The surgical implementation of osteoceramic cement in total hip arthroplasty: an in vivo study in canines

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The surgical implementation of osteoceramic cement in total hip arthroplasty: an in vivo study in canines

by

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A thesis submitted to the graduate faculty in partial fulfillment of the requirements for the degree of

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Thomas McGee, Major Professor
Steve Martin
Kejin Wang

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This thesis is dedicated to my amazing fiancée Katie, who is my constant source of inspiration and purpose, and who I know has always dreamed of having a lengthy scientific paper dedicated to her. Katie, you’re everything to me, and I love you.
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Abstract
Osteoceramic cement (OC-cement) is a novel, ceramic-ceramic composite bone cement that has many properties that are superior to traditional polymethyl methacrylate (PMMA) cement. Prior to this research, the mechanical, chemical, biological, and setting properties of the cement had been studied, but \textit{in vivo} testing was the necessary next step in developing it for use in joint replacement. In order to be able to perform surgery using OC-cement, an extensive amount of testing was done on properties that pertain to the handling and behavior of the cement in a surgical setting. This testing included investigations into cement rheology, working time variation, particle size distribution, cement sterilization, and several other areas. In addition to the studies of OC-cement properties, new surgical tools and techniques were developed for precise handling of the cement during the hip replacement procedures. \textit{In vivo} testing of the cement was done by performing unilateral hip arthroplasties on five dogs. Dr. James Toombs and Dr. Stanley Wagner performed the surgeries at the Small Animal Clinic of the ISU College of Veterinary Medicine. One surgery was performed on a cadaver canine, three surgeries were non-survival, and the final surgery was a successful survival total hip replacement. Examination of post-surgical radiographs was done to judge the completeness of the cement space-filling, the mechanical integrity of the cement, and the quality of the bone-cement interfaces. The dog was monitored after the surgery to gage its systematic response to the cement and surgery, as well as to gain more information about the mechanical integrity of the cement. By performing these surgeries and monitoring the dogs afterwards, we have been able to further show the effectiveness of OC-cement in joint arthroplasty.
1. Introduction - Need for Research

The mechanical and biological properties of osteoceramic cement (OC-cement) have been shown in previous studies to be a good match with the requirements of a bone cement. To continue the study of OC-cement and its potential for use in joint replacement, the next necessary step was an *in vivo* study. This was conducted in the present work by performing unilateral total hip arthroplasties on canines and observing the outcomes of the surgeries and the OC-cement’s performance. Before surgeries could be performed with OC-cement, a great deal of additional study was needed on properties of the cement that were relevant to surgical use. These included cement rheology, working time variation, particle size distribution, and cement sterilization. Additionally, new tools and techniques for handling OC-cement during surgery needed to be developed before the hip replacements could be carried out. Surgeries were performed on five dogs. The first was a cadaver surgery, followed by three non-survival surgeries, and finally a successful live, survival surgery. The non-survival and cadaver surgeries were necessarily performed so that the researchers and surgeons could learn about the techniques and tools needed to successfully complete hip replacements using OC-cement. This thesis will begin with a discussion on the need for improvement over the current bone cement standard. The next section will cover previous research performed with OC-cement and background on its properties. Sections 3 and 4 will then describe the current thesis work performed in preparation for and in follow up to the hip replacement surgeries.

Total joint arthroplasty (TJA) is a very common and important procedure that is performed hundreds of thousands of times per year. Since its development in the 1960s, the TJA procedure has been refined into a successful and commonplace operation with a very high
success rate. In 2003 there were over 500,000 TJAs performed, including 220,000 total hip arthroplasties (THA).\(^1\) 36,000 of these were revision surgeries.\(^1\) The total replacement of a joint is performed when the joint is too damaged to be repaired by other procedures. This damage is very often brought on by symptoms of either rheumatoid- and osteo-arthritis.\(^2\) Other conditions that may necessitate TJA include avascular necrosis, congenital dislocation, and Paget’s disease.\(^3\)

Because a large number of patients who undergo THA are elderly and thus at increased risk for serious complications during surgery, minimizing the factors that could potentially necessitate a revision follow-up surgery should be a primary goal when performing a hip replacement. Additionally, with THAs being performed on increasingly younger patients, there is a need to increase the lifetime of prostheses above the average of 10-15 years that is currently accepted. THA is a major invasive procedure, so a complication in any part of the surgery could be damaging enough to cause the implant to fail. Research into new biomaterials and methods for THA is driven by the desire to eliminate these complications.

1.1 PMMA Cement – Problems with the current standard

It has been the goal of Dr. McGee and the Bioceramics research group at Iowa State University to develop a bioactive bone cement that can help eliminate the problems that arise from the use of polymethyl methacrylate (PMMA) bone cement. With OC-cement, we hope to increase the lifetime of hip prostheses while lowering the risk of problems that lead to revision surgery. While PMMA has long been the standard bone cement used in TJA and has been shown to be reasonably successful in these surgeries, it is not without some fairly
serious problems. These problems result from PMMA’s polymeric nature, its undesirable tissue response reactions, its mechanical properties, and the exothermic nature of its setting reaction.

1.1.1 Bioactivity and PMMA cement

Because PMMA is non-bioactive, the body’s response to its presence is to encapsulate the cement with a fibrous layer of tissue. This prevents bonding between the cement and surrounding bone, which can lead to low interfacial strength and loosening of the implant. Additionally, this fibrous layer can cut off the supply of blood to bone that is regenerating after having been removed during surgery. Bone that is without a good supply of blood will tend to resorb, leaving empty space at the interface between the bone and cement. Because there is no direct bonding between the PMMA cement and surrounding bone, the interfacial strength is entirely a function of interdigitation. This interlocking bond suffers when bone resorption occurs or when the surrounding bone surface is smooth, which is often the case in revision THA surgeries. Bioactive bonding between cement and bone is therefore preferable.

1.1.2 Problems with particulate PMMA

In addition to PMMA’s non-bioactivity, problems can arise from the cytotoxicity of the monomer component of PMMA cement. The monomer can get into the body either through some non-polymerized portion of the implanted cement or inadvertently during the implant procedure. The presence of the monomer in the body causes a severe foreign body response that can lead to inflammation and a large drop in blood pressure.
Another problem with PMMA can arise through the release of cement particles and the abrasion they cause at the bone-cement or cement-implant interfaces.\textsuperscript{10} These particles can be the result of articulating surface wear in the joint or of cement fragmentation. Joint fluid can distribute particulate matter throughout the joint cavity very easily, so cement wear in any part of the implant has the potential to damage critical sections.\textsuperscript{13} Numerous studies have shown that particulate debris, particularly polymeric debris, is the primary cause of bone resorption around joint implants.\textsuperscript{11-13} This resorption can lead to implant loosening, in some cases necessitating a revision of the joint prosthesis.

1.1.3 Physical property problems of PMMA

In addition to the problems caused by its polymeric nature and non-bioactivity, PMMA cement has some drawbacks that are related to its physical properties. As PMMA sets and ages in the medullary cavity, it can tend to contract and pull away from the surrounding bone.\textsuperscript{14} This is obviously deleterious to the strength of the implant bond. Additionally, PMMA’s somewhat low compressive strength can lead to cracking under the loads applied by the motion of the limb.\textsuperscript{15} Cracking is detrimental to the physical integrity of the cement and can lead to resorption or loosening. Also, wear of PMMA at the cement interfaces can release polymeric particles, which can invoke an inflammatory tissue response. A cement with a stronger interfacial shear strength would be more resistant to interfacial wear, and thus the release of particulate debris.
1.1.4 Exothermic setting of PMMA

Finally, because the exothermic polymerization process of PMMA cement can produce temperatures that reach in excess of 100°C, the use of this cement in the body can cause tissue cauterization leading to avascular necrosis.\textsuperscript{16, 17} This is very damaging to the regrowth of bone and tissue after the arthroplasty procedure and weakens the bond that forms between the cement and surrounding bone.

1.2 Proposed bioactive bone cements

A great deal of research has been done in the area of bioactive bone cements with the goal of eliminating some or all of the problems with PMMA discussed above. Bone cements made from calcium phosphates have been developed to attempt to address these issues, as well as many types of composite cements. However none so far have shown the combination of properties needed to avoid all of the problems associated with PMMA.

1.2.1 Calcium phosphate-based biocements

Cements composed of calcium phosphate powders have been developed for use in the body. These cements are mixed with an aqueous phase and set to produce hydroxyapatite, which is the naturally occurring mineral phase in bone. They are therefore very bioactive and produce excellent response from tissue.\textsuperscript{18} Calcium phosphate cements can also be made to be injectable.\textsuperscript{19} These properties would seem to make calcium phosphate cements excellent candidates for use in joint arthroplasty. However, the cements’ inherently very low strength makes their use in this application impossible. Calcium phosphate cements have compressive
strengths that are many times lower than PMMA cement and OC-cement; they are therefore used primarily in space filling and dental applications, or as a part of composite cements.\textsuperscript{20}

\textit{1.2.2 Polymer/Bioactive particle composite biocements}

Several composite bone cements have been developed that are comprised of a polymeric resin matrix with hydroxyapatite or other bioactive material as an aggregate.\textsuperscript{21} These cements aim for increased bioactivity over PMMA cement while maintaining high strength and good flow properties. Many use various binders or deflocculants as well as materials such as fumed silica to increase the injectability of the cement.\textsuperscript{30} Crack formation and lack of enduring high strength have so far been the greatest setbacks for these types of composite cements. Several have shown good tissue response in trials, but have been hindered by polymer-induced cancellous bone resorption that weakens the cement/bone bond and leads to failure in the long term.\textsuperscript{17} This is due primarily to the fact that tissue compatibility with polymers is in general not as good as with more bioactive materials, and the tissue/polymer interaction is still dominate in these composite cements. While many of these composite cements may have potential for use in hip replacements for people, none have shown the combination of excellent properties that we believe OC-cement will exhibit \textit{in vivo}. 
2. Osteoceramic Cement Background

OC-cement is a ceramic/ceramic composite cement composed of calcium aluminate hydraulic cement and \( \beta \)-tricalcium phosphate aggregate. These powders are combined and mixed with a 2.0 molar calcium chloride solution to create a paste, which then sets in the body. The calcium aluminate is the component of the cement that undergoes hydration reactions with the liquid to cause setting. Calcium aluminate cement is used in non-biological applications for its relatively rapid setting and high early and sustained strength compared to ordinary Portland cement. It is also a biocompatible material. The \( \beta \)-tricalcium phosphate aggregate gives OC-cement its bioactive properties. \( \beta \)-tricalcium phosphate is very similar in chemical composition to hydroxyapatite, the mineral phase in bone, and therefore bone is able to bond to it directly without the fibrous encapsulating layer that is usually formed around foreign bodies. Together, the calcium aluminate and beta-tricalcium phosphate phases give OC-cement very desirable properties for a bone cement: high strength, rapid setting, and bioactivity for an excellent bond with surrounding bone. In place of water, a 2.0 molar calcium chloride solution is used to hydrate the cement because it shortens the setting time from hours to minutes and reduces the temperature rise on setting to an acceptable level. Both attributes are due to the fact that the normal hydration reactions of calcium aluminate cement are replaced by faster reactions that form calcium aluminate chlorohydrates when CaCl\(_2\) solution is used to set the cement. This makes the cement practical for use in a joint replacement surgical procedure.\(^{22}\)
2.1 Conventional setting of calcium aluminate (CA) cement

When discussing setting reactions in a cement system, a shorthand notation is frequently used to describe chemical reactions in place of writing out the entire chemical formula for the compounds involved. This makes it much easier to read the stoichiometry of the reactions and greatly clarifies how hydration is occurring. The following shorthand is used for the calcium aluminate cement system and the compound involved:

\[
\begin{align*}
\text{CaO} & \rightarrow \text{C} \\
\text{Al}_2\text{O}_3 & \rightarrow \text{A} \\
\text{H}_2\text{O} & \rightarrow \text{H}
\end{align*}
\]

Another deviation from standard chemical notation is the fact that, when writing cement hydration reactions, water is generally left out of the reactant side of the equation and the reaction is left unbalanced. This is done because it is assumed that water is in excess in hydration situations, and therefore the water reactant is unnecessary and cluttering to the written equation. In order to cause cement to flow during its working time, water in excess of the amount needed to form the hydration products must be added. However, when this excess water leaves the cement system through evaporation, it leaves voids that decrease the strength of the set cement. Therefore, to achieve high strength, the lowest water/cement (w/c) ratio that is adequate for flow should be used. The implications that stem from this use of low water content will be discussed in the OC-cement flow properties section of this paper.
CA cement gains high strength quickly after mixing and sustains this strength over time. This makes it advantageous for use in many applications. As a hydraulic cement, it sets by forming hydrate precipitates that bond together to form a paste. As excess water leaves the paste, the hydrates remain, bonded into a hard, strong mass. Kinetics dictates that, after mixing CA cement with water, a number of hydration reactions will occur in series, continuing long after the initial mixing, and producing several different hydration products before the equilibrium product is finally formed. It is often the case that the equilibrium product does not form throughout the cement mass until months or even years after initial setting. The CA cement used in OC-cement is primarily composed of the phases CaAl$_2$O$_4$ (shorthand CA) and CaAl$_4$O$_7$ (shorthand CA$_2$). At low temperatures, CA cement goes through a series of three primary reactions in sequence when mixed with water. They are:

\[
\begin{align*}
\text{CA} & \rightarrow \text{CAH}_{10} \quad (1) \\
\text{CAH}_{10} & \rightarrow \frac{1}{2}\text{C}_2\text{AH}_8 + \frac{1}{2}\text{AH}_3 \quad (2) \\
\text{C}_2\text{AH}_8 & \rightarrow \frac{2}{3}\text{C}_3\text{AH}_6 + \frac{2}{3}\text{AH}_3 \quad (3)
\end{align*}
\]

AH$_3$ is an amorphous alumina phase that forms in a gel state that fills the area between calcium aluminate particles. It slowly transforms to the mineral gibbsite in the cement. This series of reactions occurs with increasing time at constant temperature. However, the same series also occurs as temperature is increased. Reaction (1) is the dominant reaction below approximately 20°C. Between 20 and 30°C, reaction (2) is dominant. Above 30°C, C$_3$AH$_6$ is the primary hydration product that forms. This is advantageous for our work, because it means that the most thermodynamically stable product, C$_3$AH$_6$, is the first product formed at
the temperature of the body, 37°C. Therefore there is no concern about the cement transitioning from one phase to another in the body and thus changing density and volume. The temperature dependence of the hydration products of CA cement is shown below in Figure 1.28

![Figure 1 - Temperature dependence of CA cement hydration products](image)

2.2 Setting of CA cement using CaCl₂ solution

Because OC-cement is hydrated with a 2.0 M CaCl₂ solution instead of with water, the initial hydration products of the CA cement component are different than those discussed above. CaCl₂ acts as an accelerant to the setting of CA cement because it lowers the pH of the solution, thereby increasing the CA dissolution rate. It also increases the concentration of Ca²⁺ ions, enhancing precipitation. After mixing, calcium aluminate chlorohydrates and AH₃ are formed. AH₃ is the hydrated alumina phase that has poor crystallinity and fills space
between chlorohydrates particles. Calcium aluminate chlorohydrates are complex salts that have the formula

$$C_3A\cdot CaY_2\cdot mH_2O$$

where Y is one of the monovalent ions Cl$^-$ or OH$^-$ and m is 10-12. These products form until the Ca$^{2+}$ and Cl$^-$ ions in solution are depleted. After this occurs, cement hydration continues with water as explained in the previous section, and $C_3AH_6$ is the primary phase precipitated. The depletion of Ca$^{2+}$ and Cl$^-$ ions has been found to occur about three weeks after setting.$^{29}$

Calcium aluminate chlorohydrates are more thermodynamically stable than calcium aluminate hydrate products. This is advantageous for OC-cement use because it implies that conversion will not occur after the chlorohydrates are formed. Conversion can happen in water-set CA cement systems when hydration products go through the series of reactions discussed above to form different phases over time. This can be detrimental to physical properties because of the change in density associated with the conversions. The stability of calcium aluminate chlorohydrates implies that there will be no drop in strength over time such as can occur in CA cement systems set with water.$^{29}$ It should be noted that the water/cement ratio of the most stable calcium aluminate product that forms in OC-cement, $C_3AH_6$, is the same as the water/cement ratio used for the OC-cement as a whole. Therefore when $C_3AH_6$ does precipitate after the CaCl$_2$ is depleted, there will be no loss in cement strength caused by a change in volume.
A final advantage that comes from hydrating OC-cement with CaCl₂ solution is the fact that the precipitation reactions that form calcium aluminate chlorohydrates are less exothermic than those of calcium aluminates.²⁹ Therefore the setting of OC-cement in CaCl₂ solution produces lower temperatures in the cavity than would occur with water, meaning there is less risk of cauterizing surrounding tissue when the cement is used in the body. This helps to overcome one of the problems with PMMA cement, as discussed above.

2.3 The interaction of calcium phosphate and bone

As a way of classifying materials, the term biocompatible refers to a material or system that will not cause damage to tissue with which it comes in contact or cause a severe immunological response from the body. As a minimum requirement, any bone cement must be biocompatible. However, it is also advantageous for bone cements to be bioactive. A bioactive material is one that bone will interact with and bond to directly, without the intervening fibrous layer that is present with inert biocompatible materials.

The β-tricalcium phosphate (β-TCP) phase that is included in OC-cement is chemically very similar to hydroxyapatite (HA), the mineral component of bone. β-TCP’s chemical formula is Ca₃(PO₄)₂ and its Ca/P ratio is 1.5. Calcium phosphate materials with Ca/P ratios between 1.0 and 2.0 are generally considered to have the potential for bioactivity. The chemical formula of hydroxyapatite (HA) is Ca₁₀(PO₄)₆(OH)₂ and its Ca/P ratio is 1.67. The Ca/P ratio of hydroxyapatite found in bone, as opposed to stoichiometric HA, is generally somewhat lower, usually 1.62. This is caused by ion substitutions for OH⁻ in the mineral. It is clear that β-TCP and HA are very similar materials, and it should be expected that the body
react to them in similar ways. This is in fact the case. It is well accepted that the tissue response to \( \beta \)-TCP is excellent. Its chemical similarity to bone causes tissue to bond and grow on it in the same way it does to natural bone.

When \( \beta \)-TCP is placed in the bone during surgery, the body responds by rebuilding bone tissue on the \( \beta \)-TCP using the same process as is used when repairing bone damage. Of course, because bone is reamed away during arthroplasty, damage repair is essentially what is occurring. Rather than encapsulating the material with a fibrous layer to try to isolate it, the body begins building new bone directly on the \( \beta \)-TCP surface. This is what creates the direct bond between bone and \( \beta \)-tricalcium phosphate. The first step in this process is the release of fibroblasts from the outer layer of the periosteum and osteogenic cells from the inner layer of the periosteum, which is the vascularized layer that encapsulates dense bone. Together these cells create a fibrous layer of collagen matrix. The osteogenic cells then evolve into osteoblasts, which are bone-forming cells, and they begin calcifying the collagen matrix. This process creates trabeculae, which are the structural elements of bone. Trabecular (spongy) bone is the first type to form at the bone/ \( \beta \)-TCP interface. The medullary cavity is primarily occupied by trabecular bone, and so in the case that \( \beta \)-TCP is placed in the medullary cavity, the newly formed interfacial bone generally remains trabecular. However, the bone is able to respond to stresses and become cortical bone, which is much denser and stronger, if needed.\(^{15}\)

2.4 Mechanical and bonding properties of OC-cement

Previous work has been done with OC-cement to study its mechanical properties, flow characteristics, setting properties, and induced tissue reactions. The worked showed that the
cement developed a compressive strength of 70 MPa four hours after mixing and that a compressive strength of 90 MPa was maintained from 24 hours to 52 weeks after mixing.22 These values compare favorably to the mechanical properties of PMMA cement. Push-out testing was performed on OC-cement samples that had been implanted in the medullary cavities of canine femurs to measure the bonding strength between the cement and the surrounding bone. The interfacial shear strength between OC-cement and cortical bone was found to be several times higher than that of PMMA cement implanted in the same manner.23 This indicates that the bond between bone and OC-cement is inherently much stronger than the bond between PMMA and bone. The reason for this increased strength is that bone is able to bond directly to OC-cement, while interdigitation is essentially the sole attachment method between bone and PMMA. Additionally, OC-cement expands slightly upon setting, while PMMA cement contracts slightly, giving OC-cement much tighter cement/bone and cement/implant interfaces.22

2.5 Setting properties of OC-cement

The setting properties of OC-cement were found to vary based on temperature, composition, and water content of the paste.23 At 37°C, which is approximately human body temperature, the cement sets with the calcium chloride solution in approximately 18 minutes, with a working time of about 9 minutes. These times give a surgeon enough time to insert the cement and implant into the joint cavity, while setting is achieved in a short enough time to be practical during an arthroplasty procedure. The setting time characteristics of osteoceramic cement are comparable to those of the currently used PMMA cement.
Temperature dependence of OC-cement setting and working time is shown in Figure 2 below.

![Setting of OC-cement](image)

*Figure 2 - Temperature dependence of working and setting time of OC-cement*

2.6 OC-cement flow properties

OC-cement has very unique flow characteristics. It is strongly thixotropic and exhibits dilatant flow. Thixotropy is a flow characteristic that refers to the decrease in viscosity of a liquid with time when it is subjected to constant or increasing rate of shear. Dilatant flow refers to an increase in viscosity with increasing shear rate. OC-cement exhibits dilatant properties only after it has been caused to flow thixotropically by vibration. Thixotropy arises when shearing breaks down the internal microstructure of a liquid, which in this case is formed by the hydraulic bonding of the CA cement. When the shear stress is removed, the internal structure rebuilds itself. If the liquid’s rebuilding time is longer than the gap between applications of shear, thixotropy will result because the liquid will not have time to recover
its structure before it is broken up again. This results in a decrease in viscosity as the structure that is giving the liquid resistance to shear is removed.\textsuperscript{26} Shear thinning is closely related to thixotropy. With shear thinning, the internal structure of the liquid is also broken down by shear, and this effect increases with increasing rate. However, a shear thinning liquid's recovery time is fast enough as to not lag behind the applications of shear, and therefore its viscosity will not decrease with constant shear rate.\textsuperscript{26}

In many cases, the distinction between thixotropy and shear thinning is somewhat vague, with many liquids showing characteristics of both. A common way of measuring the thixotropy of a liquid is by constructing a graph of shear rate versus shear stress and plotting the stress while both increasing and then decreasing shear rate. A thixotropic liquid will show anisotropy between the increasing and decreasing cycles, producing a hysteresis loop. The area contained by this loop is indicative of the degree of thixotropy of the liquid. An example of this type of plot is shown below in Figure 3. Sample A has a large hysteresis loop, indicating a high degree of thixotropy. Sample B, with its increasing and decreasing curves almost overlapping, would likely be described as a shear thinning liquid.\textsuperscript{25} However, Sample B does show a small thixotropic loop, so it is clear that the classification is not completely simple. Both curves show a decreasing slope with increasing shear rate, which indicates non-Newtonian flow behavior.
A thixotropic fluid that has a fairly rapid recovery time, such as is the case with OC-cement, will show a decrease in viscosity with constant shear rate, but the viscosity will quickly reach a steady state value rather than continuing to decrease. A balance is reached between breakdown by shear and partial structure recovery. When shear is removed, the fluid will quickly regain its internal structures and gel state.

The practical consequence of these flow characteristics is that OC-cement is extremely responsive to applied vibration. When OC-cement is mixed, the resulting paste has almost no flow until moderate vibrations are applied. When vibrated and flowing, the cement behaves as a high viscosity, dilatant liquid and will flow slowly and fill spaces. The change between the two states occurs very quickly, and removal of vibration stops the cement flow almost immediately.\textsuperscript{23} Vibrational motion subjects the cement to a constant rate of shear, which acts on its thixotropic properties to lower viscosity. The frequency of the vibrations applied is generally in the range of 200 Hz, so the shear rate is high enough that the cement’s internal
structure does not have time to rebuild while vibration is applied. Because of OC-cement's thixotropic properties, this high rate of shear also lowers viscosity. Further evidence of thixotropic behavior comes from the fact that increasing vibrational frequency and thus, shear rate, will decrease cement viscosity and increase flow.

These flow properties present a unique challenge to the use of osteoceramic cement in surgical applications, but one which can be met by the development of special tools and procedures for handling the cement and causing precise and accurate flow. The preciseness with which the flow of OC-cement can be controlled because of its responsiveness to vibration can be advantageous to its use in a surgical setting because there is less of a risk of unwanted flow or spillage into areas not intended for the cement. Additionally, there is less risk of blood dilution, as OC-cement is less absorbent to surrounding fluids through the cement surface. When using PMMA cement in joint repair operations, pressure is applied to the cement to cause it to fill the space in the medullary cavity and interdigitate with the surrounding cancellous bone. This can sometimes have the negative side effect of walling off the blood supply to regrowing bone. OC-cement will have less of a tendency for this side effect because vibration is used rather than pressure to cause it to fill space. Finally, because the flow of OC-cement is dictated by its thixotropy rather than by the addition of excess water, it will have high strength due to the lack of pores and open spaces that are left when excess water exits the cement. OC-cement's flow properties are one of its most unique aspects and greatly influence its handling characteristics and many of its other properties.
2.7 Biological compatibility of OC-cement

The tissue compatibility of OC-cement has been studied previously by implantation of cement into the femoral medullary cavities of adult canines. The dogs were observed for their systemic and tissue responses to OC-cement. Overall response to the cement was found to be excellent. The dogs used in the study remained healthy and active after the surgeries. There were no complications in recovery for any of the dogs. Additionally, direct contact between the cement and cortical bone was observed in harvested specimens, and there were no adverse tissue reactions to the cement during the length of the study.\textsuperscript{23}

Figure 4 shows an image from the study of a femoral section made with fluorescent microscopy. The image shows the intimate contact between the bone and OC-cement at 12 weeks. Fluorescent microscopy makes use of bone-labeling agents that are administered at known times to gauge the growth of regrowing bone after surgery. The agents fluoresce in the bone under near ultraviolet light and their movement in radiograph sequences shows the growth pattern, or lack thereof, in bone after the surgery. In Figure 4, the bright green rings are from the fluorescent agent, and the fact that they are dispersed throughout the bone indicates that this is live, growing bone. Bone that is not growing due to trauma imposed by the surgery would not show the agent dispersed throughout the section.
Figure 4 - Fluorescent microscopy image of OC-cement in canine femur 12 weeks after implantation showing cortical bone (red arrow) and OC-cement (yellow arrow).

\(^{23}\)
3. Materials and Methods

In any major surgery, and especially when the surgery is experimental, all efforts must be given to ensure high quality in every step of the procedure. This is the only way a reliable outcome can be achieved. Because a problem in any part of the hip replacement could result in failure of the procedure as a whole, a great deal of preparation needed to be done to fully prepare for the challenges presented by the use of this new material. This included thoroughly testing the properties of the cement and its raw materials, studying its rheological properties, devising sterilization plans for all materials involved in the surgery, and developing a procedure and tools for using the cement in arthroplasty. This last step was especially important because OC and PMMA cements have very different flow properties and thus need to be handled quite differently when used in surgery. The following is a description of the thesis work done in preparation for and in follow up to the canine surgeries.

3.1 Modified surgical tools and procedures

Developing tools and techniques for handling OC-cement was one of the most critical aspects of this thesis work, because without them, an in vivo study of the cement would have been impossible. Information gained from the non-survival surgeries, discussed below, as well as from discussions with veterinary surgeons, provided a framework for the development of tools for handling OC-cement in a surgical setting. There are many requirements that these tools must meet in order to be used in surgery. The cement must be handled and dispersed in very tight quarters. Tools used for placement must operate in such a way as to not damage the surrounding tissue. Because of OC-cement’s flow properties, it
must be vibrated during mixing, as it fills the cavities, and during the placement of the implant components. A single tool should be used to apply all vibrations as well as for placing the femoral component. This reduces clutter in the limited space of the surgical environment and simplifies the procedure. The tools and procedure need to be designed so that one surgeon can perform each step from mixing through implant placement with minimal assistance. Having fewer hands involved reduces complications in handling the cement and increases accuracy of both cement and implant placement.

To meet these requirements, a tool was developed that applies vibration through a tip, onto which can be attached various ends that vibrate the cement and hold the femoral implant. Instead of the current method of forcing PMMA bone cement into place using pressure, the procedure was modified to allow the cement to flow under vibration through a tube into the medullary cavity. These tools and techniques greatly improved the ability to use OC-cement in hip replacement surgery. Detailed discussion and photographs of the tools are given in the Results section of this paper.

3.2 Cement and raw material properties

In addition to the development of new tools and techniques, much more information on certain properties of the cement was needed before live surgeries could be performed. Many properties of OC-cement, such as flow characteristics and working time, are extremely sensitive to environmental and other factors. Because small changes in these cement properties can greatly affect a surgical outcome, periodic verification is quite important. Verification of the cement and raw materials’ physical properties was done using methods
including XRD, Laser Diffraction, and compressive strength testing. Setting time verification was also done periodically on the cement and liquid used to ensure that these characteristics remain consistent and predictable.

3.2.1 OC-cement Particle Size Distribution

The particle size distributions (PSD) of both the CA cement and B-tricalcium phosphate have been found to be extremely influential on the properties of the OC-cement. The packing density of the B-TCP is particularly important, because if this powder takes up too large a volume in the cement, it is impossible to hydrate the cement with the needed amount of liquid. Additionally, the PSDs of the powders affect the flow properties of the cement. A mixture that contains a fairly uniform distribution through a wide spectrum of particle sizes is considered ideal to obtain a cement paste that will flow readily over itself.

It has been found that only a select few suppliers provide powders with PSDs that work for the OC-cement. Because many of these suppliers do not make detailed PSD data available, it was necessary to measure the PSD of each powder and of the powders combined into OC-cement. This made it possible to better determine the precise PSDs in the powders that gave the desired properties in the cement. A laser diffractometer was used to perform particle size distribution analysis on the B-TCP (using a Horiba LA-930) and CA cement (using a Malvern Mastersizer 2000) powders to obtain specific PSD information. Laser diffraction was also performed on the powders combined as OC-cement (Horiba LA-930), and this data was compared with that of the powders tested separately.
3.2.2 *Working time as a function of CaCl$_2$ concentration*

The working time of bone cement is a critical factor for its use in surgery. It is useful to be able to adjust the working time with close precision. One way this can be done is by altering the concentration of the CaCl$_2$ solution used to set the cement. The changes in concentration should be fairly small so as not to greatly alter the hydration products formed in the cement and the mechanical properties that are derivative of those hydration products. However, small concentration changes can have very significant and useful effects on working time, so it is useful to understand the exact nature of the relationship between these two variables. To study the effect of CaCl$_2$ concentration on working time, samples of OC-cement were prepared with CaCl$_2$ solutions with concentrations ranging from 1.0 M – 3.0 M. The working times of five samples from each concentration were determined. This was done by using the vibrating spatula to make a cut in the cement paste and then making a parallel cut approximately one centimeter away. If the cement was not past its working time, making the second cut would cause the cement to flow and eliminate the first cut. If the working time was past, the first cut would remain. This information was used to create a plot of CaCl$_2$ concentration versus cement working time.

3.2.3 *Cement hydration products and CaCl$_2$ concentration*

Changing this concentration of the CaCl$_2$ solution used to make the cement paste also changes somewhat the hydration products that form upon setting. Specifically, increasing the amount of CaCl$_2$ would increase the prevalence of calcium aluminate chlorohydrates in the set mass and decrease the amount of C$_3$AH$_6$, because this product only forms when the CaCl$_2$ is used up.
In order to verify these hypotheses and to understand with certainty what products will form should the CaCl₂ need to be adjusted, X-ray diffraction (XRD) was performed on OC-cement samples set with varying concentrations of CaCl₂ solution. A Siemens D500 X-ray diffractometer with a diffracted beam monochromator was used to collect data with 50 kV Cu Kα radiation. Data was collected over a Bragg angle range of 5-40° 2θ, with a scan rate of 1° 2θ/min. Based on previous work, the XRD peaks are known for CA, CA₂, C₃AH₆, and calcium aluminate chlorohydrate. These are shown in Figure 5. XRD was used to determine the amount of calcium aluminate chlorohydrate products present for OC-cement set with concentrations of CaCl₂ varying from 1.75M to 2.75M. Each OC-cement sample was made in pellet form and stored at 37°C in Ringer’s solution for 40 days. After 40 days, the pellets were removed from the Ringer’s solution, ground to a powder smaller than 100 mesh, and stored in moisture-tight containers until XRD was performed. The 40 day hydration time allowed the relevant hydration products to be formed to great enough degree to facilitate comparative measurement. The data was analyzed to determine the areas of the calcium aluminate chlorohydrate peaks for each sample. The areas were used as a metric for the amount of calcium aluminate chlorohydrates that had formed with varying concentrations of CaCl₂.
Figure 5 - Characteristic XRD peaks for C₃AH₆, calcium aluminate chlorohydrate, and CA₃₀

3.2.4 Working time as a function of temperature

Although previous work with the OC-cement had studied the affect of temperature on cement working time, this work looked at a wide temperature range and measured working time at temperature intervals of 10°C or more. It has been found that the working time of the cement can vary significantly with small temperature changes around room temperature. Because this is the temperature range in which the cement will be used in practical situations, and because it is very important to be able to accurately predict working time when in surgery, it was necessary to obtain more precise information on the temperature effect on OC-cement working time. This was done by measuring the working time as function of temperature over a range of 19-27°C, using the method discussed above in section 3.2.2. Working times were measured in 1°C increments, and five samples were measured for each temperature. The working time of the cement was determined by observing the time after mixing at which it became unresponsive to vibration.
3.3 Rheological properties of OC-cement

The study of the rheological properties of OC-cement is critical to understanding its behavior under the conditions in which it will be used. As discussed above, the flow of OC-cement is greatly dependent on applied vibration. While previous work had used vibration to manipulate the cement, no detailed study of the vibrational effects on OC-cement flow properties had been done prior to this work.

Because no quantitative study of vibration and OC-cement flow had been done previously, a procedure was developed to quantify the flow caused by various vibrations. The equipment was not available to do detailed studies using viscosity as the dependent variable, so it was decided that gravitationally caused flow would be the variable measured. As will be discussed in section 4.7, this turned out to be a more useful variable than viscosity, which is closely related. A test apparatus was designed to measure the amount of flow undergone by a set shape and mass of cement when vibration was applied. Several independent variables could be changed to vary the conditions under which cement flow percent was measured. These included time after mixing, vibrational frequency, time of applied vibration, as well as several changes to the cement paste itself. In this series of studies the time of applied vibration was kept constant for each experiment. Other variables were changed depending on what dependence of cement flow was being studied.

The quantitative effect of vibration on the cement was measured using a modified version of ASTM Standard C1437 – Standard Test Method for Flow of Hydraulic Cement Mortar. This test measures the amount that a conical mass of cement flows outward under a specified
agitation. The standard is included as Appendix A. The test was scaled to be compatible with the smaller volumes used in working with OC-cement. In the ASTM Standard method, the cement is caused to flow by repeatedly dropping the table from a set height. Because OC-cement’s flow is dependent on vibration, the flow table was designed to be vibrated with varying frequency. A pneumatic vibrating motor (Vibrolator BD-13, Martin Engineering) was used to apply vibration to the table. By changing the air pressure to the motor, the frequency could be varied and calculated. The flow of cement tested with this setup was quantified by its flow percentage. The calculation method for flow percentage can be found in the ASTM Standard in Appendix A.

Figure 6 shows an example of the plate on which the cement mass was placed during the tests. The four radial lines on the plate allow the average change in diameter of the mass to be measured. Figure 7 shows the conical mold used for the cement. The conical shape assures that the cement will flow uniformly outward under vibration from the table. The bottom diameter of the mold was 3.7 cm, the top diameter was 2.4 cm, and the height was 2.1 cm. These dimensions gave a mold volume that held approximately 30 grams of OC-cement, which was a standard batch size. Shown in Figure 8 is the test setup for the flow testing. The cement is removed from the mold on the glass plate. At the specified time after mixing, the plate is firmly coupled to the vibrating table, which is set at a specified frequency. In each of the experiments, the plate was coupled to the table for five seconds. The diameter of the resulting cement mass was then measured with precision calipers and the flow percent was calculated. Figure 9 shows the attachment at the air supply of the tubing that supplies the
pneumatic motor. The air pressure gage shown was used to determine and vary vibrational frequency.

Figure 6 - Glass plate used to measure cement flow. The four numbered lines are used to calculate the average change in diameter of the cement mass after leaving the mold.

Figure 7 - Mold used for cement flow testing. The mold is conical in shape, with a bottom diameter of 3.7 cm.
Figure 8 - The test setup for cement flow testing, showing the vibration table, cement mold, and flow plate. The yellow tubing attaches the vibrating motor to the air supply. The legs are sprung to increase the amplitude at the table.
3.3.1 Vibrational frequency effect on OC-cement flow

Knowledge of the effect of vibrational frequency on the resulting flow properties of OC-cement is very important for a number of reasons. The ease of filling the femur with cement increases as the degree of the cement flow increases. It is therefore pertinent to understand how the flow of the cement changes with vibrational frequency. For a thixotropic fluid such as OC-cement, viscosity would decrease as the applied strain rate (vibrational frequency) was increased. This would seem to dictate that the highest possible frequency be applied to the cement during use. However, it was not known exactly how the viscosity of the thixotropic OC-cement translated into gravitationally caused flow. Because the goal of all of the cement properties studies was to understand the cement's behavior in a surgical context, it was most
important to know exactly how the flow, and not the viscosity, would be affected by different frequencies.

To measure the effect of vibrational frequency on cement flow, a series of tests were performed using the vibration table setup described above. Frequency was varied by changing the air pressure to the motor on the vibrating table. The resulting cement flow from four different vibrational frequencies was measured. Vibration was applied to the samples for five seconds at four minutes after mixing. At each frequency, the resulting flow percent of the cement was measured in five samples. The data was used to construct a plot of vibrational frequency versus cement flow percent.

3.3.2 Cement flow over working time

The modified ASTM standard was used to measure the change in flow of OC-cement over its working time. This information can be used as means of determining the working time of the cement, as well as to understand how the cement flows towards the end of its working time. These pieces of information each give a more accurate idea of the amount of time that the surgeon has to complete the placement of the implant. Samples of cement were tested for flow at times beginning at four minutes after mixing up until the working time was clearly past. Each cement sample was mixed and placed into the conical mold. Approximately one minute prior to the specified time for testing, the cement was removed from the mold and placed on the vibrating plate. At the testing time, the flow of the cement was measured using the vibrating table apparatus. Samples were vibrated for five seconds with a frequency of
11,800 VPM. Five samples were tested for each time after mixing. The resulting data was used to construct a plot of time versus cement flow percent.

3.3.3 Change in cement flow with added water

It was determined during the first two non-survival surgeries that a slightly lower apparent cement viscosity would be preferred for surgeries in mid-sized dogs. In order to accomplish this, small amounts of de-ionized (D.I.) water were added to the cement during the mixing process. This slightly increased the amount of liquid in the mixture without increasing the amount of CaCl₂, therefore leaving the hydration products and their relative amounts unchanged. In order to determine the amount of D.I. water to add to obtain ideal flow, the flow percent of the cement was tested as a function of added water using the vibration table. The water was added at levels of 0.20g, 0.40g and 0.533g H₂O to 30 grams of cement powder and 9.4 g CaCl₂ solution. The flow percents of the resulting cement pastes were measured at 11,800 vibrations per minute (VPM) with a five second application time. Five samples were tested for each amount of added water. The data was used to construct a plot of amount of added water versus cement flow percent.

3.4 Surgical sterilization methods

Sterilizing a material for surgical use involves choosing a sterilization method, verifying that the method was effective to a chosen Sterility Assurance Level and then testing for any changes in properties that may have occurred due to the sterilization process. Successfully sterilizing a material in a way that is not damaging to it is one of the most important parts of preparing for a surgery. This is especially true in experimental procedures such as those done
in this thesis work, where there is little room for error and when there is no prior knowledge of successful techniques. Because OC-cement is a powder composite material that reacts strongly with water, ensuring that its properties stay satisfactory during sterilization is a particular challenge. Two sterilization methods have been chosen as potentially compatible with OC-cement. They were electron-beam irradiation and dry heat sterilization.

During electron-beam sterilization, energy is imparted on the material to be sterilized by a stream of electrons emitted from a linear accelerator. When an electron strikes an ion in the material, it ejects an electron from it. This electron then strikes and ejects additional electrons, and the process continues through the material as a compounding chain reaction. The electron radiation produced, usually on the order of 25 kGy, is sufficient to kill any microorganisms present. Because of the compounding nature of the process, the material furthest from the e-beam source receives the highest dose of radiation. The amount of radiation that the material receives is given as an average reading from several measurements. It is therefore important to ensure that the minimum measured radiation amount still be above the chosen dosage for sterilization. E-beam sterilization was performed using a linear accelerator at the ISU Meat Laboratory facility.

Dry heat sterilization is a very simple sterilization method that involves heating the sample to a high temperature and holding it there long enough to destroy all microorganisms present. The sample is heated in the absence of moisture, as compared to the autoclave method, where high temperature, pressurized steam is used to heat the sample. Steam is obviously incompatible with a cement that reacts with water, so dry heat sterilization is more
appropriate for OC-cement if it is able to fully sterilize it without affecting its properties. For sterilization trials, OC-cement was heated to 200°C and held for 30 minutes. Previous work has shown that 200°C is close to the highest temperature that the cement may be heated without altering its properties.

Samples of OC-cement powder were sterilized by both of these methods. The sterilized samples were then tested for their compressive strength, degree of flow under vibration, and working time. The effectiveness of the sterilization treatments was tested by culturing samples of sterilized cement and monitoring for bacterial growth. Based on the results of this testing, as well as on factors such as availability of facilities, the sterilization method to be used for OC-cement for surgery was selected.

3.5 Non-survival surgeries

Four non-survival hip replacement surgeries were performed at the ISU College of Veterinary Medicine in order to gather needed information on the use of OC-cement in canine surgery. A description of the THA procedure used in the surgeries taken from the ISU Research Compliance Review Form on the Use of Animals in Research is included in Appendix B. The first surgery was performed on a cadaver dog, and three subsequent surgeries were performed on live dogs under non-sterile conditions that were euthanized following the procedures. The cadaver surgery was the first surgical procedure performed with OC-cement and was done to gain basic information about using OC-cement in the body. This procedure was done prior to the development of OC-cement-specific tools and procedures, and therefore used standard laboratory tools to manipulate the cement. While the
surgeons were able to place the cement and implant and complete the surgery, there are many areas of the procedure that needed improvement before the cement was able to be used in live surgeries. The cement was placed in the medullary cavity with a small spatula and a vibrating shoulder massager was used to apply vibration to the implant components during placement. These methods, while adequate for the task at hand, were awkward and not precise enough for live procedures.

Three non-survival surgeries were performed prior to the survival surgery. These hip replacements were performed using new surgical tools and procedures as they were being developed. Information gained from each surgery was used for further development, resulting in the final versions of each tool that were ultimately used in the live hip replacement surgery. In order to assure that proper care of the dogs was taken throughout the study, a research protocol was submitted to the ISU Institutional Animal Care and Use Committee for approval. This group reviews all research at the University that will use animals to assure that the planned care and procedures will be ethical and humane. Approval of the submitted protocol is necessary for any animal research to take place. The protocol submitted for this research detailed the surgical procedures that were ultimately carried out during the non-survival and survival surgeries, as well as all pre- and post-surgical care. The protocol was approved by the Committee, so the study was allowed to move forward.

Prior to each surgery, radiographs of the dog’s hip were examined to determine the appropriate size for the implant to be used. The diameter of the inner section of the femur containing trabecular bone was measured. This diameter was used to determine the diameter
of tubing that would fit into the femur after the trabecular bone had been removed. Using the diameter of the trabecular-filled section of the bone and the implant size, the amount of cement needed to fill the cavity was estimated.

For the sake of convenience and consistency, OC-cement had been mixed in two standard batch sizes containing 15 grams and 30 grams of dry cement. The density of wet OC-cement after mixing is known, and therefore the volumes of each of the batch sizes can be calculated. By estimating the volume of wet cement needed to fill the reamed femoral cavity, it was determined which standard batch size of cement should be used during the surgery. Once this preparatory work was completed prior to each surgery, the procedure was performed using the latest tools and procedures. The relative success of each procedure was judged by the surgeons and the osteoceramics research group.

3.6 Live surgery and post-surgical evaluation

The performance of a live total hip replacement surgery and the evaluation of the procedure and the OC-cement in vivo was a central part of this thesis work. The important factors studied for evaluation included the efficacy of performing the modified procedure smoothly and consistently, the ability of the cement to perform mechanically under real world conditions, and the dogs’ systemic response to the surgery and the new cement. The successfulness of the modified procedure was determined by qualitative observations made during surgery as well as by observing the cement’s behavior over time in the dog. Radiographs were taken regularly over the life of the dogs to examine the cement’s filling
ability in the joint cavity. The integrity of the cement/bone and cement/implant interfaces was closely monitored.

3.6.1 Mechanical behavior of cement in vivo

The mechanical integrity of the cement in the body was studied over time with radiography. The radiopacity of OC-cement lends itself to observation by x-ray, and radiographs of the dog’s limbs were a good way to study how the cement maintained physical integrity to the stresses induced in the body. Additional information on the mechanical stability of OC-cement over time was gained by observing the dogs’ physical activity and apparent pain level after the surgeries were performed.

3.6.2 Systemic and tissue response to surgery and cement

The systemic response of the dogs’ to the surgery and OC-cement was observed by monitoring the general health of the dogs after surgery for signs of infection or adverse foreign body responses. Any adverse effects that caused by the OC-cement would be readily apparent in the dogs after surgery, so monitoring was a good indicator of success in this area. The dogs' vitals were monitored regularly for two weeks after the surgery, and any abnormalities were noted. The level of activity and food intake of the dogs was also regularly recorded. Radiography was used to study the interface between the cement and bone for signs of resorption, which is an indicator of adverse tissue response. Radiographs of the bone-cement interface were also used to study the level of success had in filling the femur and acetabulum with OC-cement during surgery. A good fill is essential to the longevity of the prosthesis.
4. Results and Discussion

The results from this thesis work are divided into three areas: the development of surgical tools and procedures for working with OC-cement, the testing of properties important to using the cement in surgery, and the completion of the hip arthroplasty procedures. These results are presented below. Because the results from some areas influenced those from another as the thesis work progressed, there is some overlap in the presentation of the results. For example, information gained from non-survival surgeries informed the further development of surgical tools, and vice-versa. The results from this work are laid out below in what is hopefully a logical and easy-to-follow manner.

4.1 New surgical tools and procedures

Several new tools were developed for handling OC-cement during hip arthroplasty, and several iterations of each tool were created before the final version of each was decided upon. The devices that were created include a stainless steel funnel, a polyvinyl tube, a hand-held vibrating instrument, and several heads that attach to the vibrator for handling the cement. The function of each of these tools is described below, along with the process undergone for their development.

The hand-held vibrator is the most important tool for handling OC-cement, and was the key development for successfully implementing the cement in surgical settings. The vibrator was made by modifying a vibrating engraving tool. A chuck was designed to fit into the hole for the engraving tip. This chuck accepts the spatula end that is used for mixing and pouring the cement and which is secured with a hex bolt. The hand-held vibrator with the spatula
attachment is shown in Figure 10. A closer view of the chuck and spatula end is shown in
Figure 11. The top of the chuck can be covered with a thick rubber layer, which facilitates
the coupling of the top to the PFA tubing to cause cement to flow out of the tube. This can be
seen in Figure 12. The vibrators power can be varied with a dial that can be set to nine
different power levels. This feature is useful in surgery, where more flow is needed when
moving the cement through the tube and less when inserting the femoral prosthetic into the
femur.

*Figure 10 - hand-held vibrator with spatula tip attached*
Figure 11 - View of hand-held vibrator as it is held to mix and manipulate OC-cement

Figure 12 - View of hand-held vibrator being pressed to the funnel and tubing to couple vibration and cause OC-cement to flow through tube.
To maximize the versatility of the hand-held vibrator, a system was designed by which various components could be used with the vibrator to handle the cement and implant components at various stages of the surgery. Each component incorporated a small piece of metal rod that was used to attach it to the vibrator by inserting into the vibrator's chuck and securing with a setscrew. This creates a tight attachment between the head and component, and allows for vibrational coupling to occur. Using this system allows vibration to be applied through the vibrator head to any reasonably sized component by attaching the correct size rod at some point on the component. This affords great flexibility in designing components for handling OC-cement at various stages of surgery. An example of this method of attachment to the vibrator is shown in Figure 13 below (red arrows).

*Figure 13 - View of hand-held vibrator showing the setscrew attachment method*
Inserting the femoral implant component was one important challenge that needed to be overcome before the successful survival surgery was possible. In traditional hip replacement surgeries using PMMA cement, the femoral component can be pushed through the cement in the medullary cavity with force and can be rotated into position simply by applying pressure. With OC-cement, however, the application of force causes no flow. Therefore the femoral component must be vibrated while being inserted into the OC-cement-filled medullary cavity. This is challenging, because the applied vibration must be strong enough to cause the cement in contact with the implant to flow, but be applied in such a way as to not damage the implant. Especially prone to damage during implantation is the stem of the femoral component, which must not be scratched or marked in any way that could compromise its ability to attach to the ball of the implant. It was also essential that the component used to attach the vibrator to the femoral implant not impede the surgeon's view of the bone while in use. Precise positioning of the implant in the bone is essential to reconstructing the joint.

With these requirements in mind, three different components were designed to couple vibration to the femoral implant. Feedback gained from the surgeons during the non-survival surgeries was used to improve the designs and create a component that was able to be successfully used in the survival surgery. The femoral component attachment that was used in the survival surgery used a thin rod to couple to the femoral component. The rod fit into the hole at the top of the implant. This is somewhat similar to the method of placing the femoral component in PMMA cement, in which the implant is pushed into the cement with a rod that fits into the hole in the implant. The rod fitted into the hole in the femoral implant component is shown in Figure 14 (red arrow). In addition to the rod used to couple the
vibration, the femoral component attachment used a plate with two holes that allowed the rod and the implant’s stem to be inserted. This gave greater vibrational coupling to the implant, as well as allowing the implant to be rotated to the correct orientation in the femur by simply turning the vibrator. The femoral component attachment is shown attached to an implant in Figure 15.

*Figure 14 - Rod attachment shown fitted into the hole in the femoral implant component. The rod is pressed into the hole about 5 mm and used to push the vibrating implant into the femur*
Another attachment developed for placing the femoral implant component was a clamp-type implant attachment that used a three-pronged clamp to hold the implant stem while being coupled to the vibrator. The three prongs were tightened and secured around the stem with thumbscrews and nuts. This attachment also coupled the femoral implant tightly to the handheld vibrator and allowed the implant to be rotated in the femur by turning the vibrator. This attachment was the first one developed for the femoral component and was used during the non-survival surgeries, but not the survival surgery. The clamp-type attachment is shown attached to a femoral stem in Figures 16 and 17.
Figure 16 - The clamp-type attachment shown connected to the vibrator

Figure 17 - The clamp-type attachment shown holding the implant stem. The hold is tight, and controlled by the screws on the set of the attachment. The nuts are used to keep the screws from backing out during vibration.
Thin-walled perfluoroalkoxyethylene (PFA) tubing was used to deliver the OC-cement to the femur and acetabulum during surgery. This allowed the cement to be placed into tight spaces with great precision. Precision placement of the cement is critical in a surgical setting to minimize contamination of the surrounding tissue. OC-cement’s thixotropic flow properties greatly enhanced the ability to avoid spillage during surgery, because the flow of the cement was able to be stopped immediately by removing vibration. It was critical that the tubing used have as thin of walls as possible. Thin-walled tubing allows a tube with an outer diameter that fits into the reamed femur to carry the highest possible amount of cement. The cylinder of cement that leaves the tube while in the femur will then have a diameter very close to that of the reamed area of the femur, and will therefore be able to spread out and fill the cavity more easily.

In addition to thin walls, it was necessary for the tubing to have an appropriate stiffness. The tubing needed to be substantially stiff enough to fully couple the vibration from the vibrator and funnel. However, some flexibility was needed to allow a small amount of bending in the tube while it was placed in the femur. The necessary stiffness was determined through many trials working with various types of tubing in simulated implant trials. Several different types of tubing were tested before the final type was decided upon. The tubing used in all surgeries and work with the cement was Cole-Parmer Standard PFA tubing. The two sizes used were 6.4 mm and 8.0 mm inner diameter.

A very tight fit between the PFA tubing and the stainless steel funnel was need for good vibrational coupling to occur. Stainless steel funnels were only available in standard sizes,
none of which had stem diameters that matched the inner diameter of the proper sized tubing. To obtain the tight fit, the funnels were modified by adding a custom sized stem which had an outer diameter that was slightly larger than the inner diameter of the tubing. Stretching the tubing over the stem produces a very tight fit and good vibrational coupling. Two sizes of tubing were selected to accommodate differences in canine femur sizes. In order to maximize the usefulness of the stainless steel funnels, the custom stems were designed so that they formed a tight fit with the larger sized tubing. The same funnels could also be used with the smaller sized tubing by making an adaptor from the larger sized tubing. In this way the smaller tubing fits tightly into the larger tubing and the funnel stem fits tightly into the other end of the larger tubing. The smaller tubing is therefore vibrationally coupled to the funnel. This setup with the funnel, adaptor, and small tubing is shown in Figures 18 and 19 below.

*Figure 18 - Custom stainless steel funnel, PFA tubing, and tubing size adaptor (red arrow).*
The development of these tools and techniques has allowed handling of OC-cement to be done with enough precision to successfully perform hip replacement surgery using the cement. The tools are made in such a way as to allow several options for the attachments used for handling, pouring the cement, and placing the implant. This allows flexibility during the surgery, which is extremely valuable and makes a successful procedure much more likely. The progress made in cement handling has taken OC-cement from a novel, experimental material to a fully realized, function biomedical material which can be used \textit{in vivo}. 

\textit{Figure 19 - View of inside of funnel and tubing showing the tab used for vibrational coupling}
4.2 Cement working time variation with CaCl₂ concentration

The measured working time of OC-cement as a function of CaCl₂ solution concentration is shown below in Figure 20. The notable feature of this plot is the minimum working time found at approximately 1.25 M. Based on previous study of cement working time and concentration, this was a surprising result. Because OC-cement set with D.I. H₂O has a working time of more than one hour, and that 2.0 M CaCl₂ decreased the working time to approximately 10 minutes, it had previously been thought that increasing the CaCl₂ concentration above the standard 2.0 M would cause a further decrease in working time. However, this was found to not be the case. As can be seen in Figure 24, the working time decreases very rapidly with concentration from 1.0 M to approximately 1.25 M, and then begins a gradual increase. This increase continues until 3.0 M, which is the highest concentration tested because it would be the highest practical concentration considered for use in surgical applications.

Although these results were unexpected, they are still very useful for fine-tuning the working time of OC-cement. As can be seen from Figure 20, the working time can be increased by several minutes by increasing the CaCl₂ concentration. This ability can be very useful in situations where placing the cement is unusually difficult or there are other reasons for needing more time to work with the cement.

The chemistry that causes the minimum in working time at an intermediate CaCl₂ concentration is, at this point, unknown. It is likely that, around the working time minimum
concentration, the hydration products that are forming in the cement paste begin to change abruptly. That is, once there exists in solution an adequate amount of CaCl$_2$, a product begins to be preferentially created that forms more rapidly than the product that forms when there is not adequate CaCl$_2$ present. However, the kinetics of these reactions are beyond the scope of this thesis work, so the precise cause of this phenomenon has not been determined.

Using this information, it will be possible to accurately adjust the working time of OC-cement by varying CaCl$_2$ concentration. As previously discussed, the working time can also be altered by changing the temperature at which hydration takes place. However, should there be a need for a longer working time during surgery, it is clearly easier to use a solution with a different concentration than to adjust the temperature of the operating room. The ability to finely adjust the working time of OC-cement without appreciably altering its properties further increases the practicality using the cement for joint replacement. The raw data from this working time versus concentration study, as well as from the other working time studies performed, is given in Appendix C.
4.3 Cement working time variation with temperature

Figure 21 below shows a plot of the working time of OC-cement measured at various temperatures. The temperatures at which working time was tested ranged from 19 to 27°C. Working times were measured at 1°C temperature increments. This range is adequate to account for all ambient temperatures at which a surgery might be performed.

Figure 21 shows a clear downward trend in the working time as temperatures is increased. This is consistent with previous data on working time and temperature. The working time decreases fairly linearly with temperature. Over the 8°C temperature range, the working time decreased by over 6 minutes, which is a decrease of 42.8%. This is clearly a significant
change in working time over the fairly small range of temperatures that can be considered room temperature. A six-minute change in the amount of time that the surgeon has to place the cement and implant, if unaccounted for, could certainly mean the difference between a successful implantation and a failure.

These findings indicate that it is critical to precisely measure the ambient temperature of the operating room before beginning work with OC-cement. By using the results of this study, an accurate prediction of the available working time of the cement can be made based on the temperature of the operating room. This knowledge makes successful placement of the cement in the body more likely, leading to a higher probability that the joint replacement will be a success. This obviously is a very positive development. As will be discussed in section 4.7, the plot of working time versus temperature can also be used in predicting the nature of flow over the entire working time at various temperatures.
Temperature vs OC-cement Working Time

\[ y = -0.8268x + 29.799 \]
\[ R^2 = 0.9659 \]

Figure 21 - Ambient room temperature vs OC-cement working time, showing a linear decrease in working time with room temperature.

4.4 CaCl₂ concentration and hydration products

Shown in Figure 22 is a plot of the XRD spectra for the five OC-cement samples tested. The concentration of CaCl₂ solution used to make the samples varies from 1.75-2.75M from top to bottom in the Figure. As can be seen from this overview, the spectra were all very similar. The spectra all show identical peak patterns and the magnitude of the peaks appear, at least from this macro view, to be unchanged from sample to sample. This was to be expected, as the changes in CaCl₂ concentrations used were not large enough to cause significant changes in the hydration products.

Examination of the peak areas and heights revealed the changes brought about by the concentration differences in the amount of calcium aluminate chlorohydrates present in the
set cement. Four characteristic peaks were examined for this purpose. The peaks were located at approximately 11.31°, 22.7°, 38.8°, and 39.2° in each sample’s spectra. Table 1 below shows the peak heights and areas of these four characteristic peaks from samples set with each of the five different CaCl₂ concentrations used. In the Table, the columns are labeled with A- or H- in front of the characteristic Bragg angle of the peak in question, referring to the peak area and height, respectively. To allow for easier visualization of the trends in this data, Figure 23 shows 3-D plots of the four peaks for each of the five concentrations, with peak areas shown in the top graph and peak heights in the bottom. In the plots, the CaCl₂ concentration increases from back to front. Interestingly, these plots do not show the direct increase in area and height of the calcium aluminate chlorohydrate peaks that was expected for increasing CaCl₂ concentration. Instead, the peak sizes change somewhat erratically with increasing concentration. With some 0.25M increases in concentration the peak areas and heights increased, but in others the peak sizes went down. Also observed was the fact that the four peaks did not always change uniformly with concentration. For the same concentration increase, there were occasions where some of the peaks increased while others decreased.
Figure 22 - XRD spectra for the five samples tested. From top to bottom, the CaCl$_2$ concentration used to make the samples varies from 1.75M - 2.75M in steps of 0.25M. The four characteristic calcium aluminate chlorohydrate peaks are indicated with red vertical lines at the bottom of the figure.

Table 1 - Peak area and height data for the calcium aluminate chlorohydrate products in OC-cement samples set with five different concentrations of CaCl$_2$

<table>
<thead>
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<td>1851</td>
<td>177.8</td>
<td>641</td>
<td>184.4</td>
<td>302</td>
<td>129.3</td>
<td>217</td>
</tr>
<tr>
<td>2.5</td>
<td>642</td>
<td>2545</td>
<td>115.7</td>
<td>524</td>
<td>214.4</td>
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<td>165.9</td>
<td>206</td>
</tr>
<tr>
<td>2.75</td>
<td>567.1</td>
<td>2022</td>
<td>156</td>
<td>577</td>
<td>188.8</td>
<td>307</td>
<td>196.8</td>
<td>220</td>
</tr>
</tbody>
</table>
Figure 23 - Peak areas (top) and heights (bottom) of the calcium aluminate chlorohydrate products from the XRD spectra of OC-cement samples set with five different CaCl$_2$ concentrations.
There are two conclusions that can be drawn from these somewhat unexpected results. The first is that, for the range of concentrations tested, the concentration of CaCl₂ used to set the cement has only a small affect on the resulting calcium aluminate chlorohydrate products. The XRD spectra from all samples were very close to identical, and the areas and heights of the peaks in question changed only minimally with concentration. The second conclusion is that uncontrolled factors appear to have a greater effect on chlorohydrate formation than CaCl₂ concentration, essentially indicating that these two factors can be separated. These uncontrolled factors could, for example, include room temperature and humidity at the time the samples were made or the time between grinding and sealing the powder in its container. The important point is that CaCl₂ concentration cannot be considered to be the most important factor affecting the calcium aluminate chlorohydrate products in the set cement within the range of concentrations studied. This fact, combined with the small magnitude of the differences observed between the spectra, means that CaCl₂ concentration can be used to make small changes to the OC-cement working time without having to worry about appreciably altering the hydration products. This is a positive outcome, as it gives surgeons more options when using OC-cement in a surgical setting.

Although XRD was a fairly good characterization method for evaluating the hydration products of the cements, it is possible that better results could be obtained through a more precise test. A method such as thermal gravimetric analysis (TGA) may provide more accurate assessment of the changes in products that occur with the small changes in CaCl₂
concentration. This work can be carried out in the future if it is determined that more accurate information on hydration products is needed.

4.5 Cement flow over working time

Shown in Figure 24 is a plot of OC-cement flow percent as a function of time. Flow percent data was collected at one-minute intervals over the working time of OC-cement. The first time at which flow was tested was four minutes after mixing, and the last time was 12 minutes after mixing. Five samples were tested for each time, for a total of 45 samples tested. The resulting data gives a good, quantitative indication of how the flow behavior of OC-cement changes over its working time.

The plot shows a clear downward trend in the flow percent of OC-cement over its working time. This corresponds with an increase in viscosity of the cement as hydration products form in the paste. The rate of decrease in the flow of the cement increases as the time after mixing increases, with very rapid hardening of the cement paste occurring near the working time. Based on the temperature at which these test were carried out, 25°C, the working time of the OC-cement was 8.8 minutes. From this data, the cement has approximately 10% flow at the working time. Below this flow value, the cement is unable to be manipulated in a useful way.
Figure 24 - OC-cement flow behavior over its working time at 25°C. The flow begins to decrease gradually with time, but then shows a rapid decrease as the working time approaches.

Quantifying cement flow and working time in this way is useful in examining how the cement behaves at various stages of its working time. When working with OC-cement in surgery, different amounts of flow are needed for different tasks, which occur at different periods during the cement's working time. For example, placing the cement into the reamed femur using the PFA tubing requires more flow than does pushing the femoral implant component into the cement-filled femur. The former task can only be accomplished relatively early in the cement's working time, while enough flow is present even late in the working time for the later task to be performed. By determining exactly how much cement flow is needed during each handling stage and referencing those numbers to the above data, a timetable for placing the cement and implant components can be constructed. This type of
information is much more useful than the single-value working time that is commonly given for a cement.

From the plot of cement flow versus time and the previous plot of working time versus temperature, it becomes possible at any reasonable room temperature to estimate the amount of cement flow that will be present at any time during the working time. The flow versus time tests were carried out at a constant temperature, so from these tests it was determined that at the qualitatively determined working time, the cement flows 10% under the standard testing conditions. This value will not change with temperature, so it is therefore possible to fit the shape of the flow over time curve to the appropriate working time, using the working time versus temperature plot. For example, at 22 °C, the qualitative working time given by Figure 21 is approximately 11 minutes. Therefore there are two known points to the flow percent versus time graph, approximately 100% flow at four minutes after mixing and 10% flow at 11 minutes after mixing. Using these two points, the shape of the flow percent versus time plot, the data for which was collected at 25 °C, can be fitted to this new temperature. The resulting plot can be used to create a timing schedule for the various procedures that need to be done before the cement working time is up, as discussed above.

4.6 Cement flow variation with added water

As discussed previously, results from the early non-survival surgeries made it apparent that a lower viscosity of the cement would be advantageous to handling during the procedure. To lower the viscosity, small amounts of D.I. water were added to the cement while mixing.
Quantifying the effects of the added water on the cement paste’s viscosity was done by adding varying amounts of water by weight and measuring the resulting flow using the flow table setup. Each amount of added water was tested with n=5 samples. The effect of various levels of water on flow is shown below in Figure 25. This plot shows an increase in cement flow with the amount of water added which is nearly linear. This linearity is advantageous because it makes it possible to choose the precise amount of water to add to the cement based on the desired level of flow. This information, combined with the data collected on the vibrational frequency effect on flow and the data on cement flow over working time, makes it possible to obtain the desired level of flow under given operating conditions.

When it became apparent during the non-survival surgeries that added water was needed to lower cement viscosity, the water was first added by drops from a pipet. Water was added to 30 grams of OC-cement powder in amounts of 6, 12, and 16 drops. For the flow table study of added water, these amounts in drops were converted to mass, which is obviously a more precise metric. It was decided that only these three different amounts of added water would be used in this study. From the non-survival surgeries, it was known that 0.40 grams of added water produced adequate flow. As this series of tests was conducted for primarily practical reasons, it was only necessary to know the effect on flow of amounts of water slightly lower and slightly higher than 0.40 grams. This data, combined with flow data using no added water, produced a very linear relationship between added water and flow, and one that could be used to calculate the amount of water needed to produce any desired flow.
Figure 25 - Flow % of OC-cement vs amount of additional D.I. water added during mixing. The flow of the cement increases linearly with the volume of water added to the paste.

Adding small amounts of additional water to the cement paste will theoretically cause a decrease in strength in the cement mass after hydration due to the formation of voids after the added water is evaporated. However, any strength decrease that does occur would be very small, because the amount of water added is only 4.25% of the total fluid. Initial compressive strength testing has confirmed that the strength decrease from the added water is not appreciable, and the cement is still easily strong enough for use in joint replacement. The raw data from this flow versus added water study, as well as from the other cement flow studies performed, is given in Appendix D.
4.7 Effect of vibrational frequency on flow of OC-cement

Shown in Figure 26 is a plot of the measured vibrational flow of OC-cement versus the frequency of vibration applied to the cement paste in vibrations per minute. The flow percent was measured for each sample at four minutes after mixing was begun, with \( n=5 \) samples tested at each frequency. The results from these experiments are somewhat inconclusive. It could be expected that increasing the frequency of the applied vibration would increase the amount of flow in the cement, which would be consistent with the behavior of a traditional thixotropic fluid. However, this is not what is observed. Instead, the flow percent of the cement increases initially with increasing frequency, but then decreases to the next frequency point before rising again at the highest frequency tested. The highest measured flow occurred at 11,800 VPM, which was the second lowest frequency tested. These results indicate that there is not a direct relationship between vibrational frequency and gravitationally caused cement flow. Because all of the flow that OC-cement will experience in surgery will be gravitational, rather than pumped or otherwise compelled, it is more useful to measure cement flow percent rather than viscosity, which is closely related. In some situations, measuring viscosity as a function of vibrational frequency could be a good indicator of the gravitational flow that occurs, but in this situation, it appears that this is not the case. Based on thixotropic flow characteristics, it is reasonable to assume that the viscosity of the cement does indeed decrease with increasing frequency. However, this is not reflected with increasing cement flow.
The reason for this is likely that, although the viscosity of the cement may have been lower at higher frequencies, this did not translate into higher flow because the vibration was not productive. Higher frequency, more powerful vibrations caused the cement to move erratically, which slowed its outward, gravitationally caused flow. At lower frequencies, there was less non-productive movement in the cement, and it was able to flow outwards more readily. These effects translate well into surgical use of OC-cement, where the cement must flow through tubes directionally, and too much erratic movement would hinder this.

From these experiments, it appears that the highest flow of OC-cement is caused not by the highest possible vibrational frequency, but rather by an intermediate frequency that is high enough to cause a low viscosity, but not so high as to cause erratic cement movement. This finding is significant for the understanding of how to best manipulate OC-cement in tight spaces and limited time frames. Using these results, it will be possible to accurately choose the proper vibrating motors to power new OC-cement tools developed in the future. Although cement flow was only measured at four frequencies in this study, it is unlikely, based on observing the results collected, that a directional trend would have emerged had flow been tested at more frequencies. This reinforces the conclusion that the highest flow is caused by an intermediate frequency rather than by the highest possible frequency.

While the results from this study are not as directly comparable to other research as they would have been if viscosity had been used as the dependent variable, they are repeatable and controlled. The vibration table testing was the best way to obtain results that were the most
relevant to the task at hand, which was to make it possible to practically implement OC-
cement in hip replacement surgery. The results from this study are significant, and have led
to a new understanding of the type of vibration that should be applied to OC-cement to
maximize flow. This information would not have been obtained by measuring the change in
cement viscosity with vibrational frequency.

![Graph showing vibration frequency vs OC-cement flow percentage](image)

*Figure 26 – Frequency of applied vibration versus the flow of OC-
cement, indicating that there is not a direct relationship between
vibrational frequency and resulting flow.*
4.8 OC-cement Particle Size Distribution

As discussed above, the particle size distribution (PSD) of OC-cement is critical to its flow and mechanical properties. PSD measurement was performed on OC-cement as well as on the CA cement and β-tricalcium phosphate that are its basic components. These PSDs gave quantitative information on the powders that are known to make OC-cement with the correct properties. This information will be useful for knowing exactly what types of CA cement and β-TCP powders are needed to reproduce OC-cement’s flow and mechanical properties.

The PSDs for β-TCP and CA cement powders are shown below in Figures 27 and 28. The β-TCP powder PSD shows a very narrow distribution of particle sizes, with a mean size of 3.34 μm. The PSD of CA cement is much broader, encompassing greater than two orders of magnitude. Unlike β-TCP, CA cement does not have one narrow particle size peak, but rather shows three broader, overlapping peaks. This indicates that CA cement is made from multiple particle sizes mixed together, while β-TCP is essentially composed of one main particle size, with a rapid decline in size frequency on either side of this.

The PSD of OC-cement is shown in Figure 29. It is evident from examination of the three Figures that the PSD of OC-cement is a weighted mixture of the PSDs of CA cement and β-TCP powder. The particle sizes encompass two orders of magnitude, with the smallest sizes present being around 0.067 μm. From the minimum, the particle size frequency increases approximately linearly with increasing particle size to a maximum, which is located at the same point as the peak in the β-TCP PSD. The maximum is at a fairly sharp peak. After the maximum, the particle size frequency decreases approximately linearly with increasing
particle size to a maximum size of around 80 μm. The resulting particle size distribution of OC-cement somewhat resembles that of β-TCP with a sharp peak at 8.8 μm. The peak in the OC-cement PSD is not as narrow as that in the β-TCP PSD, and the particle sizes are distributed over a broader range. While the distribution is not as flat and even as that of CA cement, it is broadly distributed enough to allow OC-cement to pack densely and to flow over itself. This is what gives the cement the properties needed for used in hip replacement procedures.

Figure 27 - Particle size distribution for -tricalcium phosphate powder
Figure 28 - Particle size distribution for CA cement

Figure 29 - Particle size distribution and for CA cement and β-TCP combined into OC-cement
These PSDs will be useful in ensuring that OC-cement with the needed properties can be obtained even in the event that suppliers or their products change. Because only very specific powders can be used to make OC-cement with these properties, it is advantageous to long-term development to have as much quantitative information on the cement as possible. Additionally, if at some point it is decided that the affect of altering OC-cement's PSD on its properties will be studied, these three PSDs will provide a necessary starting point of comparison.

4.9 Sterilization of OC-cement

For the live survival surgery, the dry heat sterilization method was selected for sterilizing the OC-cement. The method was selected because of the convenience of its use and the superior availability of the facilities to perform it. Before sterilized cement was used in the procedures, samples underwent extensive testing to ensure that the flow and mechanical properties of the cement were unaffected by the sterilization process. The flow properties of the sterilized cement were tested using the flow table apparatus discussed above. Using the standard test of the gravitationally caused flow at four minutes after mixing, it was determined that sterilized cement flowed no differently than non-sterilized cement under vibration. Additionally, quantitative observations made throughout the testing of the sterilized cement indicated that it handled no differently than cement that had not been heated. Unchanged handling characteristics were essential to using the cement in a live surgery. The working time of the sterilized cement was measured by noting the time at which
the cement stopped responding to applied vibration. This was done with the method described above in section 3.2.2 using parallel cuts in the cement.

Testing for mechanical strength changes in the cement after sterilization was critical for obvious reasons. The most important strength parameter for a bone cement is its compressive strength, which is the primary type of load that is undergone when it is in the bone. Compressive strength testing of OC-cement pellets is a procedure that is very frequently performed by the Osteoceramics research group, so verifying the strength of sterilized OC-cement was simply a matter of testing a number of samples made from the cement. The results of these tests indicated that there was no significant difference in the compressive strengths of sterilized and non-sterilized cement.

From these tests, it was found that dry heat sterilization of the cement did not affect its properties in any meaningful way. Therefore, it was concluded that this method would used for surgery, and a number of cement batches were prepared to be sterilized. In sterilizing the cement for surgery, it was critical that not only was the cement sterilized, but also was the container holding the cement that would be handled during surgery.

OC-cement was dry heat sterilized in glass jars in 15 gram and 30 gram batches. The openings of the jars were covered with aluminum foil before the lid was partially screwed shut. After heating, the lids were screwed tightly shut, creating a seal with the aluminum foil. Before being placed in the furnace, the jars were sealed in an envelope made from two layers
of aluminum foil. This was done so that the envelopes could be handled by non-sterile hands without contaminating the jars within. During the surgery, the envelopes could be opened by technicians without touching the jars, and a person whose hands were sterile could remove the jar and handle it without contamination. Pictures of a sterilization jar in an opened and closed envelope are shown in Figure 30 below.

Figure 30 - OC-cement sterilization setup showing foil-sealed glass jar in foil envelope. (a) shows the envelope closed and (b) shows it after being opening without touching the jar.

To assure that the heat sterilization of the cement had been effective, a sample of sterilized cement was taken and cultured. The sample was from the same sterilization batch as the cement used in the surgery. Had the sterilization been unsuccessful, bacterial growth would have appeared on the culture. However, no bacteria were observed, indicating that the heat sterilization was effective. As a means of additional testing, two swabs were taken from the open wound area during the survival surgery. These swabs were also cultured and monitored for bacterial growth. A single colony of bacteria was observed in the culture, so the dog was kept on antibiotics for an additional time to ensure that infection would not occur in the
prosthesis area. This was not considered to be a serious development, so post-surgical treatment of the animal continued as planned.

The use of dry heat sterilization for OC-cement in surgery is advantageous to the expansion of *in vivo* testing of the cement. The method is very easily to carry out, and is relatively inexpensive when compared to techniques such as electron-beam irradiation. The only equipment needed, a programmable furnace, is available at almost any facility. The aluminum foil envelopes used to maintain sterility on the surface of the jars have been shown to be effective and are extremely easily prepared. Because dry heat sterilization does not negatively affect the flow, working time, or mechanical properties of OC-cement, it can easily be used as the sterilization method in larger scale trials of OC-cement, which will be necessary to its development as a biomedical product.

4.10 Non-survival surgeries

Three non-survival surgeries were performed on live dogs that were euthanized after the surgeries were complete. These surgeries used the new cement tools and techniques as they were being developed, and were undertaken as a necessary step to gain information about the requirements of performing the procedure with OC-cement. Prior to these surgeries, there was an exploratory procedure performed on a canine cadaver. This surgery was done before any of the new cement tools were developed, and was done to gain basic information about procedure itself and the handling of OC-cement in the body.
4.10.1 Canine cadaver surgery

The hip replacement procedure on the cadaver dog yielded some interesting and informative results. After the procedure the limb was harvested and the femur and acetabulum were removed and sectioned. Initial examination of the sections showed that the cement was able to fill space in the bone and make intimate contact with surrounding bone. The femoral component was well fixed. These results were encouraging for the use of OC-cement in live dogs. The cadaver procedure, however, highlighted the need for further work to make total hip replacement using OC-cement possible.

4.10.2 Non-survival surgery #1

In addition to the hip replacement performed on the cadaver dog, there were three non-survival surgeries performed on dogs that were living at the time of the procedure, but were euthanized upon completion. Valuable information was gained from each of these surgeries, information without which the success of live surgeries with OC-cement would have been impossible. The first non-survival surgery was performed using early versions of the cement handling tools that were eventually used in the survival surgery. While the general handling techniques used in this surgery worked fairly well, a few problems arose that necessitated further development of the techniques and additional non-survival surgeries before a survival procedure could be completed. The first surgery used PFA tubing with 8.0 mm inner diameter. This was the only tubing that was brought to the surgery, and due to difficulties in performing measurements on the varying scale of the radiographs, it proved to be too large to
fit into the reamed femur. It was therefore very difficult to completely fill the femur with cement.

A second difficulty that was encountered during the first non-survival surgery was that the viscosity of the cement was unacceptably high. No added water was used in this surgery. This fact, combined with the fact that a full 30 gram cement batch was placed into the PFA tube, meant that it took much too long to fill the tube. After the four minutes that it took to fill the tube with cement, there was not enough remaining time before the working time to place the cement in the femur and place the implant in the cement. This difficulty was compounded by the fact that the tubing was too large for the dog's bone and the cement could therefore not flow smoothly from the tube. The result of these problems was that the femoral implant component was not placed within the bone. The implant did not sit correctly on the lip of the reamed femur, and in fact protruded above the bone by approximately one centimeter. In a live surgery, this placement would have made it impossible to reconstruct the joint and complete the procedure.

After completion of the first non-survival surgery, the limb was harvested and sectioned. Light microscopy images of the sections reveal that the contact was good between the bone and cement and cement and implant, despite the difficulties encountered during the surgery. Shown in Figure 31 are examples of light microscopy images taken of bone sections from surgery. Figure 31a shows contact between the cement and cortical bone. Figure 31b shows
the interface between the cement and femoral implant component. Figure 31c shows cement penetration into trabecular bone in the medullary cavity.
The techniques and tools used in the second non-survival surgery were modified using information gained in the first surgery. Changes to the tools included the use of smaller diameter PFA tubing and a shorter length of tubing used. A 15 gram batch of OC-cement was used instead of the 30 gram batch that was used in the first surgery. These factors shortened the time needed to fill the PFA tube with cement by more than one minute.

4.10.3 Non-survival surgery #2

The difficulties experienced during the second non-survival surgery were mostly unrelated to cement handling tools. The main issue encountered in the surgery was the surgeons’ lack of experience with handling the cement. Because the flow characteristics of OC-cement are so
different than those of PMMA cement, it takes a great deal of practice to understand how to manipulate the cement effectively. Because the surgeons did not have the practice, they attempted to use standard handling techniques with the OC-cement. This was most prevalent when the cement was placed in the reamed femur. Filling the femur took a great deal longer than it did in simulations up to that point. There was confusion and difficulty in communicating to the surgeons what they needed to do to get the cement to flow out of the tubing. This confusion wasted valuable working time of the cement, and delayed the filling of the femur. Further delay was caused by the extremely tight fit between the outer diameter of the tubing and the reamed area of the femur. The tight fit absorbed much of the vibrational energy from the tubing, slowing the cement flow at the tip of the tube where it was exiting to the bone.

The second non-survival surgery was not a success primarily because of the difficulty in filling the femur. The three factors that combined to cause the problem were surgeon inexperience, tight fit between tubing and bone, and high cement viscosity. These issues were all addressed prior to the third non-survival surgery. Meetings were held with the surgeons to demonstrate the proper handling methods for OC-cement. Radiographs were carefully examined to ensure that the proper tubing size was available A sample tube was inserted into the reamed femur during the surgery to ensure that it had been reamed to the proper diameter and the fit was not overly tight. To address the viscosity issue, a study was done on the effects of added D.I. H$_2$O on cement flow. Based on the results of the study, it was decided that 0.4 grams of water would be added to the 30 gram batches of cement used. The resulting
increase in cement flow was not large, but it was enough to greatly increase the ability to move the cement through the tube into the femur.

4.10.4 Non-survival surgery #3

These changes made filling the femur go very smoothly during the third non-survival surgery. The third surgery was very nearly a complete success, in that, had the procedure been performed using sterile methods, the dog could have survived. In addition to the changes discussed above, the author took a more active role in coupling vibration to the tubing while filling the femur. This brought greater experience and feel to the procedure, and made for a smoother fill.

The only difficulty encountered during this surgery was that an excessive amount of blood was mixed with the cement during the filling of the acetabulum. This was due to the fact that the acetabulum was filled not all at once, but in a number of smaller portions as the surgeons saw how much cement was needed. After each pour, blood flowed into the acetabulum and in this way was able to mix thoroughly with the cement, lowering its viscosity. After the acetabular implant component was placed initially, it was apparent that it was not securely held by the cement. To fix this, the component and cement were removed from the acetabulum, and a new batch of cement was prepared. Greater care was taken with the new batch to place the correct amount of cement into the acetabulum with the first pour. When the acetabular component was put in place on the second try, the hold was good, and the joint was able to be reconstructed and closed.
Based on the success of the third non-survival surgery, it was determined that the procedures for using OC-cement in hip arthroplasty were developed enough that a live, survival surgery would be possible. The third non-survival surgery was therefore the last, and preparation began for the survival surgery.

The cadaver and non-survival surgeries provided invaluable information, without which the completion of the successful live hip replacement would not have been possible. Several changes to the techniques and tools were made based upon the surgical experiences. The cement viscosity was lowered slightly by the addition of small amounts of sterile D.I. water. More care was taken in assuring that the tubing fit easily into the femur after reaming. Tools used to place the femoral implant component in the bone were modified to increase visibility in the field and thereby make placement of the implant more accurate. Steps were taken to reduce blood mixing with the cement while filling the acetabulum with cement. The most important outcome from the non-survival surgeries was, however, the practice gained by the surgeons in handling the cement and tools in the procedure. This experience in how to properly fill the cavities and place the implants would have been impossible to obtain without performing non-survival surgeries.
4.11 Live total hip arthroplasty using OC-cement

A successful Total Hip Arthroplasty was performed on a four year old 66-pound female boxer mix using OC-cement. Information on which techniques and procedures brought the greatest success in the non-survival surgeries was used to design the procedure for this survival surgery. Sterile handling practices were critical in every step of the surgery, and every effort was taken to prevent infection. The lead surgeons on the surgery were Drs. Toombs and Wagner from the ISU College of Veterinary Medicine. They were assisted by two resident surgeons from the College, as well as by two anesthesiologists who monitored the vitals of the dog throughout the procedure. The author assisted during the surgery in preparing the cement and placing it in the femur and acetabulum.

The surgery was performed using the hand-held vibrator to mix and pour the cement. Stiff, thin-walled PFA tubing was used to place the cement in both the acetabulum and femur. The precision control offered by the use of the tubing proved very advantageous in delivering the cement to the acetabulum. As discussed above, in previous surgeries a substantial amount of blood was mixed into the cement during the process of placing it into the acetabulum. By delivering the cement from the tubing rather than from the mixing cup, it was easier for the surgeons to monitor the amount that was placed into the acetabulum. Therefore, the correct cement volume was placed initially and there was less opportunity for blood to reach the cement while additional cement was being added, and the amount of blood mixed with the cement was reduced. This was one area of substantial improvement over the non-survival surgeries.
To obtain the needed viscosity of the cement paste, 0.40g of D.I. H₂O was added to the 30 gram OC-cement batch used to fill the femur during the surgery. The resulting lowered viscosity made placing the cement into the femur with the PFA tubing a complete success. The femoral implant component was able to be vibrated into the cement-filled femur, and the displaced cement flowed smoothly out of the femur as the implant was pushed in. This was exactly as the procedure had been designed. Because a lower viscosity was not needed to successfully fill the acetabulum, no additional liquid was added to 15 gram OC-cement batch used for the acetabulum. The acetabular implant component was vibrated into place in the cement, and after setting, the hold was deemed very satisfactory.

With both implant components successfully placed, the artificial femoral head was placed on the implant stem and the joint was reconstructed. The placement of both components was good, allowing the joint to rotate correctly when completed. At this point the arthroplasty was deemed a success, and the surgeons closed the joint and completed the surgery. The dog was kept sedated for 12 hours after the surgery to assure that it would not disturb the cement while it was gaining strength or destroy the sutures. This was likely a longer time than necessary to allow for the cement to build strength, but since this was the first in vivo trial of the cement, greater precautions were taken. The dog was kept on cephalosporin antibiotic for two weeks after the surgery to ensure that infection would not occur. It was confined to limited physical activities for six weeks, but daily exercise was provided by an assistant walking her on leash and observing her wound healing and gait. At six weeks after surgery, the dog was allowed to return to normal, unrestricted activity.
The successful completion of a survival hip replacement surgery using OC-cement has been the first step in the next stage of cement development, in vivo testing. Although a great deal of information was gained about the feasibility of OC-cement as a biomedical product from the work leading up to and including the surgery, much more testing is needed to move forward in the cement development. The completion of the live surgery provides an excellent basis from which further testing can occur. The successful live surgery has shown that OC-cement’s very different handling and flow properties can be adapted to by surgeons. The arthroplasty procedure is relatively unchanged when OC-cement is used, and remains a fairly routine operation. These two factors mean that continued in vivo testing of the cement will be possible. Additionally, because the procedure with OC-cement can now be readily performed and failure is unlikely, further in vivo testing will be more able to measure the merits of the cement as a biomaterial.

4.11.1 Mechanical integrity of cement post-surgery

The mechanical integrity of the OC-cement in the joint can be evaluated in the live dog by observing the dog’s use of the limb and overall activity, as well as by studying radiographs of the joint. Both of these factors indicate that the cement is mechanically sound in the joint. The dog was walking and putting weight on the limb within three days after the surgery, which is an excellent indication that the hip replacement and the cement were successful. The function of the limb increased fairly readily in the days after the procedure, and the dog had close to normal use of the limb within 10 days.
Radiographs of the hip joint were taken immediately after the replacement was completed. Many of these images are shown below, along with a radiograph of the joint taken prior to the arthroplasty, shown in Figure 32. Several important observations can be made from examination of these radiographs. The first is that there appears to be very good filling around both the femoral and acetabular implant components. There are a few small voids present, indicated by the red arrows in Figure 33, but these are very small, non-continuous, and will very likely not affect the mechanical integrity of the cement mantel. The other imperfection in the cement that can be seen in the radiographs is a small hairline crack that appears just distal of the femoral component. This is shown by the blue arrow in Figure 33. The crack was likely caused by the pounding force that was used to fit the head onto the stem of the femoral component. This force probably traveled through the implant and created the crack in the brittle cement. As can be seen from the radiographs, the crack is very small. By comparing Figure 33 to Figure 34, it can be determined that the crack is only present in a small angular section of the cement, and does not go completely around the mantel. This is a good thing for the mechanical integrity of the cement, as the mantel is continuous all the way to the cement plug in the distal part of the femur.
Figure 22 - Anterior-Posterior radiographs of the dog’s pelvis and hips before and after hip replacement
Figure 23 - Medial-lateral view of the hip prosthesis showing very small voids in the cement mantel (red arrows), and a hairline crack (blue arrow) at the distal end of the cement mantel.

Figure 24 - Medial-lateral view of the hip prosthesis shown at a different view from Figure 31. No hairline crack is visible in this radiograph, indicating that the crack does not extend around the cement mantel.
Figure 35 shows the acetabular implant component surrounded by OC-cement in the reamed acetabulum. Shown in the radiograph are the three holes drilled into the acetabulum for cement fixation (red arrows). These holes were successfully filled with cement, which will enhance the stability of the acetabular component's seating. Also shown in Figure 35 is a solid layer of OC-cement surrounding the acetabular component. This indicates a very good fill of the reamed acetabulum and a strong mantel to support the joint. Shown in Figure 36 are two more views of the acetabulum that also show a solid, continuous mantel of cement surrounding the implant, indicated by the red arrows. These radiographs provide strong evidence of excellent filling around the acetabular component leading to high mechanical integrity of the OC-cement.

Figure 25 - Medial-lateral radiograph of the hip prosthesis showing the acetabular component. Three holes drilled to help anchor the implant were successfully filled with cement (red arrows).
Figure 26 – Radiographs showing a solid layer of cement going all the way around the acetabular component (red arrows). A complete layer such as this will provide excellent support to the implant.

Overall, the radiographs taken post-surgery show cement mantels around both the femoral and acetabular components that appear to have very good mechanical integrity. The completeness in filling the cavities is an indication that the cement will be able to support the loads placed on it by the joint. The voids and small crack that were observed seem to be superficial and not large enough to meaningfully affect the cement mantels mechanical
integrity. Of particular significance is the completeness of the cement layer around the acetabular component. This was a particularly important result, as the fixation of the acetabular component was an area of concern for the surgeons and researchers. The forces applied to the acetabular component in the body and the manner in which it is secured by the cement mean that a very good cement mantel that fully fills the space between the component and surrounding bone is need for good, lasting fixation. As can be seen from the radiographs, this desired result was achieved.

Continually improving the results with every surgery is always a goal, so the results from this first surgery will be used to further improve the filling of the cavities and the resulting mechanical integrity of the cement. To more fully eliminate the small voids that were present after the first surgery, two steps can be taken. The first is to apply a short period of vibration to the implant once it is fully in the femur and in its final position. This vibration will not move the implant, but will cause the cement in the femur to flow and eliminate more of the small voids. The second step that can be taken is to further work to remove all of the fluids from the reamed femur before filling it with cement. Some of the voids seen in the radiographs may actually be filled with blood that remained in the femur and was dispersed in the cement upon filling. Eliminating more of this remaining blood by such methods as keeping the femur elevated until it is filled and applying suction can reduce the prevalence of voids, which would lead to greater cement strength and integrity.
4.11.2 Bone-cement interface

Figure 37 shows two views of the femoral implant component in the femur. The red arrows highlight the bone cement interfaces. From these images, the interfaces appear excellent. The cement mantel continues right up to the bone, and appears very continuous with both the cortical and trabecular bone. There are no signs of significant gaps at the interfaces, indicating that there were no systematic errors in placing the cement in the femur.
Figure 27 - Radiographs showing two views of the femoral implant component. The interfaces between the cement and surrounding cortical bone are indicated with red arrows. Cortical (yellow arrow) and trabecular bone (green arrow) can be seen in both images.

Although the initial bone-cement interfaces obtained by this surgery appear excellent, the important information in this regard will not be able to be obtained until more time has passed after the procedure. The tissue response to the cement will greatly affect the interfaces, so more useful study will only be able to be done once the cement has been in contact with the tissue for a longer period of time. Further study of the bone-cement
interfaces will be done with periodic radiographs beginning at six weeks after surgery and continuing throughout the dog’s life. For very detailed study, however, it is necessary to observe the interfaces after the dog has died, to take advantage of techniques such as sectioning, microradiography, and fluorescent microscopy. To facilitate fluorescent microscopy, the dog will be given bone labeling indicators beginning at six weeks after surgery and continuing annually until the dog’s death.

4.11.3 Systematic and tissue response to surgery

At this early stage after the surgery, the dog’s systematic and tissue response to the surgery and cement can be evaluated by monitoring the dog’s vitals, general health, and wound healing. Much more detailed evaluation will be performed after the cement has been in the body for a longer period of time. This will be done by continued monitoring of the dog’s health, and with fluorescent microscopy and microradiography after the dog’s death. Early monitoring indicated that the dog’s systematic responses to the surgery with OC-cement were very good, and at least on par with normal responses to hip replacements performed with PMMA cement. The dog was able to walk with weight on the limb within three days of the surgery, which is an excellent indication of its health. The dog was walked daily at the College of Veterinary Medicine starting three days after surgery until six weeks post-surgery, when unrestricted, normal physical activity was allowed to resume. This is a good indication both of the health of the dog and of the mechanical integrity of the cement, as discussed above. Also as discussed above, the bacteria that were found in the culture from the swab taken during surgery appears not to have had any detrimental effects on the health of the dog
following surgery. This further supports the conclusion that this bacterial growth was minor and was successfully treated with antibiotics. Overall the systematic and tissue response of the dog to the surgery and cement was very good, with no undesirable reactions observed thus far in the study.
5. Conclusions

This thesis work has shown that it is possible to successfully use OC-cement as the fixation method in total hip arthroplasty surgery. The live surgery performed with the cement was a complete success, indicating that the tools and techniques developed for handling the cement worked well for the job. Although the time available to evaluate the dog post-surgery was limited, early observation indicated that the mechanical integrity of the cement and the tissue responses were excellent. These are both indications that further in vivo testing of OC-cement would be very successful.

The work done prior to the surgeries to study OC-cement’s flow and setting properties was critical to the eventual success of the hip replacements. It was found that the cement working time decreases linearly with increasing room temperature. This makes it possible to easily predict the working time at any measured room temperature. Also linear was the relationship found between cement flow and amount of added D.I. water. The degree to which the cement flows under vibration can therefore be fine tuned by changing the volume of water added during mixing. Cement flow was found to decrease with time after mixing at a rate which increased over the working time. Using these results, it is possible to quantify the flow needed for different tasks during surgery and use the plot to create a schedule for the tasks. It was found that OC-cement working time decreases rapidly to a minimum when \( \text{CaCl}_2 \) concentration is increased. After the minimum around 1.1M, the working time increases with \( \text{CaCl}_2 \) concentration. Although this behavior is not yet fully understood, the plot of working time versus concentration can be used to fine tune cement working time by changing the
CaCl$_2$ solution. It was found that cement flow does not increase directly with increasing vibrational frequency as was previously expected, but rather has a maximum value at an intermediate frequency. This was due to the non-productivity of the higher frequency vibrations. This information can be used to determine the ideal frequencies used in future tools for handling OC-cement. It was found that OC-cement can be effectively sterilized using dry heat without appreciably altering its flow, mechanical, or setting properties. Because of this, the cement can be easily sterilized at any facility, which will make further in vivo testing much more accessible.

Based on the surgeries performed and the study of pertinent cement properties, it appears likely that OC-cement can be successfully utilized in total hip arthroplasty. Because this is true, it will be possible to continue and expand in vivo testing of OC-cement, which is the necessary next step in evaluating its potential use as a biomedical product. OC-cement has the potential to greatly increase the long-term success rate of total joint replacements, thereby improving the quality of life of a great many people. It is hoped that this work will contribute to the eventual commercial implementation of OC-cement, and in this way help to improve the lives of those in need.
6. References

   <http://www.aaos.org/wordhtml/research/stats/stats.htm> 


Appendix A - ASTM Standard C1437

Designation: C 1437 – 01


1. Scope

1.1 This test method covers the determination of flow of hydraulic cement mortars.

1.2 The values stated in SI units are to be regarded as the standard. Values in parentheses are for information only.

1.3 This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.

2. Referenced Documents

2.1 ASTM Standards:

C 109 Test Method for Compressive Strength of Hydraulic Cement Mortars (Using 2-in. or [50-mm] Cube Specimens)

C 185 Test Method for Air Content of Hydraulic Cement Mortar

C 230 Specification for Flow Table for Use in Tests of Hydraulic Cement

3. Significance and Use

3.1 This test method is intended to be used to determine the flow of hydraulic cement mortars, and of mortars containing cemenitious materials other than hydraulic cements.

3.2 While flow is not usually included in hydraulic cement specifications, it is commonly used in standard tests that require the mortar to have a water content that provides a specified flow level.

4. Apparatus

4.1 Flow Table, Flow Mold, Conforming to the requirements of Specification C 230.

4.2 Caliper, Conforming to the requirements of Specification C 230. Alternatively, any outside-measuring caliper constructed of corrosion-resistant material may be used, provided that it is incremented in millimetres and its maximum extent of measuring is at least 260 mm (10 in.).

4.3 Tamper, conforming to the requirements of Test Method C 109.

4.4 Trowel, having a steel blade 100 to 150 mm (4 to 6 in.) in length, with straight edges. The edges when placed on a plane surface shall not depart from straightness by more than 1 mm (0.04 in.) (Note 1).

4.5 Straightedge, made of steel, shall be at least 200 mm (8 in.) long and not less than 1.5 mm (0.06 in.) nor more than 3.5 mm (0.14 in.) in thickness. Its edge shall not depart from a plane surface by more than 1 mm (0.04 in.) (Note 1).

Note 1—The trowel specified in Test Method C 109 and the straightedge specified in Test Method C 185 may be used for this purpose, providing they comply with the planeness indicated.

5. Temperature and Humidity

5.1 The temperature of the air in the laboratory shall be maintained between 20 and 28°C (68 and 82°F) and its relative humidity shall not be less than 50%.

6. Materials

6.1 Hydraulic Cement Mortar—A mortar for which the determination of flow is specified or desired.

7. Procedure

7.1 Determination of Flow:

7.1.1 Carefully wipe the flow table clean and dry, and place the flow mold at the center. Place a layer of mortar about 25 mm (1 in.) in thickness in the mold and tamp 20 times with the tamper. The tamping pressure shall be just sufficient to ensure uniform filling of the mold. Then fill the mold with mortar and tamp as specified for the first layer. Cut off the mortar to a plane surface flush with the top of the mold by drawing the straightedge or the edge of the trowel with a sawing motion across the top of the mold. Wipe the table top clean and dry, being especially careful to remove any water from around the edge of the flow mold. Lift the mold away from the mortar 1 min after completing the mixing operation. Immediately drop the table 25 times in 15 s, unless otherwise specified.

7.1.2 If using the caliper specified in Specification C 230, measure the diameter of the mortar along the four lines scribed in the table top, recording each diameter as the number of
caliper divisions, estimated to one tenth of a division. If some other caliper is being used, measure the diameter of the mortar along the four lines scribed in the table top, recording each diameter to the nearest millimetre.

8. Calculation

8.1 The flow is the resulting increase in average base diameter of the mortar mass, expressed as a percentage of the original base diameter.

8.2 If using the caliper specified in Specification C 230, add the four readings, and record the total. This gives the flow in percent. If using some other caliper, compute the flow in percent by dividing "A" by the original inside base diameter in millimetres and multiplying by 100.

where:

\[ A = \text{average of four readings in millimetres, minus the original inside base diameter in millimetres.} \]

Report the flow to the nearest 1%.

9. Precision and Bias

9.1 Precision—The single-operator, within-laboratory standard deviation has been found to be 4% flow. Therefore, results of two properly conducted tests by the same operator on similar batches should not differ by more than 11% (Note 2).

9.1.1 The multilaboratory standard deviation has been found to be 11%. Therefore, results of two different laboratories on similar batches should not differ by more than 31% flow (Note 2).

Note 2—Data produced when water content is being varied to obtain a given flow is not applicable for this purpose. Only data where flow has been determined using a given cement and fixed water content is applicable. Consequently, the only data currently available is that extracted from the CRL Proficiency Sample Program for CS Flow of C 109 mortars (dropping the flow table 25 times in 15 s). The data for Sample Nos. 109, 110, 111, and 112 have been used to develop the precision statements given.

9.2 Bias—Since there is no accepted reference material suitable for determining flow available, no statement on bias is made.

10. Keywords

10.1 flow; hydraulic cement; mortar
8. Appendix B – Description of total hip arthroplasty procedure from ISU Research Compliance Review Form – Use of Animals in Research

No food in the previous 12 hours. The right rear leg will be clipped form the hock to the midline of the animal’s back. Following a sterile surgical preparation, an approach will be made to the greater trochanter. An entry through the joint capsule will be made and then retracted to expose the hip joint. The femoral ligament will be severed to permit separation of the joint. The femoral head and neck will be severed with a reciprocating saw and removed. The femur will be reamed to a depth 1 cm deeper than the length that the femoral implant component will occupy. A dam will be inserted to restrict cement flow and inhibit medullary bleeding. The cavity will be rinsed with saline and the fluids removed. OC-cement will be mixed in the correct proportions. The medullary cavity will be filled with the cement using an insertion tube, vibrated to enhance the flow. (This is an important step that must be accomplished successfully and that has been studied in vitro and in a cadaver.) Then the femoral component will be inserted into the cement-filled cavity using vibration. Excess cement will flow from the cavity and will be removed.

The acetabulum (socket) will be reamed to size with a reamer designed for the acetabular implant. Cement will be mixed and vibrated through a tube to fill the reamed site. Then the acetabular component, attached to a placement tool, will be vibrated in place and the tool released. When the cement is strong, about 20 minutes, the capsule will be cleaned, the joint set in place, and the capsule will be closed with sutures. The incision will be closed with 2-0 polydioxanone sutures and the skin will be closed with surgical staples. While under general anesthesia the operated leg will be radiographed to confirm physical orientation and cement
placement. A sterile bandage will be placed over the incision site during the recovery period, checked daily and removed on the fifth day.

Post operative the animals will be transferred to the critical care unit for monitoring until awake and with normal vital signs for a post-op animal. It will be transferred to a small, warm cage and analgesics will be ordered for comfort as necessary. The following day the animal will be transferred to a standard, single-dog cage. Dr. Wagner will monitor the dog’s condition periodically during the day. He will be responsible for on-call for after hours, weekends, and holidays during recovery period. As soon as practical a veterinary student will exercise the dog daily, until it is transferred to the farm.
9. Appendix C – Data from cement working time studies

Table 2 - Data for CaCl₂ concentration versus OC-cement working time plot

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10. Appendix D – Data from cement flow studies

Table 4 - Data for cement flow over working time plot

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### Table 5 - Data for added water versus OC-cement flow plot

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Table 6 - Data for vibrational frequency versus OC-cement flow percent plot

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