Design and Validation of an External Fixator for use in *In Vivo* Fracture Studies

By:

Marc Nash

****

Submitted in partial fulfillment
of the requirements for
Honors in the Department of Bioengineering

UNION COLLEGE

June, 2011

ABSTRACT

NASH, MARC Design and Validation of an External Fixator for use in *In Vivo* Fracture Studies. Program of Bioengineering, June 2011

ADVISOR: Jennifer Currey

This thesis explores how a new external fixator effects the healing process in the fracture site of a mouse tibia. Studies have shown that the amount of time it takes a fracture to heal can vary based on the type of fixator used. An external fixator was designed using SolidWorks and fabricated by Medical Micro Machining (Colfax, Washington). Rubber disks where created from a mold and inserted in the bottom piece of each fixator.

Using a dental drill and a variety of clamps, the fixator was attached to an already removed tibia. A Dremel saw was used to create a 1 mm fracture in the middle of the tibia and Reprorubber was inserted into the fracture site to act as a mock callus. The Daqbook 2020 data acquisition system was instrumental in helping validate the callus stiffness formation system. A micro linear actuator was used to measure the displacement of the mock callus. The Reprorubber material had a stiffness of 0.016 N/µm. The total experimental stiffness collected was 0.036 N/µm. Even though the experimental stiffness varied slightly from the theoretical stiffness (0.032 N/µm), these results validated the callus stiffness system. Lastly, a biaxial mouse stage was designed to allow for easy callus stimulation.

Introduction:

Research has been done to investigate the influence of mechanics on fracture healing. Documentation has shown that one in every twenty fractures result in a non-union or a malunion, which further emphasizes the need for new treatment methods [National Health Statistics]. The rate that a fracture heals is influenced by many different factors. The first factor is the health of the patient; an osteoporotic patient will take longer to recover. Secondly, the geometry of the fracture will have a significant impact on the rate of recovery. Lastly, stability of the fracture influences the healing mechanisms (i.e. the less stable the fracture the longer it takes to heal).

Studies have shown that the amount of time it takes a fracture to heal can vary based on the type of fixator used. The time it takes for a fracture to heal is roughly six to eight weeks. The first step in fracture healing is formation of a blood clot. In the next few days the blood clot will be replaced with a soft callus which is comprised of granulation tissue and cartilaginous tissue (Figure. 1).

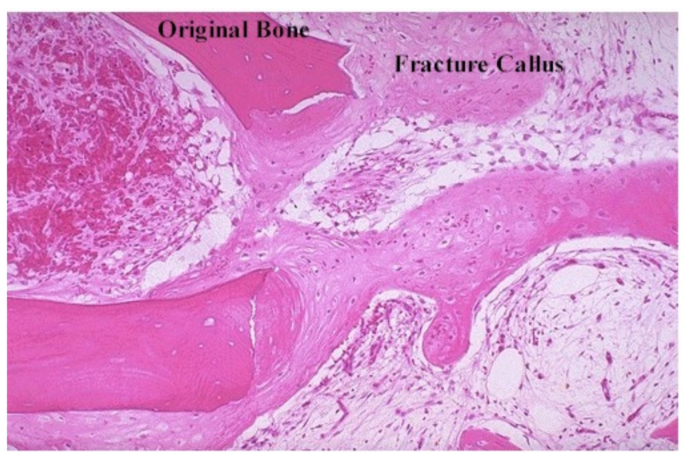


Figure 1: Illustrates the formation of a soft fracture callus in the fracture gap [11].

The degree of soft callus formation is an indication of the amount of motion (i.e. the more motion there is the larger the callus). Some fractures cannot move past the soft callus phase due to instability. The hard callus phase is marked by the calcification of the soft callus. Osteoblasts (bone formation cells) and blood vessels invade the soft callus and bone is laid down. Studies have shown that the mechanical environment can be manipulated to enhance fracture healing [1, 2, 3, 4, 5, 7, 8, 9].

The overall theme of this research is to develop a methodology to determine the effects of controlled fracture motion on the healing process. For my senior project, I will be researching how a new external fixator effects the healing process in the fracture site of a mouse tibia.

Background:

The use of axial dynamization to promote fracture healing is a currently accepted treatment for non-unions [4]. Dynamization is theorized to lead to the stimulation of the proliferation of a periosteal (the membrane surrounding bone) callus in the early stages of fracture healing and accelerates the response of normal bone cells in the late healing phase. However, little is known about when the fixator should by dynamized postoperative and how much motion is beneficial.

A study was done Egger et al. to investigate the effects of axial dynamization of a fracture midway through the healing process. Seven adult mixed-breed dogs where used in the study. Each canine had a fixator attached to their tibiae via six pins. Seven days postoperative each dog had one of its fixators telescoping mechanism unlocked allowing dynamization to occur. It is important to note that compression was not controlled, that once the mechanism was unlocked the canines were allowed to resume normal behavior. The other fixator was the control and would stay rigid for the duration of the experiment to allow for a maintained 2mm gap. After 42 days the canines were euthanized and their tibiae harvested. Several tests including a histological evaluation, a fixator rigidity evaluation, and a biomechanical analysis were done on the tibiae to examine the effects of dynamization. Mechanical tests found that axial loading in compression on the dynamized tibiae was significantly greater than that of the control tibiae. However, torsional, anteroposterior and mediolateral stiffness of the dynamized tibiae were not significantly greater than that of the control. The biomechanical analysis confirmed that with torsion testing, the dynamized osteotomies were significantly greater than the control ($p<0.05$). Furthermore, the results indicated that the fracture gap was significantly smaller in the dynamized tibiae ($p<0.0016$). The researchers explained that there was more variation between the canines then there was between the dynamized and control tibiae. From these findings it is believed that dynamization allows for an adaptation from a delayed union to accelerated normal healing [6].

The length and quality of fracture healing is influenced by both biomechanical and biological factors. The most important biomechanical factor is interfragmentary movement (same as dynamization). IFM is small axial movement that is known for stimulating bone growth, however the exact amount has yet to be determined [5]. IFM depends on a few factors, the stiffness of the fixator, the load applied to the operated leg, and the number of load cycles. Claes et al. conducted a study to explore whether early dynamization leads to improved healing and if a rigid fixator is better at promoting healing then a flexible fixator.

Twenty-four male Wistar rats were divided into three groups, the rigid fixator group (group R) with a stiffness of k=74 N/mm, the flexible fixator group (group F) with a stiffness of k=10 N/mm and the dynamization group (group D). The fixator consisted of two rectangular steel and aluminum pieces that attached to the bone via four pins. Dynamization was allowed one week postoperative by removing the inner bar of the fixator. The rats were observed and examined for five weeks. Using a motion detection system, the researchers were able to measure the activity of the rats. A three point bending test was done, in which the rigid fixator had a flexural rigidity (force couple needed to bend a rigid structure) of 82% (anterior-posterior direction) and 93% (medial-lateral direction) greater than the dynamization group. In addition, the µCT results indicated that the rigid fixator had a 9% great bone volume fraction (bone volume divided by total volume) then the dynamization group. The rigid fixator also had a flexural rigidity 87% (anterior-posterior direction) and 58% (medial-lateral direction) greater than the flexible fixator group. The researchers believe that in prior studies improved fracture healing was not due to dynamization but rather due to the effect of closing the fracture gap. Furthermore, the researchers presume that the rigid fixator provided improved healing compared to the flexible fixator because the less stable flexible fixator might have resulted in reduction in activity by the group F rats. This was seen in a previous study where sheep with flexible fixators applied less weight to those specific tibiae [13]. Even though the researchers rejected the hypothesis that early dynamization will lead to improved healing, more research is necessary to determine if later dynamization could stimulate the fracture healing process [3].

A study was done by Claes et al. to investigate whether temporary fracture distraction/compression could accelerate fracture healing by strain-induced bone formation. It was hypothesized that interfragmentary movements of a fractured tibia could lead to healing by strain-induced bone formation. The researchers believe this to be true based on Ilizarov's findings (1989) that tension stress around a fracture gap will lead to new bone formation during callus distraction [10]. The fixator used was a custom built fixator with six stainless steel screws. It was surgically attached to the right leg of fourteen female mountain sheep. The sheep were separated into two groups. Group TD had cyclical interfragmentary movement of the fixator. Group C had constantly stabilized fixators. The researchers distracted the tibia in the TD group by 0.5mm twice a day for two days. On the third day they shortened the fracture gap by 1.0mm. It is important to acknowledge that after three days the fracture gap distance was at its original distance (3mm). This procedure was carried out for twelve days. The researchers made two important observations when performing the procedure. First, they discovered that compression of the tibia resulted in significant pain for the sheep. This is important because when performing surgery we might need to provide medicine to the mice in order to eliminate any pain. Secondly, they discovered that the sheep in the TD group were careful with the amount of weight they put on the operated leg. The researchers should not have relied on the weight bearing force as a controllable force because the sheep might not have been putting their entire weight on that leg. After the researchers analyzed their results, they confirmed that quasi static tension and compression stimulates bone growth and leads to improved healing. The bone volume and volume of "whole callus" was significantly greater in the TD group. In addition, histology showed that the TD group had more bone formation in the site of the fracture, while the C group had a lot more cartilage; however, the results were not statistically significant [2].

Several studies have been done to confirm that mechanical stimulus during fracture healing leads to increased healing in the site of the fracture. However, despite these studies little is known about the relationship between the mechanical environment and the patterns of bone repair. A study was done by Smith-Adaline et al. to investigate the association between mechanical strain stimulus and the patterns of tissue growth in the site of a fracture. Seventy male Sprague-Dawley rats had a custom fixator attached to both femurs via four threaded pins. Seven days postoperative, the femur was bent in the anterior-posterior direction in a custom built stimulation device. One fracture in each rat was stimulated three times a week for 17 minutes at 0.5 Hz (from day seven to day eighteen). Once the animal was sacrificed, the tibia and fracture gap tissue were harvested. Microcomputed tomography (μCT) images showed substantial bone growth in the region that was under tensile stress. Where as the region under compressive stress showed minimal bone formation. Compressive regions contained less cartilage and less bone. This demonstrates that less cartilage does not necessarily correlate to more bone. Tensile regions had an increase in mesenchymal cells, which transformed to cartilage then quickly to bone once removed from tension. In addition, from the results the researchers believe that tensile strains tend to increase the amount of bony bridging present in fracture gaps. While compressive strains favor direct intramembranous bone formation. It is important to mention that the none of the results presented in this paper were statistically significant and that due to the simplification of the shape of the callus more research is needed to be done to further confirm their findings [12].

The four major factors in determining the mechanical environment of fracture healing are: fixator rigidity, fracture configuration, accuracy of fracture reduction and the amount/type of stresses occurring at the ends of the bone. Even though many of these factors have been studied in depth, little is known about the relative efficiency of primary and secondary fracture healing mechanisms. Primary fracture healing is when a fracture gap closes by direct bridging of the two bones via new bone. Secondary healing is when a fracture heals with the help of a periosteal callus. Aro et al. investigated the four major effects (listed above, rigidity was held constant) on fracture healing. Twenty-four dogs were divided up into three groups. Group 1 had a unilateral fixator attached to both of their tibiae via six pins. The fracture gap in group 1 was less then 1mm and was maintained by a bilateral transverse osteotomy (the gap was horizontal). Two weeks postoperative one of the fixators was dynamized by releasing the telescoping mechanism in the fixator. Group 2 had fixators attached to both tibiae however one of their fractures was transverse and one was at 60° oblique. Group 3 had a fixator attached to either tibiae and had a transverse fracture gap of 2mm. One tibiae in group 3 was dynamized using the same method as group 1 after four weeks. After 12 weeks the dogs were euthanized, their tibiae harvested and experiments were done to see the progress of fracture healing. The results from a histological and microradiography analysis indicated that between weeks 6-12 external modeling occurred more rapidly in transverse fractures compared to oblique fractures, which was indicated by the reduction of the callus formation. This signifies that fracture healing was further improved in transverse fractures. Furthermore, the tibiae of the dynamized transverse osteotomies had a significantly ($p<0.01$) reduced fracture gap. The researchers concluded that excessive gap size (greater then 1mm) tends to prevent bridging of secondary osteons and results in the presence of cartilage in the fracture gap. In addition, the results indicated that secondary healing (callus formation) occurred predominantly in dynamized fractures. Lastly, the researchers believe that dynamization might be best used in delayed fractures, or fractures which have an excessive gap size (dynamization will bring the two bones closer together) [1].

The orientation and design of the fixator is a crucial aspect of fracture healing. A study was done by Goodship et al. to investigate the effects of different 'offset' distances between the bone and the fixator. The researchers hypothesized that modifications solely in fixator stiffness would directly correlate to differences in fracture healing. The Oxford fixator, a rigid, unilateral fixator was attached to the right tibiae of twelve female sheep. The fixator was attached by use of six screws. The sheep were divided evenly into two groups. Group A had an offset distance of 35mm and group B had an offset distance of 25mm. The fixators movement was not controlled, postoperative the animals were allowed to walk around freely. After twelve weeks the system (fixator and tibia) stiffness was measured in response to axial compression. Group A's system stiffness was 500 N/mm, while group B's was 700 N/mm. Researchers also carried out a bone mineral content (BMC) analysis, where they found that between weeks 4-10 group A had a significantly ($p<0.05$) greater BMC then group B. Furthermore, they found that at twelve weeks of healing the individuals in group A walked normally, while individuals in group B were still cautious when putting weight on their right tibia. A regression analysis was also performed, in which it indicated that if the fixator is properly orientated, rapid growth in fracture stiffness can occur in the first few weeks of healing. From these results, the hypothesis was confirmed, that small differences in fixator geometry can lead to major changes in fracture healing. Previous studies also support this hypothesis, however this is the first study that has confirmed that differences in fixator geometry solely effects the healing process [9].

Studies have shown that a more rigid fixator influences fracture healing. In addition, other studies have demonstrated that dynamization while maintaining the fracture gap could lead to improved healing. However, the researchers failed to control and measure the degree of motion or the applied load. In these studies, dynamization was achieved by removing a pin or a part of the fixator allowing the weight of the animal to compress the bone. In our research we will dynamize the fracture with a custom built unilateral fixator that will allow the fracture to be stable or dynamic. The healing tissue will be stimulated with 150 µm of pure axial motion. Periodically throughout the healing process the fracture gap will be examined to provide insight into the relationship of mechanical stimuli and tissue differentiation.

<u>Methods</u>:

Alex Guernon, class of 2010, created a fixator using SolidWorks that would fit on the tibia of a mouse. After further analysis, a few changes were made. The inner diameter of the bottom piece of the fixator was 1.5mm which did not allow for the top piece to move freely inside the bottom piece. The inner diameter was increased to 1.6mm to allow for more clearance. The six holes for the retention pins and stabilization bar were reduced in diameter (from 0.7mm to 0.6mm to minimize the chance of a fracture near the pin). One challenge was finding 0.6 mm diameter threaded pins longer than 1 mm in length. The pin needed to be at least 10 mm in length in order to fit through the fixator and into the bone. Retention pins known as a Filpins (Filhol Dental, Ireland) were found which are 0.6mm in diameter and 10 mm in length (Figure 2).

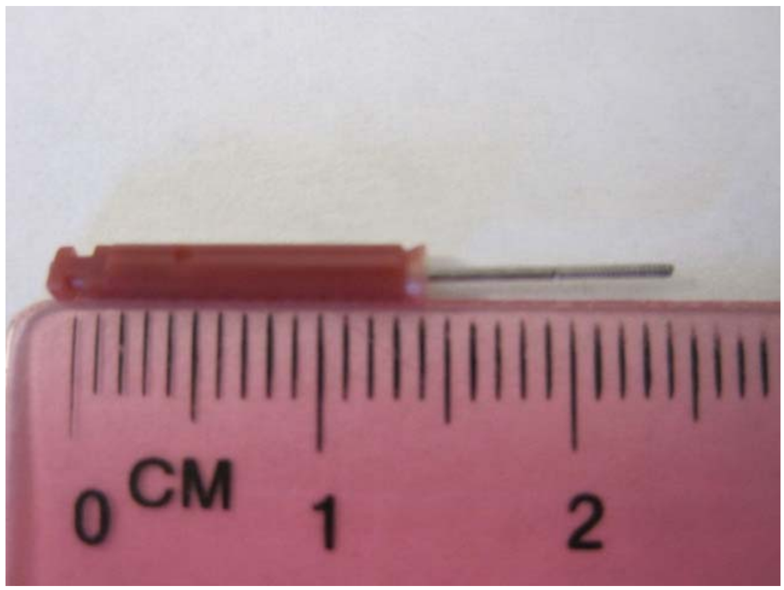


Figure 2: The Filpin, with a diameter of 0.6mm and a length of 1 cm.

The Filpins are made of pure (99.8%) titanium which is a highly biocompatible material. It was decided that the stabilization holes, through which the stabilization bar is inserted, should be the outer most holes. They would be rotated ninety degrees in order for the fixator to fit on the tibia and to not interfere with the retopins (Figure 3A, Figure 3B). The stabilization bar had to be lengthened in order for the pins to fit in the outer most holes (Figure 4). Medical grade Loctite was used to secure the pins to the stabilization bar. A zip tie will be used to temporarily yet securely fasten the stabilization bar to the fixator when the tibia is not being stimulated.

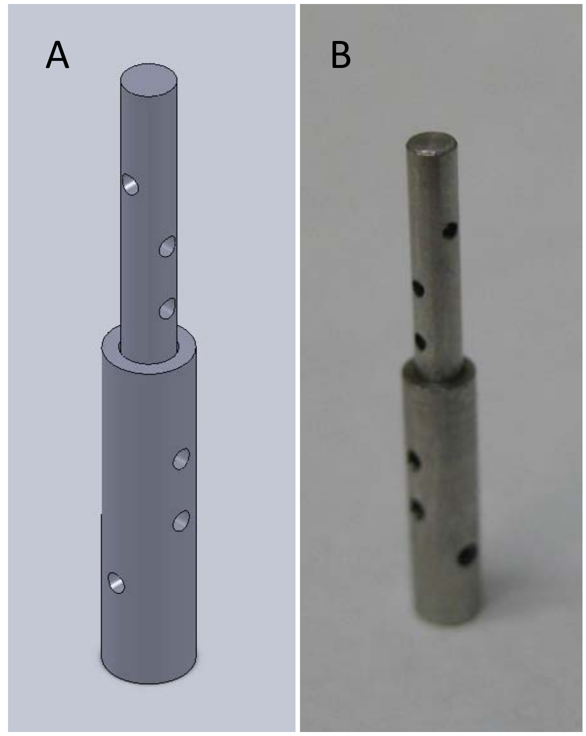


Figure 3: Fixator with stabilization holes at the top and bottom [A]. Fabricated Fixator [B].

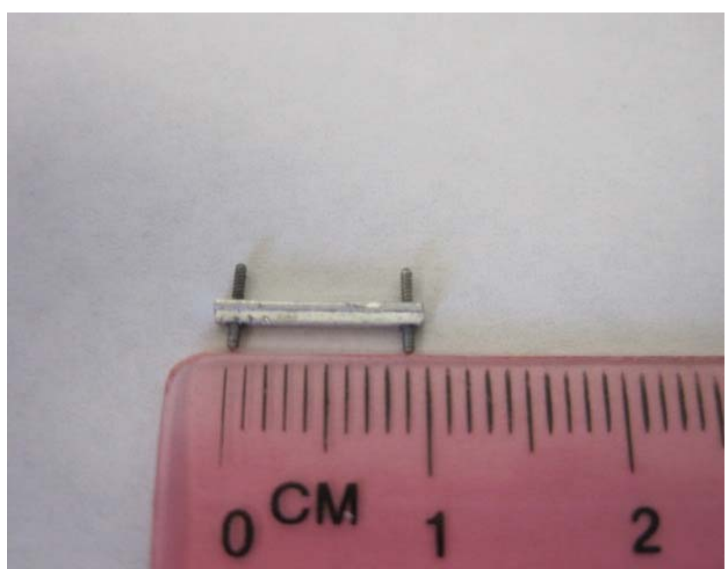


Figure 4: Stabilization bar with 0.6 mm retention pins.

With the fixator fully assembled a technique was needed to capture the stiffness at the fracture site. A method was developed to measure the amount of displacement and load applied to the fixator during the motion studies. A data acquisition system (DaqBook 2020, DBK43A and Zaber Console) will record the load and displacement applied to the fixator (Figure 5.). This data will then be used to calculated the overall stiffness.

Figure 5: The Data acquisition system.

Connected to the DBK43A is a load cell which will measure the force applied to the tibia.

A rubber spring was created to fit in between the two pieces of the fixator to help with returning it to its original position. SolidWorks was used to create a mold for a rubber spring and then the mold was fabricated in the machine shop (Figure 6).

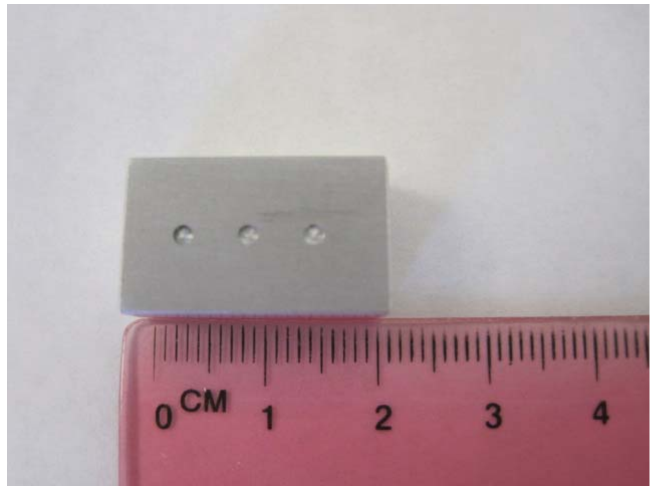


Figure 6: Rubber spring mold.

We can compute the stiffness of the rubber spring because the Reprorubber material has a known Young's modulus. The data acquisition software will collect the overall stiffness, which includes both the soft callus and the rubber spring (Equation 1). The callus and the fixator are modeled as two springs in parallel. If we know the stiffness of the rubber spring we will be able to determine the stiffness of the soft callus (Equation 2).

$$K_o = K_c + K_s \quad \text{Equation 1}$$

$$K_c = K_o - K_s \quad \text{Equation 2}$$

Where K_o is the overall stiffness, K_c is the stiffness of the soft callus and K_s is the stiffness of the rubber spring.

Fracture healing is a multistep process. As fracture healing progresses the tissue at the fracture site becomes stiffer. A rubber callus was made to validate the fixator and the data acquisition system. The rubber callus and rubber spring both have a known stiffness, which means the sum of the stiffness should match the stiffness calculated from the load and displacement data acquired by the data acquisition system. A callus mold was created using SolidWorks and then was fabricated in the machine shop (Figure 7A). The mold consisted of two identical pieces that with the help of steel rods came together. The callus was created by injecting Reprorubber into the mold (Figure 7B). The callus was spherical and had a diameter of 2.5 mm.

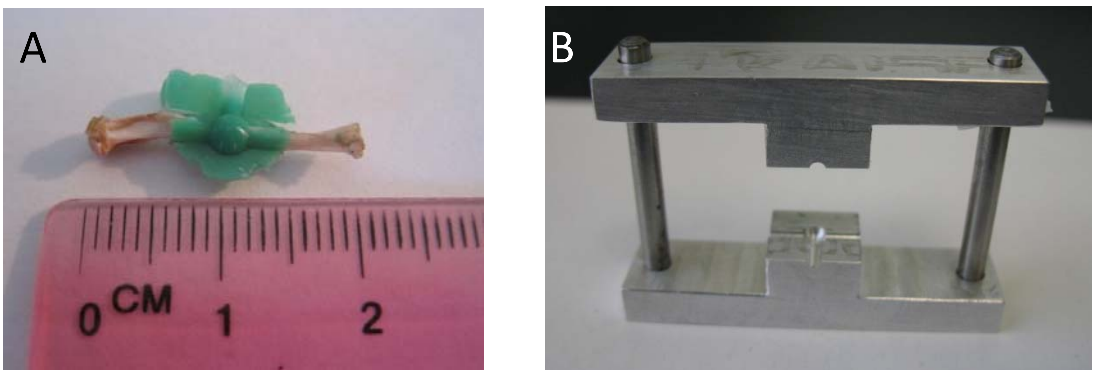


Figure 7: A fractured tibia with a rubber soft callus [A]. The rubber callus mold [B].

Procedure for removing tibiae:

Tibiae were harvested from previously deceased mice. A diagonal incision was made a few centimeters below the ilium. Using tweezers the skin was pulled back and a scalpel was used to separate the femur from the ilium (Figure 8). The hind limbs were removed from the mouse at which time the tibiae was separated from the femur and the foot. The scalpel was then used to remove any tissue or muscle that was present on the tibia. The extracted tibia was then placed in water to prevent the bone from becoming brittle.

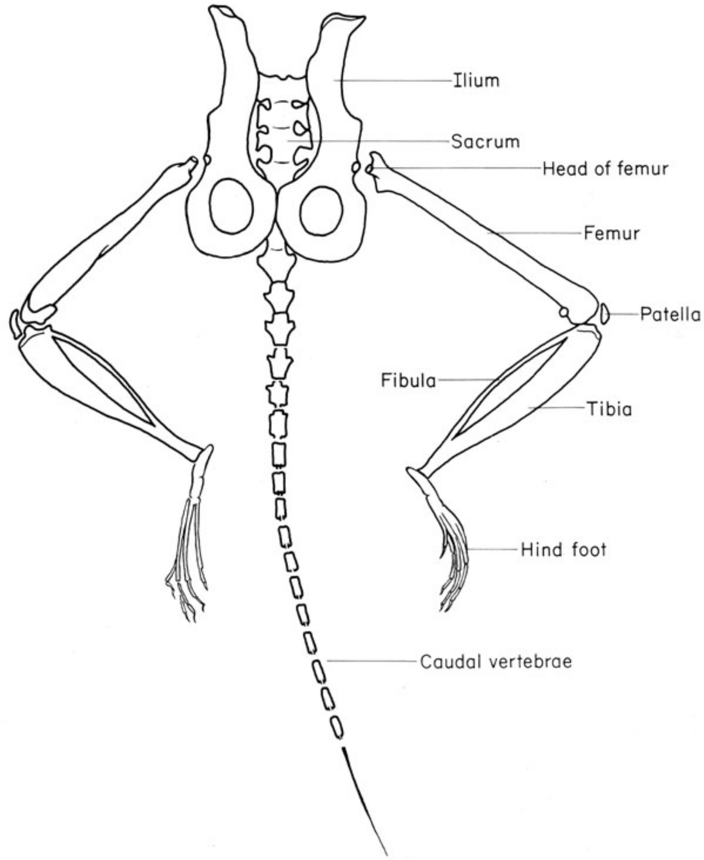


Figure 8: Anatomy of a laboratory mouse [15].

Process to attach fixator:

Prior to drilling, the bone was secured in a clamp. Using a dental drill the most distal hole was created first. The distal part of the tibia is very narrow, which makes it extremely difficult to drill into. The creation of the end hole had the greatest chance of breakage, which is why it was drilled first. The fixator was used as a drill guide for the remaining three holes. After each hole was created, a retopin was inserted through the fixator and into the bone (Figure 9). Once the fixator was attached, the stabilization bar was inserted. The stabilization bar was inserted to help keep the fixator together once the mock soft callus was created.

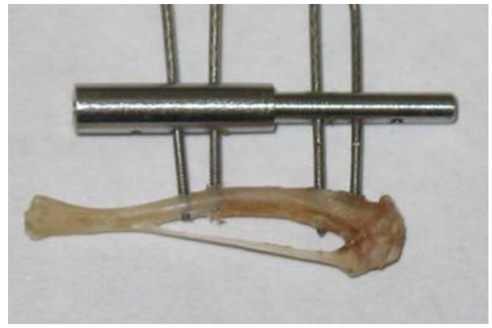


Figure 9: The fixator attached to a tibia.

Procedure to create soft callus when fixator attached:

Once the fixator was fully attached to the tibia the soft callus could be created. A 1mm osteotomy was made in the middle of the tibia using a Dremel Diamond Wheel. The tibia was then placed in the soft callus mold and Reprorubber was injected into the mold. The soft callus mold was left to set overnight. Using a scalpel, the tibia was carefully removed from the mold and placed on moist gauze to help prevent the bone from becoming brittle (Figure 10).

Figure 10: The fixator attached to the tibia with a mock soft callus at the site of the fracture.

Measuring displacement:

Initially displacement was going to be measured using a LVDT (Linear Variable Differential Transform). However, it became apparent when collecting data that the desired distance of 150 µm would be extremely hard to measure with an LVDT. The data being collected had a lot of noise, which made it difficult to determine the exact displacement of the fixator. After researching displacement instruments, the ideal apparatus to displace the fixator 150 µm is a linear actuator.

A micro linear actuator (T-NA08A25-KT01) was purchased from Zaber Technologies Inc based in Vancouver BC. The actuator has a travel range of 25.4 mm, with an accuracy of ±8 µm. However, the actuator is more accurate at smaller displacements. When traveling 150 µm, the accuracy is ± 2 µm. Using the Zaber Console the actuator was programmed to displace 150 µm, return home, and repeat at a frequency of 1 hz every 60 seconds. The Zaber Console measures distance in microsteps. One microstep is equivalent to 0.047625 µm, therefore 150 µm is equal to 3150 microsteps. An adapter was created using SolidWorks to connect the linear actuator to the load cell. In addition, the adapter that pushed the fixator had to be redesigned to fit on the other end of the load cell. Figure 11 illustrates the connection of the linear actuator to the load cell and the load cell to the fixator. The distances measured in the Zaber Console and the forces measured in Daqview where then exported to Excel, where they could be analyzed.

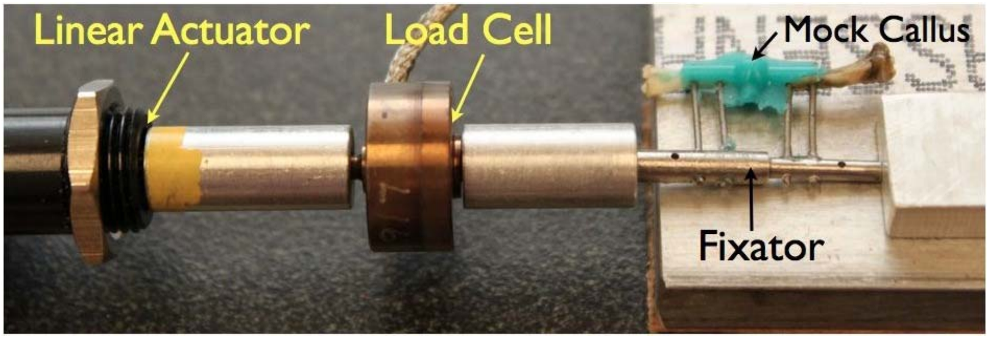


Figure 11: The linear actuator, load cell and fixator connected to one another via two different adapters.

Validation of system:

Prior to receiving IACUC approval the callus stiffness formation system needed to be validated. The system is set up similarly to two springs in parallel. The overall stiffness is collected using DaqView data acquisition software (Iotech, Measurement Computing Corp, MA). The mock callus has a know stiffness of 0.016 N/µm. The rubber spring inside the external fixator has the same stiffness as the mock callus because they are made of the same material (Reprorubber©, Flexbar Machine Corp. Long Island, NY). The stiffness of two springs in parallel when summed together provides the overall stiffness of the system. Theoretically the overall stiffness of the system should be 0.032 N/µm. Figure 12 illustrates a load vs. time plot, from which the overall stiffness was calculated. The experimental overall stiffness of the system was 0.036 N/µm. The experimental results vary slightly from the theoretical because of two possible errors. First, the linear actuator has an accuracy of ± 2µm. This could allow for the total distance moved to be a slightly greater than or less than 150 µm. Secondly, the two cylindrical pieces of the fixator might have created some drag because the fixator was fabricated at Union College's engineering machine shop. The machines used in the shop are not intended to fabricate parts on the micro scale.

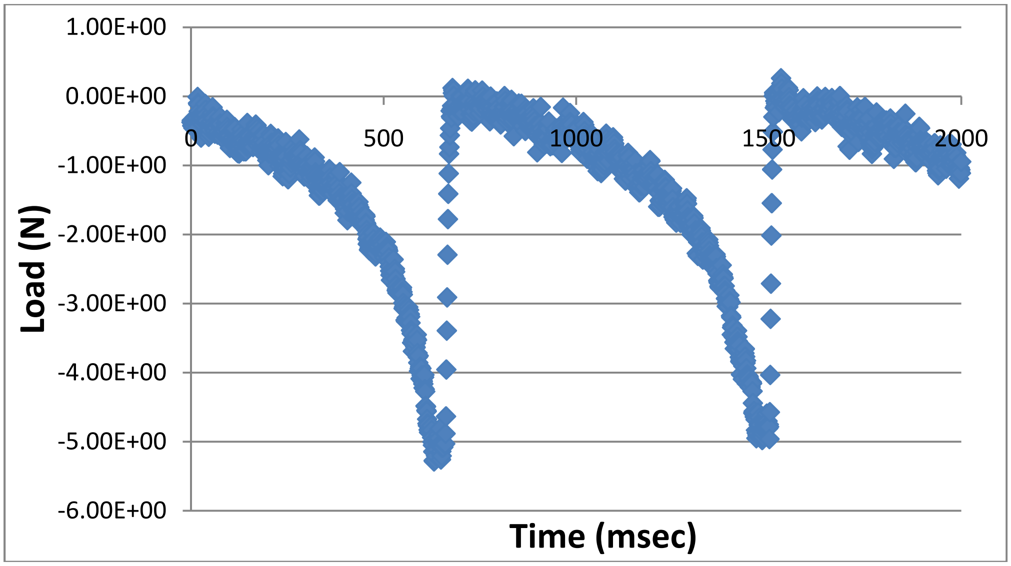


Figure 12: Load vs. time plot of a displacement of 150 µm during 2 complete cycles.

To further validate the system a force vs displacement graph was produced (Figure 13). From plotting the total force vs. displacement an R^2 value of 0.85 was obtained. This value indicates a system linearity of 85%. We are assuming that Reprorubber is a linear elastic material; however, in reality it is not. An actual soft callus will also not be completely linear.

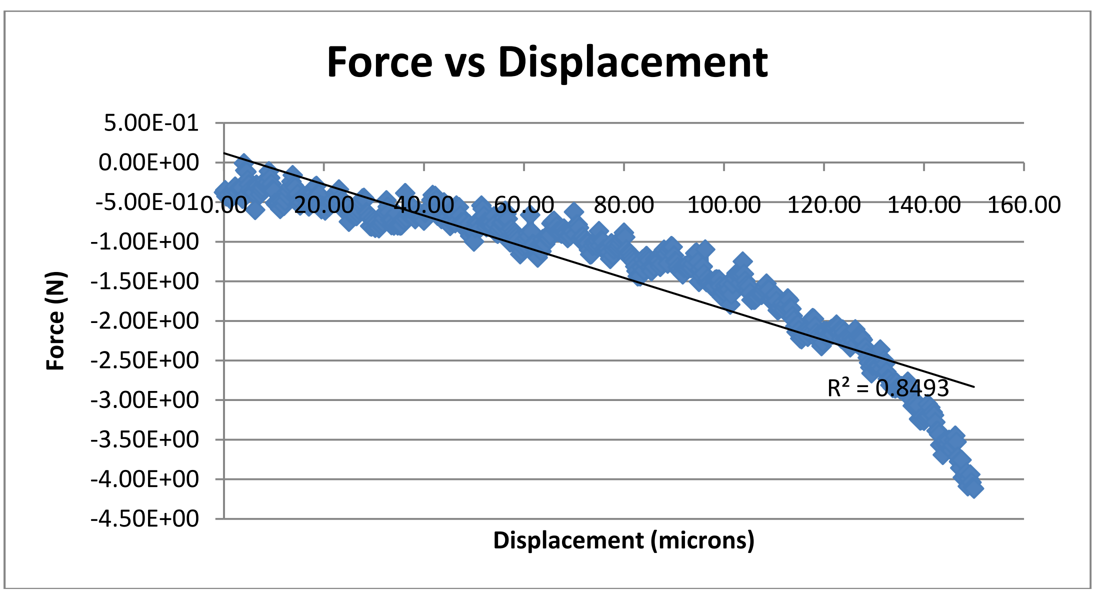


Figure 13: Force vs. displacement plot for a displacement of 150 µm

Stage for callus stimulation:

Upon validating our two springs in parallel system it became apparent that a mouse stage would be needed during callus stimulation. A mouse stage will be used to help keep one end of the fixator fixed while the other ended is being compressed via the linear actuator. In SolidWorks a two-axis stage was designed and then fabricated by the Union College engineering machine shop (Figure 13).

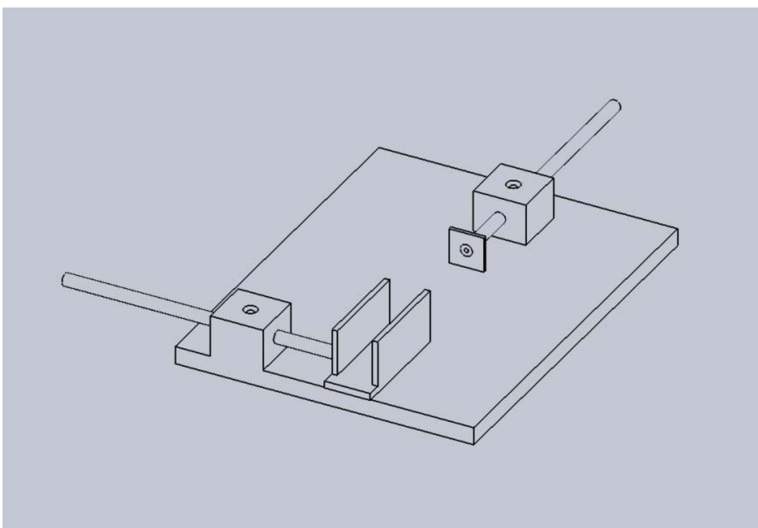


Figure 13: CAD of mouse stage

The stage consists of two square blocks with moveable rods through the center of each. The linear actuator is connected to the y-axis rod, while a flat square piece is connected to the x-axis rod. The rods are independent of each other and can be secured by a thumb screw. The anesthetized mouse will be placed in the center of the stage and the rods will be moved so that the top of the fixator is flush with flat piece on the x-axis rod (Figure 14).

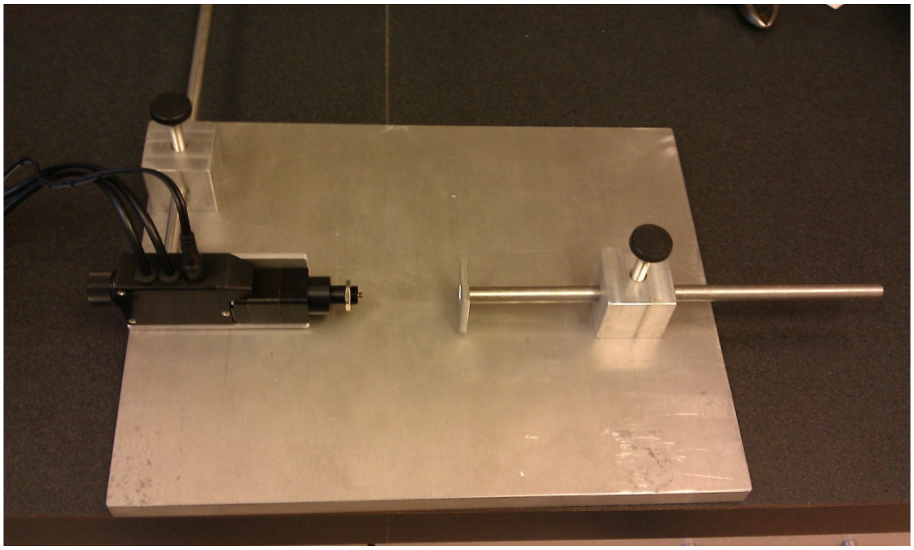


Figure 14: Image of mouse stage with linear actuator connected to y-axis rod.

Conclusion:

Fracturing bones is a common medical condition that many individuals go through in their life. Majority of bones heal properly within six to eight weeks; however, one in twenty fractures results in either a malunion or non-union. The goal of Professor Jennifer Currey's research is to develop a methodology to determine the effects of controlled fracture motion on the healing process. An external fixator was designed using SolidWorks and fabricated by Medical Micro Machining (Colfax, Washington). Rubber disks where created from a mold and inserted in the bottom piece of each fixator.

Using a dental drill and a variety of clamps, the fixator was attached to an already removed tibia. A Dremel saw was used to create a 1 mm fracture in the middle of the tibia and Reprorubber was inserted into the fracture site to act as a mock callus. The Daqbook 2020 data acquisition system was instrumental in helping validate the callus stiffness formation system. Originally a LVDT was going to be used to measure the displacement of the mock callus; however, in order to be more precise with the distance (150 μm) a micro linear actuator was purchased (Zaber Technologies). The Reprorubber material had a stiffness of 0.016 N/µm. The total experimental stiffness collected was 0.036 N/µm. Even though the experimental stiffness varied slightly from the theoretical stiffness (0.032 N/µm), these results validated the callus stiffness system.

A biaxial mouse stage was designed to allow for easy callus stimulation. The x axis rod contains a flat metal piece which the fixator will push up against. The y axis rod contains the linear actuator. In the upcoming months, the mouse stage will tested using already deceased mice. Furthermore, a procedure to perform a microCT analysis will be created by the next Union College research assistant. Hopefully over the summer the mandatory IACUC non survival surgeries will take place.

Acknowledgements:

First, I would like to thank Professor Jennifer Currey for her endless support and insight into my senior project. Without her many of my achievements would not have been possible. I would also like to thank Paul Tompkins (Union College machine shop) for his continual effort and support. Lastly, I would like to extend my gratitude to Filhol Dental for their generous gift of thirty-seven Filpin retention pins.

References:

1. Aro HT, Chao EY. Bone-healing patterns affected by loading, fracture fragment stability, fracture type, and fracture site compression. Clin Orthop Relat Res. 1993;293:8–17

2. Claes L, Augat P, Schorlemmer S, Konrads C, Ignatius A, Ehrnthaller C. Temporary distraction and compression of a diaphyseal osteotomy accelerates bone healing. J Orthop Res. 2008;26:772–777.

3. Claes L, Blakytny R, Gockelmann M, Schoen M, Ignatius A, Willie B (2009) Early dynamization by reduced fixation stiffness does not improve fracture healing in a rat femoral osteotomy model. J Orthop Res 27:22–27

4. De Bastiani G, Aldegheri R, Brivio LR: The treatment of fractures with a dynamic axial fixator. J Bone Joint Surg 66B: 538, 1984

5. Duda, G.N., Eckert-Hubner, K., Sokiranski, R., Kreutner, A., Miller,R., Claes, L., 1998. Analysis of inter-fragmentary movement as a function of musculoskeletal loading conditions in sheep. Journal of Biomechanics 31, 201–210.

6. Egger, E. L.; Gottsauner-Wolf, F.; Palmer, J.; Aro, H. T.; and Chao, E. Y.: Effects of axial dynamization on bone healing. *J. Trauma,* 34: 185-192, 1993

7. Gardner MJ, Ricciardi BF, Wright TM, Bostrom MP, vanderMeulen MC (2008) Pause insertions during cyclic *in vivo* loading affect bone healing. Clin Orthop and Relat Res **466**: 1232-1238.

8. Gardner MJ, van der Meulen MC, Demetrakopoulos D, Wright TM, Myers ER, Bostrom MP. In vivo cyclic axial compression affects bone healing in the mouse tibia. J Orthop Res. 2006;24(8):1679–1686

9. GoodShip, A. E., and Kenwright, J.E.: The influence of induced micromovement upon the healing of experimental tibial fractures. *J. Bone and Join Surg.* 67-B (4): 650-655, 1985.

10. Ilizarov GA.1989. The tension-stress effect on the genesis and growth of tissues. Part I. The influence of stability of fixation and soft-tissue preservation. Clin Orthop Relat Res 238:249-281

11. "Mechanical Effects on Fracture Healing." *Michigan Engineering| College of Engineering-Home.* Web. 10 Nov. 2010. www.engin.umich.edu/class/bme456/bonefracture/bonefracture.htm

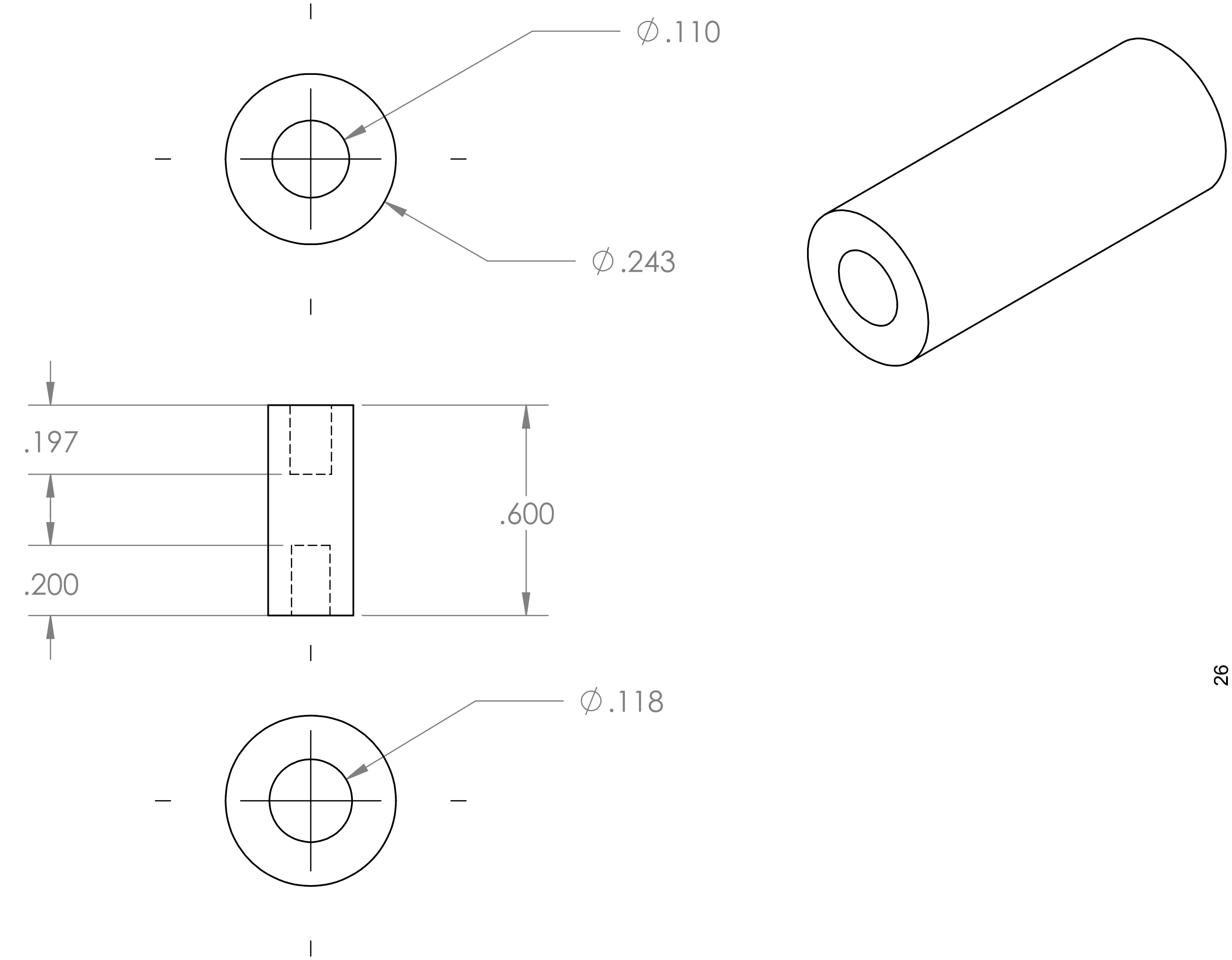
12. Miclau T, Lu C, Thompson Z, Choi P, Puttlitz C, Marcucio RS, Helms JA. Effects of delayed stabilization on fracture healing. Journal of Orthopaedic Research 2007; 25:1552-8.

13. Seebeck P, Thompson MS, Pawani A, et al. 2005 Gait evaluations: a tool to monitor bone healing? Clin Biomech 20:883-891.

14. Smith-Adaline EA, Volkman SK, Ignelzi MA Jr, Slade J, Platte S, Goldstein SA (2004) Mechanical environment alters tissue formation patterns during fracture repair. J Orthop Res 22:1079–1085

15. "The Anatomy of the Laboratory Mouse." *MGI-Mouse Genome Informatics-The International Database Resource for the Laboratory Mouse*. Web. 13 Nov. 2010. <http://www.informatics.jax.org/cookbook/figures/figure39.shtml>.

Appendix A



PROPRIETARY AND CONFIDENTIAL

THE INFORMATION CONTAINED IN THIS DRAWING IS THE SOLE PROPERTY OF <INSERT COMPANY NAME HERE>. ANY REPRODUCTION IN PART OR AS A WHOLE WITHOUT THE WRITTEN PERMISSION OF <INSERT COMPANY NAME HERE> IS PROHIBITED.

NEXT ASSY	USED ON
APPLICATION	

UNLESS OTHERWISE SPECIFIED:

DIMENSIONS ARE IN INCHES
TOLERANCES:
FRACTIONAL ±
ANGULAR: MACH ± BEND ±
TWO PLACE DECIMAL ±
THREE PLACE DECIMAL ±

INTERPRET GEOMETRIC TOLERANCING PER:

MATERIAL

FINISH

DO NOT SCALE DRAWING

	NAME	DATE
DRAWN	Marc Nash	
CHECKED		
ENG APPR.		
MFG APPR.		
Q.A.		

COMMENTS:

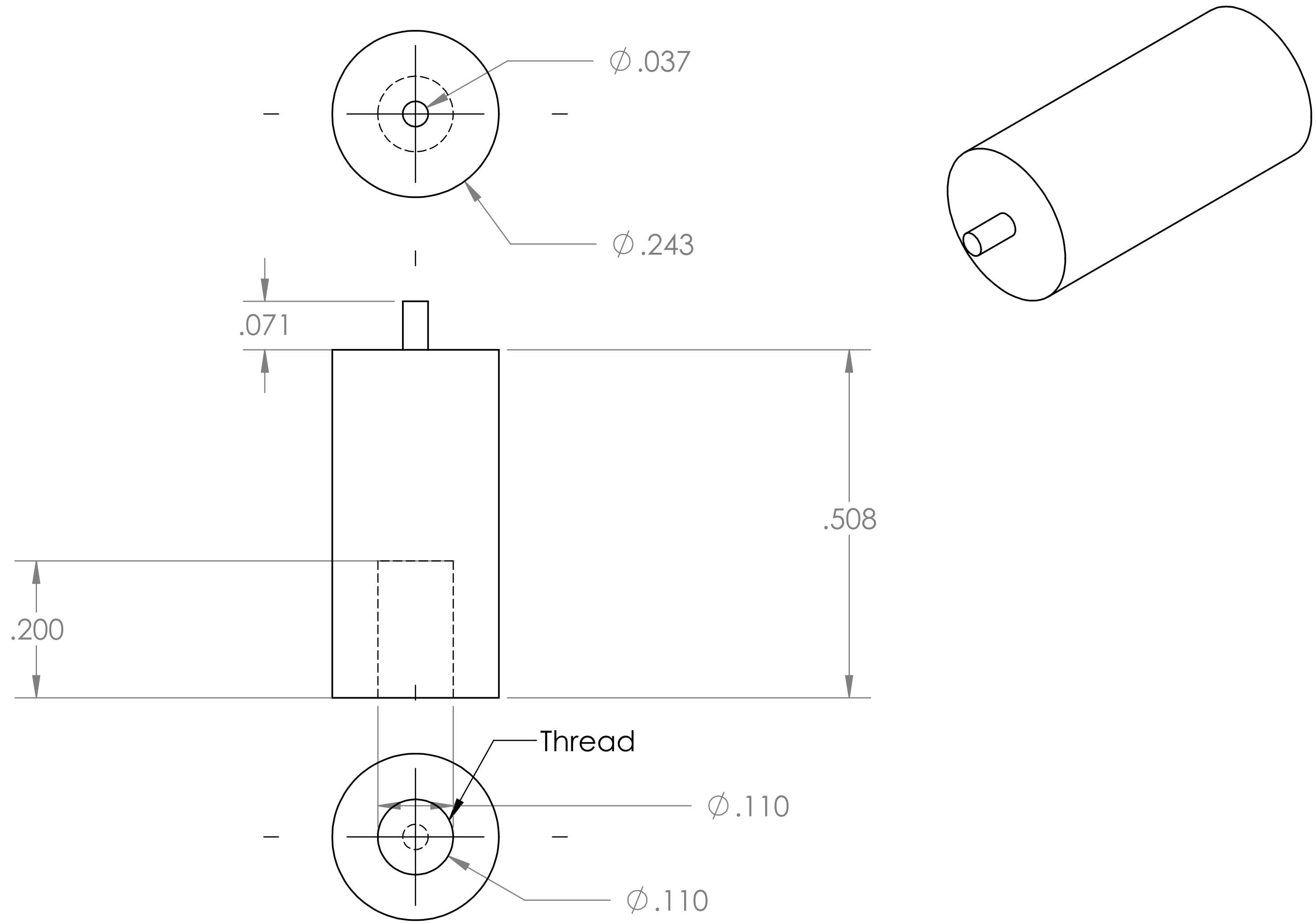
TITLE:

Adapter From Linear Actuator to Load Cell

SIZE A | DWG. NO. | REV

SCALE: 4:1 | WEIGHT: | SHEET 1 OF 1

5 4 3 2 1



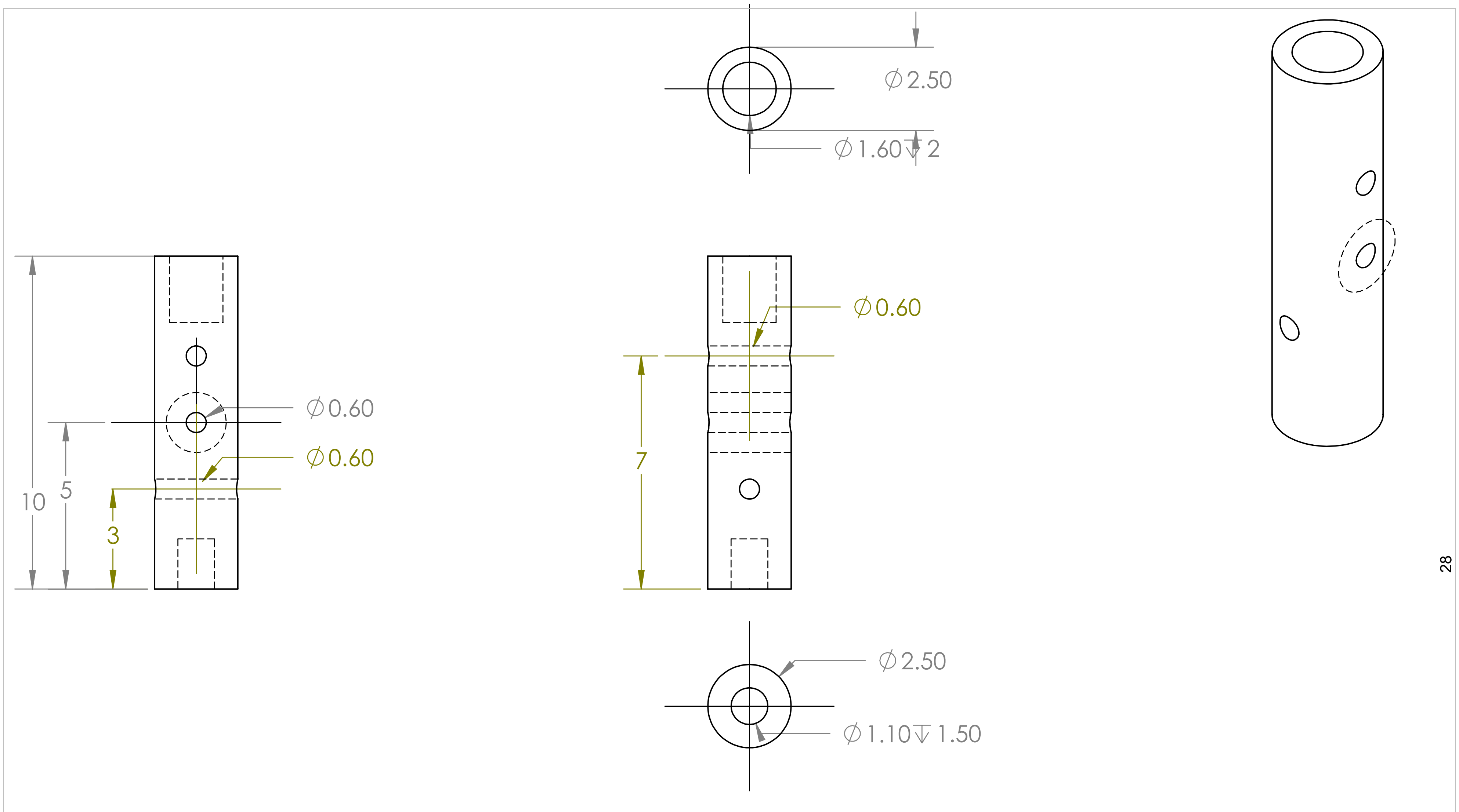
		UNLESS OTHERWISE SPECIFIED:		NAME	DATE
		DIMENSIONS ARE IN INCHES TOLERANCES: FRACTIONAL ± ANGULAR: MACH ± BEND ± TWO PLACE DECIMAL ± THREE PLACE DECIMAL ±	DRAWN	Marc Nash	
			CHECKED		
			ENG APPR.		
			MFG APPR.		
		INTERPRET GEOMETRIC TOLERANCING PER:	Q.A.		
		MATERIAL	COMMENTS:		
NEXT ASSY	USED ON	FINISH			
APPLICATION		DO NOT SCALE DRAWING			

TITLE:

Adapter for Load Cell to Fixator

SIZE	DWG. NO.	REV
A		
SCALE: 4:1	WEIGHT:	SHEET 1 OF 1

5 4 3 2 1



UNLESS OTHERWISE SPECIFIED:

DIMENSIONS ARE IN INCHES
TOLERANCES:
FRACTIONAL ±
ANGULAR: MACH ± BEND ±
TWO PLACE DECIMAL ±
THREE PLACE DECIMAL ±

INTERPRET GEOMETRIC TOLERANCING PER:

MATERIAL

FINISH

DO NOT SCALE DRAWING

	NAME	DATE
DRAWN	Marc Nash	
CHECKED		
ENG APPR.		
MFG APPR.		
Q.A.		

COMMENTS:

NEXT ASSY	USED ON
APPLICATION	

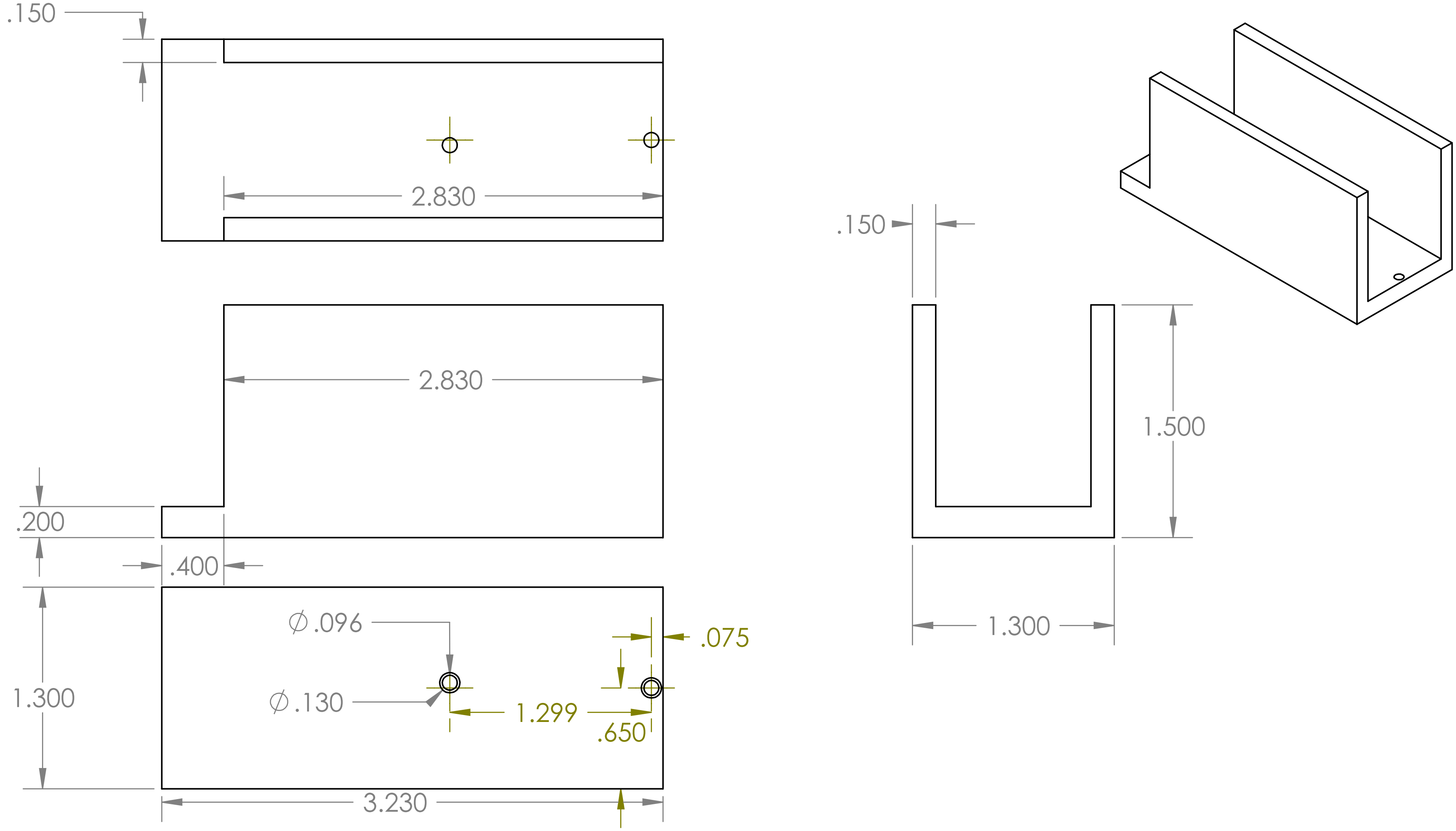
TITLE:

Bottom Part of Fixator

SIZE A | DWG. NO. | REV

SCALE: 8:1 | WEIGHT: | SHEET 1 OF 1

5 4 3 2 1

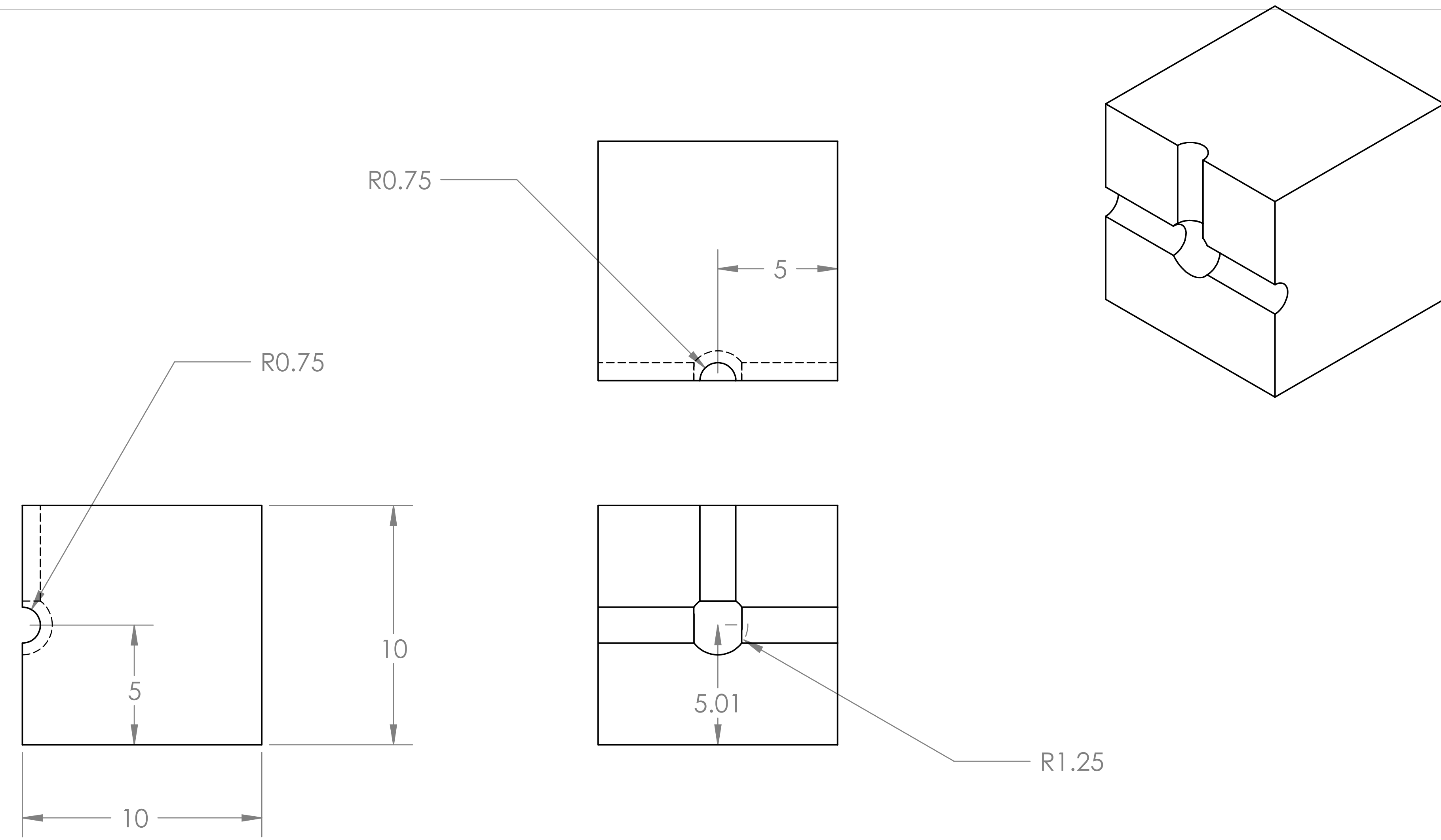


		UNLESS OTHERWISE SPECIFIED:		NAME	DATE	
		DIMENSIONS ARE IN INCHES TOLERANCES: FRACTIONAL ± ANGULAR: MACH ± BEND ± TWO PLACE DECIMAL ± THREE PLACE DECIMAL ±	DRAWN			TITLE:
			CHECKED			bracket for linear
			ENG APPR.			
			MFG APPR.			
		INTERPRET GEOMETRIC TOLERANCING PER:	Q.A.			
		MATERIAL	COMMENTS:			SIZE A — DWG. NO. — REV
NEXT ASSY	USED ON	FINISH				
APPLICATION		DO NOT SCALE DRAWING				SCALE: 1:1 — WEIGHT: — SHEET 1 OF 1

PROPRIETARY AND CONFIDENTIAL

THE INFORMATION CONTAINED IN THIS DRAWING IS THE SOLE PROPERTY OF <INSERT COMPANY NAME HERE>. ANY REPRODUCTION IN PART OR AS A WHOLE WITHOUT THE WRITTEN PERMISSION OF <INSERT COMPANY NAME HERE> IS PROHIBITED.

5 4 3 2 1



NEXT ASSY	USED ON
APPLICATION	

UNLESS OTHERWISE SPECIFIED:

DIMENSIONS ARE IN INCHES
TOLERANCES:
FRACTIONAL ±
ANGULAR: MACH ± BEND ±
TWO PLACE DECIMAL ±
THREE PLACE DECIMAL ±

INTERPRET GEOMETRIC TOLERANCING PER:

MATERIAL

FINISH

DO NOT SCALE DRAWING

	NAME	DATE
DRAWN	Marc Nash	
CHECKED		
ENG APPR.		
MFG APPR.		
Q.A.		

COMMENTS:

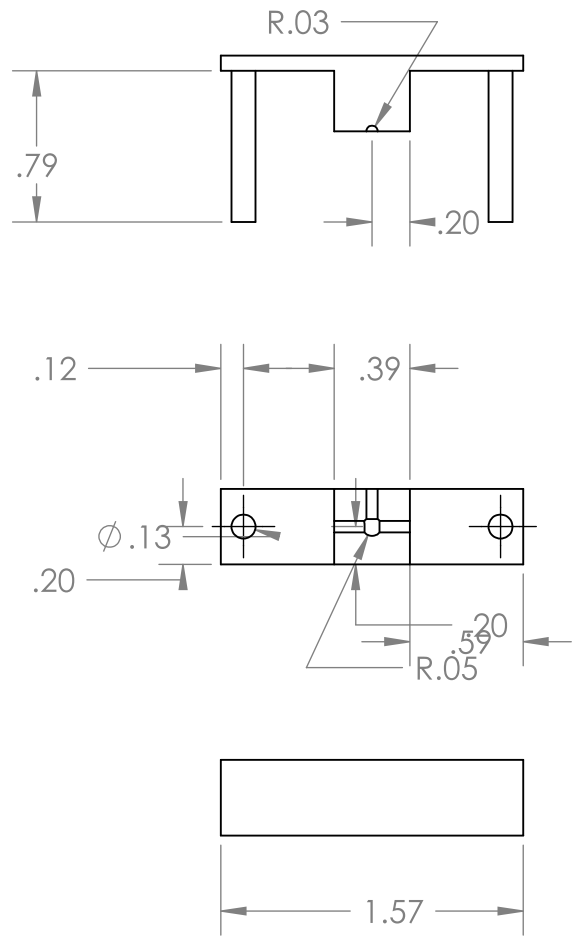
TITLE:

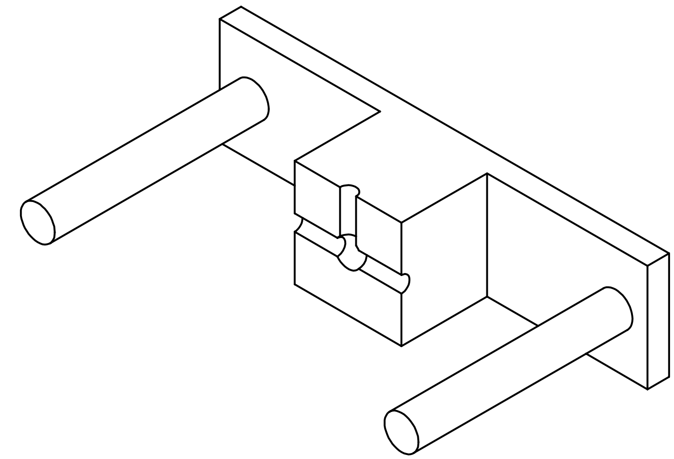
Callus Mold Attempt 1

SIZE	DWG. NO.	REV
A		

SCALE: 4:1 | WEIGHT: | SHEET 1 OF 1

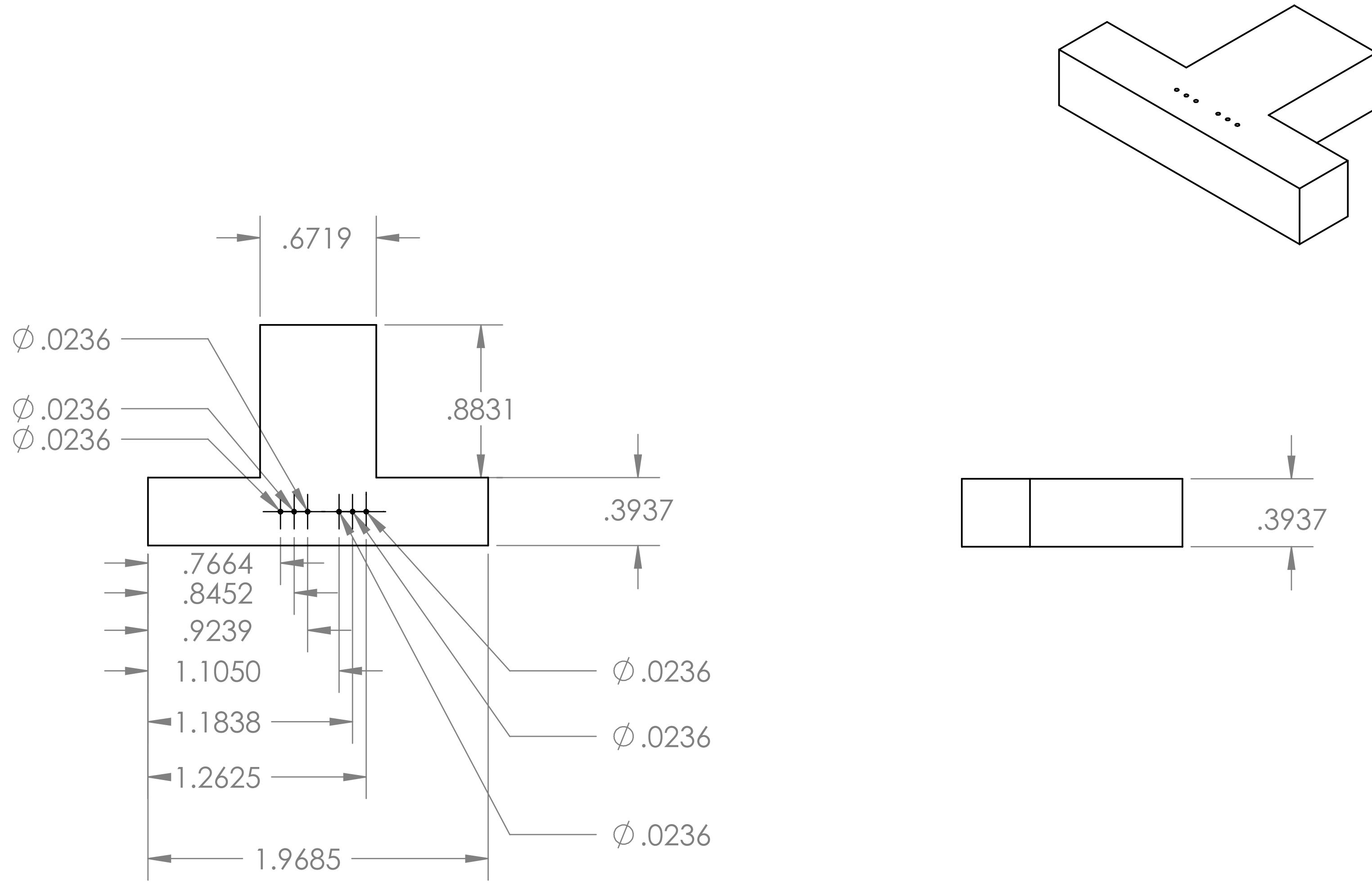
5 4 3 2 1





		UNLESS OTHERWISE SPECIFIED:		NAME	DATE	
		DIMENSIONS ARE IN INCHES TOLERANCES: FRACTIONAL ± ANGULAR: MACH ± BEND ± TWO PLACE DECIMAL ± THREE PLACE DECIMAL ±	DRAWN	Marc Nash		TITLE:
			CHECKED			Callus Mold-Final Design
			ENG APPR.			
			MFG APPR.			
		INTERPRET GEOMETRIC TOLERANCING PER:	Q.A.			
		MATERIAL	COMMENTS:			SIZE A · DWG. NO. · REV
NEXT ASSY	USED ON	FINISH				
APPLICATION		DO NOT SCALE DRAWING				SCALE: 2:1 · WEIGHT: · SHEET 1 OF 1

5 4 3 2 1



PROPRIETARY AND CONFIDENTIAL

NEXT ASSY	USED ON
APPLICATION	

UNLESS OTHERWISE SPECIFIED:

DIMENSIONS ARE IN INCHES
TOLERANCES:
FRACTIONAL ±
ANGULAR: MACH ± BEND ±
TWO PLACE DECIMAL ±
THREE PLACE DECIMAL ±

INTERPRET GEOMETRIC TOLERANCING PER:

MATERIAL

FINISH

DO NOT SCALE DRAWING

	NAME	DATE
DRAWN	Marc Nash	
CHECKED		
ENG APPR.		
MFG APPR.		
Q.A.		

COMMENTS:

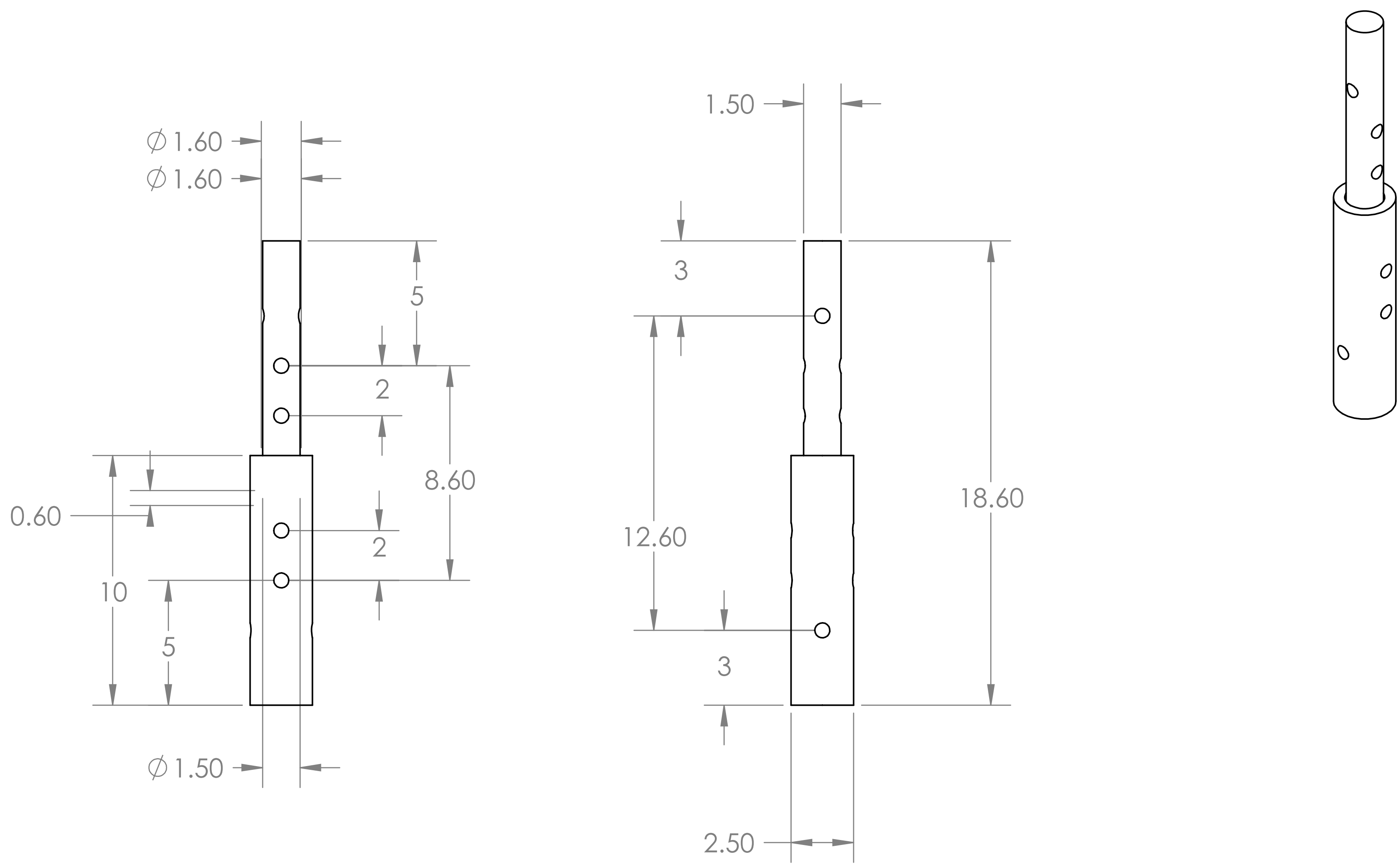
TITLE:

Drill Guide

SIZE	DWG. NO.	REV
A		

SCALE: 1:1 WEIGHT: SHEET 1 OF 1

5 4 3 2 1



PROPRIETARY AND CONFIDENTIAL

NEXT ASSY	USED ON
APPLICATION	

UNLESS OTHERWISE SPECIFIED:

DIMENSIONS ARE IN INCHES
TOLERANCES:
FRACTIONAL ±
ANGULAR: MACH ± BEND ±
TWO PLACE DECIMAL ±
THREE PLACE DECIMAL ±

INTERPRET GEOMETRIC TOLERANCING PER:

MATERIAL

FINISH

DO NOT SCALE DRAWING

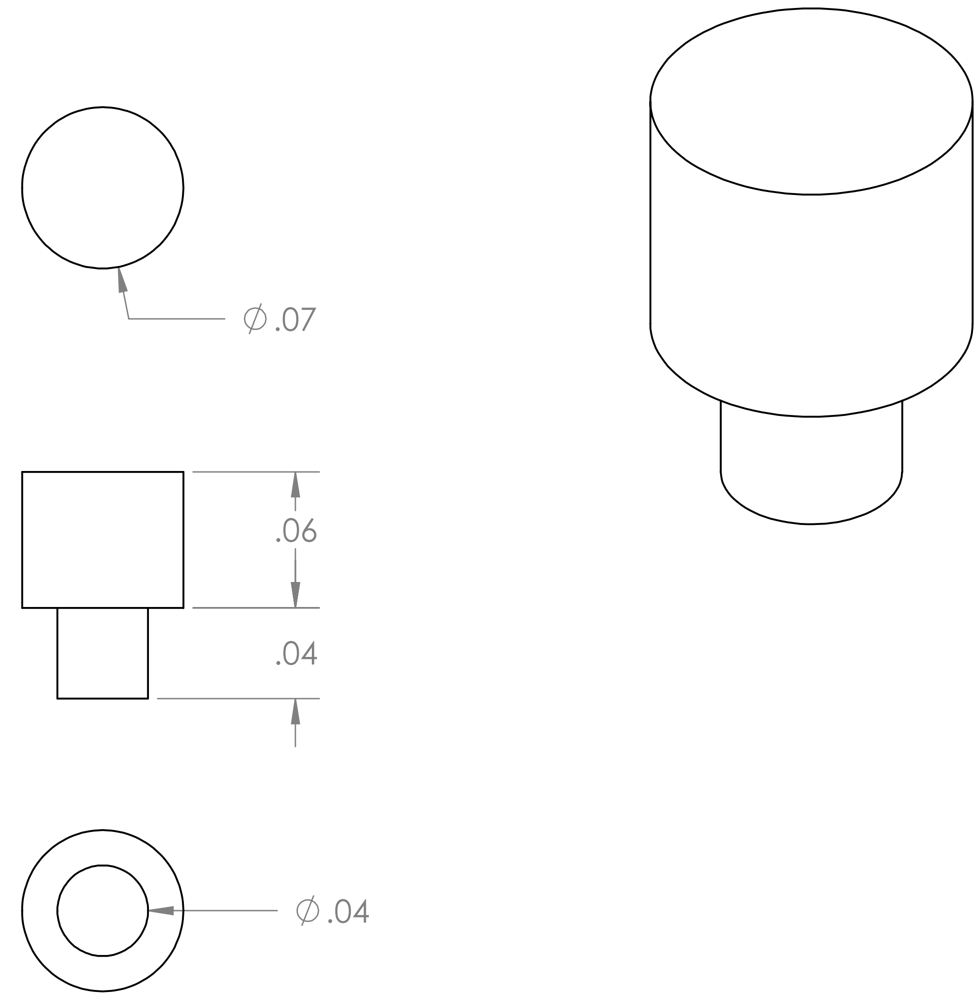
	NAME	DATE
DRAWN	Marc Nash	
CHECKED		
ENG APPR.		
MFG APPR.		
Q.A.		
COMMENTS:		

TITLE:

Assembled Fixator

SIZE	DWG. NO.	REV
A		
SCALE: 4:1	WEIGHT:	SHEET 1 OF 1

5 4 3 2 1



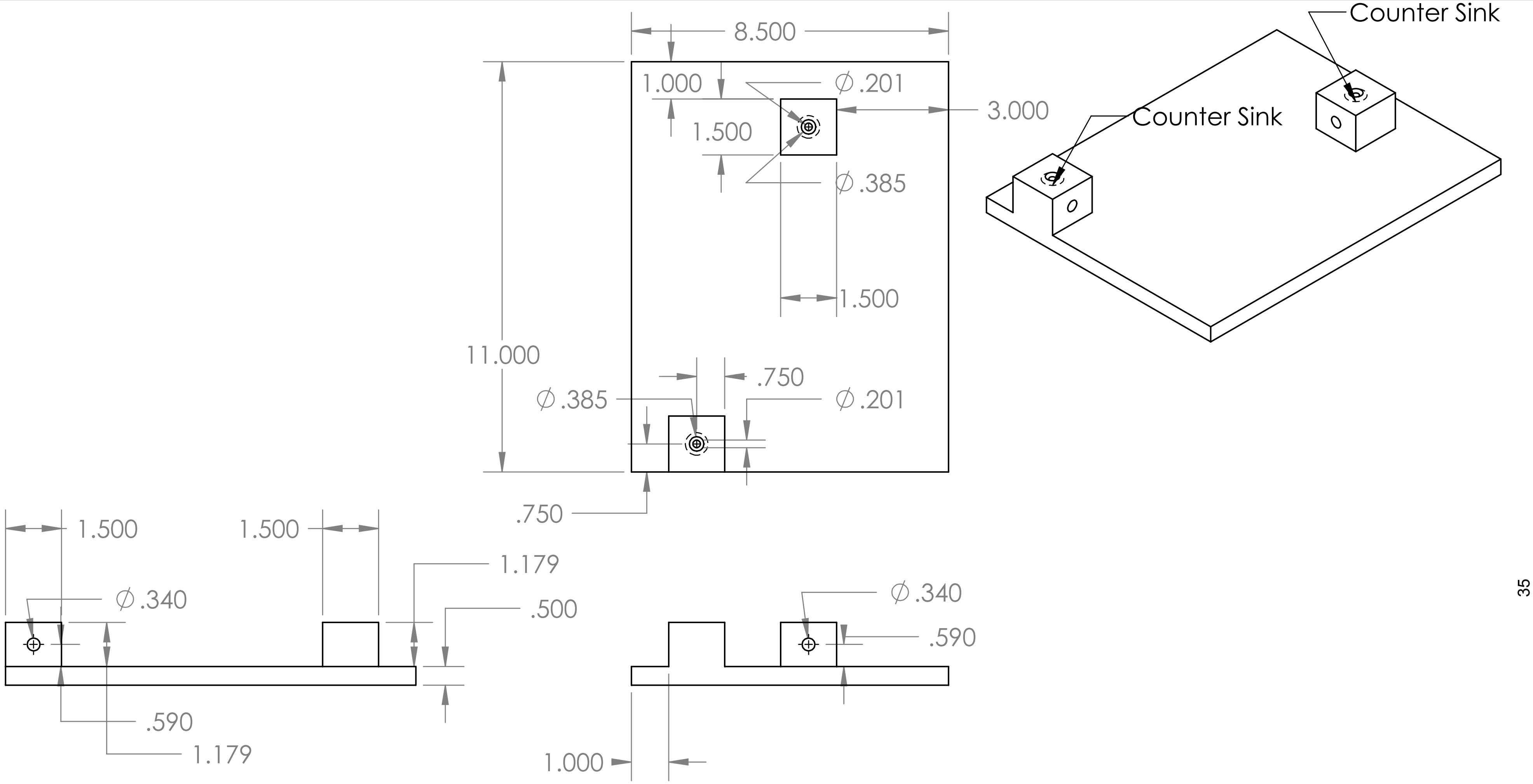
		UNLESS OTHERWISE SPECIFIED:		NAME	DATE
		DIMENSIONS ARE IN INCHES TOLERANCES: FRACTIONAL ± ANGULAR: MACH ± BEND ± TWO PLACE DECIMAL ± THREE PLACE DECIMAL ±	DRAWN	Marc Nash	
			CHECKED		
			ENG APPR.		
			MFG APPR.		
		INTERPRET GEOMETRIC TOLERANCING PER:	Q.A.		
		MATERIAL	COMMENTS:		
NEXT ASSY	USED ON	FINISH			
APPLICATION		DO NOT SCALE DRAWING			

TITLE:

Middle Adapter Between LVDT and Load Cell

SIZE	DWG. NO.	REV
A		
SCALE: 24:1	WEIGHT:	SHEET 1 OF 1

5 4 3 2 1



UNLESS OTHERWISE SPECIFIED:	NAME	DATE
DIMENSIONS ARE IN INCHES TOLERANCES: FRACTIONAL ± ANGULAR: MACH ± BEND ± TWO PLACE DECIMAL ± THREE PLACE DECIMAL ±	DRAWN: Marc Nash	
	CHECKED	
	ENG APPR.	
	MFG APPR.	
INTERPRET GEOMETRIC TOLERANCING PER:	Q.A.	
MATERIAL	COMMENTS:	
FINISH		
DO NOT SCALE DRAWING		

NEXT ASSY	USED ON
APPLICATION	

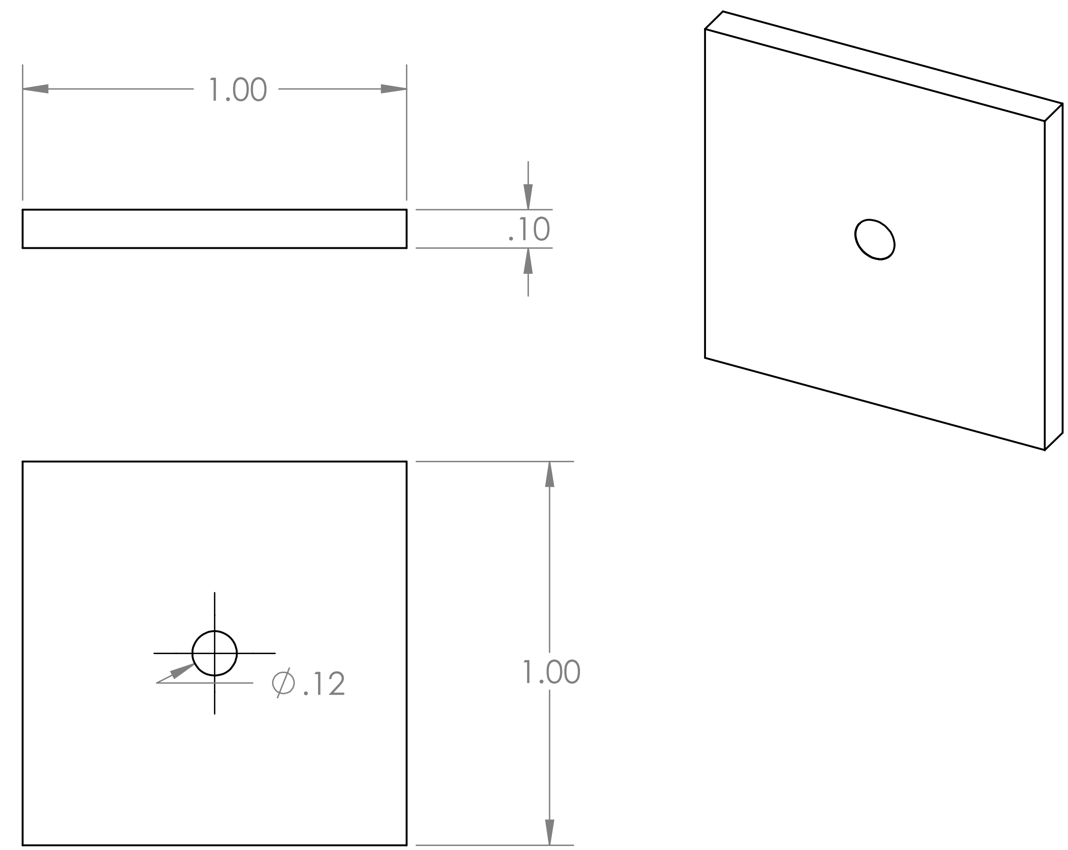
TITLE:

Mouse Stage

SIZE A | DWG. NO. | REV

SCALE: 1:4 | WEIGHT: | SHEET 1 OF 1

5 4 3 2 1



UNLESS OTHERWISE SPECIFIED:		NAME / DATE
DIMENSIONS ARE IN INCHES TOLERANCES: FRACTIONAL ± ANGULAR: MACH ± BEND ± TWO PLACE DECIMAL ± THREE PLACE DECIMAL ±	DRAWN	Marc Nash
	CHECKED	
	ENG APPR.	
	MFG APPR.	
INTERPRET GEOMETRIC TOLERANCING PER:	Q.A.	
MATERIAL	COMMENTS:	
FINISH		
DO NOT SCALE DRAWING		

NEXT ASSY	USED ON
APPLICATION	

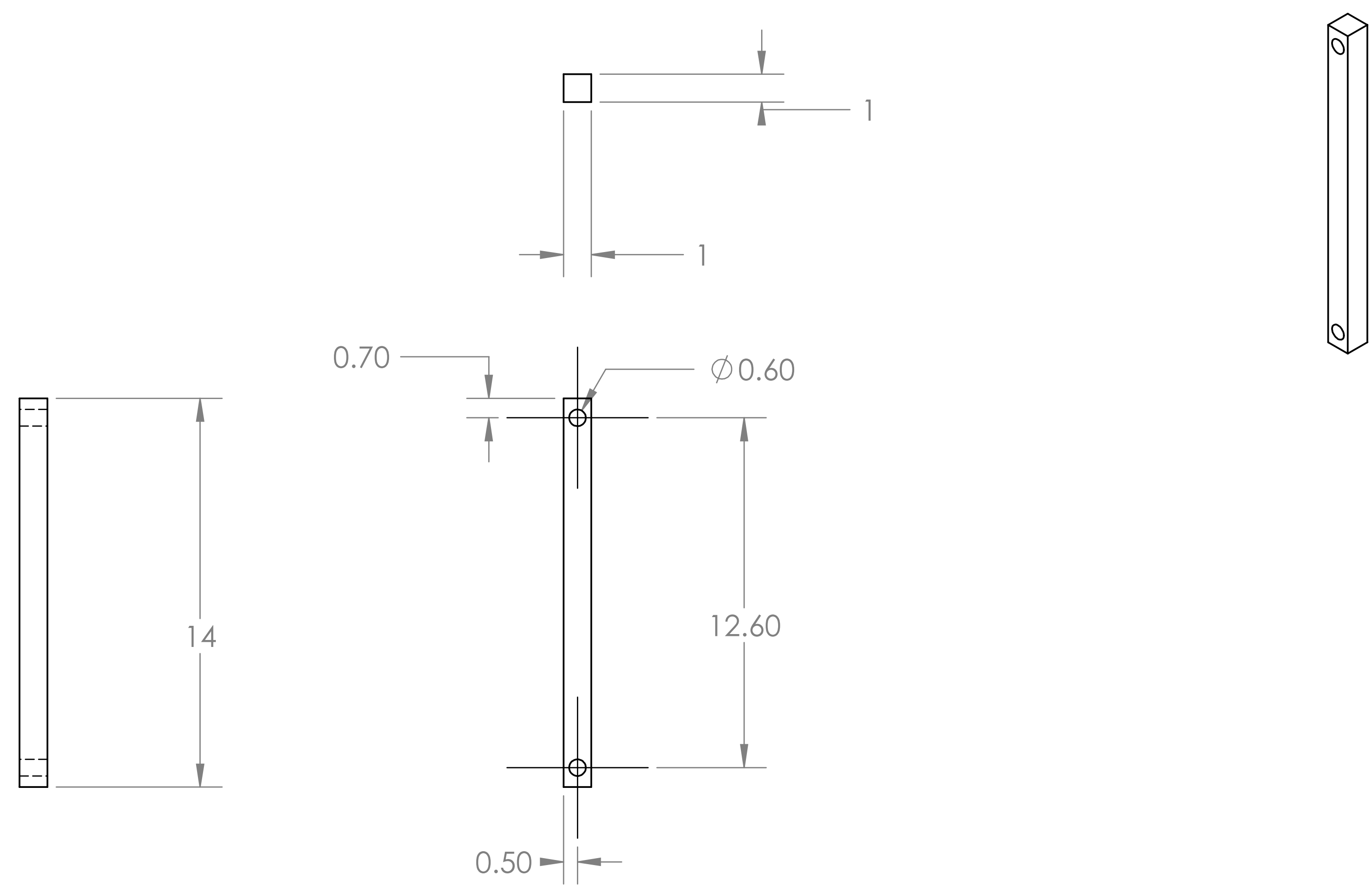
TITLE:

Pusher Block-X axis

SIZE A | DWG. NO. | REV

SCALE: 4:1 | WEIGHT: | SHEET 1 OF 1

5 4 3 2 1



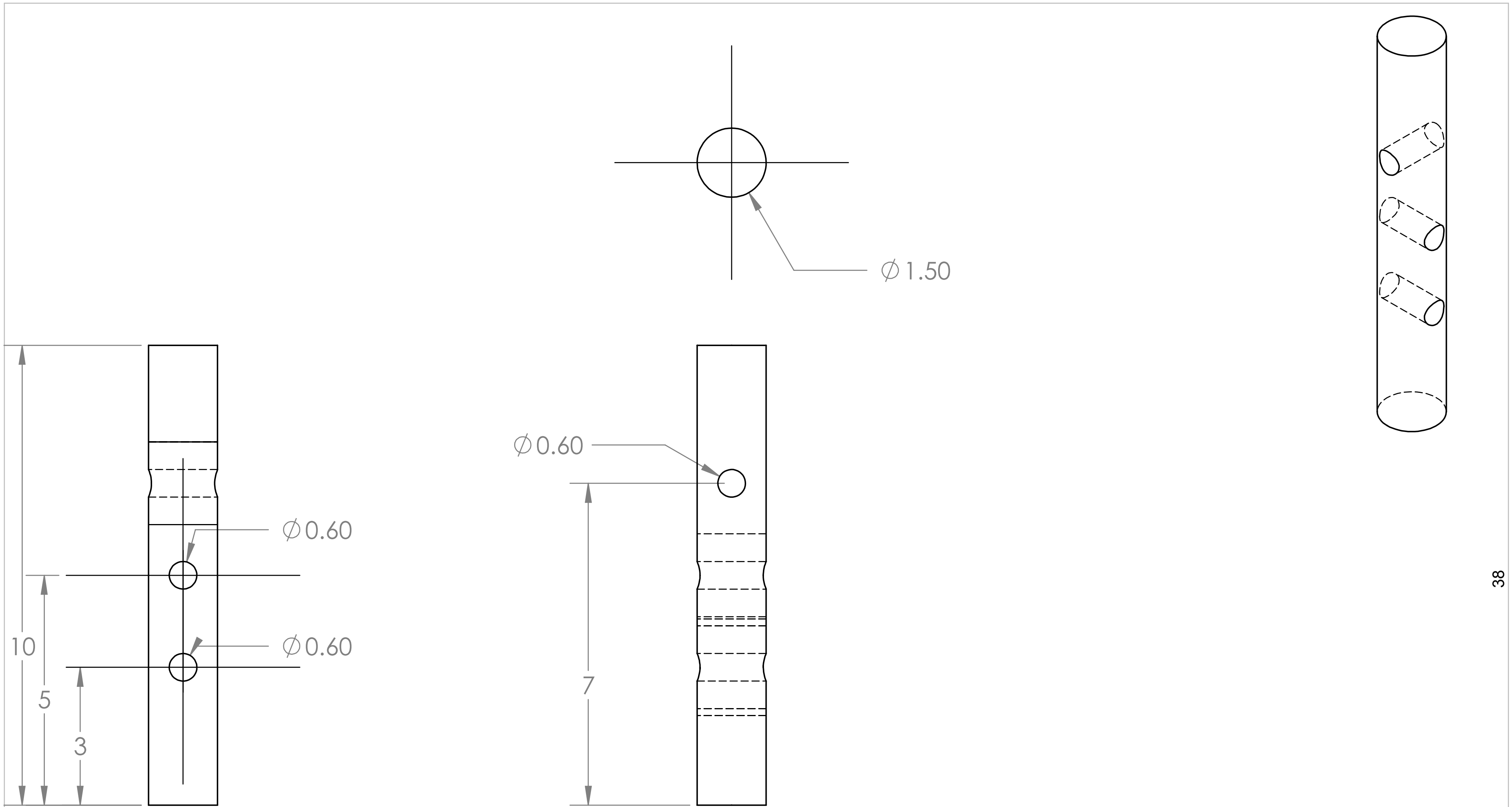
		UNLESS OTHERWISE SPECIFIED:		NAME	DATE
		DIMENSIONS ARE IN INCHES TOLERANCES: FRACTIONAL ± ANGULAR: MACH ± BEND ± TWO PLACE DECIMAL ± THREE PLACE DECIMAL ±	DRAWN	Marc Nash	
			CHECKED		
			ENG APPR.		
			MFG APPR.		
		INTERPRET GEOMETRIC TOLERANCING PER:	Q.A.		
		MATERIAL	COMMENTS:		
NEXT ASSY	USED ON	FINISH			
APPLICATION		DO NOT SCALE DRAWING			

TITLE:

Stabilization Bar

SIZE	DWG. NO.	REV
A		
SCALE: 4:1	WEIGHT:	SHEET 1 OF 1

5 4 3 2 1



PROPRIETARY AND CONFIDENTIAL

THE INFORMATION CONTAINED IN THIS DRAWING IS THE SOLE PROPERTY OF <INSERT COMPANY NAME HERE>. ANY REPRODUCTION IN PART OR AS A WHOLE WITHOUT THE WRITTEN PERMISSION OF <INSERT COMPANY NAME HERE> IS PROHIBITED.

NEXT ASSY	USED ON
APPLICATION	

UNLESS OTHERWISE SPECIFIED:

DIMENSIONS ARE IN INCHES
TOLERANCES:
FRACTIONAL ±
ANGULAR: MACH ± BEND ±
TWO PLACE DECIMAL ±
THREE PLACE DECIMAL ±

INTERPRET GEOMETRIC TOLERANCING PER:

MATERIAL

FINISH

DO NOT SCALE DRAWING

	NAME	DATE
DRAWN	Marc Nash	
CHECKED		
ENG APPR.		
MFG APPR.		
Q.A.		

COMMENTS:

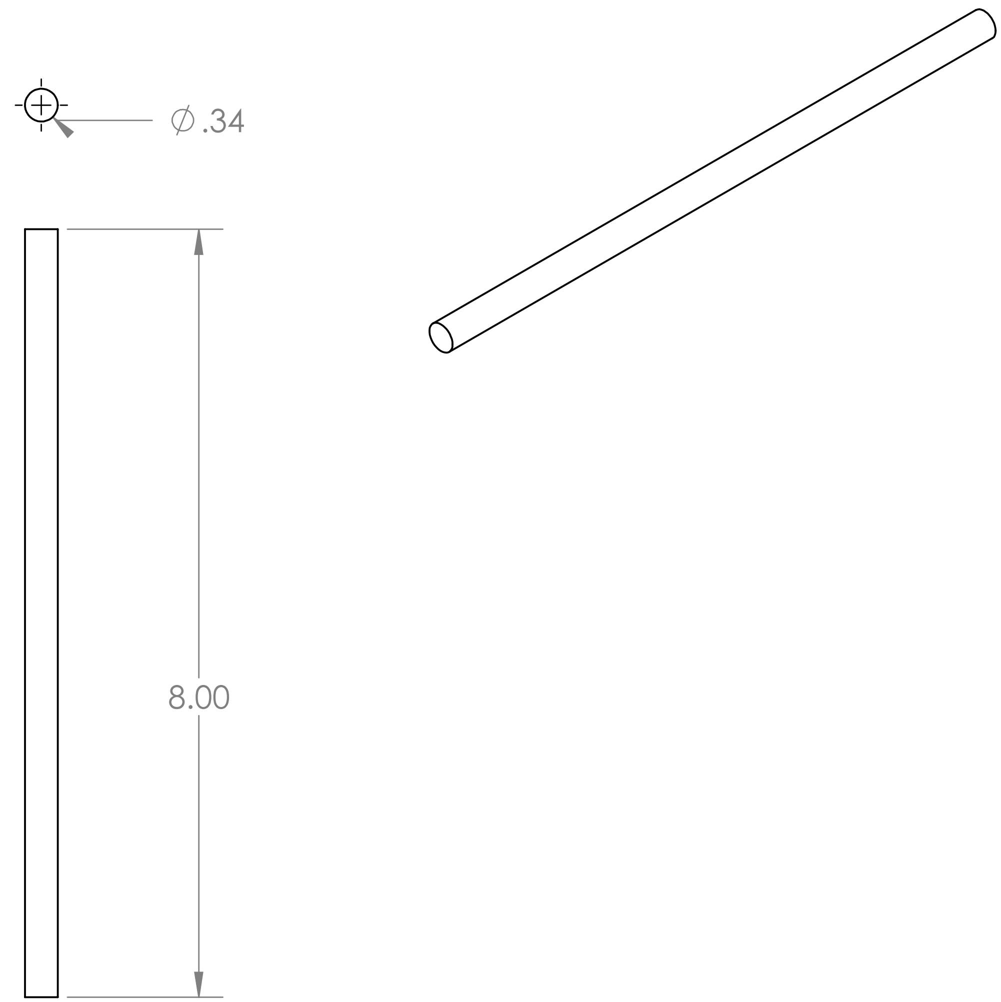
TITLE:

Top Part of Fixator

SIZE	DWG. NO.	REV
A		

SCALE: 8:1 WEIGHT: SHEET 1 OF 1

5 4 3 2 1



NEXT ASSY	USED ON
APPLICATION	

UNLESS OTHERWISE SPECIFIED:

DIMENSIONS ARE IN INCHES
TOLERANCES:
FRACTIONAL ±
ANGULAR: MACH ± BEND ±
TWO PLACE DECIMAL ±
THREE PLACE DECIMAL ±

INTERPRET GEOMETRIC TOLERANCING PER:

MATERIAL

FINISH

DO NOT SCALE DRAWING

	NAME	DATE
DRAWN	Marc Nash	
CHECKED		
ENG APPR.		
MFG APPR.		
Q.A.		

COMMENTS:

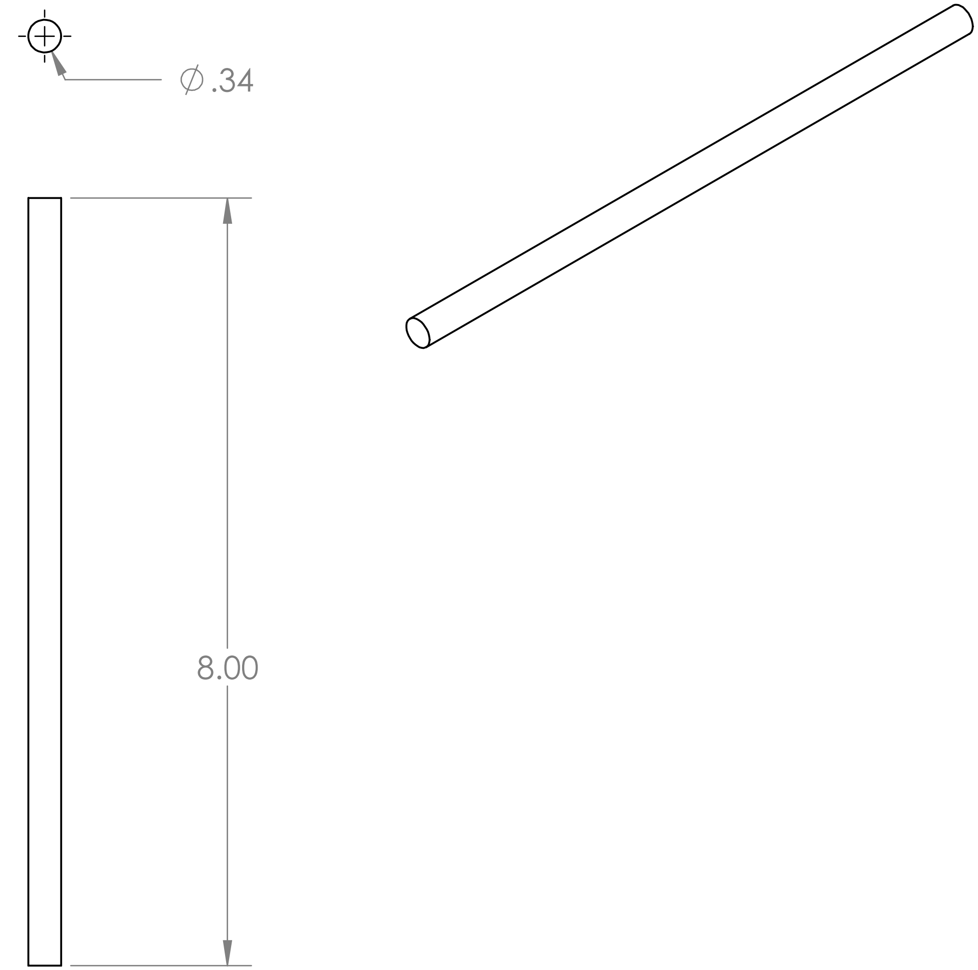
TITLE:

X Axis Rod for Mouse Stage

SIZE	DWG. NO.	REV
A		

SCALE: 1:2 WEIGHT: SHEET 1 OF 1

5 4 3 2 1



		UNLESS OTHERWISE SPECIFIED:		NAME	DATE
		DIMENSIONS ARE IN INCHES TOLERANCES: FRACTIONAL ± ANGULAR: MACH ± BEND ± TWO PLACE DECIMAL ± THREE PLACE DECIMAL ±	DRAWN	Marc Nash	
			CHECKED		
			ENG APPR.		
			MFG APPR.		
		INTERPRET GEOMETRIC TOLERANCING PER:	Q.A.		
		MATERIAL	COMMENTS:		
NEXT ASSY	USED ON	FINISH			
APPLICATION		DO NOT SCALE DRAWING			

TITLE:

Y Axis Rod for Mouse Stage

SIZE	DWG. NO.	REV
A		
SCALE: 1:2	WEIGHT:	SHEET 1 OF 1

5 4 3 2 1