Injection Catheter for Stem Cells

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Abstract

The purpose of this design was to create a catheter that can provide multiple injections in a reduced amount of time than it takes the current procedure. The catheter will be used by the client in his research of injecting stem cells into the heart to determine if it will produce new cardiomyocytes. The final design consists of three components that can provide multiple injections at a certain height in the heart. The height can then be adjusted so more injections can be made at a different level in the heart. The final prototype would have an external and internal component made of extruded polyurethane with an injection catheter that has a nitinol needle for injections.

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Problem Statement

Our client is Tim Hacker who is part of the UW-Department of Medicine. Different methods have been tried to deliver stem cells to damaged cardiac tissue caused by a heart attack or other disease. These methods include injecting cells into the general circulatory system, injecting directly into the coronary arteries or open heart surgery to inject cells directly into the heart muscle. These methods have been ineffective for delivering a large number of cells to the damaged tissue or are invasive. A minimally invasive method of delivering stem cells directly into and around the damaged tissue is needed.

Currently, injection catheters are inserted in the femoral artery and advanced to the left ventricle (LV). Once in the LV, the catheter can be steered to the desired locations on the LV walls and a needle can be extended out from the tip of the catheter to penetrate the heart muscle to inject stem cells. This is a very time consuming process to make the multiple injections of stem cells necessary to heal the damaged tissue. In addition, with current tip designs lack of anchoring the needle in the muscle wall during the injections leads to fewer cells injected into the muscle. It is also time consuming to calibrate the depth of needle penetrations as needle depth is altered by the curve of the catheter as it is bent into the necessary positions to reach damaged tissue. Therefore, a new catheter which can speed up the process of stem cell injection will be of critical importance to successful delivery of stem cells to the heart. A method is needed to improve precision of needle penetration and lessen the time to complete the procedure. This could be done by having multiple injections into the heart without adjusting the catheter and employing a corkscrew needle or other designs to securely anchor the needle in the tissue and control the depth of penetration.

Background

Heart Disease

Tim Hacker and Amish Raval of the UW Department of Medicine are conducting research to determine to what extent stem cells can regenerate dead heart tissue. The American Heart Association reports that there are 1,260,000 new and recurrent coronary attacks occur per year. About 37% of people who experience a coronary attack in a given year die from it (Heart Attack and Angina Statistics). Additionally, an estimated 5.7 million Americans live with heart failure with 670,000 new cases diagnosed each year (Heart Attack and Angina Statistics). By creating a method where tissue in the heart could be regenerated, many of these cases could be better treated. A heart attack occurs when blood flow is blocked and the myocardial tissue gets starved of blood. Without oxygen from the blood, myocardial cells die and the muscle tissue can become permanently damaged without treatment. The goal of this research is to discover if direct injection of mesenchymal stem cells isolated from bone marrow can be effectively injected into dead heart tissue, and if so, how these cells could be used to treat cardiovascular disease. Mesenchymal bone marrow cells are able to differentiate into myocardial cells and show great promise for heart tissue regeneration (Wu). Hope is that this treatment will be able to regenerate dead heart tissue caused by heart attacks in a minimally invasive manner.

For a typical procedure, our client begins by inducing heart attacks in swine models, which creates regions of dead tissue in the heart. He then enters the left ventricle of the heart with a single injection catheter via the femoral artery. The current catheter used is the Myostar made by Biosense-Webster (see figure 1). This catheter incorporates a retractable needle tip and exhibits a single degree of freedom. Our client can steer the catheter and protrude the needle by

using its handle. Currently, there are no commercial catheters that have multiple needles for injections into the heart. A patent exists for a catheter that has two needles that come out in opposite directions which can be used for injections (Hofling).

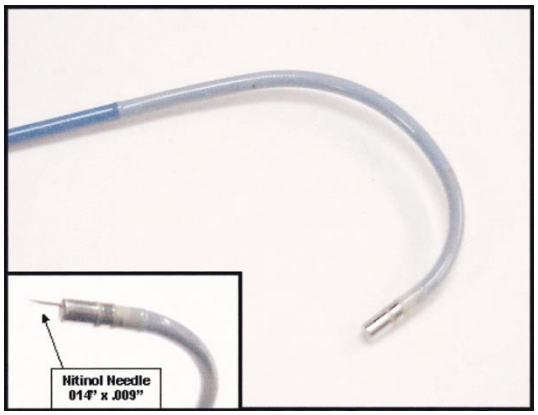

Figure 1: The Myostar injection catheter made by Biosense Webster currently being used by the client (Callans et al).

However, each procedure using the Myostar catheter is very time consuming, and the area of dead myocardial tissue is often large which requires numerous injections. In addition, the Myostar catheter must be repositioned for each injection, which is extremely difficult. With only one degree of freedom, it is hard for our client to position the tip of the catheter accurately, and during the procedure the heart remains beating, which adds to the difficulty. The duration of the procedure is not our client's only concern, however, and our client has brought to our attention other problems with the current procedure's technique.

Currently, the retractable needle of the Myostar catheter does not protrude at a consistent length. It was found that the needle length varies depending on the extent of bending in the catheter. It is important for our client to gauge needle depth in the tissue and have it be consistent, so as to not waste stem cells. In addition, the stem cells should be injected into the

middle of the tissue to get the maximum effect of the cells capabilities. If the needle depth is incorrect, the cells may leak out of the tissue and go to waste. These cells are of high value, which is why consistent needle depth is a high concern. We have been asked to design an injection catheter that will address these issues.

Client Procedure

Our client performs stem cell injections for his research at the University of Wisconsin hospital. The procedure is performed on anesthetized pigs, using an ECG to monitor heart activity and continuous x-ray imaging to view the left ventricle. The ECG is also used to determine whether the needle has penetrated the heart muscle. At the beginning of the procedure, a contrast agent is injected into the heart to provide a reference of the ventricular walls. While the contrast agent is in the ventricle, our client takes a still image and traces the ventricular walls on a transparency (see figure 2). This transparency can then be placed on the monitor to show where the heart wall is located in the continuous live image. They then insert the injection catheter into the femoral artery and guide it to the left ventricle. When the catheter is in the desired position for injection, the needle is extended from the catheter, and the ECG is used to determine if the needle has entered the tissue. Once it has, there should be a rise in electrical activity on the ECG. Before the stem cells are injected, they wait for the ECG to stabilize. Finally, the ventilator is stopped to reduce movement of the pig and then the stem cells are injected. After that, the needle can be retracted and the catheter can be repositioned for another injection. This procedure would be repeated for multiple injections.

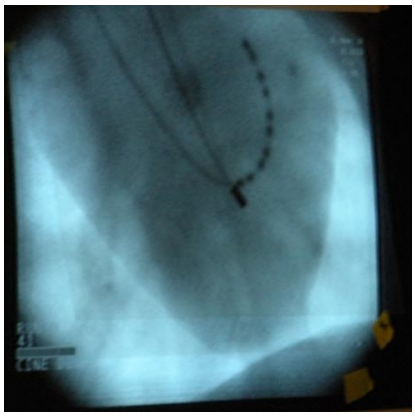

Figure 2: Image of the heart with a catheter on the inside during a procedure done by the client (Callans, D.J, et. al)

Client Specifications

To address the problems with the current stem cell injection procedure, we have compiled a list of client specifications for an alternate design (the full Product Design Specifications can be found in the Appendix). The most important is that our design should be able to make multiple injections per catheter location in the heart. This would eliminate the need of constant repositioning and should drastically cut down on the time of the procedure. Our design must take into account that the heart is beating during the procedure, and as a result incorporate a method that will stabilize the catheter during injection. Our design must be small enough in diameter so that it is able to easily fit through the femoral artery of the pig and into the left ventricle. Specifically, the catheter must have a maximum diameter of 14 French or 4.66 mm. Our design must also be flexible enough so that it is able to travel up the artery, around the bend of the aorta, and down into the apex of the left ventricle. Our catheter must be able to make injections at a constant depth in the ventricle wall, between 2-6mm. Finally, the injections made should be as accurate and consistent as the injection catheter that our client currently uses.

Design Alternatives

To provide our client with a prototype that met his specifications, three initial designs were developed. The designs developed are only for the tip of the catheter, or the portion that would enter the left ventricle. However, the entirety of the catheter must follow the specifications of the design given to us by the client, most importantly size and flexibility.

1. **Balloon Catheter**

Overview

The first design was developed to accomplish injections at multiple locations, and has the ability to provide stem cells to much of the ventricle with a single injection. The design consists of a balloon catheter on the end as shown in Figure 3. The balloon would be able to be inflated for injections and deflated within the diameter of the catheter so it would be able to fit through the arteries and into the left ventricle. However, unlike most balloon catheters, it would consist of two different chambers. The first chamber would be similar to a typical balloon chamber in that it would be filled with air. This chamber would be made of either natural rubber latex or polyurethane, both of which are compliant materials (devicelink.com). The second chamber is designed to hold the stem cells. It would consist of another layer around the balloon, probably made of polyvinyl chloride tubing, and would also hold the needles for injections. It would be very difficult to put needles on the balloon chamber, and this is why there would be a second chamber surrounding it.

When the catheter is ready for use, the balloon would be deflated so it can travel through the arteries and into the left ventricle. Once positioned in the heart, the balloon would be blown

up until the needles penetrate into the heart tissue. The stem cells could then be injected from the outer plastic chamber into the myocardial tissue.

Advantages and Disadvantages

The major advantage of this design is its ability to cover many injection locations at one time, with an outer plastic chamber that would be covered with many needles to perform injections. A method of "spray-painting" the heart would result from this, and most of the left ventricle would receive stem cells. However, even with this advantage, this design has many drawbacks. First, when the balloon is inflated to fill most of the ventricle, it could stop the flow of blood through the heart and be harmful to the pig. Even though the time of the procedure would be greatly reduced using this design, it may not be worth the risk of damaging the heart further. Also, even though the client would like to cover the heart with stem cells, it could lead to a waste of stem cells in locations that do not need them.

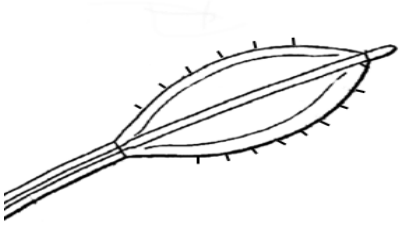

Figure 3: Image of the balloon catheter with the two chambers and the needles attached to the outer plastic chamber.

2. **Multiple Needle Catheter**

Overview

The second design was developed because it has the ability to provide multiple injections at one time. Cardiac ablation is a method used to destroy heart tissue that acts as a short circuit to return the heart to normal heart rhythms (Cardiac Ablation). Often, cardiac ablation catheters

have hollow tapered ends to damage tissue. The image seen in figure 4 is a cardiac ablation catheter made by AngioDynamics. The catheter has hollow prongs that can be retracted and protruded (StarBurst™ Talon). The second design alternative involves using this type of cardiac ablation catheter and making modifications to it so it could be used for injecting stem cells. Since the prongs already have tapered ends, they would not need to be modified because they can already be used to penetrate heart tissue. However, it would need to be modified so that it is hollow and stem cells could travel through the entire catheter and eventually out of the prongs. The handle of the device would also need to be modified so a syringe could be attached and stem cells could be inserted.

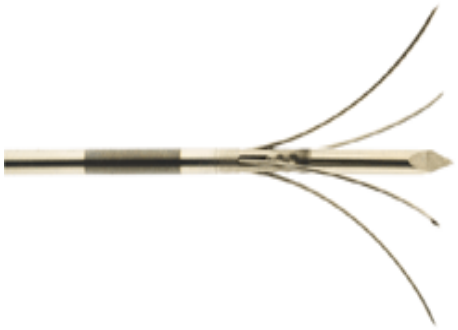

Figure 4: A cardiac ablation catheter made by AngioDynamics that would be modified to create the multiple needle catheter design alternative (StarBurst™ Talon)

To use the design, it would be inserted into the heart with the prongs retracted. The tip would then be placed up against the wall of the ventricle, and when the injection is ready to be administered, the four prongs could protrude into the tissue, and the stem cells could be injected. For addition injections, the prongs could be retracted again and the catheter would be re-positioned. The same procedure would be followed for each injection.

Advantages and Disadvantages

The major advantage of using this type of catheter is that it can perform four injections per catheter location. This would allow for the stem cells to be administered over a larger area. However, one drawback of this design is that the four prongs would not enter the tissue at a consistent depth if the tip were not perpendicular to the heart wall when extended. Additionally, the four prongs would only create injections in a single circular area and would require continuous readjustment to administer multiple injections.

3. **Guided Track Catheter**

Overview

The final design developed would consist of a catheter with a single needle that could easily be repositioned for multiple injections. It would incorporate three different components: an external, internal, and injection component. The injection component could be a smaller version of the injection catheter the client currently uses, and would be inserted into a track within the internal component. This track would guide the needle out of the catheter at a consistent angle, lining up with holes along the side of the external component so injections could be made at different heights within the heart. See figure 5 for an image of the internal and external component.

This catheter could be stabilized within the heart by placing the external component against the apex. During the entire procedure, the internal component and injection component would be inside the external component. The track of the internal component height would be

aligned at the desired height for injection, lining up with one of the holes on the external component. The injection component could then be extended from the catheter to the heart wall, and an injection could be performed. After the injection component is retracted, the track of the internal component could be adjusted, and another injection could be performed.

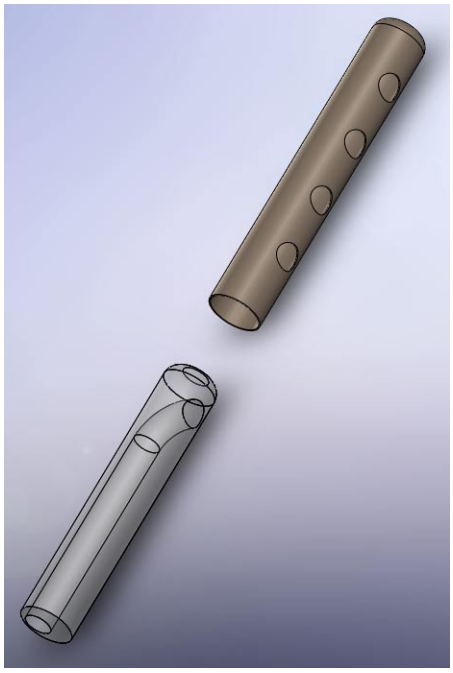

Figure 5: The guided catheter design with the internal component incorporating the track and the external component with the holes for the injection component to exit.

Advantages and Disadvantages

The guided catheter design would provide a way to more easily administer multiple injections when compared to the current catheter used by the client. Placing the outer component in the apex of the heart will also provide stability in the heart, and could improve the accuracy of injections. Injections could be made at various heights along each wall of the heart by adjusting

the inner component and rotating the entire device. The only disadvantage of this design is that it would have decreased flexibility due to the three components.

Design Decision

After coming up with three design ideas, a design matrix was created in order to determine which design to pursue. There are five factors that were chosen that weigh into the design matrix: cost, time reduction of the procedure, accuracy of injection, flexibility, and ease of manufacturing. The cost and flexibility were chosen to weigh the least (0.05), as they are the least important factors. It was decided that cost is not very important because it will be expensive to manufacture any design, and the actual function of the catheter is much more important than the cost. Flexibility is not as important because the design will have to, at the very least, be flexible enough to curve through the pig's aorta. Any more flexibility could be beneficial, but it is not absolutely essential.

It was decided that the three most important factors are time reduction of the procedure, accuracy of injection, and ease of manufacturing. These three factors were weighted an equal amount (0.30). Time reduction of the procedure is our client's main goal, which explains its importance. Accuracy of the injection is important because the stem cells should be directed to the damaged heart tissue. We do not want to build a catheter that is inaccurate and could potentially waste stem cells by injecting them into healthy heart tissue. Finally, ease of manufacturing was also weighted heavily. This is because it is important that we are actually able to find resources and build the design for our client.

As can be seen in Table 1, the balloon catheter scored the lowest of our three designs. This was primarily due to its ease of manufacturing being low (0.3 out of 3). It received this rating because we do not know how needles could be properly positioned on an inflatable balloon. We also are not sure how we could get the needles to lay flat upon insertion and removal of the catheter. The accuracy of this design also did not score well because of the method of injection for this design. Our client would not be able to pick specific points for injection, but instead inflate the balloon and inject at many places inside the ventricle. The main benefit of this design is that it is able to greatly reduce the time of the procedure because the catheter requires minimal positioning and only one injection would need to be made. Despite the large time reduction, this design fell short because of its inaccuracy and manufacturing difficulty.

The multiple needle catheter was rated above the balloon catheter but below the guided catheter. This design would reduce the time of the procedure, but not by much because the catheter would still have to be repositioned multiple times during the procedure. Additionally, the accuracy of injections from the four prongs would not be constant if the tip were not positioned perpendicular to the heart. The only true benefit of this design is that similar products exist, which would make this catheter the easiest of the three to manufacture.

The guided catheter scored the highest in the design matrix, and is the design that was chosen for our final prototype. This catheter scored well because it maintains a high degree of accuracy while drastically reducing the time of the procedure. This design would be able to reduce the time of the procedure by only requiring one position within the ventricle. From this one position, this design would be able to make multiple, accurate injections. We are concerned,

however, about the catheter's ease of manufacturing due to it containing three separate components in such a small diameter. In addition, the three components would reduce the overall flexibility of the catheter when compared to the other designs. Despite these deficiencies, the guided catheter scored the best in our design matrix.

Design Option	Cost (0.05)	Time Reduction (0.30)	Accuracy of Injection (0.30)	Flexibility (0.05)	Ease of Manufacturing (0.30)	Total
#1 Balloon	1 (0.05)	9 (2.7)	4 (1.2)	8 (0.4)	1 (0.3)	4.65
#2 Guided	5 (.25)	7 (2.1)	8 (2.4)	5 (.25)	4 (1.2)	6.2
#3 Multiple Needle	7 (.35)	4 (1.2)	6 (1.8)	6 (.3)	8 (2.4)	6.05

Table 1: Design matrix showing how each aspect was weighted for the three alternative designs.

Final Design

Guided Catheter

The final true-to-scale design proposed involves a catheter that could be stabilized in the apex of the heart and perform multiple injections at different locations using a single needle. This would be accomplished by constructing a catheter with three main components: An exterior component that would be stabilized at the apex, an interior component with a track to guide a needle out of the external component at roughly a 60 degree angle, and the injection component

containing the needle. The exterior component would have slots at different heights along the side from which the injection component could exit, and the entire device could be rotated 360 degrees within the ventricle. This way, injections can be administered at different heights along each wall of the left ventricle.

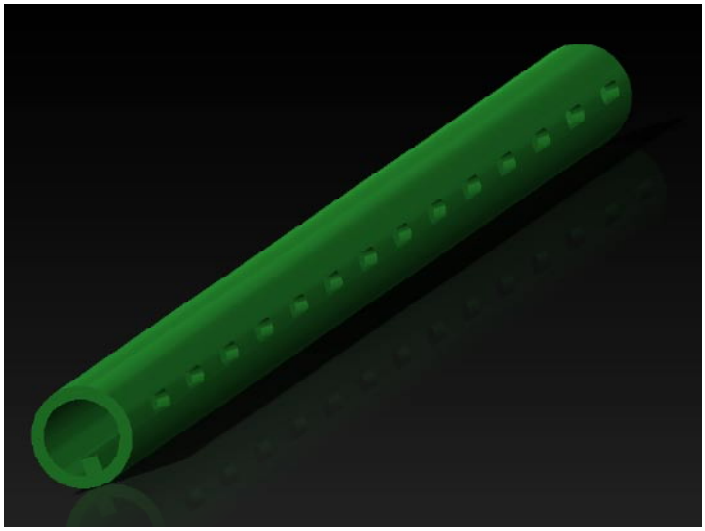

Figure 6: External component with 14 slots and track for internal component to travel

External Component

The exterior component is a cylindrical tube of 3 mm OD (9 French) x 2.25 mm ID made of polyurethane plastic. The lumen would be continuous from the handle of the catheter to its tip. This tip, which would be rounded as to not damage heart tissue, would be placed at the apex of the heart to stabilize the catheter during injections. Starting 2 mm from the tip, placed linearly along the side, there would be 14 slots with dimensions of 0.5 x 2 mm and 2.25 mm between each slot (Figure 6). The needle would be able to come out of these slots at various heights within the ventricle. Slots were chosen rather than circular holes because they are able to maximize the variability of injection height while retaining consistent structure of the catheter. For example, if a single 0.5 x 60mm slit were used instead of smaller slots, the 0.5mm width of the long slit would vary (widen/close) if the catheter were bent. This could potentially damage the catheter or its surrounding tissue. Due to this, a 2.25 mm gap between each slot was chosen to maintain consistent catheter structure. In addition, 2 mm slots make it easier for the surgeon to align the internal track properly. With slots of length 1 mm or less it would be difficult to align

the internal component track because the surgeon would have to be accurate up to 0.5 mm or less. Finally, along the side of the lumen of this component, there would be a track (0.5 x 0.5mm rectangular cross section) to guide the interior component so the track of the interior component would always be aligned with the 2 mm long slots. The entire structure would be able to rotate 360 degrees within the ventricle.

Internal Component

Within this external component, an internal component containing a track for the needle would be able to slide along the lumen, allowing the surgeon to position the needle at different heights within the ventricle. This internal component can be seen in Figure 7. The entire component would be 2.25 mm in diameter, made out of polyurethane plastic. The track within it would be 0.5 mm in diameter, located 0.375 mm from the edge, traveling from the handle to near the tip where it would curve to guide the injection component out of a hole located 1 mm from its tip. This curve would allow the needle to exit the catheter at a 60 degree angle. Along the side of this component, there would be a 0.5 x 0.5mm rectangular cut in which the track inside the external component would be inserted. This is to ensure the needle is consistently aligned with the slots of the external component.

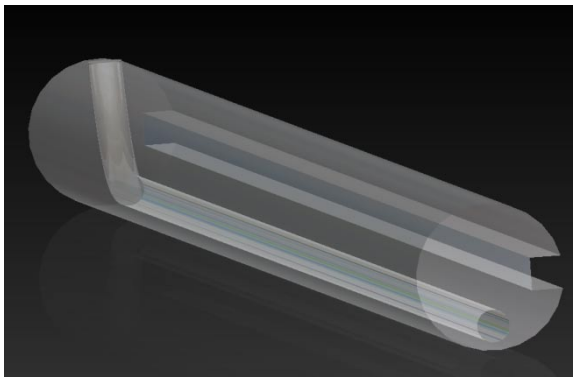

Figure 7: Internal component with track for injection component. Extruded rectangular track would for alignment with external

Injection component

Located inside the track of the internal component, there would be a cylindrical tube 0.45mm OD x 0.25mm ID leading to a 3 mm long 27 gauge needle (Figure 8). This would exit the catheter through the slots along the external component and eventually penetrate the myocardium for injection.

Figure 8: Injection component with 3mm long polyurethane tubing and a nitinol needle on the end for injections

Handle

Until the tip of the catheter has been constructed and tested, the design of its handle will be kept relatively simple. Each internal component would simply slide within the lumen around it with a plastic, like polypropylene, as the cylindrical base that would be used as a grip. For the internal component, there would be marks along the outside of the shaft, designating where each slot of the external component is located. This allows the surgeon to properly align the interior component's track with these slots. For the injection component, there would be mm markings along its base beginning from the point where the needle exits the external component to be used as a reference for the surgeon. Although the x-ray images would be the primary determinant of needle location, these markings could be used as well to determine how far the needle is from the

external component. For example, if the surgeon uses the mm markings as a guide and protrudes the injection component x mm from the catheter, the perpendicular distance of the needle from the external component would be approximately x*sin(60) mm.

Materials

Polyurethane is to be used for the plastic portions of each component. This is because it is very compatible with blood, has good stiffness for insertion and softening for removal, has a great combination of flow rate, stiffness, and kink resistance, and has reduced catheter assembly costs when compared to most other typical catheter materials. Depending on roughness, it also has low thrombogenicity or is resistant to clot formation (Lamba). Additionally, most catheters used on animals are made of polyurethane (Alzet Catheters).

Dimensions

Our client requested that the catheter be less than 14 French (4.66mm) in diameter so it would not damage tissue while traveling through the vasculature. The 9 French (3mm) diameter of the catheter was chosen because it would be safer and easier to use than a 14 French catheter while still allowing the injection component to curve 60 degrees from the longitudinal axis of the catheter. As discussed above, 2 mm slots were used on the external component so the surgeon could more easily align the internal track with them while retaining the structural integrity of the catheter. Detailed dimensions are shown in Figures 9 and 10.

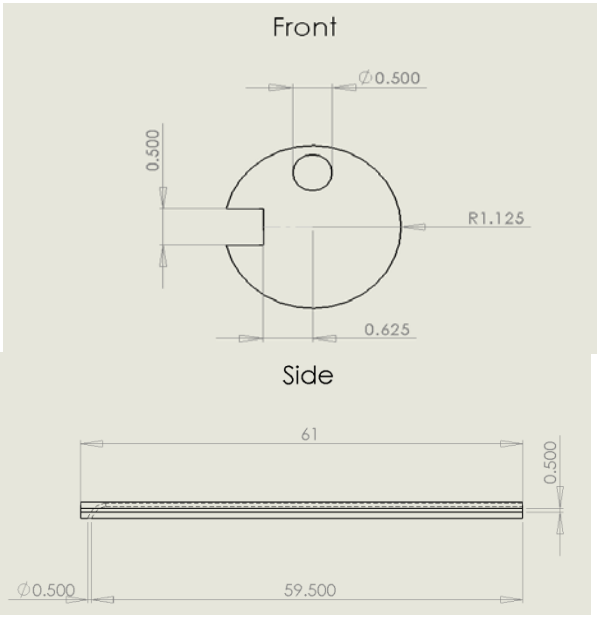

Figure 9: Dimensions of Internal Component in mm.

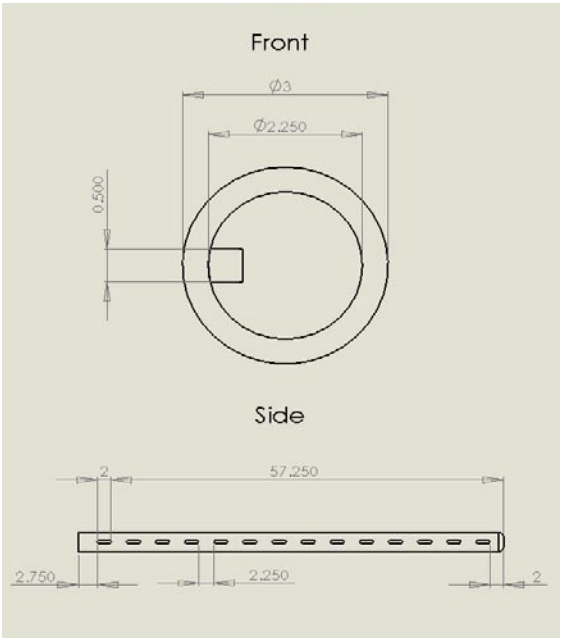

Figure 10: Dimensions of External Component in mm.

Prototype - Guided Catheter

Due to cost and time limitations, a true-to-scale prototype has not yet been constructed. However, a prototype that is 25.4x larger was constructed as proof of concept (see figure 11). A 25.4mm (1in) OD tube was used for external component, with holes drilled in the side to simulate the slots for the needle to exit, and a plastic cap to simulate the rounded tip. The internal component consisted of a 19 mm (3/4 in) clear vinyl tube filled with silicon, with a 3.5 mm vinyl tube within it to serve as the track to guide the injection component. All these items were accurately scaled 25.4 times greater than the true-to-scale design other than the internal track and injection component diameter. The internal component track should have been 0.8 mm greater in diameter (4.3 mm rather than 3.5 mm), and the injection component should have been ~2 mm greater in diameter. Once constructed, this prototype was used to test the concept of the guided catheter design. See appendix C for the cost of producing the enlarged prototype.

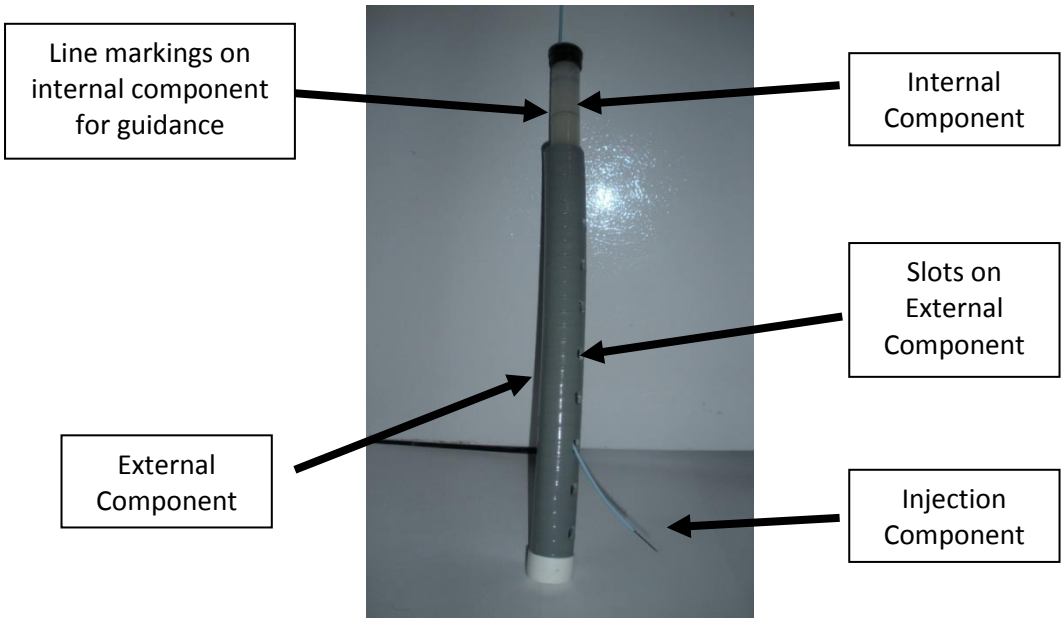

Figure 11: Picture of the constructed prototype with parts labeled.

Testing

The main purpose of this design is to reduce the time of the procedure by providing multiple injections throughout the heart while still maintaining accuracy. However, since the true-to-scale design that would be used by our client could not be produced, it could not be determined to what extent the time would be reduced for the procedure. Therefore, the constructed prototype was used to test the accuracy of injections at certain hole heights. Using the conversion that was determined for the enlarged prototype to the true-to-scale of 25.4 mm to 3 mm was used for the accuracy testing. The enlarged prototype was place approximately 90 mm away from a piece of graph paper (see figure 12). This distance was chosen because using the scaling conversion; it would about equal to the distance from the center of the heart to the ventricle wall which is about 15 mm during systole and 20 mm during diastole (Hacker).

Figure 12: The enlarged prototype being used in the accuracy testing.

For conducting the accuracy testing, twelve trials were completed at three different holes. For each trial, the injection component would come into contact with the graph paper. Each contact point would be marked and the injection component would be removed from the internal component. The next trial could then be completed by inserting the injection component back in and following the same procedure. Once all twelve trials were completed, twelve more trials were complete in the hole above (hole 7). The third trial was done in the hole above 7 (hole 8). Once all trials in the three holes were complete, a coordinate system was added to the graph paper. Using this coordinate system, the location of each trial was measured and recorded. Once all data was recorded, the mean point was determined for each hole. Using the location of each injection and the mean point, a scatter plot was created to show all the trials in each set (see figure 13) Using the mean points, the standard deviation was determined for each set of holes. This standard deviation told us how far each point, on average, was away from the mean point or the accuracy of the injections compared to the average. Additionally, the mean points were used

to determine the y-distance between them. The importance of this measurement was to compare the actually distance between injections and the distance between the holes on the external component.

Using the data of standard deviation and mean points of the enlarged prototype, these values were estimated for the true-to-scale design using the scaling conversion used throughout the design. The estimated standard deviation for the x-direction was 0.36 mm and 0.42 mm for the y-direction. The y-distance between mean points was also determined to be 2.40 mm and 2.28 mm between holes 6 to 7 and 7 to 8 respectively. This distance is very comparable to the 2.25 mm that would be between the holes in the true-to-scale external component. See appendix B for the table of data collect.

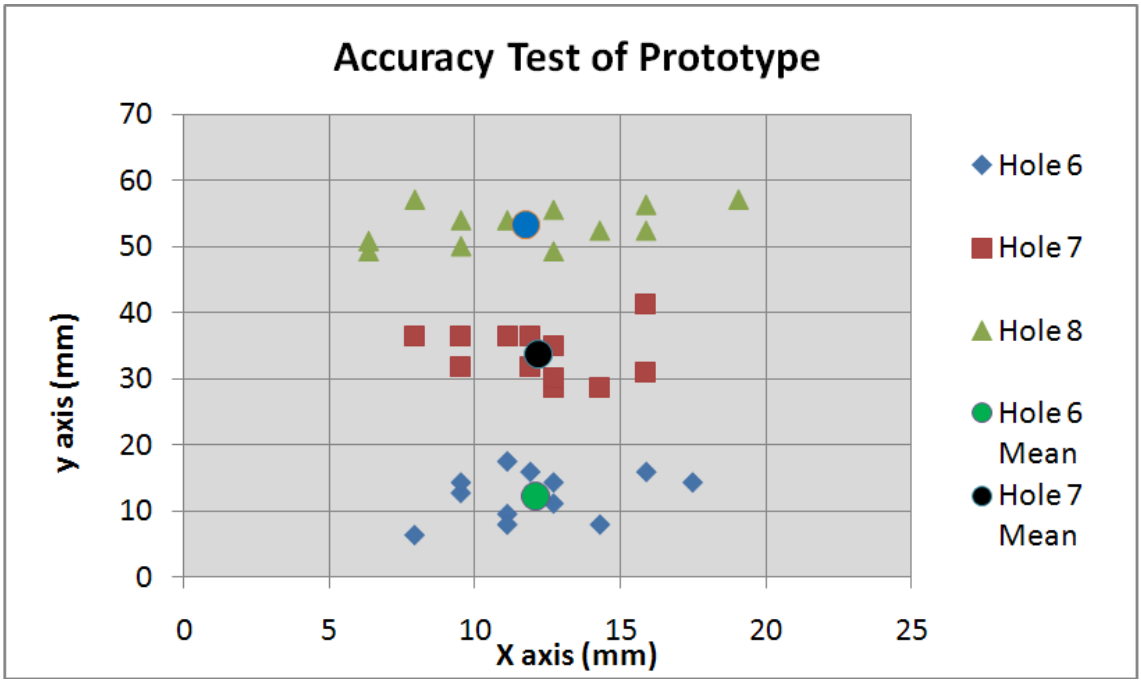

Figure 13: A scatter plot of all twelve trials in the accuracy testing at 3 different holes. The mean point is also displayed for the twelve trials of each hole.

During the testing, there is a possibility for experimental error and it is also possible in the estimations for the true-to-scale prototype using the conversions. One possible error of

estimation in the data for the true-to-scale design would be the size of the slots. If the slots are too small, the injection component could hit the external component as it exits causing a change in trajectory and injection location. This would increase the standard deviation of the accuracy testing and possibly the y-distance between mean points. Additionally, the catheter can become bent after using multiple times. Therefore, after using the catheter in multiple trials of testing it could of become deformed compared to a straight catheter that is always use for the procedure. This could affect the location of different trials in the testing we completed for the enlarged prototype.

Future Work and Ethical Considerations

The proposed final design given in the solidworks would theoretically be able to improve accuracy and reduce the time of the client's procedure. The current enlarged prototype is still a proof of concept design which would need to be scaled down to our true-to-scale design. The difficulty of making this small of catheter by hand made it so it could not be created over one semester's time. However, it would be possible to create the final design through two possible methods of production. One is through the UW Polymers lab on campus that can extrude pieces of plastic using their equipment. They would be able to extrude a piece of polyurethane plastic for the inner component with a channel down the middle for the inner track. We could also have the outer component machined as just a hollow tube and drill the slots in it after completion. The drawback of using this method is it would cost about $5,000 to create the required resin to have both components produced. It would also take at least six weeks to create (Osswald). Another possible option for production could be through rapid prototyping. One way of producing the prototype using this method would be through a company called Proto Lab. They are capable of

taking 3D CAD models and creating machined parts made from a variety of different materials. The part takes between 1-3 business days to create and the price depends on the type of material used (First Cut CNC Machining Service). However, they currently don't make parts made of Polyurethane. Further future work could include finding a company similar to Proto Lab that could create a Polyurethane part with the dimensions required. The first area of future work would be to determine which of these methods would be best for production of the true-to-scale prototype.

Once the true-to-scale prototype is constructed, there are a few more modifications that could improve the accuracy and usability for the client. The first addition would be to develop a mechanical handle to ensure the slots of the external component line up with the track on the internal component. Possible ideas for the handle could be a screw mechanism that after one complete turn, the track would line up with the next slot above. Both the internal component and external component would have to have grooves for the handle design. A second idea would still involve the user pulling on the internal component. However, it would involve grooves on the internal component with a lock component that would need to be releed before moving to the next hole. These handles would create a fool proof method of lining up the hole with the track so it doesn't need to be based on the client's judgment. A second modification would be determining the proper sizing of the slots based on further testing. The slots can't be too small that it would be difficult for the client to accurately match up the slots with the track. The slots also can't be too large so that they would affect the structural integrity of the catheter. If the slots are too large, bending the catheter could cause the catheter to deform in such a way that the slots would close up preventing the injection component from exiting through the slots. There

has to be a medium so that the client still has flexibility of different heights within the slot but still able to easily pass through the slots with the injection component. The final modification would be to determine the proper length of the needle. This would have to be determined using the true-to-design prototype. The proper length would have to be determined to get through the channel in the internal component while still maximizing it to allow penetration into the heart tissue.

Usability Testing

Once the true-to-scale design is developed, it would need to be tested to ensure its quality and desired outcome meets the expected functionality of the client's specifications. These tests include the accuracy, consistency, and time reduction of the client's procedure. The same test could be done that was used for the enlarged prototype to determine the accuracy and standard deviation of injections at certain slots. The client would have to use the catheter in the procedure to determine time of reduction. Additionally, using the MRI images they develop could be examined to determine accuracy and consistency of the prototype.

Since this design would be used in living animals it would be important to be safely used without causing any excessive harm to the pig. Our client currently has animal testing protocol and already does induce heart attacks in them but the device should not cause any further damage when injecting stem cells. Additionally, the design should effectively use the stem cells and not put any to waste when injecting and throughout the procedure. Stem cells are an important area of research so the design should be able to conduct the client's research without the loss of stem

cells. Even though the client isn't using embryonic stem cells which are much more valuable, the mesenchymal bone marrow stem cells he uses are still valuable and should not be wasted.

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Appendix A: Product Design Specifications (PDS)

Project: Injection Catheter for stem cells

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Problem Statement:

Different methods have been tried to deliver stem cells to damaged cardiac tissue caused by a heart attack or other disease. These methods include injecting cells into the general circulatory system, injecting directly into the coronary arteries or open heart surgery to inject cells directly into the heart muscle. These methods have been ineffective for delivering a large number of cells to the damaged tissue or are invasive. A minimally invasive method of delivering stem cells directly into and around the damaged tissue is needed.

Currently, injection catheters are inserted in the femoral artery and advanced to the left ventricle (LV). Once in the LV, the catheter can be steered to the desired locations on the LV walls and a needle can be extended out from the tip of the catheter to penetrate the heart muscle and inject stem cells. This is a very time consuming process to make the multiple injections of stem cells necessary to heal the damaged tissue. In addition, with current tip designs lack of anchoring the needle in the muscle wall during the injections leads to fewer cells injected into the muscle and it is also time consuming to calibrate the depth of needle penetrations as needle depth is altered by the curve the of the catheter as it is bent into the necessary positions to reach damaged tissue. Therefore, a new catheter which can speed up the process of stem cell injection will be of critical importance to successful delivery of stem cells to the heart. A method is needed to improve precision of needle penetration and lessen the time to complete the procedure. This could be done by having multiple injections into the heart without adjusting the catheter and employing a corkscrew needle or other designs to securely anchor the needle in the tissue and control the depth of penetration.

Client Requirements:

- **Multiple Injections:** The catheter must be able to create multiple, quick injections to decrease time of procedure.

- **Size:** Must be small enough to fit through the arteries and aorta
  - < 14 French diameter (4.66 mm)

- **Flexibility:** The catheter must be made out a flexible enough material to curve through aorta.

- **Consistency:** The needle must enter the muscle wall of the heart with a constant depth.

- **Accuracy:** The catheter must be positioned accurately in the heart to improve accuracy

of injections

Design requirements:

Physical and Operational Requirements

a. *Performance Requirements* – The catheter must work throughout the whole procedure without any complications. The insertion procedure will always be the same but different injection locations are required so the catheter must be flexible enough to reach all areas of the left ventricle. Stem cells will also be injected using the same method for each procedure.

b. *Safety* – The unit cannot cause any additional harm the animal in any way by being too bulky to be inserted into the arteries. Tissue of the heart should not be damaged by the catheter or needle by being inserted too far.

c. *Accuracy and Reliability* – The unit should be able to do multiple injections when being used with the ability to know how far the needle is in the tissue of the heart.

d. *Life in Service* – The unit should be able to withstand frequent use in a controlled, clinical environment for a long duration.

e. *Shelf Life* – The unit should not degrade while in storage.

f. *Operating Environment* – The unit should be able to withstand contact with blood in the heart and arteries and not cause any harmful effects. It also must not affect the stem cells that are injected.

g. *Ergonomics* – The unit should not provide enough force to break arteries or damage tissue. The catheter should easily be rotated so injections can be in a 360^{o} fashion.

h. *Size* – The unit must be able to fit inside the femoral artery and up through the aorta into the left ventricle

i. *Weight* - The weight should be as minimal as possible.

j. *Materials* – The internal and external component will be made out of polyurethane which is what a majority of catheters are made of. The injection component will be made of an existing catheter.

k. *Aesthetics* – The catheter should be circular and smooth without any protrusions to prevent movement through the arteries.

Product Characteristics

a. *Quantity* – Only one catheter is required.

b. *Target Product Cost* – Budget will be adequate for the manufacturing of these units.

Miscellaneous

a. *Standards and Specifications* – The unit will fit within the client's current injection procedure, thus no further board approval is necessary.

b. *Customer* – Clinicians working with pigs to inject stem cells will use the unit in a clinical setting. A fool proof method of using the device is preferred

c. *Patient-related concerns* – The pigs should not be harmed during the insertion of the catheter and injection of stem cells.

d. *Competition* – Only a patent exists for a multiple injection catheter that has two needles that come out the tip.

Appendix B: Table of data collected in accuracy testing

Distance Test								
Hole		Coordinates (in)			Converted Coordinates (mm)		Coordinates (mm)	
1	Trial	X	Y		X	Y	X	Y
	1	0.31	0.25	0	0.9375	0.75	7.9375	6.35
	2	0.44	0.38	0	1.3125	1.125	11.1125	9.525
	3	0.44	0.31	0	1.3125	0.9375	11.1125	7.9375
	4	0.56	0.31	0	1.6875	0.9375	14.2875	7.9375
	5	0.50	0.44	0	1.5	1.3125	12.7	11.1125
	6	0.38	0.50	0	1.125	1.5	9.525	12.7
	7	0.38	0.56	0	1.125	1.6875	9.525	14.2875
	8	0.50	0.56	0	1.5	1.6875	12.7	14.2875
	9	0.69	0.56	0	2.0625	1.6875	17.4625	14.2875
	10	0.47	0.63	0	1.40625	1.875	11.90625	15.875
	11	0.44	0.69	0	1.3125	2.0625	11.1125	17.4625
	12	0.63	0.63	0	1.875	1.875	15.875	15.875
Mean		0.48	0.48		1.4296875	1.453125	12.1046875	12.303125
STDV		0.11	0.14		0.322599582	0.431472275	2.731343124	3.653131926
2	1	0.56	1.13	0.13	1.6875	3.375	14.2875	28.575
	2	0.50	1.13	0.13	1.5	3.375	12.7	28.575
	3	0.50	1.19	0.19	1.5	3.5625	12.7	30.1625
	4	0.63	1.22	0.22	1.875	3.65625	15.875	30.95625
	5	0.47	1.25	0.25	1.40625	3.75	11.90625	31.75
	6	0.38	1.25	0.25	1.125	3.75	9.525	31.75
	7	0.63	1.63	0.63	1.875	4.875	15.875	41.275
	8	0.47	1.44	0.44	1.40625	4.3125	11.90625	36.5125
	9	0.38	1.44	0.44	1.125	4.3125	9.525	36.5125
	10	0.50	1.38	0.38	1.5	4.125	12.7	34.925
	11	0.31	1.44	0.44	0.9375	4.3125	7.9375	36.5125
	12	0.44	1.44	0.44	1.3125	4.3125	11.1125	36.5125
Mean		0.48	1.33		1.4375	3.9765625	12.17083333	33.66822917
STDV		0.10	0.16		0.289187243	0.465256871	2.448451989	3.939174841
3	1	0.25	1.94	0.19	0.75	5.8125	6.35	49.2125
	2	0.25	2.00	0.25	0.75	6	6.35	50.8
	3	0.75	2.25	0.50	2.25	6.75	19.05	57.15
	4	0.50	1.94	0.19	1.5	5.8125	12.7	49.2125
	5	0.50	2.19	0.44	1.5	6.5625	12.7	55.5625
	6	0.31	2.25	0.50	0.9375	6.75	7.9375	57.15
	7	0.44	2.13	0.38	1.3125	6.375	11.1125	53.975
	8	0.63	2.06	0.31	1.875	6.1875	15.875	52.3875
	9	0.38	2.13	0.38	1.125	6.375	9.525	53.975
	10	0.38	1.97	0.22	1.125	5.90625	9.525	50.00625
	11	0.63	2.22	0.47	1.875	6.65625	15.875	56.35625
	12	0.56	2.06	0.31	1.6875	6.1875	14.2875	52.3875
Mean		0.46	2.09		1.390625	6.28125	11.77395833	53.18125
STDV		0.16	0.12		0.35078038	0.35078038	4.030802771	2.969940551

Appendix C: Itemized cost to produce enlarged prototype

Material/Product	Price
Tubing for outer component	$ 9.97
Tubing for inner component	$ 7.92
Silicone filling	$ 5.97
Miscellaneous	$11.34
Total	$ 35.20