Effect of Curing Time on Mechanical Properties of PMMA Bone Cement

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DEDICATION

I dedicate this thesis to my parents and spouse.

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List of Abbreviations

PMMA	Poly methyl methacrylate
Ti	Titanium
3PB	Three Point Bend

List of Technical Symbols

B	Thickness of the 3PB specimen
d	Deflection of the 3PB specimen
E	Young's modulus
N	Number of fatigue cycles
P	Load
S	Span of the 3PB specimen
σ_f	Flexural strength or Fracture Strength
υ	Poisson's ratio
W	Width of the 3PB specimen

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Abstract

Bone cement is commonly used in orthopedic surgeries of human and animal. The most common bone cement material used is poly methyl methacrylate, or PMMA. Most commercially available PMMA bone cements for human are Cobalt (Biomet, Inc.), Simplex (Stryker, Inc.), and Palacos (Heraeus Company) while for animal, available PMMA bone cements are Biomedtrix, Jorgensen, etc. One of the major drawbacks of PMMA cements that are used for human and animal orthopedic surgeries is strong exothermic reaction that happens during the curing of PMMA cement. The increased temperature can cause damage to the surrounding bone cells as well as the tissues. There are significant differences in the maximum temperature rise of the bone cement samples for different curing time of the PMMA. The thermal expansion of the cement would have generated large residual stress which would affect the cement stress distributions at the stem cement interface. The residual stresses, caused by the exothermic temperature difference, can influence the local strain energies and the fracture at the bone-cement interface. Properties of bone cements are investigated by many researchers but the effects of curing time on the mechanical properties remain unaddressed. In addition, the effects of curing time on the interfacial strength between implant and cement interface due to pull out tensile force under static and cyclic loading are not known yet. Such knowledge has clinical importance since the clinicians will know the time period requires for the cement to reach to its maximum mechanical capabilities after surgery. The goal of this study is to understand how the mechanical behavior of implant-cement interface is influenced by the change of mechanical properties of two different bone cements, which are differentiated by curing time.

This study hypothesizes that the curing temperature and time influence the mechanical properties of the cement adjacent to the implant, which resulted in the variability in bonding strength between the implant and cement. To test this hypothesis, this study measured the flexural strength, hardness, and morphology of the human bone cement (HBC) and veterinary bone cement (VBC) at different curing times. In addition, this study measured the shear strength at the interfaces of implant/HBC and implant/VBC samples during static and stepwise cyclic tests at different curing times. Stryker Simplex P and BioMedtrix 3 poly methyl methacrylate (PMMA) cements were used as an HBC and VBC, respectively. The HBC and VBC cement samples were cured for 10, 30, and 60 min and then conducted flexural, hardness, and interface fracture tests to evaluate the curing effect on mechanical behavior of each of the cements. It has been found that the curing time significantly increases the values of flexure and hardness properties of each cement and shear strength of implant/HBC and implant/VBC.

CHAPTER 1

Introduction

1.1 Summary

The cemented total joint prosthesis is one of the most frequent operations in the orthopedic fields. Polymethyl methacrylate (PMMA) bone cements are widely used to fix artificial joints for filling the free space between bone and prostheses. The big challenges of orthopedic research are the loosening introduction of implant or breakage of cement at the implantation sites[1]. The mechanical failure of the implant-cement interfaces has been proposed as one of the most possible causes for eventual clinical loosening of cemented total joint prosthesis. It is an active area of research to develop an optimal implant-cement interface by improving mechanical performances of PMMA bone cement. PMMA bone cement, which are used in human and veterinary orthopedic surgeries show fast and slow curing characteristics. The difference of mechanical performances between fast and slow curing of PMMA bone cement is not known. Specifically, the fast and slow curing characteristics of these bone cement on bonding strength between implant and cement interface is unknown. A comparative study is required to determine the effect of different curing time on the mechanical properties of PMMA bone cement. The suitability of inclusion of the additives to overcome problems of conventional human and animal PMMA bone cement for the orthopedic applications requires complete understanding of the influence of the curing on the mechanical properties. In addition, such studies are required for the design of novel PMMA based composite bone cement.

1.2 Bone Cement

Bone cement is used in various orthopedic surgeries for both human and animals. Among the many potential bone cement materials, polymethyl methacrylate (PMMA) bone cement has been successfully used in those surgeries mostly because of its strong mechanical bonding with implant. PMMA bone cements commercially available as two-component materials, a powder (PMMA beads) and a liquid (MMA monomer). These two components are mixed at 2:1 ratio and polymerization occurs. The current most commercially available human PMMA bone cements are Cobalt (Biomet, Inc.), Simplex (Stryker, Inc.), and Palacos (Heraeus Company). Figure 1.1 (a) shows Simplex (Stryker, Inc.) bone cement, which is used as a human PMMA bone, cements in this study. The current most commercially available animal PMMA bone cements are BioMedtrix, Patterson, Jorgensen Labs

veterinary bone cement. Figure 1.1 (b) shows Bio Medtrixbone cement, which is used as a veterinary bone cement in this study.

(a)

(b)

Figure 1.1 PMMA bone cement used in the study: (a) Stryker surgical Simplex P Human bone cement and (b) Biomedtrix 3 Veterinarian bone cement.

Several drawbacks associated with PMMA bone cement limit its efficacy. Some of the drawbacks are: (1) PMMA cement adheres inadequately to the bone surfaces (no bioactivity)[2], (2) it has a high exothermic reaction temperature[3] and (3) it exhibits monomer toxicity[4].Particularly, enough bonding strength of cement with the implant and bone is required for the design of optimal bone cement, which may be greatly influenced by the high exothermic temperature. It is important to

determine temperature changes in the PMMA bone cements during curing and how the different level of curing time and temperature influences the mechanical properties of bone cement and bonding strength between implant and cement. The knowledge regarding change of mechanical properties of bone cements with different curing time is required for their use in bone cement.

1.3 Titanium Implant

Titanium alloys exhibit attractive properties such as biocompatibility, mechanical strength, corrosion resistance, safety and ductility. Titanium (Ti) is used as an orthopedic and orthodontic implant material for excellent biocompatibility [5]. The dissolution of Ti into body is very trivial because Ti metal surface can spontaneously form a stable and inert layer of titanium dioxide (Ti_2O), which will prevent Ti metal from reacting with body fluid [6]. Ti has its excellent biocompatibility (high corrosion resistance, low ion-formation tendency, low level of electronic conductivity, etc mostly owing to this oxide layer. Comparing to commercial pure Ti, Ti alloys such as Ti-6Al-4V exhibit solid solution hardening and have lower fusion temperatures and better ductility [7]. Among the various Ti alloys, Ti-6Al-4V, which was used in this study, is the most widely used as implant because of its better physical and mechanical properties in comparison to pure Ti. Figure 1-2 shows the Ti-6Al-4V rod (76 mm long x 3.96 mm diameter) that has been used in this study as Ti implant.

Figure 1.2 Ti-6Al-4V rod that was used in the study.

The titanium alloy (6Al-4V ELI) was manufactured according to ASTM B 348 standard. It is grade 23 and biocompatible. All Ti rod was cut using precision shear cut machine from a same lot.

1.4 Curing Time

PMMA bone cement is a polymeric material. It cures by exothermic reaction during its polymerization process[8]. The reaction time (curing time) and temperature (curing temperature) creates thermal stress to the bone cement as reported by various researchers [9, 10]. When the bone cement is injected into bone in the pliable state, it starts polymerizing to solidify. This process will generate great

amounts of heat causing the temperature at which the cement is located to be higher than body temperature and cause damage on the body tissue. The prolonged curing time and temperature can cause damage to the surrounding bone tissues around implant. Different types and concentrations of additives (e.g $BaSO_4$, gentamicin, ZrO_2) added to the PMMA bone cement affect the exothermic reaction differently resulted in different curing time. The viscosity of cement depends upon curing time. Low and high curing time bone cement corresponds to high viscous and low viscous bone cements. Human PMMA cement (Stryker Simplex ® P bone cement) usually takes 10 minutes for full curing, whereas Bio Medtrix Veterinary bone cement usually takes 30 minutes for full curing. This study will measure the effect of different curing time on the surface roughness, hardness, flexural strength, and fatigue properties of Stryker Simplex ® P bone cement and Bio Medtrix 3 Veterinary bone cement.

Penetration tests (Kallol et al., Materials Journal 2019) showed it takes at least 10 minutes for complete curing of HBC. Since it is irrational to conduct mechanical tests before full curing therefore, this study conducted mechanical tests on HBC after 10 minutes of curing. Similar penetration tests showed that at least 30 minutes is required for complete curing of VBC. Therefore, this study conducted mechanical tests on VBC at 30 minutes of curing. Thermal tests (K. Serbetci et al., Polymer Testing, 23, 145–155, 2004)) on PMMA based bone cement shows that it takes at least 60 minutes for the cement to reach human body temperature (37°C). Therefore, this study used 60 minutes as the limiting value for mechanical experiments for HBC and VBC. Thirty and sixty minutes for both HBC and VBC were selected since the aim of this study was to compare the mechanical properties after complete curing at different time. Longer time of curing could not be done due to the shortage of materials.

Orthopedic surgery types and required curing time guides the types of cement to be used. When cement needs to be applied as a paste (low viscous) to the defect sites by injection (for example vertebral fusion), it is preferable to use long curing and low viscous cement. When cement needs to be applied as doughy (semi-cured) phase to the defect site (for example total hip, knee joint replacement orthopedic surgeries), short curing process of cement is used for anchoring artificial joints. So both short and long curing times are practiced in orthopedic applications.

1.5 Implant Fixation Problem

Although cemented fixation provides more long-term stability, the clinical loosening of cemented replacement has been reported also. In USA, there are approximately 600,000 cases of poor union and 100,000 cases of nonunion of implant with surrounding tissue each year[11]. Many manufacturers have recalled their hip implants (including Johnson & Johnson, DePuy, and Zimmer Durom)[12]. A patient's age, sex, weight, diagnosis, activity level, surgery condition, and implant choice influence the longevity of the cemented fixation. The primary cause of failure of cemented joint replacements is aseptic loosening of the components, which may arise from mechanical failure of the cement mantle surrounding the implant [13]. It has been pointed out that the debonding of stem-cement interface enables gapping and sliding between the stem and cement[14, 15]. Revision surgeries are required for implant failures that are costly and painful.

1.6 Factors Affecting Cement with Adjoining Material Bonding Properties

In every case where dissimilar materials are bonded together and undergo a subsequent change of dimension due to change of temperature, loading, or moisture content, stresses develop at the interface due to mismatch of material properties. The magnitude of the stresses can be very large and may have a significant influence on the life of each material in the bond as well as the interface. Research found that strength mismatching controls the fracture of bimaterial interface made with different kinds of steel [16], bone-cement interface [17] and bonded dental ceramics [18].There is hardly any data available in literature which shows the effect of material mismatch created by difference of curing properties (curing time and temperature) on the fracture resistance of the implant/cement interface. There is a need to evaluate the material mismatch effect on interface strength of an implant and cement for modeling the fracture behavior of implant and cement. This study will measure the effect of different curing time on the bonding strength of Stryker Simplex ® P bone cement and BioMedtrix 3 Veterinary bone cement with titanium implant under both static and cyclic loading conditions.

1.7 Measurement Approaches for Evaluation of Curing Effect

The purpose of this project was to measure mechanical properties of two different PMMA cement samples based on curing time: low curing time (HVBC) and high curing time (LVBC). To evaluate the impact of the internal morphology on cement mantle having different curing time, internal microstructure (roughness) and mechanical performance (flexural strength) of each group of cement were measured for each group of bone cements. Three Point Bending (3PB) tests using ASTM standard were performed at room temperature on each specimen to test the flexural stress-strain properties of the bone cements with various curing time. The main reason of using 3PB test is the ease of specimen

preparation and testing. Interface fracture strength is the stress when the bonded specimen failed. Fatigue life defines the number of stress cycles that a specimen sustains before failure occurs. Universal testing machine (UTM) is usually used to conduct the static and fatigue pull out and compression test. The interface fracture stress of implant-HVBC and implant-LVBC were compared to determine whether the curing time has any effect on the bonding strength of the implant-cement union.

The type of mechanical testing that has been used most frequently for the evaluation of the implant-cement interface is a force-based or stress based test such as tensile or push-out test [19, 20]. Wang et al. [21] found that these tests cannot reveal the actual bonding property of the interface because of the significant influence of surface roughness on the measured adhesion and failure to account for the mismatch of elastic modulus across the interface [22]. The results obtained from the pull out tension experiment of implant/cement interface can be used to predict the strength mismatch effect that is created by different bone cement on their respective interface fracture strength. This study will measure the effect of different curing time on the bonding strength of Stryker Simplex ® P bone cement and BioMedtrix 3 Veterinary bone cement with titanium implant at two different loading conditions: static and cyclic loading.

1.8 Hydration Effect on Implant/Cement Interface

Very few works are reported in literature about the effect of corrosive environments on the mechanical properties of adhesive joints[23]. Therefore, the present study intends to contribute for a better understanding of the effect of saline solution on the mechanical properties of single-lap adhesive joints. Numerous hydration methods have been reported in the literature to imitate the physiological condition of bone cement *vivo* condition. These methods include exposure to formalin [24, 25] and saline [25, 26]. The majority of the hydration methods have been shown to have some measure of irreversible effects on the material properties of biomaterials. Accurate knowledge of interface fracture strength of titanium/cement is the central for the prediction of failure and development of injury treatment protocols. Often when the cement properties are measured experimentally, the cement specimens have to be chemically preserved prior to or during testing under hydrated condition. Understanding the effect of the hydration on the material properties of the bonding strength between implant and cement is important. Degradation of properties due to hydration may lead to reduction of values of the cement mechanical properties. A salient question is, therefore, whether the preservation of titanium/cement using saline affects the bonding strength of titanium/cement interface. To answer these questions, a pull out tension test setup was constructed to perform experiments after keeping the titanium/cement samples in Human Buffer Saline for 5 days at about 37ºC.

1.9 Exothermic Temperature Effect on Implant/Cement Interface

Residual stresses resulting from the shrinkage of poly methyl methacrylate (PMMA) bone cement have been implicated in the formation of cracks in cement mantles following total hip arthroplasty[27]. High stress intensity are inherent at the corner of the bi-material joints due to both thermal and mechanical loading [28]. According to Reedy [29], stress intensity can exist at an interface corner within the context of both elasticity and work hardening plasticity theory. Therefore, the initiation and propagation of cracks from the bi-material interface is a major problem in the design of bi-material joints [30]. The magnitude of the stress intensity of a bi-material specimen depends on the material and geometric properties of the joining materials[31]. The residual stresses, which are caused by the exothermic temperature difference, can influence the material properties of cement and fracture energies at the implant-cement interface [32]. This study investigates whether two cements with differentiated solidification characteristics (i.e. working and setting times), display significant differences in their residual stress characteristics at the titanium/cement interface.

1.10 Literature Review

As stated before, PMMA bone cements commonly used in human and animal orthopedic surgeries. The current most commercially available human PMMA bone cements are Cobalt (Biomet, Inc.) [33], Simplex (Stryker, Inc.) [34], and Palacos (Heraeus Company) [35]. The current most commercially available animal PMMA bone cements are BioMedtrix [36], Jorgensen Labs veterinary bone cement [37].

One of the major drawbacks of using PMMA cements for those surgeries is strong exothermic temperature that happens during the curing of PMMA cement [9]. Hingston, *et al.* [27] have showed that thermal stresses resulting from the shrinkage of polymethyl methacrylate (PMMA) bone cement have been implicated in the formation of cracks in cement mantles following total hip arthroplasty. High stress intensity are inherent at the corner of the bi-material joints due to both thermal and mechanical loading as studied Blanks-Skills, *et al*.[28]. According to Reedy [29], stress intensity can exist at an interface corner within the context of both elasticity and work hardening plasticity theory. Therefore, the initiation and propagation of cracks from the bi-material interface is a major problem in the design of bi-material joints [30]. Glieich, *et al*. [31] reported that the strength of a bi-material specimen depends on the material and geometric properties of the joining materials. The thermal stresses, which are caused by

the exothermic temperature difference, can influence the material properties of cement and fracture energies at the implant-cement interface, as studied by Zor, *et al*.[32]. The magnitude of the developed stresses during the curing can be very large and may have a significant influence on the bonding of the interface, which is unknown yet. The interfacial mechanics at the implant/cement interface is a critical issue for implant fixation and the filling of bone defects created by tumors and/or their excision as has been demonstrated by Moiduddin, *et al*. [38]. The fixation of human and animal bone cement with implants may not be the same, since the mechanism of curing of the cement is different.

1.11 Research Questions

This study was conducted based on three research questions: (1) Is there any significant difference in the morphology of cured bone cement due to the difference in curing time? (2) Is there a significant difference in the mechanical performances between high and low viscous bone cement that occurs due to difference of curing time? and (3) How does curing time influence the performances of high and low viscous bone cement under hydrated and non-hydrated condition?

1.12 Hypothesis

The interfacial mechanics at the implant/cement interface is a critical issue for implant fixation and the filling of bone defects created by tumors and/or their excision. The mechanical properties of fast and slow curing cement with implants may not be the same. Similarly the mechanism of bonding of fast and slow curing cement with implants is also different. The present study is based on the hypothesis that the differences of the material properties at implant/cement interface due to rate of curing may have significant influence on the quality of implant/cement union.

1.13 Motivation and Goal

The majority of cemented hip replacements fail due to implant loosening. One of the important factors that may affect implant loosening is the mechanical behavior of cement at the implant-cement interface. The motivation of this study is to design implant loosening free PMMA bone cement for human and animal orthopedic surgeries. The goal of the study is to understand how mechanical behavior of implant-cement interface is influenced by the change of mechanical properties of a human and animal orthopedic bone cements, which are differentiated by curing time.

1.14 Objectives

This research is aimed to study Poly Methyl Methacrylate (PMMA) bone cement having fast and slow curing properties that are used for human and veterinary orthopedic surgeries as different cement materials. This thesis has following objectives:

(1) To measure hardness of human and animal bone cement materials for different curing times (10, 30 and 60 minutes) to determine the impact of curing time on hardness.

(2) To investigate the effect of curing time on the flexural properties of bone cement materials (human and animal) by testing the specimens of 10, 30 and 60 minutes curing.

(3) To measure the interface fracture strength of titanium/cement implant from the human and animal bone cements under static loadings after curing the cement for 10, 30 and 60 minutes.

(4) To investigate the effects of curing time on the surface roughness of the bone cement materials.

(5) To measure the effect of soaking of the cured titanium/cement implant in human buffer saline (HBS) on the interface fracture strength of titanium/cement implant.

(6) To measure the interface fatigue strength of titanium/cement implant from the human and animal bone cements under cyclic loadings.

(7) To evaluate the correlation between the interface fracture strengths and hardness of the bone cement materials for different curing time.

1.15 Organization of the Thesis

There are six chapters. Chapter 1 is the introduction. Followings are the scope of works for each chapter:

Chapter 2

Experimental setup for measuring curing effect on human and veterinary bone cement

Chapter 3

1. To measure hardness of fast curing bone cement (human and high viscous) for different curing times (10, 30 and 60 minutes) to determine the impact of curing time on hardness.

2. To investigate the effect of curing time on the flexural properties of fast curing bone cement (human and high viscous) by testing the specimens of 10, 30 and 60 minutes curing.

3. To measure the interface fracture strength of titanium/cement implant from the fast curing bone cements under static loadings.

4. To investigate the effects of curing time on the internal morphology (e.g. roughness, voids) of fast curing bone cement.

Chapter 4

1. To measure hardness of slow curing bone cement (veterinary and low viscous) for different curing times (30 and 60 minutes) to determine the impact of curing time on hardness.

2. To investigate the effect of curing time on the flexural properties of slow curing bone cement (veterinary and low viscous) by testing the specimens of 30 and 60 minutes curing.

3. To measure the interface fracture strength of titanium/cement implant from the slow curing bone cements under static loadings.

4. To investigate the effects of curing time on the internal morphology (e.g. roughness, voids) of slow curing bone cement.

Chapter 5

1. To measure the interface fatigue strength of titanium/cement implant from the fast and slow curing bone cements under cyclic loadings.

2. To measure the effect of soaking of the cured titanium/cement implant in human buffer saline (HBS) on the interface fracture strength of titanium/cement implant.

CHAPTER 2

Experimental Setup for Measuring Curing Effect on Human and Veterinary Bone Cement

2.1 Summary

The goal of the study is to understand how the curing characteristics of a human bone cement (HBC) and veterinary bone cement (VBC) influence the mechanical behavior of each cement and cement bonding with an implant. This study hypothesizes that curing temperature and time influence the mechanical properties of the cement adjacent to the implant, which resulted in the variability in bonding strength between implant and cement. To test this hypothesis, this study measured flexural strength, hardness and morphology of a HBC and VBC at different curing times. In addition, this study measured shear strength at the interfaces of implant/HBC and implant/VBC samples during static tests at different curing times. This study used Stryker Simplex P and BioMedtrix 3 poly methyl methacrylate (PMMA) as a HBC and VBC, respectively. This study cured HBC cement for 10, 30 and 60 minutes and VBC cement for 30 and 60 minutes and then conducted flexural, hardness and interface fracture tests to evaluate the curing effect on mechanical behavior of each of the cements.

2.2 Introduction

PMMA bone cements commonly used in human and animal orthopedic surgeries. The current most commercially available human PMMA bone cements are Cobalt (Biomet, Inc.), Simplex (Stryker, Inc.), and Palacos (Heraeus Company). The current most commercially available animal PMMA bone cements are BioMedtrix, Jorgensen Labs veterinary bone cement. One of the major drawbacks of using PMMA cements for those surgeries is strong exothermic temperature that happens during the curing of PMMA cement. Thermal stresses resulting from the shrinkage of polymethyl methacrylate (PMMA) bone cement have been implicated in the formation of cracks in cement mantles following total hip arthroplasty. High stress intensity are inherent at the corner of the bi-material joints due to both thermal and mechanical loading. According to Reedy, stress intensity can exist at an interface corner within the context of both elasticity and work hardening plasticity theory. Therefore, the initiation and propagation of cracks from the bi-material interface is a major problem in the design of bi-material joints. The strength of a bi-material specimen depends on the material and geometric properties of the joining materials. The thermal stresses, which are caused by the exothermic temperature difference, can influence the material properties of cement and fracture energies at the implant-cement interface. The magnitude of the developed stresses during the curing can be very large and may have a significant

influence on the bonding of the interface, which is unknown yet. The interfacial mechanics at the implant/cement interface is a critical issue for implant fixation and the filling of bone defects created by tumors and/or their excision.

2.3 Materials and Methods

2.3.1 Materials

This study used Stryker Simplex® P bone cement as a HBC and BioMedtrix 3 veterinary bone cement as a VBC and titanium (Ti) alloy (Ti-6Al-4V ELI, ASTM B 348 standard, grade 23, biocompatible) of dimension 76 mm long × 3.96 mm diameter as an implant. Ti alloy from Supra Alloys, Camarillo, CA. Among the various Ti alloys, this study used Ti-6Al-4V Eli because of its better physical and mechanical properties in comparison to pure Ti for orthopedic surgeries.

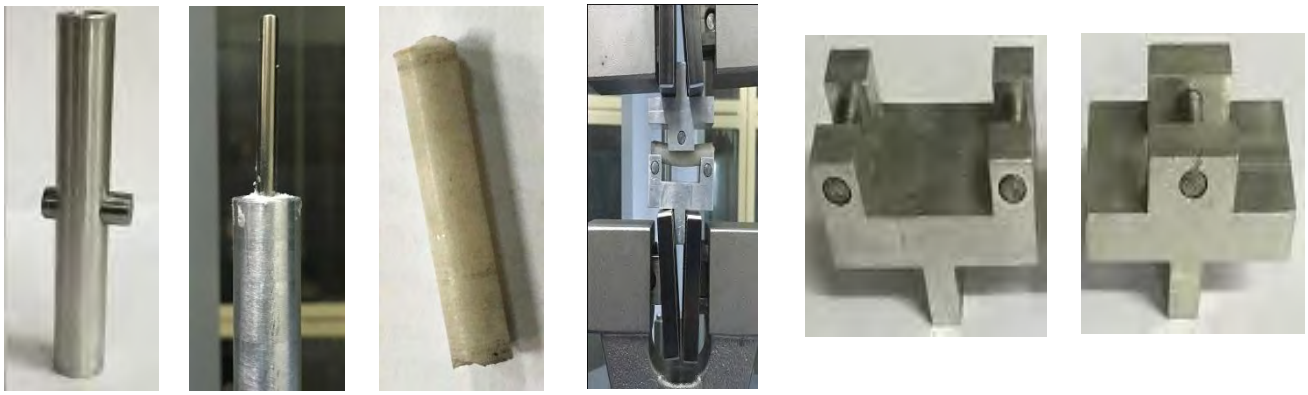
2.3.2 Experimental Design

Flexural and hardness tests were conducted on HBC and VBC samples at different curing times. Pullout static tests were conducted on Ti/HBC and Ti/VBC samples. The pre-load resulted during the curing of Ti/HBC and Ti/VBC samples was measured during the pullout static tests. This study also determined the roughness of cement joining the implant after the pullout static tests to measure the morphology of the cement near the interface between implant and cement. This study cured cement for 10, 30 and 60 minutes for HBC and 30 & 60 minutes for VBC before conducting the above tests. The reason for the selection of the 30 and 60 minutes curing time for VBC is that within 30 minutes complete curing occurs.

2.3.3 Three-Point Bend Test

A hollow cylindrical aluminum holder was prepared (length = 80 mm, outside diameter = 8.4 mm and inside diameter = 8 mm) as shown in Fig 2.1 (a) for the three-point bend tests. A rod pushed into the side hole of the holder so that cement can be cured in the hole of the cylinder without leakage. The top gripper of Shimadzu ASG -X series universal testing machine (UTM) fastened with a mirror polished Ti implant, whereas the bottom gripper of UTM fastened with the aluminum holder. The inside surface of aluminum holder was polished so that small amount of push force is necessary for breaking the interface between cement and aluminum after curing. The top gripper of UTM that contains the implant was slowly lowered so that the implant touches the top of side rod. Each group of cement was prepared by mixing 0.62 gram of PMMA powder and 310 microliter of MMA monomer. The cement was hand-mixed and poured in to the gap between implant and holder. Fig 2.1(b) shows a cured PMMA

with Ti in the holder. After the curing of HBC and VBC for a specific amount of time, the Ti rod were pulled off from cement by moving up the Ti rod with a rate 1 mm/min. To remove cylindrical cement sample from aluminum holder, a 7.5 mm diameter rod was mounted at the top gripper of UTM that pushed off the top edge of the cement. Fig 2.1(c) shows a cylindrical PMMA samples that was used for a 3PB test. Three point bend tests were performed on the cured samples using a custom made supporter and indenter (Fig 2.1(d). Two steel rollers were press-fitted in the supporter at a distance equal to the span length (32 mm). A steel roller was press-fitted in the indenter at the center. The specimens were mounted on the custom-made 3PB indenter and supporter in the test stage during the flexural tests. Shimadzu ASG -X series universal testing machine (UTM) was used for the flexural tests (2.1(d). The load and displacement were continuously recorded using trapezium X software until the failure of the specimens.



(a) (b) (c) (d) (e) (f)

Fig. 2.1(a) Aluminum mold used to prepare Ti/cement samples for 3PB and pull-out tension tests, (b) A fabricated Ti/PMMA samples, (c) A 3 PB cement samples prepared by removing the rod and aluminum rod, and (d) A 3PB bend experiment on a prepared sample (e) 3PB supporter, (f) 3PB indenter.

Flexural strength, σ_b, was calculated using:

$$\sigma_b = \frac{P_{max} S R_0}{\pi\left(R_0^4 - R_i^4\right)} \quad (1)$$

where P_{max} is the ultimate load (force at failure), S is the span length (32 mm), R_0 outer radius of cylindrical sample, and $R_i$is the inner radius of the cylindrical sample.

2.3.4 Hardness Test

A hollow cylindrical aluminum holder (length = 30 mm, outside diameter = 8.4 mm and inside diameter = 8 mm) was prepared for hardness test samples (Figure 2.2 (a). A 10 mm length and 8 mm diameter PMMA was produced following the same 3PB test samples preparation protocol as described above. Figure 2.2 (b) shows a prepared PMMA samples for a hardness test. Indentations were done at three different places on each sample for the selected curing times. Rockwell hardness number (scale R) was read out from the scale from each indentation. According to this scale, a 1/2" steel ball was used, 30 kg of preload and 60 kg of test force was applied. The load was applied for 15 s. The test was conducted at room temperature. The same test condition was applied for both HBC and VBC samples.

(a) (b) (c)

Fig 2.2(a) Hardness test sample holder, (b) a fabricated sample that be tested to find the Rockwell hardness number and (c) hardness test setup.

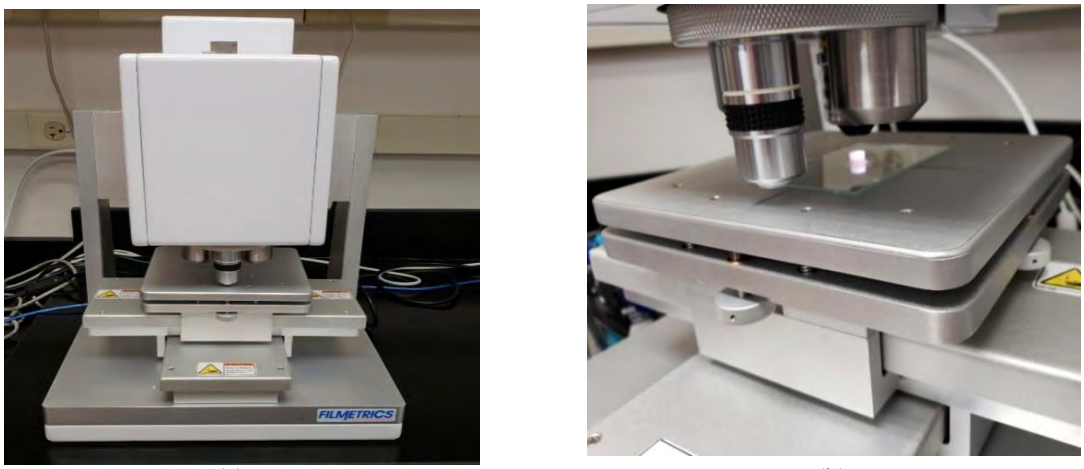
2.3.5 Pull-Out Tension Test

Another custom-made cylindrical aluminum holders with same dimension as the 3PB test holder Ti/cement samples for pull out test were prepared using the same method as 3PB tests samples. After curing each group of cement with specific time, the pullout static test was performed on the Ti/cement samples at strain rate 0.05 mm/sec until the break of Ti rod from cement. The maximum shear strength was calculated by dividing the force at the point of failure, F_{max} by the surface area of the implant in contact with the cement, $2\pi R_i L$, where R_i is the radius of implant and L is the length of implant in contact with the cement.

2.3.6 Surface Roughness Test

A Profilm three dimensional (3D) optical profiler a) from Filmetrics, Inc-USA[58] to measure the roughness of the surface at the interface between Ti and cement. The Profilm 3D uses state-of-the-art vertical scanning interferometry (VSI) combined with optional high-accuracy phase shifting

interferometry (PSI) to collect physical information of surfaces. This includes both surface morphology and topography from sub-nanometer to millimeter scale.



(a) (b)

Figure 2.3 (a) Profilm 3D optical profiler and (b) Mounting of a cement sample in the profiler.

After the mechanical test, the samples were sectioned in to 10 mm long cement samples using diamond saw cutter. Then each coupon was longitudinally cut in to four equal coupons using the saw. The inside curved surface of the section sample (were mounted on a glass slide and scanned by Filmetrics digital profiler (Fig 2.3 (b)). Profilm software was used to measure arithmetic mean height, S_a, and root mean square height, S_q, values from the captured images. S_a is the extension of R_a (arithmetical mean height of a line) to a surface. It expresses, as an absolute value, the difference in height of each point compared to the arithmetical mean of the surface. S_q represents the root mean square value of ordinate values within the definition area. It is equivalent to the standard deviation of heights. S_a and S_q parameters are used generally to evaluate surface roughness of planar surface.

(a) (b)

Figure 2.4 The sectioned samples for measuring the roughness at the interface between Ti and Cement: (a) longitudinal section view and (b) transverse section view.

2.3.7 Statistical Analysis

An independent samples t-test assuming unequal variances was performed to determine if there is a significant difference in the mean experimental test parameters of the 10, 30, and 60 minutes cured sample groups. For all statistical analysis, statistical significance was considered at $p<0.05$.

2.4 Conclusion

The novelty of the setup is that experiment can be conducted at consistent condition. Additionally, the cured sample blocks for the setup can further be used for various mechanical testing. The results of the study can be used for the determination of the appropriate time required for the PMMA cements to restore its full functional capabilities for orthopedic or orthodontic surgeries.

The limitation of the study is that there was no study conducted to find the relation of curing time on exothermic behavior of cement, which could be important in understanding the residual stress build up due to the exothermic reaction. Such experiment is important to develop a theoretical model to find a correlation between the residual stress due to curing and interface shear strength of implant/cement. The knowledge of understanding the curing effect on interface fracture strength of a titanium and cement is important for modeling the fracture behavior of titanium/cement interface due to thermal stress created by different curing temperatures.

CHAPTER 3
Effect of Curing Time on the Mechanical Behavior of Human Bone Cement

3.1 Summary

It has been found from previous studies that the time of curing of high viscous poly methyl methacrylate (HV-PMMA) cement influences the shear strength of titanium (Ti) implant/ HV-PMMA cement samples during pull out static tests, although the reason for the influence is not understood yet. This study hypothesizes that time of curing of cement influences the strength and hardness of the cement adjacent to the implant, which resulted in the variability of the shear strength between Ti and cement. To test this hypothesis, this study has conducted ASTM standard three point bend (3PB) test on a HV-PMMA cement to measure the flexural strength of HV-PMMA cement that has been cured for 10 and 60 minutes. In addition, this study has conducted pull out tension tests on Ti/ HV-PMMA cement to measure the shear strength between Ti and HV-PMMA cement that has been cured for 10,30 and 60 minutes. The hardness of the HV-PMMA cement at the adjacent to Ti has been measured using a Rockwell R hardness test scale. Two groups of samples have been produced for each type of experiments by varying the curing times: 10,30 and 60 minutes. The cement during the liquid phase has poured into a custom made mold to create the 3PB cylindrical samples. For the pull out tension tests on Ti/cement samples, the Ti implant has been fastened at the top gripper and a custom made holder that has a hole was fastened at the bottom gripper of universal mechanical test system. Cement has been poured in to the gap between implant and holder. The cement has been cured for variable time. This study found that the curing time significantly increases the values of bending and hardness properties. The study concludes that the variability of the shear strength between Ti and cement depends on the strength and hardness of the cement adjacent to the implant.

3.2 Introduction

Bone cement is commonly used in orthopedic and orthodontic surgeries. The most common bone cement material used is poly (methyl methacrylate), or PMMA. One of the major drawbacks of PMMA cement is strong exothermic reactions. Most commercially-available PMMA bone cements such as Cobalt (Biomet, Inc.), Simplex (Stryker, Inc.), and Palacos (Heraeuscompany) have been known to produce an exothermic reaction during their polymerization process. There is increase of temperature

due to the exothermic reaction that can cause damage to the surrounding bone cells as well as the tissues. Other reported problems include loosening of the bone cements at the bone-cement interface[39].The residual stresses, caused by the exothermic temperature difference, can influence the local strain energies at the bone-cement interface[32]. In our previous study, it was found that significant differences in the curing properties (maximum curing temperature and time to reach maximum curing temperature) present between PMMA (control) and various nano particles added to the cements[40]. The thermal expansion of the cement would have generated large residual stress which would affect the cement stress distributions at the stem cement interface [41]. The accumulation of stresses due to modulus and temperature differences at the interface of implant-cement can be varied with the curing time. According to the author's knowledge, there is no study conducted to determine the effect of curing time on the strength and hardness of PMMA cement. Such knowledge has clinical importance since the clinicians will know the time period requires for the cement to reach to its maximum mechanical capabilities after surgery.

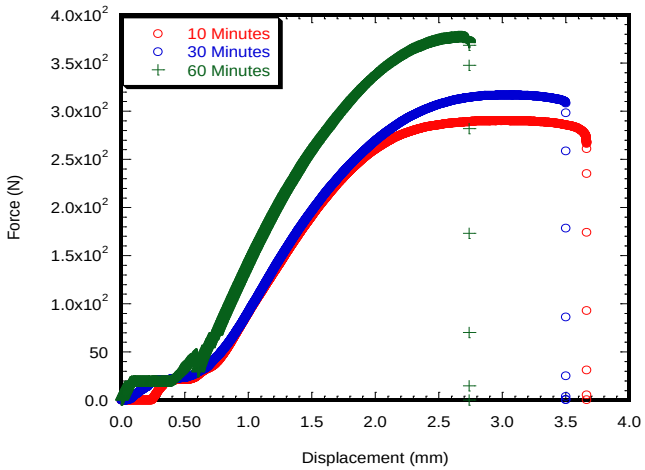
3.3 Materials and Methods

Discussed in Chapter 2

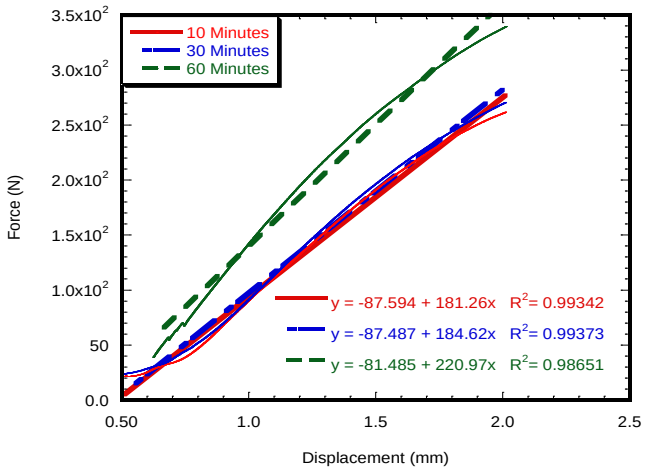
3.4 Results and Discussion

3.4.1 Effect of Curing Time on Flexural Strength

The effects of curing time on the HV-PMMA samples can be observed in Figure 3.1. The red curve corresponds to the curing time of 10 minutes and the green curve corresponds to the curing time of 60 minutes. It is observed from the figure that as the curing time increases from 10 minutes to 60 minutes, the maximum bending load increases from about 275 N to 375 N, suggesting more than 35% increase of the maximum load. Furthermore, the stiffness also increases as the curing time is increased. However, the maximum deformation is decreased with increasing the curing time because the cement becomes harder at the longer curing time.



(a)



(b)

Figure 3.1(a) Load-displacement graph and (b) slope for an implant-cement during 3PB test with respect to curing time (HBC).

Figure 3.2 shows a comparison of the average maximum bending forces between 10, 30 and 60 minutes curing time for multiple numbers of tests. The dispersions of the measured data in each case are also shown in Figure 3.2 through the respective error bars. The graph indicates that the impact of the curing time is more significant on the bending force for 60 minutes curing, although in both cases forces are increasing with the curing time.

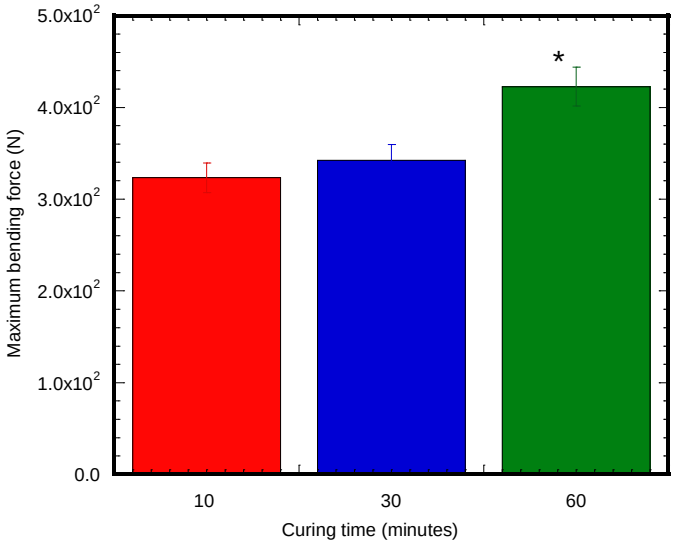


Figure 3.2 Bar diagram showing the curing effect on the maximum bending force (HBC).

Table 3-1 Summarizes the calculated results of the average bending strengths and the hardness for the three different curing times (10 minutes, 30 minutes and 60 minutes). It can be observed that as the curing time is changed from 10 minutes to 60 minutes, the average bending strength increases by 24% .

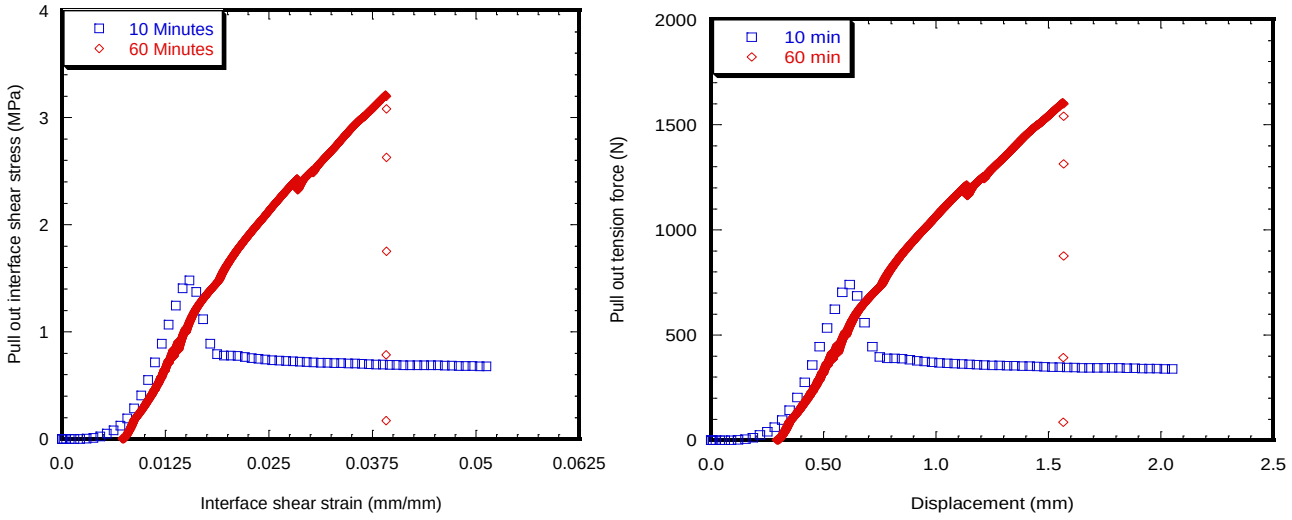
Table 3-1 Curing effect on bending and hardness in relation to curing time (HBC)

Experimental parameters	**Curing time**		
	10 min	**30 min**	**60 min**
Bending Strength (MPa)	50.56 ± 0.28 (n=4)	56.24 ± 2.55 (n=6)	62.57 ± 0.21 (n=7)
Hardness (Rockwell R)	64(n=3)	64 (n=3)	79(n=3)

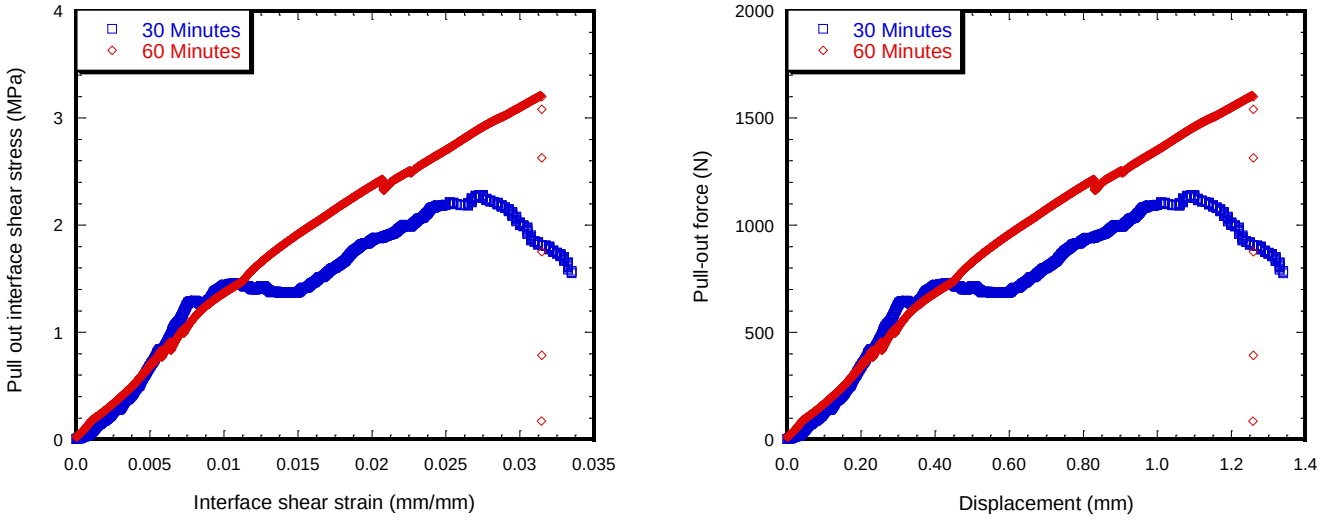
3.4.2 Effect of Curing on Interface Shear Strength

Figure 3.3 shows the pull out test results of the Ti/PMMA samples made with Simplex (human) bone cement at three different curing times (10, 30, and 60 minutes). The results show that it takes about 500

N to take the Ti rod out of the implant-cement when the curing time is 10 minutes. As the curing time is increased to 60 minutes the force also increases to about 1500 N.



(a)



(b)

Figure 3.3 Pull out shear stress-interface shear strain and pull out force-displacement graph for an implant/cement during pull out tension test under static loading condition with respect to curing time made with HBC.

Table 3-2 summarizes the calculated results of the average pull out shear strengths for the three different curing times. It is clear from the data that when the curing time is changed, the average pull out shear strength increases significantly. When comparing the effect of curing time on bending strength and pull-

out shear strength, it can be concluded that the curing time has more impact on the interfacial shear strength than on the bending strength results for human bone cement.

Table 3-2 Curing effect on pull out shear strength (MPa) in relation to type of human bone cement.

Type of bone cement	**Curing time**		
	10 min	**30 min**	**60 min**
Human	1.71 ± 0.09 (n = 5)	1.71 ± 0.09 (n = 5)	3.08 ± 0.07 (n = 4)

The observed difference of the mechanical properties between 10, 30 and 60 minutes sample may be due to the residual stress build during curing. When cement was curing, tension preload build up on the titanium, when the cement became solid. The preload may produce compressive residual stress in titanium. This preload during the pull out tension tests was observed for every sample that fluctuates with curing time. It was typically +30N for 10 minutes of curing and + 70 N for 60 minutes of curing.

3.4.3 Effect of Curing on Material Hardness

Besides, we have observed the change in hardness of the sample with the change of the curing time. From table 3-1 we can see that the average Hardness in Rockwell R scale has increased by about 23% as the curing time increases from 10 minutes to 60 minutes for HBC.

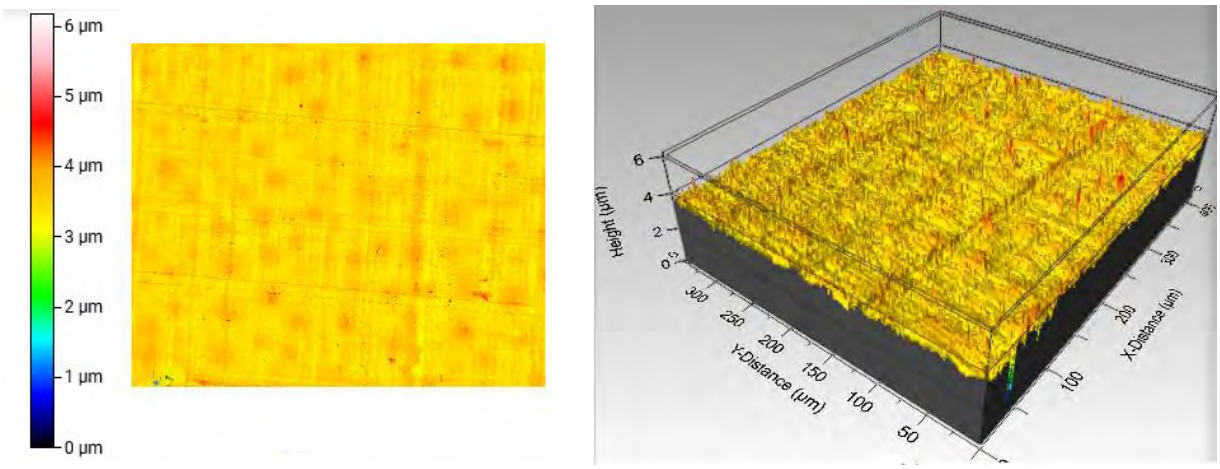
By analyzing the hardness data and the measured pullout shear strength between Ti/HBC and Ti/VBC the following correlations between the hardness of the bone cement samples and the interfacial shear strength have been obtained.

For human cement: $IS = 1.8571H + 39.855$ MPa (1)

Where, IS = Interfacial shear strength and ‘H’ stands for hardness.

3.4.4 Effect of Curing on Surface Roughness

Figure 3.4(a) show the surface topographical view of a HBC samples from pullout tension tests. The dimension of scanned images of the corresponding samples with 3D surface profile is shown in Fig. 3.4(b). For HBC, the differences of values of S_a and S_q for different curing time were not significant (p>0.05) (Table 3-3 and 3-4).



(a) (b)

Figure 3.4(a) Two-dimensional views of scanned surface profile and (b) three-dimensional views of scanned surface profile of HBC sample.

Table 3-3 Curing effect on arithmetic mean height, S_a (µm) in relation to HBC.

Experimental Parameters	**Curing time**		
	10 min	**30 min**	**60 min**
Human	0.161 ± 0.011	0.16 ± 0.01	0.180 ± 0.025

Table 3-4 Curing effect on Root mean square height, Sq (µm) in relation to HBC.

Experimental Parameters	**Curing time**		
	10 min	**30 min**	**60 min**
Human	0.226 ± 0.013	0.23 ± 0.01	0.243 ± 0.032

It has been observed that in longitudinally sectioned HBC samples SEM images show large amount of voids in HBC samples (Fig 3.5).

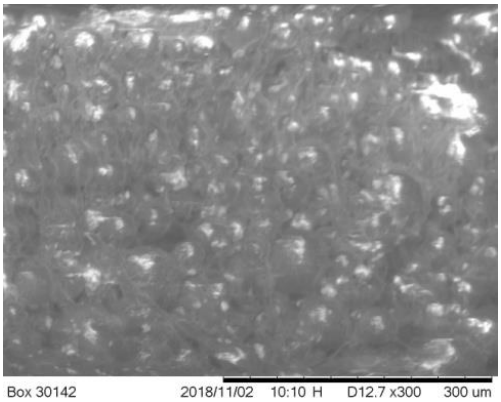


Figure 3.5 Scanning electron microscope images of a longitudinal sectioned HBC sample.

3.4.5 Significance of Obtained Results Based on Potential Applications

From Eq. (1) it is clear that there exists a linear relationship between hardness of bone cement and interface shear strength of titanium implant–cement interface. There is material test standard readily available to measure hardness of bone cement. On the other hand, there is no standard for the measurement of interface shear strength of titanium implant–cement and requires custom made setup for the experiment. Clinicians or bone cement researcher can readily get idea about interface shear strength of implant-cement interface without conducting the experiment from the measured empirical relationship.

The results of this study can be used to determine the relative influence of waiting time after cementing implant during the orthopedic surgery on the mechanical, thermal, and surface properties of traditional human and veterinary bone cements.

Results obtained in this thesis can be used in biomedical research and industries particularly cemented implant technology (total hip, knee, shoulder, vertebral) to design an optimal bone cement which will ensure maximum developed mechanical properties with minimum possible curing time.

Finite element modeling is a common method for designing novel total joint arthroplasty (TJA) implant system and evaluating the effect of physiological loading on the designed implant. The results of the mechanical (fracture, fatigue and bending) properties obtained from this study can be used during material assignment steps for the finite element modeling of cemented TJA.

The test set up and results obtained in this thesis can be used to improve the design of bone cemented implant by modifying the cement properties with additives such as nano particles and nano fibers.

This study developed a novel experimental setup for interface fatigue and fracture tests on PMMA-type samples. The novelty of the setup is that a wide variety of bone/cement interface samples can be tested using the system.

3.5 Conclusions

It can be concluded that the cement curing time control the structural properties of the test samples during the preparation of flexural and hardness test samples. The cement setting time changes the hardness and strength of the cement adjacent to the implant. The following conclusions can be drawn from the present investigation:

(1) The flexural strength of cement samples under three point bend loadings were significantly higher for 60 minutes cured cement samples in comparison with the flexural strength of cement samples cured for 10 and 30 minutes.

(2) The hardness of cement samples were significantly higher for 60 minutes cured cement samples in comparison with to the hardness of cement samples cured for 10 and 30 minutes.

(3) Mechanical test results concluded that curing time increases the interface bonding strength between implant and cement.

(4) Surface roughness at the interface between implant and cement concludes that curing time has little influences on surface characteristics between implant and HBC.

CHAPTER 4
Effect of Curing Time on the Mechanical Behavior of Veterinary Bone Cement

4.1 Summary

The goal of the study was to determine the effect of time of curing of BioMedtrix Veterinary Bone Cement, a low viscous bone cement (VBC), on the bending strength and hardness of the cement adjacent to the implant as well as to determine the shear strength between Ti and cement. This study conducted ASTM standard three point bend (3PB) test on the cement to measure the flexural strength of the cement that was cured for 30 and 60 minutes. In addition, this study conducted pull out tension tests on titanium/VBC to measure the shear strength between titanium and LVBC that was cured for 30 and 60 minutes. The hardness of the cement at the adjacent to Ti was measured using a Rockwell R hardness test scale. Two groups of samples were produced for each type of experiments by varying the curing times. The cement during the liquid phase poured in to a custom made mold to create the 3PB cylindrical samples. For the pull out tension tests on Ti/cement samples, the Ti implant was fastened at the top gripper and a custom made holder that has a hole was fastened at the bottom gripper of universal mechanical test system. Cement was poured and cured in to the gap between implant and holder. This study has found that the curing time significantly increases the values of bending and hardness properties. It can be concluded that the variability of the shear strength between Ti and cement depends on the strength and hardness of the cement adjacent to the implant.

4.2 Introduction

BioMedtrix Veterinary Bone cement is a sterile form of polymethyl methacrylate (PMMA) originally formulated for use in hip replacement. It is available with a range of viscosities[43]. In addition to hip replacement bone cement, veterinarians have found a wide range of other applications[36]. There are to types that offer different viscosities for different applications. All consist of liquid/powder portions that are mixed together with and without gentamycin.

BioMedtrix Veterinary Bone Cement is used to embed titanium (Ti) implant/bone samples for measuring the mechanical stability of implant with bone after the implantation of the implant in an animal model[44]. The Ti-bone sample was embedded in a custom made cylindrical cup using a low-

viscosity acrylic bone cement in the Test Resource universal testing machine (Figure 4.1). The acrylic cup was used to permit coaxial alignment of the implant in the direction of pull-out force. The bottom of the cup was fastened in the bottom of the test machine. The implant was carefully fastened to the top gripper in the mechanical tester and slowly lowered to embed the Ti-bone sample in a low-viscosity acrylic bone cement (BioMedtrix veterinarian bone cement) and cured for an hour. Pull out tension tests were conducted on each sample at room temperature after the curing. Variable preload(tension forces) was induced in the titanium/bone samples during the curing of the cement, which varies with curing period of time. Similar phenomena was also observed for titanium/high viscous bone cement [45]. It is not known how is the curing time effect on the preload of the implant/bone sample that lead to this study.

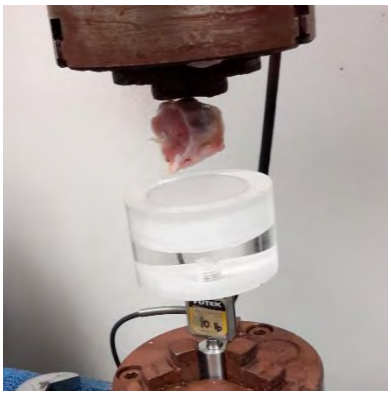


Figure 4.1 Mechanical stability tests on a titanium/bone sample.

4.3 Material and Method

Discussed in chapter 2.

4.4 Results and Discussion

4.4.1 Effect of Curing Time on Flexural Strength

The effects of curing time on the bending behavior of low viscous PMMA samples can be observed in. The tests are performed for 30 and 60 minutes curing. After some initial slippage between grip and sample (up to about 1 mm displacement), the force increases with displacement. The red curve corresponds to the curing time of 30 minutes and the green curve corresponds to the curing time of 60 minutes. It is observed from the Figure 4.3 that as the curing time increases from 30 minutes to 60 minutes, the maximum bending load increases from about 350 N to 375 N, suggesting more than 10% increase of the maximum load. Furthermore, the stiffness also increases as the curing time is increased.

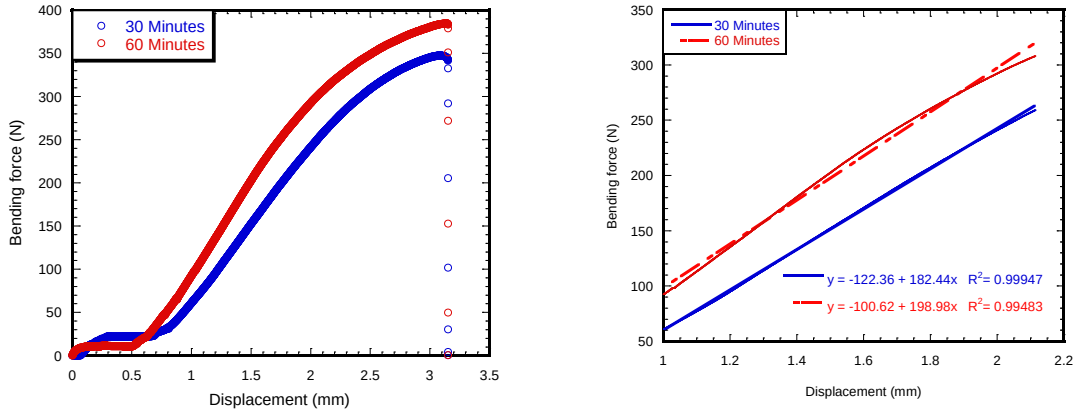


Figure 4.2 Load-displacement graph and slope for an implant-cement during 3PB test with respect to curing time (VBC).

Figure 4.3 shows a comparison of the average maximum bending forces after 30 minutes and 60 minutes curing time for multiple numbers of tests. The dispersions of the measured data in each case are also shown in Figure 4.3 through the respective error bars. The graph indicates that the impact of the curing time is more significant on the bending force for 60 minutes curing, although in both cases forces are increasing with the curing time.

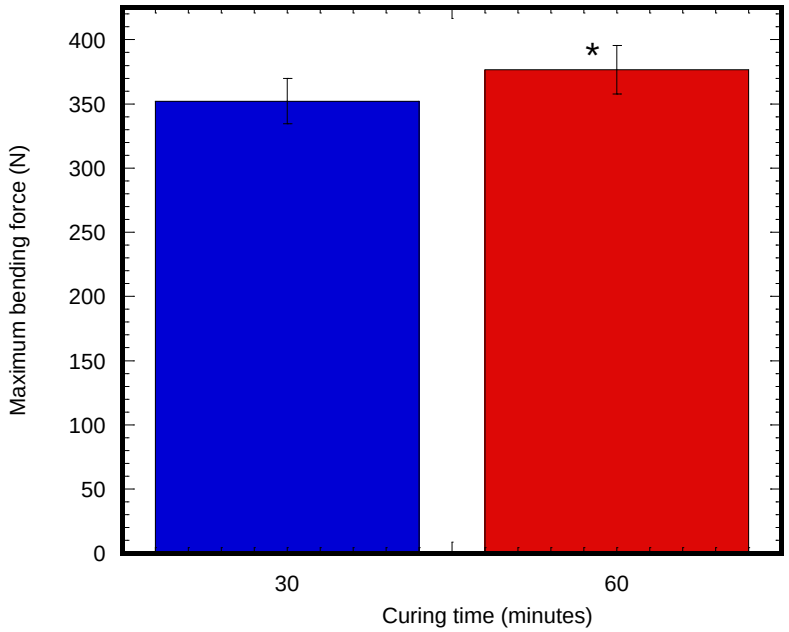


Figure 4.3 Bar diagram showing the curing effect on the maximum bending force.

Table 4-1 summarizes the calculated results of the average bending strength and the hardness for the two different curing times (30 minutes and 60 minutes). It can be observed that as the curing time is changed from 30 minutes to 60 minutes, the average bending strength increases by 7%.

Table 4-1 Curing effect on bending and hardness in relation to curing time.

Experimental Parameters	Curing Time	
	30 min	60 min
Bending Strength (MPa)	59.77±1.26(n=5)	63.95±.0.76(n=5)
Hardness (Rockwell R)	42±0.71(3)	71±1.63(3)

4.4.2 Effect of Curing Time on Interface Shear Strength

There is an enormous increase of the pull out tensile force as the curing time changed from 30 minutes to 60 minutes. Figure 4.5 shows the pull out test results of the Ti/PMMA samples made with Biomedtrix (veterinary) bone cement at two different curing times (30 and 60 minutes). The tests are performed for 30 and 60 minutes curing. After some initial slippage between grip and sample (up to about 0.11 mm and 0.19 mm displacement for 30 and 60 minutes cured samples, respectively), the force increases linearly with displacement until break. The experiment found that it takes about 420 N to take the Ti rod out of the implant-cement when the curing time is 30 minutes. As the curing time is increased to 60 minutes the force also increases to about 525 N. So, there is significant increase of the pull out tensile force as the curing time changed from 30 minutes to 60 minutes.

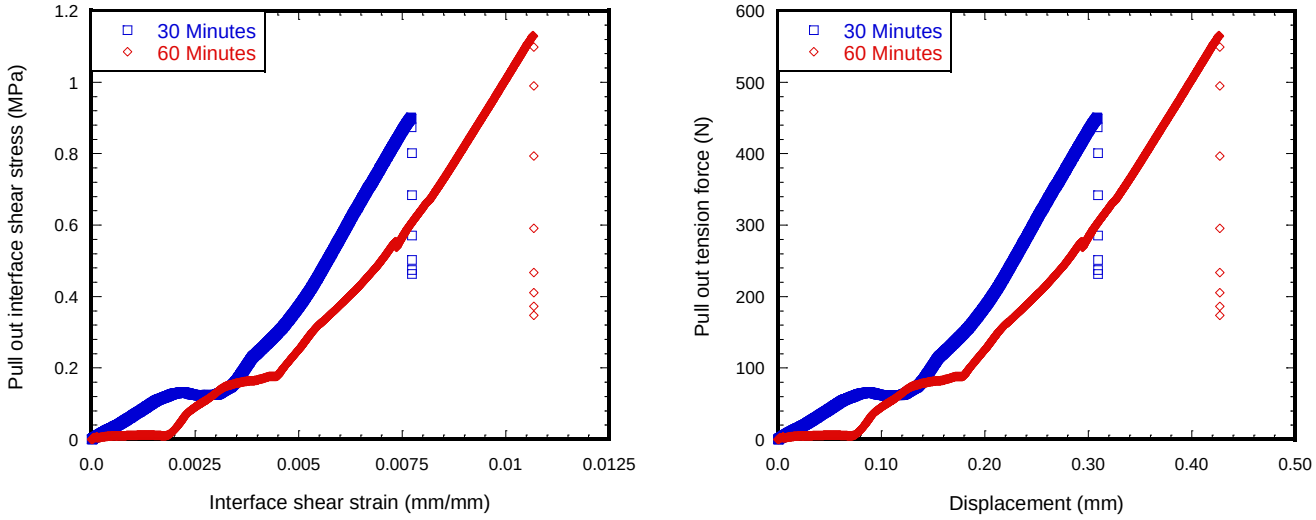


Figure 4.4 Pull out shear stress (MPa)-Interface shear strain and pull out force-Diplacement graph for an implant/cement during pull out tension test under static loading condition with respect to curing time made with VBC.

Table 4-2 summarizes the calculated results of the average pull out shear strengths for three different curing times. It is clear from the data that when the curing time is changed, the average pull out shear strength increases significantly. When comparing the effect of curing time on bending strength and pull-out shear strength, it can be concluded that the curing time has more impact on the interfacial shear strength than on the bending strength.

Table 4-2 Curing effect on pull out shear strength (MPa) in relation to type of cement.

Type of bone cement	Curing time	
	30 min	60 min
Veterinary	0.84±0.05 (n=3)	1.045±0.05 (n=4)

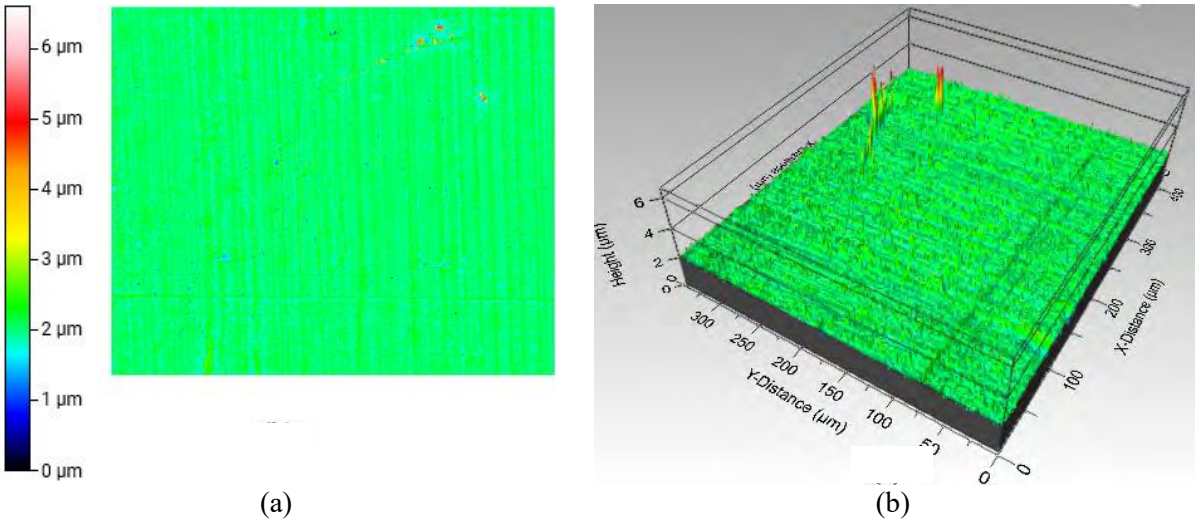
The observed difference of the mechanical properties between 30 and 60 minutes sample may be due to the residual stress build during curing. When cement was being cured, tension preload build up on the titanium, when the cement became solid. The preload may produce compressive residual stress in titanium. This preload during the pull out tension tests was observed for every sample that fluctuates with curing time.

4.4.3 Effect of Curing on Material Hardness

Besides, we have observed the change in hardness of the sample with the change of the curing time. In fact, the average Hardness in Rockwell R scale has increased by about 69% as the curing time increases from 30 minutes to 60 minutes and the great amount of increase of hardness occurs between 30 to 60 minutes.

4.4.4 Effect of Curing Time on Surface Roughness

Figure 4.5(a) show the surface topographical view of VBC samples from pullout tension tests. The dimension of scanned images of the corresponding samples with 3D surface profile is shown in Fig. 4.5(b). For VBC, the differences of values of S_a and S_q for different curing time were not significant (p>0.05), but there was a significant difference of S_a and S_q values observed between HBC and VBC (Table 3-3, 3-4, 4-2 and 4-3).



(a) (b)

Figure 4.5 (a) Two-dimensional views of scanned surface profile and (b) three-dimensional views of scanned surface profile of VBC sample.

Table 4-3 Curing effect on arithmetic mean height, S_a (μm) in relation to type of VBC.

Experimental Parameters	**Curing time**	
	30 min	**60 min**
Veterinary	0.105±0.004	0.127±0.008

Table 4-4 Curing effect on Root mean square height, Sq (μm) in relation to type of VBC.

Experimental Parameters	**Curing time**	
	30 min	**60 min**
Veterinary	0.177±0.010	0.168±0.007

In longitudinally sectioned VBC samples SEM images show lesser amount of voids in VBC samples (Fig 4.6) when these are compared to HBC samples.

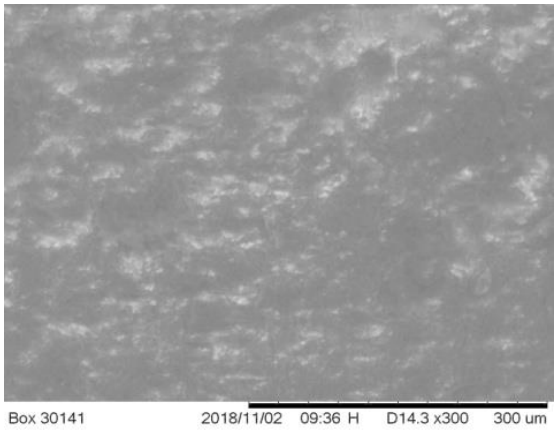


Figure 4.6 Scanning electron microscope images of a longitudinal sectioned VBC sample.

4.5 Conclusions

It can be concluded that the cement curing time control the structural properties of the test samples during the preparation of flexural and hardness test samples. The cement setting time changes the hardness and strength of the cement adjacent to the implant. The following conclusions can be drawn from the present investigation:

(1) The flexural strength of cement samples under three point bend loadings were significantly higher for 60 minutes cured cement samples in comparison with the flexural strength of cement samples (VBC) cured for 30 minutes.

(2) The hardness of cement samples (VBC) were significantly higher for 60 minutes cured cement samples in comparison with the hardness of cement samples cured for 30 minutes.

(3) The hardness of VBC with the change of the curing time might influence the bonding of implant with the cements.

(4) Mechanical test results concluded that curing time increases the interface bonding strength between implant and cement.

(5) Surface roughness at the interface between implant and cement concludes that curing time has little influences on surface characteristics between implant and cement, whereas cement type has great influence on surface characteristics between implant and cement. As has been observed, surface roughness values are higher for HBC samples than that of VBC samples.

CHAPTER 5

Saline and Curing Effects on Fatigue Characterization of a Poly methyl Methacrylate Bone Cement

5.1 Summary

The effect of storing the cemented implant system, an implant/PMMA cement interface, at hydrated condition prior to testing is vital, since the cement is always hydrated at *in vivo* implantation conduction. Degradation of properties due to storing methods leads to incorrect numbers and false conclusions. The aim of this study was to determine if saline, (a common storage media) had any effects on the interface fracture strength of implant/PMMA interfaces over a certain storage periods (5 days). Three specific aims were used to answer this question. First, design and manufacture of a pull-out tension holder to find fracture strength under cyclic load of implant/cement interface. Second, measure the effect of curing time difference (slow vs. fast curing) on interface fracture strength of implant/cement. Third, examine the effect of storing specimens in saline for extended periods of time on fracture strength of implant/cement. For achieving the first specific aim, a custom pull-out setup was designed and manufactured. This study used titanium (Ti) as implant material and two groups of PMMA bone cement (slow and fast cured) to prepare Ti/PMMA specimen. Each specimen was tested to failure through cyclic load. Each group of Ti/PMMA was tested under three condition: (1) non-salinized and curing for an hour, (2) non-salinized and curing for 5 days and (3) salinized and curing for 5 days. The data collected from these tests was analyzed for its average fracture load and number of cycles for failure. This study concludes that the custom setup has high repeatability and accuracy. Also, the type of specimens (fast vs slow) and the storage of specimens for 5 days has significant effect on the average fracture load and number of cycles for failure. Although, the study found storing the specimen in physiological saline for 5 days has insignificant statistical effect on the interface fracture strength of Ti/PMMA under stepwise cyclic load.

5.2 Background and Significance

There are two main ways of conserving biomedical specimens prior to testing its material properties. These are conservation in a fluid or temperature change. The most common type of temperature change is to freeze bone. This is done at different temperatures such as -20 °C to -70 °C. Another way to use temperature as a conservation method is to dry it. This can be done either by autoclaving (heating) or drying (vacuum). An alternative to temperature conservation is using a fluid.

Many fluids have been used to store bone including formalin, methanol, chloroform, saline, and alcohol. Each has its benefits but also its drawbacks.

Physiological saline preservation shows a decrease in fracture toughness of bone due to elution of calcium and magnesium [25]. Sasaki *et al*. [26] found that saline conservation of as little as one week degrades the material properties of cortical bone. Yet, Sasaki *et al.*[26] and Gustafson *et al.*[59] concluded that material properties are not affected by the preservation in calcium buffered saline solution. This is due to the fact that the calcium contained in the solution is matched to the calcium in the cortical bone samples and therefore elution is reduced. The limitation with using calcium buffered saline is you have to use the right amount of calcium in the saline. Too much calcium and calcium in absorbed by the cortical bone, too little and calcium is defused from cortical bone into the solution [59]. However, material properties of the surface such as reduced elastic modulus and Nano hardness of enamel have been found to be reduced in as little as one day when being preserved in calcium buffered saline and deionized water, with a drastic reduction of around 50 percent at 14 weeks [60]. There is no study conducted on finding the effect of storing a cemented implant in saline on its fracture strength, which was one of the aim of this study.

There is variability in increase in temperature and curing time for various PMMA used in human and animal orthopedic surgeries. It has found that curing properties (temperature and time for curing) affect creep rate [61], fatigue life [62], even affect deformation characteristics [63] of biological materials. Yan *et al.*[64] found that the fracture toughness of cortical bone decreased with an increase in temperature. The effect of curing on the fracture strength of Ti/PMMA specimen was unknown and found in this study.

5.3 Materials and Methods

5.3.1 Specimen Types and Preparation

This study used titanium alloy, Ti-6Al-4V Eli (ASTM B 348 standard, grade 23, biocompatible) as the implant material. Among the various Ti alloys, Ti-6Al-4V Eli is used in this study because of its better physical and mechanical properties in comparison to pure Ti for orthopedic surgeries. This study used Stryker Simplex ® P bone cement, which is a low curing time (fully cured within 30 minute) PMMA bone cement using in human and BioMedtrix veterinary bone cement, which is a high curing time PMMA bone cement (fully cured within 1 hour). The cement was cured for 1 hour and 5 days in

two different curing conditions: saline and non-saline for 5 days. This study used human buffer saline as shown in Figure 5.1

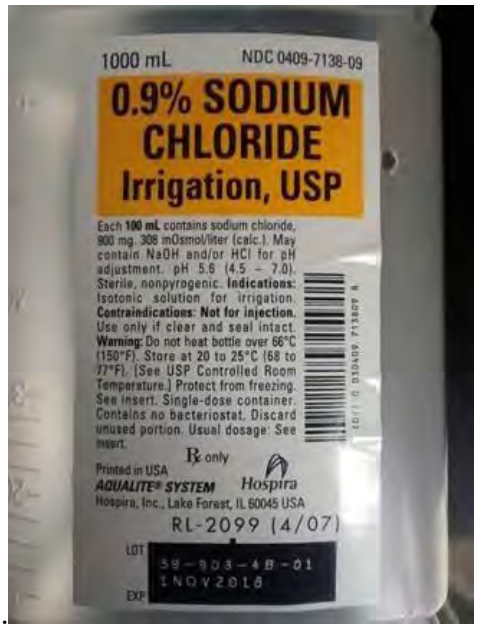


Figure 5.1 Human Buffer Saline that was used in this study.

5.4 Experiment and Analysis

5.4.1 Pull out Fatigue Test

To prepare the pull out fatigue test samples, the implant was fastened at the top gripper and the hollow cylindrical aluminum holder was fastened at the bottom gripper of the UTM (Fig 1b). PMMA cement was prepared by mixing 0.62 gram of powder and 310 micro liter of liquid. The cement was poured into the gap between implant and holder. The top gripper of UTM that contains the implant was slowly lowered so that the implant touches the top of the round rod. The samples were considered for non-saline treated condition for 1 hour, non-saline treated condition for 5 days, and human Buffer Saline treated condition for 5 days constantly at 37℃.

Cyclic pulling tests were performed using Shimadzu AGS -X series universal testing machine (UTM). After curing with specific time period, the fatigue test was done to determine the number of cycles to break the contact between the bone cement and the Titanium rod. For human cement, first stage fatigue test was run for 1000 cycles. Fatigue test parameters were given as: mean load = curing load =150 N , amplitude = 20% of curing load (150N x 0.2=30N) and frequency = 2 hz. After finishing

the 1000 cycles, the 2nd stage fatigue test is run for another 1000 cycles where the mean load = curing load+50 N=200, amplitude = 20% of curing load and frequency = 2 hz as the fatigue test parameters. Then the study was continued until the sample was loaded to a mean load of 600 N (average human weight) with amplitude 20% and frequency = 2 hz until the break of the specimen. From the machines, the study recorded the maximum cycles for the failure of the specimen. For animal cement, this study followed the above protocol except the samples were loaded up to 300 N (average weight of Shepherd breed Dog) instead of 600 N.

Figure 5.2 Fatigue test on a Ti/Cement samples in the UTM.

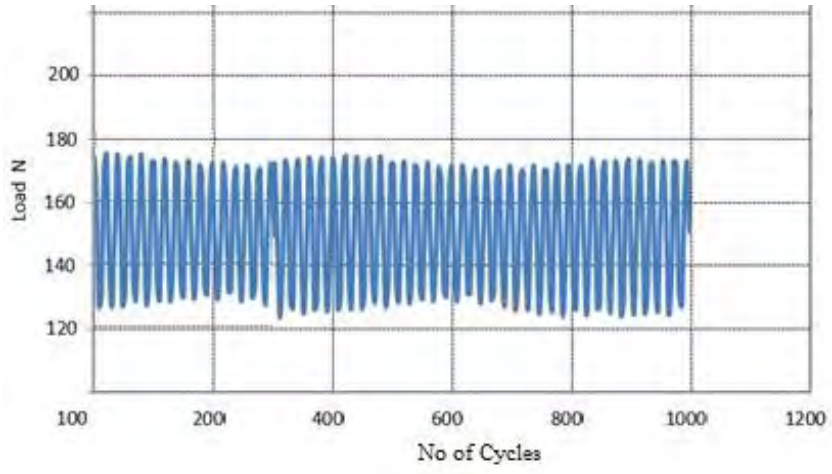


Figure 5.3 Fatigue cyclic load from the UTM.

5.4.2 Surface Roughness

The sample surface roughness parameters of saline and non-saline samples were measured using the 3D optical profiler according to the same way as discussed in chapter 2.

5.4.3 Statistical Analysis

The independent-samples t-test compares the means between two or more unrelated groups on the same continuous, dependent variable. An independent samples t-test assuming unequal variances was performed to determine if there is a significant difference in the mean experimental test parameters of the saline and non-saline treated sample groups. For all statistical analysis, statistical significance was considered at $p < 0.05$.

5.5 Results and Discussions

5.5.1 Pull out Fatigue Test

Figure 5.4 Shows the pull out test results of Ti/PMMA implant-cement made with slow and fast curing PMMA cements at the three different curing conditions. The tests are performed after 1 hour and 5 days curing under non-salinized and salinized conditions. There is significant increase of the pull out tensile force as the curing time is changed from 1 hour to 5 days. As the curing time is increased to 5 days the average fracture force also increases to about 300 N from 250 N under cyclic load for veterinarian bone cement (slow cured PMMA cement), whereas average force increases to about 450 N from 400 N under cyclic load for human bone cement (fast cured PMMA cement). The results also found that the interface fracture load and number of cycles of human bone cement is about 2.2 times higher than the veterinary bone cement for non-salinized samples, whereas the values are 2 times higher for salinized samples. In the figure, * represent the statistical significant value of the test samples with respect to non-salinized 1 hour cure samples for veterinary bone cement and † represent the statistical significant value of the test samples with respect to non-salinized 1 hour cure samples for human bone cement.

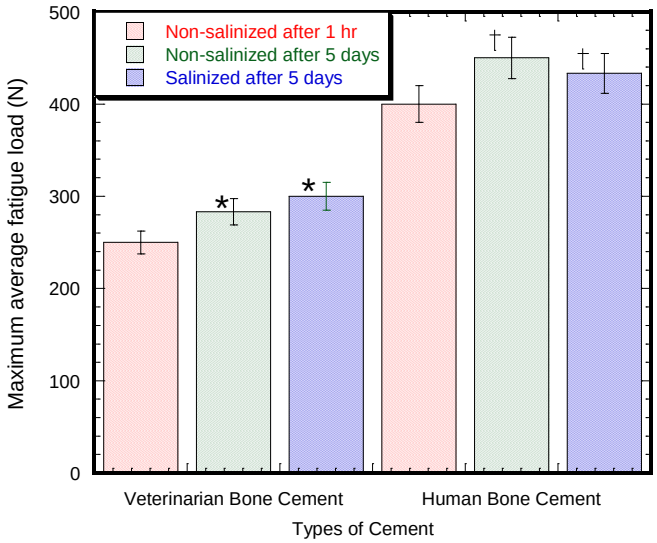


Figure 5.4 Bar diagram of implant-cement fatigue test results of veterinary and human bone cement during pull out stepwise cyclic test showing the effect of curing time and saline condition on the fatigue fracture load.

Figure 5.5 shows that one hour cured VBC cement samples can sustain more than 2000 fatigue cycles. Mean fatigue stress before failure of the specimen is 0.45 Mpa.

Figure 5.5 shows that one hour cured HBC cement samples can sustain more than 5000 fatigue cycles. Mean fatigue stress before failure of the specimen is 0.72 Mpa.

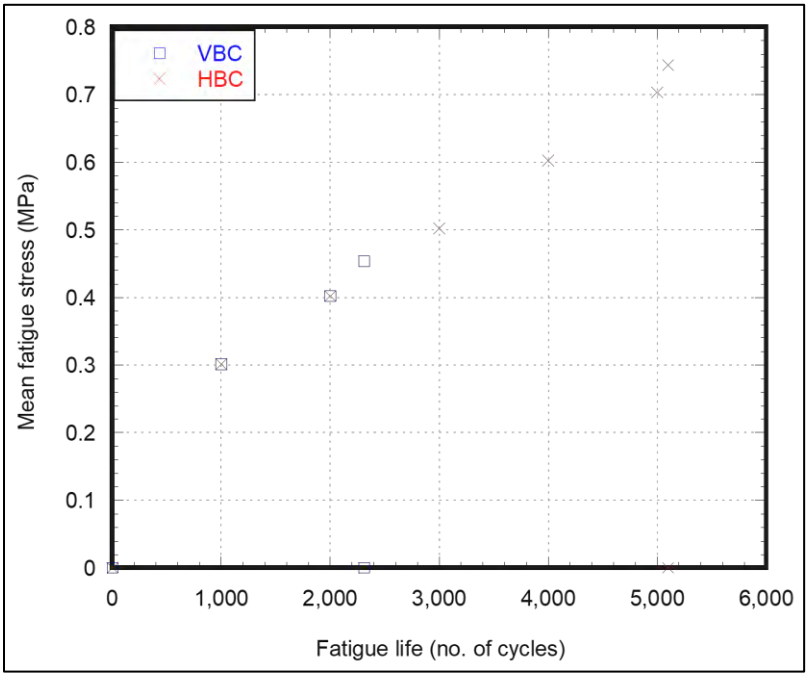


Figure 5.5 Maximum average fatigue stress in relation to fatigue cycles of veterinary and human bone cement during pull out stepwise cyclic test after 1 hour of curing.

The effects of curing time on the fatigue fracture behavior of high curing time PMMA samples (veterinary bone cement) can be observed in Figure 5.5 The tests are performed again after 1 hour and 5 days of curing. It is observed from the non-salinized samples that as the curing time increases from 1 hour to 5 days, the mean total number of cycles required for the failure of the specimen increases from 2309 cycles to 3027 cycles, suggesting more than 31% increase of the fatigue cycles. For salinized samples, the fatigue cycle increases as the curing time is increased was 32%. However, the fatigue cycles difference was not significantly changed with salinization that shows that there is no degradation of material properties or no weakness of Ti/PMMA interface because of the salinization of the cement.

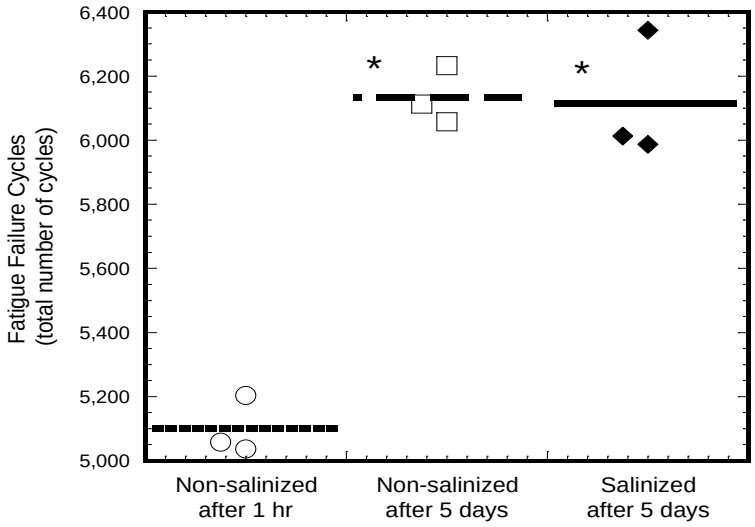


Figure 5.6 Dot plots of implant-cement fatigue test results during pull out stepwise cyclic test of veterinary bone cement with respect to curing time and saline condition. In the figure, *represent the statistical significant value of the test samples with respect to non-salinized and 1 hour cure samples.

The effects of curing time on the fatigue fracture behavior of low curing time PMMA samples (human bone cement) can be observed in Figure 5.6. As like as high curing PMMA cement, the tests were performed on Ti/PMMA samples again after 1 hour and 5 days of curing. It is observed again from the non-salinized samples that as the curing time increases from 1 hour to 5 days, the mean total number of cycles required for the failure of the specimen increases from about 5099 cycles to 613 4cycles, suggesting more than 20% increase of the fatigue cycles. For salinized samples, the fatigue cycle increases was almost same as the nonsalianized PMMA cement. So, as like as high curing time PMMA cement, the fatigue cycles difference was not significantly changed with salinization that shows that there is no degradation of material properties or no weakness of Ti/PMMA interface because the salinization of the cement.

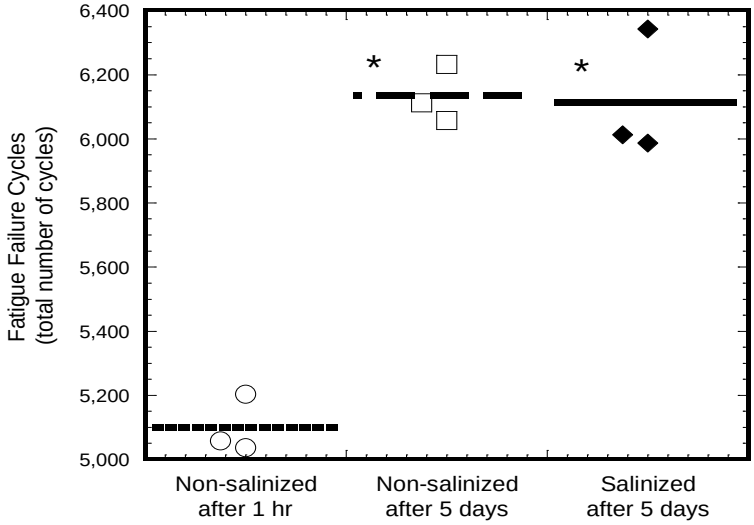


Figure 5.7 Dot plots of implant-cement fatigue test results during pull out stepwise cyclic test of human bone cement with respect to curing time and saline condition. In the figure, *represent the statistical significant value of the test samples with respect to non-salinized and 1 hour cure samples.

The observed difference of the mechanical properties between the various samples may be due to the residual stress that build up during curing for different type of bone cement. When cement was being cured, and become solid tension preload build up on the titanium. The preload may produce compressive residual stress in titanium. This preload during the pull out tension tests under stepwise cyclic load was observed for every sample that fluctuates with curing time.

The limitation of the study is that it was not studied how long curing time effects on the interface fracture toughness behavior of Ti/PMMA cement, which could be important in understanding the degradation and interface saline build up due to the hydrated condition. In future, Ti/PMMA cement will be cured longer time to evaluate whether degradation due to saline storage has any influence on the mechanical behavior of Ti/PMMA interface. In addition, a theoretical model will be developed to find a correlation between the curing time and the mechanical properties.

5.5.2 Surface Roughness

The study didn't find any significant difference of surface roughness parameters between saline and non-saline treated samples for human bone cement (Table 5-1). Therefore, it can be concluded that the saline does not have any effect on the internal morphology of bone cement.

Table 5-1 Difference of surface roughness parameters between saline and non-saline treated samples after 5 days of curing a human bone cement

Surface roughness parameters	Saline Samples			Non-saline samples			p value
	Sample # 1	Sample # 2	Sample # 3	Sample # 1	Sample # 2	Sample # 3	
Peak height, Sp	10.76	3.76	2.37	3.00	5.22	3.94	0.61
Valley depth, Sv	3.71	9.87	4.41	3.02	8.64	3.75	0.76
Maximum peak to valley depth, St	14.47	13.63	6.78	6.02	13.86	7.69	0.51
Arithmetic mean height, Sa	0.39	0.42	0.42	0.46	0.38	0.39	0.95
Root mean square, Sq	0.62	0.58	0.54	0.58	0.50	0.51	0.24
Skewness, Ssk	3.61	-1.88	-0.05	-0.33	-1.18	-0.04	0.58
Kurtosis, Sku	42.62	26.15	4.02	3.34	19.82	4.52	0.32

5.6 Conclusions

To recapitulation, veterinary and human cement curing time control the structural properties of the test samples during the preparation of the pull out fatigue Ti/PMMA samples. The cement setting time changes the hardness and strength of the cement adjacent to the implant that may be the cause for this effect. The following conclusions can be drawn from the present investigation:

1. Interface fracture strength of Ti/PMMA cement samples were significantly higher for human cement samples in comparison to veterinary bone cement samples under stepwise cyclic load.

2. Interface fracture strength of Ti/PMMAcement samples under step wise fatigue loadings were significantly higher for 5 days cured Ti/PMMAcement samples in comparison with the bonding strength of Ti/PMMAcement samples cured for 1 hour only.

3. Interface fracture strength of Ti/cement samples under step wise fatigue loadings were significantly higher for 5 days cured Ti/cement samples in comparison with the bonding strength of Ti/cement samples cured for 1 hour only.

CHAPTER 6
Achievement, Significance and Future Works

6.1 Conclusions

This study was conducted based on three research questions:

(1) Is there a significant difference in the mechanical performances between high and low viscous bone cement that occurs due to difference of curing time?

(2) Is there any significant difference in the morphological behavior occurs due to difference of curing time of a bone cement? and

(3) How does the curing time influence the performances of high and low viscous bone cement under hydrated and non-hydrated condition?

This study found the following conclusions:

(1) Statistically significant differences of mechanical properties (bending, pull-out shear strength and hardness) occurs due to the difference of curing time of a bone cement and type of cement.

(2) Difference of surface roughness occurs due to difference of curing time of a bone cement although the difference was not significant for curing time, but varies with the type of cement (human vs. animal).

(3) Statistically significant difference of pull-out shear strength under cyclic load occurs due to difference of curing time of a bone cement and type of cement. The effects of hydration are not significant on the performances of bone cements.

6.2 Significance

The novelty of this research is the comparative study to determine the relative influence of curing time on the mechanical properties of traditional low viscous bone cements for veterinary applications and traditional high viscous bone cements for human applications. This study also developed a novel experimental setup for the hardness, flexural strength, pull out shear strength, and fatigue tests on Ti/PMMA-type samples. The novelty of the setup and experimental protocol is that experiment can be conducted at consistent condition. Additionally, the setup can further be used for fatigue testing of other biomaterials. The results of the study can be used for the determination of the appropriate time required for the PMMA cements to restore its full functional capabilities for cemented orthopedic surgeries.

6.3 Future Works

Residual stress build up due to thermal load difference at different curing time may have influence, on mechanical properties of Ti/PMMA interface which can be investigated in future.

REFERENCES

[1] W. Lu, J.S., and X. Jiang, "Recent advances in electrospinning technology and biomedical applications of electrospun fiber,″Journal of Materials Chemistry B, 2014. 2: p. 2368-2380.

[2] G. Cunin, H.B., H. Petite, C. Blanchat, G. Guillemin, "Experimental vertebroplasty using osteoconductive granular material,″ Spine, 2000. 25(9): p. 1070-1076.

[3] J.X. Lu, Z.W.H., P. Tropiano., "Human biological reactions at the interface between bone tissue and polymethylmethacrylate cement,"J Mater Sci Mater Med, 2002. 13(8): p. 803-809.

[4] J.E. Barralet, T.G., A.J. Wright, I.R. Gibson, J.C. Knowles, "Effect of porosity by compaction on compressive strength and microstructure of calcium phosphate cement," J Biomed Mater Res (Appl Biomater), 2002. **63**(1): p. 1-9.

[5] E.P. Lautenschlager, P.M., "Titanium and titanium alloys as dental materials," International dental journal, 1993. **43**(3): p. 245-253.

[6] Elias CN, L.J., Valiev R, Meyers MA, "Biomedical applications of titanium and its alloys," JOM, 2008. 60(3): p. 46-49.

[7] O. Okuno, H.H., Dent. Jpn., 1989. 26: p. 101-104.

[8] Khandaker, M. and Z. Meng, "The Effect of Nanoparticles and Alternative Monomer on the Exothermic Temperature of PMMA Bone Cement," in 6th BSME International Conference on Thermal Engineering *(ICTE 2014)*. 2015: Gazipur, Bangladesh.

[9] Liu-Snyder, P. and T.J. Webster, "Developing a New Generation of Bone Cements With Nanotechnology,"Current Nanoscience, 2008. 4(1): p. 111-118.

[10] Orr, J.F., N.J. Dunne, and J.C. Quinn, "Shrinkage stresses in bone cement," Biomaterials, 2003. 24(17): p. 2933.

[11] Bishop, J.A., et al.,"Assessment of compromised fracture healing,"J Am Acad Orthop Surg, 2012. 20: p. 273-282.

[12] U.S., F. Food and Drug Administration. http:// www.fda.gov/ medicaldevices/ productsandmedicalprocedures/implantsandprosthetics/metalonmetalhipimplants/ucm241770.htm.

[13] J.R. Jeffers, M.B., A.B. Lennon, P.J. Prendergast, M. Taylor, "Cement mantle fatigue failure in total hip replacement: experimental and computational testing," Journal of Biomechanics, 2007. 40: p. 1525-1533.

[14] Ramos, A.S., J.A., "The influence of cement mantle thickness and stem geometry on fatigue damage in two different cemented hip femoral prostheses," Journal of Biomechanics, 2009. 42(15): p. 2602-2610.

[15] Gravius, S.W., D.C. ; Siebert, C.H. ; Andereya, St. ; Mueller-Rath, R. ; Maus, U. ; Mumme, T., "In vitro interface and cement mantle analysis of different femur stem designs,"Journal of Biomechanics, 2008. 41(9): p. 2021-2028.

[16] Ohata, M., F. Minami, and M. Toyoda, "Local approach to strength mis-match effect on cleavage fracture of notched material," Journal De Physique Iv, 1996. 6(C6): p. 269-278.

[17] An, Y.H. and R.A. Draughn, "Mechanical Testing of Bone and the Bone-Implant Interface," 2000: CRC.

[18] Yi, Y.J. and J.R. Kelly, "Effect of occlusal contact size on interfacial stresses and failure of a bonded ceramic: FEA and monotonic loading analyses," Dental Materials, 2008. 24: p. 403-409.

[19] Mann, K.A., F.W. Werner, and D.C. Ayers, "Mechanical strength of the cement-bone interface is greater in shear than in tension," Journal of Biomechanics, 1999. 32(11): p. 1251-1254.

[20] Macdonald, W., E. Swarts, and R. Beaver,"Penetration and shear-strength of cement bone interfaces invivo," Clinical Orthopaedics and Related Research, 1993(286): p. 283-288.

[21] Wang, X.D., et al., "Testing of bone-biomaterial interfacial bonding strength: A comparison of different techniques," Journal of Biomedical Materials Research, 1996. 33(3): p. 133-138.

[22] Lucksanasombool, P., et al., "Interfacial fracture toughness between bovine cortical bone and cements," Biomaterials, 2003. 24(7): p. 1159-1166.

[23] Pereira, A.M., et al., "Effect of saline environment on mechanical properties of adhesive joints," International Journal of Adhesion and Adhesives, 2013. 47: p. 99-104.

[24] Ohman, C., et al., "The effects of embalming using a 4% formalin solution on the compressive mechanical properties of human cortical bone," Clinical Biomechanics, 2008. 23(10): p. 1294-1298.

[25] Kikugawa, H., T. Asaka, and M. Miyake, "Effect of preservative solution on fracture characteristics of bovine femoral cortical bone," Materials Transactions, 2007. 48(6): p. 1417-1421.

[26] Sasaki, N., et al., "Effect of mineral dissolution from bone specimens on the viscoelastic properties of cortical," Journal of Biomechanics, 2008. 41(16): p. 3511-3514.

[27] Hingston, J.A., et al.,"Effect of curing characteristics on residual stress generation in polymethyl methacrylate bone cements," Proc Inst Mech Eng H, 2008. 222(6): p. 933-45.

[28] Banks-Sills, L., Y.Y. Yang, and D. Munz, "An influence function for stress intensity factors of bimaterial notched bodies," International Journal of Fracture, 1997. 85(4): p. 333-350.

[29] Reedy, E.D., "Free-Edge stress intensity factor for a bonded ductile layer subjected to shear," Applied Mechanics Review, 1993. 60: p. 715-720.

[30] Akisanya, A.R. and N.A. Fleck,"Interfacial cracking from the free-edge of a long bi-material strip," International Journal of Solids and Structures, 1997. 34(13): p. 1645-1665.

[31] Gleich, D.M., M.J.L. Van Tooren, and A. Beukers, "A stress singularity approach to failure initiation in a bonded joint with varying bondline thickness," Journal of Adhesion Science and Technology, 2001. 15(10): p. 1247-1259.

[32] Zor, M., M. Küçük, and S. Aksoy, "Residual stress effects on fracture energies of cement–bone and cement–implant interfaces," Biomaterials, 2002. 23(7): p. 1595-1601.

[33] Biomet, I. *Cobalt™ HV Bone Cement*. 2010; Available from: http://www.biomet.com/orthopedics/productDetail.cfm?category=7&product=250.

[34] Mousa, W.F., et al.,"Biological and mechanical properties of PMMA-based bioactive bone cements," Biomaterials, 2000. 21(21): p. 2137-2146.

[35] Tunney, M.M., et al. "Incorporation of chitosan in acrylic bone cement: Effect on antibiotic release, bacterial biofilm formation and mechanical properties," in Special Section: Selected Papers from the 21st European Conference on Biomaterials, Brighton, UK, 9-13 September 2007. Guest Editors: Andrew Lloyd and Matteo Santin.2008. Van Godewijckstraat 30, Dordrecht, 3311 GZ, Netherlands: Kluwer Academic Publishers.

[36] Inc., B. The Total Hip Replacement. 2017; Available from: https://biomedtrix.com/.

[37] Inc, J.L. Jorgensen Bone Cement. 2018.

[38] Moiduddin, K., et al., "Structural and mechanical characterization of custom design cranial implant created using additive manufacturing," Electronic Journal of Biotechnology, 2017. 29: p. 22-31.

[39] Lewis, G.,"Alternative acrylic bone cement formulations for cemented arthroplasties: Present status, key issues, and future prospects,"Journal of Biomedical Materials Research - Part B Applied Biomaterials, 2008. 84(2): p. 301-319.

[40] Khandaker, M. and Z. Meng, "The Effect of Nanoparticles and Alternative Monomer on the Exothermic Temperature of PMMA Bone Cement," Procedia Engineering, 2015. 105: p. 946–952.

[41] Nuño, N.A., G. Journal of Biomechanics,"Residual stresses at the stem–cement interface of an idealized cemented hip stem,"2002. 35(6): p. 849-852.

[42] Ritchie, R.O., et al., "Measurement of the toughness of bone: A tutorial with special reference to small animal studies," Bone, 2008. 43(5): p. 798-812.

[43] Kwong, F.N.K. and R.A. Power,"A comparison of the shrinkage of commercial bone cements when mixed under vacuum," J Bone Joint Surg Am., 2006. 88-B: p. 120-2.

[44] Khandaker, M., et al., "Effect of collagen- polycaprolactone extracellular matrix on the in vitro cytocompatibility and in vivo bone responses of titanium," Journal of Medical and Biological Engineering, 2017. 38: p. 1-14.

[45] Khandaker, M., et al., "Plasma nitriding of titanium alloy: Effect of roughness, hardness, biocompatibility, and bonding with bone cement,"Bio-Medical Materials and Engineering, 2016. In Press.

[46] McCormack, B.A.O. and P.J. Prendergast, "Microdamage accumulation in the cement layer of hip replacements under flexural loading," Journal of Biomechanics, 1999. 32(5): p. 467-475.

[47] Race, A., K.A. Mann, and A.A. Edidin, "Mechanics of bone/PMMA composite structures: An in vitro study of human vertebrae," Journal of Biomechanics, 2007. 40(5): p. 1002-1010.

[48] Race, A., et al., "Early cement damage around a femoral stem is concentrated at the cement/bone interface," Journal of Biomechanics, 2003. 36(4): p. 489-496.

[49] Wang, X.D. and C.M. Agrawal, "A mixed mode fracture toughness test of bone-biomaterial interfaces," Journal of Biomedical Materials Research, 2000. 53(6): p. 664-672.

[50] Wood, J.D., et al. "Mechanical behavior of the dentin-enamel interface," in 9th Intl. Cong. Soc. Experimental Mech. 2000. Orlando, FL.

[51] Mann, K.A. and L.A. Damron, "Predicting the failure response of cement-bone constructs using a non-linear fracture mechanics approach," Journal of Biomechanical Engineering-Transactions of the Asme, 2002. 124(4): p. 462-470.

[52] Wang, X.D. and C.M. Agrawal, "Interfacial fracture toughness of tissue-biomaterial systems," Journal of Biomedical Materials Research, 1997. 38(1): p. 1-10.

[53] McCormack, B.A.O. and P.J. Prendergast, "Analysis of crack propagation paths at implant/Bone-Cement interfaces," Journal of Biomechanical Engineering, Transactions of the ASME, 1996. 118(4): p. 579-585.

[54] Staninec, M., et al., "Ultimate tensile strength of dentin: Evidence for a damage mechanics approach to dentin failure," Journal of Biomedical Materials Research, 2002. 63(3): p. 342-345.

[55] Lucksanasombool, P., et al., "Comparison of failure characteristics of a range of cancellous bone-bone cement composites," Journal of Biomedical Materials Research - Part A, 2003. 64(1): p. 93-104.

[56] Vallo, C.I., "Influence of load type on flexural strength of a bone cement based on PMMA," Polymer Testing, 2002. 21(7): p. 793-800.

[57] Stratasys, Dimension Elite.

[58] Filmetrics Inc-USA. [cited 2018; Available from: https://www.filmetrics.com/opticalprofilers/profilm3d.

[59] Gustafson, M.B., et al., "Calcium buffering is required to maintain bone stiffness in saline solution,"Journal of Biomechanics, 1996. 29(9): p. 1191-1194.

[60] Habelitz, S., et al., "Nanoindentation and storage of teeth," Journal of Biomechanics, 2002. 35(7): p. 995-998.

[61] Rimnac, C.M., et al., "The effect of temperature, stress and microstructure on the creep of compact bovine bone," Journal of Biomechanics, 1993. 26(3): p. 219-228.

[62] Carter, D.R. and W.C. Hayes, "Fatigue life of compact bone- I. Effects of stress amplitude, temperature, and density," Journal of Biomechanics, 1976. 9: p. 27-34.

[63] Bonfield, W. and C.H. Li, "The temperature dependence of the fracture mechanics of cortical bone,"Journal of Biomechanics, 1968. 1: p. 323-329.

[64] Yan, J.H., et al., "Effect of temperature on the fracture toughness of compact bone," Journal of Biomechanics, 2007. 40(7): p. 1641-1645.

[65] Davies, J. and W. Harris, "Strength of cement-metal interfaces in fatigue: comparison of smooth, porous and precoated specimens," Clinical Materials, 1993. 12(2): p. 121-6.