Design of Hot Extrusion Molding Device for the Continuous Production of Pharmaceutical Tablets

by

Giorgio Zampierollo

SUBMITTED TO THE DEPARTMENT OF MECHANICAL ENGINEERING IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

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ABSTRACT

Currently, pharmaceutical tablets are manufactured in large batch operations that have inefficiencies associated with the stopping, re-configuration and testing between batches. Continuous manufacturing has the potential to lower manufacturing costs and energy consumption while enhancing process reliability and flexibility. Although there are many manufacturing processes that could make an impact in this sector, I focused on hot extrusion molding. Hot extrusion molding consists of heat melting a pharmaceutical resin in an extruder and packing it in a mold where it is allowed to solidify until it is ready to be ejected. I designed a hot extrusion molding system after estimating the injection pressure and cooling parameters needed to meet functional requirements. As a result, I realized the importance of using a hot runner system in order to meet criteria and be able to produce the tablets. The hot runner allows for the temperature of the melt to be controlled up until it is to be extruded into the mold, preventing pre-mature solidification and clogging in the system. From the estimations and available hardware I was able to fabricate the components for the hot extrusion molding system. The components were then assembled to be tested.

Thesis Supervisor: Jung-Hoon Chun
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Author's Biographical Note

I will be graduating with my Bachelors of Science in Mechanical Engineering, with a Minor in Management Science, and taking it to work as a mechanical engineer for Procter and Gamble in South Boston for the brand Gillette. There I will be part of the Advanced Manufacturing Technologies group which focuses on the design and implementation of manufacturing alternatives for company products. I am originally from San Juan, Puerto Rico. I would like to personally acknowledge my loving parents, Giorgio A. Zampierollo, and Jeanette Jaramillo, for without them I would never have achieved my dream of graduating from MIT. I also want to thank my sisters, Annabella and Giovanna, for their love and support and for putting up with me all our years growing up together. Finally I would like to thank all of my friends, both at MIT and from Puerto Rico, who provided the healthy balance I needed even in the most stressful of times.

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Salvatore Mascia, Erin Bell, Tushar Kulkarni and the rest of the Novartis-MIT team– They gave me the freedom to explore alternatives for this design as well as served as strong pillars of support and understanding. It was an honor working with them and learning from them.

Table of Contents

List of Figures and Tables

Chapter 1: Introduction

Every year the pharmaceutical industry contribute to saving the lives of millions of people from various diseases by developing and producing a variety of products that allows many people suffering from illness to recover and lead productive lives.

The pharmaceutical industry is consistently near the top of the Fortune 500 survey of most profitable industries. In 2006, global spending on prescription drugs was above $643 billion, despite a halt in growth in Europe and North America. The United States is the industry's largest consumer with $289 billion in annual sales. The sales in the United States were followed by the European Union and Japan. Emerging markets like China, Russia, Mexico and South Korea grew 81 percent the same year.

Despite slowing profit growth, the pharmaceutical industry continues to be the most profitable business in the U.S.

Much of the industry's achievements in the United States are attributed to the research and development (R&D) of new drugs. However, this comes at a high price with the high proportion of revenue that needs to be reinvested into the firm. Although millions of compounds are tested, it is not uncommon to find less than one hundred new prescription medicines.

Manufacturing is a substantial part of the total cost structure. According to some estimates, these costs can be as high as 27-30% of sales for manufacturers of brand-name pharmaceuticals, more than double the share of costs for research and development.[1,2] In spite of R&D largely focus on drug innovations or improvements, and much less is the focus on solving the inefficiencies in manufacturing. The cost of bringing a new drug is projected to require an investment of over $2 billion to progress from a laboratory idea to a successful commercialization. [1]

Chapter 2: Current Tablet Manufacturing Process

Pharmaceutical tablets are primarily produced in large batch operations, where components are made in a single workstation before being moved on to the next one. Traditional pharmaceutical manufacturing processes consist of pharmaceutical active ingredients being synthesized in a chemical manufacturing plant. These ingredients are then shipped to a manufacturing facility, often at another site, where milling and micronizing machines pulverize substances into fine particles. These fine particles reduce bulk chemicals into required sizes. Finished chemicals are later combined and processed further in mixing machines, until when (in the case of tablets) they are pressed to their final shape. With multiple interruptions, including transport to separate locations, each batch may take weeks to produce. In addition, manufacturing design and scale-up for a new drug are very costly and time-consuming.

Batch manufacturing procedures are useful in reducing the initial capital outlay by only requiring a single production line that can be used with little modification to produce several products. Batch manufacturing processes does have its fair share of disadvantages as well. The stopping and restarting of machines is not time efficient, and results in additional operational costs. Reconfigurations and output testing also contributes to additional downtime and slower cycle times. The direct alternative to batch manufacturing is continuous manufacturing.

Chapter 3: Novartis-MIT Center for Continuous Manufacturing

The 10 year partnership, between Novartis and MIT, is working to develop new technologies that aim to replace traditional batch production processes with continuous manufacturing processes. When asked about the partnership Dr. Daniel Vasella, Chairman and CEO of Novartis, said "This partnership demonstrates our commitment to lead not only in discovering innovative treatments for patients but also in improving manufacturing processes, which are critical to ensuring a high-quality, efficient and reliable supply of medicines to patients. Our collaboration with MIT, a worldwide leader in developing cutting edge technologies, holds the promise to achieve a quantum leap in the production of pharmaceuticals, a field which has received rather little attention in the past."

The Novartis-MIT Center for Continuous Manufacturing aims to benefit patients, healthcare providers, and the pharmaceutical industry by:

- Accelerating the introduction of new drugs through efficient production processes
- Requiring the use of smaller production facilities with lower building and capital costs
- Minimizing waste, energy consumption, and raw material use
- Monitoring drug quality on a continuous basis rather than through post-production, batch-based testing
- Enhancing process reliability and flexibility to respond to market needs

Chapter 4: Hot Extrusion Molding

One of the manufacturing alternatives being explored by the Novartis-MIT Center for Continuous Manufacturing for the production of medicinal tablets is the direct injection of tablets with a hot extrusion molding system. The main difference between hot and wet extrusion is that hot relies on heat to melt the resin being used while wet extrusion relies on the mixing of the resin with water and other agents that can be hardened into shape by drying. Traditional injection molding machines produce parts from thermoplastic and thermosetting plastic materials. Essentially the polymer is fed into a heated barrel, where it is mixed and forced into a mold cavity where it solidifies as it cools and takes the shape of the mold cavity in which it is being retained, until the part is ready to be ejected.

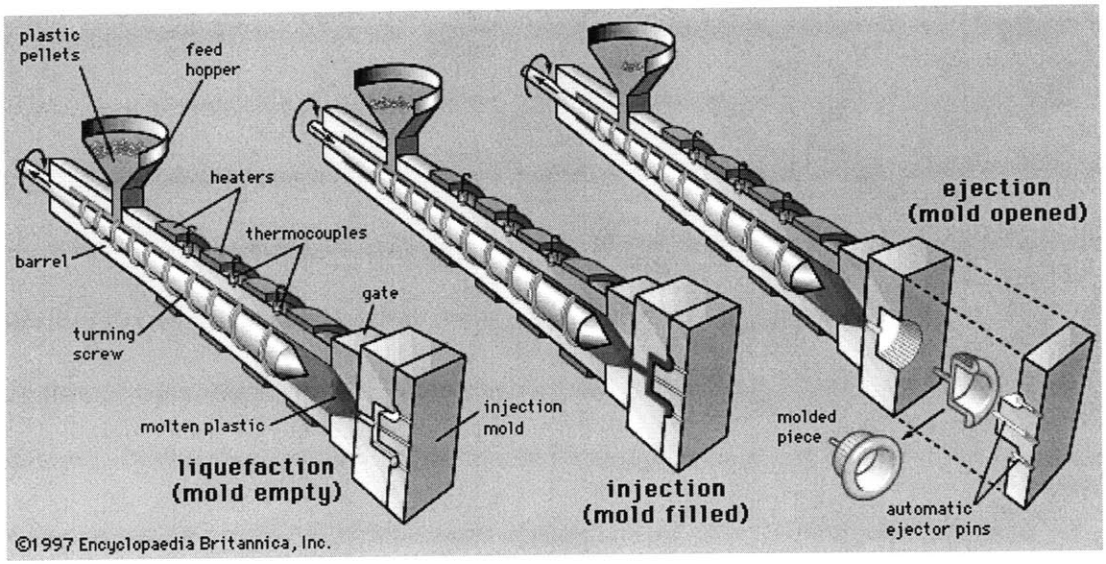

Figure 1: *Simplified injection molding component and operations*

Injection molding machines have three basic components in order to achieve its function. The first is the injection unit, often called the plasticator, which prepares the proper plastic melt and transfers it into the second component, the mold. The third basic component is the clamping system which opens and closes the mold. Injection molding machines all perform certain necessary functions:

1. *Plasticizing:* heating, melting and mixing of the plastic in the injection unit,
2. *Injection:* controlled shot is injected from the plasticator into a close mold were it begins to solidify on the mold's cavity wall,
3. *Packing:* maintains injected material under pressure for a specified period of time to compensate for decrease of volume during solidification and prevent backflow,
4. *Cooling:* cooling of the plastic in the mold until it is ready to be ejected,
5. *Part Release*: mold opens and part is ejected.

Once the part is successfully released the mold closes, and a new shot of melt is ready to be introduced into the cavity.

Injection molding is a well understood and largely employed process which provides an interesting alternative to the batch method. Although initially designed to perform as a non-continuous extruder, advances in the process have opened the doors for injection molding to run as a continuous process. For this project we are interested in a continuous manufacturing process, but the differences in processing conditions and functional requirements of a pharmaceutical extrusion molding machine poses a different challenge.

Chapter 5: Mixing criteria – Twin barrel screw

Before joining the project the team had acquired and began the use of a twin barrel screw extruder to be used as the plasticator in the hot extrusion molding machine. The twin barrel screw extruder is better suited to thoroughly mix the active pharmaceutical ingredient with any excipient that might be used in the formulation of the tablets. The extruder used was a Leistritz Twin Barrel extruder which is capable of generating pressures up to 2,030 PSI. This is a much lower range than traditional injection molding plasticators, which generally operate on pressures of 8,000 PSI and above. This meant that pressure drop calculations had to be conducted to see whether if the filling/packing of the molds would be possible with the current set-up.

Another big limitation in the use of a twin barrel screw instead of a traditional reciprocating (single screw) screw is that there is no axial movement of the screw which acts as a piston which allows for greater pressure control and can act as a shut off valve to regulate the flow of the melt into the mold cavity.

Chapter 6: Feasibility and Injection Pressure Requirement

As mentioned before, the first and most critical calculation needed to be employed was the pressure drop calculations, to see whether the extruder could adequately force the material through the runner and into the mold cavity. For this calculation, the Darcy-Weisbach equation[3] was used to obtain the pressure drop, Δp, as:

$$\Delta p = f \cdot \frac{L}{D} \cdot \frac{\rho V^2}{2} \tag{1}$$

where f is the friction factor, L and D are the respective lengths and diameters of different segments of the runner, ρ corresponds to the density of the active pharmaceutical ingredient and V to its velocity.

The value of the friction factor changes depending if the flow is laminar or turbulent, so the Reynolds number, Re, for the flow at the different segments of the system needed to be calculated. The Reynolds number is expressed as: [4]

$$\mathrm{Re} = \frac{\rho V D}{\mu} \tag{2}$$

where, μ, corresponds to the material's viscosity.

The Density of the material was obtained by measuring the volume of a hand pressed tablet made from the melt. The same tablet was then weighed, and the density was derived from those values.

The velocity of the active pharmaceutical melt was obtained by dividing the known mass flow rate, $\dot{m}$, of the extruder by the cross sectional area of each segment as shown

$$V = \frac{\dot{m}}{\frac{D^2}{4} \cdot \pi} \tag{3}$$

The viscosity was obtained from rheometry experimental setup conducted by Erin Bell and shown in Figure 2.

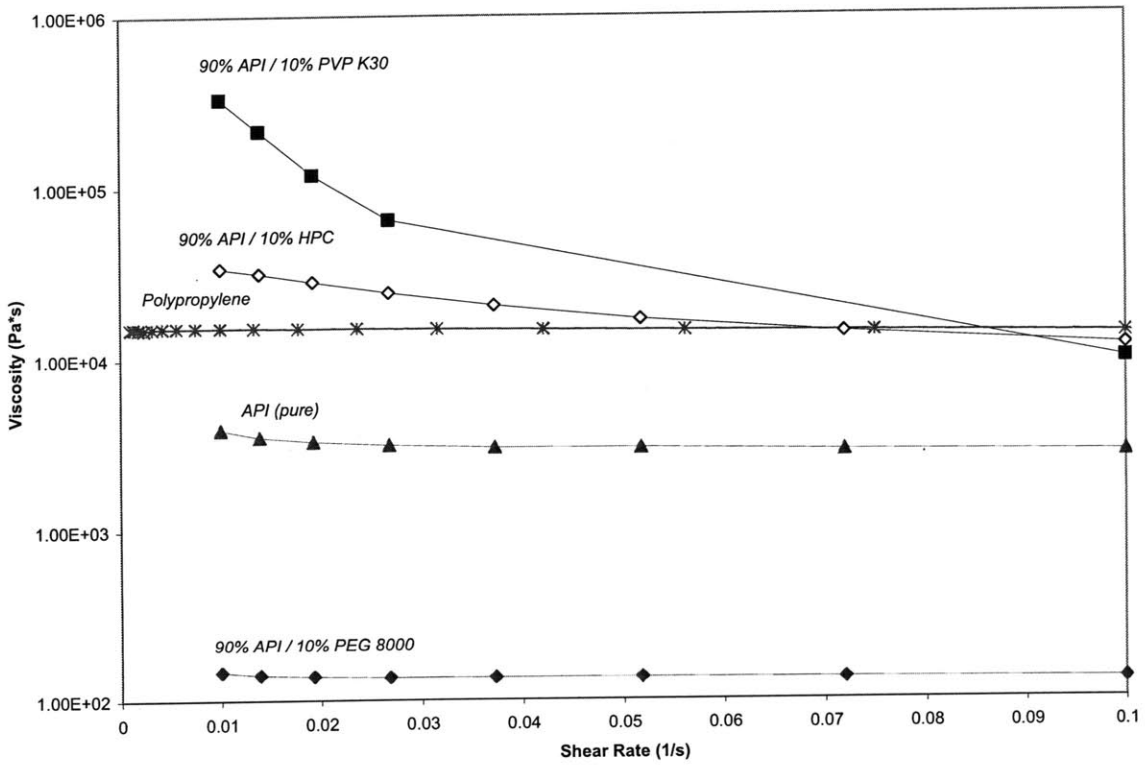

Figure 2: *Viscosity of pharmaceutical melts and polypropylene*

For the different segments of the gate, runner and cavity the Reynolds numbers were obtained as shown in Table 1.

Table 1: *Reynolds numbers of different hot extrusion system segments*

Segment	Reynolds number
Runner	2.44×10^{-10}
Gate	1.22×10^{-9}
Cavity	7.32×10^{-11}

The flows are always in the laminar regime, so the friction factor can be obtained from [4]

$$f = \frac{64}{\mathrm{Re}} \tag{4}$$

Using Equation 1 the total pressure drop was estimated to be 1117 psi, which is less than the maximum pressure of the extruder.

Chapter 7: Temperature Considerations

One of the key challenges with the hot extrusion molding process of pharmaceutical melts is that the material(s) used in the melt are much more expensive and need to be meticulously controlled during production. Excess material in plastic injection molding is not a problem since scraps can be collected and re-melted later, whereas in pharmaceutical applications the melt can not be re-melted after solidifying since the active pharmaceutical ingredient can degrade, and the dosage specifications can be lost.

Another problem we encounter is that there is a much narrower processing window in order to prevent melt degradations. Unlike plastic injection molding, where the melt is maintained at temperatures above 200°C until reaching the mold, we are limited by a much lower temperature limit of about 95°C before risking active pharmaceutical ingredient degradation. This gives a window of approximately 10°C between melting temperature and degradation temperature that has to be carefully controlled in order to avoid both the premature solidification of the melt and the excessive heat degradation of the melt. Additionally over exposure of the drugs to even 95°C can also lead to active pharmaceutical ingredient degradation, so the total time at a melted state needs to also be considered in the machine design process.

Chapter 8: Cooling, Degradation and Coefficient Estimates

As mentioned before, there is a strong design concern of premature cooling in a hot extrusion molding machine for pharmaceutical applications. Premature cooling can result in clogging of the system or short shots when filling the molds. For this reason cooling calculations were needed to be conducted to quantify the potential for premature cooling.

Before being able to set any particular cooling models, some material thermal parameters had to be obtained. Since little information was available about the material being used some quick experiments to estimate the thermal diffusivity were conducted.

I insulated a hand formed tablet with Styrofoam leaving only both ends of the cylinder uncovered. A temperature sensor was attached to both exposed ends. One end was then placed on top of a heat plate, while the other was exposed to the ambient temperature. The heat plate was incrementally raised up to 80°C, which is just under the melting temperature of the material. At each temperature setting the temperature reading from each sensor was recorded as well as the room temperature. The thermal conductivity, *k*, of a material can be obtained from[5]

$$k = \dot{Q} \cdot \frac{h}{A(\Delta T)} \tag{5}$$

Where $\dot{Q}$ corresponds to the heat flux, *h* to height of the tablet, *A* to the cross-sectional area of the tablet and ΔT to the difference in temperature readings between the sensors.

Since thermal conductivity is an intrinsic property we can make the assumption that for all the measured values, *k*, should be constant, this restriction and the known heat flux at maximum temperature was used to derive an expression for the heat flux at different temperature settings.

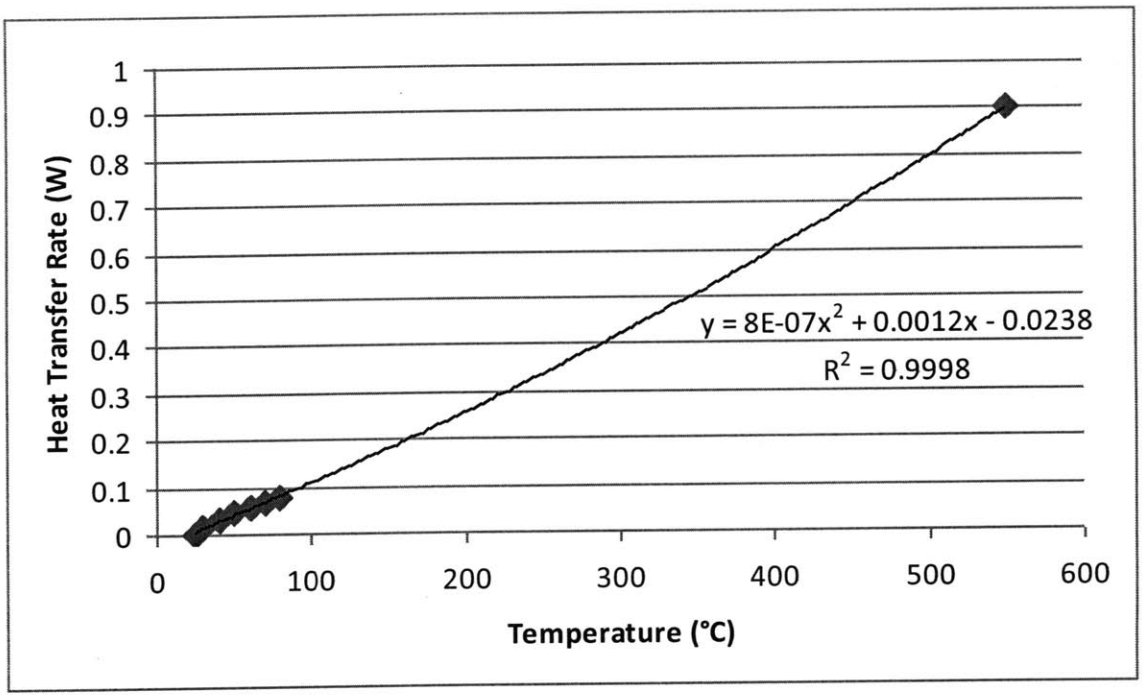

***Figure 3**: Heat transfer rate vs Temperature for experimental set-up with fitted curve*

The line fit from Figure 3 was then use to back calculate the thermal conductivity, which was then used to obtain the thermal diffusivity, α, of the material being study by using the relation[5]

$$\alpha = \frac{k}{\rho \cdot c_p} \tag{6}$$

where c_p is the specific heat. The specific heat can range between 0.84 and 2.30 J/(g·K).[6][7]

The thermal conductivity was calculated using Equation 5 to be 0.893 ± 0.189 W/mK and the thermal diffusivity was calculated using Equation 6 to be within the range of $2.6 \cdot 10^{-7}$ m^2/s and $3.7 \cdot 10^{-7}$ m^2/s.

With these thermal parameters now available, the cooling time can now be obtained. The centerline cooling times, t_c, and the average part cooling time, t_a, are respectively [8]

$$t_c = 0.173\left(\frac{h^2}{a\pi^2}\right)\ln\left[1.6023\left(\frac{T_m - T_W}{T_e - T_W}\right)\right] \quad (7)$$

$$t_a = 0.173\left(\frac{h^2}{a\pi^2}\right)\ln\left[0.6916\left(\frac{T_m - T_W}{T_e - T_W}\right)\right] \quad (8)$$

where T_m, T_W and T_e correspond to melt temperature, mold wall temperature and ejection temperature, respectively.

When inputting the calculated thermal diffusivity ranges from above into the cooling equations the time for centerline to reach ejection temperature ranged from 7.1 to 9.9 s, and time for average part to reach ejection temperature ranged from 5.7 to 7.9 s. This was an issue since the cooling time was less than the actual filling time, 9 s, which indicated that the material would prematurely cool clogging up the runner leading to the tablet.

Degradation is also another big concern, exposure to too high temperatures will damage the active pharmaceutical ingredient, but if not melted enough we risk clogging the system by premature freezing before reaching the cavity. Also the time exposed to heats even close to the melt temperature can have adverse effect on the material. In order to test the effect of

exposure to heat at different intervals of time, the active ingredient was melted and kept at a melted state for different intervals of time and was then allowed to cool until solidifying. The solid material was then tested to see the purity of the solid. Figure 4, obtained by Erin Bell, shows the area percent of the impurity in the active pharmaceutical ingredient, Y-axis, when exposed to a set temperature, X-axis, for 5 and 20 minutes. The melt can stay at a temperature between 85-100°C for 5 minutes without showing signs of degradation.

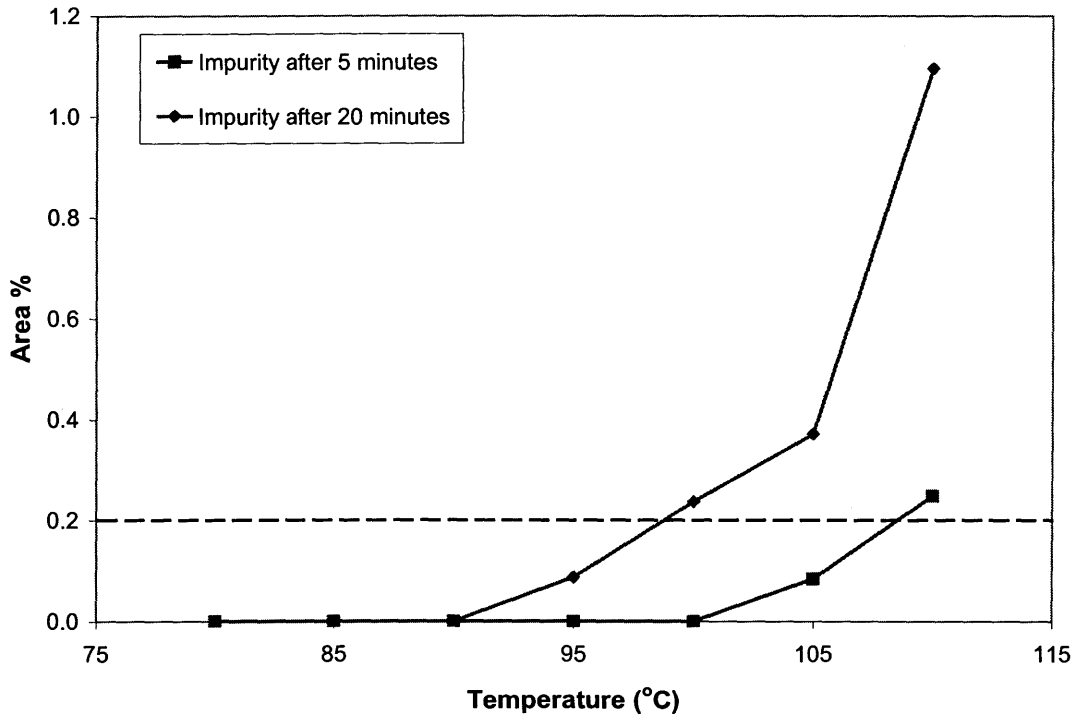

Figure 4: *Impurity area percent of active pharmaceutical ingredient at different temperatures and time spans*

The melt was observed to take between from 3.5 to 4.0 minutes to go from the feeding location to the die of the extruder. So there is only about 1.0 to 1.5 minutes of time it can remain in the melted state until deformations begin to appear.

Chapter 9: Hot Runner System

A hot runner system in injection molding differs from the more common cold runner system in that the plastic is maintained heated at the melted state throughout by heated components in addition to the plasticator. A typical hot runner system usually includes heated manifolds and nozzles. The manifolds distribute the plastic entering the mold to the nozzles, which in tern meter it to the injection points in the cavities.

Hot runners have many advantages since they reduce material scrap, since there is no need for a cold runner to freeze off since the nozzle takes care of directly injecting the melt to the cavity. Since the cycle time of the mold is largely influenced by the cooling cycle, minimizing the material that needs to cool down can increase the production output. As a result hot runner systems are generally attributed with overall reduction in cycle times.

Injection time is also reduced since there is no wasted time in filling a cold runner, and, with no runner to interfere, parts molded with hot runner better lend themselves to automated part removal. However, hot runner systems do require additional controls and add an additional level of complexity in the design of an injection molding machine, but since the cooling time is preventing the use of a typical cold runner system due to premature clogging, and since it provides a solution to the wasted resin material.

Since we were interested in producing a prototype, and are limited by the extruder mass flow rate, it is not necessary to include a manifold for our system, which meant that the pharmaceutical melt could flow from the extruder barrel directly to the nozzle which in turn fills the mold cavity.

When selecting the nozzle to purchase for the application the main design consideration criteria were:

- Large material processing window – Since we are using pharmaceutical melts that are not traditionally injected molding, it was important to verify that it could operate with material property range.
- Nozzle tip and size – Medicinal tablets are small and require a nice surface finish, so the nozzle needs to leave a small impression on the tablet, and for this it needs to be of small bore dimensions, under a millimeter.
- Nozzle length – Since the overall time in melted state is proportional to the length of the flow channel, the longer the nozzle length the longer the melt is exposed to high temperatures and risks decaying.

After looking for different hot runner nozzles a Synventive Series 03 S01 open nozzle was selected. This nozzle has an overall length of 56 mm, with a hot runner gate diameter of 0.6 mm. The W02T gate tip had a large material processing window and allowed for shot sizes as small as 100mg, it also is an open torpedo gate which helps in the control and finish of the part.

Chapter 10: Clamp Force

The clamping unit is one of the most critical components in the design of an injection molding machine. It needs to be able to withstand the force that gets accumulated within the molds. It also needs to be able to be controlled and operable.

When selecting an appropriate clamp for an application the clamp force, F_{clamp}, is used to determine the proper tool. Clamp force is determined as

$$F_{clamp} = A_{projected} \cdot \Delta p_{\max} \tag{9}$$

where $A_{projected}$ corresponds to the projected area of the cavity and $\Delta p_{\max}$ corresponds to the maximum pressure which is limited by the extruder. This yields a clamp force of 200.2 lbs. Although automation of the production is an eventual goal of the Novartis-MIT Center for Continuous Manufacturing, it was decided to proceed with the purchase of a hand-operated clamp. The reasoning behind this decision was that a programmable clamp is an additional complexity that shouldn't be included in the proof of concept prototype that was going to be built.

I purchased a De-sta-co 630-R line clamp for the machine. This model had holding forces maximums of 2500 lbs and is a single line clamp which meant that the force can be directly aligned on to the center of the mold to provide the right amount of support and rigidity.

Chapter 11: Pressure Accumulation

Injection molding machines must be capable of handling and sustaining large pressures inside, so safety precautions against pressure build-up within the machine should be in place to prevent damaging the machine or injuring the operator. The extruder sets the limit of the amount of pressure that can build up in the machine, since it stalls out at 2030 psi. The hot runner was built to run with pressures of 8000+ psi so we don't expect any trouble with that component. The clamp is rated to hold 2500 lbs, and is acting directly in line with the runner so the extruder should stall out before risking any material failure.

However, the extruder stalling out is not an optimal solution if the system over-pressurizes since, continuous restarting and cleaning of the machine is not aligned with the aim of the project. For this reason a mechanical release was introduced into the system using a heavy load die spring that can compress and release the pressure if it goes above a certain limit, limiting the stopping as a result of extruder stalling. The die spring also helps add preload to the system.

Chapter 12: Additional Design Considerations and Material Selection

Since we are working with pharmaceutical grade material it is important that all the components that come in contact with the melt wont compromise the purity of the melt. The melt also has the characteristic of being rather sticky, of almost taffy-like texture, so surface finishes are important to facilitate material ejection and removal. For these reasons all components that come in direct contact with the melt are made from (304) stainless steel. The parts that come in contact with the melt, in addition to the extruder and hot runner nozzle, are the attachment die that connects the extruder to the hot runner nozzle and the mold core/cavity.

Primary weight supporting materials, i.e rails, are to be made with steel to take advantage of the high material strength for the relatively low cost. The remaining parts can be fabricated from aluminum to keep overall weight of the attachments low and eases the machining.

Proper alignment of the system is also important for the successful performance of the system. Concentricity tolerances for this reason are important to be maintained and self alignment features like key and slot mates with flexing elements should be included.

Chapter 13: Overall Design Layout

The hot extrusion injection molding system is incorporating the twin screw extruder, a hot runner nozzle and a linear clamp, but these elements by themselves can not make a complete machine by themselves. The molds have to be designed and fabricated to fit the hot runner nozzle tip and to keep the cavity size consistent with the tablet weight specifications set by Novartis. They also must align properly with respect to each other.

It would be counter cost effective and limit flexibility of the system if the molds are rigidly attached as part of the machine. For this reasons the molds should be held in place by back-plates that can be adjusted in location, and translate to allow the mold to open and close. In order to allow the plates to slide and to support the weight of the machine, rails will be used to support the back-plates. To help align the linear action of the clamp with the molds, the rails will also support an additional back-plate to be where the clamp will be mounted.

The clamp-mold will be attached with a bolt that screws into the clamp plunger and is attached to the mold cavity back plate to transfer the clamping force to the mold when closed. On the other side the mold core is to constrain the hot runner nozzle with the use of the spring die and a locking plate to prevent unwanted rotation. The hot runner nozzle is then linked to the extruder through an extruder die that can fit the hot runner entrance.

Figure 5 shows the labeled overall design layout that was described in this chapter. Additional information regarding the specifics of the different individual components is presented in the next chapter.

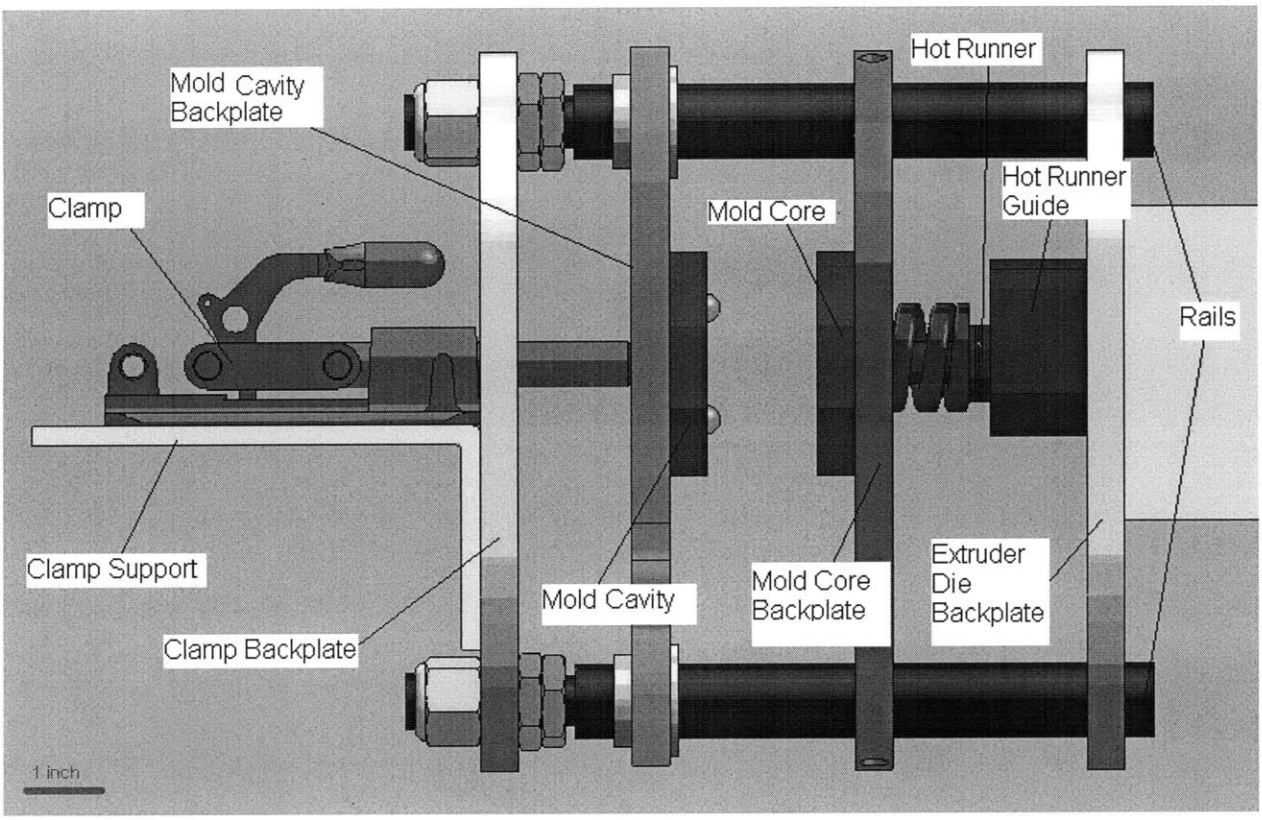

Figure 5: *Hot Extrusion Molding System Layout*

Chapter 14: Individual Components

Pictures and CAD drawings are attached in the appendix for all the following parts.

14.1 Clamp Support and Backplate

The before mentioned clamp is held in place by a combination of a 6061 aluminum backplate that was also made on the waterjet to match the other pieces. This one is held in place by a combination of think hex jam nuts and a nylon reinforced locknut on the threaded side of the rail. The support is essentially a wide aluminum L-bracket with through holes for attachment to the backplate and to the clamp. The holes are either oversized or slotted to allow for minor adjustments for alignment in assembly.

14.2 Mold Cavity Backplate

The mold cavity backplate is also made from 6061 aluminum using the waterjet. This piece was designed with a flexure piece to allow for rail misalignment when sliding, and so that the locating pins in the molds can conform to be aligned with each other. FEA was conducted on the flexure so that under 1% of the force applied of the clamp the flexure could displace a minimum of 1/8 in either direction perpendicular to the rails, but it is yet stiff enough to withstand the axial forces applied by the clamp over the

mold section. This piece is free to slide on the rails and is open / closed by a bolt screwed into the clamp plunger.

14.3 Mold Cavity

The mold cavity is made from 304 Stainless Steel and together, with the core mold, makes the second half of the cavity where the tablet is formed. This part contains the male key that match up with the core's female ends for proper alignment. The male key is made from steel dowel pins pressed fit into the mold. Like the mold core, the mold cavity also is bolted down to the back plate using socket head cap screws.

14.4 Mold Core

The mold core is also made from 304 Stainless Steel. The tablet cavity is made so that when matched up with the mold cavity it has the theoretic volume for a 300 mg dose of the active pharmaceutical ingredient being molded. The opposite end of the mold is the suggested dimensions for the cutout for the nozzle end. The mold is then attached on to the back-plate with socket head cap screws that don't interfere with the mold opening and closing. The mold core also contains female ends to where the mold cavity can sink slip in, and align with respect to each other.

14.5 Mold Core Backplate

The mold core backplate is made from 6061 Aluminum using a waterjet to make the shape and inner features. This piece is clamped on to the rails after being slid into place. The center hole is used to keep the spring positioned in the system, the combination of this with the core mold tube keep the spring properly constrained.

14.6 Extruder Die Backplate and Hot Runner Guide

The extruder die backplate is the last waterjetted part of 6061 aluminum in the assembly. It bolts on to the extruder die in the extruder machine directly and locks on to the rails using a pair of set screws. The hot runner guide is then bolted on to this piece. The guide provides alignment support for the hot runner and can serve as a mounting plate for additional customization.

14.7 Extruder Die

The extruder die was made out of stainless steel since it comes in contact with the material. This attachment is responsible for the transfer in interior diameter between the extruder barrel and the hot runner. It steps down the diameter with a 60 degree angle to limit the pressure drop as a result of kinks, or the uncontrolled flow of pharmaceutical melt.

14.8 Rails

The 1117 steel rails are 1 inch in diameter. A flange was milled on to one end to allow a place for the set screw to hold on to, while the other side was threaded so that the clamp backplate could be bolted tight.

Chapter 15: Assembly Results and Discussion

The fabrication and assembly was tedious and required small modifications reflected in the CAD drawings in the assembly. The hardest part to manufacture were the stainless steel molds as a result of their small tolerance, and required the manufacturing of special tooling to be able to make them. Type 304 stainless steel is very hard to work with, so if possible for future work a softer grade stainless steel may be substituted if it meets the additional specifications. Another large obstacle that we had to overcome resulted from the supplied hot runner controller and its connections. There was confusion over the wiring documentation and some connecter pieces were missing. After meeting with a representative the doubts were cleared and the right plug was bought for the application.

The last issue in the build was interference. I overlooked travel path of the clamp handle while opening and closing. It interferes with rail extending above it so modifications have to be made to it so that it doesn't strike the rail or nuts while traveling. It may be possible that the dowel pins might have to be faced down as well as there seems to be some gap between the molds at a close state, which might result from the locating dowel pins coming in contact with the backplate. After fine tuning alignment and running the machine we should have a better idea of the severity of the potential issue, if any.

There is still some doubt about the capability of the furnished extruder to have the power necessary to overcome the pressure drop across the molding system. If the problem

exists, depending on the gravity of the situation, there are some ways to deal with it. First of all, modifications to the API by blending it with other materials we can alter the properties of the melt. If it is less viscous pressure drop as a result of friction can be reduced. The interconnections between the different elements of the runner can add unwanted pressure drops in the system as well. Another possibility is having an additional component between the extruder and the hot runner system to increase the pressure of the system without affecting the other design parameters.

Chapter 16: Conclusion

Throughout the course of completing this thesis I really learned the value of planning in advance and allocating time to things going wrong and having unexpected, and not hard to resolve obstacles. I also got a firsthand look as to how delivery and lead time can delay a project. Overall I am glad I took part in this thesis. It allowed for me to take responsibility, make mistakes, and learn from those mistakes at an academic level, which I will soon not forget when working in projects at a professional level.

References

1. Reinhardt UE. Perspectives on the pharmaceutical industry. Health Aff. 2001;20(5):1363–70.
2. Suresh P, Basu PK. Improving pharmaceutical product development and manufacturing: impact on cost of drug development and cost of goods sold of pharmaceuticals. Pharmaceutical Technology & Education Center, Purdue University, February 2006.
3. Denevers, N., (1970). *Fluid Mechanics*. New York: Harper Perennial.
4. J.P. Holman, *Heat Transfer*, McGraw Hill.
5. Halliday, David; Resnick, Robert; & Walker, Jearl(1997). *Fundamentals of Physics* (5th ed.). John Wiley and Sons, INC., NY
6. Tipler, Paul A., Physics for Scientists and Engineers, 4th Ed., W.H. Freeman, (1999).
7. R.J. Crawford, Rotational molding of plastics
8. Rao, Natti S.; Schumacher, Gunter Design Formulas for Plastics Engineers (2nd Edition). Hanser Publishers.

Appendix

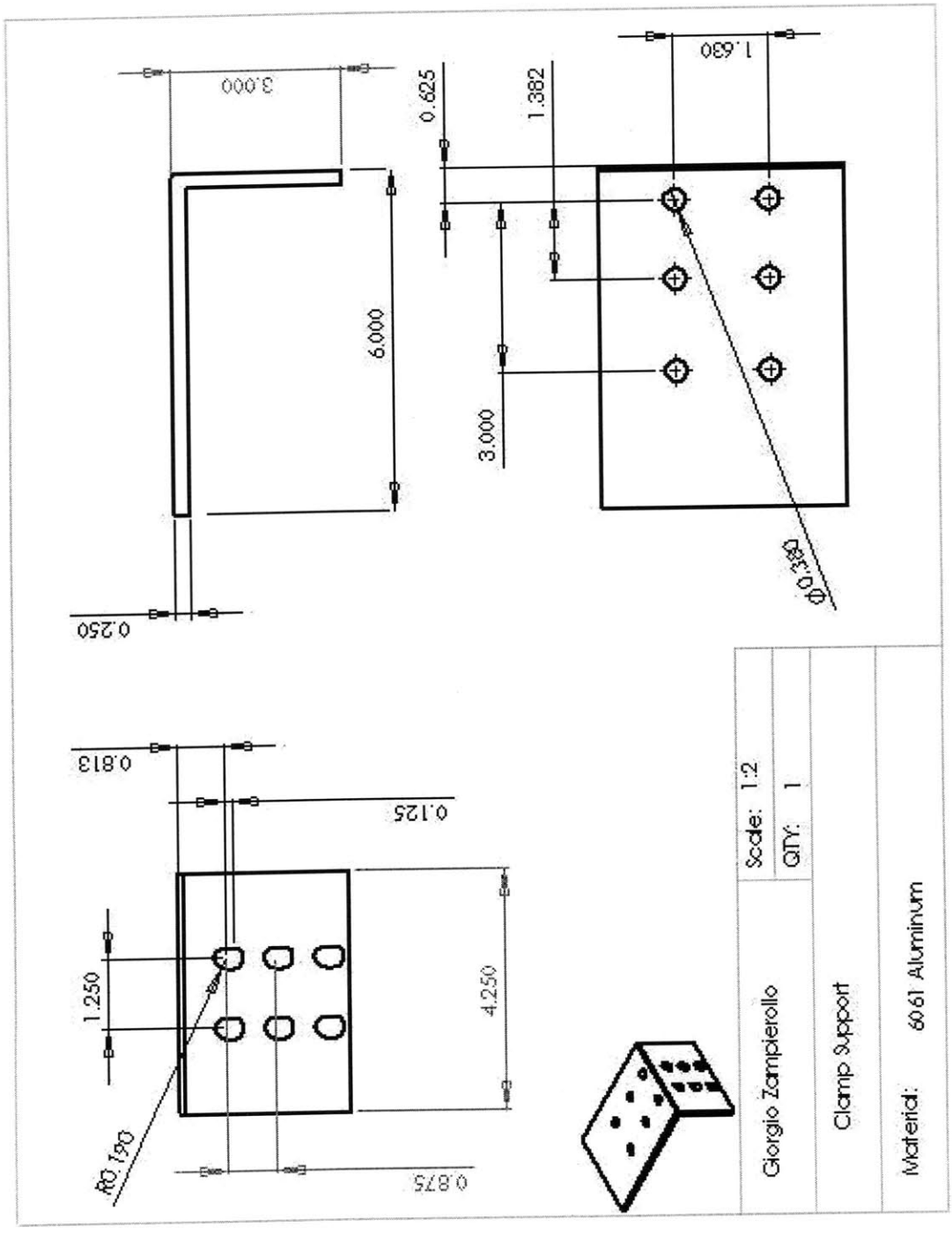

Figure A1: *Clamp Support Drawing*

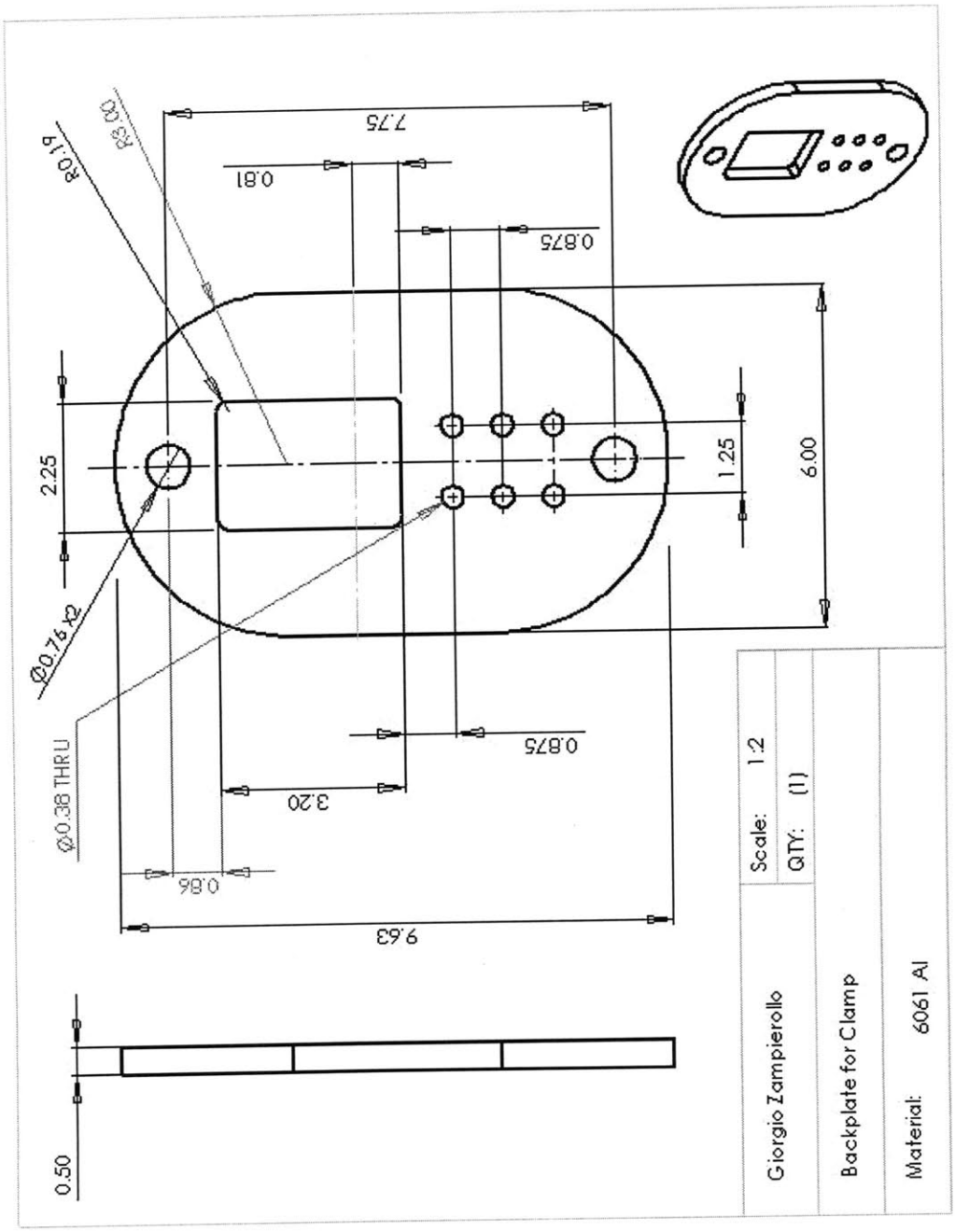

Figure A2: *Clamp Backplate Drawing*

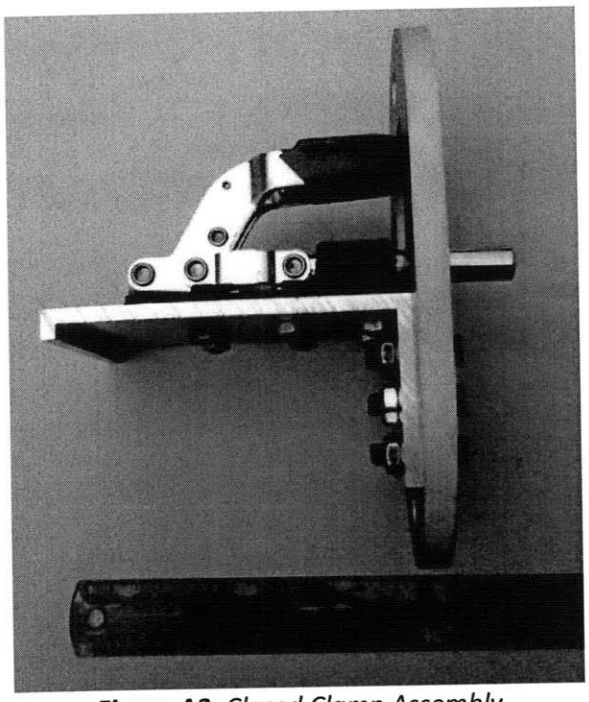

Figure A3: *Closed Clamp Assembly*

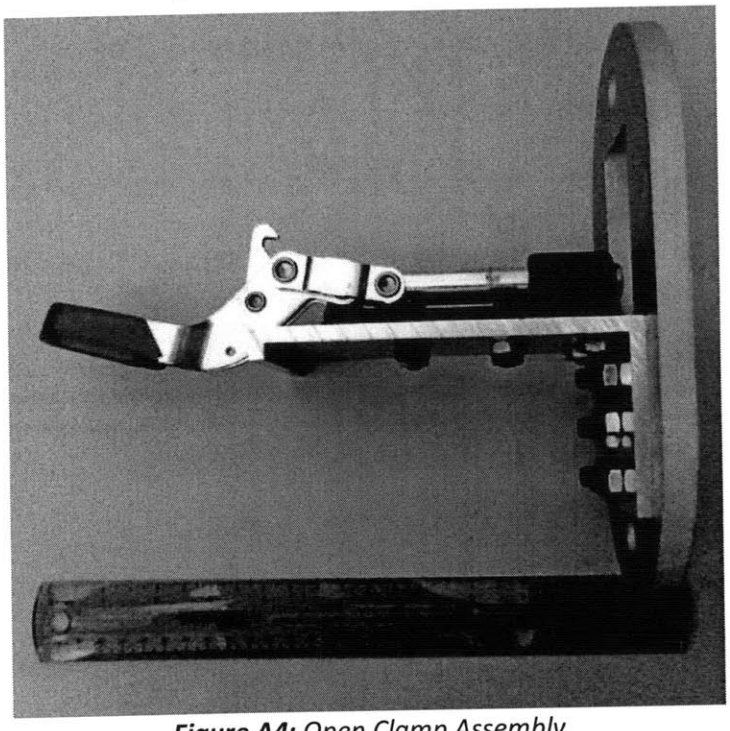

Figure A4: *Open Clamp Assembly*

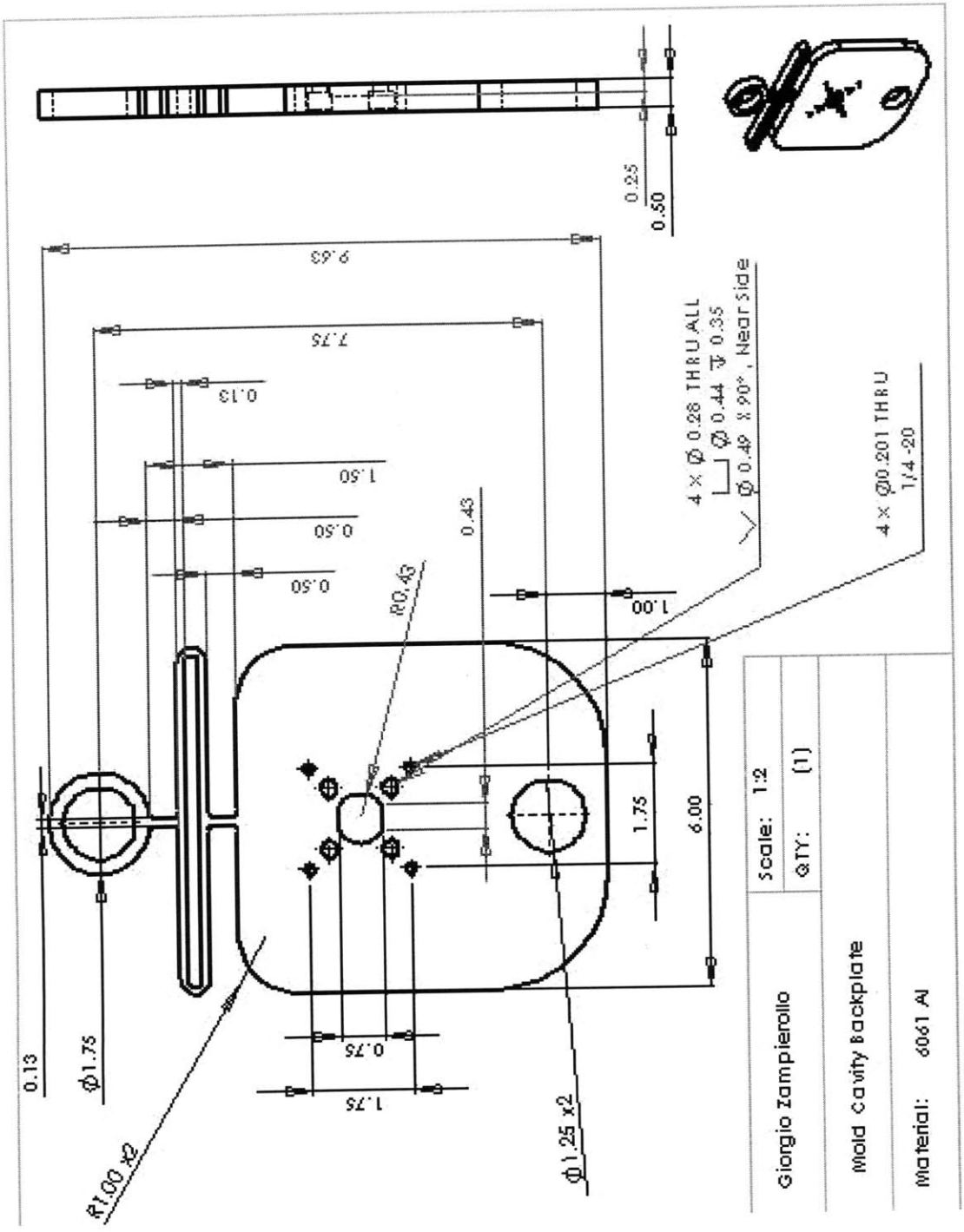

Figure A5: *Mold Cavity Backplate Drawing*

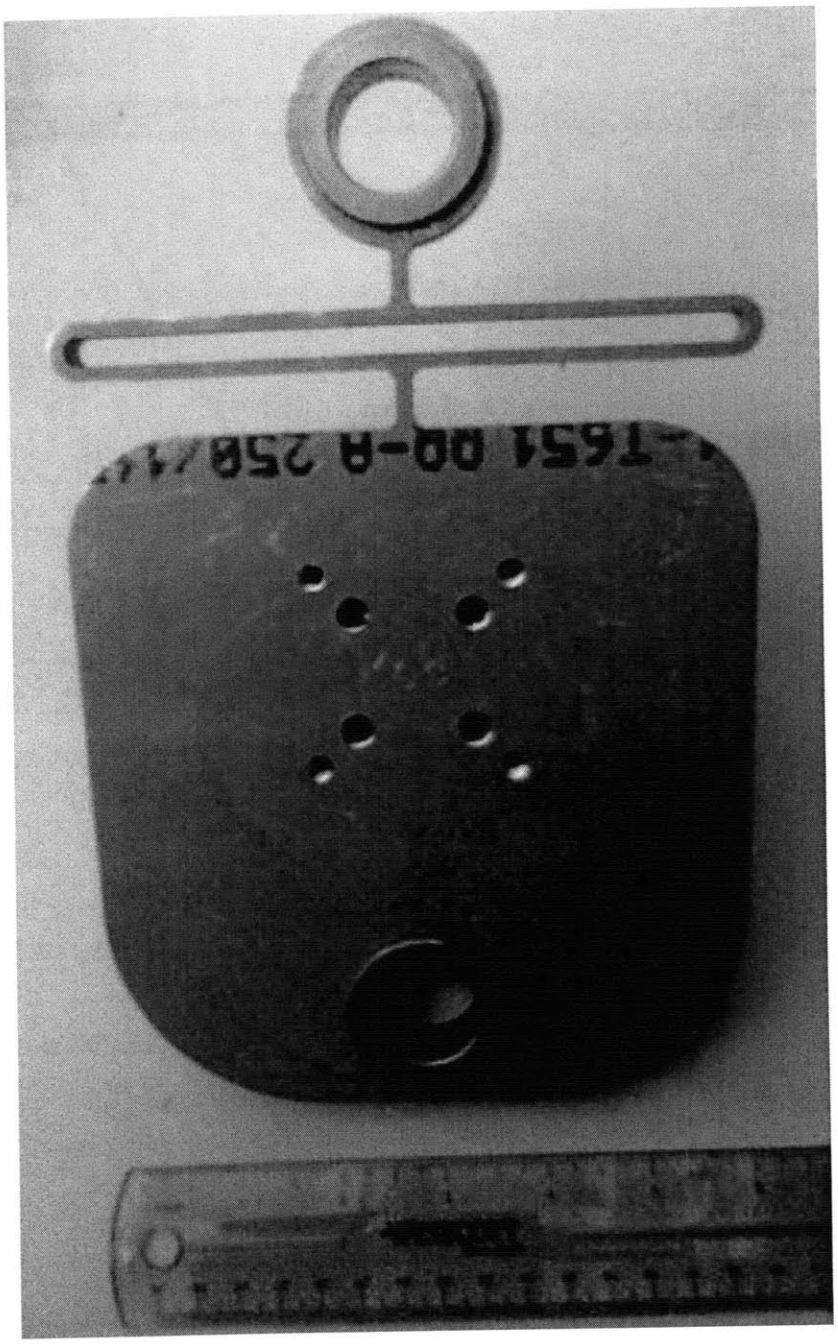

Figure A6: *Mold Cavity Backplate*

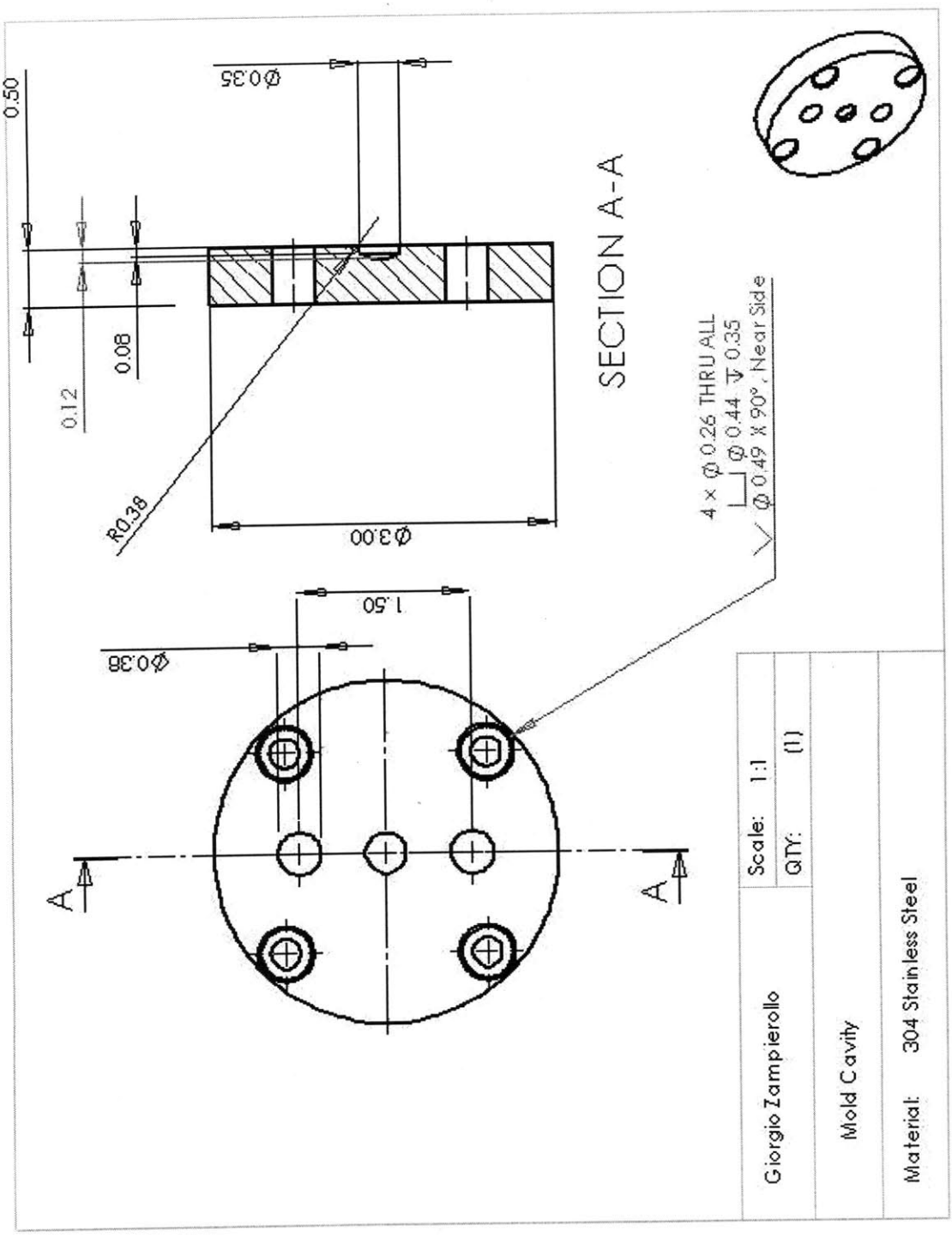

Figure A7: *Mold Cavity Drawing*

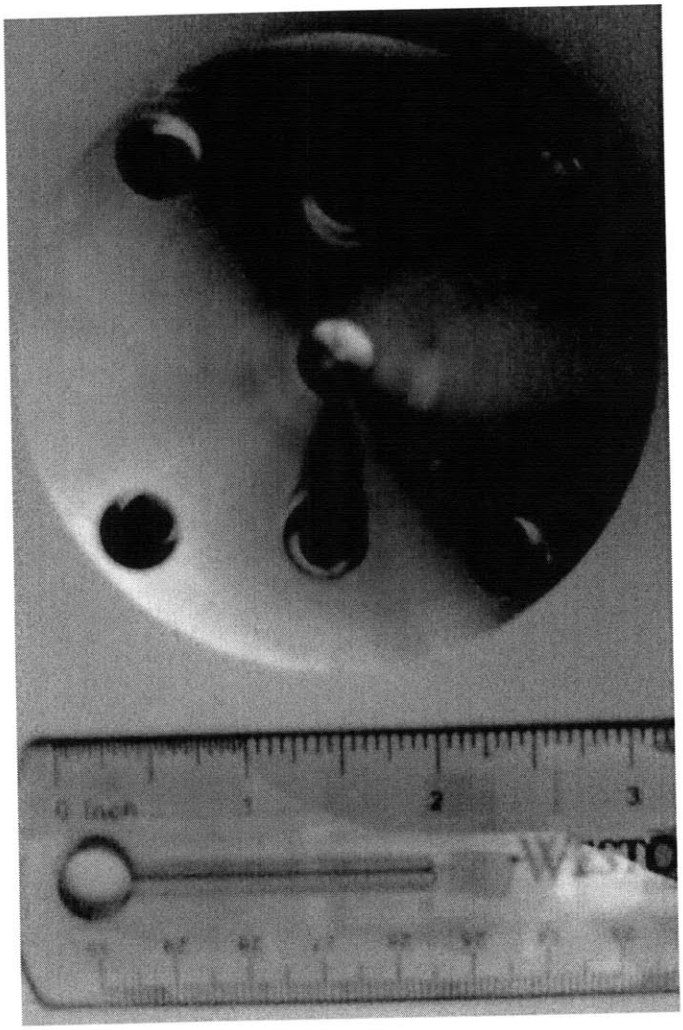

Figure A8: *Mold Cavity*

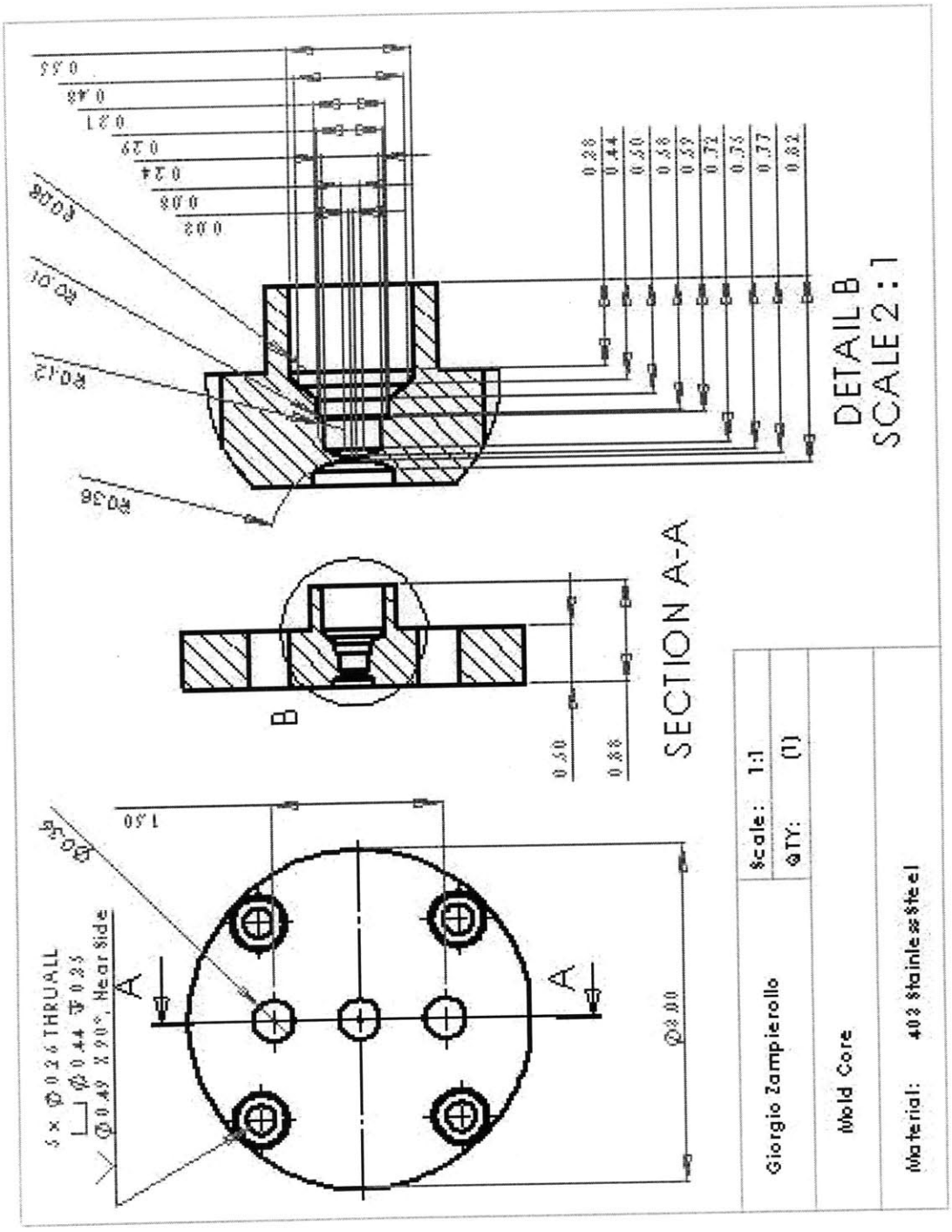

Figure A9: *Mold Core Drawing*

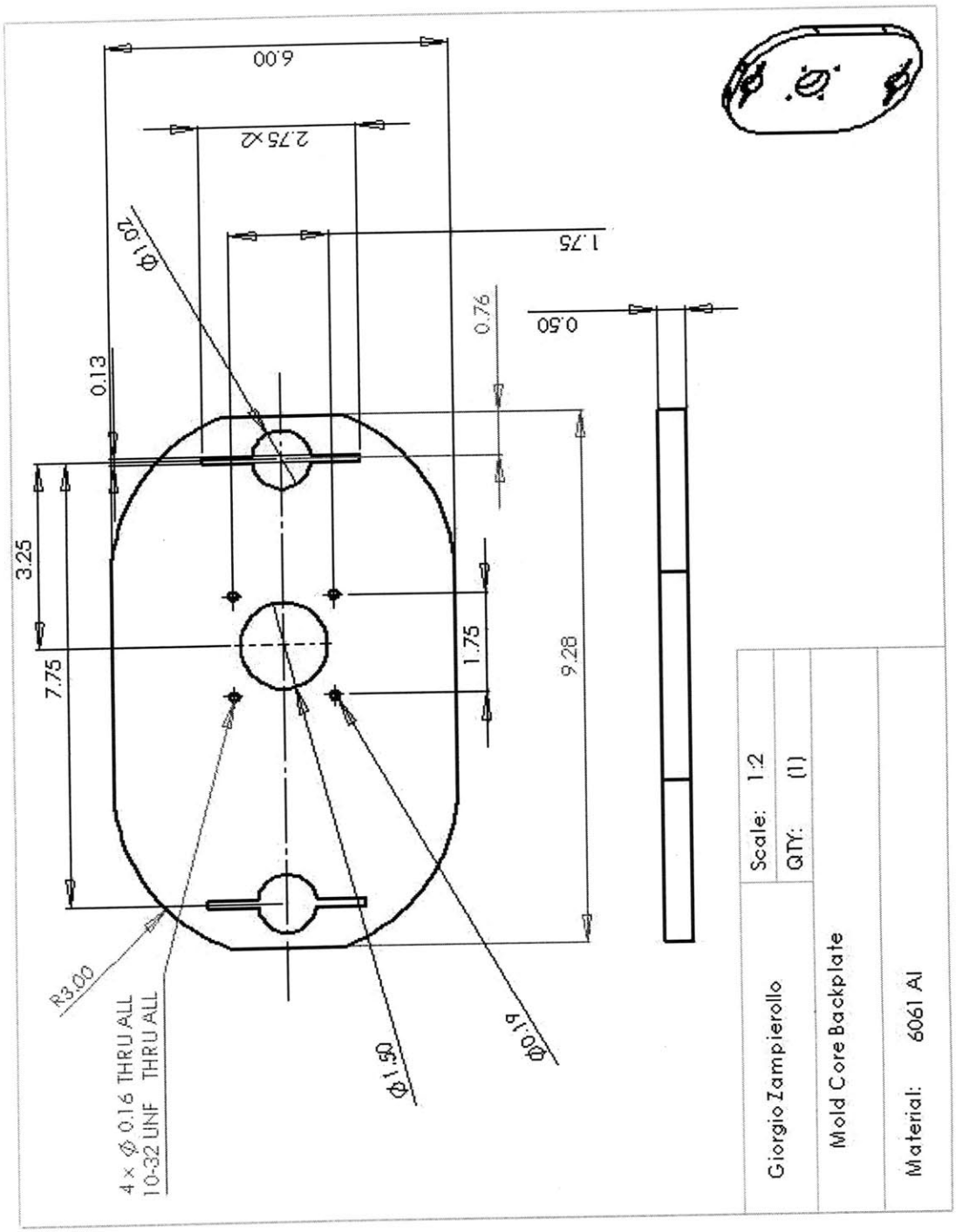

Figure A10: *Mold Core Backplate Drawing*

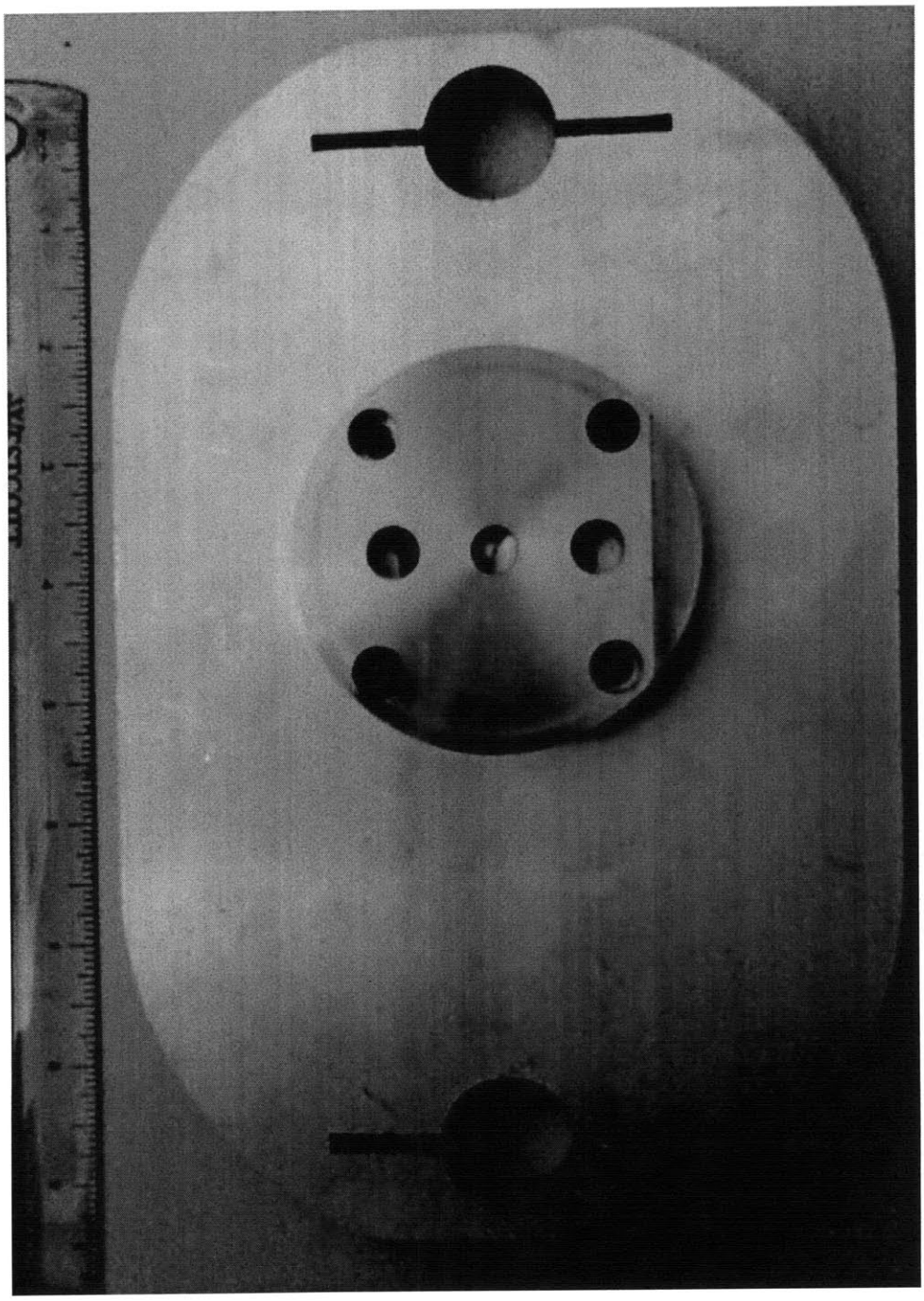

Figure A11: *Mold Core and Backplate Assembly*

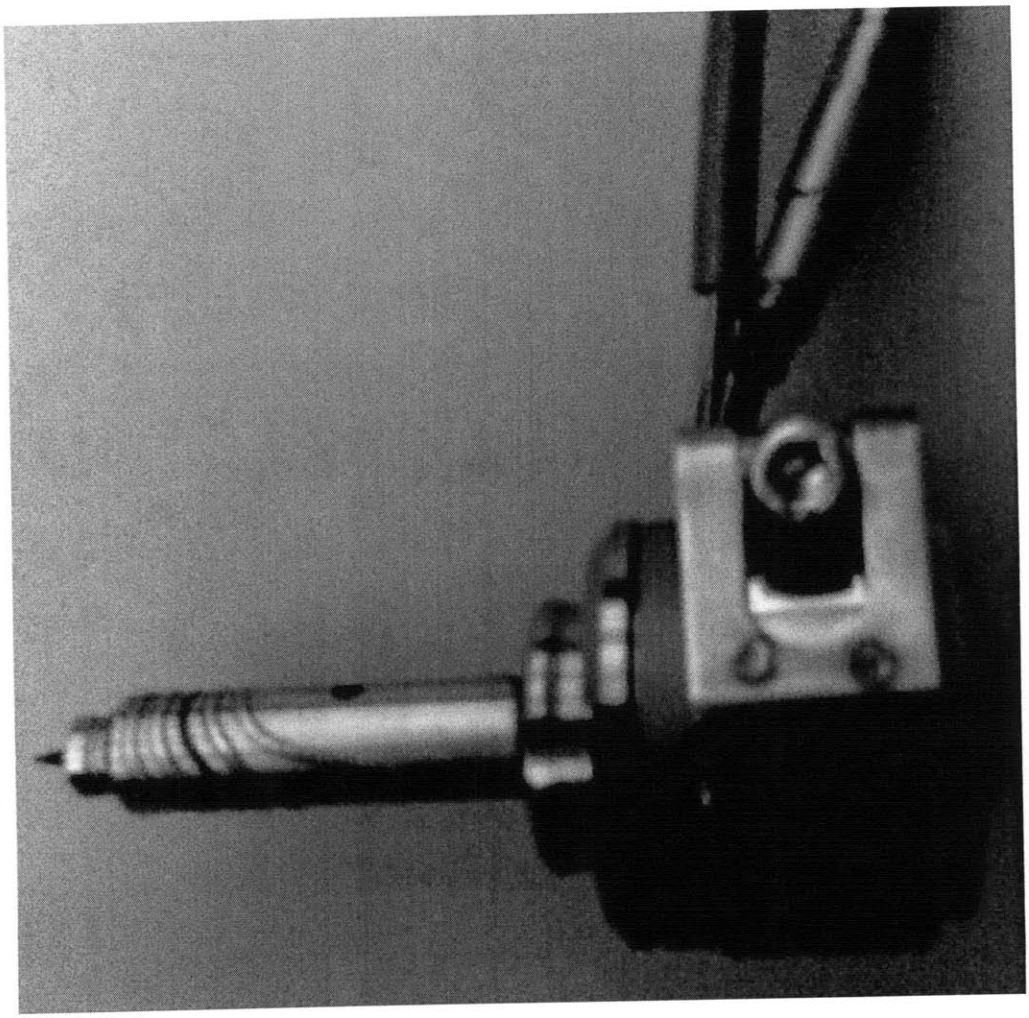

Figure A12: *Hot Runner*

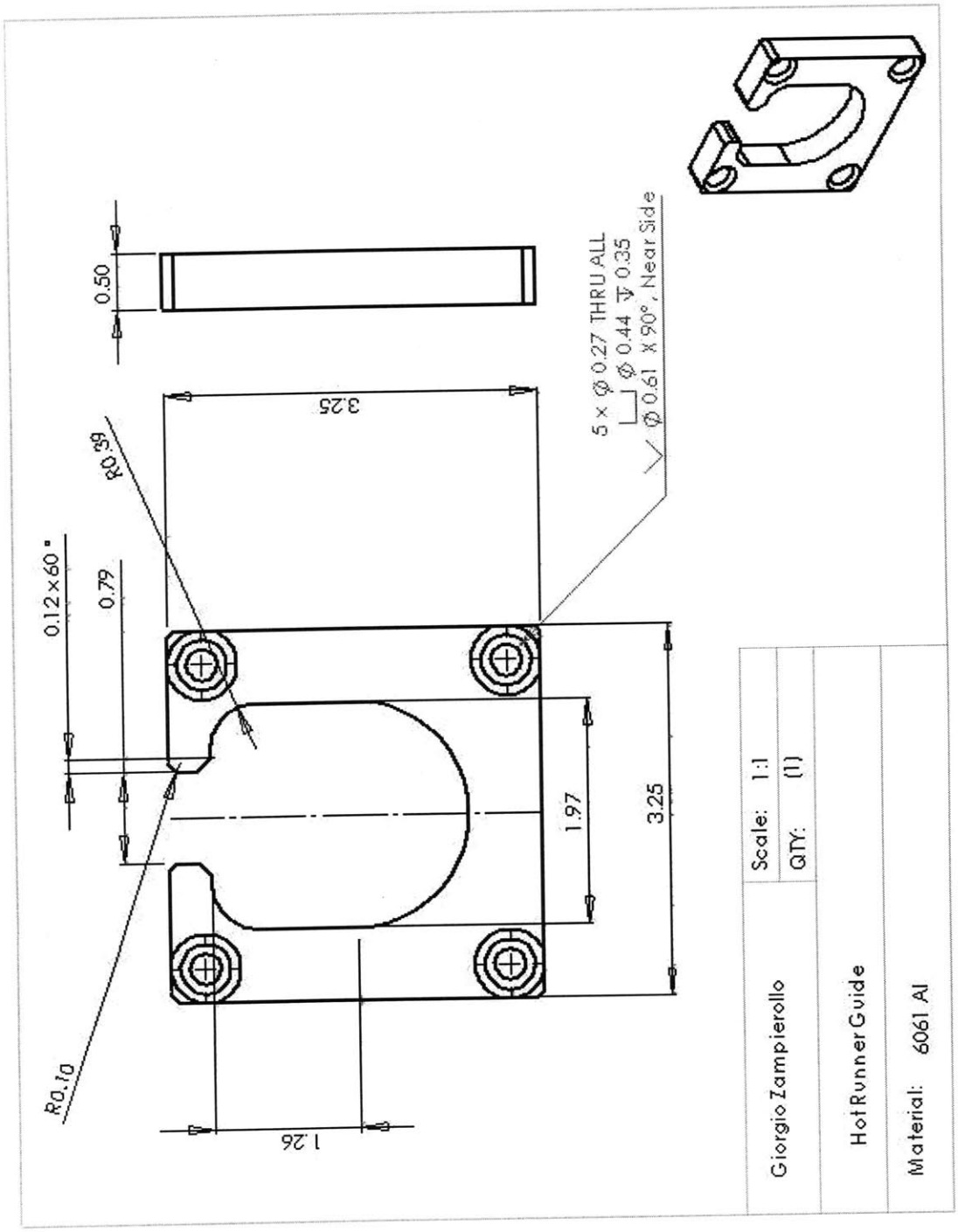

Figure A13: *Hot Runner Guide Drawing*

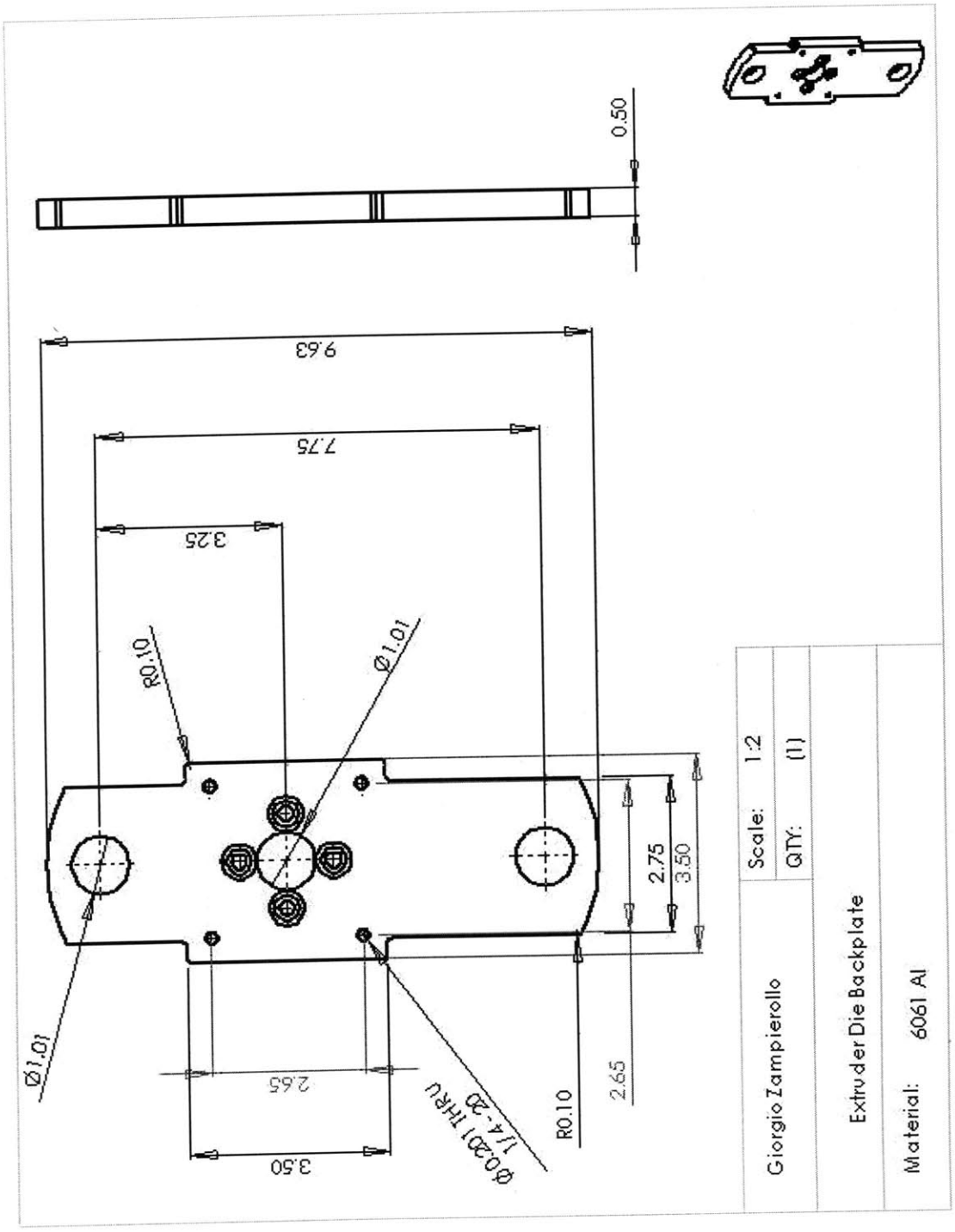

Figure A14: *Extruder Die Backplate Drawing*

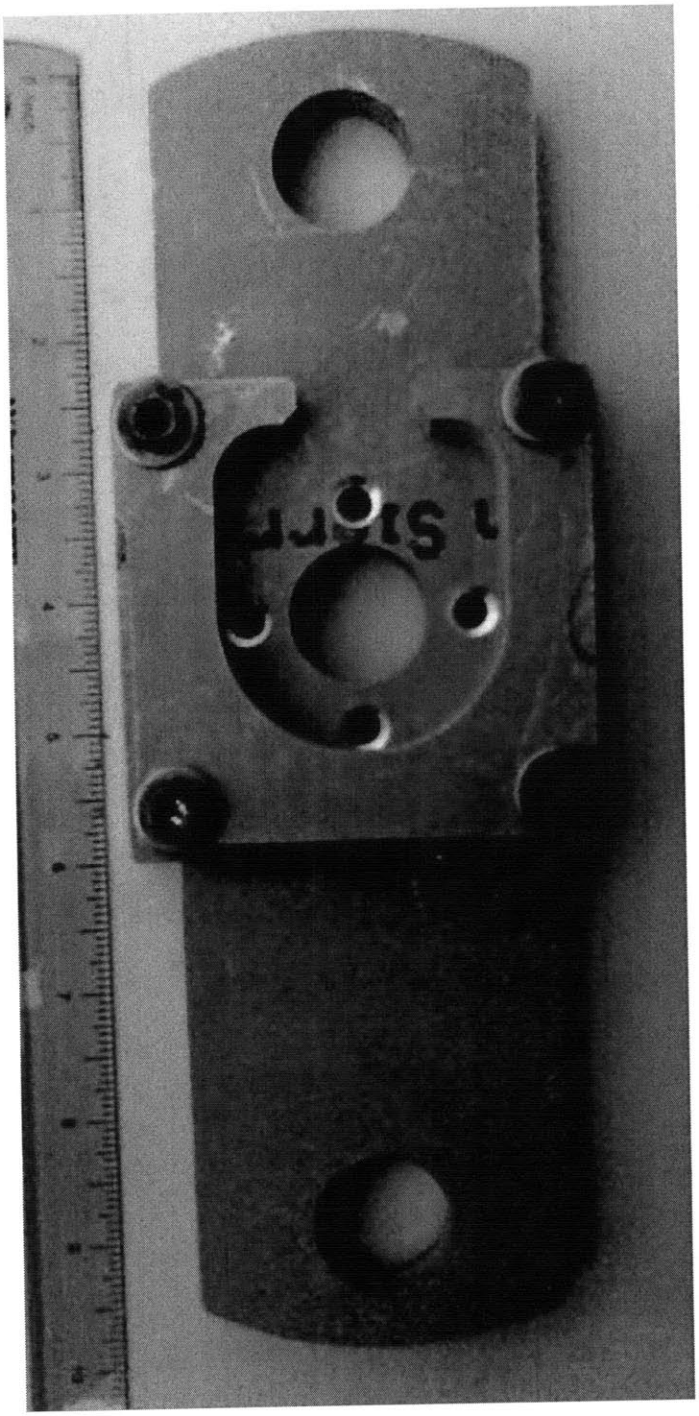

Figure A15: *Hot Runner Guide and Extruder Die Backplate*

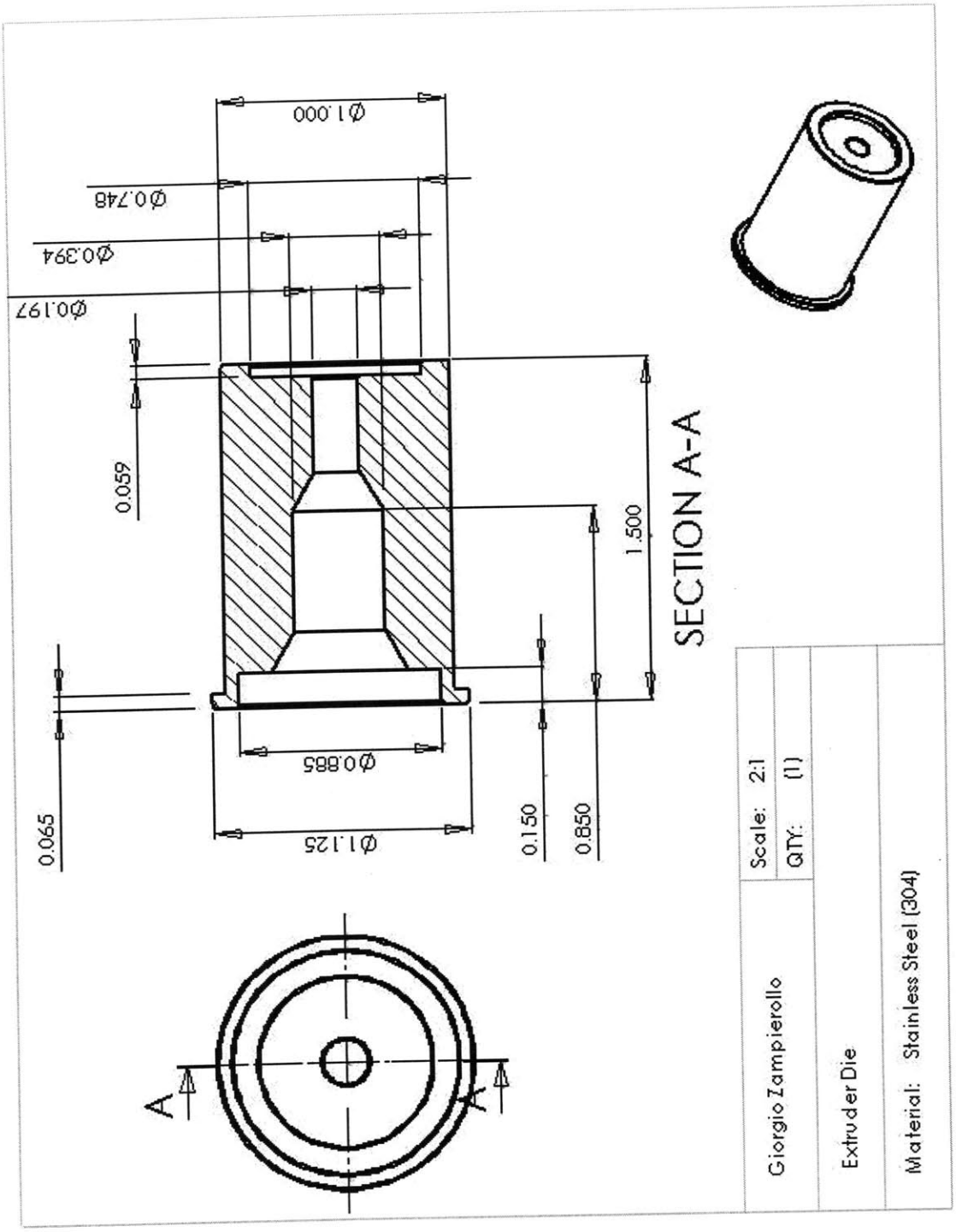

Figure A16: *Extruder Die Drawing*

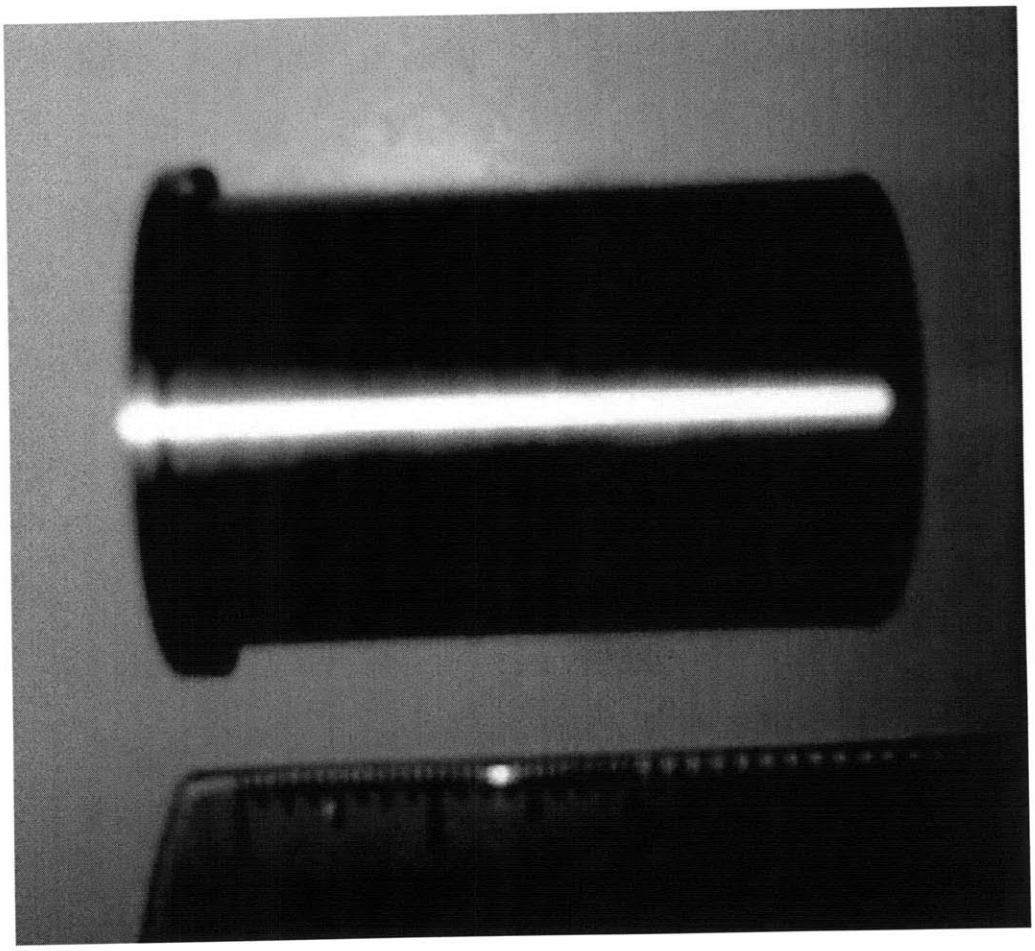

Figure A17: *Extruder Die*

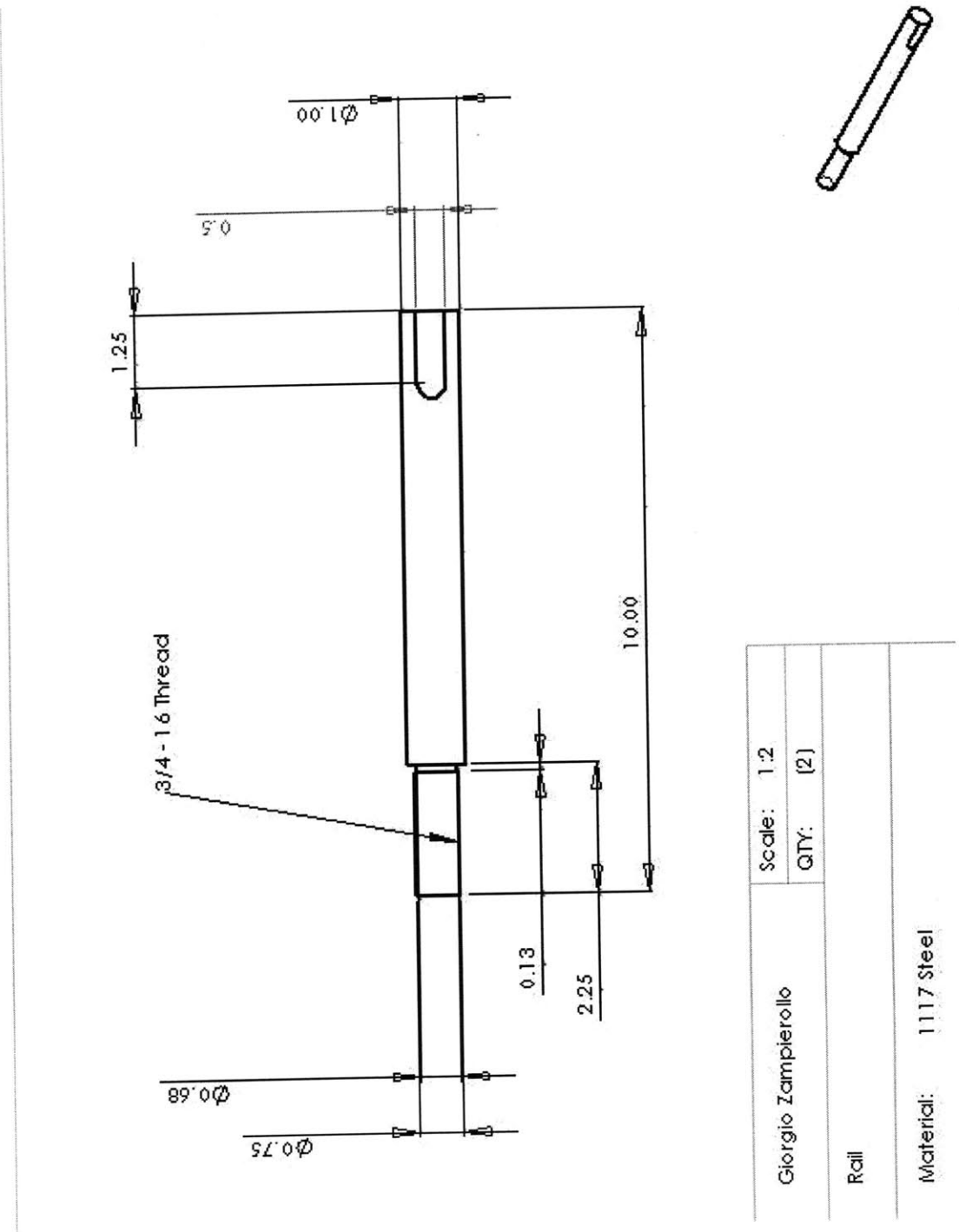

Figure A18: *Rail Drawing*

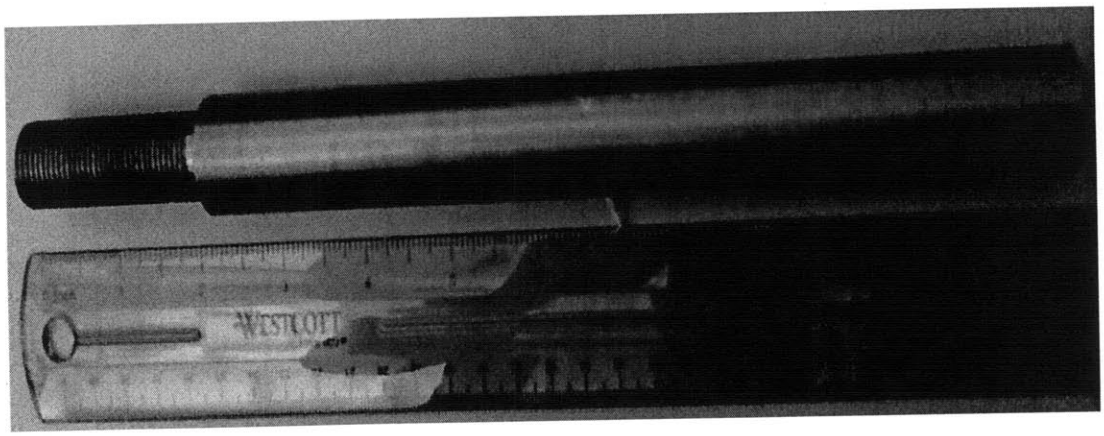

Figure A19: *Rail*

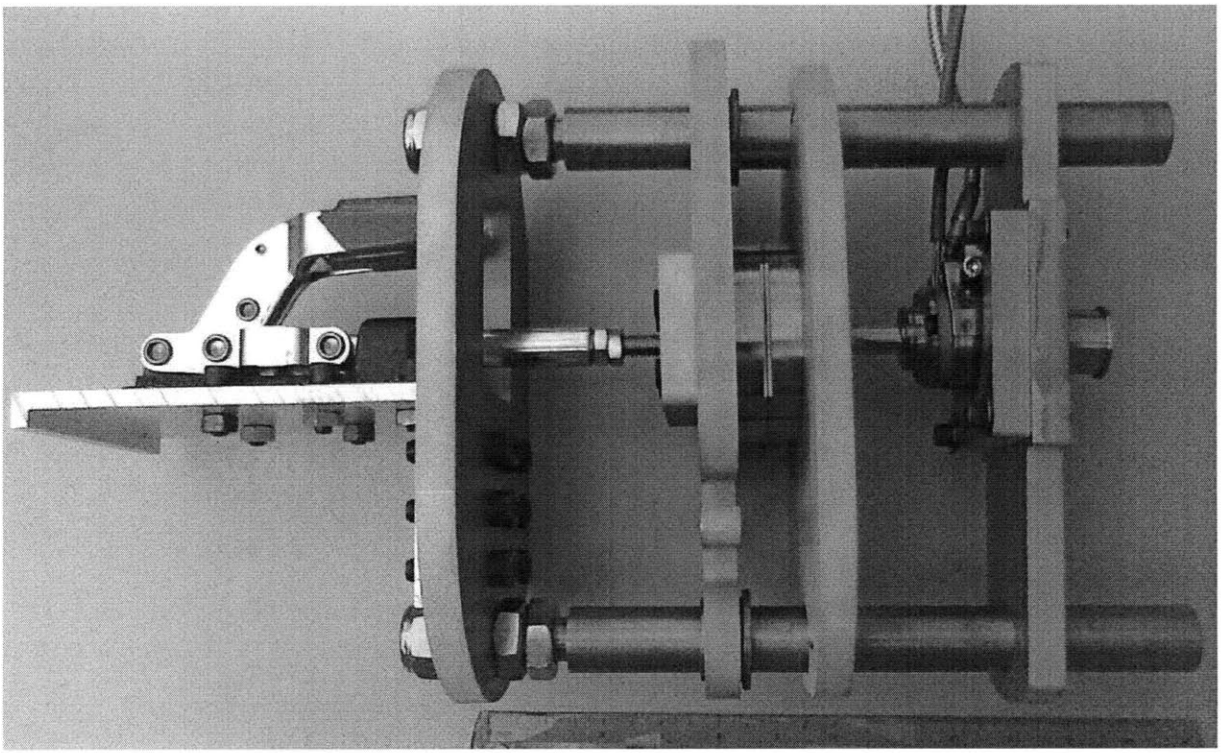

Figure A20: *Hot Extrusion Molding System Assembly*