OSTEOCHONDRAL ALLOGRAFT TRANSPLANT SYSTEM

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Abstract

Osteochondral allograft transplantation is an increasingly popular procedure that repairs osteochondral defects by introducing mature cartilage and subchondral bone to facilitate defect healing. These defects can arise from trauma, osteonecrosis, osteoarthritis, and other degenerative cartilage disorders. Existing surgical systems are detrimental to chondrocyte viability and limit vertical graft adjustment, which are both crucial for successful surgical outcomes. To address both challenges, we developed a novel surgical system that creates threads on the graft and receiving site to produce a screw-in graft. Testing revealed a significant improvement in chondrocyte viability with the screw-in graft over the traditional impaction method. However, matching the surface of the graft with the surface of the receiving site was not fully addressed with our current device. Using the threading approach couples graft rotation and translation presenting a unique graft alignment challenge as aligning the graft correctly in the receiving site is important to avoid cartilage incongruencies. We tested an approach to graft threading with the aim of ensuring accurate graft placement at the desired height and rotation. Testing in a synthetic bone model revealed that when the graft is inserted to the desired rotation, there is a mean graft-height error of 0.37 ± 0.198 mm ($n = 26$). The small height error is clinically insignificant and showed that graft threading allows for accurate graft placement. Having shown that the threading method maintains chondrocyte viability while allowing for accurate graft insertion, additional work will show that these key advantages of the threading procedure can be achieved simultaneously in ex-vivo testing.

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Background

Osteochondral Defect Etiology

Osteochondral defects can arise from traumatic injury, or degenerative cartilage diseases like osteoarthritis or osteonecrosis [1]–[3]. The leading concomitant knee pathology for this defect is a tear in the medial meniscus, which reduces support of the knee and results in greater joint contact forces [4]. Other pathologies leading to osteochondral defects include abnormal bone growth and excessive stress in the knee [5]. OCA transplantation represents an end-stage solution to cartilage repair after other repair techniques (like debridement, microfracture, or autologous chondrocyte implantation) have failed. The rate of OCA transplantations performed is increasing by 5% annually and is expected to reach 3500 procedures by the year 2020 [6].

Osteochondral Allograft Transplant Procedure

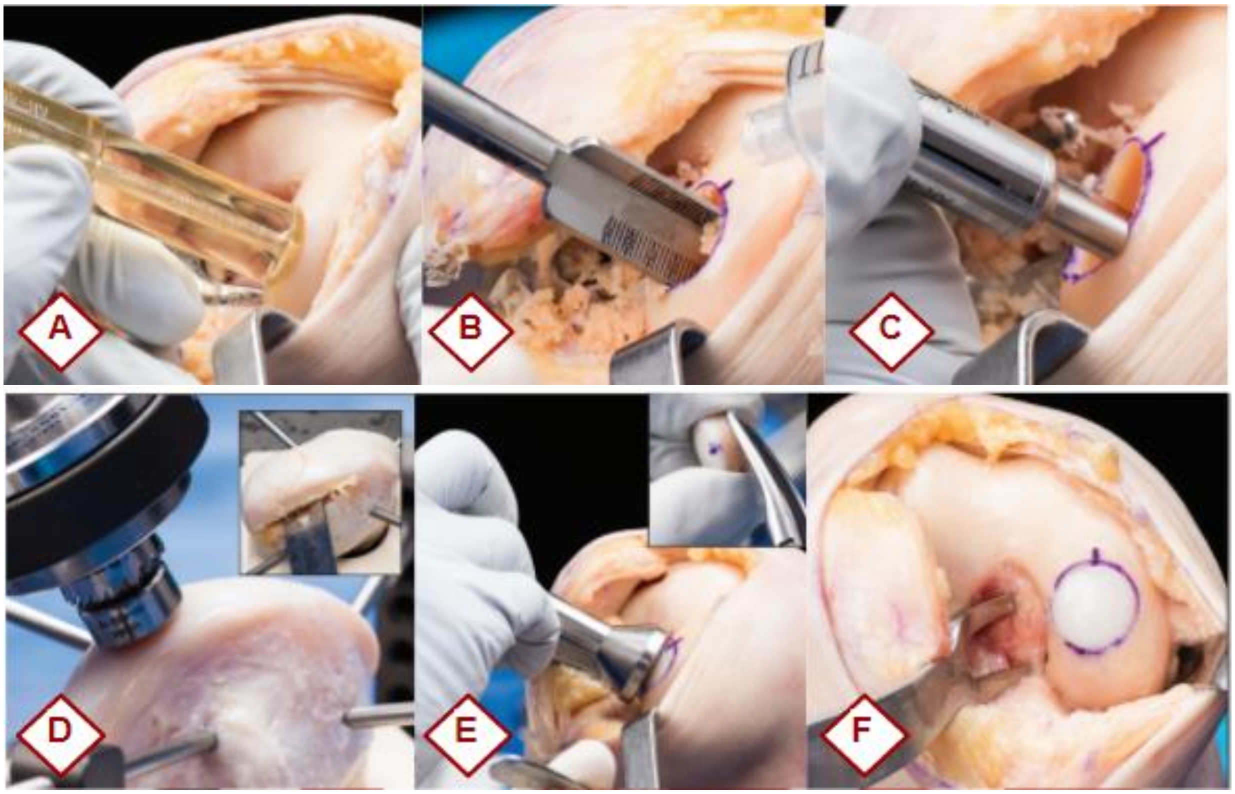

Figure 1: OCA transplant procedure as outlined by the current surgical guide. (4A) Sizing the defect with plastic sizing rod. (4B) Drilling the recipient site to desired depth with a cannulated reamer. (4C) Measuring depth of recipient site with plastic measuring rod. (4D) Cutting donor graft with surgical hole saw. (4E) Impacting donor graft into recipient site with impacting rod. (4F) A successfully implanted graft. [7]

The most common surgical approach to implanting an osteochondral allograft is the dowel technique. This procedure begins by preparing the recipient site for the allograft. The focus of this preparation is to create a cylindrical void that is perpendicular to the surrounding cartilage. To ensure perpendicularity, a guide wire is inserted orthogonal to the condyle at the defect site. A cannulated dowel reamer is passed down the guidewire and advanced to a depth of between 7 mm -14 mm, clearing a void 10 mm-25 mm in diameter.

The allograft is created from fresh cadaver tissue, and its geometry is matched to the recipient site on the patient. To harvest the graft, a surgical hole-saw is passed through a guide ring on the articular cartilage creating a cylindrical dowel. Then, the measurements of the recipient site depths are used to guide the surgeon as they cut the graft to a complementary length with an oscillating saw. The allograft is then positioned directly above the recipient site, and impacted until the graft lies flush with the surrounding cartilage [7].

Physiology

Impaction force used to press fit osteochondral allografts into place during a transplant procedure induces cell death in the superficial portion of the articular cartilage. The impaction impulse deforms mechanoreceptors in the cell. This initiates an intracellular signaling cascade ultimately activating executioner caspases, triggering cell apoptosis (Figure 2).

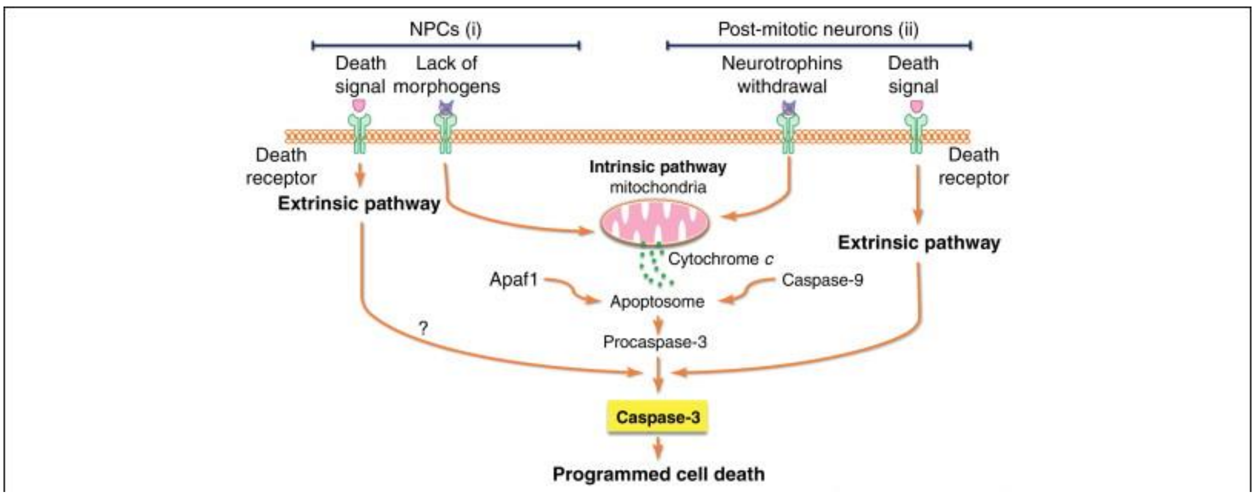

Figure 2: Bio-signaling pathway leading to chondrocyte death following impaction. Mechanoreceptors initiate a signal cascade ultimately activating executioner caspases and leading to apoptosis [8].

This mechanism was discovered in a study to assess the effects of impaction on chondrocyte viability during OCA transplantation. In this study, grafts were taken from the distal aspect of the femoral head and inserted into their recipient sites. Additional grafts were taken from each donor knee and used as controls. The grafts were assessed after forty-eight hours, and the impacted grafts had an average of 47% greater cell death, particularly on the superficial layer of the cartilage (Figure 3). The impacted grafts showed increased levels of caspase 3 activity which is a known enzyme involved in programmed cell death [8].

A separate study was conducted to assess the optimal ratio between the number of impacts, and the total force required for graft implantation. Allografts were impacted with 37.5, 75, 150, and 300 N loads 74, 37, 21, and 11 times respectively. One unimpacted allograft was kept as a control. The researchers found a direct relationship between cell viability and the force to strike ratio: lower impulses with more strikes yielded higher cell viability. The unimpacted control allograft had little to no cellular death [9]. This study demonstrated that graft impaction forces during OCA are deleterious to chondrocyte viability.

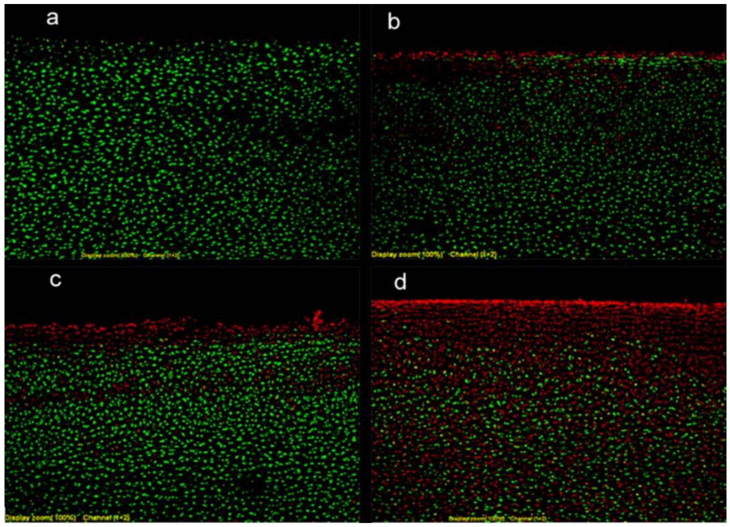

Figure 3: Live/dead chondrocyte cell staining following impaction at varying loads. Red indicates cell death; green indicates viable cells. (a) control (b) 75 N (c) 150 N (d) 300 N [9].

The effects of impaction on chondrocyte viability is an important medical concern for this procedure as chondrocyte viability at the time of impaction is the primary determinant of allograft success. A study was performed in canine models to assess the effects of chondrocyte viability at the time of impaction on allograft success. Subjects received an osteochondral allograft and graft cell viability was assessed at the time of impaction where viability ranged from 23-99%. Six months post-surgery, procedural success was compared to initial chondrocyte viability. The researchers found that no graft with an initial chondrocyte viability below 70% was successful [6]. While other factors contributed to procedural success, none were as significant as initial chondrocyte viability.

Motivation

Osteochondral allograft (OCA) transplantation is a surgical procedure that fuses a healthy cartilage and subchondral bone implant from cadaver donor tissue into the patient's cartilage lesion site, particularly in young, active adults [1]. Despite the prevalence of this procedure, the failure rate is as high as 15.5% at 5 years and can certainly be improved [1]. Nevertheless, the benefit of this procedure over total knee arthroplasty is the promising possibility of restoring full-range of motion and maintaining the patient's quality of life [10]. The motivation in this project, therefore, is to improve full-graft integration and long-term integrity by protecting chondrocyte viability—a significant factor in determining procedure success [4].

Existing Devices

Arthrex Osteochondral Allograft Transfer System (OATS)

The Arthrex Osteochondral Allograft Transfer System (OATS) uses several different tools to prepare the donor site and harvest the graft before impacting it into the patient [2]. As shown in Figure 4A, OATS contains a translucent plastic sizing guide that is used to determine how large of a graft must be placed to completely repair the defect. The surgeon places this guide over the defect to ensure that it is completely covered, selecting a larger or smaller size as needed. Once the proper size is determined, the sizing rod is held orthogonal to the surface of the defect and the guidewire (4B) is inserted through the hole in the center of the sizing guide, and a drill screws the guidewire through the center of the defect and into the bone. After the guidewire is positioned, the cannulated reamer (4C) (with a diameter corresponding to the sizing guide) is inserted over the guidewire to drill a receiving hole to the proper depth (typically 7-14 mm). Miscellaneous tools (not pictured) are used to remove loose tissue from the bottom of the hole, as well as from the cartilage surrounding this hole.

To harvest the donor graft, the cadaver tissue is placed in a vice (not pictured) or another similar fixture to secure it for cutting. The shape of the condyle surrounding the prepared donor site is noted and the best geometric match on the donor tissue is selected. A surgical hole saw guide (4D) is held over the matched geometry of the cadaver graft and the hole saw (4E) is then used to cut the graft cylinder. The graft is inserted using the impaction rod (4F) and a surgical hammer until it sits flush with the surface.

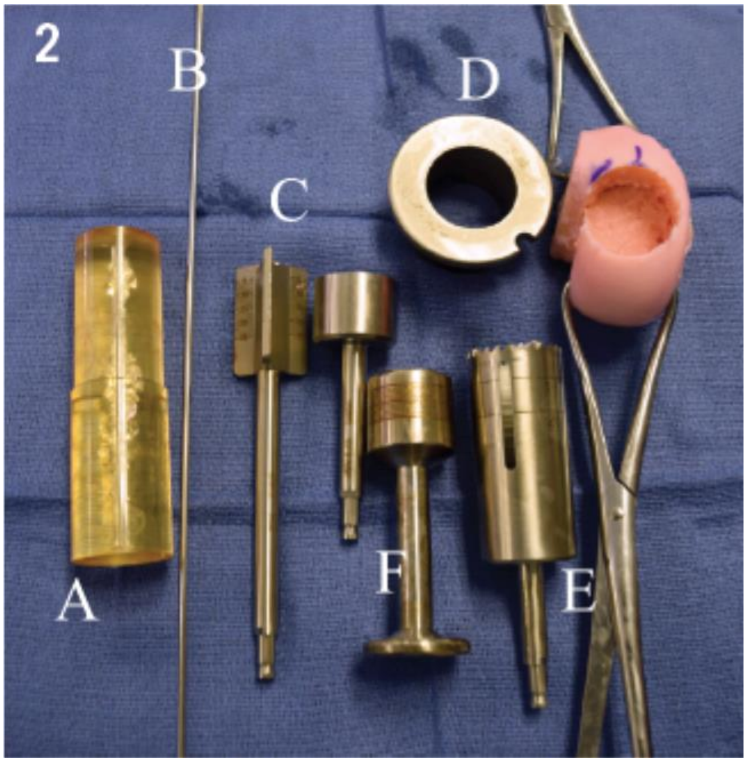

Figure 4: Arthrex Osteochondral Allograft System. (*A*) Locating and sizing guide. (*B*) Stainless steel guide wire. (*C*) Cannulated reamer. (*D*) Surgical hole saw guide ring. (*E*) Surgical hole saw. (*F*) Impacting rods.

Zimmer Chondrofix Osteochondral Allograft System

The Zimmer Chondrofix Osteochondral Allograft system (Figure 5) relies on a pre-made, decellularized osteochondral graft. This eliminates the need to prepare an allograft from cadaveric tissue during surgery. The steps leading up to graft insertion are similar to the Arthrex system. A plastic sizing rod determines the size of the graft that the surgeon will insert. A hollow punch of corresponding size is pounded into the bone over the defect while the surgeon keeps it perpendicular to the condyle surface. Depth markings on the side of the punch allow for greater control over the depth of the receiving hole. After punch insertion, the impacting handle is removed to expose a center hole that accepts a corresponding drill bit which removes the remaining bone inside the punch and leaves a perfectly sized graft receiving hole. Unlike the Arthrex system, this drilling system has a built-in depth stop allowing greater depth control, which can be challenging for surgeons. The drill bit and punch are removed, and the hole depth is verified before cutting the pre-made graft to length. The graft is inserted using the insertion tool, leaving it slightly proud of the surface, and the impaction tool pushes it flush with the surface. This system is designed for arthroscopic use, unlike with the Arthrex system [11].

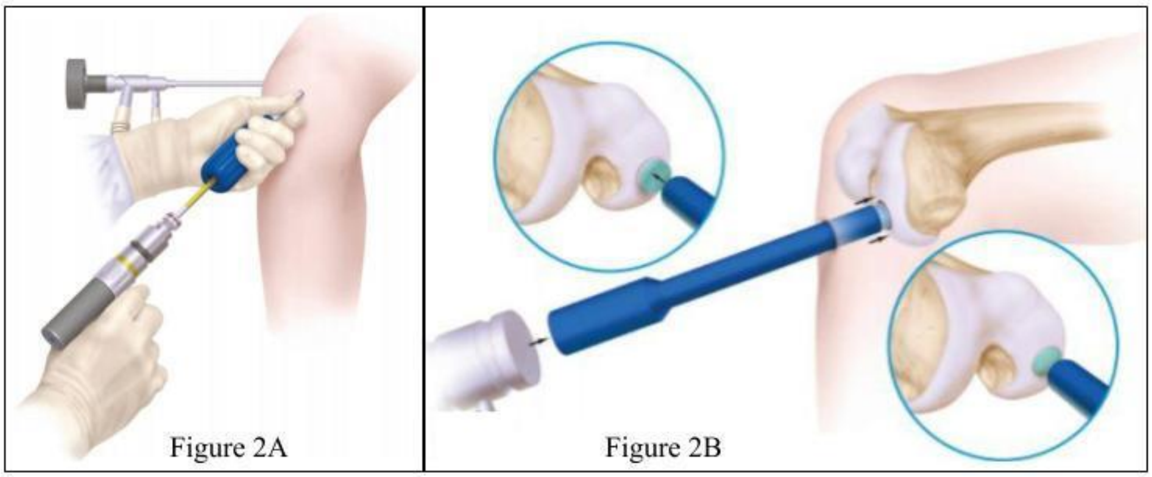

Figure 5: Zimmer Chondrofix Osteochondral Allograft System. (2A) Recipient site arthroscopic drill guide prepares the receiving site. (2B) Arthroscopic impactor secures the decellularized osteochondral allograft into the patient.

DePuy Synthes COR ® Precision Targeting System

The COR ® Precision Targeting System boasts ease of use and improved accuracy, but its claim to protect chondrocyte viability defines it from other systems. Using "no-impact transfer" and "low-impact delivery", it is designed to be used to surgically treat femoral articular cartilage lesions via autograft transplantation. However, the claims of improved chondrocyte viabilities are unsubstantiated by the provided literature. Use of an autograft is another concept unique to this system. To harvest the donor graft, the graft harvesting tool is placed on a non-weight-bearing articular surface (Figure 6A), and a mallet drives the cutter to the desired depth, indicated by measurements on the tip of the tool (Figure 6B). Rotating the tool scores the bottom of the graft to free it from the patient. The graft inside the graft transfer tube is then aligned with the recipient site and impacted until it is fully inserted (6C) [12].

Figure 6: COR® Precision Targeting System. (A) Graft harvesting tool placement. (B) Graft harvesting tool impacted into bone and rotated to score the graft for removal from the patient. (C) Graft transfer tube is placed over the receiving site, and a low impact insertion tool secures the graft into the patient.

These three systems indicate that there is little variation in methodology to OCA transplantation procedures. Every OCA system currently on the market relies on impaction to set the graft in place. This represents a significant gap in the market that an improved osteochondral grafting system can fill.

Problem Statement

Osteochondral transplantation procedures are becoming increasingly common but maintain a procedural failure rate of 15.5%. Current surgical methods involve impaction of an osteochondral allograft into the region of the defect. The goal of this treatment is to introduce mature hyaline cartilage and subchondral bone that will ultimately integrate with the native tissue and repair the defect. The main problem with current OCA surgical systems is that they all rely on graft impaction which is deleterious to chondrocyte viability, and this directly affects the success of the procedure. To address this concern, we developed a novel OCA surgical system with our client, Dr. Brian Walczak, that cuts matching threads on the graft and recipient site resulting in a screw-in graft.

Testing showed the chondrocyte viability was significantly improved using the screw in method compared to impaction. However, matching the surface of the graft with the surface of the receiving site was not fully addressed with our current device. Since our device relies on threading, the vertical and rotational alignment of the graft with the receiving site are coupled once the threads are defined. Aligning the graft correctly in the receiving site is important to avoid incongruencies in the receiving site surface, which can lead to overloaded joints and premature graft failure [13]–[15]. Therefore, further testing of the device is necessary to develop a threading procedure that ensures correct rotational and vertical alignment of the graft with each use of the device. To validate the device, we also must develop a measurement tool to assess how well the surfaces of the graft and receiving site match.

Design Specifications

The chief aim of the system is to improve chondrocyte viability, which has a positive relationship with procedure success. The system must therefore maintain chondrocyte viability above 70%, which has been shown to be a threshold for procedure success. Any damage to the graft beyond current surgical techniques should be avoided. Additionally, the surface of the graft should match the surface of the receiving site, and the total height difference between the two surfaces must not exceed 1 mm. Rotational and vertical alignment between the graft and receiving site should be optimized to minimize irregularities in the implant surface. Furthermore, the procedure for threading the graft into the donor site should be easy for the surgeon and should integrate with the current surgical technique. Ideally, the system will require minimum skilled input from the surgeon to prevent avoidable errors and to promote widespread adoption of the device. The entire system must be easily sterilizable, and operable in a surgical environment. For more detailed product specifications, refer to Appendix A.

Previous Design Work

Overview of Prototype

The current prototype consists of three components: a tap, a die and die base, and graft screwdriver. The die base, shown in Figure 7, is made of aluminum but could easily be transitioned to stainless steel for application in a surgical setting. It consists of two parallel plates separated by vertical stainless-steel pins. In the bottom plate, a removable supporting cup holds the graft. Two thumb screws tighten down the graft and prevent it from rotating when the die is threading it. In the top guiding platform, there is a hole cut through it that matches the size of the die. This hole lies directly over the supporting cup, which ensures axial alignment between the threads and the graft.

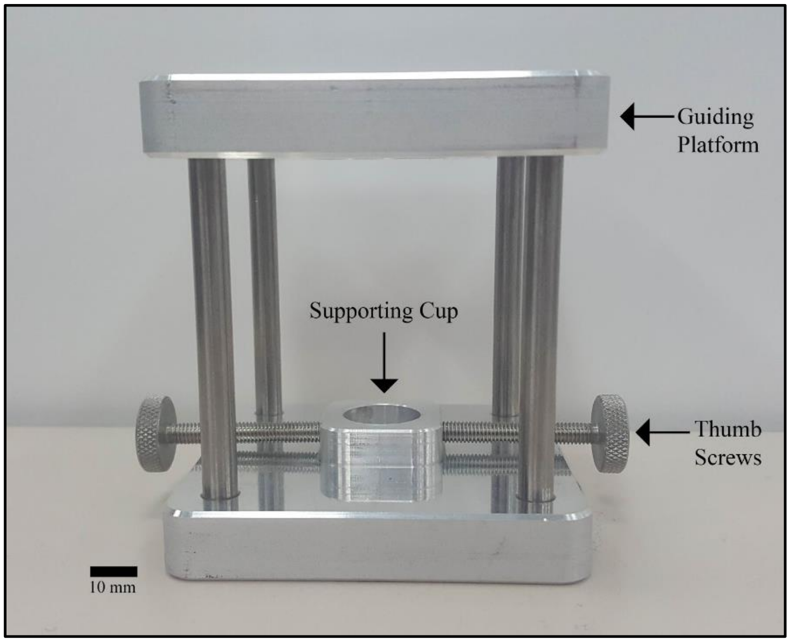

Figure 7: The above image is the final prototype of the stand used to hold the allograft in place while external threads are created. The guiding platform ensures axial alignment. The allograft would be inserted cartilage side up into the supporting cup, and the thumb screws would tighten around the allograft.

The die, as depicted in Figure 8, consists of a stainless-steel body and handle. The handle is removable and offers the surgeon a comfortable grip when using the tool. The die body consists of an open-ended cylinder. The open end has 4 flutes built in to allow the bone shavings created during the threading process to escape. The threads have a 1.5 mm pitch, allowing the surface of the graft to always remain 0.75 mm of the native surface. A previous iteration of this prototype used a 2 mm thread pitch. Finally, the die threads begin as a taper and lead in to allow more consistency during the threading process while requiring less pressure from the surgeon.

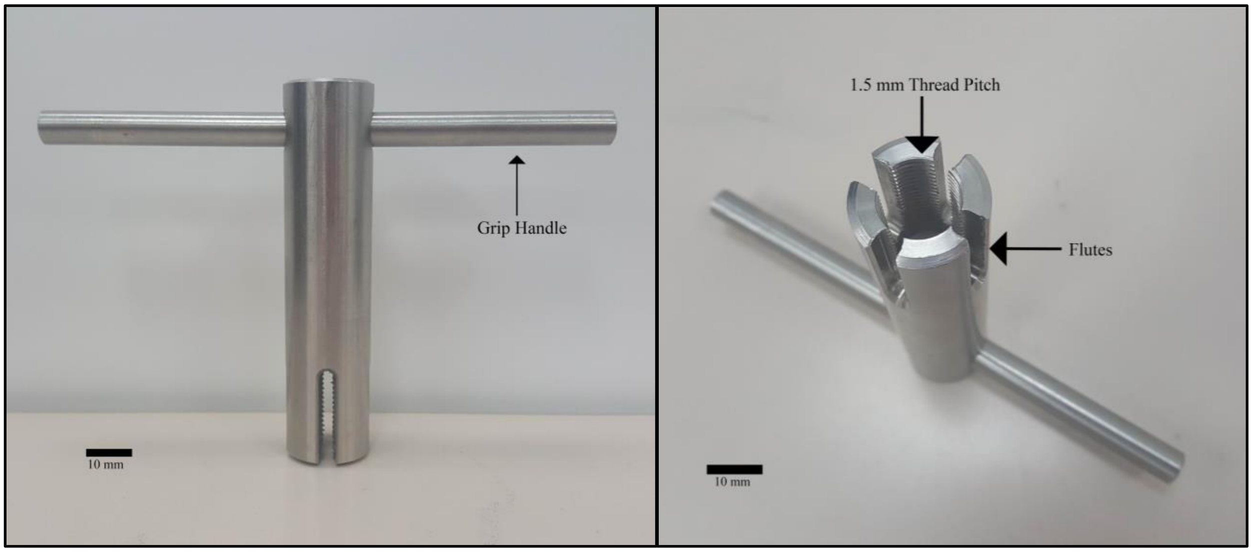

Figure 8: Depicted is the die system used to create threads on the external profile of the graft before insertion into the recipient site. The die would be inserted through the guiding platform to maintain alignment as it creates the external threads in the cartilage and subchondral bone. The image on the left is the die from a head-on perspective, showing the handle and the base cylinder. The right image is an overhead view of the device, showing the internal threads and flutes used to thread the bone.

The tap, as depicted in Figure 9, consists of a stainless-steel body and handle. The die body consists of a cylinder with a hole along the central axis, and threads protruding from working end. The central hole matches the guidewire currently used in surgical systems and is used to slide the tap along said guidewire. This ensures the threading axis is perpendicular to articular surface. The tap has 4 flutes built in to the threads that allow the bone shavings created during the threading process to escape. The threads have a 1.5 mm pitch, matching that of the die above. Finally, the tap threads begin as a taper and lead in to allow more consistency during the threading process while requiring less pressure from the surgeon. The handle is removable and has a guide hole to slide over the guide wire.

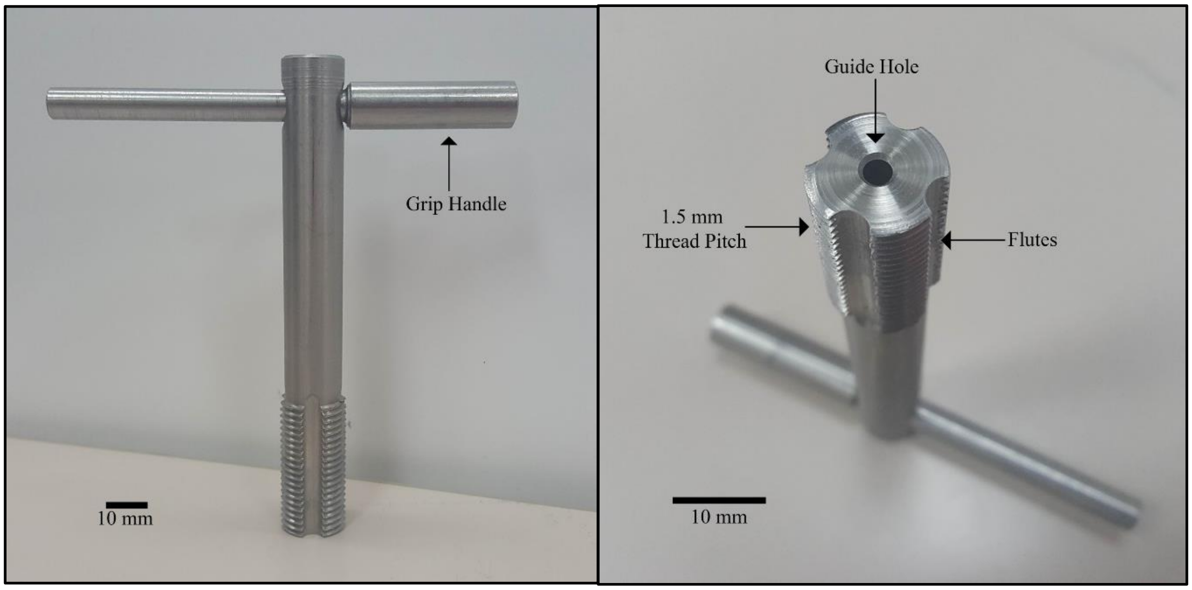

Figure 9: Seen above is the tap system used to create sister-threads within the recipient site when preparing it for graft receipt. A guide wire is to be slid through the guide hole and inserted into the center of the recipient site to ensure proper alignment. The left image shows the tap and handle as a system. The image on the right shows a closeup of the threads and flutes on the tap as well as the hole along the tap's central axis through which the guidewire will be inserted.

The graft screwdriver, as shown in Figure 10 is designed to aid in screwing the graft into the receiving site because hand screwing was found to be difficult. The device is made from two easily sterilizable materials: stainless steel and silicone. It utilizes a hex-bit to attach to a standard screwdriver handle, which is a familiar tool for most people. The working end utilizes two 1 mm diameter tines and a disposable silicone cap to protect the chondrocytes from overhead force when the device is in use. The tines are tapped through the cartilage into the subchondral bone, securing the graft for the surgeon to screw into the receiving site. Additional damage to the chondrocytes due to the tines was found to be minimal. There was localized death, but the viability returned to above the 70% threshold within 400 microns and the overall viability was not significantly altered from the control samples. Additionally, in the current system when particularly large defects requiring multiple grafts, similar pins are used to secure the first graft while the second is being inserted. This appears to have minimal effect on the outcome of the procedure, further justifying their use in this device.

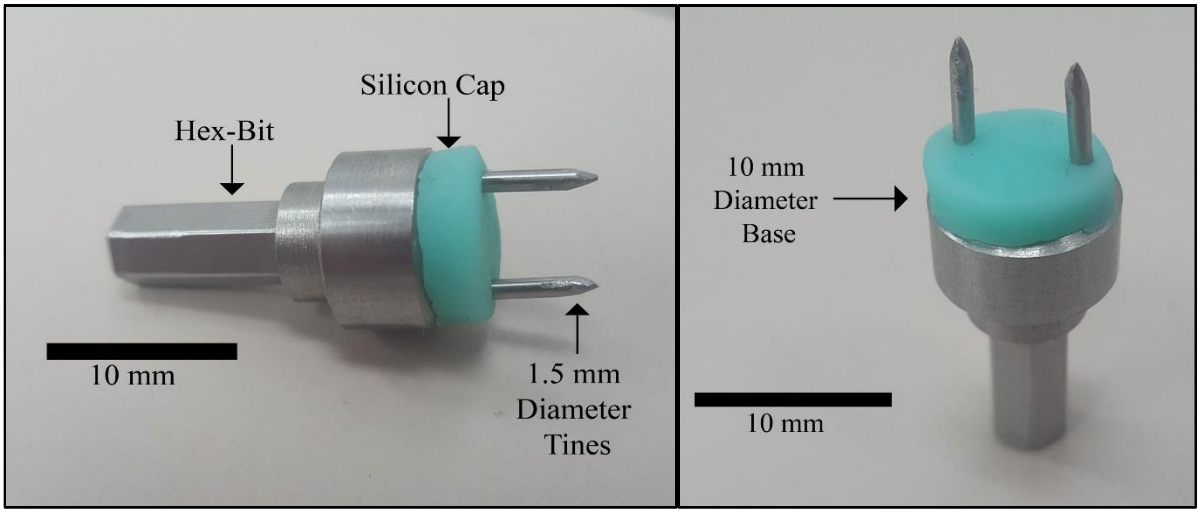

Figure 10: The novel bident tool design depicted above attaches to a standard screwdriver via the hex-bit extrusion. The tines are comparable in size to wires that are used to secure large osteochondral allografts into the patient. As such, they do not increase tissue damage beyond what is already clinically accepted. The silicon cap is a failsafe intended to protect the cartilage from unwarranted impact in the case of accidental over-insertion of the bident into the cartilage.

Prototype Shortcomings

The primary challenge with the current prototype is that it lacks a robust protocol for ensuring that the graft is properly aligned with the native tissue upon insertion into the recipient site. The surgeon aims to insert graft such that it sits flush with the articular cartilage when fully inserted, however the surface geometry of the native cartilage surrounding the graft insertion site is non-planar. Thus, the distance from the base of the recipient site to the top of the articular cartilage varies throughout the circumference of this area. Therefore, it is imperative that the graft is inserted in a specific orientation such that local graft height is complementary to recipient site depth.

In the traditional osteochondral allograft transplant procedure, a surgeon has two degrees of freedom when inserting the graft: rotation and vertical translation. This allows the surgeon to first place the graft in the in the proper rotational alignment, so that throughout the circumference of the graft the local height of the graft is the same as the local depth of the recipient site. Then, the surgeon uses an impaction rod to drive the graft to a depth equal to the recipient site.

Due to the threaded nature of our system, rotation and vertical adjustment of the graft are coupled. Thus, we are limited to one degree of freedom when inserting the graft. As a result, threading of the graft must be both precise and accurate, to ensure that the graft sits flush and properly aligned with the articular cartilage.

Analysis Techniques

3D Laser Scanners

Measuring the geometry of the threaded graft and receiving site presents a unique engineering challenge. As it is difficult to accurately measure the point where threading starts on both components using conventional methods (i.e. calipers, ruler, protractor), and even more difficult to full characterize the size of the components using these techniques, we were forced to investigate more robust measurement techniques. 3D laser scanning provides a convenient method for obtaining a complete and accurate characterization of the surface geometry of the threaded receiving site and threaded graft. 3D laser scanners can be used to compile a highly accurate digital recreation of our threaded graft and receiving site, which will allow us to quantitatively determine how the two components will align, and ultimately allow our team to determine a method for properly aligning the surfaces of both components.

The University of Wisconsin-Madison Makerspace has two 3D laser scanners available to students. The first of these scanners is the Creaform Handyscan 700. This laser scanner is handheld and collects measurements of a component as it is passed over the object by the user. This scanner has a theoretical maximum resolution of 0.05 mm. However, the practical resolution of the scanner is limited by the stability and speed of the user's arm as the collect measurements, and rarely achieves the theoretical resolution.

The second laser scanner that the Makerspace offers is the Einscan SP. The Einscan SP reports a resolution of <0.05 mm, which is similar to the Handyscan. However, the Einscan SP connects the scanner to a measurement stage with a support arm. This feature of the Einscan SP fixes the relative point of reference of the system and makes the system independent of user technique. Thus, it is possible for the Einscan SP to consistently achieve the maximum limit of resolution.

3D Point Cloud Analysis

For analysis of different laser scans, even when collected with the same scanner, it is necessary to register the coordinate systems of the scans to ensure that any measurements are not affected by global rotations or translations during scan measurements. There are two algorithms that have been implemented in MATLAB that should allow for easy registration between the different scans.

The normal distribution transform (NDT) algorithm was developed to reconstruct 3D renderings of rooms given 2D scans from images, or more importantly from LIDAR range finders. Individual points are grouped into 2D objects called cells. Once the point cloud data are split into these cells, mean position values are calculated for each cell and this mean is termed q. Once the mean is found, the convergence matrix is found given equation 1.

$$\Sigma = \frac{1}{n}\sum_i (x_i - q)(x_i - q)^t \tag{1}$$

The convergence matrix is used in an optimization to find convergence of the system through varying rotation angles and translations within this 2D plane. These standard rigid transformations yield potential solutions to the registration x' and y' as in equation 2.

$$\begin{pmatrix} x' \\ y' \end{pmatrix} = \begin{pmatrix} \cos\emptyset & -\sin\emptyset \\ \sin\emptyset & \cos\emptyset \end{pmatrix}\begin{pmatrix} x \\ y \end{pmatrix} + \{t\} \tag{2}$$

A score of p is used as the optimizing parameter given the transformed coordinates x' and y' as in equation 3 [16].

$$score(p) = \sum_i \exp(\frac{-(x_i' - q_i)^t \Sigma_i^{-1}(x_i' - q_i)}{2} \tag{3}$$

Once convergence is found, the MATLAB function returns the point cloud data that have been transformed to the reference coordinate system for analysis.

A different registration algorithm used in MATLAB is the iterative closest point (ICP) algorithm. This algorithm works to find the closest corresponding point between the reference data $\boldsymbol{X}$ and un-registered data $\boldsymbol{P}$ where the difference between individual points $\boldsymbol{x}$ and $\boldsymbol{p}$ is calculated by equation (4).

$$d(\boldsymbol{p}, \boldsymbol{x}) = min\|\boldsymbol{x} - \boldsymbol{p}\| \quad \boldsymbol{x} \in \boldsymbol{X} \quad \boldsymbol{p} \in \boldsymbol{P} \tag{4}$$

The points $\boldsymbol{p}$ having minimum distance to $\boldsymbol{X}$ are stored as the closest points in $\boldsymbol{Y}$ and represents the registration of $\boldsymbol{P}$ with respect to $\boldsymbol{X}$ using a least squares registration method until convergence of the mean-square error [17].

While both the NDT and ICP registrations appear to be applicable to our laser scanning application, the ICD algorithm was developed for registering distinct 3D objects, whereas the NDT algorithm was developed to create a 3D shape out of a series of 2D images. Given the parallel between the ICP algorithm and our laser scanning application, we intend to pursue this algorithm for registering the different laser scans.

Threaded Graft Mechanical Integrity

Given the novel method of using a threading system to secure the graft into the patient, it is critical to characterize its mechanical strengths and ensure that the graft will not fail unexpectedly. In this case, the graft is usually unsupported at the bottom of the hole—this space is left to afford the surgeon a degree of adjustment to the vertical graft placement. Consequently, the only portion of the graft supporting tibiofemoral contact forces is the thread. Given contact forces applied to the axis of the graft, the threads are most likely to experience shear-stress failure.

Shear stress at the threads can be modeled based on the applied axial compressive load, and the geometry of the thread [18]. In this case, the thread shear area (AS_S in mm^2) is related the length of engagement (LE); thread pitch (p); the maximum minor diameter of the internal thread (D_{1max}); and the minimum pitch diameter of the external thread (d_{2min}) (equation 5). The diameter and pitch specifications are easily gathered from a table of thread dimension standards for each given thread size [19].

$$AS_s = \frac{\pi * LE * D_{1max}}{p}\left[\frac{p}{2} + 0.57735\,(d_{2min} - D_{1max})\right] \tag{5}$$

Shear stress V can be calculated by dividing the thread shear area by the applied force F (equation 6). The applied force F was estimated based on numerous assumptions of extreme loading circumstances. The graft was assumed to have been placed on the femoral condyle and sitting proud of the surface so that it bears the entirety of any tibiofemoral contact force. Such forces have been found to exceed 6.2 body-weights during large loading activities such as stair climbing [20]. Assuming the individual weighs 150-pounds (667 N), this corresponds to a simulated tibiofemoral contact force of over 4100 N.

$$V = \frac{F}{AS_s} \tag{6}$$

Given that F = 4100 N, the shear stress V was calculated for numerous graft sizes from 10-25 mm encompassing the most common sizes of osteochondral allografts across typical graft insertion depths (represented by the length of engagement LE in the equation). The results were plotted in Figure 11.

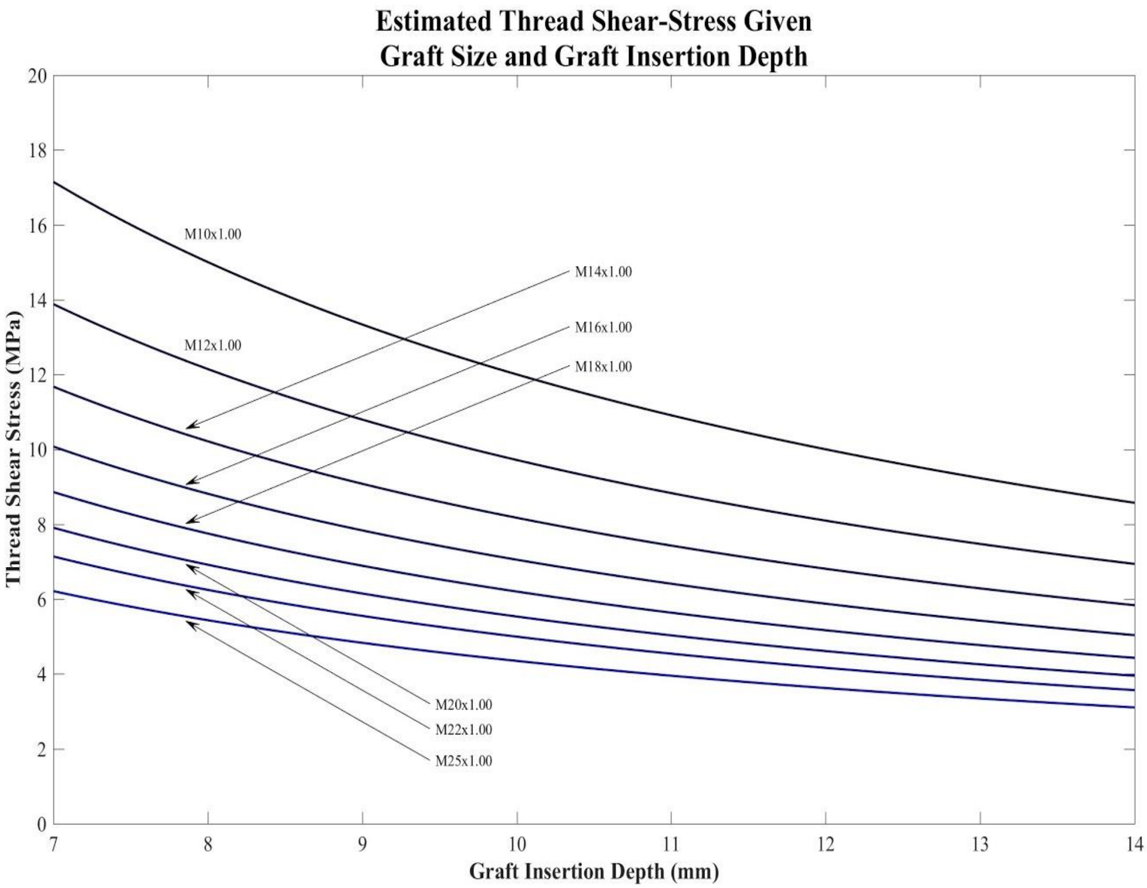

Figure 11: Plot of thread shear stress with various thread geometries varying with graft insertion depth. The simulated load comes from a 150-pound individual climbing stars generating a tibiofemoral contact force of 4100 N.

Cortical bone, such as that present surrounding the receiving hole for an osteochondral allograft, can support a shear stress of approximately 50 MPa [21]. Given the results of the simulation in Figure 11, shear stress in the smallest graft (a 10-mm graft with an M10x1.00 thread) at the minimum insertion of 7-mm only experiences a shear stress of 17 MPa—this is well below the prescribed failure criterion of 50 MPa. Given the extreme (and very unlikely) loading parameters described in this simulation, the contact forces acting directly on the graft will result in shear stress far below the failure stress. Ultimately, these data indicate that the graft can readily support moderate loads until the donor bone can integrate with native bone and reform a solid foundation.

Additionally, threads with a finer pitch exhibit a decreased shear stress and thus are less likely to fail under extreme loading. (The thread pitch *p* decreases in equation 5, which results in an increases shear area and consequently decreases the shear stress on the graft demonstrated with equation 6). Considering the application of the grafts, the finer threads also allow for finer adjustment by the surgeon to match the surface geometries. Previous testing with different thread types showed that the finer threaded tap and dies initiate the threading process with less force required by the operator. However, the finer pitches were also found to be less consistent than the coarser threads and tend to experience more friction between the graft and the donor site. The testing results may attributable to the differences in bone we used for each thread pitch. The coarser thread was tested on hard, mature bovine tissue while the finer thread was tested on softer, adolescent porcine tissue. One goal of this semester is to resolve these inconsistencies and determine a balance between the thread pitch, graft adjustability, thread quality, and initial threading location and difficulty.

Regulatory Standards

FDA Manual Orthopedic Device Standards

The U.S. Food and Drug administration outlines medical device regulations in CFR Title 21- Subchapter H [22]. There are exemptions to the requirement of sending premarket notifications to the FDA, provided that the device has existing characteristics of commercially distributed devices of that generic type [23]. In the case of intention to use a device for a different purpose than that of pre-existing devices of the same type, notification is still required. In addition, a modified device operating on a different fundamental technology requires notification of the FDA. For the purposes of manual orthopedic surgical instruments, exemptions apply in the same manner, so long as they are classified within a particular group, as well as adhere to specific limitations [24]. A generic device, such as a bone tap with minor modifications, would likely necessitate little regulation, and perhaps qualify for exemption, in contrast to a novel instrument for threading donor tissue.

Surgical Instrument Material Standards

Various grades of stainless steel are used in biomedical applications. Corrosion resistance is an essential aspect of any surgical instrument. The International Organization for Standardization (ISO) specifies metals commonly used to manufacture standard surgical instruments [25]. There are many alloys of stainless steel available, however martensitic alloys are generally chosen for surgical instruments, due to its substantial hardness [26]. This grade of surgical steel meets the requirements of ISO product standards, passing corrosion tests based on the methods of sterilization normally encountered by these products (i.e. autoclaving) [27].

Prototype Evaluation

Graft Alignment Testing

Materials and Methods

The aim of this testing was to ensure the surface of the graft, when inserted into the receiving site, does not differ in height from the native surface by more than 1 mm. The first step to evaluate with our device is assessing how consistently we can thread the graft and receiving site. Consistent threading is important because if we are unable to consistently define threads where we want them, then it will be impossible to develop a reliable procedure that ensures rotational alignment of the graft. Essentially, we need to evaluate if we can start threading exactly where the threading tools are placed.

High Density Polyethylene (HDPE) was initially employed for our threading efficiency testing. However, due to the elastic properties of this material, it proved to be an unsuitable model for characterizing threading efficiency of our device. The threading tools did not cut the plastic as expected, but rather formed the material to make the threads. The forming action was not suitable because it altered the effective dimensions of the receiving site and graft making them impossible to thread together. To quantify threading accuracy, a more representative bone model was needed.

Biologic bone samples are expensive, have complex geometry, and variable mechanical properties making controlled testing challenging. To better represent the mechanical properties of bone that our devices will be threading we performed testing in Sawbone. Sawbone is a synthetic polyurethane foam bone analog with material properties closely matching those of actual human bone. The density and Young's Modulus of the foam was chosen to mimic cancellous bone. The average density of cancellous bone in human femoral condyles is 0.346 g/cm^3 which was closest to the 0.32 g/cm^3 density foam which was used to conduct this threading testing [28].

To perform the testing, receiving sites were milled to the appropriate 14.5 mm diameter and either 6 mm or 9 mm deep. These depth measures are multiples of the thread pitch (1.5 mm/revolution) so if threading was performed as expected, the tap rotation should end where it started. For the receiving site threading, an arbitrary reference mark was made, and it was aligned with a mark on the tap denoting the start of the threads. Light downward pressure was applied to the tap handle as the tap was twisted to initial threading. The tap was threaded into the receiving site until it hit the bottom of the hole at which point the location of the thread starting point on the tap was transferred to the surrounding Sawbone to mark where the tap ended. This mark is known as the tap error and is quantified as the angular deviation from the arbitrary reference mark on the receiving site where tapping started.

A similar procedure was repeated in threading the graft. An arbitrary reference mark was placed on the graft and the starting location of the die threads was aligned with the graft mark before threading. Light downward pressure was applied to thread the graft and threads were cut at least 9 mm down the graft to ensure that there was enough thread to screw into the receiving site. After threading, the graft was cut to a length matching the receiving site depth. The bident was tapped into the graft and the graft was screwed into place. After screwing the graft into place, the graft reference mark was compared to the tap end mark and this angular offset was taken to be the die error. Similarly, the angular offset between the graft reference mark and receiving site mark was measured and is interpreted as the total error corresponding to the accuracy with which the graft can be inserted given errors in the tap and die. The angular errors are visualized in Figure 12.

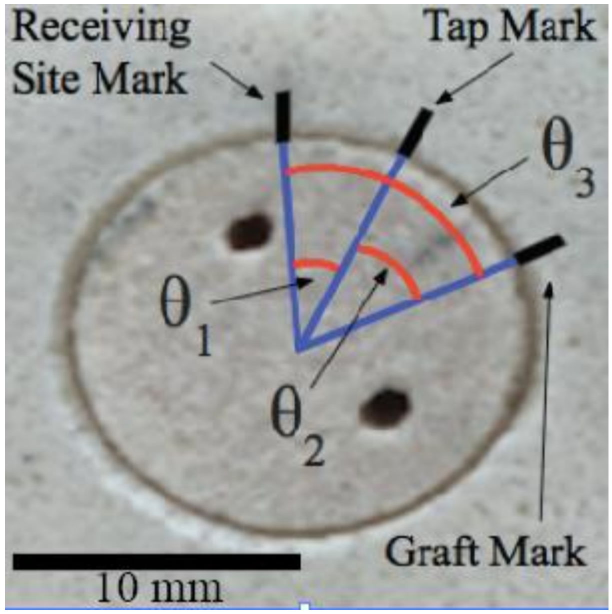

Figure 12: Sawbone graft inserted into Sawbone receiving site. The receiving site mark indicates the intended position for the tap and graft alignment marks. The tap mark indicates the tap position when fully inserted, and the graft mark shows the alignment when the graft is fully inserted. θ_1: tap angle error, θ_2: die angle error. θ_3: total angle error.

Results

From our testing, we found the average total angle misalignment is 89.25° with a standard deviation of 47.49° across 26 samples from 4 test subjects at 2 different depths. This angle offset translates to an average height offset of 0.37 mm and standard deviation of 0.20 mm calculated based off thread pitch (1.5mm / revolution). The angle error, as well as the corresponding height offset, for the die, tap, and overall system can be found in Table 1 and Figure 13.

To calculate the significance of the threading angle difference testing results, a one-sided, one sample t-test with a significance level of $\alpha = 0.01$ is used. The testing results can be compared to the null hypothesis of a 540-degree difference between intended and actual thread starting locations, which translates to a 1 mm height difference. The alternate hypothesis is that our threads have a greater start angle than zero. The t-test can be calculated using equation 7.

$$t_{n-1} = \frac{X\sqrt{n}}{s} \tag{7}$$

In this equation, n is the number of samples, X is the mean sample absolute value of angle difference, s is the sample standard deviation, and t is a test statistic which can be compared to a standard T-table to obtain a p-value. With our data, we can also create a 1-α = 99% confidence interval of where the observed threads begin relative to the intended beginning using equation 8.

$$1 - \alpha = \left[X - \frac{t_{n-1,\frac{\alpha}{2}}(s)}{\sqrt{n}}, X + \frac{t_{n-1,\frac{\alpha}{2}}(s)}{\sqrt{n}}\right] \tag{8}$$

Using equations 7 and 8, the p-value and confidence interval for the Sawbone samples can be calculated. These values can then be transformed to the height offset as a function of thread pitch. To do this, the angle is divided by 360 degrees and multiplied by the thread pitch of 1.5 mm. Table 1 shows the results in the height offset between the graft and the native surface.

Table 1: Graft alignment testing results, including average offset angle, average height difference, p-value at $\alpha = 0.01$ compared to the 1 mm threshold, and a 99% confidence interval for the graft height offset compared to the native tissue surface.

	Tap	Die	Total
Mean angle difference (°)	95.0 ± 50.9	75.9 ± 48.24	89.25 ± 47.6
Mean height offset (mm)	0.40 ± 0.21	0.32 ± 0.20	0.37 ± 0.20
p-value	<0.00001	<0.00001	<0.00001
Confidence Interval (mm)	[0.289, 0.503]	[0.215 0.418]	[0.272, 0.472]

Together, these stats indicate that the height offset using the screw-in method is significantly less than the 1 mm threshold given by our client, Dr. Walczak. Additionally, we are 99% confident that the height offset on Sawbone is below 0.5 mm.

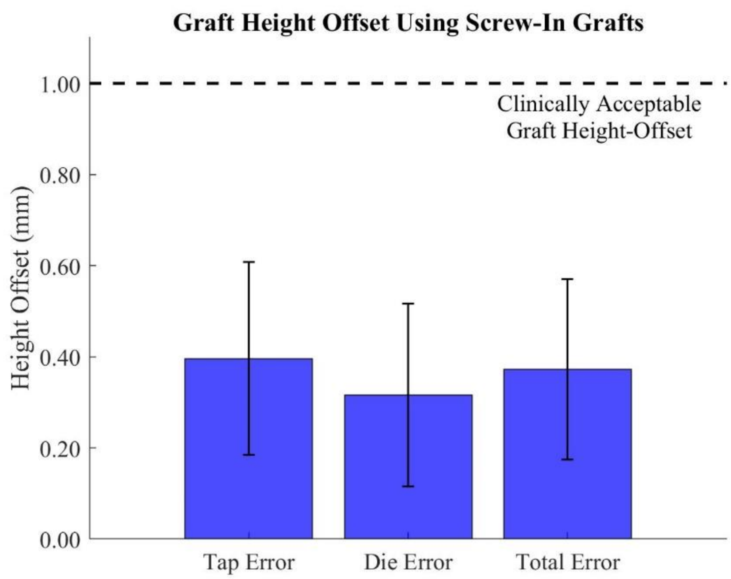

Figure 13: Mean height offset between the graft and receiving site as a result of measured angle difference (n=26). Error bars indicate one standard deviation. The total height difference was less than the clinically acceptable graft height-offset threshold of 1mm.

3D Laser Scanning

To characterize the height differences in the implanted grafts from the native tissue, 3D laser scans and resulting point cloud analysis will be used. To prepare for these measurements, a MATLAB processing routine was developed to quantify the graft height offsets above a native reference surface. To start, a laser scan will be taken of the exposed joint without any modification (i.e. grafting). This scan will serve as a reference coordinate system for registration, and as a ground-truth for graft-height comparisons (i.e. how far from this native surface does the graft lie after implantation?). The grafting procedure will be performed with our threading method, as well as with the traditional impaction method. After the grafting is complete, the articular surfaces will be scanned again to measure any geometry changes. These scan data will be imported to MATLAB and registered to the unaltered joint scan using the ICP algorithm. This will allow for a direct comparison between the reference and grafted scans. The point cloud data collected from the laser scanning is fit with a scattered data interpolant function to quantify the out-of-plane (z-direction) sample heights as a function of in-plane (x-y plane) position. A one-million cell mesh-grid was applied to the interpolant and the values in each cell in the reference scan were subtracted from those of the grafted scan to yield a height difference between the two states. The resulting height difference is attributed to imprecise grafting and allows it to be easily quantified despite the torturous measurement geometry. Sample pilot laser scans are shown in Figure 14.

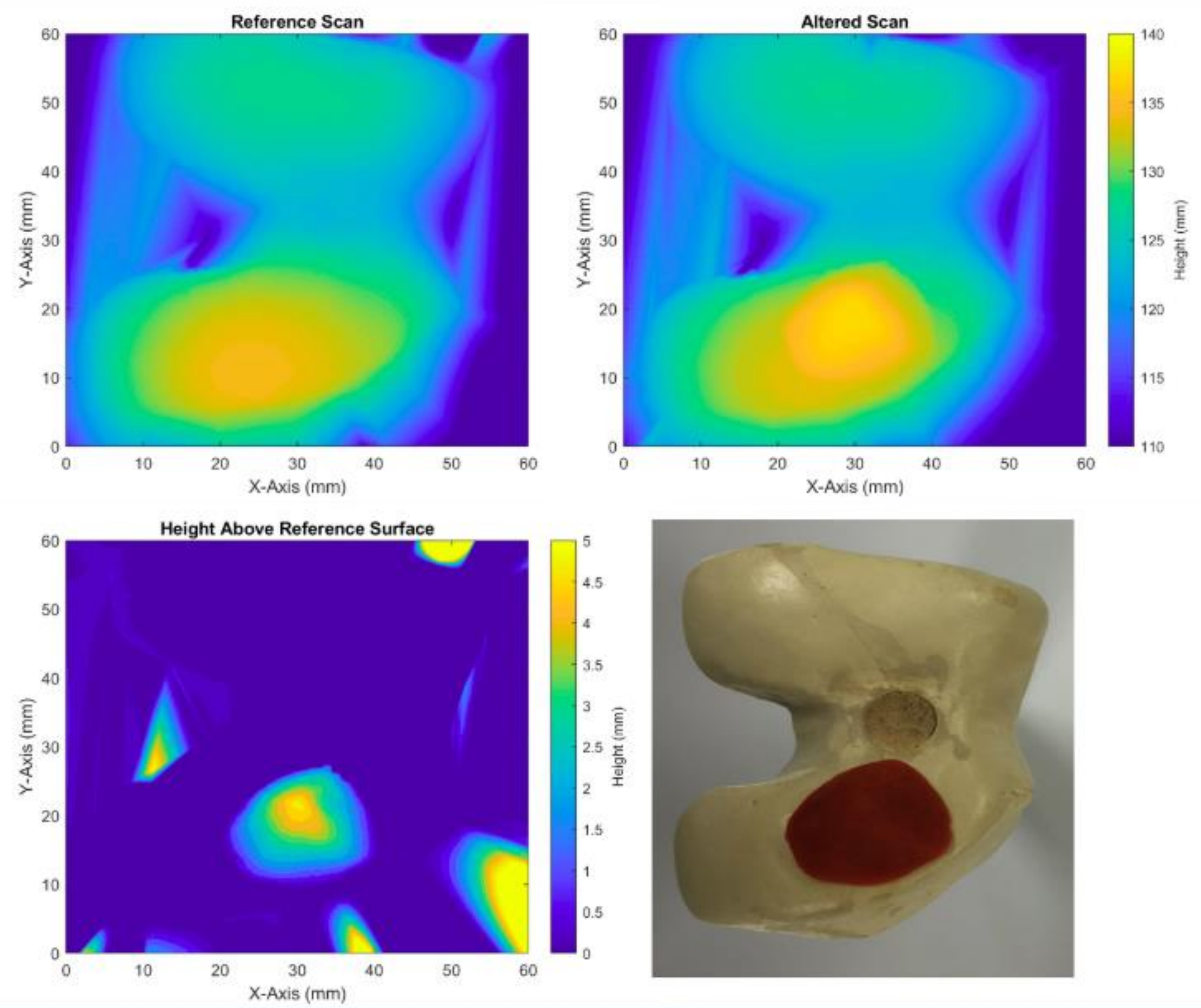

Figure 14: Laser measurements of simulated graft height offset above articular surface in a model femur. The reference scan is the geometry of the unaltered bone. The altered scan shows the bone with the simulated graft and this height offset is quantified by subtracting the reference scan from the altered scan. Image depicts the altered bone model.

Discussion

When compared to the current surgical threshold of a 1 mm height offset, the Sawbone thread testing results are significantly less at an average of 0.37 mm. From the confidence interval, 99% of graft transplantations will be within 0.5 mm. This result is important because the surgeon can be confident in the graft alignment. Additionally, it ensures there is enough cartilage for chondrocyte integration after the surgeon finishes making the graft flush by removing proud cartilage. The large standard deviation is primarily a result of the amount of downward pressure applied during the threading process, which constitutes a large source of error between both operators and individual testing sample. The surgeon, through training, will naturally become more consistent over time and can compensate for his or her particular tendencies when threading.

The Sawbone used in this testing can be considered an idealized sample due to its flat surface. However, in practice the device with be used to thread imperfect, round condyles. Therefore, it is important to quantify the height offsets that result in such procedures and ensure that it remains under 1 mm. Due to the curvature of the surface, the height offsets can no longer be quantified as a function of thread pitch. Instead, 3D laser scanning can be used to quantify maximum and average graft height offsets.

The novel graft threading device has some advantages over current surgical system. The first advantage is that the graft can be adjusted once it has been inserted by using the graft screwdriver. For example, if the graft is inserted too far, the surgeon can simply back the graft out. However, this may affect the surface geometry matchup between the graft and native surfaces if they were improperly matched. Additionally, the design is simple and intuitive to use, as described by a UW Health orthopedic surgeon who used it for the first time. This surgeon also complimented the mechanical integration of the graft by using the threads to keep it in place with a decreased risk of graft loosening.

Future Work

Training Medical Professionals

While we have demonstrated that our novel system provides both improved chondrocyte viability, the individuals who are performing this procedure must be comfortable with using this device if it is to ever be implemented in the operating room. Therefore, we have recruited several orthopedic surgeons from UW Health to provide feedback on our prototype. We will train them on how to use our device, explain how it fits into the current procedure, and allow them to test the system. Following this event, we will elicit feedback, via an exit survey, on what they believe could be improvements to our device, and how it compares to the current industry standard.

Comparing System to Industry Standard

Previously we have compared our threading system to an impaction procedure, by performing mock impaction transplants using a tool set that our team fabricated. However, the Arthrex Osteochondral Allograft Transplant system is currently the standard commercially available product for performing this procedure. Therefore, in order to reliably compare our novel threading system to the industry standard, we aim to obtain this system and for a direct comparison. We will perform replicate transplants using both devices and assay tissue viability post insertion, as a surrogate end point for procedural success.

Viable Tissue Testing

Finally, we will perform the full OCA transplant procedure with viable tissue to simultaneously evaluate geometrical alignment and chondrocyte viability in our device. We will conduct a series of comparative surgeries in porcine models obtained from the Clinical Sciences Center at the University of Wisconsin-Madison. Surgeries will be performed using both the standard impaction protocol and our new threading protocol. If possible, we will have an experienced surgeon, such as our client Dr. Walczak, to perform the procedures as they would be performed in a clinical setting.

A single biopsy of cartilage will be taken from the center of each allograft. These biopsies are intended to be a relative sample of the gross tissue viability of impacted grafts. An additional biopsy of cartilage that has not been implanted will be taken from each of the knees. This biopsy will be used to normalize the initial tissue viability of each sample.

All biopsies will be cultured in Dulbecco's Modified Eagle Medium and stained with Calcein AM and Ethidium Homodimer-1. This stain is a form of a live/dead assay which is intended to characterize tissue viability. Calcein AM is a green fluorochrome that binds to the membrane of living cells and will fluoresce green when excited using confocal microscopy. Ethidium Homodimer-1 is a red fluorochrome that integrates into dead cells and will fluoresce red when excited using confocal microscopy. Following staining, all biopsies will be sliced to reveal a cross section of the cartilage from the articular layer to the subchondral bone. This will provide a representative sample of cell viability at multiple heights through the cartilage. All samples will then be imaged using an A1RS confocal microscope at the Wisconsin Institute for Medical Research Imaging Core. Analysis of cell viability from these images will then be performed using Cell Profiler.

Conclusion

OCA transplantation corrects osteochondral defects through the implantation of a donor graft. This procedure is becoming increasingly common but maintains a relatively high failure rate. Current surgical methods impart high forces on the graft through impaction, which is deleterious to chondrocyte viability and negatively affects procedural outcome. We previously designed a device that utilizes a screw system, which aims to eliminate the force applied to the graft by the current impaction method. Testing showed that our device significantly improves chondrocyte viability compared to the standard impaction method. However, this design did not address how well the surface of the graft matches the recipient site surface. Since we are using a screw system, the rotational and vertical alignment are coupled in the graft. We performed graft alignment testing in Sawbone, which is a polyurethane foam that mimics the mechanical properties of cancellous bone. In this idealized testing, we found there was a 99% confidence interval of the height difference being below 0.5mm, which is well below the clinically accepted height difference of 1mm. Additionally, we developed a 3D laser scanning method of measuring the difference in height between the surface of the graft and recipient site. In the future, we will use the 3D laser scanning during viable tissue testing to evaluate geometry and chondrocyte viability considerations simultaneously. We also plan to have orthopedic surgeons use both the OATS and our system to further determine if our procedure is a viable model to improve OCA transplantation procedure outcomes.

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Appendix

Appendix A: Product Design Specifications

Osteochondral Allograft Tapping System

Product Design Specifications

Team: Alex Teague

Alex Babinski

David Fiflis

Zach Wodushek

Function: Osteochondral allografts (OCAs) are used to repair chondral defects in young, active patients. The current procedure involves cutting the graft from cadaveric tissue, then using impaction to drive the graft into a low-clearance receiving hole drilled over the defect. The large impulse associated with graft impaction often leads to decreases in grafted chondrocyte viability, and negatively affects procedure outcomes [1]. To avoid deleterious impaction, we created a screw-in system which taps the patient receiving site and threads the donor graft allowing the graft to be screwed into the patient. Testing revealed that this new system has significantly higher implanted chondrocyte viability when compared to the impaction protocol. A challenge unique to our system, however, is that the one degree-of-freedom (DOF) nature of a screw mechanism limits graft adjustment relative to the traditional two DOF impacted graft. Therefore, the aim of this project is to develop a protocol for threading the graft and receiving site such that desired graft rotation and height can be achieved simultaneously when the graft is fully inserted into the patient.

Client Requirements

1. The protocol must permit a graft height offset from native tissue of no more than ±1.0mm.
2. After graft preparation and insertion, chondrocyte viability must be consistently greater than 70%, which has been shown to be a threshold to successful graft integration [1].
3. The entire system must be sterilized before use in surgery.
4. The threading protocol must be quick and easy to learn so as not to drastically alter the current surgical practice.
5. Damage to the chondral surface must be no greater than what presently occurs during OCA transplantation.

Design Requirements

1) Physical and Operational Characteristics
   a) Performance Requirements

i) Threading the graft and receiving site should not damage the articular cartilage
   (1) It should limit gouging, scratching, and other mechanical alterations to the native, or graft cartilage.
   (2) It should not result in significant chondrocyte death after use
ii) Insertion of the graft must be easily executed to minimize the risk of tissue damage.
iii) During the procedure, the graft should be easy to insert and remove allowing the surgeon to adjust the graft depth.
iv) The threading protocol must cut threads in the graft and receiving site that result in predictable graft placement.

b) Safety
   i) The threading system should not increase the chances of postoperative complications, including (but not limited to) infection, tissue death, or graft dislocation.
   ii) Long term, the threaded graft must not lead to an associated cartilage disorder, significant fissuring or fibrous tissue infiltration, or improper tissue integration.

c) Accuracy and Reliability
   i) The threading protocol should allow for successful graft integration into the recipient site. This means that the procedure should maintain at least 70% chondrocyte viability after implantation.
   ii) The measurement protocol should ensure that, after graft insertion, the donor curvature closely matches that of the recipient site within ±1.0 mm of height difference.

d) Life in Service
   i) Non-disposable components must be serializable to allow for repeated use
   ii) Life of device materials will vary depending on chosen stainless steel alloy.
   iii) Disposable components should be minimized in the design to prevent excessive recurring costs.

e) Shelf Life
   i) Capable of storage at room temperature.
   ii) Must be compliant with hospital regulations of storage.
   iii) Shelf life is not likely to present as a significant design consideration.

f) Operating Environment
   i) Protocol must not compromise sterility of the device or surgical field.
   ii) Must function within range of operating room temperatures, in addition to *in vivo* conditions.

iii) Must be usable in concurrence with all other orthopedic tools and materials.

g) Ergonomics
   i) The devices must be designed for comfortable handheld use by the orthopedic surgeon during the procedure.
   ii) To promote easy rotation, the tool must be easy to locate over the central-axis of the graft.

h) Size
   i) Tools will be appropriately sized for handheld usage by orthopedic surgeon.
   ii) The device should accommodate bone graft sizes 10 mm - 25 mm in diameter and 7 mm - 14 mm deep.

i) Weight
   i) Since the device will be hand-held, its total weight should not be so heavy that it is cumbersome or fatigues the surgeon during use.

j) Materials
   i) All materials must pass ISO regulations to corrosion resistance and excessive wear from use [2].
   ii) Tools involved in the procedure must be sterilizable or disposable.
   iii) These materials will be a stainless-steel alloy and not the standard high-speed steel alloy that these threading tools are traditionally made from.

k) Aesthetics
   i) Aesthetics will serve as a secondary initiative to the function of the final product.

2) Production Characteristics
   a) Quantity
      i) One prototype capable of inserting the graft into the patient.
         (1) The prototype may have more than one component.

   b) Components
      i) The final product must consist of a mechanism for inserting the graft into the recipient hole.
         (1) A component must hold the graft in place and align a threading mechanism.
         (2) An external threading component must create threads on a harvested graft.

(3) An internal threading component must create threads in the patient receiving site.
(4) A component will function as a screwdriver to screw the graft into the recipient site.
(5) A final component must define the starting threading position on the graft threading component to ultimately allow for predictable graft placement.

3) Miscellaneous
   a) Standards and Specifications
      i) The final product must comply with the FDA standard for manual surgical instruments as stated by CFR 21 - Subchapter H - Medical Devices [2]

   b) Customer
      i) Orthopedic surgeons implanting an osteochondral allograft.

   c) Patient Related Concerns
      i) Decreasing chondrocytes cell viability leads to diminished graft integrity.
      ii) Unwanted debris and fragments of the graft may be released into the synovial fluid environment and cause other complications.
      iii) A graft with an articular surface homologous to the native tissue is necessary for long term grafting success and patient health.

4) Current Systems
   a) Arthrex Osteochondral Allograft Transfer System (OATS). This system is the prototypical system used in osteochondral transplant procedures (and is most similar to the system Dr. Walczak uses). It uses a sizing guide, guide wire, and cannulating reamer to size, locate, and ream the chondral defect. The allograft is prepared using the hole saw which is guided by a manually held ring. The impaction rods forces the graft into the receiving hole [3].
   b) Zimmer Chondrofix Osteochondral Allograft. This system uses a hollow punch hammered into the bone to guide the drill bit during receiving site preparation. There is no need to prepare an allograft since it comes with a pre-made, decellularized allograft that fits precisely in the hole created by the punch and drill bit. The graft is inserted most of the way using the insertion tool and is pounded in the reminder of the way using an impaction rod [4].
   c) COR Precision Targeting System. This is the only surgical system that claims to address chondrocyte viability concerns associated with OCA transplantation. The tool encloses the graft during harvesting and insertion to protect it from mishandling. The surgical guide also claims to use “low impaction insertion” but does not describe how impaction forces are minimized relative to traditional tools. Despite the promise with the system, it is not currently in use in human OCA transplantation. [5]

d) There are no direct competitors, and of the ones currently in use, all rely on graft impaction.

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Appendix B: Fabrication and Testing Material Expenses

Use	Product	Part Number	Supplier	Quantity	Unit Price	Total Price
Mock graft for geometric fitting in plastic	Rod Stock, HDPE, ⅝ in., 48 in.	22JL48	Grainger	1	$9.40	$9.40
Mock receiving site for geometric fitting in plastic	Sheet Stock, 12” LX 12” W X 1.000” Thick, 176 Max. Temp. (F), Off-White	1ZAH3	Grainger	1	$22.15	$22.15
Mimic of cancellous bone for geometric fitting in physiologically relevant model	Sawbone, 20 pcf Block	1522-03	Sawbone	2	$17.75	$35.50
Drill bit for creating recipient sites	Flat-Blade Drill Bit for Wood	2894A65	McMaster-Carr	1	$3.44	$3.44
Testing models for training surgeons on the device	Cow knuckles	N/A	Conscious Carnivore	5.12 lbs.	$4.99/lbs.	$25.54
					Material Total:	$96.03
					Tax:	$3.89

					Shipping:	$28.59
					Total:	$128.51

Table 1: Complete list of all materials used to make the prototype. Total project expenses are $128.51.