Mechanical Comparison of a Type II External Skeletal Fixator and Locking Compression Plate in a Fracture Gap Model

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ABSTRACT (ACADEMIC)

The purpose of this study was to compare the stiffness of a Type II external skeletal fixator (ESF) to a 3.5 mm locking compression plate (LCP) in axial compression, mediolateral, and craniocaudal bending in a fracture gap model. The hypothesis was that the Type II ESF would demonstrate comparable stiffness to the LCP. A bone simulant consisting of short fiber reinforced epoxy cylinders and a 40 mm fracture gap was used. The LCP construct consisted of a 12 hole 3.5 mm plate with three 3.5 mm bicortical locking screws per fragment. The Type II ESF construct consisted of 3 proximal full fixation pins (Centerface®) per fragment in the mediolateral plane, and 2 carbon fiber connecting rods. Five constructs of each were tested in non-destructive mediolateral and craniocaudal bending, and axial compression. Stiffness was determined from the slope of the elastic portion of force-displacement curves. A one-way ANOVA and a Tukey-Kramer multiple comparisons test were performed, with significance defined as $p < 0.05$. In mediolateral bending, the stiffness of the Type II ESF (mean ± standard deviation; 1584.2 N/mm ± 202.8 N/mm) was significantly greater than that of the LCP (110.0 N/mm ± 13.4 N/mm). In axial compression, the stiffness of the Type II ESF (679.1 N/mm ± 20.1 N/mm) was significantly greater than that of the LCP (221.2 N/mm ± 19.1 N/mm). There was no significant difference between the constructs in craniocaudal bending. This information can aid in decision-making for fracture fixation, although ideal stiffness for healing remains unknown.

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ABSTRACT (PUBLIC)

Optimum fracture stabilization requires a balance between providing a stable mechanical environment and preserving the blood supply to healing tissues. When the complexity of a fracture precludes reconstruction of the bony column, the fixation method chosen for repair must counteract the forces of weight bearing, including compression and bending. Knowledge of the relative construct stiffness is important for a clinician to determine the ability of a fixation technique to withstand all forces acting on a fracture, while supporting bone healing. The purpose of this study was to compare the stiffness of a Type II external skeletal fixator (ESF) and a locking compression plate (LCP) when non-destructive physiologic loads are applied in axial compression, mediolateral bending, and craniocaudal bending. Five constructs of each were tested in non-destructive mediolateral and craniocaudal bending, and axial compression. Stiffness was determined from the slope of the elastic portion of force-displacement curves. There was a significant difference between the stiffnesses of the Type II ESF and the LCP in all modes of loading except craniocaudal bending. The Type II ESF was significantly stiffer in mediolateral bending than the LCP, and the Type II ESF was significantly stiffer in axial compression compared to the LCP. There was no statistically significant difference in stiffness in craniocaudal bending. This information will aid a clinician in selecting an appropriate fixation method for a non-reconstructable fracture, but further studies are required to assess the importance of increased stiffness in a clinical setting.

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LIST OF ABBREVIATIONS

AMI	Area Moment of Inertia
ANOVA	Analysis of Variance
ASTM	American Society for Testing and Materials
AO	Arbeitsgemeinschaft für Osteosynthesefragen
ASIF	Association for the Study of Internal Fixation
BMPs	Bone Morphogenetic Proteins
BMP-2	Bone Morphogenetic Protein 2
BMP-7	Bone Morphogenetic Protein 7
DCP	Dynamic Compression Plate
ESF	External Skeletal Fixator
GAGs	Glycosaminoglycans
GPa	Gigapascals
IL-1	Interleukin-1
IL-6	Interleukin-6
KE	Kirschner-Ehmer
LC-DCP	Limited Contact Dynamic Compression Plate
LCP	Locking Compression Plate
LVDT	Linear Variable Differential Transformer
MSCs	Mesenchymal Stem Cells
m	Meters
m^2	Meters^2
mm	Millimeters
mm^2	Millimeters^2
MIPO	Minimally Invasive Plate Osteosynthesis
MTS	Materials Testing System
N	Newtons
PDGF	Platelet Derived Growth Factor
PC-Fix	Point-Contact Fixator
PGE_2	Prostaglandin E_2
RNA	Ribonucleic Acid
TGF-β	Transforming Growth Factor β

Chapter 1: Background Information and Literature Review

1) Bone Anatomy: Structure and Function

a. Histologic Anatomy

Bone is a unique composite tissue that is composed of both organic and inorganic materials[1,2]. Histologically, it consists of mainly collagen, which prevents tensile fracture, and hydroxyapatite, which prevents excessive deformation of the collagen and provides compressive strength[2]. An additional important part of bone anatomy to consider is the periosteum. The periosteum consists of an inner osteogenic layer, called the cambium layer, which invests the outer surface of the bone, and an outer fibrous sleeve, which carries the vascular and nerve supply[3-7]. The cambium layer serves as an important source of pluripotential mesenchymal stem cells (MSCs), particularly in situations of fracture healing[8-11].

b. Osteon Structure and Bone Properties

The fundamental unit of cortical bone is the osteon, part of the Haversian system, with a central canal through which the vascular and nerve supply as well as lymphatic channels pass[6]. Bone is deposited in concentric layers of mineralization around the central canal, and a cement line of glycosaminoglycans (GAGs) surrounds each Haversian system[6]. Osteons form in two fashions: primary or secondary. Primary refers to appositional bone growth, which occurs during skeletal immaturity, where osteons form nearly parallel to the longitudinal axis of the bone[6]. Secondary osteon formation occurs throughout life with bone deposition and remodeling, where concentric rings of lamellar bone are deposited on the trailing edge of cutting cones[6]. Cutting cones are composed of osteoclasts and osteoblasts, and are described later in the chapter. The bone of the cortex is made up of longitudinally compact Harversian systems, with a porosity, or ratio of volume of open space to total bone volume, of 5-30%, while cancellous bone is composed of less compact Haversian systems with a porosity from 30% up to 95%[1,2,12]. When discussing long bones, cortical bone is stiffer and stronger when loaded longitudinally versus transversely and stores more energy with rapid loading[12]. Cancellous bone is more compliant, with lower stiffness and a longer plastic phase in compression, whereby although progressive collapse can occur, the energy absorbed can exceed that of cortical bone[12]. Bone strength ultimately varies according to osteonal type and load orientation, as compressive strength comes from a transverse collagen fiber orientation and tensile strength from longitudinal collagen fiber orientation[12]. This heterogeneous nature of osteon arrangement contributes to the anisotropic and viscoelastic nature of bone[1,2,12]. Anisotropy refers to bone having different mechanical properties when loaded in different axes, meaning the strength and stiffness are related to the direction of loading[1,2]. The strength and stiffness are greatest when bone is loaded parallel to the orientation of osteons, hence long bones tend to resist loads better if loaded longitudinally to the axis of their diaphysis[2]. Viscoelasticity is a time dependent phenomenon whereby the rate of loading of bone affects the total energy absorbed, as in a higher rate of loading leads to higher strength and higher energy absorbed before fracture[1,2,12]. The clinical significance of this property is that higher velocity injury leads to increased energy release, bone fragmentation, and surrounding soft tissue trauma, and ultimately a bone is "stronger" when loaded rapidly[2,12].

c. Cell Types

There are multiple cell types found in bone, including osteocytes, osteoblasts, and osteoclasts. These are considered osteogenic cells, which are responsible for bone turnover and remodeling[6]. Osteoblasts originate from undifferentiated MSCs from the periosteum, bone marrow, and endosteum[4,7,13,14]. Their main function is to deposit osteoid, an unmineralized structural scaffold, which is made up of mostly type I collagen, proteoglycans and GAGs[6]. The organic matrix secreted provides a framework for the accumulation of inorganic soluble crystals, mostly calcium and phosphorus, but also sodium, magnesium, iron, and others[6]. In bone healing, osteoblasts form the tail end of “cutting cones” and deposit osteoid across fracture lines[15]. They also regulate the transport of extracellular substrates, such as calcium and phosphorous, to the osteoid boundary to facilitate subsequent mineralization[6]. A subset of osteoblasts will becomes osteocytes after becoming completely encased in the matrix[7]. Osteocytes function to maintain the surrounding matrix and control the extracellular concentrations of calcium and phosphorus[4,6]. They communicate via cytoplasmic processes that radiate outward via canaliculi and generally have fewer energy utilizing organelles, such as endoplasmic reticulum, and more lysosomes compared to their osteoblast ancestors[6]. Osteoclasts are large, multi-nucleated cells that originate from pluripotent bone marrow cells and are found in groups near the surface of the bone, called Howship’s lacunae[4,6,7]. Their form follows their function of bone resorption, with a ruffled border whose contractile proteins facilitate attachment to the bone surface, and they secrete collagenase and other degradative proteins, as well as transforming growth factor-β (TGF-β)[6,7]. Osteoclasts form the front end of “cutting cones” during direct bone healing, creating channel to be ultimately filled by osteoid deposited by osteoblasts[15]. Bone resorption plays a pivotal role in the initial phases of fracture healing, and ultimately the balance between resorption and deposition forms the basis of fracture remodeling.

d. Blood Supply and Biologic Considerations

Optimal fracture fixation requires an understanding of the inherent biologic environment. This can be divided into the patient's systemic biologic environment and the local biologic environment, or the fracture site[16]. Systemically, many factors can influence bone healing, such as growth factors and hormones, nutrition, pH, oxygen tension, and the electrical environment[17]. The local biologic environment also asserts influence, in terms of blood supply to the bone and the condition of the surrounding soft tissues[16]. The afferent blood supply to bone consists of the nutrient artery, which supplies the medullary cavity and inner 2/3 of the cortex, metaphyseal arteries, and periosteal arteries, which supply the outer 1/3 of the cortex[1,2,6]. The nutrient artery travels through the cortex and into the medullary cavity, where it divides into ascending and descending branches[6]. These further branch into arterioles, which enter the cortex and supply the Haversian systems[6]. The proximal and distal metaphyseal arteries tend not to play a large role in intact bone, but can hypertrophy to assume cortical blood supply if there is damage to the nutrient artery, such as in a fracture[2,6]. Periosteal arterioles run longitudinally within the periosteum of young animals, but atrophy with skeletal maturity, resulting in bone surface contact only at points of fascial or ligamentous attachment[6,18]. An extraosseous blood supply is derived from the surrounding soft tissues to supply the fracture callus and cortical bone, which is paramount in the initial stages of fracture healing until the intramedullary supply is re-established[2,12]. It is vital to preserve any remaining intrinsic bone supply while also encouraging extraosseous blood supply by limiting soft tissue damage and periosteal stripping during fracture repair[12].

e. Mechanical Environment and Strain Theory

The influence of the mechanical environment on bone healing and the indications for fracture fixation can be described via interfragmentary strain theory. Strain theory refers to the notion that a tissue cannot be produced under strain conditions that exceed that tissue's capacity for elongation before rupture[2,19]. A changing mechanical environment will favor differentiation of tissue compatible with the next phase of healing, and it has been suggested that cell fate is determined within 3-4 days of fracture [20,21]. Pluripotential cells are responsive to local deformation within the fracture gap[2]. Granulation tissue can withstand 100% deformation before failure, thus can form in a high strain environment[1,2,16]. Cartilage will form in a <10% strain environment[1,2,16]. Osteoblasts require a low strain, <1-2%, so ossification requires stabilization of the fracture gap and progressively stiffer tissue in a callus[1,2,12,16]. Conditions can vary within a fracture callus such that the external callus ossifies first to bridge the fracture gap and provide a lower strain environment, which then allows ossification of the interfragmentary tissue[16,22,23]. There are naturally occurring mechanisms undertaken to decrease strain at the fracture gap. Osteoclasts will facilitate resorption of cellularly dead bone at fragment ends to increase interfragmentary distance, which will decrease the amount of local strain[2,12]. In addition, granulation tissue will become increasingly fibrous during the formation of callus to reduce the movement between fracture fragments, thereby enabling survival of tissue with lower deformation tolerance and increased inherent stiffness[2,12]. These natural mechanisms are augmented by surgical implants, which will provide stability to further decrease interfragmentary movement and deformation, but attention must be paid to also minimizing vascular injury[2].

2) Bone Healing and Fracture Fixation

a. Direct (Primary) Bone Healing

Primary bone healing refers to direct bony union with no formation of intermediate callus[12]. This is also referred to as primary osteonal reconstruction[2]. This requires anatomic alignment of fracture fragments and absolute stability[2]. There is less contribution from the periosteum in direct cortical healing; osteoprogenitors come from perivascular sites[24]. Generally, this can only occur at areas of contact or with a very small fracture gap and there is no vessel ingrowth[2,16]. The two manifestations of direct bone healing are "contact healing" and "gap healing".

i. Contact Healing

Contact healing occurs in areas where there is no gap, and thus no interfragmentary motion, which leads to an environment with minimal strain[2,12]. With direct contact, osteonal remodeling occurs directly across the fracture plane and results in longitudinally oriented osteons[2,12]. This occurs by the formation of "cutting cones". Osteoclasts form the front part of the cutting cone and move across the fracture line to create longitudinal cavities from bone resorption at a rate of about 50-100 µm/day[1,2,15,16]. Osteoblasts form the tail portion and follow with bone deposition to re-establish continuity of longitudinally oriented compact Haversian systems[1,2,15,16].

ii. Gap Healing

Gap healing occurs between zones of contact where small fragment gaps less than 800 µm to 1 mm are present and deformation is less than 2%[2,12]. The gap is filled with medullary blood vessels that are oriented perpendicular to the fracture line and loose connective tissue[1,2,6,15,16,25]. Blood supply is generally re-established after 2 weeks, and osteoblasts deposit lamellar bone in the gap, which can be a slow process over 3-8 weeks[1,2,6,15,16,25]. This initial bone is mechanically weak, as it is oriented perpendicularly to the fragment ends, but it becomes longitudinally oriented over time, which reestablishes the mechanical integrity of the cortex in the diaphysis of long bones[1,2,6,12,15,16,25]. Secondary osteonal reconstruction refers to when an implant does not provide stability to reduce fracture gap deformation to allow direct deposition of bone initially[2]. Bone resorption occurs to lengthen the fracture gap and decrease strain, and external callus is formed to stabilize the fracture ends, as an intermediate step[2]. If the deformation at the fracture gap is small enough once the callus unites to allow bone tissue to survive, gap healing can proceed[2]. If not, indirect bone healing will occur.

b. Indirect (Secondary) Bone Healing

Direct bone healing requires specific circumstances of stability and generally cannot occur without outside intervention. Indirect or secondary bone healing will proceed naturally when circumstances for direct bone healing are not met, and is generally considered to be quicker. There are numerous descriptions of indirect bone healing, which can ultimately be summarized into the following main phases: inflammation/hematoma formation, formation of a cartilaginous and periosteal bony callus, mineralization and resorption of the cartilaginous callus, and bone remodeling[5,15].

i. Inflammation and Fracture Hematoma

Upon initial bone fracture, there is hemorrhage from the periosteum, endosteum, and surrounding soft tissues[2,12,16]. This disruption in the microvasculature results in regional hypoperfusion, which leads to bone necrosis at the fracture site due to a decrease in oxygen tension and lack of nutrient delivery to osteocytes[16]. The extent of necrosis is dependent on the degree of blood supply disruption, which is associated with both the level of comminution and displacement of fracture fragments, as well as the amount of periosteal stripping from surround soft tissues[1]. The disrupted bone canaliculi at the fragment ends cause dying osteocytes to release lysosomes that trigger degradation of the organic matrix[6]. Osteoclasts are activated and begin to resorb bone debris[6]. Concurrently, the coagulation cascade is triggered by the exposure of endothelium and release of tissue factor, which results in an influx of inflammatory cells. The resultant hematoma is an important source of bone healing potential[12,16]. Platelets and macrophages release cytokines and acute phase proteins, such as platelet-derived growth factor (PDGF), TGF-β, interleukin-1 (IL-1), interleukin-6 (IL-6), and prostaglandin-E_2 (PG-E_2)[6]. Bone morphogenetic proteins (BMPs) play an important role in recruitment of MSCs (BMP-7), initiation of the healing cascade, and ultimately callus formation (BMP-2)[15,26,27]. Macrophages activate complement, initiate fibroplasia, and mediate angiogenesis as the hematoma becomes more organized with platelet activation and fibrin deposition. This organization serves as a scaffold and source of cells for the formation of granulation tissue[2,6]. Fibroblasts migrate into the fibrin meshwork and new capillaries are formed, beginning the transition into granulation tissue[6]. The hematoma also contains multipotent stem cells that originate from the cambium layer of the periosteum, the bone marrow and the endosteum, as well as those recruited from the surrounding soft tissue and ingrowth of capillaries[6,12,28]. The lineage of these cells is ultimately determined by biological and mechanical stimuli and the hematoma itself can serve as a stimulus for new bone formation via a cartilaginous callus and ultimately endochondral ossificiation[6,24,29].

ii. Callus Formation and Mineralization

As the inflammation phase terminates, mesenchymal cells begin to proliferate and differentiate into cells with osteogenic potential to initiate the repair phase, namely fibroblasts, chondroblasts, and osteoblasts[12,16]. Depending on the biologic and mechanical environment, cells may follow a path of endochondral ossification, intramembranous ossification, or some combination thereof[2,12]. Endochondral ossification involves the formation of a "soft" fracture callus, which is eventually replaced by "hard" callus[1,16]. MSCs are committed to a chondrogenic cell lineage pathway to primarily produce type I collagen[6,16]. The dedication to the chondrogenic pathway can be explained by a combination of biologic and mechanical factors. Variations in oxygen tension due to the hypoperfusion associated with the injury can lead to formation of capillary buds and differentiation in chondroblasts, due to their decreased oxygen demand compared to osteoblasts, whose minimal oxygen tension requirement is higher[5,6,12]. Fibrous tissues tend to form at the periphery where blood supply is more abundant, while fibrocartilage forms in the middle where blood supply is limited[2]. Concurrently, MSCs will differentiate along a fibroblastic, chondroblastic, or osteoblastic lineage based on the type and magnitude of mechanical forces applied, provided that the necessary biologic factors, such as growth factors and chemical stimulation, are present[12,16,30]. Fibroblasts respond to tension, chondroblasts to shear forces, and osteoblasts respond to compression and distraction[16,30]. It has been suggested that fibroblast tolerance to axial strain is due to a more highly developed actin cytoskeleton compared to osteoblasts and that direction of load applied is impacts cell response[31,32]. Osteoblasts will show increased ribonucleic acid (RNA) synthesis and cell division in vitro when exposed to cyclic strain, as well as changes in alignment in reference to the load applied[33]. Decreased stability at the fracture site predisposes to cartilage formation, as demonstrated in a study showing histological evidence of cartilage formation in non-stabilized fractures[20]. The soft callus can bridge the fracture, and as the callus increases radially in diameter due to inherent instability, its ability to resist bending and rotation will eventually increase, further decreasing local strain[2,12].

Ultimately, chondrocytes undergo apoptosis, which allows new blood vessel ingrowth, and osteoblasts can deposit osteoid on the remaining type I collagen framework, which further limits gap deformation, eventually to less than 2% strain[1,2,12,20,34,35]. With the deposition of calcium hydroxyapatite crystals, the callus continues to be mineralized[16]. Intramembranous ossification does not involve a cartilaginous intermediate, and there is no expression of cartilaginous proteins[20]. MSCs derived from the periosteum differentiate into osteoblasts, which synthesize type I collagen, and there is direct generation of calcified tissue[16,20]. If the periosteum remains intact despite injury, a callus bridge can form directly from the cambium inner layer, but if it is damaged, cuffs of callus will grow outward and join each other to bridge the fracture gap[1]. Preservation of the periosteum is vital in surgical repair of fractures, as it is a mechanobiological environment conducive to osteogenesis[20,36]. Intramembranous ossification is the method of bone formation that occurs when utilizing distraction osteogenesis. Bone formation is essentially mechanically induced by placing the osteotomy or fracture gap under tension, after which a radiolucent zone is created[12]. This represents a fibrous interzone made up of longitudinally oriented collagen, and there are areas of vascular ingrowth on either side[12]. Osteoblasts deposit osteoid along the collagen, and once distraction ceases, the fibrous zone completely mineralizes[12].

iii. Remodeling

The final stage of indirect bone healing is remodeling. Bone is unique in its ability to remodel over time and attain its pre-injury strength and structure. Wolff's law states that the structure of bone will change in response to mechanical demands placed upon it, which allows for optimization of bone growth such that bone will form in areas of high stress and be resorbed in areas of low stress[12,16]. Certain levels of strain, or the change in length of a given material when a given force is applied, will lead to net bone resorption or deposition over time[1,16]. Initially collagen fibers have random orientation, which leads to formation of woven bone upon mineralization[16]. Woven bone has decreased ability to withstand forces, but remodeling allows replacement of woven cancellous bone with longitudinally oriented lamellar bone, with a more highly ordered microarchitecture[2,12,16]. In addition to strain, piezoelectricity also impacts bone remodeling. Piezoelectricity is the generation of electric polarity by pressure exerted in a crystalline environment[6,37]. As force is applied across a concave surface, an electronegative polarity is created, enhancing osteoblastic activity, leading to net bone deposition[6,12]. Force applied to a convex surface generates electropositive polarity and enhances osteoclastic activity, favoring bone resorption[6,12]. This remodeling ability provides the basis for the need to return to function early, as weight bearing can benefit fracture healing[12].

c. Biologic Osteosynthesis

Many factors must be considered when choosing the best method of fracture repair: biological factors, such as fracture environment, mechanical factors, such as forces acting on the fracture, and clinical factors, such as patient status and client compliance[38]. Emphasis was once placed on anatomic reconstruction and rigid fixation to promote primary bone healing[39,40]. This is both difficult and time-consuming when dealing with comminuted fractures and inevitably, small fragment gaps can still exist, which eliminates any load sharing effect[41]. The soft tissues surrounding small fragments are disrupted, and the environment between fracture fragments can still be high in strain and preclude bone formation[19,41]. Recently, paradigms have shifted towards biologic osteosynthesis, in which effort is made to establish an optimal environment for rapid bone healing by preserving the surrounding soft tissues[41]. With semi-rigid stabilization and preservation of blood supply, indirect bone healing progresses with resorption of fracture ends to decrease local strain, and external callus forms to increase stability for an overall shortened healing time[2,19,42]. Principles of biologic osteosynthesis include indirect or closed reduction of fracture fragments to focus on adequate spatial alignment[43,44], minimal disruption of the soft tissue envelope, and placement of implants rigid enough to stimulate osteosynthesis and achieve relative stability without vascular insult to bone, as opposed to absolute stability[39-41,45].

d. Goals of Fracture Fixation

The goal of any fracture fixation is to maximize the biologic environment of the bone to bring early union and return to function while minimizing complications[1]. Healing is thus determined by the efficacy of the implant in providing stability and the biologic environment at the fracture site[1,2]. The mechanical environment involves forces acting on a fractured bone and the mechanical stability of a repair[16,46]. Deformation of the tissues at the fracture site can also influence the differentiation of the MSCs and predispose to either primary or secondary bone healing[46]. Tissue at the site of fracture is subjected to microstrain due to interfragmentary motion, which will stimulate secondary bone healing by way of callus formation[16,47]. Both the quality of this tissue and the width of the gap between fragments dictate the mechanical quality of healing bone[16,47]. Controlled micromotion under functional load can stimulate cartilage and bone growth and facilitate osteogenesis. This is referred to as “relative stability”[1]. In contrast, with absolute stability, such as in anatomic reconstruction and fixation in compression, no interfragmentary motion occurs. This lack of mechanical stimulus inhibits callus formation[16]. Early cyclical axial micromotion may stimulate earlier fracture healing and might be preferable in the early phases of healing[16,48]. Studies have demonstrated that semi-rigid fixation leading to increased interfragmentary movement results in a more cartilaginous callus, but successful fracture healing, and that while macromotion (strain > 2%) can inhibit osteogenesis, micromotion (strain $\leq$ 1%) does stimulate osteoblast proliferation[49-52]. Another study demonstrated that small interfragmentary strains stimulated tissue differentiation, but too much strain did not allow further bone healing. This study concluded that stable yet flexible fixation to induce a pathway of secondary healing is still preferable to the extremes (too rigid or too unstable a fixation method)[47]. Other types of micromotion, such as off axis or shear loading, is thought to impede callus formation, although this has been refuted in some studies[16,47,53]. Another mechanism of cyclical axial micromotion promoting and accelerating bone healing is through creation of piezoelectrical alterations[54]. Overall, while some degree of cyclical axial micromotion is beneficial, the upper limit of stability of a fracture fixation method necessary for successful healing is not known[49,54].

e. Fracture Biomechanics

Bone is subjected to physiologic and non-physiologic forces. Physiologic forces are generated by weight-bearing and muscle contraction and are generally uniaxial, while non-physiologic forces are applied directly to the bone and can potentially lead to fracture if they exceed a bone's ultimate strength[2,12]. Weight bearing of a quadruped involves the limb contacting the ground, which generates an equal and opposite ground reaction force[2]. This force can vary depending on the acceleration of the body and distribution of body weight, and must be balanced by muscle contraction[2]. Quadruped species, including canines, carry approximately 30% of body weight is carried on each forelimb, and 20% on each hindlimb during standing[2,55]. Weight bearing leads to both eccentric and concentric physiologic forces being applied to the long bones[2]. These forces can be summarized as axial, bending, and torsion forces[2,12]. These forces lead to local deformations within the bone and consequent internal strains, and the type of force and shape of the bone dictate the impact of those strains[2]. Axial compressive and shear forces act parallel or tangential to the long axis of the bone and can cause collapse of comminuted or oblique fractures[2,12]. Axial tension, such as gravity, although still considered a physiologic force, tends not to be clinically significant, as it would cause lengthening, not collapse[2,12]. Bending results in tensile internal stresses on one side of the bone, creating a convex surface, while causing compressive internal stress on the opposite side, creating a relative concave surface[2,12]. These forces can act on a bone in a pattern of cantilever bending, 3-point, or 4-point bending[2,12]. Torsion is a twist about the long axis of the bone. This causes a shear stress in the bone, which increases with distance from the center axis, and is most significant when the line of muscle force is perpendicular to the longitudinal axis of bone[2,12]. In vivo strain analysis has shown that 85-89% of physiologic internal stress in long bones is from bending[2]. When fractures occur due to non-physiologic forces, internal stresses now present at the fracture site need to be neutralized, and failure to do so will result in collapse of the cortical surface[2]. Optimal fracture stabilization requires knowledge of an implant's ability to resist these inherent stresses.

The biomechanical properties of bone, or bone fixation construct, are quantified using measurements obtained when the given sample is subjected to controlled loading. When referring to a material, the material response is referred to as a stress/strain curve, while when referring to a structure or construct, the structural response is called a load-displacement or force-deformation curve[2]. Engineering stress is defined as units of force in Newtons (N) per unit area (usually meters squared, m^2) or Pascals (Pa), and engineering strain is a local deformation expressed as units of length per length, or the change in length over the original length as a percent[12]. The stiffness of a material is known as the elastic modulus, or Young's modulus, and defines the stress/strain relationship inherent in linear elastic materials[12,56]. The material, such as bone, is subjected to increasing load until deformation results in critical failure, with the ultimate strength being defined as the ultimate stress a bone can withstand before breaking[2,12]. Loading initially proceeds in a linear fashion, called the elastic region, in which the bone or construct can return to its original shape once the force is removed[2,12]. The point at which a permanent change in shape occurs is called the yield point, and the following region is called the plastic region, indicating that covalent bonds have been broken at the molecular level and permanent deformation has occurred[2,12]. In living and post-mortem bone, plastic deformation means that microstructural damage has occurred[2]. The slope of the curve in the elastic region of a stress/strain or load-displacement curve is the elastic modulus or stiffness, respectively, of the material or construct[2,12]. The area under the curve refers to the energy absorbed by bone before failure[2,12]. Figure 1 shows a generic example of a load-displacement curve.

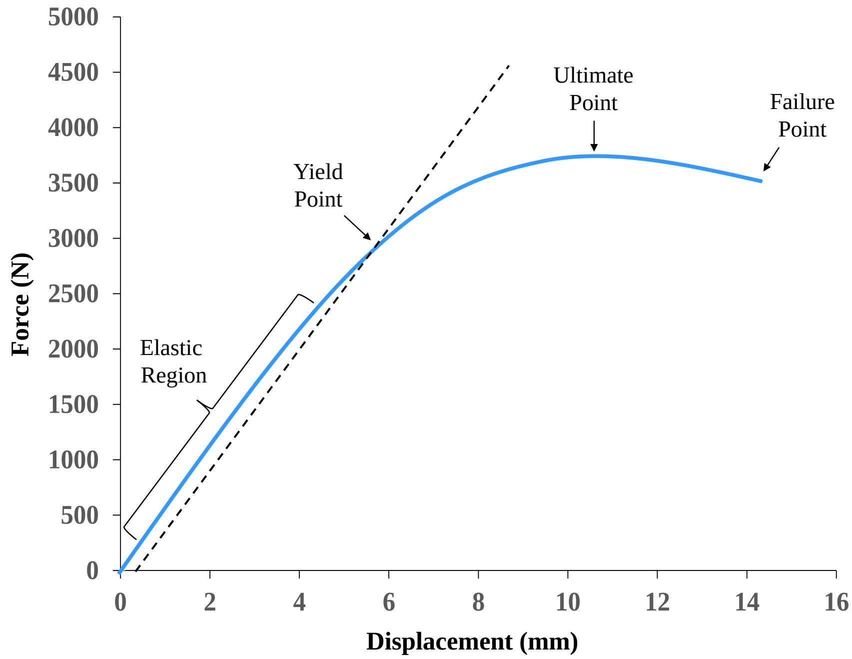

Figure 1: Example of generic load-displacement curve

3) Methods of Fracture Fixation

a. External Skeletal Fixation

There are many advantages to external skeletal fixation (ESF). The most important advantage is versatility. There are multiple ESF systems available, including the Kirchsner-Ehmer (KE) ESF, the SK® Linear ESF (IMEX Veterinary Inc., Longview, TX, USA) and Securos ESF (Securos Surgical, MWI Veterinary Supply Co., Fiskdale, MA, USA) systems. ESFs have the capacity for multiplanar constructs, and the most common configurations are Type Ia (unilateral uniplanar), Type Ib (unilateral biplanar), Type II (bilateral uniplanar), and Type III (bilateral biplanar) [57-59]. Type III ESFs are the strongest compared to all others in axial compression, shear, and torsion, but both Type II and Type III ESFs are limited in their application[60-62]. Unilateral uniplanar constructs have been shown to be inferior to both bilateral and biplanar constructs in stiffness, but can be modified to increase their stiffness by altering pin spacing/placement, clamp orientation, and number of connecting rods[57,60,61,63-66]. Type Ia constructs can be combined with other implants, such as interlocking nails, intramedullary pins, or supplemental plates, to achieve more rigid constructs and promote earlier return to function[67-73]. In addition, lower stiffness frames have been shown to achieve healing in radial and tibial diaphyseal fractures with lower morbidity than once thought[74]. Using acrylic connecting columns affords additional adaptation and has been shown to be stronger in compression than a traditional KE splint and potentially promotes earlier return to function[60,75-77]. ESF is particularly useful in open or infected fractures as well as non-union fracture situations[45,60]. External skeletal fixators can be utilized in both closed and open reduction of fractures[6] and can be implemented to stimulate both primary and secondary bone healing, the combination of which has been suggested to be optimal[60,78]. In studies comparing bone healing between external fixator constructs, less stiff constructs, such as Type Ia, demonstrated increased osteogenesis and increased and stronger callus formation, while more rigid fixation induced less callus formation and demonstrated more direct bridging by osteons[79-82]. Ultimately, there were no differences in the quality of callus, the strength of the healed bone, nor the time to bony union[79]. Callus free gap primary healing can be achieved via rigid neutralization fixation using external fixation and axially dynamized stable fixation, which applies compression across the fracture gap, can stimulate direct contact healing with periosteal bone formation[81]. It has been shown that stiffer external fixation in the early stages of healing permits greater weight bearing, but can lead to less advanced healing later and slower rate of fracture stiffness compared to less rigid fixation, although less rigid constructs may demonstrate more pin loosening complications[80,82]. Stress protection, or bone resorption and increased porosity due to decreased mechanical load, has been shown to occur with external fixation[83]. Staged disassembly of ESF constructs may offset this tendency and prove beneficial in skeletally mature dogs[48,83-85]. Despite theories of a limited time frame for the benefit of staged disassembly, there is no consensus and it remains a judgement call on the part of an experienced clinician[48,83-85].

Despite the innate versatility of external fixation, there are drawbacks that must be considered. The most commonly reported complications are pin tract inflammation and premature pin loosening[45,60,73,86]. Although percutaneous application is ideal for avoiding disruption of the fracture's biologic environment, it represents a breach of normal defense barriers that can lead to irritation or entrapment of soft tissue, causing pain or infection[45]. Mechanically, the extracorporeal apparatus necessitates that connecting rods be placed eccentric to the central axis of a long bone leading to large moments acting on the pins[45]. This contributes to failure at the pin-bone interface. Despite this impediment, advances have been made to improve this aspect of external fixation and decrease the risk of complications. For example, the use of threaded positive profile fixation pins results in increased stiffness and axial extraction resistance[60]. Additionally, the method of application, including predrilling, low speed placement of pins, and loading under stable fracture fixation has been shown to impact the pin-bone interface, leading to improved resistance to loosening[60,87-89].

b. Conventional Bone Plate

As with ESFs, there are many advantages to stabilizing a fracture via bone plating. The most important advantage of bone plating is that it provides a stable internal fixation and reduces post-operative care[90]. Since bone plates resist all forces acting on a fracture, bone plating allows early mobilization and weight bearing without the need for any additional external immobilization[91,92]. The stability afforded by an appropriately placed bone plate can maintain a level of interfragmentary strain that is compatible with fracture healing[93]. Bone plates can also be placed in different modes to suit different needs, including neutralization, buttress, bridging, and dynamic compression. With simple fractures, bone plates can be placed to generate compression, which allows osteons to travel directly across the fracture line allowing for primary bone healing[40]. Neutralization mode requires that force is being borne by the bone and the plate, implying some degree of load-sharing in a reconstructable fracture[12]. Buttress and bridging plating both refer to situations in which the plate must withstand all forces, such as in severely comminuted fractures. The terminology has evolved with the advent of bridging plating systems such that "buttress" plating primarily refers to spanning trans-cortical defects in the metaphyseal region of the bone, while "bridge" plating is used to achieve relative stability and promote secondary bone healing[12]. In addition, it has been suggested that in situations in which the blood supply to bone is damaged, more rigid fixation is preferable to provide protection for longer term internal remodeling[40]. Although bone plating can be utilized to achieve anatomic reconstruction and rigid fixation, bone plates can also be placed in minimally invasive fashion, thereby in keeping with the principles of biologic osteosynthesis[39].

Although bone plating has a number of advantages, there are a number of disadvantages and complications associated with the application of bone plates. Bone plates can require an extensive approach, which may damage the biologic environment, leading to devascularized bone fragments. This can predispose the patient to sequestration, necrosis, and infection[40]. It has been speculated that a bone plate, particularly a non-locking plate due to its dependence on compression and friction with the bone surface, can lead to decreased vascularity of the cortical bone[90]. The resultant increased porosity, initially thought to be due to decreased mechanical load as in stress protection, may be more accurately as secondary to temporary necrosis due to disturbance of circulation[94]. The limited contact dynamic compression plate (LC-DCP) was developed to decrease bone-plate contact and preserve cortical blood flow. However, studies have failed to show definitive proof that limited bone-plate contact reduces porosity[92]. There is a reduction of interface contact area, which is supposed to reduce interference with vascular efflux via the cortical bone. However, studies have shown similar cortical blood flow between a dynamic compression plate (DCP) and LC-DCP[95]. Studies have also indicated that there is no distinct advantage over the traditional dynamic compression plate in terms of porosity formation, although there was a trend towards more new bone formation with the LC-DCP[95,96]. Another possible drawback to bone plating is mechanical stress protection, which has been suggested to retard bone healing and potentially lead to non-union[90,97]. Increased bone porosity has not been uniquely linked to bone plating and some have claimed that it is not a true phenomenon[91,98]. However, the degree of strain protection is related to porosity and a plate can contribute to bone weakening once a stable mechanical union is formed[91]. Once satisfactory bone healing has occurred, it is suggested that plate removal and normal weight bearing would lead to infilling of cortical porosis[91]. Other possible complications with plate application include loss of reduction or fracture during screw tightening, screw loosening, and the fact that unfilled screw holes serve as stress risers, or an area where stress is locally increased due to the decreased area of the plate-screw construct, which is more prone to failure[93,97,99].

c. Comparison between External Fixators and Conventional Bone Plates

Given the breadth of options for fracture stabilization, much has been done to compare fracture fixation methods. It has been shown that both dynamic compression plating and external skeletal fixation lead to comparable results in terms of strength of healed bone, time to healing, hospitalization time, and time to unrestricted activity[100-103]. Many studies have sought to characterize the modes of bone healing stimulated with different fixation methods. Plate fixation in neutralization demonstrated mostly gap primary healing with some contact primary healing and maintenance of gap size[104]. Dynamic compression plating also shows both forms of primary healing, but with more contact healing and a reduction of gap size[104]. In rabbit tibiae, neutralization plate fixation demonstrated more rapid bone healing compared to ESF; however, mechanical testing of bones in the later stages of healing after plate removal were found to be weaker due to stress protection[101]. One study demonstrated that unilateral ESF yielded less mature bone with more bone resorption and porosity at 120 days compared to plate fixation and was less stiff in axial compression, distraction, craniocaudal bending, mediolateral bending, and torsion[105]. A more recent study demonstrated ilial osteotomies stabilized with external fixation had equivalent stiffness as well as greater yield and failure load compared to those stabilized with a bone plate and screws[86]. Overall, ESF has been reported as having more complications, but fewer major or catastrophic complications compared to bone plates or plate-rod constructs[100]. Specifically, bone plate complications, such as osteomyelitis and implant failure, tend to be more major or catastrophic and necessitate a second surgery[100,102]. The use of ESF is also associated with more recheck veterinary visits, and shorter surgery times[102].

d. Locking Compression Plate

With the increasing recognition of the importance of biologic osteosynthesis, it has become important for bone plating techniques to evolve to keep these concepts in mind. The advent of locking plate technology is promising both for general fracture stabilization and for the growing practice of minimally invasive plate osteosynthesis (MIPO) [39,40,106]. Conventional plating relies on compression to the bone, which converts axial compression to shear stress at the bone interface, leading to possible screw failure[107,108]. The frictional force of the plate against the bone counters that shear force, and the force inherent to the plate equals the axial force generated by torque applied to the screws[108]. Therefore, the weakest point in conventional bone plate fixation is the screw-bone interface, and increased contact area between the screw and plate will increase the frictional coefficient, but at the risk of decreasing periosteal perfusion[108]. In addition, osteoporotic or comminuted bone cannot resist shear forces as well, so adequate screw torque cannot be generated to prevent motion at the fracture site, whereas locking plates obviate this concern[108-110]. Locking plates are designed to have screw heads lock into the screw hole at a fixed angle by varying mechanisms, which resists shear forces and creates a single beam construct that provides axial stability[107,108,110]. The design of a conventional screw includes a coarser pitch to resist pullout and a smaller core diameter, while locking screws are more symmetric with a finer pitch and greater core diameter[107,109]. This imparts 2 times improved resistance to shear forces and 3 times improved resistance to bending; the strength of the fixation equals the sum of all the screw-bone interfaces[56,107]. In terms of mode of failure, conventional plates fail by sequential pullout of screws, while locking screws would have to pull out simultaneously with the plate, as one construct[107]. Given that locking screws are not subjected to the same pullout force as conventional screws and the plate-screw interface provides axial stability, it is not necessary to engage 2 cortices, i.e., monocortical screw placement in locking constructs can achieve comparable strength[107,110]. There was no significant difference in stiffness in mediolateral nor craniocaudal bending for monocortical versus bicortical screw placement in a fracture gap model using LCPs, although monocortical screws were approximately 30-37% less stiff in torsional testing[111]. In addition, no biomechanical differences were noted between monocortical and bicortical locking plate-rod constructs when axially loaded in a fracture gap model[112]. Monocortical screw use is also beneficial, as it can make screw measuring easier in minimally invasive approaches or when a plate is used in conjunction with an intramedullary pin, and can decrease endosteal blood supply damage[108].

The lack of reliance of compression to the bone affords locking plates other advantages compared to conventional plates. The angular and axial stability of locking plates decrease the need for plate contouring, which minimizes the risk of primary loss of reduction[108-110]. Conventional bone plating comes with the risk of delayed union or non-union and infection, secondary to damage to periosteal blood supply[108,109,113]. Locking plates are thought to be more effective in cancellous or poor quality bone, and the lack of reliance on frictional compression to the bone preserves periosteal blood supply, and thus decreasing the incidence of infection and non-union[107-110,113]. This minimal bone contact produces greater increases in cross-sectional diameter of bone growth around the plate, and can lead to easier plate removal if that becomes necessary[114]. Locking plates can be placed with up to 2 mm distance between the bone and the plate without compromising stiffness[115-117]. Conventional plating can also predispose the bone to re-fracture after plate removal due to stress shielding, which is not found in locking plates[108]. Contrary to conventional plating, which seeks to facilitate direct bone healing, locking plates enable indirect bone healing via callus formation[108,109,113]. Some studies have demonstrated inconsistent callus formation with locking plates, with more stable fixation leading to decreased healing of femur fractures, and longer plate spans leading to increased callus formation[118,119]. Locking plates have been shown to be equally stiff as non-locking plates in axial compression testing, and stiffer than external skeletal fixators when indirectly compared to values generated in older studies, although the ideal stiffness for optimal bone healing is unclear[118]. It has been suggested that a low initial stiffness promotes axial interfragmentary motion of 0.2-1 mm during weight bearing, which stimulates initial callus formation[118]. Progressive stiffening of the construct under higher loads can provide more consistent fracture healing[118].

The locking compression plate (LCP) was designed to incorporate the advantages of an internal fixator system (the point-contact fixator or PC-Fix) with those of a dynamic compression plate, which allows flexibility in how the plate can be utilized[120]. The LCP limits the implant bone contact to minimize impairment of the vascular supply to the bone, with a similar shape and cross sectional geometry to the LC-DCP, but with a tapered end to facilitated submuscular insertion for minimally invasive approaches[121]. Mechanically, it has been suggested that the lower stiffness and higher elasticity of the LCP compared to stiffer implants may be preferable for long term stability[122].

In order to maximize the benefit of using locking plate technology, certain recommendations have been made in terms of screw density, screw configuration, and plate span width, depending on the fracture[107,110]. In particular, the LCP was designed to serve as an “internal fixator”, and can also be used as a compression plate, due to the unique “combi hole” design, which allows for either a locking screw or non-locking cortical screw to be placed[114,123].

The LCP has very specific guidelines for its application in particular fracture types according to mechanical testing[116,123]. Plate span width refers to the length of the plate divided by the length of the fracture, and it is recommended for a plate span width of higher than 2-3 in comminuted fractures, versus higher than 8-10 in simple fractures[111,123]. Screw density refers to the number of screws inserted divided by number of screw holes in a plate[123]. It is recommended for LCP screw density to be less than 0.4-0.5, or fewer than half the screw holes occupied, with at least 2 monocortical screws per fragment; more than 3 screws per fragment does not equate to more axial nor torsional stability[111,114,116,123]. Because of this, locking plate constructs do not require all screw holes to be filled. The axial stiffness and torsional rigidity is mainly influenced by the distance of screws from the fracture site, with stiffness of the construct increasing the closer a screw is placed to the fracture gap[116]. In fact, locking screw configuration has been found to be more important than number of locked vs. non-locked screws in terms of stiffness in bending and strength in torsion, with entirely locked constructs being the most stiff, but hybrid constructs achieving comparable stiffness[117,124]. The LCP has been mechanically compared to the LC-DCP, and no significant difference was found in bending stiffness, although the LCP had improved values in mediolateral bending and outperformed the LC-DCP in rotation to failure in one study[114,125,126]. However, another study demonstrated LCP as having a consistently lower stiffness than LC-DCP in a diaphyseal gap model when tested in eccentric cyclic loading, suggesting a balance between the mechanical and biologic is still important to consider[127]. Similarly, in a humeral metaphyseal gap model, LCP was less stiff than LC-DCP in dynamic testing but showed greater stiffness in monotonic loading[128]. The LCP has proven easy to apply with a less invasive surgical approach, potentially faster healing rate than plate-rod constructs, and external skeletal fixators, and a relatively low complication rate in appendicular fracture fixation[121]. It is important, however, to adhere to the recommended guidelines to maximize the function of the LCP and decrease risk of complications in fracture repair[121].

4) Conclusion

Fracture fixation must afford the patient sufficient stability to enable formation of bone, while preserving the necessary biologic environment to optimize and expedite bone healing. To achieve this, a balance must be struck between biologic and mechanical factors acting at the fracture site, both those inherent to the patient and those that are influenced by surgeon intervention. Many studies have been undertaken to understand the biology of fracture healing and to discover the ideal stability necessary to achieve bony union, and paradigms have shifted from anatomic reconstruction and rigid stability to biologic osteosynthesis with relative stability to reflect this evolving perspective. Consequently, further study is required to focus on how best to achieve relative stability with an ever-advancing array of surgical implants by understanding the mechanical properties of these fixation methods in the context of biologic osteosynthesis.

Chapter 2: Mechanical Comparison of a Type II External Skeletal Fixator and Locking Compression Plate in a Fracture Gap Model

5) Introduction

Comminuted long bone fractures are commonly encountered in veterinary orthopedics. Traditionally, fracture repair consisted of rigid fixation and anatomic reconstruction of bone fragments. However, recent shifts towards biologic osteosynthesis emphasize minimizing surgical trauma and preservation of blood supply for optimum healing[41], especially when reconstruction of the bony column is not possible. Thus, the use of minimally invasive methods to achieve these goals is becoming increasingly important. Bone plating and linear external skeletal fixators (ESF) are popular methods for comminuted fracture fixation. Both of these methods can be adapted to achieve biologic osteosynthesis via minimally invasive technique[45,129].

Traditional dynamic compression bone plating provides stable internal fixation and allows early weight bearing with reduced post-operative care without external immobilization[90-92]. However, bone plates require an extensive approach, which may result in devitalized bone fragments, which can predispose the bone to sequestration, necrosis, and infection[40]. Another possible complication is stress protection, which has been suggested to retard bone healing and potentially lead to non-union[90,97]. Other possible complications include loss of reduction during screw tightening, screw loosening, and unfilled screw holes that can be stress risers and thus locations of potential failure[93,97,99]. The advent of locking plate technology is promising both for general fracture stabilization and for the growing practice of minimally invasive plate osteosynthesis (MIPO) [39,40,106]. Locking plates have been referred to as “internal fixators”, forming a fixed angle mechanism in which the screw heads lock into a threaded plate hole[107,114].

This eliminates the need for compression of the plate against the bone decreasing the risk of stress protection and damage to the blood supply[98,107,108]. Advantages of locking plates include the lack of dependence on plate contouring, the promotion of both primary and secondary bone healing, comparable stiffness to dynamic compression plates, and the improved fixation in osteoporotic or pathologic bone[107-109,113,118]. Although it is an evolving field, the steep learning curve and potential need for specialty equipment (fluoroscopy, specialized instrumentation) for minimally invasive application currently preclude the use of MIPO in every clinic[39,40,106], but locking plates are gaining widespread popularity for comminuted fracture repair with minimally invasive and "open but do not touch" approaches. LCP was designed to incorporate the advantages of an internal fixator system with those of a dynamic compression plate, which allows flexibility in how the plate can be utilized[120]. Mechanically, it has been suggested that the capacity for relative stability and higher elasticity of the LCP compared to stiffer implants may be preferable for long term stability[122].

As with bone plates, ESFs can be utilized in both closed and open reduction of fractures and can be applied to stimulate both primary and secondary bone healing[60,78]. The most commonly reported complications are pin tract inflammation and premature pin loosening[45,60,73,86]; however, advances have been made to decrease risk of complications[60,87-89]. External fixators can be modified to increase their stiffness by altering pin spacing/placement, clamp orientation, and number of connecting rods[57,60,61,63,65,66]. Stiffness and load to failure increases from Type Ia ESF (unilateral, uniplanar) to Type III ESF (bilateral, biplanar), with Type III ESFs being the strongest in axial compression, shear, and torsion[60,61].

It has been shown that both dynamic compression plating and external skeletal fixation lead to comparable results in terms of strength of healed bone, time to healing, hospitalization time, and time to unrestricted activity, but no research exists on the comparison of an ESF construct to the LCP in the current literature[100-103].

Although biologic osteosynthesis emphasizes the importance of preservation of the soft tissue, any fracture healing demands minimal motion in the fracture gap during loading. Thus, achieving the ideal fracture-healing environment requires knowledge of the mechanical profile, including stiffness, for any type of fixation method. Although mechanical testing of LCPs and ESFs has been performed in many studies, no studies to date have directly compared the mechanical response of LCPs to that of ESFs in a comminuted fracture model through matched testing[116,130]. Obtaining objective and quantifiable data comparing ESF to the LCP would provide valuable information for determining the best method to achieve the stability needed for optimal healing of a particular fracture. The purpose of this study was to quantify and compare the stiffness of a Type II ESF to a 3.5 mm LCP in axial compression, mediolateral, and craniocaudal bending in comminuted long bone fracture model. Our hypothesis was that the Type II ESF would demonstrate comparable stiffness to the LCP in compression and bending in a model mimicking a non-reconstructable fracture.

6) Materials and Methods

Bone Model

A previously validated bone simulant[131] was utilized to minimize variation between samples. This bone model consisted of hollow short fiber reinforced epoxy cylinders (Sawbones®, Pacific Research Laboratories, Vashon Island, WA, USA) with a 3 mm wall thickness and 20 mm outer diameter were used. The cylinders were cut into 100 mm segments to simulate fracture fragments and a 40 mm fracture gap was used to mimic a non-load sharing comminuted fracture, as previously described (Figure 2)[132]. A custom jig was fabricated to ensure a consistent 40 mm gap between fragments.

Figure 2: Bone composite cylinders with a 40 mm gap with LCP applied

Study Design

Two distinct constructs were created: the LCP and the Type II ESF. Ten replicates were made of each, for a total of 20 constructs. Five constructs of each were tested in non-destructive mediolateral and craniocaudal bending; five of each were tested in non-destructive axial compression, for a total of 30 tests. Preliminary tests were performed to determine the displacement necessary to ensure testing was sub-yield; repeats tests were also performed to confirm/refute outlying results.

Locking Compression Plate

A 316L stainless steel 12 hole 3.5mm LCP (157 mm) (DePuy Synthes Vet, West Chester, PA, USA) was used. The plates were applied according to Arbeitsgemeinschaft für Osteosynthesefragen (AO)/Association for the Study of Internal Fixation (ASIF) guidelines[133] using 3.5mm locking self-tapping cortical bone screws (DePuy Synthes Vet, West Chester, PA, USA). A locking screw drill guide (DePuy Synthes Vet, West Chester, PA, USA) was used in the appropriate plate holes and a 2.8 mm diameter drill bit was used to drill the cis and *trans* cortices of the bone composite for bicortical screw placement. A 1.5 Nm torque limiter (DePuy Synthes Vet, West Chester, PA, USA) was used and a pre-fabricated jig was used to ensure accuracy and precision of screw placement, and fracture gap distance of 40 mm (Figure 3). Three screws were placed per fragment for a plate screw density of 0.5, as recommended for the LCP with comminuted fractures[123]. The two screw holes nearest to the fracture gap were filled, as well as the furthest from the fracture gap on either end, for a 4-hole working length. The plate was applied flush to the composite cylinders[115].

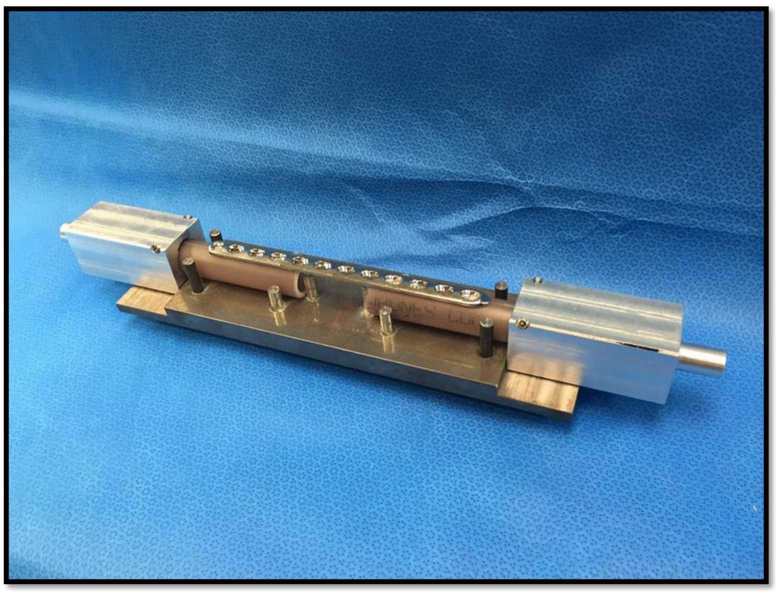

Figure 3: The LCP construct in custom jig and aluminum pots

External Skeletal Fixator

A Type II ESF was applied to the composite cylinders using 3 proximal full fixation pins and 3 distal full fixation pins in the mediolateral plane. Centerface® (IMEX Veterinary Inc., Longview, TX, USA) positive profile fixation pins [3.2mm/4.0 mm (1/8”/5/32”)] representing

20% of the bone model diameter were used. Pre-drilling was performed using a 3.1 mm diameter drill bit using a power drill at slow speed (150 rpm). The distance between a fixation pin and fracture gap was 10 mm, and the distance between fixation pins was 20 mm. Single large SK® clamps (IMEX Veterinary Inc., Longview, TX, USA) were used to attach 2 carbon fiber connecting rods to complete the constructs tightened to 7.68 Nm of torque using a torque wrench (Sturtevant Richmont Torque Measurement Systems, Franklin Park, IL, USA) (Figure 4)[134]. A pre-fabricated jig was use to maintain a distance of 20 mm from the cylinders to account for soft tissue in a clinical setting.

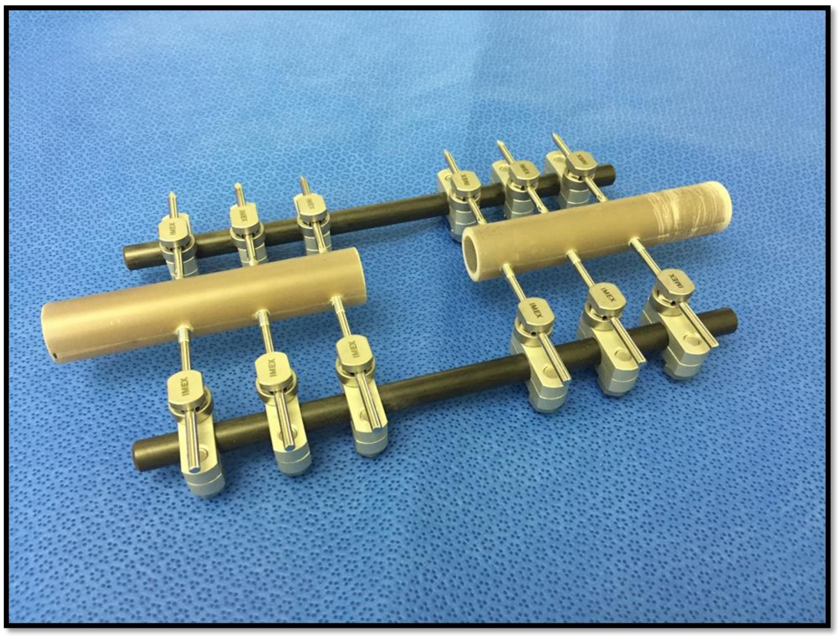

Figure 4: The completed ESF construct

Mechanical Testing

A servo-hydraulic material testing system (MTS 810, 13.3 kN; Eden Prairie, MN) with a 500 lb. load cell (Interface, 1210ACK-500, Scottsdale, AZ, USA) used for all testing. The load cell was recalibrated in house to a range of 0-60 lbs. to correspond to the range over which non-destructive testing would take place. Displacement was measured with the internal LVDT attached to the MTS piston. The constructs were tested non-destructively in 3 loading modes. Five constructs of each type were tested first in four-point bending in the mediolateral plane, and were then rotated orthogonally to be tested in the craniocaudal plane. Five additional constructs of each type were tested in axial compression. Data were collected by data acquisition hardware (DTS, TDAS Pro, Seal Beach, CA, USA) and sampled at 250 Hz (DTS, TDAS Control Ver. 6.8K6, Seal Beach, CA, USA).

Four-Point Bending

Custom aluminum pots with squared ends were used to mount the constructs and prevent rotation about the long axis. The constructs were manually placed to ensure a 300 mm gap between the support points and a 220 mm gap between the load points, resulting in a constant bending moment, as previously described[132]. Due to variations in the constructs, one or more 0.001 inch shims were placed between the pots and the loading points to minimize differences in contact time between the left and right load points. The constructs were loaded for 3 cycles under displacement control at 10 mm/min, after manually setting the point of contact between the load rollers and the pots as zero displacement. This was done by placing a 0.001 inch shim between the pot with the largest gap and the corresponding loading point and then lowering the MTS piston until the loading point contacted the shim. The MTS displacement was then zeroed and the shim was removed. The pots were lubricated to minimize friction between the pots and the contact points. Hysteresis loops of force versus displacement were generated with practice LCP constructs to establish a load range that would be non-destructive, i.e. sub-yield [Maximum load 133 N (30 lb.)]. Subsequent tests were then conducted to remain in this range. The mediolateral bending tests were performed first, and screws were re-tightened with the 1.5 Nm torque limiter.

The constructs were then rotated orthogonally 90 degrees and loaded in craniocaudal bending (Figures 5-8). If irregular loading, i.e., asymmetric loading due to the construct not being perfectly straight, was encountered during the first test on a given construct for a given loading condition then a repeat test was performed on the same construct and used in lieu of the first test. It should be noted that this only occurred for two ESF constructs in mediolateral bending (ESF-C2-ML and ESF-C3-ML). In addition, repeat tests were performed on several other constructs to evaluate whether or not any damage or yielding occurred as a result of the level of loading or repeated loading. Bending tests were also performed on the two intact bone simulant samples without a construct attached. The bending direction could not be defined for tests, as there was no construct to delineate directionality. Stiffness was quantified by curve fitting the force-displacement curve between 20-40N, i.e., the linear elastic portion of the load-displacement curve, during the 3rd loading cycle using a linear curve (Microsoft Excel, Microsoft Corporation, Redmond, WA, USA).

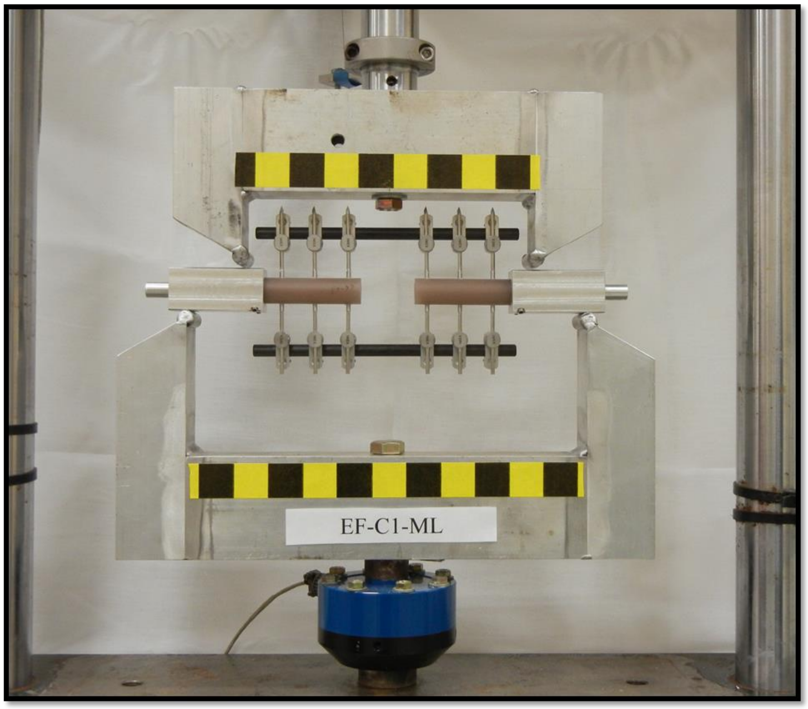

Figure 5: Mediolateral bending testing apparatus with Type II ESF construct

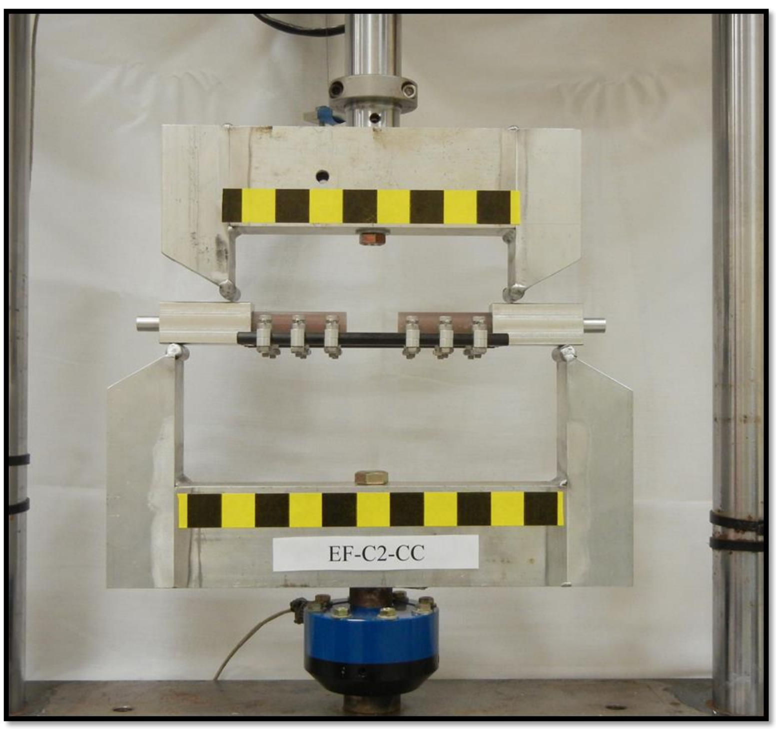

Figure 6: Craniocaudal bending testing apparatus with Type II ESF construct

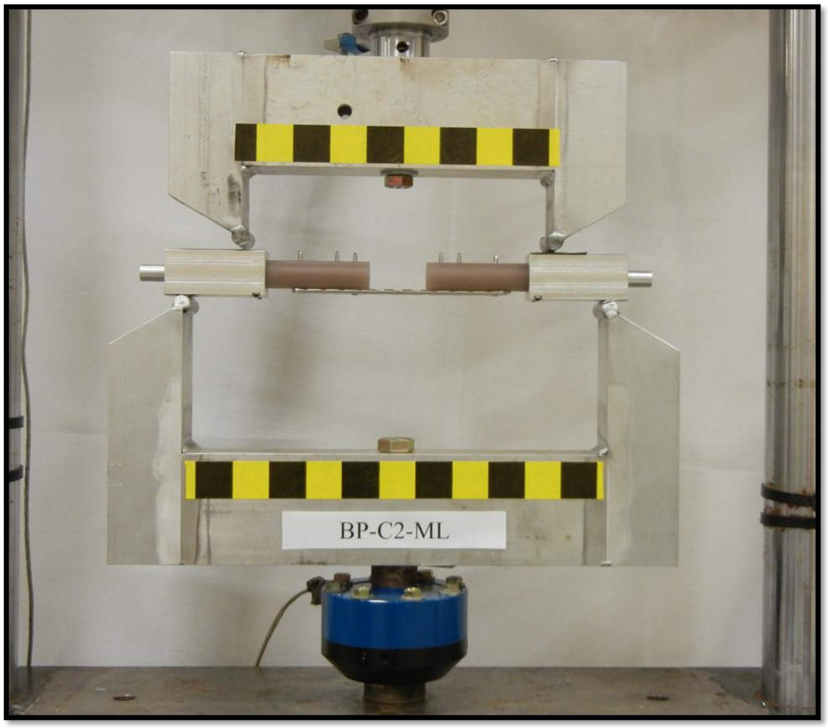

Figure 7: Mediolateral bending testing apparatus with LCP construct

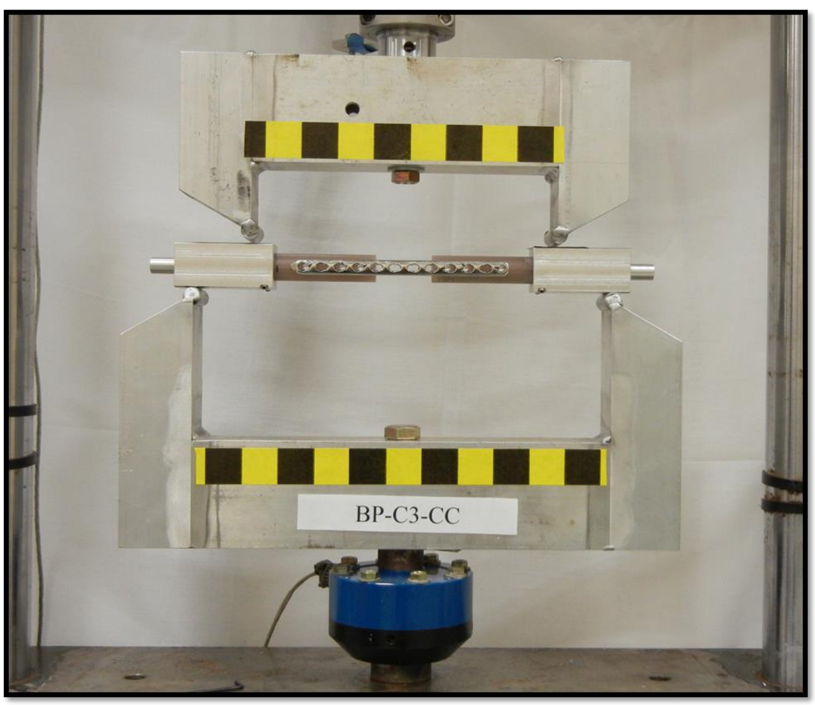

Figure 8: Craniocaudal bending testing apparatus with LCP construct

Axial Compression

The pots attached to the constructs were mounted to universal joints on either end, with the use of set screws, to prevent the formation of any moments. The system was preloaded to 1 lb. in compression to remove any slack in the system and the displacement was then manually zeroed. The constructs were loaded for 3 cycles under displacement control at 10 mm/min to a maximum load of 44N (10lb). (Figures 9-10). Stiffness was quantified by curve fitting the force-displacement curve between 20-80N, i.e., the linear elastic portion of the load-displacement curve, during the 3rd loading cycle using a linear curve (Microsoft Excel, Microsoft Corporation, Redmond, WA, USA).

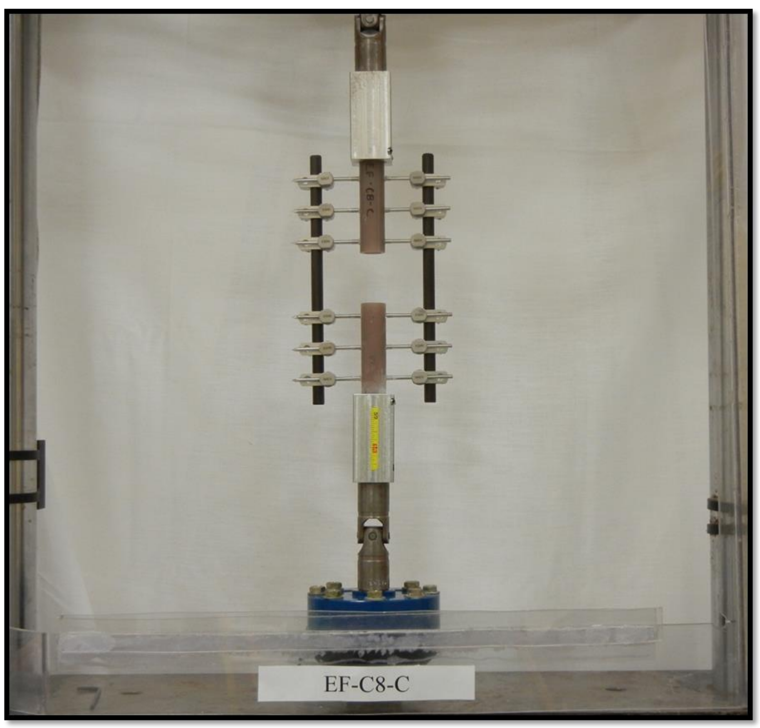

Figure 9: Axial compression testing apparatus with Type II ESF construct

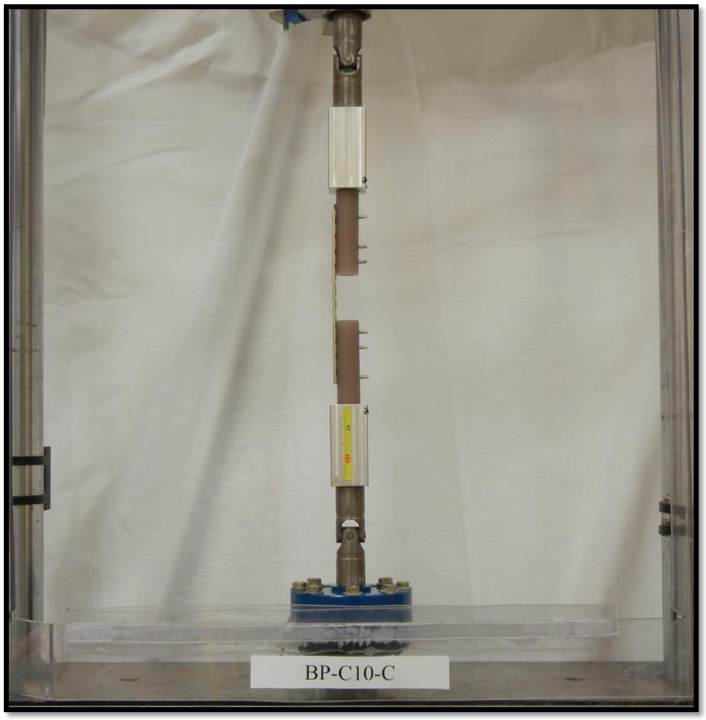

Figure 10: Axial compression testing apparatus with LCP construct

Data Processing and Statistical Analysis

A preliminary power analysis using data from previous studies indicated that 5 per group would adequately detect a statistically significant difference between groups with an alpha of 0.05 and a power of 0.80. A low pass software filter (SAE J211; 4 pole phaseless butterworth filter) was applied to the raw load and displacement data to reduce signal noise. It should be noted that filtered data plots were overlaid on unfiltered data plots to confirm that the filters did not adversely affect the data. Stiffness data were reported as means with standard deviations, and were found to be normally distributed. Separate one-way ANOVAs were performed on the bending and compression datasets to accept or reject the null hypothesis, which was that there were no differences between the constructs. For the bending tests, a Tukey-Kramer multiple comparison test was then performed to detect pairwise difference between means. Statistical significance was defined as $p < 0.05$. All statistical analyses were performed utilizing statistical software (NCSS, Kaysville, UT, USA).

7) Results

Bending Tests

The stiffnesses of the constructs and bone simulant in each mode of bending are expressed as means and standard deviations in Table 1. The one-way ANOVA showed that there was a statistically significant difference between the groups ($p = 0.00000$), and the Tukey-Kramer multiple comparisons test showed the groups that were statistically significant from each other ($p<0.05$). The comparisons between each group and the statistical significance are summarized in Table 2. The stiffness of the Type II ESF in mediolateral bending (1584.2 N/mm ± 202.8 N/mm) was significantly greater than the stiffness of the LCP in mediolateral bending (110.0 N/mm ± 13.4 N/mm). The stiffness of the Type II ESF in mediolateral bending was significant greater than that of the Type II ESF in craniocaudal bending (584.8 N/mm ± 36.6 N/mm). The stiffness of the LCP construct in craniocaudal bending (744.3 N/mm ± 66.7 N/mm) was significantly greater than that of the LCP construct in mediolateral bending (110.0 N/mm ± 13.4 N/mm). There was no statistically significant difference between the stiffnesses of the Type II ESF and the LCP constructs in craniocaudal bending. The stiffness of the bone simulant (1026.3 N/mm ± 43.1 N/mm) was significantly different from both of the constructs in all modes of loading. A graphic depiction of the linear portion of the elastic region of the force-displacement curves for all the bending tests is shown in Figure 11. A graphic representation of the linear elastic portions of the force-displacement curves for the Type II ESFs and LCPs in mediolateral bending is shown in Figures 12 and 13, respectively. A graphic representation of the linear elastic portions of the force-displacement curves for the Type II ESFs and LCPs in craniocaudal bending are shown in Figures 14 and 15, respectively. A graphic representation of the linear elastic portions of the force-displacement curves for all constructs, including the bone simulant, in bending, are shown in Figure 16. The consistency in the response curves and stiffness values between the first tests and the repeated tests (designated with the number "2") indicate that the testing did not alter the measured stiffness of the constructs ($p>0.05$) outside the range of normal variation (see Appendix A for figures and statistics). Therefore, any observed differences can be attributed to the differences in loading conditions or construct type, and not to any changes due to repeated loading.

Table 1: Summary of bending results for Type II ESF construct, LCP construct, and Bone Simulant

Construct	Mode of Bending	Stiffness (N/mm)	
		Mean	Standard Deviation
LCP	Mediolateral	110.0	13.4
Type II ESF	Mediolateral	1584.2	202.8
LCP	Craniocaudal	744.3	66.7
Type II ESF	Craniocaudal	584.8	36.6
Bone Simulant	Bending	1026.3	43.1

Table 2: Summary of statistically significant relationships for bending according to Tukey-Kramer multiple comparisons test

Construct	Stiffness Comparison	Construct	Significance
ESF-ML	>	LCP-ML	*
ESF-ML	>	ESF-CC	*
LCP-ML	<	LCP-CC	*
LCP-CC	=	ESF-CC	

Note: * denotes statistical significance of $p < 0.05$

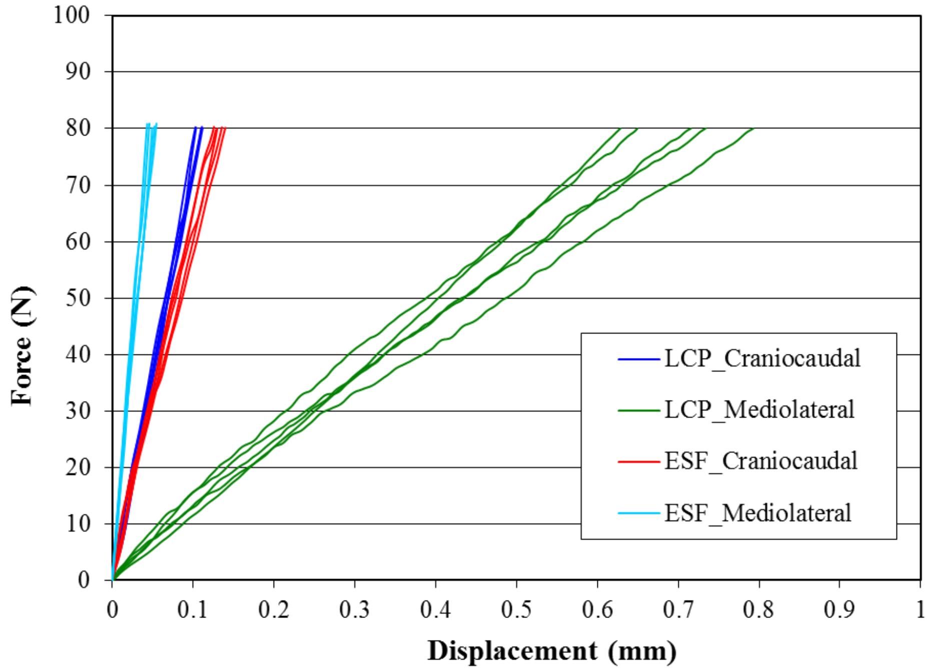

Figure 11: Summary of linear elastic portion of force-displacement curves for all bending tests

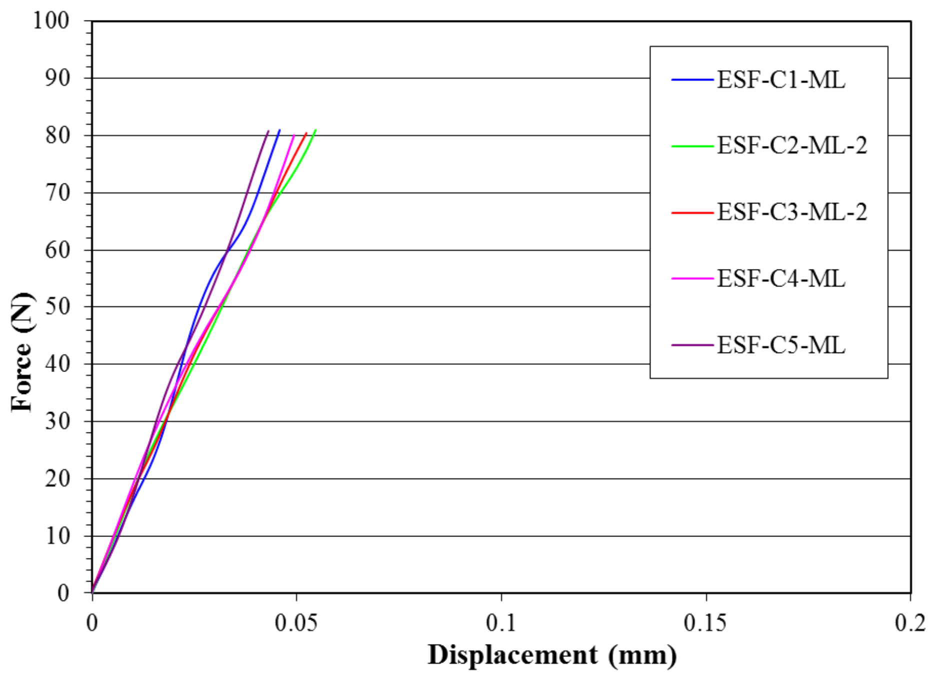

Figure 12: Linear elastic portion of force-displacement curves for Type II ESF constructs in mediolateral bending

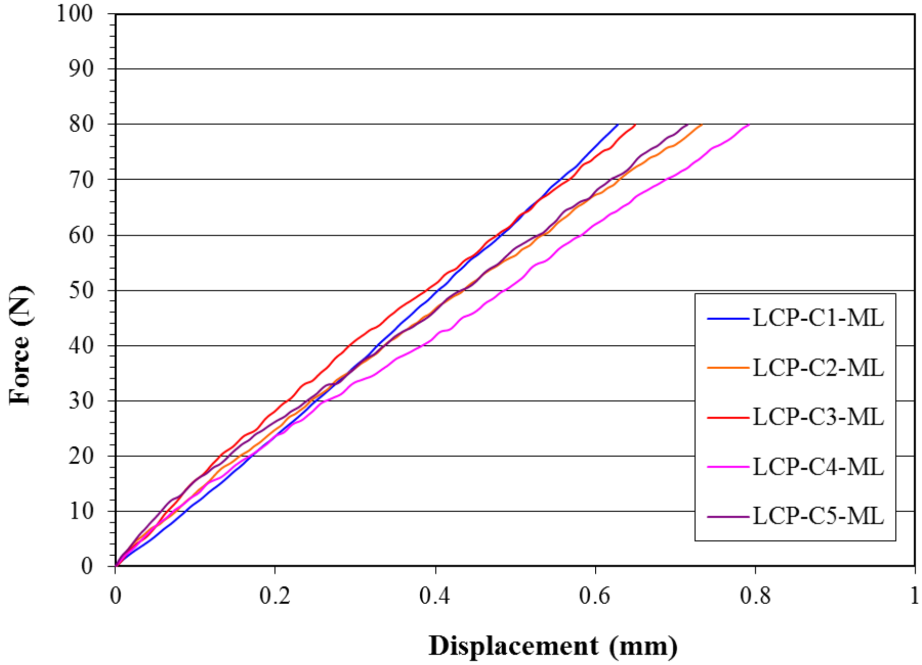

Figure 13: Linear elastic portion of force-displacement curves for LCP constructs in mediolateral bending

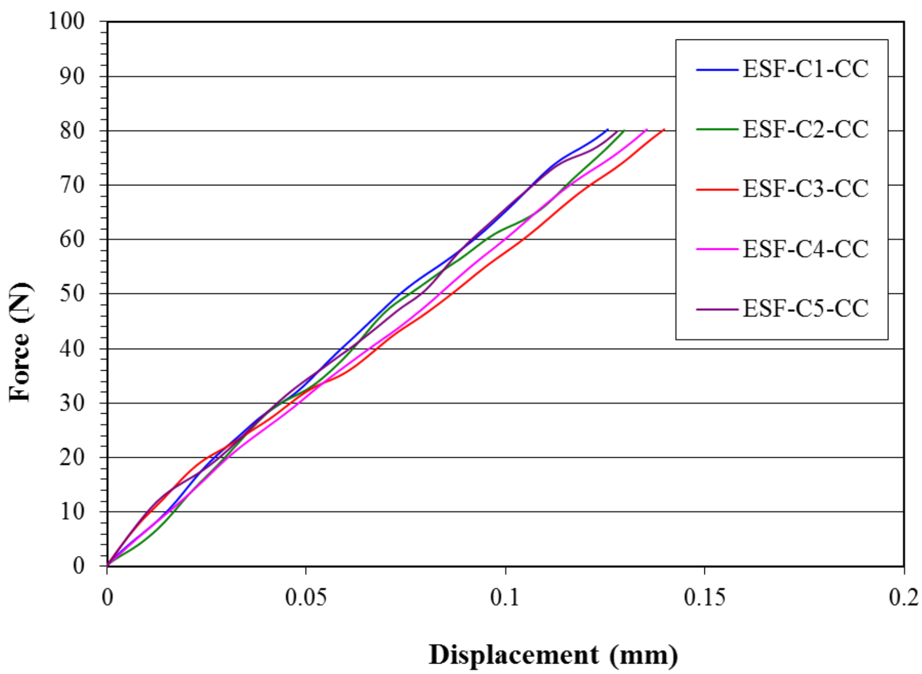

Figure 14: Linear elastic portion of force-displacement curves for Type II ESF constructs in craniocaudal bending

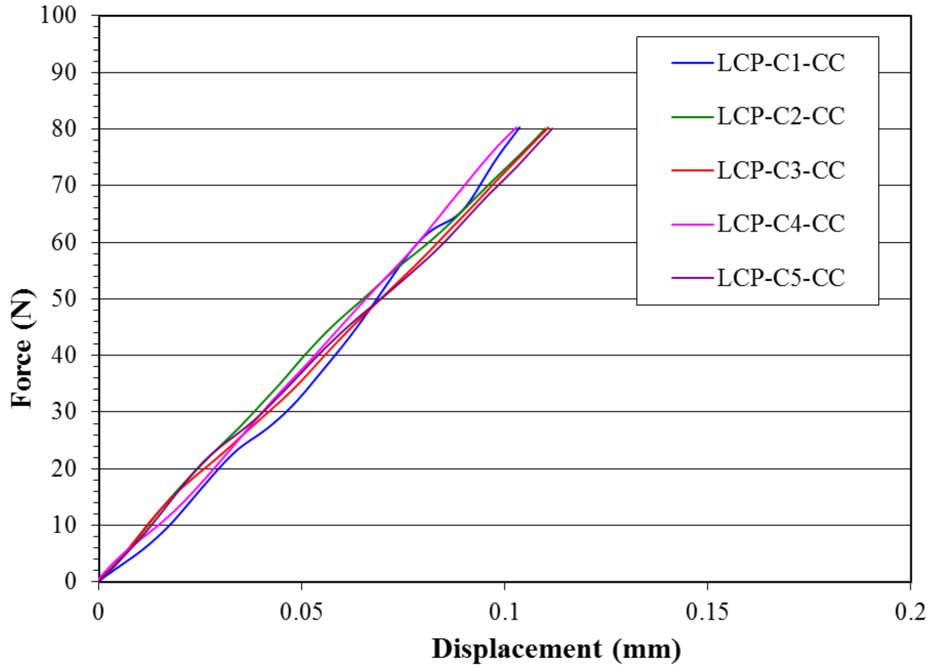

Figure 15: Linear elastic portion of force-displacement curves for LCP constructs in craniocaudal bending

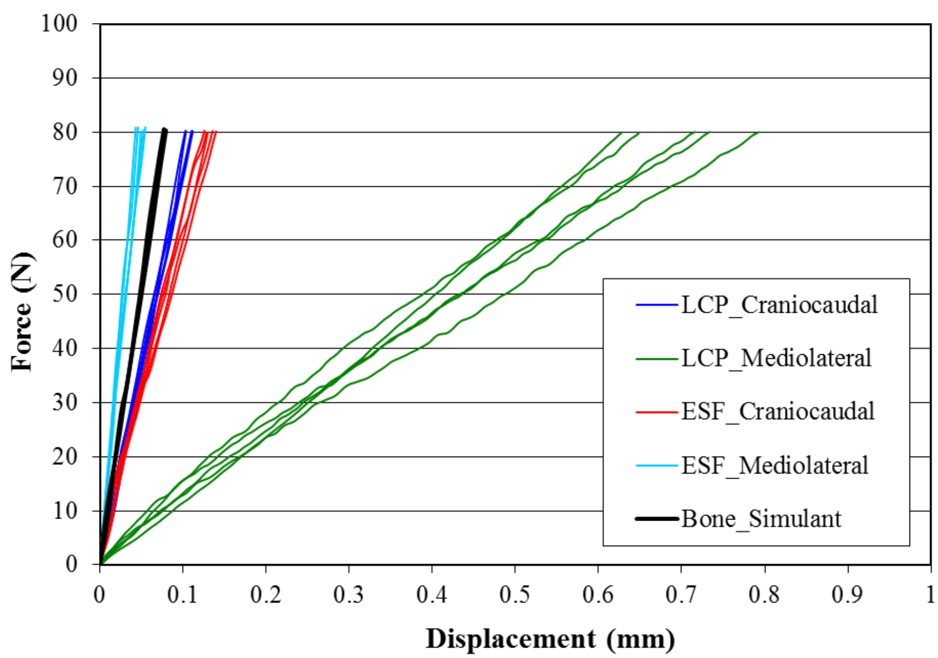

Figure 16: Summary of linear elastic portion of the force-displacement curves for all constructs, including bone simulant, in bending

Compression Tests

The stiffnesses of the Type II ESF and the LCP constructs in axial compression are expressed as means and standard deviations in Table 3. The one-way ANOVA showed that there was a statistically significant difference between the groups (p = 0.0000). The stiffness of the Type II ESF in axial compression (679.1 N/mm ± 20.1 N/mm) was significantly greater than that of the LCP construct in axial compression (221.2 N/mm ± 19.1 N/mm). The linear portion of the elastic regions of the force-displacement curves for the Type II ESF and LCP in axial compression are depicted in Figure 17. The linear elastic portions of the force-displacement curve for the Type II ESFs and LCPs separately in axial compression are shown in Figures 18 and 19, respectively.

Table 3: Summary of axial compression results for Type II ESF and LCP constructs

Construct	Mode of Loading	Stiffness (N/mm)	
		Mean	Standard Deviation
LCP	Axial Compression	221.2	19.1
Type II ESF	Axial Compression	679.1	20.1

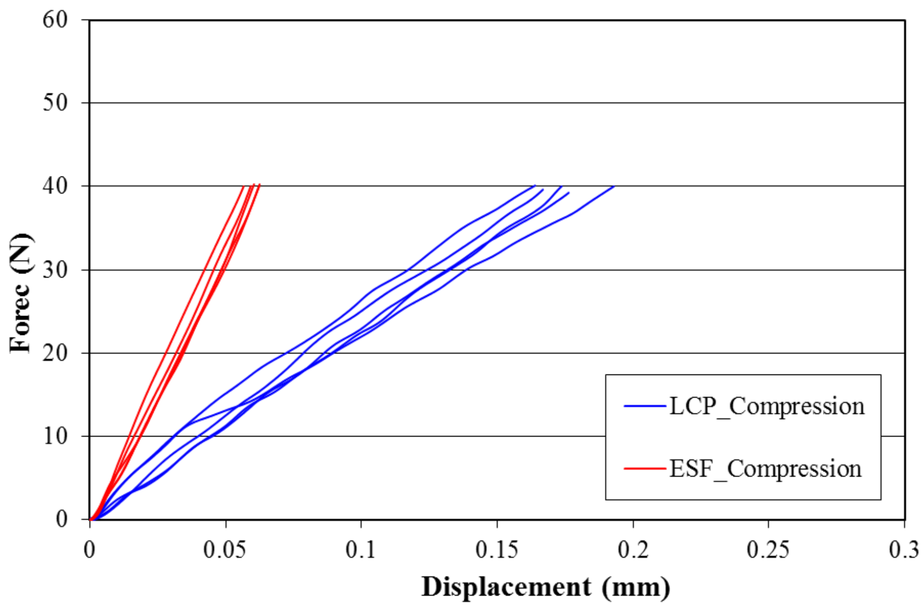

Figure 17: Summary of linear elastic portion of force-displacement curves for all compression tests

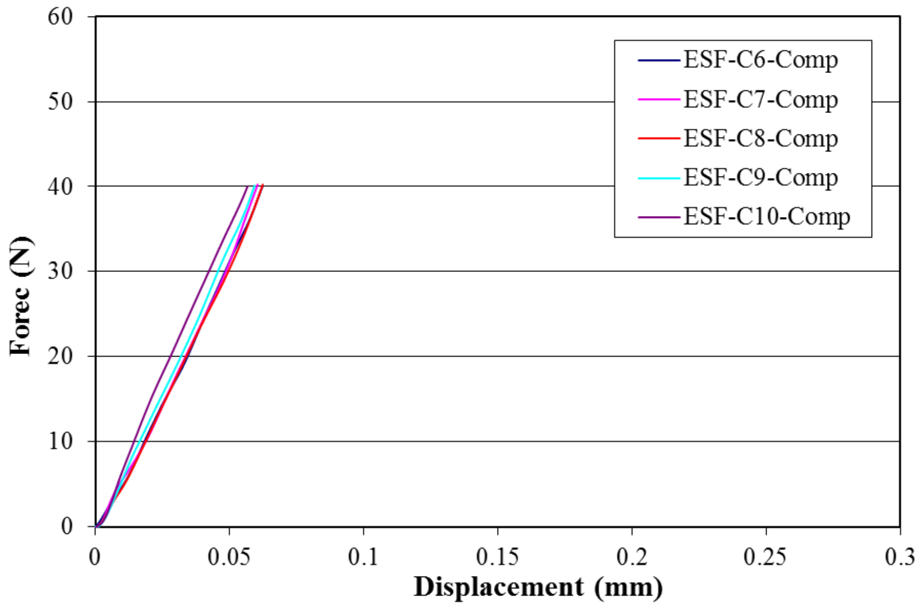

Figure 18: Linear elastic portion of force-displacement curves for Type II ESF constructs in axial compression

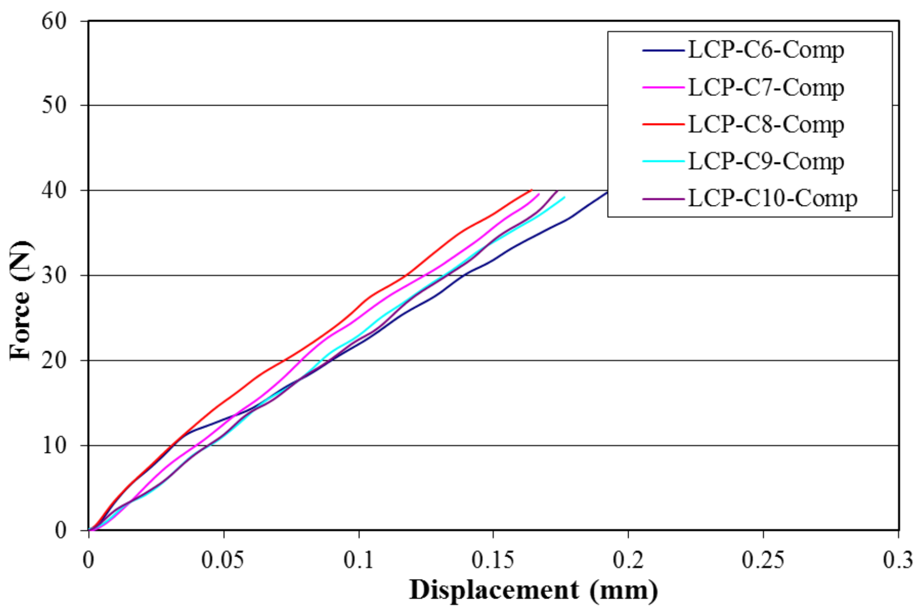

Figure 19: Linear elastic portion of force-displacement curves for LCP constructs in axial compression

8) Discussion

The results of this study demonstrate that a Type II ESF is significantly stiffer than an LCP in mediolateral bending and axial compression, but there is no significant difference in stiffness between the two constructs in craniocaudal bending. These data lead to the rejection of the stated hypothesis. There are no other mechanical studies to date that compare a Type II ESF and LCP construct in a comminuted fracture model.

Previous studies have been performed to evaluate quality and strength of bone healing achieved with ESF compared to conventional bone plating methods. In rabbit tibiae, plate fixation and ESF yielded a similar amount of periosteal callus, had similar times to radiographic union, and demonstrated comparable strength and stiffness of the healed bone; however, plated bones demonstrated decreasing strength in the later stages of healing, attributed to stress protection, although this did not reach significance[101]. Another study demonstrated that unilateral ESF yielded less mature bone with more bone resorption and porosity at 120 days compared to plate fixation[105]. In addition, the healed bone was less stiff in axial compression, distraction, craniocaudal bending, mediolateral bending, and torsion for the unilateral ESF[105].

In the present study, the data revealed substantial differences in stiffness of the Type II ESF in mediolateral bending compared to the LCP construct both due to the ESF construct itself and to some inherent differences in the mechanics of an LCP versus a conventional bone plate. The bilateral biplanar design of the Type II ESF construct affords the most stiffness in mediolateral bending, as opposed to craniocaudal bending[57]. Bouvy et al. compared different ESF constructs, and concluded that the Type II ESF would have optimal stiffness in mediolateral bending compared to craniocaudal bending in a small gap model. Similarly, the comparatively decreased stiffness of the LCP construct can be potentially attributed to some inherent factors. The LCP is placed eccentrically on the model, introducing an inherent asymmetry in response to the loading conditions. While both sides of the Type II ESF are eccentric, they are not asymmetric. The LCP is designed similarly to the LC-DCP, with a scalloped underside such that contact is decreased while maintaining even stiffness along the long axis of the plate, and stress is minimized at the screw holes by reducing the cross-sectional area between them[135 129,136]. The area moment of inertia of a bone plate with a rectangular cross-section is relative to its thickness to the third power, and a greater area moment of inertia confers increased resistance to bending, i.e., increased bending stiffness[137]. When loaded in mediolateral bending, the thickness of the LCP is less than when the LCP is loaded in craniocaudal bending, so it would follow that a greater resistance to bending would be achieved in craniocaudal bending. The LCP can function to afford relative stability particularly in a comminuted fracture situation where screw holes are left open over the fracture, so an increased flexibility in this situation can be expected. In addition, adaptations can be made to the LCP construct to increase stiffness in mediolateral bending if necessary, including the addition of an intramedullary pin, as well as a lateral buttress plate[111,138]. It is important to note that the optimal level of stiffness to stimulate osteosynthesis and prevent non-union is not known, so although quantifying stiffness of these constructs provides valuable comparative information, it is still important to consider each clinical fracture scenario individually, as greater stiffness does not definitively correlate with optimum fracture healing[47,49].

Previous studies have reported stiffness for various LCP constructs in bending and axial compression[112,126,131,132]. In a comparable model, Pearson et al. concluded the stiffness calculated for a comparable LCP construct was much lower than the values obtained in the current study. An approximately 32% increase in stiffness was noted in mediolateral bending, a 280% increase in craniocaudal bending, and an approximately 190% increase in axial compression in this study compared to Pearson et al. Although some of this discrepancy could potentially be attributed to slight variations in methodologies and the testing apparatus, it is likely that the discrepancy is primarily due to the inherent differences in stiffness of the composite material used in the bone model. Pearson et al utilized acetal tubes (Delrin® Acetal Polymer; Plastics International, Eden Prairie, MN, USA) and polyurethane foam (Sawbones™ Pacific Research Laboratories Inc., Vashon Island, WA, USA) to simulate cortical bone. The area moment of inertia (I) of a hollow cylinder is based on the inner diameter (D_I) and the outer diameter (D_O). The I of both bone model cylinders were calculated using $I = \pi/64\ (D_O^4 - D_I^4)$. The I of the acetal tubes is 2737 mm^4 versus approximately 5968 mm^4 for the composite cylinders used in this study. This represents an approximately 118% increase in area moment of inertia for the composite compared to the acetal tubes, which would lead to a 118% increase in stiffness assuming that all else is equal, i.e., same test conditions and modulus of elasticity. In addition, the reported elastic modulus for the acetal tubes ranges from 3-6 GPa, depending on what type was used. The elastic modulus for the short fiber reinforced epoxy cylinders was 16 GPa, which represents a 167-433% increase in stiffness between the two models. Therefore, comparable values cannot necessarily be expected between mechanical studies. In future studies, reporting data as "bending structural stiffness" according to the American Society for Testing and Materials (ASTM) may allow direct comparison between normalized stiffness values as reported in other studies[126,131,139].

This study sought to simulate a comminuted fracture, in which reconstruction of the bony column is considered impossible. This represents a commonly encountered clinical scenario in which biologic osteosynthesis methods will be utilized and all stability must be afforded by the imposed surgical fixation due to the lack of load sharing. The model in this study was designed with a large enough fracture gap to eliminate the risk of contact between fracture fragments and without any stability afforded from load sharing, as in other fracture gap studies[132,140]. The LCP construct was designed to model the ideal use of an LCP in a comminuted fracture with a gap of 40 mm, according to published recommendations[116,123]. Given the importance of screw configuration and working plate length in affording stiffness in biomechanical studies, the LCP construct had 2 bicortical locking screws placed nearest to the fracture and 1 farthest away per fragment to provide the greatest stiffness possible from 3 screws per fragment[111,116,132]. Similarly, the Type II ESF was chosen as it represents a clinically feasible ESF configuration for use in a comminuted fracture. The ESF construct was designed to be in keeping with current recommendation in terms of number of pins per fragment, pin configuration and type, and pin placement[42,57,66,87,141-145]. Other reasonable options would have been Type IB, Type III ESF or hybrid fixators, but time and finances precluded the evaluation of all of these constructs in the course of one study. Earlier ESF studies have suggested that uniplanar bilateral fixations (Type II in the mediolateral or craniocaudal plane) may be inadequate at counteracting *in vivo* bending forces generated in the canine tibia, and that placing a construct craniomedially (Type IB) will better address *in vivo* bending forces, which is grounds for further evaluation in future studies[146,147].

In order to render data most applicable to a clinical setting, modes of loading were chosen to most closely simulate forces of weight bearing encountered *in vivo*, including bending and axial compression[56,132]. Bending is considered to be responsible for a large proportion of strain in most bones, and is often chosen for mechanical testing[2,111,132,148]. A 4 point bending scenario was chosen in order to apply a constant moment along the construct, as previously reported, although no *in vitro* or *ex vivo* bending condition has been shown to precisely duplicate physiologic bending *in vivo*[90,111,124,125]. In addition, mediolateral bending and craniocaudal bending were both performed previously[111,132]. In a fractured bone scenario, mediolateral bending will induce a tensile force on the medial or lateral side of a bone, while craniocaudal bending will induce such a force on the cranial or caudal surface, depending on the direction of bending. This forms the basis for the AO recommendations for bone plate application to the "tension side" of a bone[133]. This phenomenon has been demonstrated in an *in vivo* study using external fixation and it is considered the most accurate method to assess the mechanics of a construct in both modes of bending, if possible. Similarly designed mechanical studies have tested in axial compression[112,127,149]. There are some that argue that with a large fracture gap model, axial compression is not as clinically relevant due to the possibility of generating a bending moment during testing[140]. This was not observed during the sub-yield testing in the current study; however, preliminary attempts to test to failure did demonstrate significant bending of the eccentrically placed LCP implants. This precluded the ability to accurately assess pure axial load to failure, as discussed later. It is the opinion of the author that this situation marks a legitimate concern for accuracy in assessing failure of a large fracture gap construct in axial loading, but not necessarily for measuring stiffness in sub-yield loading assuming the construct does not deform considerably.

This study did not evaluate these constructs in torsion, unlike some comparative mechanical studies[111,125,128,131,140,150]. Previous studies have noted differences between LC-DCP constructs and LCP constructs in cyclical torsion, where the LCP construct has been less stiff[125,128]. In contrast, other studies have shown no significant difference in stiffness between locking and non-locking constructs, or even increased stiffness with locking constructs, in cyclical torsion[151-153]. Previous mechanical studies have prioritized other modes of loading over torsion, citing force plate analyses demonstrating a decreased rotational demand on canine femora *in vivo*[90,154,155]. Thus, while torsion may not unilaterally be considered among the most relevant forces to evaluate, it remains an area of interest for future expansion of this study.

This study sought to maximize the information gained from a limited number of constructs by rotating the same constructs orthogonally to test in mediolateral and craniocaudal bending, as previously performed[132]. This is in contrast to other studies, in which each mode of loading and test order were assessed with distinct constructs[111]. In order to verify that the repeat testing would not affect the measured stiffness, repeat tests were conducted on several constructs. The results of these tests showed that there was no change to the measured stiffness after replacing the constructs in the testing apparatus, re-tightening screw, re-zeroing, and re-loading (see Appendix A). In other words, these test confirmed that the constructs were not altered by repeated loading, i.e., the loading was sub-yield. Additionally, preliminary sub-yield testing performed with alternating order of testing (mediolateral first, followed by craniocaudal and the reverse) confirmed that test order did not impact the measured stiffness. Therefore, any observed differences can be attributed to the differences in loading conditions or construct type, and not to any changes due to repeated loading.

A limitation of this study is the use of a synthetic bone model in lieu of cadaveric bone, which is considered to have the most accurate representation of bone material properties[156]. The use of the bone substitute minimizes variability during testing and may lead to increased power of a mechanical study, but it is not an accurate representation of living tissue. Similar models have been used to mimic a non-load sharing fracture and the short fiber epoxy reinforced cylinders have been validated as an acceptable bone substitute in mechanical testing[131,132,157]. Being hollow, it may more accurately predict the behavior of cortical bone, especially in regards to the “bone”-screw interface versus solid cylindrical materials, although the screw holding capacity may yet still be suboptimal compared to cadaveric bone[158]. Thus, although allowing for comparisons between constructs, caution must be used in extrapolating conclusions from this mechanical study for use in a clinical scenario.

An additional limitation to this study was the lack of evaluation of yield point or load to failure, as reported in similar mechanical studies[111,112,125,131,132,150]. The yield point could not be accurately determined due to constraints inherent in the design of the testing apparatus for the bending tests. The boundary conditions were constrained by the distance between the contact points, which was based on the setup used by Pearson et al., being too narrow and the lack of rollers to provide a nearly frictionless surface. Although the surface of the contact points and the aluminum pots were lubricated, this did not duplicate a truly frictionless boundary condition. Due to narrow distance between the contact points and the presence of friction, the angle of the aluminum pots, and thus the constructs being tested, increased quickly, but the pots did not translate towards the center of the construct to a large extent. This resulted in an increased tensile load on the construct, which in turn affected the force-displacement curve. Consequently, there was not a distinct inflection point to define yield. Similarly, destructive testing was not performed in axial compression, in contrast to similar studies[132]. Preliminary load to failure testing conducted on LCP constructs in axial compression showed that the constructs underwent visible bending, i.e., buckling. The load cell used, however, was a single axis load cell and not a multi-axial load cell. Therefore, a crosstalk compensation matrix could not be used to compensate the measured axial force for the effects of shear forces. Measuring failure force under those conditions would lead to inaccuracies due to the limitations of the single axis load cell. In addition, the forces applied to the construct would not be purely axial. Instead, they would be a combination of compression, shear, and bending, due to the large degree of buckling resulting from a large fracture gap model with an asymmetric eccentric LCP construct, which is a concern cited in previous studies[90,140]. In addition, this could potentially bias the testing against the LCP construct given that the LCP is unilateral and placed eccentrically on the bone, and thus more susceptible to bending forces during compressive loading[90,140]. Further studies may be conducted to failure using a multi-axial load cell.

Cyclic loading was not evaluated in this study, unlike other mechanical studies[111,112,125,127,128]. Cyclic loading is considered to be most representative of loading conditions encountered during post-operative convalescence, and cyclic fatigue is considered to be most responsible for failure of constructs in a clinical setting[111,125]. More importantly, it can approximate the micromotion that can potentiate osteosynthesis and/or the macromotion that disrupts it[16,48-52,125]. Other studies have sought to quantify and describe interfragmentary motion and gap stiffness more precisely, but this was beyond the scope of the current study[90,125]. Cyclic loading also better demonstrates the biphasic stiffness profile of the LCP, as shown in other studies, versus static loading[112,118,127,128]. It was decided to simplify this initial study to quasi-static loading in order to generate quantifiable mechanical parameters for relative comparison, as performed in previous studies[126,132,159]. Previous studies have shown varied results comparing LCPs and non-locking plate constructs in dynamic testing[125,128,151,152]. These differences are somewhat attributable to variations in experimental design and materials, which illustrates the difficulty in testing cyclic loading in a consistent, repeatable fashion that both accurately represents a clinical scenario and allows for comparisons to be made between studies. Nevertheless, performing a mechanical comparison between ESFs and LCPs in cyclic loading represents a next step in predicting how these will behave in a clinical setting.

9) Conclusions

In conclusion, due to the increased stiffness demonstrated by the Type II ESF in mediolateral bending, this construct may be the preferred choice, compared to an LCP, in a comminuted fracture requiring increased stability in the mediolateral plane. The optimal stiffness for stimulating bone healing while preventing non-union is not known, so definitive conclusions in regard to how stiff a construct must be in every scenario cannot be determined. However, this study provides quantifiable and comparable stiffness data for 2 commonly utilized constructs in a fracture gap model. These mechanical properties can augment a clinician's understanding of the capacity of implants to impose stability, and aid in their ability to balance biologic factors and mechanical factors to choose an appropriate fracture fixation method in a clinical scenario. Further studies are warranted to evaluate these methods in cyclic loading and torsion, and to prospectively evaluate fracture healing using these 2 methods in clinical patients.

10) References

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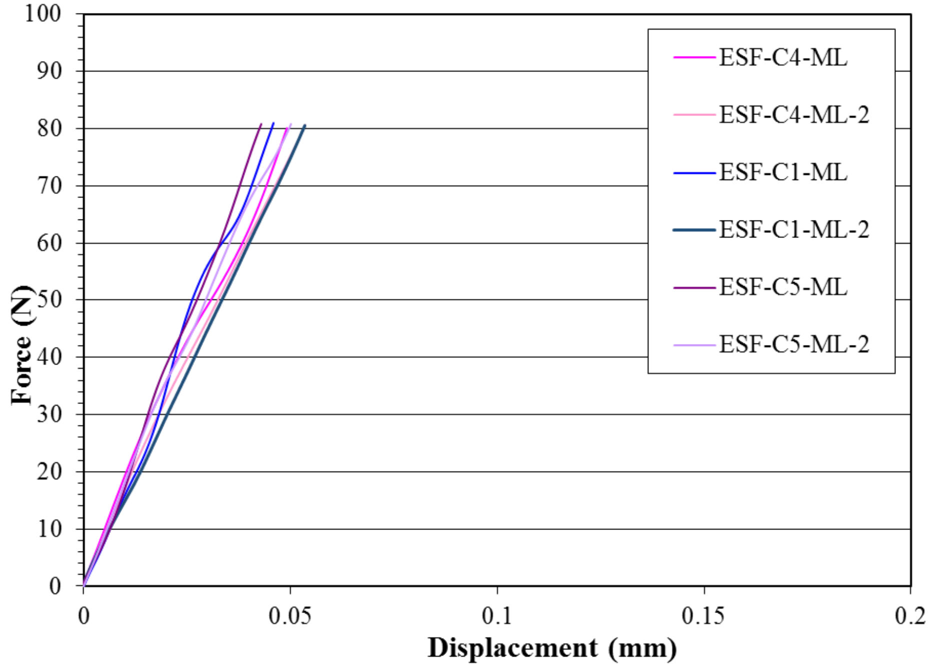
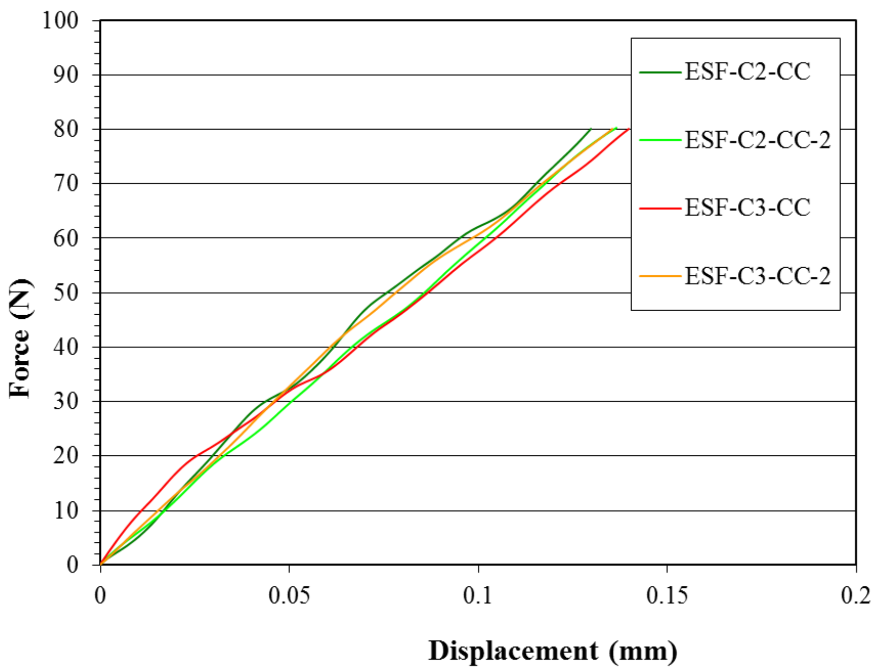
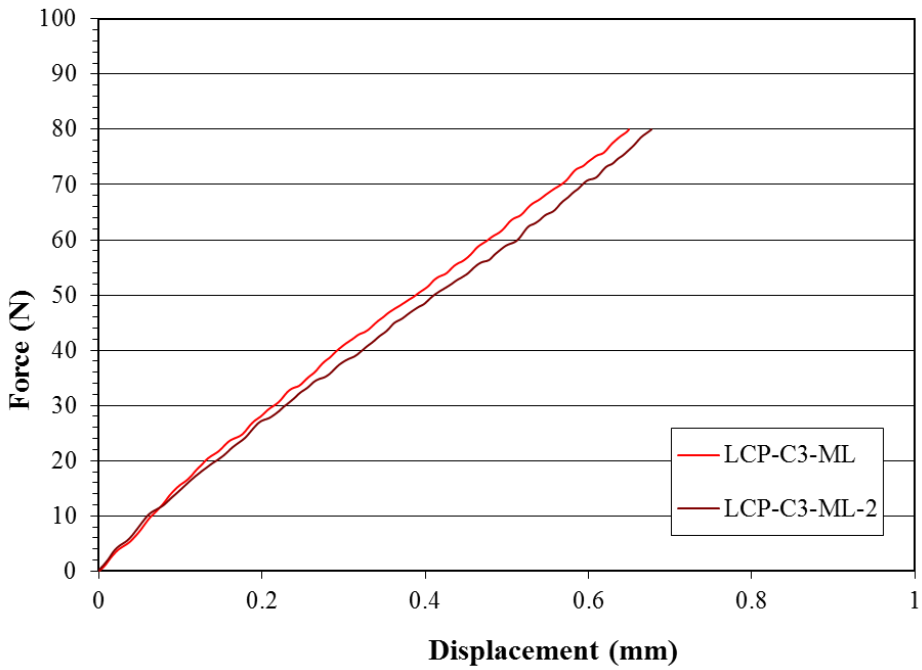
APPENDIX A
Data from repeated tests and associated statistics



Appendix Figure 1: Summary of Type II ESF constructs in mediolateral bending with repeated tests on the same constructs



Appendix Figure 2: Summary of Type II ESF constructs in craniocaudal bending with repeated tests on the same constructs



Appendix Figure 3: Summary of LCP constructs in mediolateral bending with repeated tests on the same constructs

Appendix Table 1: Summary of stiffness of Type II ESF in mediolateral bending with repeated tests with paired student's t-test

Sample Type	Loading Type	Test ID	3rd Cycle Slope N/mm
Type II ESF	Mediolateral Bending	ESF_C1_ML	1784.9
Type II ESF	Mediolateral Bending	ESF_C4_ML	1447.8
Type II ESF	Mediolateral Bending	ESF_C5_ML	1824.1
Type II ESF	Mediolateral Bending	ESF_C1_ML-2	1511.4
Type II ESF	Mediolateral Bending	ESF_C4_ML-2	1428.6
Type II ESF	Mediolateral Bending	ESF_C5_ML-2	1544.5

	p-value
Paired student's t-test	0.16

Note: Significance is set at $p < 0.05$

Appendix Table 2: Summary of stiffness of Type II ESF in craniocaudal bending with repeated tests with paired student's t-test

Sample Type	Loading Type	Test ID	3rd Cycle Slope N/mm
Type II ESF	Craniocaudal Bending	ESF_C2_CC	576.0
Type II ESF	Craniocaudal Bending	ESF_C3_CC	530.9
Type II ESF	Craniocaudal Bending	ESF_C2_CC-2	591.8
Type II ESF	Craniocaudal Bending	ESF_C3_CC-2	562.3

	p-value
Paired student's t-test	0.20

Note: Significance is set at $p < 0.05$

Appendix Table 2: Summary of stiffness of LCP in mediolateral bending with repeated tests

Sample Type	Loading Type	Test ID	3rd Cycle Slope N/mm
LCP	Mediolateral Bending	LCP_C2_ML	103.9
LCP	Mediolateral Bending	LCP_C3_ML-2	109.7

Note: Paired student's t-test not performed due to insufficient sample size