Analysis of bendable osteochondral allograft treatment and investigations of articular cartilage wear mechanics

Courtney Adair Petersen

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Abstract

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Osteoarthritis is a highly prevalent, debilitating disease characterized by the wear and degradation of articular cartilage. While many surgical interventions exist, few are consistently effective and those that are effective are not necessarily suitable for all patients. The objective of this dissertation is to improve patient care through the development of a new surgical technique and through basic science studies which seek to better understand articular cartilage wear initiation. Four studies, which address this objective are summarized below.

Osteochondral allograft transplantation provides a safe and effective treatment option for large cartilage defects, but its use is limited partly due to the difficulty of matching articular surface curvature between donor and recipient. We hypothesize that bendable osteochondral allografts may provide better curvature matching for patella transplants in the patellofemoral joint. The finite element study presented in Chapter 2 investigates patellofemoral joint congruence for unbent and bendable osteochondral allografts, at various flexion angles. Finite element models were created for 12 femur-patella osteochondral allograft pairings. Two grooves were cut into the bony substrate
of each allograft, allowing the articular layer to bend. Patellofemoral joints with either unbent (OCA) or permanently bent (BOCA) allografts were articulated from 40 to 70 degrees flexion and contact area was calculated. OCAs and BOCAs were then shifted 6 mm distally toward the tibia (S-OCA, S-BOCA) to investigate the influence of proximal-distal alignment on congruence. On average, no significant difference in contact area was found between native patellofemoral joints and either OCAs or BOCAs ($p > 0.25$), indicating that both types of allografts restored native congruence. This result provides biomechanical support in favor of an emerging surgical procedure. S-BOCAs resulted in a significant increase in contact area relative to the remaining groups ($p < 0.02$). The fact that bendable osteochondral allografts produced equally good results implies that these bendable allografts may prove useful in future surgical procedures, with the possibility of transplanting them with a small distal shift. Surgeons who are reluctant to use osteochondral allografts for resurfacing patellae based on curvature matching capabilities may be more amenable to adopting bendable osteochondral allografts.

The recent development of bendable osteochondral allografts provides the potential for improved osteoarthritis treatment for joints whose current treatment is unsatisfactory. One such joint is the carpometacarpal joint in the thumb. While the current standard of care for carpometacarpal osteoarthritis, ligament reconstruction and tendon interposition, can reduce pain in the joint, it does not restore full joint function and mobility. A proposed alternative includes using an osteochondral allograft harvested from the femoral trochlea in a donor knee, machining grooves in the bone to allow the allograft to bend, and replacing the trapezium with this bent osteochondral allograft [1,2]. Chapter 3 of this dissertation discusses adjustments to the original design of the bendable allograft and the design of a custom surgical tool to perform the proposed surgery. Specification changes of the allograft included an overall size reduction in order to better
fit within the carpometacarpal joint, minimum bone thickness requirements to avoid bone cracking during the surgical procedure, and a reduction from three grooves to two grooves, which provided sufficient bending yet avoided fracture of the allograft. The surgical tool was designed to be a custom forceps device, whose primary features included (1) jaws with an angled face to match the angle of allograft bending and (2) insertion holes for the Kirschner wire and compression screws used to anchor the allograft in the bent position. These customizations allow the tool to be used to bend the allograft, fix it in the bent configuration, and place the allograft in its proper position in the hand during anchoring of the bent allograft to the native trapezium.

The final two studies presented in this dissertation focus on furthering our current understanding of wear and structure-function relationships of articular cartilage. We hypothesize that cartilage wears due to fatigue failure in reciprocating compression instead of reciprocating friction. Chapter 4 compares reciprocating sliding of immature bovine articular cartilage against glass in two testing configurations: (1) a stationary contact area configuration (SCA), which results in static compression, interstitial fluid depressurization and increasing friction coefficient during reciprocating sliding, and (2) a migrating contact area configuration (MCA), which maintains fluid pressurization and low friction while producing reciprocating compressive loading during reciprocating sliding. Contact stress, sliding duration, and sliding distance were controlled to be similar between test groups. SCA tests exhibited an average friction coefficient of $\mu = 0.084 \pm 0.032$, while MCA tests exhibited a lower average friction coefficient of $\mu = 0.020 \pm 0.008$ ($p < 10^{-4}$). Despite the lower friction, MCA cartilage samples exhibited clear surface damage with a significantly greater average surface deviation from a fitted plane after wear testing ($R_q = 0.125 \pm 0.095$ mm) than cartilage samples slid in a SCA configuration ($R_q = 0.044 \pm 0.017$ mm, $p = 0.002$), which showed minimal signs of wear. Polarized light microscopy confirmed that
Delamination damage occurred between the superficial and middle zones of the articular cartilage in MCA samples. The greatest wear was observed in the group with lowest friction coefficient, subjected to cyclical instead of static compression, implying that friction is not the primary driver of cartilage wear. Delamination between superficial and middle zones imply the main mode of wear is fatigue failure under cyclical compression, not fatigue or abrasion due to reciprocating frictional sliding.

The final study of this dissertation, presented in Chapter 5, investigates the importance of collagen fibril distribution in articular cartilage computational models. Finite element models were created to approximate a bovine humeral head and replicate previous experimental loading conditions [3]. Five different finite element analyses were run, each using a different fibril distribution model. Three of the models used two, four, or eight discrete fibril bundles, while two models used continuous fibril distributions with either isotropic or depth-dependent ellipsoidal distributions. Two primary findings arose from this investigation. The first was the discovery that as the fibril distribution became more isotropic, the strain throughout the tissue decreased, even though the contact area between the articular surface and rigid platen remained relatively equal across distribution models. This suggests that computational models which approximate the collagen fibrils with an isotropic distribution may be underestimating the strain through the depth of the tissue. The second primary finding was that in the discrete distribution model with two fibril bundles, which followed the classically described Benninghoff structure [4], the greatest magnitude of shear strain during compressive loading was observed in the middle zone. However, the highest magnitude of shear strain observed in the isotropic fibril distribution model occurred in the deep zone near the subchondral surface. The observed results suggest that the type of fibril
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Dedication

For Papa.
Chapter 1: Introduction and Background

Osteoarthritis is one of the leading causes of disease in adults over the age of 50 [5] affecting nearly 52 million people in the United States and over 520 million people globally [6]. Classically characterized by the wear and degradation of articular cartilage, osteoarthritis often progresses from a small focal area of cartilage damage to full joint degeneration. The most common site of osteoarthritis is in the knee (61% of all cases), followed by the hand (24%), and hip (6%) [6]. Cartilage degeneration often goes unnoticed or undiagnosed until late-stage osteoarthritis progression, when symptoms begin to manifest and a patient seeks medical treatment. Pain, the most prominent osteoarthritis symptom, can be debilitating and may be experienced as a consistent aching or as surges of intense pain, at times amplified by specific activities or movements [7]. Other common symptoms include joint stiffness, instability, or weakness [7]. The objective of this dissertation is to improve osteoarthritis care and reduce patient pain through (1) developing a new osteoarthritis treatment method and (2) furthering understanding of mechanical contributions to cartilage wear and degeneration.

Required to meet this objective is a comprehensive understanding of both the disease (osteoarthritis) and the tissue (articular cartilage). The following sections detail current clinical treatments, both standard and novel, and outline the structure and function of articular cartilage. Understanding mechanical contributions leading to articular cartilage wear directly affect how osteoarthritis should be studied, treated, and prevented.

1.1 Osteoarthritis

1.1.1. Common Treatment Techniques

As an avascular tissue with low cell density, cartilage has limited capability to self-repair and surgical intervention is typically required to alleviate pain [8,9]. The standard of care for late-
stage osteoarthritis is artificial joint replacement, or arthroplasty, where the articular cartilage and underlying bone is removed and replaced with metal, plastic, or ceramic. Though this treatment is typically viewed as the gold standard osteoarthritis treatment, it is not suitable for all patients. Prior to surgical interventions, other treatment modalities may be suggested by a physician, such as physical therapy, exercise, bracing, activity modification, steroid injection, or hyaluronic acid injection. These treatments, however, have neither proven to be disease-reversing nor have consistently effective outcomes [7]. Some groups have advocated for treating osteoarthritis with techniques such as microfracture [10], mosaicplasty [11], or autologous chondrocyte implantation [12], however none of these treatments have shown consistently positive long-term results.

1.1.2. Osteochondral Allograft Transplantation

One biologic technique that has emerged over the last two decades is the transplantation of osteochondral allografts. Healthy articular cartilage and the underlying bone recovered from qualified donor tissue can be preserved for several weeks in tissue banks before being transplanted to replace arthritic focal defects or even entire articular surfaces [13-15]. This technique preserves more of the native tissue relative to artificial joint replacements and the use of osteochondral allografts to treat osteoarthritis has shown good clinical outcomes [16-20]. Though the results of this technique are encouraging, osteochondral allograft procedures are often considered salvage techniques and have not been widely adopted. One reason surgeons hesitate to recommend an osteochondral allograft procedure more readily is the inability to match curvature between donor and recipient anatomy [21-23]. Even when the donor osteochondral allograft is recovered from the same location for which it will be transplanted, current methods are only able to approximate curvature matching rather than guarantee it.
This dissertation (Chapter 2) discusses a method for adapting osteochondral allografts to the curvature of the recipient anatomy with the hypothesis that the ability to manipulate the articular surface curvature of the allograft will result in improved clinical outcomes and more widespread use. Previous work investigated this method by adapting the curvature of cartilage tissue from the femoral trochlea to match the curvature and replace the articular cartilage surface of the trapezium in the carpometacarpal joint of the thumb [1,2]. In this dissertation, the design and use of osteochondral allografts will be discussed using the patella due to its propensity for osteoarthritis, the difficulty to treat patellofemoral arthritis, and the relatively recent clinical application of fresh osteochondral patellar allograft resurfacing (FOPAR) procedures during which an entire patellar surface is replaced with a size-matched donor patella [13,15,22,24-27].

1.2 Articular Cartilage

Articular cartilage is a load bearing tissue covering the ends of bones in synovial joints and can be considered the “shock absorber” of the body. Cartilage is primarily made up of three structural components: (1) water, (2) proteoglycans, and (3) collagen, with water making up approximately 80% of the tissue wet weight, proteoglycans making up approximately 30% of the dry weight of cartilage, and collagen making up the remaining 70% of the dry weight with collagen II being the primary type of collagen in articular cartilage [28]. The unique composition and structure of articular cartilage produce its load-bearing capabilities, providing both low friction and low wear in joints and distributing applied loads between bones [28].

As a network of fibrils, collagen is generally presumed to determine the tensile properties of cartilage tissue, while the compressive properties are generally attributed to the proteoglycans. In reality, proteoglycans and the collagen network work together to produce the complex material response of articular cartilage [29]. Proteoglycans, which are negatively charged, attract water and
cause the tissue to swell. This swelling is then restrained by the collagen network and when the tissue is loaded, the fluid pressurizes [30]. Therefore, even when the bulk tissue is loaded in compression, the collagen fibrils may be loaded under tension as they restrain tissue deformation.

1.2.1. Interstitial Fluid Load Support and Friction

Generally, the friction coefficient between cartilage surfaces is extremely low, which is an important function of the tissue. As cartilage is loaded, the interstitial fluid, which makes up 70% – 90% of the entire weight and is largely responsible for the load-bearing capabilities of cartilage [28,31-33], is depleted from the tissue. If the fluid pressurization and therefore load support in the tissue decreases, the friction coefficient rises [34,35]. Friction coefficients for cartilage sliding against cartilage measured in synovial joints has ranged from 0.001 to 0.08 varying with joint type and testing parameters [36]. For small explants, the friction coefficient of cartilage against glass has been reported to vary from 0.002 to 0.2 [36].

In physiologic loading conditions, cartilage slides against cartilage and the point of contact between the two surfaces moves across the tissue, producing a migrating contact area (MCA) configuration. This MCA configuration allows the tissue to re-imbibe lost fluid and sustain an elevated fluid load support, resulting in a low friction coefficient [37]. Conversely, in a stationary contact area (SCA) configuration, the tissue does not have the opportunity to recover its interstitial fluid pressurization, resulting in an increased friction coefficient [35,37]. For example, Caligaris and Ateshian reported a 60-fold increase in friction coefficient in the SCA configuration relative to the MCA configuration for cartilage sliding against glass [37].

Though the lubricating properties of synovial fluid are often attributed as the primary source of low friction in articular cartilage [38-40], the effects of interstitial fluid pressurization have a significantly greater effect on the friction coefficient of articular cartilage surfaces. In fact,
orthopedic surgeon, John Charnley found that the friction coefficient in his experiments was not altered after wiping away the synovial fluid layer from the articular surfaces [41]. Results reported in Chapter 4 further support this finding by showing that the greatest difference in friction coefficient comes from maintaining fluid pressurization rather than by sliding in a synovial fluid bath. The lubricating properties of synovial fluid (boundary lubrication) work together with interstitial fluid pressurization to provide the remarkably low friction coefficient reported in articular cartilage [42].

1.2.2. Friction and Wear

An implicit assumption has been made throughout the literature that surface friction is directly related to cartilage wear [38,43-46]. This assumption would suggest that the friction coefficient should increase with the advancement of osteoarthritis or the progression of cartilage damage. While some studies have provided tentative evidence to support this hypothesis [47-49], others have either remained inconclusive or observed the opposite [46,50]. Caligaris et al. reported that increasing levels of OA in human cartilage tissue did not result in increasing friction coefficients [50]. In another study, Durney et al. showed that the friction coefficient in a cartilage against glass configuration remained low even when gross visual wear or subsurface damage was observed, and no statistical difference was found in friction coefficients between damaged and undamaged samples [51]. Furthermore, Zimmerman reported only a small increase in damage due to the addition of friction in computational models of cartilage sliding against glass [52].

The assumption that friction and wear are directly related could also suggest that abrasive wear is the primary wear mechanism in articular cartilage. Cartilage wear studies show subsurface failure prior to surface failure, either in the form of delamination between the superficial and middle zones of articular cartilage [51,53] or splits along the direction of primary collagen
If cartilage failed due to abrasion, we would expect to see the superficial zone worn away first, leaving the middle zone initially intact.

One classic example in orthopedic tribology of friction not necessarily being a direct predictor of wear is the switch made in the early 1960s from polytetrafluorethylene (PTFE, commonly known as Teflon), which was chosen for its low-friction properties, to ultra-high-molecular-weight polyethylene (UHMWPE) in hip implants [55]. While the friction coefficient between Teflon surfaces is lower than between UHMWPE surfaces [56], Teflon showed unsatisfactory wear properties, with significant wear observed even just one year after hip implantation [57]. Taking all this together, we can conclude that while friction plays an important role in joint motion, it is not the sole indicator of articular cartilage wear or the onset of osteoarthritis. Further details on this topic are discussed in Chapter 4.

1.2.3. Collagen Structure

The fibrillar structure of collagen is presumed to be well known and exhibits a varying orientation through the tissue. At the articular surface, known as the superficial zone (SZ), collagen fibrils lie tangent to the surface, while deep zone (DZ) collagen fibrils are oriented perpendicular to the subchondral bone [4,28,58-60]. These two zones of highly aligned collagen are separated by a transition zone known as the middle zone (MZ). Although this depth-dependent structure is believed to be well understood, the specific functions resulting from the inhomogeneous collagen alignment have not been entirely elucidated. Additionally, the exact dispersion of collagen fibrils around each preferential axis has not been sufficiently quantified due to the difficulty of imaging collagen II fibrils.

Finite element models implementing depth-dependent material properties with an isotropic fibril distribution for the articular cartilage were able to replicate experimental contact pressures
and indicated reasonable agreement between stress within the tissue and collagen orientation [61]. However, this material model has not produced accurate depth-dependent strain results within the tissue. We hypothesize that developing an accurate depth-dependent strain material model requires explicitly modeling the precise collagen fibril orientation throughout the tissue. Therefore, in order to better understand the relationship between collagen structure and cartilage function, we seek to develop a cartilage material model which accurately models the depth-dependent strain of articular cartilage. The first study to address this aim is included in this dissertation and investigates the influence of different fibril models on strain distribution and strain magnitude (Chapter 5).

1.3 Significance and Specific Aims

Osteoarthritis is a painful and debilitating joint disease affecting over 500 million people globally [6]. Typically, articular cartilage can withstand millions of loading cycles with minimal damage. However, because the tissue does not have an apparent self-repair mechanism, once wear is initiated the articular cartilage will continue to degenerate until significant loss of tissue reveals the underlying bone. The primary function of articular cartilage is to distribute stresses across the joint; arthritic tissue cannot support this primary function. In seeking to alleviate patient pain from osteoarthritis, two overarching questions arise: (1) How can we better treat patients with severe osteoarthritis for whom joint arthroplasty is not an option? (2) What mechanical factors initiate articular cartilage degeneration?

In regard to the first question, “How can we better treat patients with severe osteoarthritis for whom joint arthroplasty is not an option?”, we must first look at current treatments and ask ourselves what could be improved. As briefly described above, the gold standard treatment for late-stage osteoarthritis is joint arthroplasty, or artificial joint replacement. This type of surgical intervention generally results in effective clinical outcomes, especially for knee, hip, and shoulder
replacements [62-66]. Though this is the case, arthroplasties are typically considered a last-resort treatment and are not always the appropriate solution. A major limitation of an artificial joint replacement is the lifespan of the implant, which may not exceed the life expectancy of a patient. Studies have reported good clinical outcomes after 10-15 years [62,67-69]. However, while idiopathic osteoarthritis typically affects adults over the age of 60, post-traumatic osteoarthritis, which begins with an initial insult or injury to the joint, can affect people of all ages [8]. Ten to 15 years with an artificial joint prior to a necessary revision is not enough time for a young patient. Furthermore, artificial joint implants are typically intended to treat full-joint osteoarthritis and younger patients are more likely to experience osteoarthritis in isolated areas rather than across the full-joint. Patients who are not indicated for an artificial joint replacement because of their age or location and degree of disease progression may be encouraged to wait and continue to live with the pain.

The need exists for a treatment which can be implemented earlier in the progression of the disease and can be a suitable alternative to, or way of delaying, joint arthroplasty, especially for younger patients for whom arthroplasty is not an option. A promising biological surgical intervention that has emerged over the last two decades involves the use of osteochondral allografts (OCAs). Healthy articular cartilage and the underlying bone recovered from qualified donor tissue can be preserved for several weeks in tissue banks before being transplanted to replace arthritic focal defects or even entire articular surfaces [13-15]. This technique preserves more of the native tissue relative to joint arthroplasty and the use of OCAs to treat osteoarthritis has shown good clinical outcomes [16-19]. Previous work investigated a novel method of expanding the use of OCAs by adapting the curvature of the femoral trochlea to match the curvature and replace the articular surface of the carpometacarpal joint in the thumb [1,2]. The following dissertation
expands on that work. The first two specific aims include the clinically translational portion of this dissertation by first, investigating the feasibility of adapting the technique of conforming OCAs to be used in the patella and second, developing a custom surgical forceps tool to bend and surgically implant OCAs in the carpometacarpal joint to replace an arthritic trapezium.

In regard to the second overarching question this dissertation seeks to address, “What mechanical factors initiate articular cartilage degeneration?”, we must understand the mechanical influences on tissue response. The etiology of osteoarthritis, though somewhat unclear, is generally considered to be multifactorial, with biochemical and mechanical contributions [70-72]. While mechanical loading, such as stretch, shear stress, or osmotic pressure, can trigger chemical responses or cell signaling cascades [73-75], tissue loading will also have purely mechanical effects. The objective of the studies presented here are to investigate cartilage wear initiation from a mechanical perspective. Previous work has shown that cartilage fails in fatigue in the form of delamination between the superficial and middle zones [51,53,76]. During physiologic joint articulation, cartilage experiences two main types of repeated loading that could cause fatigue failure: (1) reciprocating frictional forces acting on the articular surface and (2) reciprocating compressive loading of the tissue as the contact area migrates across the surface during sliding motion. Previous work has discussed various mechanisms of cartilage wear in isolation (i.e. studies have included compressive [54,76,77], tensile [78,79], or shear fatigue [80]), but none have directly compared multiple loading mechanisms. The third aim of the present work seeks to determine the primary mechanical factor in articular cartilage wear and degeneration.

The delamination observed in articular cartilage after experimentally-induced wear [51,53,76], as well as in histological cross-sections of human arthritic cartilage [51], occurs between the superficial and middle zones. The fibrillar structure of collagen is presumed to be well
known and exhibits a varying orientation through the tissue. As discussed previously, at the articular surface, or superficial zone, collagen fibrils lie tangent to the surface. Directly beneath this highly aligned superficial zone is a transition zone, known as the middle zone, where the collagen fibrils appear to be randomly oriented. It is at this interface between the superficial and middle zones that delamination wear is observed, suggesting that the fibril orientation may play a significant role in how and where cartilage fatigue failure occurs. The specific functions resulting from this inhomogeneous collagen alignment, relating to cartilage wear, stress distribution, or strain distribution throughout the tissue, have not been entirely elucidated. Furthermore, collagen II in cartilage can be imaged on a broad level to determine primary alignment using imaging modalities such as polarized light microscopy or scanning electron microscopy [51,81], but because of the small ~20 nm diameter size of the collagen fibrils [82], imaging alone has not been able to conclusively quantify fibril dispersion through the depth of the tissue. One group used X-ray diffraction to quantify fibril dispersion at three different depths through the cartilage [58] and another group has used small angle X-ray scattering to quantify collagen fibril dispersion [83], however comprehensive characterization of the fibril dispersion throughout the full thickness has not been reported. The final aim of this dissertation examines how different fibril distribution models influence the depth-dependent strain responses. This aim is intended to be the first of a series of studies which (1) seeks to develop a strain-validated depth-dependent cartilage material model and (2) examines whether computational modeling can be used as another tool to elucidate the exact fibril dispersion through the thickness of articular cartilage by using fibril dispersion within the model to replicate experimental results. Developing a more accurate material model of articular cartilage with an accurate collagen fibril architecture would strengthen each of the previously discussed studies. With a strain-validated cartilage model, chondrocyte viability could
be predicted in osteochondral allografts under sustained bending. It also would be possible to use a cartilage sliding model to examine collagen fatigue failure in relation to depth-dependent tissue deformation.

Specific Aim 1: Test the hypothesis that transplanted bendable patellar allografts improve patellofemoral joint congruence compared to standard allografts. Use finite element models to develop bendable patellar osteochondral allografts (OCAs), whose articular surface curvature can adapt to the native femur curvature. Examine whether bendable OCAs increase the patellofemoral contact area and congruence, suggesting improved clinical outcomes relative to OCAs which are not adapted to match the native femur surface curvature.

Specific Aim 2: Develop a surgical tool to be used during carpometacarpal joint allograft bending and transplantation. Design, manufacture, and patent a forceps-like surgical tool to assist in the bending and transplantation of an osteochondral allograft to replace an arthritic trapezium. Though osteoarthritis of the hand is relatively common, the current standard of care to treat carpometacarpal osteoarthritis is ligament reconstruction and tendon interposition, which reduces pain, but does not restore full joint function, strength, and mobility. The recent development of bendable osteochondral allografts [2] provides the potential to better treat osteoarthritis in joints, such as the carpometacarpal joint, whose current standard treatments are unsatisfactory. Essential to a successful surgery are the surgical tools used to carry out the surgery. In attempting to replace the trapezium with a bendable osteochondral allograft during cadaver surgery, it was determined that existing standard surgical tools and forceps could not properly bend and secure the allograft.
Therefore, there exists a need to design and manufacture a new surgical tool, specifically intended for bendable osteochondral allograft surgery of the trapezium.

Specific Aim 3: Test the hypothesis that cartilage wear is due to fatigue failure from reciprocating compressive forces and not fatigue failure from reciprocating frictional forces. Perform friction tests between immature bovine cartilage and glass with one group experiencing only reciprocating frictional forces and the other experiencing both reciprocating frictional forces as well as reciprocating compressive forces. Examine both groups for surface damage and subsurface structural changes to determine which loading mechanism induces consistent fatigue failure. A more thorough understanding of the underlying mechanism of cartilage fatigue failure could help us better direct clinical treatment efforts for mitigating osteoarthritis progression.

Specific Aim 4: Investigate the functional role of collagen fibril orientation across the articular layer thickness. Develop finite element models of bovine articular layers that reflect depth-dependent collagen fibril orientation. Compare discrete fibril models to continuous fibril distributions and examine the differences in Lagrange strain, contact pressure, and contact area between each model. Use this initial study to determine best practices for collagen modeling in articular cartilage finite element analyses.

1.4 Organization

The following chapters discuss four studies which were carried out to address the above specific aims and the overarching goal for this dissertation of improving osteoarthritis care and reducing patient pain.
The first two chapters following the current one address the clinically translational portion of the dissertation, which focuses on the implementation of conforming, or bendable, osteochondral allografts as a novel surgical technique for osteoarthritis. Chapter 2 details a finite element analysis carried out to investigate the feasibility of restoring patellofemoral joint congruence by using bendable osteochondral allografts to replace an arthritic patella. Chapter 3 details the iterative design and manufacturing process for a surgical tool compatible with small bendable osteochondral allografts created for the carpometacarpal joint in the thumb.

The next two chapters, Chapter 4 and Chapter 5, make up the basic science portion of this dissertation, which seeks to provide context and further understanding for the development of osteoarthritis. Chapter 4 discusses an articular cartilage wear study comparing compressive fatigue and frictional fatigue to elucidate the mechanisms of cartilage damage initiation. Finally, Chapter 5 discusses the first of what is intended to be a series of studies investigating collagen fibril orientation within articular cartilage. The chapter specifically focuses on how varying types of fibril distribution models affect mechanical responses.

The final chapter of this dissertation serves as a conclusion to summarize the outcomes of the discussed studies and what significance they have in the context of the field of cartilage mechanics and osteoarthritis. Future work and recommended next steps will be outlined as well.
Chapter 2: Bendable osteochondral allografts for patellar resurfacing: a finite element analysis of congruence

2.1 Introduction

Osteoarthritis (OA) is a debilitating degenerative disease affecting nearly 52 million people in the United States[6]. This disease often progresses from an initial insult or injury to the articular cartilage to whole-joint degradation, which significantly compromises the main function of cartilage as a load bearing material, leading to pain and limiting activities of daily living. Though cartilage degeneration is occasionally limited to small focal areas within articular layers (~1 cm²), osteoarthritis generally becomes symptomatic when degradation has spread over much greater surface areas (e.g., > 5 cm² or > 25% of the articular layer) [84,85]. Prior to surgical intervention, non-invasive treatments are typically recommended, some of which include physical therapy, use of an assistive device such as a walker, or simply avoiding activities that exacerbate the pain, significantly impacting the typical activities of daily living of a patient [65]. Artificial joint replacements are often considered the gold standard treatment by surgeons, generally resulting in effective clinical outcomes, especially for the knee, hip, and shoulder [65]. Studies have reported good clinical outcomes after 10 – 15 years [67-69]. Though this is the case, arthroplasties are typically considered a last-resort treatment and are not always the appropriate solution.

While artificial joint replacement, or joint arthroplasty, has proven effective for treatment of end-stage osteoarthritis, it is limited by implant lifespan, associated postoperative activities, and overall patient satisfaction level [65,86]. This issue is of particular concern for younger patients afflicted with post-traumatic osteoarthritis (PTOA) [8,87,88]. Post-traumatic osteoarthritis refers to osteoarthritis initiated by a traumatic injury or impact to the joint. Injuries resulting in post-traumatic osteoarthritis may include, for example, intraarticular fractures, meniscal or ligament
tears, or joint dislocation [8]. Approximately 12% of the individuals living with osteoarthritis in
the hip, knee, or ankle are affected by post-traumatic osteoarthritis [89]. While idiopathic
osteoarthritis typically affects adults over the age of 60, post-traumatic osteoarthritis affects adults
of all ages [8]. Ten to 15 years with an artificial joint prior to a necessary revision is not enough
time for a young patient. Patients who are not indicated for an artificial joint replacement because
of their age may be encouraged to wait and continue to live with the pain. Therefore, there exists
a need for a post-traumatic osteoarthritis treatment method that has the potential to delay, or even
eliminate the need for, artificial joint replacement. In the knee, one such solution may include a
partial arthroplasty, such as a patellofemoral arthroplasty, where only the patella and femoral
trochlear articular surfaces are replaced. This type of intervention, however, has resulted in mixed
clinical performance [24,65,86,90,91] and requires resurfacing two articular surfaces even if only
one shows signs of osteoarthritis. Biologic joint restoration strategies that are less invasive and can
be implemented earlier in the course of disease are highly desirable.

A promising biological joint restoration technique has emerged over the last two decades,
involving transplantation of fresh osteochondral allografts (OCAs) recovered from qualified
human organ and tissue donors and preserved for up to six weeks in tissue banks. Osteochondral
allograft transplants can be used to fill large defects, or even to replace entire articular surfaces
[13,21,92]. Osteochondral allograft transplantation has demonstrated favorable outcomes [93],
particularly in the knee [16-18,94], but also in the ankle [20] and in the shoulder [95,96]. Typically,
OCA transplantation has primarily been considered a salvaging procedure [97], with only a few
tens of thousands surgeries performed yearly in the U.S., although some investigators have
advocated it as a standard treatment modality [98].
One of the greatest obstacles to widespread use of osteochondral allograft transplantation is the difficulty in matching the articular cartilage surface curvature of a donor osteochondral allograft with the recipient’s joint anatomy [22]. We propose a novel patella resurfacing technique to overcome this limitation by using an innovative bendable osteochondral allograft method (Figure 2.1) [2]. Allograft bending can be accomplished by machining grooves in the bony side of the osteochondral allograft to reveal the subchondral surface of the cartilage [1]. The removal of trabecular and subchondral bone gives bending flexibility to the cartilage; this results in articular surface curvature changes as the remaining bone struts are brought together (Figure 2.1) or pushed apart. The ability to safely bend osteochondral allograft cartilage to match the curvature of the host site provides more flexibility with respect to donor anatomy and presents the potential to better replace entire articular surfaces without loss of joint congruence, thereby eliminating discontinuities of the articular layer between allograft and host tissue.

Our work in this study focuses on the patella as a testbed for the proposed technology, based on it propensity for secondary osteoarthritis [26,99,100] and the relative lack of consistent success for patellofemoral arthroplasties [65,86,90,91]. The anatomy of the patella is particularly well-suited for testing the proposed technology, since an osteochondral allograft that contains the entire patellar articular layer can be created using a single planar cut [15,22]. Furthermore, the relatively thin and flat bony substrate is easily accessible for machining.

Figure 2.1: As described previously [2], cutting grooves in the bony substrate of this saddle-shaped osteochondral allograft, harvested from a human knee femoral trochlea, makes it possible to bend the articular layer and increase its convex curvature, while mostly maintaining its concave curvature.
We hypothesize that transplanted osteochondral allografts that conform better to the opposing articular surface result in better clinical outcomes than allografts that have only been size-matched for the host site. Subsequently, we hypothesize that bendable osteochondral allografts may provide better surface curvature matching for patella transplants such that patellofemoral contact areas are maintained at native levels. In this study, we use finite element analyses of the patellofemoral joint to investigate whether better conformity may be achieved with allograft bending flexibility.

2.2 Methods

Computational patellofemoral joint (PFJ) models were constructed from previously reported cadaveric human knee studies [101] and analyzed in an open-source finite element software (FEBio, febio.org; [102]) using soft tissue material properties and muscle forces reported in [61]. Experimental tibial kinematics for three of these knee models (Figure 2.2A) were used to articulate the knees at 15 degrees/s through a cycle starting at 60 degrees of flexion, extending to 40 degrees, then returning and ending at 70 degrees (Figure 2.2B-C).

The patellofemoral contact area was calculated from the models through the flexion cycle and used to quantify changes in PFJ congruence. Osteochondral allograft models (Figure 2.2D) were constructed as described in the next section and a size-matched subset of these osteochondral allografts was used to replace the patella in each of the three PFJ models to investigate congruence across the same range of knee flexion. Grooved osteochondral allografts were bent to conform to the opposing femoral trochlea of the host knee at 60 degrees of flexion (bent OCA, or BOCA, group). This bent configuration was maintained for the subsequent analysis of joint congruence over the range of knee flexion by assuming that grooves were filled with bone cement that had sufficiently stiffened.
Figure 2.2: (A) Three PFJ models were created from human cadaver knees as described in [101] and finite element models were constructed as reported by [61]. Three active contractile forces and two linear springs (depicted as thin blue lines) represented the quadriceps muscles and the patellar tendon, respectively. In this study, these PFJs were articulated from (B) 60 degrees of flexion to 40 degrees, then back from (C) 40 degrees to 70 degrees. (D) Fourteen OCA patellae were created from imaging of knee joints from cadavers and volunteers as reported in [101] and [84]. Articular surfaces seen here.
2.2.1. Three-Dimensional Solid Models

Three-dimensional geometric data of three human cadaveric knee joints (age 61-70, 1 female, 2 male; Figure 2.2A) and point cloud data for eleven additional patellae of healthy human knees (age 21-57, 5 female, 6 male; Figure 2.2D) were acquired previously using stereophotogrammetry and magnetic resonance imaging [84,101]. The usage of prior MRI scans of human volunteers was approved by Columbia University’s Institutional Review Board (protocol #AAAS1887). Smooth spline surfaces were fitted to point cloud data of the articular and the subchondral cartilage surfaces using a computer-aided design software (SOLIDWORKS 2019, Dassault Systèmes, solidworks.com, Figure 2.3A,B), then cartilage and subchondral bone smooth surfaces were combined to create a solid cartilage model for each osteochondral allograft (Figure 2.3C). The subchondral surface was extruded along its average normal direction to create the planar-ended bony substrate of the osteochondral allograft with minimum thickness of 0.3 mm relative to the cartilage layer (FreeCAD, freecadweb.org, Figure 2.3D). Using Boolean operations, two 2 mm-wide grooves were created in the bony substrate along parallel sagittal planes, resulting in three bone struts (Figure 2.3E). Grooves ran along the length of the patella median ridge [103] and were placed on either side of the ridge, subdividing both the medial and lateral articular facets into two equal halves. The grooves were filled with a material representing bone cement, whose properties were selected to be negligibly stiff during osteochondral allograft bending, and rigid either when the cement was assumed to have set or when modeling non-bending osteochondral allografts. All domains were meshed as shown in Figure 2.3F and detailed in the next section.
2.2.2. Finite Element Models

Finite element models of the patellofemoral joints from our previous study were adapted for this investigation ([61]; Figure 2.2A). Patellar osteochondral allograft models were meshed (CUBIT 13.2, Sandia National Laboratories, cubit.sandia.gov) as shown in Figure 2.2D and Figure 2.3F. The patella bone, bone cement, and articular cartilage layers were meshed with eight-node hexahedral elements. Articular cartilage meshes included five layers through the thickness, which were biased to be thinner toward the articular and subchondral surfaces. A mesh convergence analysis was performed on the cartilage layers and an approximate element size of 0.75 mm across the articular surface was determined to be sufficient for producing converged contact area results (less than 5% change in contact area between the last two consecutively refined meshes; Figure 2.2D). All finite element models were analyzed using open-source software (FEBioStudio 1.4.0 and FEBio 3.5.1, febio.org). Cartilage and patella tendon material models and properties, muscle forces, and articular contact conditions were presented in [61].
Three basic sets of analyses were completed in this study, each producing contact area results as a function of flexion angle: (1) native patellofemoral joint models (PFJ group, three models, native patellae; Figure 2.2A-C), (2) unbent osteochondral allograft models (OCA group, multiple size-matched osteochondral allografts substituted for each of the three native patellae in corresponding patellofemoral joint models; Figure 2.2D and Figure 2.4), and (3) bent osteochondral allograft models (BOCA group, same osteochondral allografts from (2) bent to conform with the native femur, Figure 2.5). In addition, a preliminary study demonstrated that the patellofemoral contact area increased when an osteochondral allograft patella was shifted distally toward the tibia relative to the position of the native patella. After conducting a parametric study that investigated a distal shift between 0 mm and 9 mm, it was found that a 6 mm distal shift (Figure 2.6) represented the smallest distal shift with the greatest contact area through the flexion cycle. This 6 mm distal shift was added to our study design, resulting in two additional sets of analyses: (4) shifted unbent osteochondral allograft models (S-OCA), and (5) shifted bent osteochondral allograft models (S-BOCA).
2.2.2.1. Native Joint (PFJ) Models

The three native patellofemoral joint models (Figure 2.2A) were used as the standard of comparison for allograft models. As described in the original human cadaver knee study [101], three muscle groups represented the quadriceps, with forces through knee flexion and extension of 89 N on the vastus medialis obliquus (VMO), 267 N on a combined group comprising the rectus femoris, vastus intermedius and vastus medialis longus (RF), and 178 N on the vastus lateralis (VL). After an initial ramp-up, these muscle forces remained unchanged throughout the range of knee flexion and extension. Insertion points of the patella tendon and quadriceps muscle groups were obtained precisely from three-dimensional geometric measurements on the cadaveric knee joints that underlie these models [101], independently of the coarse acquisition of patellar and tibial bone geometries. Therefore, while these insertion points may appear to be floating in space in these models (e.g., Figure 2.2A-C), in reality they represent the true locations of these soft tissue insertions on the patella and tibia. Patellofemoral contact area was measured through the flexion cycle and plotted as a function of flexion angle.

2.2.2.2. Unbent Osteochondral Allograft (OCA) Models

To create the unbent OCA models, we started with one of the three native patellofemoral joint models (Figure 2.2A) and replaced the native patella with one of the thirteen non-native patellae as an osteochondral allograft (Figure 2.2D and Figure 2.4). Patellae whose articular cartilage surface areas fell within 20% of any native patellae surface areas were considered suitable allografts for those native joints. Indeed, preliminary studies showed that allografts that were too small could never produce native contact area values, even after bending. On the other hand, allografts that were too large could crowd the joint space, potentially causing detrimental effects clinically and aesthetically. For each PFJ-OCA pairing, surface registration was performed
between the articular surfaces of the patellar allograft and native patella to produce an optimal alignment using an iterative closest point algorithm with translation and rotation tolerances of 0.001 mm and 0.005 degrees respectively (pcregistericp, MATLAB, mathworks.com; [104,105]). Quadriceps and patella tendon insertion points, and tibial kinematics remained unchanged in these analyses. Bone struts and bone cement were modeled together as a single rigid body.

### 2.2.2.3. Bent Osteochondral Allograft (BOCA) Models

These models were created from the corresponding unbent OCA models. To produce bent OCAs, each bone strut was modeled as a distinct rigid body and bone cement was modeled as a neo-Hookean material with an adjustable Young’s modulus, using a multigeneration framework [106]. Young’s modulus of the cement was initially set to 1 GPa, Poisson’s ratio was set to zero, and the muscle forces were increased to 10% of the values indicated previously, which was sufficient to stabilize the patella at 60 degrees of flexion (Figure 2.5A). The bone cement modulus was then reduced to 1 kPa to simulate malleable cement, while a pressure was prescribed on each of the two outer bone struts to allow the osteochondral allograft articular surface to conform to the opposing femoral trochlea (Figure 2.5B). The amount of pressure applied was adjusted for each bone strut (2.91 ± 1.41 MPa) so that the resulting force applied to each bone strut equaled the patellofemoral contact force in the corresponding native PFJ model at 60 degrees (422, 427, or 428 N). During bending, rotation of the central bone strut was fixed, to promote bending of the cartilage layer without rotation of the patella.

![Figure 2.5](image_url)
The bone cement was then ‘hardened’ to 1 GPa in this bent configuration and the pressure on the bone struts was removed, producing the desired bent osteochondral allograft geometry (exploded view in Figure 2.5C). The bone cement and bone struts were merged into a single rigid body and the analysis of this bent OCA (BOCA) was performed in the same manner as the unbent OCA models.

2.2.2.4. **Shifted Osteochondral Allograft (S-OCA and S-BOCA) Models**

Shifted unbent osteochondral allograft (S-OCA) models were created from the unbent osteochondral allograft models described previously. After replacing the native patellae with a patellar allograft, the osteochondral allograft was translated distally toward the tibia by 6 mm (Figure 2.6). The shifted-bent osteochondral allografts were created from the S-OCA models. With the osteochondral allograft patella in the 6 mm distally shifted position, a pressure was applied to the outer two bone struts as described above to bend the articular cartilage in this new position. With the shifted allograft in the bent configuration, the bone struts and bone cement were once again merged into a single rigid body creating the shifted and bent osteochondral allograft (S-}
BOCA) model. Quadriceps and patella tendon insertion points, and tibial kinematics remained unchanged in these analyses.

2.2.3. Statistical Analysis

An analysis of variance (ANOVA) with repeated measures was used to compare contact areas of OCA, BOCA, S-OCA and S-BOCA groups at 40, 45, 60, and 70 degrees (NCSS Statistical Software 2019, ncss.com) with type I error $\alpha$ set to 0.05. Normality was confirmed using a Shapiro-Wilk normality test with type I error $\alpha$ set to 0.05 (NCSS Statistical Software 2019, ncss.com). When significance was detected ($p \leq 0.05$), post-hoc testing of the means was performed using the Tukey-Kramer correction. One-way ANOVA tests were performed to compare the contact area in OCA, BOCA, S-OCA and S-BOCA models to the contact area in the native PFJs at the four flexion angles and the average over all flexion angles. In both cases, post-hoc power analyses were performed to determine type II error $\beta$ (PASS Sample Size Software 2019, ncss.com).

2.3 Results

Articular cartilage surface areas for all 14 patellae ranged from $795 - 1418 \text{ mm}^2$ with an average value of $1072 \pm 211 \text{ mm}^2$. The three native patellae had surface areas of $949 \text{ mm}^2$, $1103 \text{ mm}^2$, and $1262 \text{ mm}^2$ (Table 2.1). Size-matching each of the eleven OCA patellae and each of the three native PFJ patellae to the three native patellae resulted in 22 possible PFJ-OCA pairings (Table 2.1, *PFJ matches*). Surface registrations to position the patellar osteochondral allografts required an average of $122 \pm 68$ iterations, resulting in a root mean square error of $0.792 \pm 0.141 \text{ mm}$ between the patellar OCA and native patella articular surface point clouds.
Table 2.1: PFJ and OCA patellae (Patella ID), respective articular surface areas, possible size-matched pairings (PFJ matches), and flexion angles for which the PFJ-OCA pairing converged. ALL indicates the model converged at 60, 45, 40, and 70 degrees. NONE indicates the model did not converge at any of the listed flexion angles. N/A indicates BOCA models not analyzed because the respective OCA did not converge at all flexion angles. A set of analyses was considered “complete” when the analysis converged at all flexion angles for all models, as indicated by an asterisk * in column 3.

<table>
<thead>
<tr>
<th>Patella ID</th>
<th>Patellar surface area (mm²)</th>
<th>PFJ matches</th>
<th>OCA</th>
<th>BOCA</th>
<th>S-OCA</th>
<th>S-BOCA</th>
<th>Flexion angles converged (60, 45, 40, 70 degrees)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFJ-1</td>
<td>949</td>
<td>PFJ-2</td>
<td>60</td>
<td>N/A</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
</tr>
<tr>
<td>PFJ-2</td>
<td>1103</td>
<td>PFJ-1*</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
</tr>
<tr>
<td>PFJ-3</td>
<td>1262</td>
<td>PFJ-2</td>
<td>ALL</td>
<td>60, 45</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
</tr>
<tr>
<td>OCA-01</td>
<td>903</td>
<td>PFJ-1*</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
</tr>
<tr>
<td>OCA-02</td>
<td>795</td>
<td>PFJ-1</td>
<td>ALL</td>
<td>60, 45, 40</td>
<td>NONE</td>
<td>NONE</td>
<td>ALL</td>
</tr>
<tr>
<td>OCA-03</td>
<td>1326</td>
<td>PFJ-3*</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
</tr>
<tr>
<td>OCA-04</td>
<td>1384</td>
<td>PFJ-3</td>
<td>ALL</td>
<td>60, 45</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
</tr>
<tr>
<td>OCA-05</td>
<td>998</td>
<td>PFJ-1</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
</tr>
<tr>
<td>OCA-06</td>
<td>1121</td>
<td>PFJ-1*</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
</tr>
<tr>
<td>OCA-07</td>
<td>1418</td>
<td>PFJ-3*</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
</tr>
<tr>
<td>OCA-08</td>
<td>802</td>
<td>PFJ-1</td>
<td>ALL</td>
<td>ALL</td>
<td>60, 45, 40</td>
<td>60, 45, 40</td>
<td>60, 45, 40</td>
</tr>
<tr>
<td>OCA-09</td>
<td>1003</td>
<td>PFJ-1</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>60, 45, 40</td>
</tr>
<tr>
<td>OCA-10</td>
<td>1099</td>
<td>PFJ-1*</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
</tr>
<tr>
<td>OCA-11</td>
<td>843</td>
<td>PFJ-1*</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
<td>ALL</td>
</tr>
<tr>
<td>Total converged at all angles</td>
<td>20</td>
<td>16</td>
<td>20</td>
<td>15</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
and 70 degrees, as well as on average through the flexion cycle \( (p > 0.05) \). Normality could not be confirmed for the small number of samples in the native PFJ group.

Representative contact area plots for a PFJ-OCA pairing from each of the three recipient knees are shown in Figure 2.7. For all groups, the average contact area increased from 40 to 70 degrees, with the exception of the S-OCA models, where the average contact area decreased slightly from 60 to 70 degrees (Table 2.2). No treatment group exhibited significantly different contact areas from the native joints \( (p > 0.05) \) for all angles, Figure 2.8, Table 2.2); however, a post-hoc power analysis showed that this finding had low levels of confidence \( (\beta \) ranging from 0.68 to 0.95 for the various treatments). On average, the S-BOCA group resulted in a significantly greater patellofemoral contact area than BOCA, OCA, or S-OCA groups \( (p < 0.02, \) Figure 2.8).

Table 2.2: Contact area (mean ± standard deviation) at each flexion angle for PFJ and OCA models.

<table>
<thead>
<tr>
<th>Group</th>
<th>( n )</th>
<th>40 degrees</th>
<th>45 degrees</th>
<th>60 degrees</th>
<th>70 degrees</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Native PFJ</td>
<td>3</td>
<td>267 ± 64</td>
<td>306 ± 58</td>
<td>403 ± 52</td>
<td>453 ± 49</td>
<td>356 ± 55</td>
</tr>
<tr>
<td>OCA</td>
<td>12</td>
<td>259 ± 45</td>
<td>289 ± 40</td>
<td>358 ± 44</td>
<td>385 ± 49</td>
<td>323 ± 43</td>
</tr>
<tr>
<td>BOCA</td>
<td>12</td>
<td>263 ± 45</td>
<td>295 ± 40</td>
<td>370 ± 52</td>
<td>398 ± 53</td>
<td>332 ± 45</td>
</tr>
<tr>
<td>S-OCA</td>
<td>12</td>
<td>298 ± 43</td>
<td>329 ± 41</td>
<td>390 ± 47</td>
<td>387 ± 72</td>
<td>354 ± 45</td>
</tr>
<tr>
<td>S-BOCA</td>
<td>12</td>
<td>314 ± 44</td>
<td>347 ± 38</td>
<td>412 ± 48</td>
<td>407 ± 76</td>
<td>373 ± 45</td>
</tr>
</tbody>
</table>
Although the BOCA mean contact areas at each flexion angle were slightly higher than the OCA mean values (Table 2.2), this difference was not statistically significant ($p > 0.55$ for all angles, $\beta < 0.02$, Figure 2.8). Contact area in S-BOCA models was significantly greater than in the BOCA models between 40 and 60 degrees of flexion ($p < 0.001$), but not at 70 degrees ($p = 0.94$, Table 2.2). S-BOCA patellofemoral contact area was significantly greater than S-OCA models at 40 and 45 degrees ($p < 0.008$), but not at 60 and 70 degrees ($p > 0.08$, Table 2.2). At smaller flexion angles, the S-OCA contact area was significantly greater than the BOCA models ($p < 0.0001$ at 40 and 45 degrees, $p > 0.1$ at higher flexion angles, Table 2.2).

### 2.4 Discussion

The objective of this study was to investigate the hypothesis that a bendable patellar osteochondral allograft could improve surface curvature matching with the native femoral trochlea of a recipient knee based on patellofemoral joint contact areas at various flexion angles. The longer-term goal of this computational investigation is to explore the clinical potential of osteochondral allograft bending to improve and expand the capabilities of this biological joint restoration technique. The current investigation did not address the clinical feasibility of this strategy, but rather focused on the analysis of the underlying biomechanical hypothesis that joint
congruence may be improved when an osteochondral allograft is allowed to bend. Bending was achieved by cutting grooves in the bony substrate of a standard entire-surface patella shell osteochondral allograft and applying pressure on the allograft bone to alter the contour of the softer articular layer (Figure 2.5).

One of the primary outcomes of the current study was the finding that unbent, size-matched patellar allografts produced contact areas that were not statistically different from those of the native patellae for the three patellofemoral joints studied (Figure 2.7 and Figure 2.8). This result suggests that two-dimensional size-matching of patellar allografts may be sufficient for the purpose of matching surface contours for functional joint congruence. Indeed, clinical studies have recently advocated for the use of unbent entire-surface patellar shell osteochondral allografts, size-matched by radiographic imaging, as an effective biologic joint restoration strategy [15,22]. The findings of the current study provide support for this strategy from the perspective of maintaining reasonably similar joint contact mechanics. Nevertheless, clinicians may be reluctant to exclusively rely on unbent allografts as a standard clinical practice for patellar osteochondral allograft transplantation because of the risk of mismatch in a particular donor-recipient pair. Therefore, providing bendable osteochondral allografts may induce greater confidence among surgeons that the allograft may be suitably matched with a specific patient. In that context, another primary outcome of the current study was our finding that bendable patellar allografts produced equally good congruence as native joints, as assessed by contact areas (Figure 2.7 and Figure 2.8). One previous study quantitatively defines the concept of diarthrodial joint congruence using principal curvatures and assuming small deformations of opposing surfaces [107]. This classical approach was based on Hertz contact theory [108], which proposes measures of congruence that correlate with the Hertz contact area under a given load. However, since the patellofemoral joint
articular layers underwent large deformations in the current study, contact area was deemed a more appropriate measure of joint congruence here.

For OCAs and BOCAs, the finding that contact areas were comparable to those of native joints was somewhat compromised by the low statistical power in that analysis ($0.18 < 1 - \beta < 0.32$) since comparisons were performed between three native joints and twelve osteochondral allograft transplant simulations. Stronger statistical results were achieved when comparing the various osteochondral allograft treatment groups (OCA, BOCA, S-OCA and S-BOCA) since the statistical design involved twelve samples in each group, with repeated measures ($1 - \beta > 0.98$). In that comparison, OCA and BOCA contact areas were also not significantly different from each other, but this finding had much greater statistical power. Thus, we conclude from the present analysis that there is neither biomechanical gain nor loss when using unbent versus bendable entire-surface patellar shell osteochondral allografts. This conclusion does not account for clinical factors that might affect the risks or benefits of either approach. It is purely based on computational results, albeit using realistic models of the human knee joint. Nevertheless, as argued above, surgeons may prefer having an option to bend an osteochondral allograft to improve capabilities of matching the complex anatomy of a patient’s patellofemoral joint with donor allografts. From that perspective, the biomechanical results of this study show that there would be no downside to using bendable osteochondral allografts in relation to functional joint congruence.

In our earlier efforts to properly place patellar osteochondral allografts in the native knee computational models, prior to using surface registration to optimize this placement, we discovered serendipitously that a distal shift in the allograft placement could increase the contact area. Thus, we added two more treatment groups (S-OCA and S-BOCA) to our analysis to explore the implications of distally shifting the patellar allograft. Results showed that this distal shift
produced significantly larger contact areas in S-BOCA compared to the other groups (Figure 2.8), suggesting that this method for increasing patellofemoral joint contact area is a consideration for surgeons when technically feasible and desired. This conclusion is again based exclusively on the results of our contact mechanics analysis which does not account for any potentially compromising clinical and surgical factors. It should be noted that distally shifting a patellar allograft does not necessarily reproduce the detrimental iatrogenic condition known as patella baja or patella infera [109-114], since the process of shifting the allograft distally on the existing patellar substrate does not shorten the patellar tendon. Nevertheless, it remains unclear if there may be a clinical or surgical downside to distally shifting a patellar allograft. In future cadaver studies that examine the various treatment groups presented here, we can explore the related variables.

In principle, we could have examined other metrics such as cartilage strain or fluid pressure. However, we have chosen to forego such examinations in the current study due to the speculative nature of these results in relation to how they may affect chondrocyte viability or mechanotransduction. These responses cannot be resolved from computational studies, nor from cadaver studies. In vitro studies on live cartilage explants, however, may provide some relevant insights. Separate studies following this computational work have investigated chondrocyte responses to sustained bending of osteochondral allografts, reporting maintenance of chondrocyte viability during machining and sustained bending for up to two-weeks post-machining [115]. Additionally, an animal study has been recently initiated to further investigate surgical viability of this procedure.

Our relatively simple PFJ models excluded many of the soft tissues that help stabilize the knee, including muscle tissue, joint capsule and embedded ligaments, fat pads, and skin. Consequently, as the knee extended, the patella encountered fewer realistic constraints to keep it
tracking along the femoral trochlea. This limitation required us to maintain the flexion angle at 40 degrees or greater within the computational model. This limitation likely contributed to the lack of convergence of finite element analyses for every PFJ-OCA pair and every flexion angle (Table 2.1). Fortunately, we were able to obtain complete results for twelve PFJ-OCA pairs, giving us sufficient statistical power to produce meaningful conclusions for this biomechanical study.

Alternative groove patterns were preliminarily investigated prior to the study design discussed above. These other patterns included 1) a two-by-two groove pattern, with equally spaced medial-lateral proximal-distal grooves, and 2) two equally spaced proximal-distal grooves. Upon investigating these alternative groove patterns, it was determined that the pattern employed in this study (Figure 2.3E,F) provided a sufficient amount of bending for the least amount of allograft processing. At times, equally spacing the grooves caused one of them to lie along the proximal median ridge of the patella [103]. Bending improved when the groove positions were adjusted such that each groove ran along either side of that ridge rather than underneath it. The results presented in this study implement two proximal-distal grooves positioned on either side of the patellar proximal median ridge, rather than equally spacing the two grooves.

Three full models of human patellofemoral joints (Figure 2.2A-C), along with eleven models of human patellar osteochondral allografts (Figure 2.2D) were used in this biomechanical study, relying on prior experimental measurements of joint and articular surface anatomy [84], as well as the kinematics of the tibia and patella of the PFJs [101]. Model predictions of patellar kinematics and patellofemoral joint contact areas were previously validated against those experimental measurements [101], therefore predictions of PFJ contact areas in the current study may be considered reliable in the context of that prior validation. Nevertheless, further validation of the predictions from this study may be investigated in future cadaver experiments [116].
In summary, this study used finite element analyses to investigate the potential biomechanical benefits of a novel osteochondral allograft bending technique for patella resurfacing. Grooved patellar OCAs can provide additional flexibility to the articular cartilage surface, allowing the allograft to conform to the shape of the native femoral trochlea. The outcome of this biomechanical study produced encouraging results, motivating us to pursue future cadaveric investigations of this surgical procedure, in an effort to validate the conclusions from the finite element modeling results, and to identify surgical challenges and how they may be resolved. A natural progression of the investigation of this allografting procedure may also include future animal studies and, if outcomes are promising, clinical studies in patients indicated for biologic restoration surgery of the patella.

2.5 Acknowledgments

This study was supported with funds from the United States Department of Defense (W81XWH-18-1-0361/PR171360). Opinions, interpretations, conclusions, and recommendations are those of the authors and do not necessarily reflect those of the U.S. Department of Defense.

2.6 Conflict of Interest Statement

Some of those involved in this study are also inventors on a patent that describes the method of bending allografts [2]. As of this writing however, this technology is not currently licensed to any companies.
Chapter 3: Surgical tool for manipulating osteochondral allografts

3.1 Introduction

As the prevalence of osteoarthritis increases, the necessity arises for better treatments and preventative measures. A common site of osteoarthritis is the carpometacarpal joint of the thumb. The degeneration of articular cartilage at this joint often necessitates surgery to alleviate pain and restore normal mobility and functionality. Current surgeries, such as ligament reconstruction and tendon interposition, are not satisfactory. These surgeries relieve the pain from the bone-on-bone contact experienced due to the loss of articular cartilage, but do not restore full strength or range of motion to the joint [1].

Osteochondral allografts, which refer to healthy cartilage attached to the bone harvested from donor joints, can be used to replace the damaged articular cartilage in an osteoarthritic patient and restore joint functionality. During a surgical procedure, the osteoarthritic site is removed and replaced by an osteochondral allograft. These allografts, however, need to be carefully selected and size-matched between donor and recipient to ensure that the proper curvature is maintained. This greatly limits the number of procedures that can be performed. A new solution has been developed which can significantly increase the number of osteochondral allograft procedures that can be performed and expand the use of allografts to joints for which current procedures are unsatisfactory (Figure 2.1) [1,2]. The addition of grooves in the bone allows the articular surface of the osteochondral allograft to bend, adapting the allograft cartilage curvature to match the curvature of the host site. Specifically, in the carpometacarpal joint an arthritic trapezium is replaced by a donor allograft harvested from the femoral trochlea in the knee. The work presented in this chapter includes 1) trapezium osteochondral allograft design adjustments to implement feedback received during cadaver surgery, 2) surgical tool design to aid the surgeons in correctly
bending and fixing the osteochondral allograft before inserting it into the hand, 3) refining the original design and manufacturing the surgical tool to be used in future cadaver surgeries and clinical trials, and 4) patent submission.

3.2 Trapezium Osteochondral Allograft Design Adjustments

The original designs for the grooved osteochondral allograft resulted in a successful surgery in terms of proving the feasibility of the technology and surgical method. The cadaver surgery results, however, suggested critical feedback for future iterations of the osteochondral allograft designs, which will be discussed in this section. The original designs indicated that three grooves should be cut, resulting in four bone struts. This particular number of grooves was chosen to maximize the bending capability of the allograft without reaching strain values that harm the cartilage [1]. Cutting three grooves, however, proved more difficult than anticipated and only two grooves could be cut with the equipment available to AlloSource, the tissue bank manufacturing the allografts at the time this work was completed. Therefore, it was necessary to adjust the design of the osteochondral allografts.

Original models of the grooved osteochondral allografts included three general sizes to be chosen according to hand size and hence, trapezium size. These sizes included small, medium, and large, which each varied in length, width, and height [1]. During the surgery, it was realized that the sizes were too large. Each of the allografts was approximately 2 mm longer than necessary and therefore did not properly articulate with the trapezium bone. Additionally, the original “large” size was determined to be too wide and would not fit most hands. Therefore, it was decided to eliminate the original “large” size and instead create only two sizes, a “small/medium” (S/M) and a new “large”. Solidworks models were adjusted to implement these changes. The new large size
was designed to be 16 mm in length and 12 mm in width, while the small/medium was designed to be 15 mm in length and 10.5 mm in width (Figure 3.1).

![Figure 3.1: Sketches of small/medium (left) and large (right) osteochondral allografts. Allograft is harvested from a donor femoral trochlea, grooved, bent, secured in the bent configuration, and transplanted to replace the trapezium in the carpometacarpal joint of the thumb.](image)

Bone strut heights were adjusted as well. During the surgery, the bone struts are pinched together, which bends the cartilage, and a $\varnothing$3 mm screw is driven into the bone struts beneath the layer of articular cartilage to keep the osteochondral allograft bent in place. Oftentimes in the preliminary cadaver trials, the insertion of the screw caused the bone struts to crack at the bottom, resulting in an unsuitable allograft. We hypothesized that this issue could be resolved by requiring taller bone struts. In order to determine the minimum bone height required, we used immature bovine bone along with rubber, which simulated the cartilage, to create an OCA prototype. Small sections of bone, without cartilage, were cut using a band saw to match the grooves and sizes of the new small/medium and large designs. Each piece was made with grooves that were approximately 7 mm tall. Extra bone was left at one end of the grooves; this extra bone will be referred to as the “bone sheet”. In order to simulate cartilage bending, we cut small rectangles of rubber that matched the length and width of the bone sheet. The prototype was oriented with the bone sheet lying on the table. The rubber piece was then super glued to the open side of the bone
struts, opposite from the bone sheet. After the glue had dried, a razor blade was used to remove the bone sheet, leaving only the rubber and attached bone struts. This simulated the grooved osteochondral allograft with the rubber representing the articular cartilage.

We created multiple prototypes, all of varying heights ranging from 4 mm to 7 mm. For each of the osteochondral prototypes, the bone struts were clamped together to bend the “cartilage” (rubber) and a hole was drilled through the three struts. A Ø3 mm screw was then driven into the bone. The total bone height as well as the distance between the screw and the bottom of the bone was recorded and the osteochondral prototype was examined for cracking. After multiple variations of strut size and screw placement, we observed that cracking occurred when the bone strut height was less than 6 mm. Therefore, it was determined that the minimum bone height should be 6 mm for both the small/medium and large osteochondral allograft sizes. The Solidworks models were updated accordingly and can be seen in Figure 3.1.

3.3 Surgical Tool (“Approximator”) Design

3.3.1. First Version (V1): Aluminum Prototype

During the cadaver surgeries, difficulty arose in driving the Kirschner wire (K-wire) through the bone struts at the correct orientation. The K-wire must be driven through the bone normal to the central bone strut with the bone struts in the bent configuration. The K-wire is used to guide the insertion of the compression screw. If the K-wire is angled, the screw will also be inserted at an angle, which could result in either cracking of the bone strut or the screw being driven into, and therefore damaging, the articular cartilage.

In order to address this issue, we developed a surgical tool specifically designed to assist the surgeon in properly inserting the compression screw required to maintain the osteochondral allograft in its bent configuration. Requirements of the tool included the following, according to
surgeon feedback: must be a forceps-like hand tool, must properly bend the osteochondral allograft when pinched together, must include a guide for the K-wire, must be able to drive a compression screw through the bone while still pinching the tool closed, and must be able to insert osteochondral allograft into carpometacarpal joint without opening the tool. Using Solidworks, we constructed an initial design (V1) of this surgical tool, named the Approximator, that meets these requirements (Figure 3.2).

The jaws (opposite end of the finger holds) have two angled sides, one at the end of each individual shank. These angles are designed specifically to match the angle of the bent allograft while the jaws are designed to match the average width of the different allograft sizes. This design ensures that the osteochondral allograft will be properly bent and can be held in that position during insertion of the K-wire and compression screw. Two through holes can be seen on each individual shank of the jaws. One hole has a small diameter and is intended as a wire guide to insert the $\varnothing 1$ mm K-wire. The other hole has a large diameter and is included for the insertion of the compression screw once the K-wire has been driven through the bone. With the compression screw in place, the same tool can be used to insert the osteochondral allograft into the correct location at the trapezium. Figure 3.3 shows the tool being used to manipulate a bendable osteochondral allograft. The order of operations using this tool is as follows:

![Figure 3.2: First version (V1) of a surgical tool designed specifically for bendable osteochondral allograft trapezium surgery. Angled jaws properly pinches and bends osteochondral allograft. Small diameter hole at the jaws acts as a guide for the K-wire. Larger diameter hole at the jaws allows insertion of the compression screw. (Initial sketch. Refinements addressed later.)](image)
1) Pick up osteochondral allograft by pinching with tool. Pinch allograft until cartilage is bent to desired curvature.

2) Insert K-wire through smallest diameter hole. Drive K-wire through bone.

3) Approaching from the opposite side to that which the K-wire was inserted, guide compression screw over K-wire and drive through bone. At this point the allograft should be properly bent and held in place by the compression screw.

4) Remove K-wire from osteochondral allograft.

5) Insert bent allograft into proper location in the hand to replace the trapezium. Once osteochondral allograft is placed, finish anchoring the osteochondral allograft in position, release tool and back out of hand.

Figure 3.3: Approximator V1 from two different angles clamping an osteochondral allograft in the bent position. Black tape acts as a makeshift bumper (implemented in future designs) to prevent the jaw tips from touching. Compression screw hole, bend angles of the jaws, and pivot joint screw are all pictured.

This initial Approximator design (V1) was sent for manufacturing in Columbia University’s Mechanical Engineering Machine Shop. Features not reflected in Figure 3.2 include the rounding of all sharp edges to improve comfort during use as well as knurling on the inside of the jaws to better grip the bone. Additionally, V1 was held together at the pivot joint with a temporary screw and nut. The screw inserted through the top of the finger shank (the shank gripped by one of the fingers, usually the pointer finger, when holding the Approximator in the right hand) and mated with the nut on the other side of the Approximator, which was coincident with the
bottom face of the thumb shank. This screw/nut was used for the initial joining of the two shanks, but was not intended to be the permanent design. From this design, we manufactured an initial prototype out of aluminum. After submitting for a provisional patent (see Section 3.4), the initial prototype was used in cadaver surgeries. Surgeon, Dr. Melvin Rosenwasser, gave positive feedback, including suggested changes for future designs. Changes to be implemented in the next design iterations include the following: thinner jaws to increase ease of osteochondral allograft insertion, wire guide tube with a thinner inner diameter to decrease K-wire insertion angle variability, a permanent pivot joint to replace the screw and nut that held together the two shanks in the initial prototype, a recess on the inside of the thumb shank jaw sized to fit the compression screw, “bumpers” on the shank to prevent the jaws from touching each other, and an indication of which orientation the tool should be held by the surgeon.

### 3.3.2. Second Version (V2): Modified Prototype

New design implementations for the second version (V2) of the Approximator included a more permanent pivot joint to replace the screw and nut that held V1 together, a thinner jaw portion to allow for easier manipulation of the bent allograft during surgery, a recess on the jaw of the thumb shank (shank gripped by the thumb when holding the Approximator in the right hand) sized to the diameter of the compression screw, “bumpers” on each shank to prevent the ends of the jaws from touching each other, and an inscription of “TOP” indicating the proper tool
orientation to ensure the surgeon correctly orients the Approximator to properly clamp the allograft. Figure 3.4 shows the V2 assembly while Figure 3.5 highlights only the thumb shank.

We chose to use a solid rivet at the pivot joint as our method of permanently securing the two shanks together. In addition to building V2, we also replaced the screw in V1 with a rivet to make the pivot joint more permanent. The rivet was secured using a mechanical press while ensuring that the shanks were still able to pivot around the joint and move relative to one another. However, this resulted in somewhat of a looseness at the joint, which caused misalignment of the tips of the jaws unless carefully maneuvered. Additionally, the hole for the rivet was large compared to the surrounding material thickness. Upon initial use during practice cadaver surgeries, V2 and the modified V1 both broke. The shanks bent at the pivot joint and the thin material surrounding the rivet cracked. We attributed this failure to two major causes: 1) the material surrounding the pivot joint was much too thin and 2) the aluminum was too weak to withstand the forces undergone during surgery. To address these concerns, we iterated on our design and used finite element analysis to optimize the critical dimensions.

3.3.3. Third Version (V3): Final Design

The design was updated to increase the thickness around the pivot joint as well as to replace the rivet with a stepped pin (per suggestion of a senior engineer at Arc Precision, MN). For this Approximator third version (V3), we chose to use 420 stainless steel because of its high yield stress.
relative to other surgical grade stainless steels (Table 3.1). For the full set of engineering drawings for the final Approximator design iteration V3, refer to Appendix A.

Table 3.1: Material properties for 420 stainless steel [117].

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modulus of Elasticity</td>
<td>$29 \times 10^6$ psi</td>
</tr>
<tr>
<td>Yield Stress</td>
<td>$0.197 \times 10^6$ psi</td>
</tr>
<tr>
<td>Density</td>
<td>0.28 lb/in$^3$</td>
</tr>
</tbody>
</table>

### 3.3.3.1. Finite Element Analysis

Tetrahedral elements with 10 nodes each were used to create the Approximator geometry (Figure 3.6). In the finite element model (febio.org; [102]), we fixed the Approximator jaw inside faces in the x-, y-, and z-directions to simulate an osteochondral allograft held in the bent position. The bottom face of the stepped pin was also fixed in the y-direction (normal to the bottom face). Sliding elastic contact was applied between the circumferential pin faces and the inner faces of the pivot hole of each shank. Sliding elastic contact was also applied between the apposing shank surfaces at the joint. A 25 lbf force was applied to each of the shank ring holes in the positive or negative x-directions to simulate the surgeon using the Approximator by pinching the two ring holes together in order to clamp the bendable allograft. This force was chosen by rounding the maximum key pinch force value reported in [118] to the nearest 5 lbf. Finite element analysis showed that the maximum effective stress in the Approximator occurred...
around the pivot joint, but did not exceed the yield stress, verifying that this new design (V3) would not deform or fail due to a large applied force (Figure 3.7).

### 3.3.3.2. Machining Challenges

Manufacturing the final version (V3) of the Approximator tool required several iterations and attempts due to the complexities of machining 420 stainless steel with a variety of angled surfaces. The primary issues encountered are discussed below.

#### 3.3.3.2.1. Correct Speeds and Feeds

Stainless steel is much more difficult to machine than aluminum and the speeds and feeds will not be the same for both materials. Particularly, stainless steel requires much lower speeds and feeds than aluminum. In several instances, we did not reduce the feed rate enough (especially when turning corners or machining a circular path) and would break a tool. Breaking tools is not only expensive, but also dangerous. With more experience in the process of machining the Approximator surgical tool, we aired on the side of caution when choosing our feed rates. When the speed is too high for the given feed rate, the mill tools may wear out quicker than expected. Worn out tools will cause inaccurate dimensions. Aside from wearing out tools, different speeds and feeds may result in slight dimension differences. These are especially important to pay attention to when machining critical dimensions with high tolerances (e.g. the pivot hole or the guide wire tube hole) as well as reference surfaces. The 420 stainless steel we used was not necessarily uniformly hardened, so some areas of the metal were softer than others. The softer areas are easier to machine than harder areas and the non-uniformity required us often to adjust the speeds and feeds on the fly.
3.3.3.2.2. *Chip Clearing and Flood Coolant*

We required constant flooding of coolant and chip clearing during the entire machining process. At times the coolant pressure would decrease due to clogs in the system and would not be able to sufficiently clear the chips being produced. When this happened, chip packing would occur in the end mill and cause accuracy issues or could cause the tool to get stuck and either ruin the part being machined or break the mill tool.

3.3.3.2.3. *Proper Jigging*

The jig, which is clamped in the vice on the mill and is used to secure the material being machined, was essential to proper machining of the Approximator. We found that small discrepancies in jig hole dimensions or placement resulted in compounding inaccuracies (tolerance stack-up) in the Approximator machining. Often these inaccuracies could not be fixed or compensated for and we would need to restart. Further inaccuracies arise each time the tool has to be released from its current jigging state and moved to a new position. Aside from proper dimensioning of the jig itself, sufficient clamping of the machined material to the jig was also essential. When enough material was machined away from the stainless steel block leaving only a thin piece of material, this thin piece would vibrate and flex either causing the machining tool to cut away too much of the steel or dangerously interfering with the machining tool causing tools to break. This was fixed by adding more clamping points to the jig to better secure the steel being machined.

Due to the complex geometry of the Approximator, finding good reference surfaces became difficult and complex jigging was required. Future work could include creating a jig with machined recesses and angled surfaces for the Approximator to rest against that would create
simpler reference surfaces. An alternative would be to design clear reference surfaces as a part of
the Approximator that could later be machined off.

3.3.3.3. Machining Process

In this section, we briefly discuss the steps and process used to machine the Approximator
tool. Step-by-step informal notes are attached in Appendix A. The Approximator was machined
out of 420 stainless steel with the guide wire
tubes cut from 304 stainless steel stock and
the locking mechanism built from a
threaded rod and thumbwheel (Table 3.2).
The entire process involved two Tormach
Personal CNC 770 milling machines, eight
total operations, and 14 different tools
(Figure 3.8, Table 3.3).

Table 3.2: Materials needed to manufacture Approximator. Table includes material, part made from the material,
quantity to order, the number of parts produced, and the link to purchase.

<table>
<thead>
<tr>
<th>Material</th>
<th>Part</th>
<th>Quantity to Order</th>
<th>Number Produced</th>
<th>Link to Purchase</th>
</tr>
</thead>
<tbody>
<tr>
<td>420 stainless steel (0.25” x 3” x 24”)</td>
<td>Approximator shanks &amp; pin</td>
<td>1</td>
<td>3 sets</td>
<td><a href="https://www.onlinemetals.com/en/buy/stainless-steel/0-25-x-3-stainless-rectangle-bar-420-oversize/pid/18829">https://www.onlinemetals.com/en/buy/stainless-steel/0-25-x-3-stainless-rectangle-bar-420-oversize/pid/18829</a></td>
</tr>
<tr>
<td>18-8 stainless steel flanged knurled-head thumb nut</td>
<td>Locking mechanism</td>
<td>3</td>
<td>3</td>
<td><a href="https://www.mcmaster.com/95150A130">https://www.mcmaster.com/95150A130</a></td>
</tr>
<tr>
<td>Super-corrosion-resistant 316 stainless steel threaded rod (6-32 thread size, 1’ long)</td>
<td>Locking mechanism</td>
<td>1</td>
<td>3+</td>
<td><a href="https://www.mcmaster.com/93250A050">https://www.mcmaster.com/93250A050</a></td>
</tr>
</tbody>
</table>
The overall process is described briefly here. For more details on the machining process determined by Andrei Shylo, the Columbia University machinist who manufactured the Approximator, please refer to his notes in Appendix A. First, the stainless steel should be cut down to size. This cut piece will be used to manufacture the stepped pin followed by the two shanks.
The pin and shanks should be de-burred. The threaded rod is cut to length and two opposing sides are flattened to fit within the lock slots cut out of each shank. A hole is drilled through the end of the threaded rod to hold the pin that will secure the threaded rod in place and form the Approximator’s locking mechanism. The two shanks are brought together and joined with the stepped pin. The stepped pin is welded on the bottom only; the step keeps the two shanks together while allowing freedom of rotation. The threaded rod is secured within the aforementioned slots and a gauge pin is inserted through the shank and the rod. The gauge pin is welded on top and bottom of the shank to secure the threaded rod while letting it rotate. Once the Approximator is assembled, it is carefully polished using a stainless steel polishing kit to eliminate machining and welding marks. The thumb wheel is screwed on to the threaded rod to complete the locking mechanism. The guide wire tubes are cut to size and sanded at each edge to form a conical shape, which allows the tube to be inserted into the Approximator and secured in place without being able to slip through the guide wire hole. Several replacement guide wire tubes should be made for each Approximator. Photos of the final version can be seen in Figure 3.9.

Figure 3.9: Top view of the Approximator in (A) closed, (B) neutral, and (C) open positions. Direct view of the angled jaws inlaid in (B).
3.4 Patent Submission

In order to protect our intellectual property and the design of the surgical tool before disclosing it to collaborating teams or tissue banks, it became necessary to submit our designs for a provisional patent with the intent of later converting to a full patent. We worked with Columbia Technology Ventures (CTV) to draft and edit a provisional patent. CTV drafted the initial copy and we edited it significantly to include appropriate terminology and accurate descriptions. We also provided drawings to add clarity. The provisional patent was submitted on October 22, 2018 under the title “Systems and apparatuses for manipulating bendable allografts with tool guides” and application number 62748917. This patent application included the tool described above as well as potential modifications for future tools to be used in surgery alongside the current version of the surgical tool. The current version is known as the “Approximator” because it is used to approximate, or bring close together, the bone struts of the bendable osteochondral allograft. These modifications included a tool specifically for trimming the allograft to size and a tool specifically to be used during the insertion process. As of now, both of these processes can be accomplished with the current version of the Approximator, but the patent includes the possibility of creating separate tools for each of these processes. The patent additionally includes the option of adding a bend either in the plane of the tool or out of the tool plane. Adding said bend would allow the surgeon to leave the Approximator clamped on the osteochondral allograft during surgery while “bending” the tool toward the wrist of the patient or perpendicular to the arm (depending on bend orientation) to provide the surgeon with a clear work area for drills, screwdrivers, and other tools necessary to complete the surgery. The application for conversion of the provisional patent was submitted on October 22, 2019. The final patent (US 2021/0298780 A1) was issued on September

3.5 Acknowledgments

We thank Andrei Shylo for manufacturing all prototypes and final versions of the Approximator surgical tool. He spent an enormous amount of time and effort to develop the entire manufacturing process of the tool and additionally provided design ideas to improve manufacturability. We also thank Robert Stark for the assistance and consultation he provided during the machining process. This project was supported with funds provided by the United States Department of Defense (W81XWH-18-1-0361/PR171360). Opinions, interpretations, conclusions, and recommendations are those of the authors and do not necessarily reflect those of the U.S. Department of Defense.
Chapter 4: Immature bovine cartilage wear is due to fatigue failure from reciprocating compressive forces and not reciprocating frictional forces

4.1 Introduction

Osteoarthritis (OA) is a debilitating disease characterized by the degradation and wear of articular cartilage. While a large effort has been put forth to understand wear of articular cartilage [44,45,51,53,54,77-80,119,120], its exact mechanisms have not been fully elucidated.

Generally, the friction coefficient between cartilage surfaces is very low, representing a significant functional property of the tissue. Friction coefficients for cartilage sliding against cartilage measured in synovial joints have ranged from 0.001 to 0.08, varying with joint type and testing parameters [36]. For small explants, the friction coefficient against glass has been reported to vary from 0.002 to 0.2 [36]. Much of the cartilage wear literature focuses on friction and lubrication, often reporting increasing friction coefficient as a potential indicator of wear [38,43-46,121]. Previous studies, however, have shown the friction coefficient to remain low even with increasing OA [50] or damage [51], suggesting that the friction coefficient may not be directly implicated in cartilage wear. However, this hypothesis has not been tested directly to date.

Indeed, it remains unclear whether cartilage wear, which has been shown to occur due to fatigue failure in immature bovine cartilage loaded in a saline bath [51], initiates from reciprocating frictional forces acting on the articular surface, or by reciprocating compressive loading as the contact area migrates across the articular surface during reciprocating motion. In physiologic loading conditions, cartilage surfaces slide against one another, and the point of contact moves across one or both articular surfaces, producing a migrating contact area (MCA)
configuration. When a joint is loaded, the interstitial fluid is forced out of the tissue from the pressurized zones to surrounding unloaded areas. Interstitial fluid makes up 70% – 90% of the weight of cartilage, and is largely responsible for its load-bearing capabilities [28,31-33]. In a MCA configuration, as the loaded contact area moves across the articular surface, the unloaded cartilage can re-imbibe the lost fluid and sustain an elevated fluid load support, resulting in a low friction coefficient [37]. If fluid pressurization, and therefore fluid load support, in the tissue is depleted, such as occurs when the tissue is under static loading in a stationary contact area (SCA) sliding configuration, the friction coefficient rises as the solid matrix supports more of the applied load [34,35,37]. When investigating cartilage sliding against glass, we have previously reported a 60-fold increase in friction coefficient in the SCA configuration relative to the MCA configuration [37] as interstitial fluid pressurization reduces to zero.

Here, we hypothesize that the primary wear mechanism of articular cartilage is fatigue failure under reciprocating compressive loading rather than reciprocating frictional sliding. While past studies have examined cartilage fatigue failure in various testing environments, such as tensile [78,79], compressive [54,76,77], or shear fatigue [80], this study directly compared cyclical compressive loading versus static loading mechanisms under reciprocating sliding to better understand the progression of wear in articular cartilage. The study presented here compared (1) potential fatigue failure under reciprocating compressive loading with low-friction sliding to (2) potential fatigue failure due to reciprocating frictional sliding under static compressive loading. Improved understanding of mechanically mediated cartilage wear can lead to new insights into osteoarthritis initiation and progression.
4.2 Methods

Reciprocating sliding between glass and cartilage was prescribed in two separate testing configurations while keeping the average contact stress approximately equal between groups, to eliminate the potential role of this factor on wear. Migrating contact area (MCA) long rectangular cartilage samples were articulated against a hemispherical glass platen (a lens), resulting in a localized contact area that did not extend to the cartilage sample edges. In MCA, as a constantly-loaded glass platen moved across the surface of the cartilage sample, every point along the travel path was loaded and unloaded during a single sliding cycle, subsequently producing both reciprocating compressive and frictional sliding forces. The friction coefficient in this MCA configuration remained low in these tests, as reviewed and explained in the above Introduction (Section 4.1). For SCA, square cartilage samples were articulated against a flat glass disc (a prism) that covered the entire surface of the cartilage sample during reciprocating sliding. In this case, as the glass platen moved across the sample, the entire surface was under a static compressive load in addition to reciprocating frictional sliding. The friction coefficient in this SCA configuration increased over time as the interstitial fluid pressurization was progressively depleted, as reviewed in the Introduction (Section 4.1). The integrity of the cartilage samples was assessed before and after testing, to detect signs of surface damage and cartilage wear. The hypothesis of this study was tested using saline and synovial fluid as ambient baths.

4.2.1. Sample Preparation

Immature bovine knee joints (2-3 months old; seven right knees, six left knees) were acquired from a local abattoir (IACUC exempt) and tibial plateau cartilage layers were harvested as described previously [122]. Each tibial plateau cartilage layer was trimmed with a box cutter to 20 mm × 30 mm. Samples were then placed articular surface down on a freezing stage sledge.
microtome (Leica Biosystems #SM2400, leicabiosystems.com; Physitemp Instruments #BFS-30TC, physitemp.com) and frozen in water soluble embedding matrix (Epredia M-1, #1310, fishersci.com). Samples were trimmed to a thickness of 1.36 ± 0.04 mm and each cut into three separate cartilage strips: two 10 mm × 10 mm strips for the control (CTRL) and SCA samples and one 10 mm × 30 mm strip for the MCA sample, with the long dimension along the antero-posterior axis of the tibial plateau articular cartilage.

Samples were mounted to the center of a Ø 60 mm petri dish using cyanoacrylate and submerged in phosphate buffered saline supplemented with 0.04% isothiazolone-based biocide (Proclin 950, Millipore Sigma, #46878-U, sigmaaldrich.com) and 0.1% protease inhibitor (0.5 M Ethylenediaminetetraacetic acid, EDTA, #03690, sigmaaldrich.com) (summarized as PBS). Following mounting, articular cartilage surfaces were stained with India ink and samples with scratched or blemished surfaces were discarded. Mounted samples were then frozen in PBS at -7 °C for no more than 4 weeks until day of testing.

4.2.2. Wear Testing

Friction tests were carried out using two identical custom testing devices which collected multiaxial load and vertical position data, as described previously [122] (Figure 4.1). Mounted MCA and SCA samples were affixed to the sliding stage base of the friction testing devices with the antero-posterior axis of the tibial plateau strip oriented along the sliding x-direction. A glass loading platen, which could be moved vertically in the z-direction, was brought into contact with the cartilage strip and dead weights were added to a loading stage above the platen to apply a constant force to the cartilage samples. MCA tests were loaded against a Ø 25 mm hemispherical glass platen with an applied load of 4.45 N (Figure 4.2A,C), while SCA tests were loaded against a Ø 25 mm flat glass disc with an applied load of 44.5 N (Figure 4.2B,D). Load values were chosen
based on preliminary data in order to apply approximately equal average contact stresses between MCA and SCA test configurations. Sliding between cartilage and glass was prescribed at 1 mm/s across a distance of \( u_x = \pm 4 \) mm for 24 hours (5,400 reciprocating cycles). Mounted CTRL samples were placed next to the friction testing devices and exposed to the same environment, but did not undergo any loading or sliding. Time-dependent friction coefficient \( \mu \) and creep displacement \( u_z \) were calculated post-test using custom MATLAB codes [122]. A previously built custom LabVIEW code was used to collect loads (\( F_x \) and \( F_z \)) and displacements (\( u_x \) and \( u_z \)). Time-dependent friction coefficient and creep displacement were calculated post-test using previously written a custom MATLAB code [122]. The MATLAB code produced a spreadsheet with four columns: cycle number, friction coefficient (\( \mu \)), \( u_z \), and \( F_z \). While \( u_z \) was output in encoder units, this value could be converted to millimeters for either Device 1 (Figure 4.1, left) or Device 2 (Figure 4.1, right) by dividing the encoder value \( u_z \) by 1001.2 \( \frac{\text{units}}{\text{mm}} \) or 1002.2 \( \frac{\text{units}}{\text{mm}} \), respectively.

For \( n = 8 \) sets of MCA, SCA, and CTRL cartilage strips, samples were submerged in PBS throughout the testing duration. An additional \( n = 8 \) samples were each tested in MCA and SCA configurations, in addition to a CTRL
group, using mature bovine synovial fluid (Lampire Biological Laboratories #8620853, lampire.com). Particulates were separated and removed from synovial fluid through centrifugation (3000 g, 20 min) and synovial fluid was supplemented with 0.04% isothiazolone-based biocide and 0.1% protease inhibitor as described above (summarized as SF).

4.2.3. Contact Area Measurements

Prior to and immediately after testing, contact area between loading platen and cartilage strip was measured and used to calculate the average contact stress. Pressure-sensitive paper (Fujifilm Prescale, 4LW, pressure range of 0.05 – 0.2 MPa, sensorprod.com) was placed between the cartilage and glass surfaces mounted on the testing devices, dead weights were added to the loading stage, and load was applied for 60 seconds. Pressure-sensitive paper was then removed and photographed (Figure 4.3A,C). Photos were analyzed to measure contact area using open-source image analysis software (Figure 4.3B,D) [123]. Average contact pressure $p_{avg}$ was calculated as the ratio of applied force to contact area.

Figure 4.2: Schematic (top) and photos (bottom) of migrating contact area (MCA) testing configuration (left) and stationary contact area (SCA) configuration (right).

Figure 4.3: Representative contact pressure measurements for MCA (A,B) and SCA (C,D) configurations. Raw photos (A,C) and processed photos (B,D) of pressure-sensitive paper after loading.
4.2.4. Surface Deviation, $R_q$, Measurements

Surface scans of the articular surfaces of MCA, SCA, and CTRL cartilage strips were acquired before and immediately after wear testing using a Keyence Profilometer (LJ-V7080, keyence.com), which produced a dense point cloud of 50,000 points/cm$^2$ with a vertical resolution of ±0.046 mm. Unloaded samples were then allowed to recover in PBS at 4 °C for 48 hours and scans were taken again after recovery. Using a custom MATLAB code, point clouds were trimmed to include only the center 8 mm $\times$ 8 mm of the articular surface. Integrity of the surface geometry was then quantified by using the root mean square deviation, $R_q$, of the articular cartilage surface relative to a fitted plane.

4.2.5. Polarized Light Microscopy

Subsurface damage was analyzed by using polarized light microscopy (PLM) to examine cross-sections of the cartilage strips at the completion of testing. Each MCA, SCA, and CTRL strip was cut in half along the travel path. One half of each sample was mounted on the freezing stage sledge microtome using water-soluble embedding matrix with the center cross-section face up. Cross-sections of the cartilage along the sliding path (120 µm thick) were obtained and mounted on a glass slide. These unfixed sections were imaged using polarized light to view collagen alignment (Olympus BX60 microscope, Olympus DP72 camera, Olympus U-POT drop-in polarizer).

4.2.6. Statistical Analysis

One-way analyses of variance (ANOVAs) were performed before testing, immediately after testing, or after unloaded recovery to compare surface deviations, $R_q$, between loading configuration and testing bath treatment groups (single factor of treatment, with six levels: MCA-PBS, MCA-SF, SCA-PBS, SCA-SF, CTRL-PBS and CTRL-SF). Similar ANOVAs were also
performed to compare the average friction coefficient, $\mu_{\text{avg}}$, and maximum creep displacement, $u_{\text{max}}$, among groups. Repeated measures ANOVAs were performed within each treatment group to investigate differences in contact pressure, $p_{\text{avg}}$, or $R_q$ at three different time points (before reciprocating sliding, immediately after, and after unloaded recovery). When statistical differences were found, post-hoc testing of the means was performed using a Tukey-Kramer correction. Shapiro-Wilk normality tests were used to confirm normality of test groups. Type I error $\alpha$ was set to 0.05 and significance was set at $p \leq 0.05$ for all statistical analyses (NCSS Statistical Software 2019, ncss.com).

Based on preliminary data not reported here, a power analysis was performed to determine that the sample size used in the present investigation ($N = 8 \times 6$) was suitable for a well-powered study ($1 - \beta > 0.9$, PASS: Power Analysis and Sample Size Software 2019, ncss.com).

### 4.3 Results

All eight MCA cartilage strips tested in PBS (MCA-PBS) exhibited clear visual surface damage in the form of delamination and tearing of the superficial zone as observed by visual inspection (Figure 4.4C) and PLM (Figure 4.5C). Delamination occurred in the center of the samples, underneath the sliding path. Additionally, delamination did not extend to the edges of the sample, eliminating edge effects as a possible

![Figure 4.4: Photos (top) and laser scans (bottom) for one representative set of migrating contact area (MCA, left) and stationary contact area (SCA, right) cartilage strips shown both before and after friction testing. Arrows identify delamination.](image)
cause of damage initiation. Three of the eight migrating contact area cartilage strips tested in SF (MCA-SF) also exhibited clear visual damage both observed by inspection and visualized with PLM after testing. Conversely, all stationary contact area (SCA-PBS and SCA-SF) cartilage strips remained intact away from sample edges. Surface scans and PLM of eight of the SCA-PBS and two of the SCA-SF samples showed slight swelling or delamination at the edges of the sample only (Figure 4.4D, Figure 4.5B). No SCA samples exhibited delamination in the center of the articular surface as seen in the MCA tests.

Delamination occurred between the superficial and middle zones (SZ-MZ) of the articular cartilage, as noted from PLM (Figure 4.5B,C). This was observed for every damaged sample, regardless of testing bath (PBS or SF). PLM also confirmed that SCA samples remained intact without observable sub-surface delamination (Figure 4.5A,B).

![Figure 4.5: Polarized light microscopy (PLM) images of cartilage cross-sections for (A) CTRL, (B) SCA, and (C) MCA treatment groups. Superficial zone (SZ), middle zone (MZ), and deep zone (DZ) are labeled in (A), respectively corresponding to thin bright, thick dark, and thick bright regions. Dark spots in the DZ are cartilage canals present in immature bovine cartilage. Arrows in (B) and (C) show delamination between superficial and middle zones.](image)

These visual observations were further supported by measurements of $R_q$. In MCA-PBS cartilage strips, $R_q$ significantly increased from before testing to immediately after the friction test ($p < 10^{-3}$, Table 4.1, Figure 4.6). Additionally, immediately after frictional testing $R_q$ was significantly greater in the MCA-PBS group than in SCA-PBS or CTRL-PBS groups ($p < 10^{-4}$, Table 4.1, Figure 4.6).
No statistical difference was found in $R_q$ across treatment groups before testing ($p > 0.07$, Table 4.1, Figure 4.6). Additionally, no statistical difference was found in $R_q$ between scans taken immediately after frictional testing, and after 48 h unloaded recovery, in any test group ($p = 0.67$), implying that quantitative measures of articular surface integrity reported immediately after frictional testing were essentially permanent. Consequently, $R_q$ measurements after 48 h unloaded recovery are not reported here.

Table 4.1: Mean ± standard deviation of articular surface deviation from a fitted plane, $R_q$, and average contact pressure, $p_{avg}$, before and after testing, for each test group (MCA=migrating contact area, SCA=stationary contact area, PBS=saline, SF= synovial fluid). $p_{avg}$ was not acquired for CTRL samples. $n = 8$ per test group. Statistical differences between “immediately after” and “before” results are indicated in the “immediately after” columns, with * $p < 10^{-4}$, † $p = 0.03$. No other statistical differences were observed ($p > 0.09$).

<table>
<thead>
<tr>
<th></th>
<th>Average surface deviation, $R_q$ (mm)</th>
<th>Average contact pressure $p_{avg}$ (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>Immediately after</td>
</tr>
<tr>
<td>MCA-PBS</td>
<td>0.042 ± 0.021</td>
<td>0.196 ± 0.086*</td>
</tr>
<tr>
<td>SCA-PBS</td>
<td>0.047 ± 0.016</td>
<td>0.041 ± 0.015</td>
</tr>
<tr>
<td>CTRL-PBS</td>
<td>0.056 ± 0.024</td>
<td>0.056 ± 0.024</td>
</tr>
<tr>
<td>MCA-SF</td>
<td>0.040 ± 0.010</td>
<td>0.054 ± 0.018</td>
</tr>
<tr>
<td>SCA-SF</td>
<td>0.055 ± 0.030</td>
<td>0.047 ± 0.020</td>
</tr>
<tr>
<td>CTRL-SF</td>
<td>0.071 ± 0.030</td>
<td>0.071 ± 0.028</td>
</tr>
</tbody>
</table>

Contact pressure before the beginning of the 24-hour wear test was similar between MCA and SCA samples for both PBS ($p = 0.07$) and SF ($p = 0.22$) test groups (Table 4.1). After 24 h...
of frictional testing, $p_{\text{avg}}$ tended to decrease for both MCA and SCA test groups as the cartilage tissue deformed and the contact area expanded under loading (Table 4.1). This decrease was statistically significant only for the MCA-SF group ($p = 0.03$). However, due to the disparate temporal evolution in contact area between MCA and SCA configurations, the value of $p_{\text{avg}}$ immediately after frictional testing was significantly lower in the MCA-PBS test group compared to the SCA-PBS group ($p = 0.01$). Nevertheless, no statistical difference was observed in $p_{\text{avg}}$ after testing between SCA-SF and MCA-SF groups ($p = 0.29$, Table 4.1).

On average over the entire testing duration, and at each cycle, the friction coefficient in SCA tests was significantly greater than the friction coefficient in MCA tests for both PBS and SF groups ($p < 10^{-4}$, Table 4.2, Figure 4.7). While $\mu_{\text{avg}}$ in PBS tests was greater than in SF tests ($p < 10^{-3}$), the greatest difference in $\mu_{\text{avg}}$ resulted from the testing configuration (MCA versus SCA) and not from the testing bath (PBS versus SF, Table 4.2, Figure 4.7). The creep displacement $u_{\text{max}}$ was significantly greater for SCA relative to MCA group ($p < 10^{-4}$, Table 4.2). Similarly, the compressive creep displacement at each cycle was greater for SCA tests than MCA tests (Figure 4.7).

Table 4.2: Average friction coefficient $\mu_{\text{avg}}$ (mean ± standard deviation) and maximum compressive creep displacement $u_{\text{max}}$ (mean ± standard deviation) for frictional testing groups ($*, †, ‡ p < 10^{-4}; * p < 10^{-3}$). No statistical difference was observed for SCA-PBS versus SCA-SF ($p = 0.63$). Other legends given in caption of Table 4.1.

<table>
<thead>
<tr>
<th></th>
<th>MCA-PBS</th>
<th>SCA-PBS</th>
<th>MCA-SF</th>
<th>SCA-SF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average friction coefficient, $\mu_{\text{avg}}$</td>
<td>0.028 ± 0.005*‡</td>
<td>0.109 ± 0.020*</td>
<td>0.013 ± 0.002†‡</td>
<td>0.060 ± 0.021† *</td>
</tr>
<tr>
<td>Maximum creep displacement, $u_{\text{max}}$ (mm)</td>
<td>0.283 ± 0.076*‡</td>
<td>0.504 ± 0.084*</td>
<td>0.079 ± 0.035†‡</td>
<td>0.521 ± 0.054†</td>
</tr>
</tbody>
</table>
Figure 4.7: (A) Mean friction coefficient $\mu$ and (B) mean creep displacement $u$ per cycle, for SCA (blue) and MCA (gray) frictional tests in PBS (solid) and SF (dotted). Standard deviations are shaded. $n = 8$ cartilage samples per test group.

4.4 Discussion

Results showed that wear damage, in the form of surface delamination, was observed at the center of the articular layer only in the migrating contact area (MCA) configuration. All samples tested in saline (PBS), and three of eight samples tested in synovial fluid (SF), exhibited this form of damage. None of the samples tested in the stationary contact area (SCA) configuration showed evidence of central damage, neither in PBS nor in SF (Figure 4.5). This finding, which was confirmed quantitatively with measurements of $R_q$, occurred while the average contact pressure $p_{avg}$ remained similar between MCA and SCA (Table 4.1), whereas the friction coefficient in SCA was statistically greater than in MCA (Table 4.2, Figure 4.7). The latter result implies that a higher friction coefficient does not produce greater cartilage wear, under the same amount of contact pressure. Indeed, the only other functional difference between the MCA and SCA test groups was that MCA produced reciprocating compressive stresses on the cartilage layer, whereas SCA produced a nearly-static contact pressure (Table 4.1). Therefore, results of this study strongly support our hypothesis that the primary wear mechanism of articular cartilage is fatigue failure under reciprocating compressive loading rather than reciprocating frictional sliding.
Cartilage strips loaded in a MCA configuration exhibited significant delamination damage along the entire sliding path while cartilage loaded in SCA showed fibrillation only at the edges, most likely due to edge effects (Figure 4.5) as suggested from our computational studies of frictional contact in biphasic cartilage [124]. In the MCA configuration, cartilage experienced reciprocating compressive forces in addition to frictional sliding, but maintained a lower friction coefficient $\mu_{\text{avg}}$. Samples loaded statically in the SCA configuration only experienced reciprocating frictional forces with static compression.

Additionally, because the tissue was not able to re-imbibe the exuded fluid in the SCA tests, interstitial fluid pressurization subsided over time, raising the friction coefficient between glass and cartilage throughout the testing duration (Figure 4.7). Additional evidence in support of loss of interstitial fluid pressurization was the increased creep deformation noted in SCA cartilage samples relative to MCA samples (Figure 4.7), consistent with prior literature reports that combined experimental measurements of interstitial fluid pressurization with theoretical predictions [31,32,125,126]. The greater value of the group-averaged $u_{\text{max}}$ in MCA-PBS samples relative to MCA-SF samples could be attributed to the delamination and removal of the superficial zone, since fewer samples exhibited delamination wear in SF than PBS (Table 4.2).

This study was able to elucidate the differences between the tissue’s fatigue response due to reciprocating compressive loading versus reciprocating frictional sliding by designing experimental groups that differed in the temporal evolution of compressive loading. Average contact pressures were comparable between MCA and SCA samples before wear testing, and reduced slightly over time in MCA samples compared to SCA samples, eliminating the likelihood that higher contact pressures could be implicated as the cause of increased wear damage in the MCA configuration. In fact, due to the natural variability and surface curvature of articular
cartilage layers, SCA samples exhibited non-uniform contact pressure across their surface at the beginning of the wear test. This finding further supports the conclusion that higher localized contact pressures on the tissue were not the cause of increased wear during testing.

The common, but often implicit, assumption that frictional forces may be directly implicated in the progression of cartilage wear might suggest that cartilage wear is abrasive, releasing cartilage particulate matter into the surrounding bath in a manner similar to using sandpaper to smooth a rough surface. However, our previous study of abrasive particulate wear in immature bovine cartilage in saline had shown that it is entirely negligible prior to the observation of surface delamination [53,127]. We believe it is more likely that particulate cartilage observed, for example, during arthroscopy of an OA patient’s joint [128], results from the breakdown of delaminated portions of the articular surface. Qualitative evidence in support of this interpretation was provided in our earlier study [51] in the form of histological cross-sections of human OA cartilage, showing evidence of surface delamination similar to our in vitro findings in immature bovine cartilage.

Furthermore, to support the alternative hypothesis that frictional forces may be significantly implicated in OA progression, there would need to be evidence that frictional forces in OA cartilage are greater than in healthy cartilage, at least during the initiation phase of tissue degeneration. While some studies have provided tentative evidence to support this hypothesis [47-49], others have either remained inconclusive or observed the opposite [46,50]. We have previously reported that increasing levels of OA in human cartilage tissue did not produce higher friction coefficients [50] (in fact, the contrary was reported in that study). In another study, we showed that the friction coefficient of cartilage against glass remained low even after evidence of gross visual wear or subsurface damage was observed, showing no statistical significance between
damaged and undamaged samples [51]. The results of the present study further support these earlier findings: the samples with the greatest amount of damage (MCA) also experienced the lowest friction coefficient (compared to SCA, Table 4.2).

In this study, we found that the presence of synovial fluid reduced the likelihood of cartilage delamination over the reciprocating frictional testing duration adopted in our experimental design. While all eight MCA-PBS samples damaged within the 24 h testing duration, only three of the MCA-SF cartilage strips damaged within that time. However, it is important to emphasize that the only damage observed in SF occurred in the MCA configuration, not in the SCA configuration, supporting our hypothesis that fatigue failure initiates due to reciprocating compressive loading rather than reciprocating frictional loading. The reduction in the number of damaged samples in MCA-SF suggests that SF might delay the onset of delamination damage compared to MCA-PBS; in other words, upon longer durations of testing we may find that all MCA-SF samples exhibit delamination wear compared to none of the SCA-SF samples. While this hypothesis was not tested directly in the current study, we plan to address it in a future investigation.

Since \( \mu_{\text{avg}} \) in MCA-SF was statistically lower than in MCA-PBS (Table 4.2, Figure 4.7), there is a theoretical possibility that frictional forces might play a significant role when distinguishing the response of cartilage in healthy SF versus PBS. However, given the evidence reported above regarding the minimal role of frictional forces in OA, alternative hypotheses might also explain this difference. For example, there is a possibility that some molecular SF constituents may diffuse through the narrow thickness of the SZ and bind to/coat/decorate the type II collagen in the sub-surface region where delamination occurs, providing greater resilience to fatigue failure, perhaps by delaying the onset of denaturation of the collagen molecule under reciprocating
compressive loading. This purely speculative hypothesis would need thorough examination in a future set of studies that identify candidate molecules that might play this role, such as hyaluronan or lubricin/superficial zone protein, both of which have been implicated in relation to cartilage wear [129-132]. Though these molecules often have large molar masses, they may be able to diffuse through the ~100 µm-thick SZ over testing durations of 24 h or greater.

Another hypothetical possibility is that synovial fluid viscosity could play a role in slowing the loss of interstitial fluid pressurization by slowing the exudation of interstitial fluid, producing less creep deformation over the same loading duration. This reduced deformation may in turn protect the collagen fibril structure from denaturation. These hypotheses, generated from the outcome of the current investigation, were not the focus of the present work. They will be addressed in our future studies.

In the context of reciprocating frictional loading, an intuitive assumption may be that fatigue failure happens due to reciprocating shearing motion of the SZ above the MZ. Indeed, the shear modulus in immature and mature bovine cartilage and in adult human cartilage was shown to be lowest at the interface between the SZ and MZ [133], suggesting greater vulnerability of the tissue to shear loading in that location. Furthermore, Oungoulian et al. induced surface delamination in immature bovine cartilage using the SCA configuration [53], suggesting that fatigue failure due to reciprocating frictional forces may be feasible. However, Simon et al. reported a drop in shear moduli in bovine articular cartilage after repeated shear strain, but did not find any structural defects in the tissue [80], indicating that the lower shear modulus at the SZ-MZ interface may not have a direct influence on fatigue damage. In the context of these findings, we speculate that the delamination of cartilage observed in our earlier study [53] under SCA might have resulted from edge damage that propagated inward in the relatively small (Ø 4 mm) tissue
explants used in that study. The study presented here attempted to minimize edge effects in MCA and SCA, by using larger cartilage strips, demonstrating no delamination in SCA.

Other studies have investigated human articular cartilage fatigue failure in tension using a saline bath, showing an increased propensity for failure with increasing number of loading cycles, though results depended significantly on donor age and degenerative disease condition [78,79,120]. This testing configuration could be used in future investigations to examine the hypothesis that samples immersed in SF (or some of its constituents) fail at a higher number of cycles than those tested in PBS, under reciprocating loading conditions that preclude the putative influence of frictional contact.

Several prior studies have suggested that cartilage may fail due to compressive fatigue rather than shear fatigue. Weightman et al. reported surface fibrillation and cracks under cyclical compressive loading of cartilage with a hemispherical indenter [54], and Kaplan et al. showed delamination [76] in human articular cartilage due to cyclic compressive loading. In the porcine model, Vazquez et al. reported surface fibrillation and thinning after compressive loading of cartilage-against-cartilage [77]. Additionally, in our recent study of immature bovine cartilage-against-cartilage frictional tests, with one cartilage layer subjected to MCA and the other to SCA, delamination damage was only reported on the sample subjected to MCA [51]. In hindsight, this earlier result presaged the outcome of the current study.

In summary, the current experimental investigation demonstrated that cartilage wear progresses in the form of sub-surface delamination due to fatigue failure of cartilage at the interface of the SZ and MZ, under reciprocating compressive loading, but not under reciprocating frictional loading. This outcome may have major implications for our understanding of the mechanical mediation of OA initiation and progression in articular cartilage. This finding may also help us
better understand that the limited reparative ability of cartilage under moderate activities of daily living may rest on the activity of chondrocytes residing in this sub-surface zone, as well as cells such as synoviocytes that may infiltrate this zone [134,135].

4.5 Acknowledgements

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Chapter 5: Importance of fibril distribution in modeling of
Benninghoff arches in articular cartilage

5.1 Introduction

Articular cartilage is a load bearing tissue covering the ends of bones in synovial joints. The unique composition and structure of articular cartilage produce its load-bearing capabilities, providing both low friction and minimal wear in joints and distributing applied loads between bones [28]. Cartilage is primarily made up of three structural components: (1) water, (2) proteoglycans, and (3) collagen, with collagen making up 60-70% of the dry weight [28].

As a network of fibrils, collagen is generally presumed to determine the tensile properties of cartilage tissue, while the compressive properties are generally attributed to the proteoglycans. In reality, proteoglycans and the collagen network work together to produce the complex material response of articular cartilage [29]. Proteoglycans, which are negatively charged, attract water and cause the tissue to swell. This swelling is then restrained by the collagen network and when the tissue is loaded, the fluid pressurizes, supporting the load applied to the tissue [30]. Therefore, even when the bulk tissue is in compression, the collagen fibrils may be loaded under tension as they restrain tissue deformation. This is confirmed by Jones et al. whose computational models showed that although contact stresses in the patellofemoral joint were always compressive, the maximum principal stress in the collagen matrix was always tensile [61].

The fibrillar structure of collagen is presumed to be well known and exhibits a varying orientation through the tissue. At the articular surface, known as the superficial zone, collagen fibrils lie tangent to the surface, while deep zone collagen fibrils are oriented perpendicular to the subchondral bone [4,28,58-60]. These two zones of highly aligned collagen are separated by a transition zone known as the middle zone. Though this structure is believed to be well understood,
the specific functions resulting from the inhomogeneous collagen alignment have not been entirely elucidated. We seek to develop a cartilage material model which accurately models the depth-dependent properties as a tool for better understanding the relationship between collagen structure and cartilage function.

Depth-dependent material properties with an isotropic fibril distribution were able to replicate experimental contact pressures and indicated reasonable agreement between the directions of maximum principal stress within the tissue and collagen orientation [61]; therefore, the same material model was used in our previous study investigating patellofemoral joint contact area with bendable osteochondral allografts (Chapter 2)[136]. However, when attempting to use this same material model again in a preliminary investigation examining strain through the tissue, we were not able to replicate experimental results [137]. Previous studies include modeling discrete fibril bundles as horizontal springs [138-140], discrete arcade-like structures after Benninghoff’s observations [4,141], continuum or membrane elements with varying orientation through the tissue [142], or isotropic fibril distributions [61,136,143]. While these models successfully replicate various material properties and behaviors, none focus on replicating the inhomogeneous strain distribution through the tissue, such as that reported experimentally [3,137].

While the preferential fibril orientation in each zone is well-accepted, few studies have attempted to determine the fibril dispersion about each axis. Aspden and Hukins used X-ray diffraction to quantify the fibril dispersion as probability curves at three locations through the thickness of the articular cartilage [58]. Tadimalla et al. used diffusion tensor imaging (DTI) to determine the fractional anisotropy for the top-half and bottom-half of articular cartilage samples and compared the results to ellipticities of fiber orientation distributions acquired using small angle X-ray diffraction (SAXS) [83]. The DTI and SAXS results, however, did not correlate with one
another and there appeared to be a large amount of scatter in the results for both fractional anisotropy and ellipticity reported [83]. While attempts such as these have been made to quantify specific collagen dispersion through the depth of articular cartilage, the results have remained sparse.

We hypothesize that developing an accurate depth-dependent strain material model requires explicitly modeling a precise collagen fibril orientation throughout the tissue. Developing an accurate cartilage material model would lead to many benefits, including improved accuracy of finite element analysis results, ability to use modeling to address previously unanswered questions, and added insight toward the relationship between cartilage structure and its function within the body. Additionally, developing a computational model which adjusts fibril distribution in order to match experimentally observed depth-dependent properties, could suggest that computational modeling could function as another tool in addition to imaging techniques to determine and quantify fibril dispersion through the thickness of the articular cartilage. This study investigates the functional differences between various types of fibril distributions in a biphasic cartilage material model. The work presented here is intended to be the first in a series of studies whose overarching objective is to use computational modeling as an available alternative to imaging modalities in order to identify the collagen fibril dispersion in articular cartilage under the hypothesis that the proper choice of fibril orientation will replicate mechanical behavior of the tissue, specifically depth-dependent strain.

5.2 Methods

Axisymmetric finite element models were created to replicate the experimental setup reported in [3]. Five different fibril distribution models were implemented, with three models using discrete fibril bundles and two models using continuous fibril distributions. With the exception of
the isotropic continuous distribution, preferential fibril orientation varied through the depth such
the deep zone fibrils were generally perpendicular to the subchondral surface and the superficial
zone fibrils were generally tangential to the articular surface. For each of the five models, a static
load was applied to compress the tissue and two-dimensional depth-dependent strain was analyzed
and compared to the other fibril models.

5.2.1. Geometry Creation

Three-dimensional meshed models were created by using a tube whose wall thickness was
2.2 mm to match the cartilage thickness for immature bovine tissue reported in [3]. The tube outer
radius was 22.5 mm to approximate the shape of the humeral head and 1 mm tall, although as will
be seen below, the assigned tube height is not relevant to the final geometry. The tube was oriented
such that the height extended in the z-direction and the circular cross-section laid in the XY plane.
Eight-node hexahedral mesh elements were assigned to the part with 72 slices per 90 degree arc
of the tube (approximately 0.5 mm per element), 20 segments in the radial direction, and 1 element
along the z-direction. Radial elements were biased toward both the outer wall of the tube (articular
cartilage surface) and inner wall of the tube (subchondral cartilage surface) with a bias of 1.3, so
that the two surfaces employed a relatively fine mesh. The circular tube was trimmed to keep an
approximately 13 mm arc of the entire tube (32.5 degrees, 26 mesh slices), which was chosen to
provide a sufficiently large articular surface area to accommodate the deformation and contact area
observed in [3].

The front face (XY plane) of the geometry was duplicated and the remainder of the
geometry was deleted so that only a planar face remained. This face was revolved about the y-axis
to create a 3 degree wedge, approximating a wedge of a bovine humeral head. Eight hexahedral
elements were used through the thickness. While a 3 degree wedge was used for simplicity, in
practice the planar face could have been revolved by 180 degrees to match the experimental protocol of [3] which used half of a bovine humeral head. However, doing so would have created large inefficiencies in model run times and was not necessary to obtain the two-dimensional axisymmetric results desired. The meshed geometry is shown in Figure 5.1.

![Figure 5.1](image)

**Figure 5.1**: (A) Front view of 3 degree wedged used to approximate the articular surface of a bovine humeral head. Blue line represents the rigid platen. Articular and subchondral surfaces are indicated with arrows. (B) Top view of the subchondral surface of the articular cartilage wedge only. Red, green, and blue axes indicate x-, y-, and z-directions, respectively, for both (A) and (B).

In addition to the articular cartilage wedge, a planar surface (12 mm × 3 mm) was created and aligned with the XZ plane to represent a rigid platen, which the cartilage would be loaded against. A single hexahedral element was assigned to the rigid platen surface.

### 5.2.2. Finite Element Analyses

All finite element models were created in FEBio Studio 1.8 (febio.org, [102]). In order to utilize symmetry, the inside edge of the wedge (y-direction curve located at $x = 0$, Figure 5.1A) was fixed in the x-direction. Additionally, a symmetry plane was assigned to the back face of the wedge, preventing bulging. The front face of the wedge, aligned with the XY plane, was fixed in the z-direction to prevent bulging. A fixed effective pressure ($p = 0$), or free-draining surface, was assigned to the outside face of the articular cartilage wedge.
Sliding biphasic contact was assigned between the platen and the articular surface. The platen, which was assigned to be a rigid material, was positioned with a small overlap between the platen and the articular surface. This small overlap is necessary for proper execution of a contact interface in a load-controlled study. Note that a sliding elastic contact interface would also have been sufficient since one of the contact surfaces was a rigid surface, which does not allow fluid flow through the material. Lagrangian augmentations were turned on and the auto-penalty feature was utilized.

The subchondral surface of the articular cartilage wedge was tied to a rigid material, which did not have an associated geometry but represented the subchondral bone of the humeral head, using a rigid contact interface. The bone was fixed so that translation was only allowed in the y-direction. A load of -0.6 N in the y-direction was applied to the rigid bone over five seconds, which in turn compressed the articular cartilage against the rigid platen. This load magnitude was chosen to reproduce the loading protocol of [3]; because Canal et al. applied a compressive load of 36 N to half of the humeral head, or 180 degrees of a spherical cap, we equivalently applied 0.6 N to a 3 degrees wedge of the spherical cap. For each model, a five second transient biphasic analysis using a non-symmetric stiffness matrix and full-Newton solver was run in FEBio 3.7.0 (febio.org, [102]). Results were viewed and analyzed in FEBio Studio 1.9.

5.2.3. Material Parameters

Articular cartilage was modeled as an inhomogeneous biphasic solid mixture with a neo-Hookean ground matrix and either a continuous fiber distribution or discrete fiber bundles. Solid volume fraction was approximated to be $\varphi = 0.2$. Spatial mapping was used to prescribe the inhomogeneous Young’s modulus such that it varied with the depth of the tissue according to:

$$E = 6.0492x^4 - 9.9321x^3 + 6.9342x^2 - 0.8074x + 0.1768$$
where \( x \) is the normalized height of the tissue [144]. Permeability and fiber stiffness were chosen based off previously reported data and assigned to be \( k = 0.00116 \text{ mm}^4/\text{N·s} \) and \( \xi = 1.432 \text{ MPa} \), respectively [145]. Three zones were created in the cartilage with the superficial zone (SZ) and middle zone (MZ) occupying 4.6% and 12.1% of the total thickness, respectively, and the remaining portion of the tissue comprising the deep zone (DZ) [3].

### 5.2.3.1. Discrete Fibril Bundles

Three models used discrete fibril bundles instead of a continuous fibril distribution to model the arcade-like structures described by Benninghoff [4]. For each model that used discrete bundles, the deep zone had one fibril bundle oriented perpendicular to the subchondral surface with fiber stiffness \( \xi = 1.432 \text{ MPa} \). Fibrils in the middle zone and superficial zone arched from initially aligned with the deep zone fibrils to become tangent with the articular surface. One model used two discrete fibril bundles (Discrete-2) which arched within the local XY plane to be aligned with the local x-direction at the articular surface (Figure 5.2A,D). Each fibril bundle in the middle zone and superficial zone had assigned stiffness of \( \xi = 0.716 \text{ MPa} \). The second discrete fibril bundle model had four total fibril bundles (Discrete-4) with two arching through the middle zone to align with the local x-direction and two arching to align with the local z-direction at the articular surface (Figure 5.2B,E). Each fibril bundle had assigned stiffness of \( \xi = 0.358 \text{ MPa} \). The final model with discrete fibrils used eight distinct fibril bundles (Discrete-8) with the same four as employed in the Discrete-4 model and four additional fibril bundles rotated 45 degrees about the local y-axis (Figure 5.2C,F). Each bundle had assigned stiffness \( \xi = 0.179 \text{ MPa} \).
Figure 5.2: Front view (A,B,C) of a portion of the cartilage model with white arrows indicating fibril distribution through the thickness. Zoomed-in bottom view (D,E,F) of a portion of the articular surface with purple arrows showing the fibril dispersion about the local y-axis. Fibril distribution for Discrete-2 (A,D), Discrete-4 (B,E), and Discrete-8 (C,F). Local (element-wise) coordinate system and cartilage zones indicated in (A). Local z-axis is orthogonal to both local x-axis and y-axis, oriented perpendicular to the cartilage face. DZ = deep zone (yellow), MZ = middle zone (blue), SZ = superficial zone (orange).

5.2.3.2. Continuous Fibril Distribution

Two models used continuous fibril distributions. In one case, an isotropic, or spherical fibril distribution was assigned in each of the three zones (Isotropic). In the second case, a depth-dependent ellipsoidal distribution was employed (Ellipsoidal). In the case of the ellipsoidal distribution, semi-principal axes of an ellipsoid defined the fibril density in the local x, y, and z-directions (see Figure 5.2A for descriptions of the local material axes). Semi-principal axes were estimated based on the orientation distribution functions reported in [58]. Deep zone semi-principal axes were assigned $a = 1$, $b = 1$, and $c = 5$, where $a$, $b$, $c$ define the $x$, $y$, $z$ lengths of the ellipsoid defining the fibril distribution. In the middle zone, the distribution was isotropic such that $a = 1$, $b = 1$, and $c = 1$. Finally, in the superficial zone, $a = 3$, $b = 1$, and $c = 1$. 
5.3 Results

Lagrange strain values are summarized in Table 5.1. Magnitudes of maximum and minimum (tensile and compressive) normal Lagrange strain ($E_{xx}, E_{yy}$), minimum Lagrange shear strain ($E_{xy}$), and maximum principal strains ($E_1, E_3$) were highest in the Discrete-2 model. Upon the introduction of two more discrete fibril bundles from Discrete-2 to Discrete-4, the strain magnitudes dropped and remained similar between Discrete-4 and Discrete-8. The exception to this trend was for the maximum shear strain, $E_{xy}$, which nearly doubled in both the Discrete-4 and Discrete-8 groups relative to the Discrete-2 group.

The strains observed in the Ellipsoidal model were relatively similar to those observed in the Discrete-4 and Discrete-8 groups, with the exception of the maximum shear strain $E_{xy}$, which was at a minimum compared to all models. Magnitudes of maximum and minimum (tensile and compressive) normal Lagrange strain ($E_{xx}, E_{yy}$), maximum and minimum Lagrange shear strain ($E_{xy}$), and maximum principal strains ($E_1, E_3$) were lowest in the Isotropic model. The most notable difference in strain distribution was observed in $E_{xy}$ where the maximum shear strain magnitude occurred in the middle zone of the articular cartilage for the Discrete-2 model and in the deep zone closer to the subchondral surface for all other models (Figure 5.3).

Table 5.1: Magnitudes of maximum and minimum normal ($E_{xx}, E_{yy}$), shear ($E_{xy}$), and principal ($E_1, E_3$) Lagrange strains observed in each fibril distribution model. Minimum $E_1$ and maximum $E_3$ are 0 in all models.
Contact pressure $p$ between the articular cartilage and rigid platen once the load was fully applied was the lowest in the Discrete-2 model ($p = 1.26$ MPa) and highest in the Isotropic model ($p = 1.59$ MPa). Contact pressure was nearly equal in the Discrete-4 and Discrete-8 models ($p = 1.42$ MPa and $p = 1.41$ MPa, respectively), and slightly lower in the Ellipsoidal model ($p = 1.33$ MPa). Contact area $A$ was approximately equal between all models. In the Discrete-4, Discrete-8, and Ellipsoidal models, $A = 0.78$ mm$^2$. In the Discrete-2 and Isotropic models, $A = 0.79$ mm$^2$ and $A = 0.82$ mm$^2$, respectively.

![Figure 5.3: Normal and shear Lagrange strain plotted for Discrete-2, Ellipsoidal, and Isotropic models.](image)

5.4 Discussion

One primary outcome from this study is the observation that the more isotropic distribution of collagen fibrils in the articular cartilage model led to lower strains overall, even while contact pressures at the surface remained generally equal. This finding suggests that models which do not include the specific collagen fibril orientation may be underestimating the strain through the depth of the tissue, even when the ground matrix stiffness varies through the depth.
The development of the collagen fibril orientation has been attributed to force distribution in the tissue, allowing collagen to properly support loads typically experienced by the joint [146,147]. Support for this idea has been observed in finite element models of the patellofemoral joint, which reported that calculated principal directions of normal stress mirrored the collagen orientation [61]. Maximum principal stress in the superficial zone was found to be tangential to the surface. In the deep zone, maximum principal stress was found to alternate between plus and minus 45 degrees relative to the normal direction of the subchondral bone as the contact area migrated across the surface, which supports the observed predominantly perpendicular collagen direction in this zone [61]. The same study employed an isotropic fibril distribution and was validated for contact area and contact pressure. This cartilage model was used in Chapter 2 to examine patellofemoral contact area with bendable osteochondral allografts. The present study emphasizes that while stress distribution during loading appeared to mimic the presumed collagen orientation in the tissue, and while the model was validated for contact pressure, it may not necessarily result in accurate depth-dependent strain values. Future work should focus on implementing a depth-dependent fibril distribution to these patellofemoral joint models. Only after an appropriate fibril distribution is prescribed and after experimental validation of the computational models, can the strain in the tissue, say during allograft bending, be analyzed.

Another primary outcome of the present study was the observation that a more discrete fibril distribution shifted the shear strain to the middle zone rather than the deep zone as seen in Figure 5.3 primarily for the Discrete-2 model. Fibril dispersion clearly affects not only strain magnitude, but also strain distribution throughout the tissue. This finding may also begin to provide insight into the relationship between compressive loading and cartilage fatigue failure. In Chapter 4 we found that cartilage failed under reciprocating compressive loading. We also found
that the primary mode of wear was fatigue failure in the form of delamination, which occurred between the superficial and middle zones. The present study applies a compressive load to the articular cartilage and found that when we explicitly model the collagen after the classical Benninghoff arcade-like structures, we observe that the maximum shear strain occurs in the middle zone, the same zone where delamination occurs during failure. It is important to note, however, that while the maximum shear strain is observed in the superficial and middle zones in the Discrete-2 model, strain itself is not a valid failure criterion since it is a kinematic state variable, not a function of state describing the material’s response, and no causation should be directly associated between the observation of maximum shear strain location and observed failure location. Instead, this observation should serve as an insight in developing future hypotheses relating fibril dispersion and failure criteria. A future study could investigate the hypothesis that fibril orientation and dispersion affect the fatigue failure location within articular cartilage, incorporating an appropriate stress-related failure criterion.

One limitation of the present study is the use of a biphasic material for cartilage instead of a multiphasic material. As discussed briefly in the introduction, one of the primary roles of collagen within articular cartilage is to restrain the swelling that occurs as the negatively charged proteoglycans attract ions, bringing water into the tissue. This will in turn cause the collagen to be under tension in its reference configuration. This initial tensile pre-stress will have an effect on the overall loading response of the tissue. However, in the present biphasic analysis, the collagen did not experience any tensile pre-stress. Furthermore, when comparing the results presented above to the experimental results reported in [3], we find that our strain values are much larger than the experimental results. This could be in part due to the lack of collagen tensile pre-stress in the tissue,
which would make the tissue stiffer as the bulk compressive loading initially needs to overcome the tensile forces.

The set of models presented in this study is the first step in developing a depth-dependent strain validated patellofemoral joint finite element model. This study provides insight into the importance of specifically modeling fibril distribution in the tissue, especially when considering strain in the set of results. The next step to developing a comprehensive cartilage material model is to implement multiphasic properties. Preliminary work has begun to incorporate non-ideal osmotic swelling [148] along with depth-dependent solid volume fraction and fixed charge density [149] to optimize the zonal ground matrix and fibril stiffness necessary to match the experimental stress-strain data of human patellar articular cartilage samples reported previously [150]. With sufficient fits, these material models for the top, middle, and deep zones of articular cartilage can be prescribed to our existing patellofemoral joint models described in Chapter 2 to try to replicate the experimental patellofemoral joint loading strain data reported previously [137].

5.5 Acknowledgments

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Chapter 6: Conclusion

6.1 Motivating Questions

As of 2019, there were 527 million prevalent cases of osteoarthritis globally, having more than doubled in 30 years [6]. The majority of osteoarthritis cases reported are in the knee (61% of all cases), followed by the hand (24%) and hip (6%) [6]. In the United States, annual total healthcare costs and lost wages due to osteoarthritis is estimated to be $45 billion and $1.7 billion, respectively [151]. Furthermore, there are no satisfactory clinical interventions to reverse, halt, or delay disease progression and the current standard surgical treatment, joint arthroplasty, or artificial joint replacement, is not suitable for all patients. Osteoarthritis places a heavy burden on society. The above dissertation presents two clinically translational projects and two basic science studies all with the overarching goal of minimizing patient pain and improving patient care. The two questions motivating this work included both “How can we better treat patients with severe osteoarthritis for whom joint arthroplasty is not an option?” and “What mechanical factors initiate articular cartilage degeneration?”

While artificial joint replacement, or arthroplasty, is generally a successful surgical technique, providing many patients with relief from pain and the ability to return to normal activities of daily living [62-66], it is not an appropriate solution for everyone. For example, many young patients will outlive the lifespan of the implant itself, requiring revision surgery for the already invasive operation which removed not only the arthritic cartilage, but a significant amount of the underlying bone. Often patients will be requested to endure the pain of living with osteoarthritis until more appropriate timing to receive an artificial joint. There are other cases of patients living with severe osteoarthritis in joints where a suitable surgical intervention does not exist. Such an example may be osteoarthritis in the finger joints, where standard treatment methods
are unsatisfactory when compared to other joints in the body [152-154]. Developing a solution as a way to minimize pain and delay the need for joint replacement, or as an alternative to unsatisfactory surgical methods, could have a significant impact on patient care and satisfaction. This dissertation presents a novel biological surgical technique, conforming osteochondral allografts, as a way to meet this clinical need.

Osteoarthritis is a multifactorial disease with compounding effects from mechanical, cellular, and biochemical influences [70-72]. The purpose of the final two specific aims presented in this dissertation was to isolate the influence of specific mechanical factors that affect cartilage wear and damage. While it is clear that impacts or traumatic injuries to the joint will frequently lead to osteoarthritis [8,88], it is less clear how osteoarthritis initiates due to normal wear and tear that comes with time. Previous studies have shown that cartilage fails in fatigue [51,53,76]. We sought to determine specifically what kind of mechanical loading leads to fatigue failure in articular cartilage. We also sought to determine the functional role of collagen fibril orientation on mechanical loading and strain distribution, which presumably has an important effect on fatigue failure. This final aim was addressed using computational modeling as a tool for isolating and investigating specific influences of the types of fibril distributions used.

6.2 Work Performed, Significant Findings, and Future Directions

The work performed in this dissertation addresses the ongoing search within the field of orthopedics to better understand and treat osteoarthritis. The studies presented above sought to further progress the field by contributing novel insights into existing and new clinical treatments as well as new discoveries in regard to articular cartilage wear mechanics. The work performed and significant findings of each study are summarized below.
6.2.1. Bendable osteochondral allografts for patellar resurfacing: a finite element analysis of congruence

We investigated the feasibility of using bendable osteochondral allografts to treat osteoarthritis of the patella. The curvature of articular cartilage can be manipulated by giving bending flexibility to the cartilage. Bending can be achieved by machining grooves in the underlying bone of an osteochondral allograft to just reveal the subchondral surface of the articular cartilage [1,2]. The ability to safely bend articular cartilage to match the host site presents the potential of better allograft matching and provides more flexibility with respect to donor anatomy.

6.2.1.1. Work Performed

This aim was addressed by investigating how bending the surface of a patellar osteochondral allograft changes patellofemoral joint congruence relative to a non-bent allograft. Specifically, finite element analysis was used to model the patellofemoral joint with a native patella, a patellar osteochondral allograft, or a bendable patellar osteochondral allograft. Models generated from actual human anatomy allowed accurate congruence predictions and comparisons between different patellar configurations. While previous studies have examined contact mechanics of the native patellofemoral joint using finite element analysis [61,155-158], this work was the first to investigate how osteochondral allograft implementation affects contact mechanics. Understanding how the current fresh osteochondral patellar allograft resurfacing (FOPAR) technique changes patellofemoral joint congruence relative to the native anatomy can elucidate whether the common hesitancy in recommending the FOPAR procedure, even without bending, is warranted. More importantly, this study aimed to investigate the advantages of patellar osteochondral allograft adaptability and whether congruence between a bendable osteochondral allograft and host femur can reproduce native patellofemoral joint congruence. The ability to
manipulate the articular cartilage surface curvature during the surgical procedure would provide a novel patient-specific adaptability that current procedures lack.

6.2.1.2. Significant Findings

One primary outcome was the finding that unbent, size-matched patellar allografts produced contact areas that were not statistically different from those of the native patellae for the three patellofemoral joints studied, suggesting that two-dimensional size-matching of patellar allografts may be sufficient for the purpose of matching surface contours for functional joint congruence. Another significant outcome of the study was the finding that bendable patellar allografts produced equally good congruence as native joints, as assessed by contact areas. Grooved patellar OCAs can provide additional flexibility to the articular cartilage surface, allowing the allograft to conform to the shape of the native femoral trochlea. The outcome of this biomechanical study produced encouraging results, motivating us to pursue future cadaveric investigations of this surgical procedure, in an effort to validate the conclusions from the finite element modeling results, and to identify surgical challenges and how they may be resolved.

6.2.1.3. Future Directions

This study did not include an investigation of other metrics such as cartilage strain or fluid pressure, primarily because the results would have been speculative in nature in relation to how they may affect chondrocyte viability or mechanotransduction. At the present, these responses cannot be resolved from computational studies. However, upon the development of a material model which accurately represents the strain distribution through the depth of the tissue, computational results may elucidate valuable information about chondrocyte viability based on applied strain. One future direction could include expanding on this work and the work described in Chapter 5 to develop a strain-validated material model.
Cadaver studies have been recently completed to validate the results of the described computational models [116]. Additionally, separate studies have investigated chondrocyte responses to machining and sustained bending, showing high levels of chondrocyte viability [115]. The next steps include an animal study, which has been recently initiated, to investigate the surgical viability of this procedure. Upon the completion of the animal study, all the results of the related studies mentioned, including the computational study presented in this dissertation, will be analyzed in the context of one another in anticipation of a future clinical trial. Prior to any clinical trial, the final step to validate the end-to-end surgical procedure will include practicing various anchoring methods in cadaver models to ensure the appropriate surgical techniques and tools, such as using compression screws, pins, or bone cement, are utilized to successfully bend and anchor the patellar osteochondral allograft.

6.2.2. Surgical tool for manipulating osteochondral allografts

Previously, a novel technique was developed which involves obtaining osteochondral tissue from the femoral trochlea of a donor knee, machining grooves in the underlying bone, and bringing the bone struts together to bend the articular cartilage surface [2]. Bending the articular surface conforms the femoral trochlea osteochondral allograft to better match the surface curvature of the trapezium. While this development introduced a novel surgical technique to treat osteoarthritis in the thumb, the clinical application was limited due to the lack of appropriate surgical tools.

6.2.2.1. Work Performed

We developed a forceps-like surgical tool whose purpose was to bend and manipulate bendable osteochondral allografts developed for the trapezium in the carpometacarpal joint of the thumb. Standard tools were not able to successfully bend and hold the allograft while trimming it
to size and inserting the screws and anchors necessary to fix the allograft in its bent configuration within the carpometacarpal joint. Therefore, it became necessary to design and manufacture a custom tool which could meet the requirements of the surgical procedure, including the following: bending the osteochondral allograft by bringing the bone struts together, properly drilling the K-wire through the bone struts to ensure safe screw alignment, inserting the compression screw through the bone struts with the allograft in the bent configuration, and securely clamping the allograft during manipulation such as trimming, anchoring, or transplantation. This project included design iterations of the forceps-like custom surgical tool, finite element analyses to determine potential failure locations, appropriate choice of material which was compatible with sterilization procedures, and managing the manufacturing of all prototypes and final versions of the custom tool.

6.2.2.2. Significant Findings

A custom forceps-like device was developed specifically for the bendable osteochondral allograft procedure for the carpometacarpal joint. In addition to the standard forceps features such as knurling on the jaws to grip the allograft and a position locking mechanism, the Approximator, so the custom tool was named, includes the following unique features:

- Angled jaws to clamp the allograft in the bent position
- K-wire insertion hole and separate K-wire insertion guide to ensure proper alignment of the K-wire with respect to the allograft bony substrate
- Separate compression screw hole to allow screw to be inserted while clamping the allograft
- Height of jaws matching ideal height of allograft for easy measurements
- Flat surface on bottom of jaws to act as a trimming guide to remove excess bone
The Approximator was manufactured from autoclavable surgical-grade stainless steel in order to be sterilized to use in upcoming clinical trials. The patent for this tool was filed on October 22, 2019 and issued on September 30, 2021.

6.2.2.3. Future Directions

The next step in this project is to begin clinical trials using bendable osteochondral allografts for the trapezium and determine whether the current tool is suitable or whether modifications or additional tools need to be developed. A preliminary design was created which keeps the jaws parallel during clamping so that an oscillating saw can rest flush against the clamped tool to trim the allograft shorter while it is held in the bent configuration (see patent Figure 8, uspto.gov). Additional preliminary designs have been developed which incorporate an in-plane or out-of-plane bend at the jaws to allow for better access to the joint while the jaws are clamped in place holding the allograft (see patent Figures 10 and 11, uspto.gov).

6.2.3. Immature bovine cartilage wear is due to fatigue failure from reciprocating compressive forces and not reciprocating frictional forces

Previous work has discussed various mechanisms of cartilage wear in isolation [54,76-80], but none have examined the hypothesis that fatigue failure is produced by reciprocating compressive forces, and not reciprocating frictional forces. Therefore, we investigated the specific mechanisms of immature bovine articular cartilage fatigue failure.

6.2.3.1. Work Performed

Friction tests were conducted to investigate wear mechanisms in articular cartilage. This study tested immature bovine articular cartilage against glass in both a migrating contact area (MCA) and stationary contact area (SCA) configuration. A static load was added to the friction testers in both the MCA and SCA set-ups. However, because the cartilage samples in a MCA
configuration were larger than the contact area itself, as the MCA sample slid underneath the load, the loading area migrated across the sample, applying compressive loading/unloading to each contact area along the travel path. Subsequently, samples in the MCA configuration experienced reciprocating compressive stresses in addition to reciprocating shear from frictional sliding, while the samples in the SCA configuration, whose contact area never changed, experienced reciprocating frictional forces only. Cartilage samples were submerged in either a saline or synovial fluid bath during testing. The experimental protocol was designed to apply approximately equal contact pressures between MCA and SCA groups to eliminate contact pressure as a possible reason for the observed results. The goal of this study was to investigate whether cartilage fatigue failure occurred due to compressive loading or due to frictional sliding.

### 6.2.3.2. Significant Findings

The primary outcome of this study was that fatigue failure in immature bovine articular cartilage does not occur due to frictional forces. Rather, cyclic compressive loading resulted in consistent and significant delamination between the superficial zone and middle zone of the articular cartilage. Surface delamination was clearly visible upon inspection, confirmed with polarized light microscopy, and quantified using surface laser scanning. This outcome was observed regardless of testing bath (saline or synovial fluid), however synovial fluid appeared to delay the onset of cartilage wear. The results of this study suggest that physiologic loading in a migrating contact area configuration can lead to fatigue failure in the form of delamination because of the cyclic compressive forces applied to the tissue in this type of sliding configuration. This finding also suggests that articular cartilage must have a normal maintenance mechanism to protect against fatigue failure that would occur from normal wear and tear from millions of loading cycles over the course of a lifetime.
6.2.3.3. Future Directions

Follow up studies for this work are already underway. Future studies will include investigating whether immature bovine articular cartilage will exhibit delamination reliably after a specific number of cycles when submerged in synovial fluid, such as was observed for samples submerged in saline (i.e. 5,400 cycles for saline). This will be done by performing more friction tests in synovial fluid using the same experimental setup presented in Chapter 4 at increasing cycle counts (i.e. 10,800 cycles, 16,200 cycles, etc.) until damage is consistently observed.

One limitation of the present study was the immaturity of the tissue being used. Immature articular cartilage is more vulnerable to damage and, while this is a desirable characteristic for a more efficient experimental wear study, it is important to determine whether the theory developed in our immature bovine study is still valid in mature tissue. We will want to carry out the same testing protocol using mature bovine tissue, followed by mature human cartilage, to validate whether wear is initiated by reciprocating compressive loading.

Finally, computational studies can be performed to replicate the experimental setup discussed above to further isolate and examine the influence of friction on cartilage damage. Developing a proper fibril distribution model for articular cartilage that has been validated against experimental results would allow us to perform the same experiments in silico to compare the effect of compressive loading via sliding without friction to compressive loading via sliding with friction. This computational model could also be used to examine molecular diffusion from synovial fluid into the articular cartilage tissue and examine whether the diffusion of these molecules could protect the collagen from wear initiation.
6.2.4. Importance of fibril distribution in modeling of Benninghoff arches in articular cartilage

Lastly, we investigated the effects of fibril distribution models used in finite element analyses. Previous studies have included collagen fibrils by modeling discrete fibril bundles as horizontal springs [138-140], discrete arcade-like structures after Benninghoff’s observations [4,141], continuum or membrane elements with varying orientation through the tissue [142], or isotropic fibril distributions [61,136,143]. We hypothesize that modeling the specific fibril distribution of articular cartilage is necessary to producing accurate depth-dependent strain results. This study focused on examining the differences between modeling discrete fibril bundles and continuous fibril distributions.

6.2.4.1. Work Performed

Finite element models were created to approximate a bovine humeral head and replicate the loading conditions described in [3]. Five different finite element analyses were run, each using a different fibril distribution model. Three of the models used discrete fibril bundles, which were aligned perpendicular to the subchondral surface in the deep zone and arched through the middle and superficial zones to align tangent to the articular surface at the surface. One of the discrete models included two fibril families (Discrete-2), which followed the positive and negative local x-directions at the articular surface. The second discrete bundle model (Discrete-4) included four fibril bundles which arched through the middle zone and aligned with the positive and negative local x-directions and the positive and negative local z-directions at the articular surface. The final discrete bundle model (Discrete-8) included the four bundles from Discrete-4 and an additional four bundles which were rotated 45 degrees about the local y-axis. The final two finite element models used continuous fibril distributions. One used an isotropic distribution whose fibril
distribution was equal in all directions for each zone, while the other employed a depth-dependent ellipsoidal distribution. Load was applied to the subchondral surface to compress the cartilage tissue against a rigid platen and Lagrange strain, contact pressure, and contact area were analyzed.

6.2.4.2. Significant Findings

Two primary findings arose from this study. The first was the discovery that as the fibril distribution became more isotropic, the strain throughout the tissue decreased, even though the contact area between the articular surface and rigid platen remained relatively equal across distribution models. This suggested that computational models which approximate the collagen fibrils with an isotropic distribution may be underestimating the strain through the depth of the tissue. The second primary finding was that in the Discrete-2 model, which followed the classically described Benninghoff structure, the greatest magnitude of shear strain during compressive loading was observed in the middle zone. This observation suggests that the fibril distribution model not only influences strain magnitudes, but also has an effect on strain distribution through the thickness of the cartilage tissue model.

6.2.4.3. Future Work

This study is the first of a series, which seeks to elucidate the most accurate fibril dispersion about each cartilage zone’s preferential axis. The current study provides the groundwork and increased understanding for how to move forward with this overarching task. However, before choosing whether to model articular cartilage with a discrete or continuous fibril distribution, the biphasic study performed here should be converted to a multiphasic study, which includes depth-dependent fixed charge density and water content. This implementation will incorporate the appropriate tensile pre-stress of the collagen fibrils as they restrain tissue swelling. Preliminary work has been started on this by using previously published experimental results from human
patellar cartilage to develop appropriate cartilage models for the top zone (top 1/3 of the cartilage tissue), middle zone, and deep zone [148-150]. The next step will include combining these models to create a full-thickness cartilage model.

The results presented here can be used as preliminary data influencing the development of a patellofemoral joint model. This full patellofemoral model could be used for multiple future studies. The first study should be to validate the depth-dependent strain in the tissue by matching the two-dimensional experimental strain results reported in [137]. Once strain-validated, this model could be used to expand the study described in 6.2.1 examining bendable osteochondral allografts, potentially incorporating a strain-based chondrocyte viability model. This model could also strengthen the work described in 6.2.3 by providing a computational model which could eliminate the contributions of friction during sliding of cartilage against glass to further investigate the influences of friction and of bulk compressive loading on fatigue failure.

Aside from strengthening the work described in this thesis, an accurate depth-dependent strain patellofemoral joint model could be used to investigate the potentially protective effects of viscoelasticity during traumatic injury. For example, the previously described patellofemoral joint computational model could be developed with the incorporation of a viscoelastic damage model [159,160] to replicate the experimental study described in [161], during which an impact is applied to the patellofemoral joint at different speeds and damage is assessed. The benefit to using a computational model is that speed and impact energy can be decoupled from one another, whereas this cannot be done sufficiently during an experiment.

### 6.3 Conclusion

This dissertation aimed to contribute to the ongoing search for improved osteoarthritis treatments to reduce patient pain. In addition to the design and development of novel clinical
practices to improve patient care, treating osteoarthritis also requires a thorough understanding of
the mechanics of articular cartilage both as an engineering material and as a biological tissue.
Bendable osteochondral allografts may be the key to expanding the use of osteochondral allografts
and either delaying the need for artificial joint replacements, or providing a suitable solution when
joint arthroplasty is not an option. Investigating the mechanics of tissue fatigue failure contributes
to and strengthens our current understanding of cartilage wear and subsequent onset of
osteoarthritis by shifting the focus away from friction-induced wear. Finally, the development of
a comprehensive and accurate cartilage material model can strengthen each of the previously
discussed studies.
References


150. Chahine, N.O., Multi-scale measurements of the mechanical and transport properties of native and engineered articular cartilage. 2006, Columbia University: Ann Arbor, MI.
Appendix A: Approximator Engineering Drawings

The following pages include a copy of the final engineering drawings for the Approximator surgical tool discussed in Chapter 3. These drawings were created in Solidworks by Courtney A. Petersen (Courtney A. Shaeffer at the time the drawings were completed) and reviewed by Gerard Ateshian. These drawings, along with the 3D CAD solid models of the Approximator and its associated parts, were used by Andrei Shylo to manufacture the Approximator tool.
APPROXIMATOR

1. Bottom Shank
2. Top Shank
3. Lock Pin
4. Wire Guide
5. Stepped Pin
6. Thumb Wheel
7. Threaded Rod

Dimensions in Inches
- Laser Weld Stepped Pin to Bottom Shank
- Laser Weld Lock Pin to Top and Bottom

Material: 400 Stainless Steel
Finish: Bead Blast to Satin Matte
Angle: 0.1°

Notes:
- Do not scale drawing
- Weight:
  - Laser weld stepped pin to bottom shank
  - Laser weld lock pin to top and bottom
  - Angle ±0.1°

COLUMBIA UNIVERSITY MBL

Scale 1:1
Sheet 1 of 12
COLUMBIA UNIVERSITY MBL

TOP SHANK

DIMENSIONS IN INCHES

[Table format with dimensions and notes]

NAME  DATE  DRAWN  CHECKED  ENG. APPROV.  Q.A.

REVIEW SHEET 10 OF 12

SCALE 1/1
Appendix B: Approximator Machining Notes

The following set of notes are references which were used by Andrei Shylo and Courtney Petersen during the manufacturing of the Approximator surgical tool. These notes are informal in nature and included only as a general reference for the step-by-step manufacturing process.

Tormach 1: Machine shop’s Tormach, left machine
Tormach 2: Ateshian lab’s Tormach, right machine

*Double check that the code is edited to run the pin operation before anything else*
*Keep watch of coolant to make sure enough pressure to clear chips*
*Use round cap head screws since they are lower profile for all but last operation where countersunk screws are also used*

Turn on machine:
- Check that wall power is on
- Flip side power switch on machine (red switch on right hand side of switch board toward the bottom)
- Let computer power up
- Pull out e-stop
- Press start
- Ref Z, Ref X & Ref Y

Before running program:
- Ref Z, Ref X & Ref Y
- Set x = 0, y = 0 to top left corner of jig (use edge finder and smallest step increments)
- Set z = 0 to jig surface (use paper technique)
- Check that coolant hose pointed at tool

Load G-Code:
- Plug in USB to port on right side toward the front of Tormach base (about 1.5 feet off the ground)
- Open File tab
- Under USB section (in middle), look for file
- If nothing shows up, click USB button and check USB connections in corner of machine with cables
- Under left hand section on screen, navigate to folder where you want to save the file
- Click on file from USB and choose left pointing arrow to transfer from USB to Tormach computer
• Click on file once mounted on computer and choose “Load G-Code”

0. Setup 420 stainless steel in Tormach 1
   a. Cut to be 7.5” x 3” (width of ordered material)
   b. Using parallels, clamp in vice, hit with mallet so that parallels don’t move
   c. Reference to upper left corner
1. Run Pin Setup (Tormach 1)
   a. #43 - ¼” end mill: cuts out pins
   b. Put pins in tumbler and let tumble through rest of operations (check periodically to make sure they don’t get tumbled too much)
2. Flycut 420 SST to be perfectly parallel and correct thickness (Tormach 1)
   a. 6 mm thickness
   b. Fly cutter with carbide inserts
   c. Change gear ratio so high torque, low speed
   d. 0.002 step down
   e. 1000 rpm
   f. 20 inches/min
   g. Run with coolant (close doors)
3. Re-zero z-height now that material is correct thickness (Tormach 1)
   a. Use #48 - ⅜” tool (make sure #48 is selected before re-zeroing)
   b. Use paper moving method
4. Run op. Vice Setup for Holes Stainless (Tormach 1)
   a. #48 - ⅜” end mill: cut joint recesses
   b. #40 - center drill: center drill screw holes
   c. #41 - ⅛” drill: drill screw holes
   d. #49 - 7/32” ball end mill: joint recess inner fillets
5. Setup material in Tormach 2
   a. Screw down stainless to jig in Tormach 2
   b. Make sure to use the proper set of 4 holes
   c. Double-check that jig is referenced correctly (x, y, z = 0 at top left corner)
   d. Double-check all tool heights (!!)
   e. Double-check that all tools are tightened (!!)
6. Run Op_1 (Tormach 2)
   a. #43 - ¼” end mill: contours
   b. #45 - 0.062 corner rounding end mill: outside edge radii/fillets
      i. Check to see if edges look good or if height needs to be adjusted
   c. Take off all extra material from around the tools (everything that’s not the tool itself should come off - may need to use a blade to cut through the skin)
      i. Save this extra material for Step 11
   d. #46 - 20˚ taper: taper first side of each jaw
7. Remove shanks from jig and debur everything
8. Run Op_2 (Tormach 2; back left recess jig)
   a. Put both shanks in recesses at the same time; flat faces should be flush against the bottom
      i. Top shank is in back recess (handle down) - push jaw to back right corner of recess
ii. Bottom shank is in front recess (handle up) - push jaw to front right corner
iii. First, screw outer screws with washer, keep loose
iv. Next, screw inner screw with washer and tighten really tight (make sure washer is centered; might need to wiggle a bit to make sure it tightens properly)
v. Tighten outer screws (make sure washers are centered)

b. #44 - ⅛” end mill: slot
c. #50 - center drill: center drill for guide wire hole
d. #51 - No. 39 drill: drill guide wire hole

9. Setup for next ops
a. Remove from recess jig
b. Move shanks to original spots on jig (“Top” shank goes in the front)
c. Flip shanks so the joint recess is facing down and the flat side is facing up
d. Insert screws in center hole at pivots
e. Insert screws in hole at handles
f. (Should have 2 screws on each shank at this point)

10. Run Op_3_radius
a. #45 - 0.062 corner rounding end mill: edge radii/fillets (check to see if radius looks good or if height needs to be adjusted before moving on to next step)

11. Adjust fixtures
a. Sand tool without removing from jig (if needed)
b. Screw on 3 fixture plates (2 on “Top” shank located in front of jig, 1 on other shank located in back of jig)
c. Screw in 3 jaw supporting screws (1 on “Top” shank, 2 on other shank)
i. Use gage blocks (stacked to 0.263”) or spare material from Step 6 to support screws
d. Remove screw from “Top” shank (located in front of jig) at the center joint (!!)

12. Run Op_3_second
a. #43 - ¼” end mill: inner handle contours (cuts out extra material from inside handles)<- what do you mean? That the operation cuts out the extra material?
b. #45 - 0.062 corner rounding end mill: inner handle radius (check to see if radius looks good or if height needs to be adjusted before moving on to next step)
c. #44 - ⅛” end mill: pin recess
d. #40 - 20° taper: taper other side of jaws (carefully watch and reduce feed rate if needed, especially when coming around curve) *i’ve reduced them in code, we’ll need to check if it runs ok though.
e. #52 - diamond engraving tool: write word “TOP” on “Top” shank *see if its deep enough and if not we can adjust the spring tension and try again.

13. Setup for knurling op.
a. Remove shanks from jig and debur everything
b. Clean tools (!!) and jig (!!) with Simple Green degreaser (green degreaser found hanging at front of machine shop)
c. Glue into front left recess jig so both handles are up
i. Use 2P.10 glue and activator (glue on jig, activator on jaw, press firmly together, spray more activator)

14. Run Op_4_back (double check tool height!)
a. #53 - engraving bit: knurling
b. Check if looks good or if need to adjust height
15. Run Op_4_front (doesn’t matter if back or front is ran first)
a. #53 - engraving bit: knurling
b. Check if looks good or if need to adjust height
   i. Note that knurling required checking, possibly tweak the depth and running the operation multiple times
16. Deburr jaws and anything else that needs to be deburred
17. Tumble pins in tumbler
18. Weld shanks and pin together (double check that correct orientation with knurled jaw faces facing each other)
a. Have Andrei weld
19. Polish welding mark and anything else that needs it (Dremel polishing attachments)

Notes on the slot:
- Fusion won’t let you machine a slot that’s exactly 1/8” (for example) with a 1/8” tool. So, Andrei told Fusion that the tool was 0.124” instead of 0.125”, but still used 0.125” end mill.
- Normally, really important to input actual tool & tool holder geometry bc Fusion will show you where collisions/interferences occur.