereas the PEKK/tantalum composite should promote effective osseointegration, but have limited antibacterial activity [14]. The PEKK/tantalum composite should also exhibit improved mechanical properties compared to the pristine PEKK material [12]. In contrast, the PEKK/eADF4(C16) composite should demonstrate a significant reduction in microbial attachment and limited to no osseointegration capability. The effect of an eADF4(C16) coating on the compressive strength, modulus, and load cycles to failure of the implant will be confirmed, but it is believed that the coating will not substantially affect these properties. It is anticipated that the proposed PEKK/tantalum/eADF4(C16) composite will achieve successful osseointegration, while maintaining adequate strength and antibacterial activity.

There are several factors that are supporting the growth of the bone graft market, including: an increased incidence of bone and joint disorders as well as orthopedic diseases, a rising number of road accidents, and technological advances in surgical procedures. There has been a gradual shift from autologous grafts to bone substitutes as a result of product availability and positive clinical outcomes [20]. **It is anticipated that the suggested bone substitute will improve upon current commercial and prospective bone substitutes by maximizing both antibacterial and osseointegration capabilities while maintaining adequate mechanical strength. Due to the expanding market potential of bone substitutes and the anticipated superiority of the proposed solution, it is likely that the PEKK/tantalum/eADF4(C16) composite will be commercially viable.**

5.0 Research Objectives

The objectives of the proposal are first, to construct a polymer-metal composite made from PEKK, tantalum, and eADF4(C16), and second, to test the antibacterial, mechanical, and osseointegration properties of the implant (Figure 1). Since implant failure can result from

infection, inadequate mechanical properties, and/or lack of osseointegration, the experiments described in the following sections are warranted. The goal is to create a bone substitute that can be used successfully in future clinical applications.

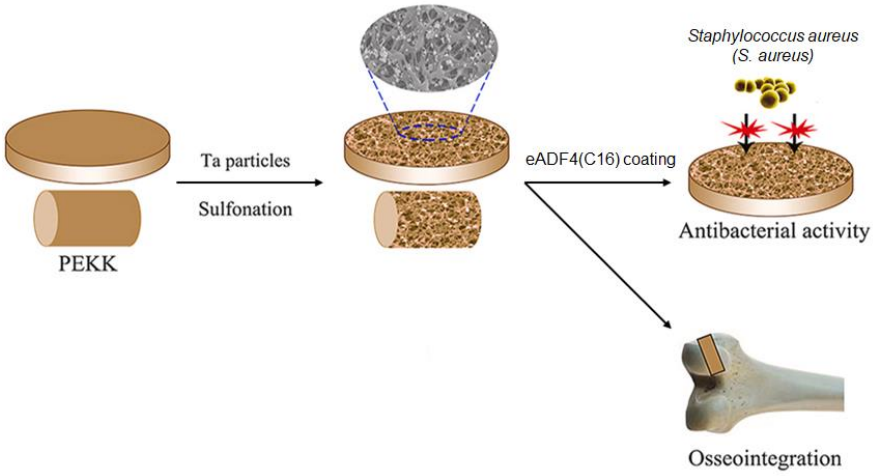

Figure 1: The development of the PEKK/tantalum/eADF4(C16) composite involves several steps. Modified from [14].

The development of the proposed polymer-metal composite will be accomplished through the following Specific Aims:

1. Prepare the polymer-metal composite made from PEKK, tantalum, and eADF4(C16).

a) Create a porous PEKK structure containing tantalum microparticles via a sulfonation reaction. Sulfonation has been used successfully to make porous PEKK structures in a previous study [14].
b) Assess the viability of dip coating the PEKK/tantalum composite in an eADF4(C16) solution to create the final product. Dip coating in eADF4(C16) has previously been used to create antibacterial silicone surfaces [17].

2. Test the antibacterial and mechanical properties of the polymer-metal composite *in vitro*.

a) Perform a bacterial counting assay to assess the adhesion of *S. aureus* to the composite [14].
b) Use scanning electron microscopy (SEM) to qualitatively assess the bacterial infestation of *S. aureus* on the composite [17].
c) Perform compression, tensile, and fatigue testing to evaluate the suitability of the composite as a bone substitute.

3. Test the osseointegration capabilities of the polymer-metal composite using a rabbit implantation model.

a) Perform histological examination of the implant interface to evaluate the extent of new bone formation.
b) Evaluate the bonding strength of the composite-to-bone interface via push-out tests.

6.0 Research Plan

6.1 Summary of Project Tasks

6.1.1 Specific Aim 1

Experiment: The first step in making the polymer-metal composite involves putting tantalum microparticles into a 98% sulfuric acid solution at room temperature. The concentrated sulfuric acid suspension with tantalum particles will be magnetically stirred for 3 hours, followed by ultrasonic stirring for an additional 3 hours to disperse the particles. After being washed and dried, dense PEKK samples will be made using a cold pressing-sintering technique. The powders will be placed into molds and pressed using a tablet machine at a pressure of 5 MPa. The samples will then be sintered in a muffle furnace operating at 355°C for 6 hours. After polishing with abrasive paper, the PEKK will be soaked for 15 minutes in sulfuric acid without particles as well as in sulfuric acid containing 20 wt% tantalum particles. The sulfonated PEKK without particles will serve as the control. All samples will be soaked in deionized water for 24 hours to remove residual sulfuric acid and then will be ultrasonically cleaned and dried [14].

Since coating PEKK with eADF4(C16) has not been done in the past, it is important to evaluate the efficacy of this technique in creating the desired composite. First, a cleaning step will be performed in which the samples will be dipped into isopropanol for 10 seconds. Afterwards, the samples will be dipped for 5 minutes into a 10 mg/mL eADF4(C16) solution and then left to dry. The samples will be cleaned with isopropanol for a second time before they are ready for use in subsequent studies [17]. To ensure efficient osseointegration *in vivo*, the ends of the cylindrical composite will be cut to expose the tantalum to the bone surface.

At the end of Specific Aim 1, the following specimens will be created: PEKK, PEKK/tantalum composite, PEKK/eADF4(C16) composite, and PEKK/tantalum/eADF4(C16) composite.

Benchmarks for Success: Fourier transform infrared (FTIR) spectroscopy can be used to confirm the presence of sulfonate groups and therefore validate the success of the sulfonation reaction in the creation of a porous PEKK structure [21]. The thickness of the eADF4(C16) coating will be measured using atomic force microscopy to ensure that the dip coating procedure was effective [17].

6.1.2 Specific Aim 2

Experiment: To assess the antibacterial properties of the proposed bone substitute, a bacterial counting assay will be performed on the samples prepared during Specific Aim 1. A *S. aureus* suspension containing 1×10^7 colony forming units will be inoculated on each sample and incubated at 37°C for 24 hours. The samples will be put into phosphate-buffered saline before being subjected to vortexing in order to detach the bacteria. A 60 µL diluted suspension of bacteria will be spread onto nutrient agar and incubated at 37°C for 24 hours, after which counting will be performed [14]. Additional samples inoculated with *S. aureus* will also be analyzed using SEM to confirm the extent of biofilm formation. The samples will be fixed in paraformaldehyde solution, washed, dried, and sputter coated with platinum before being examined [17].

Mechanical testing will also be performed on all samples to determine what effect tantalum and eADF4(C16) have on the mechanical properties. The compressive strength, modulus, and load cycles to failure will be determined using a universal testing machine [22], [23].

Benchmarks for Success: The PEKK/tantalum/eADF4(C16) composite elicits a significant reduction in bacterial adhesion compared to other samples and prevents the formation of biofilms. In addition, the PEKK/tantalum/eADF4(C16) composite exhibits similar mechanical properties to bone.

6.1.3 Specific Aim 3

Experiment: A rabbit implantation model will be used to study the osseointegration capabilities of the implant *in vivo*. A total of 16 rabbits will be divided into 4 groups to test the osseointegration of PEKK, PEKK/tantalum composite, PEKK/eADF4(C16) composite, and PEKK/tantalum/eADF4(C16) composite. The rabbits will be sedated in order to introduce a femur defect and insert the sample implants. The femurs containing the implants will be removed after 4 and 12 weeks to check the progression of osseointegration [14].

Histological tissue sections will be prepared and stained with Van Gieson's picrofuchsin which stains mineralized bone tissues red. An optical microscope will be used to visualize the implant interface to evaluate the extent of new bone formation [14].

The bonding strength of the composite-to-bone interface will be determined via push-out tests. A universal testing machine will be used to apply loads up to 600 N onto femurs containing implants [14].

Benchmarks for Success: The PEKK/tantalum/eADF4(C16) composite elicits a significant increase in new bone formation compared to other samples tested.

6.2 Performance Schedule

It is anticipated that the proposed research will take approximately 18 months to complete (Table 1).

Table 1: Performance schedule for the proposed research.

Task	Duration
Specific Aim 1	4 months
Specific Aim 2	8 months
Specific Aim 3	6 months

7.0 Commercialization Potential

7.1 Description of Company

This project will be executed by principal investigator Dr. Catherine Trojanowski, who will be assisted by 1 postdoctoral associate, 2 laboratory technicians, and 2 graduate students working in the Applied Biomaterials Laboratory at North Point University. This laboratory is outfitted

with the majority of the required equipment; the remaining equipment can be found at other facilities on campus as described in Section 10.

7.2 Commercial Applications

The global bone graft market size was valued at 2.78 billion USD in 2020 and is expected to increase at a compound annual growth rate of 5.8% from 2021 to 2028 (Figure 2). Factors supporting the market growth of bone grafts include: an increased incidence of bone, joint, and orthopedic disorders, a growing number of road accidents, and technological advances in surgical procedures. The dominant market for bone grafts is North America. In 2020, North American sales generated over 40% of the revenue in the industry. As a result of commercially accessible novel products, a strong healthcare system, and high healthcare expenditure, North America, and in particular the United States, is an ideal market for innovative bone graft solutions [24].

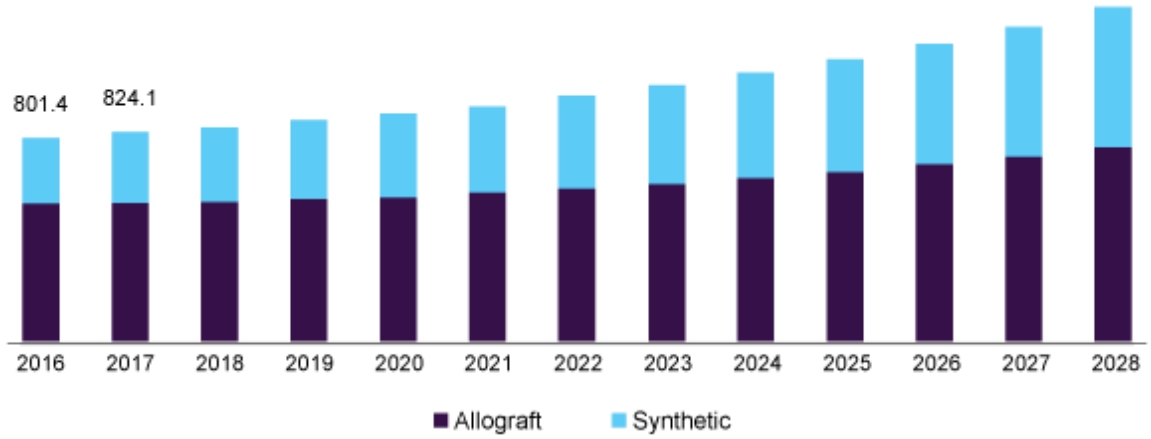

Figure 2: United States bone graft market size, by material type, 2016-2028 (USD Million). The original figure can be found in [24].

There has been a gradual shift from autologous grafts to bone substitutes as a result of product availability and positive clinical outcomes [20]. The use of bone substitutes is expected to grow significantly in the foreseeable future due to an increase in patient acceptance resulting from the products' biocompatibility and safety. Furthermore, patients receiving bone substitutes benefit from a decreased surgical duration, controlled blood loss, and reduced pain [24]. The proposed solution is a novel bone substitute that is mechanically robust, allows for osseointegration, and has antibacterial properties, making it well-positioned to succeed in today's market.

7.3 Advantages of Technology over Existing Technologies

Many current bone substitutes lack mechanical strength which limits their application to low-weight-bearing areas [3]. Furthermore, most of the commercial products available are not designed to inhibit bacterial colonization, which can cause pain, infection, implant failure, and even death [4], [5]. Commercial calcium phosphate bone substitutes are available as injectable pastes or moldable semi-solid cement and include Norian SRS, α-BSM, BoneSource, Mimix, and CopiOs. There are also tricalcium phosphate products available such as Allogran-R, Cellplex, Cerasorb M, chronOS, Conduit, and Vitoss, but these bone substitutes are notably brittle. In

addition, a coralline hydroxyapatite-based product called Pro Osteon has been developed, however it is also particularly brittle. Lastly, commercial calcium sulfate bone substitutes include Osteoset, BonePlast, OsteoMax, and Stimulan, but these products resorb faster than bone and may be associated with high rates of serous wound drainage [25].

A recent advancement in bone substitute research involved the incorporation of Si_3N_4 and tantalum microparticles into PEKK which resulted in a strong substitute capable of osseointegration and antibacterial activity. However, it was found that tantalum is more effective than Si_3N_4 in promoting osseointegration while Si_3N_4 exhibits superior antibacterial activity [14]. Since Si_3N_4 is not biodegradable, there is a constant antibacterial effect which may not be necessary for clinical applications as infections usually occur within a few months postoperatively [19]. In addition, the constant presence of Si_3N_4 reduces the osseointegration capability of the implant, as less tantalum can be embedded within the PEKK material.

To overcome these limitations, a porous PEKK implant containing tantalum microparticles will be engineered and coated with biodegradable eADF4(C16). The resulting composite should allow for enhanced strength and osseointegration, while maintaining antibacterial activity for an adequate timeframe. It is anticipated that the proposed solution will achieve a more durable bone-implant interface and enable a quicker patient recovery time compared to commercial and prospective bone substitute materials.

8.0 Qualifications of the Principal Investigator

Dr. Catherine Trojanowski has over 25 years of experience in materials science, biomaterials, and biomedical engineering. She graduated with a BEng in Biomedical Engineering from Southlake University and then went on to complete a MSc in Materials Science at the University of Newmarket. After graduating, she worked at Killarney Medical Ltd. for 3 years and was in charge of testing bone substitutes to ensure they met the necessary regulations. This experience inspired her to pursue a PhD at North Point University where she studied antibiotic release from calcium sulfate bone substitutes. Dr. Trojanowski currently runs the Applied Biomaterials Laboratory at North Point University. Her research focuses on bone tissue regeneration and the development of novel polymeric-based bone substitutes.

9.0 Consultant and Subcontracts Required to Conduct this Research

No subcontracts are needed to conduct this research, as all requisite expertise and equipment can be found at North Point University. Two professors will serve as consultants for this project and a third will assist with veterinary surgery. From the Industrial Design Laboratory, Dr. Amber Beaumont will be the advisor and point of contact. In addition, a PhD student will assist the project team with the use of laboratory equipment. Similarly, Dr. Robert Kingsley from the Advanced Material Laboratory will provide advice on material testing and characterization and a PhD student will support the team as they perform experiments. Lastly, Dr. Barbara Wilkinson will be responsible for conducting all required animal surgeries.

10.0 Equipment, Instruments, Computers and Facilities

All required facilities for conducting the research are located at North Point University, with a portion of the necessary equipment and instruments located in the Applied Biomaterials Laboratory (Table 2). The Industrial Design Laboratory contains the required tablet press machine, muffle furnace, laser cutter, and dip coating unit, while the universal testing machine, FTIR spectrometer, atomic force microscope, scanning electron microscope, and sputter coater can be found in the Advanced Material Laboratory. Lastly, animal surgery will be performed at the John Speck Surgical Ward of the School of Veterinary Studies.

Table 2: Required equipment and instruments for each specific aim.

Specific Aim 1	Magnetic and ultrasonic stirrer, laboratory oven, tablet press machine, muffle furnace, ultrasonic cleaner, dip coating unit, laser cutter, FTIR spectrometer, atomic force microscope
Specific Aim 2	Incubator, vortex mixer, scanning electron microscope, sputter coater, universal testing machine
Specific Aim 3	Surgical instruments, saw microtome, optical microscope, universal testing machine

SUMMARY

PROPOSAL BUDGET

FOR NSF USE ONLY

ORGANIZATION	PROPOSAL NO.	DURATION (MONTHS) Proposed	Granted
North Point University, Applied Biomaterials Laboratory			
PRINCIPAL INVESTIGATOR/PROJECT DIRECTOR Dr. Catherine Trojanowski	AWARD NO.		

A. SENIOR PERSONNEL: PI/PD and Other Senior Associates (List each separately with title, A.6, show number in brackets)	NSF Funded Person-mos. CAL	Funds Requested By Proposer	Funds Granted By NSF (If Different)
1. Dr. Catherine Trojanowski, PI/PD	18	$195,000	$
2. Dr. Robert Kingsley, Consultant	18	$195,000	
3. Dr. Amber Beaumont, Consultant	4	$43,000	
4. Dr. Barbara Wilkinson, Surgeon	3	$50,000	
5.			
6. (0) OTHERS (LIST INDIVIDUALLY ON BUDGET EXPLANATION PAGE)			
7. (4) TOTAL SENIOR PERSONNEL (1–5)			
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)			
1. (1) POST DOCTORAL ASSOCIATES	18	$82,000	
2. (2) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	18	$150,000	
3. (4) GRADUATE STUDENTS			
4. (0) UNDERGRADUATE STUDENTS			
5. (0) SECRETARIAL - CLERICAL			
6. (0) OTHER			
TOTAL SALARIES AND WAGES (A+B)		$715,000	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)			
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A+B+C)		$715,000	
D. PERMANENT EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.) **(Do not use for Phase I)**			
TOTAL PERMANENT EQUIPMENT			
E. TRAVEL 1. DOMESTIC (INCL. CANADA AND U.S. POSSESSIONS			
2. FOREIGN **(Do not use for Phase I)**			
F. PARTICIPANT SUPPORT COSTS 1. STIPENDS $ 20,000 and $ 23,000 2. TRAVEL _____ 3. SUBSISTENCE _____ 4. OTHER _____			
(4) TOTAL PARTICIPANT COSTS		$86,000	
G. OTHER DIRECT COSTS			
1. MATERIALS AND SUPPLIES		$60,000	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION		$4000	
3. CONSULTANT SERVICES			
4. COMPUTER (ADPE) SERVICES			
5. SUBAWARDS			
6. OTHER			
TOTAL OTHER DIRECT COSTS			
H. TOTAL DIRECT COSTS (A THROUGH G)		$865,000	
I. INDIRECT COSTS (SPECIFY RATE AND BASE)		$715,000 × 2.5	
TOTAL INDIRECT COSTS		$1,787,500	
J. TOTAL DIRECT AND INDIRECT COSTS (H+I)		$2,652,500	
K. FEE (If requested; maximum equals 7% of J)			
L. TOTAL COST AND FEE (J + K)		$2,652,500	$

PI/PD TYPED NAME & SIGNATURE	DATE	FOR NSF USE ONLY
Dr. Catherine Trojanowski *CTrojanowski*	8/24/2021	INDIRECT COST RATE VERIFICATION
CO. REP. TYPED NAME & SIGNATURE	DATE	Date Checked / Date of Rate Sheet / Initials-DGA
Dr. Kevin Johnson *KJohnson*	8/24/2021	

12.0 References

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