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Design of an Implanted Vascular Access Device with a Mechanical Septum

Mallory Ann Moffett
University of Mississippi

Katherine Rose O'Quinn
University of Mississippi

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by

Mallory Moffett and Katherine O'Quinn

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Approved by

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Advisor: Professor Troy Drewry

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Reader: Dr. Thomas Werfel

_____

Reader: Dr. Dana Nikki Reinemann

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DEDICATION

We would like to dedicate our thesis to the Ole Miss Biomedical Engineering department for providing all the support and education we needed to complete this document. We would also like to dedicate this to our families for the time and energy they have invested in us.

ABSTRACT

As populations continue to age, their need for medical care continues to rise. This is seen by the large need for implanted vascular devices (IVADs). IVADs are essential for individuals with poor venous access and patients requiring long-term venous delivered drugs. This document will explore the existing IVADs, where they fall short, and where our device, the IrisPort system, works to solve the unmet needs of patients. The IrisPort system is a needle-less port system that allows for repeated venous access without the use of a non-coring needle. Prior art searches have shown that the IrisPort is a novel solution as it does not require a needle for access. The IrisPort system will follow the FDA regulatory pathways, by citing several predicate devices, and will be considered a Class II device. Following these necessary validation steps, the IrisPort will provide patients with a better quality of life due to its smaller dimensions and needless nature, whilst meeting necessary flowrate, pressure, and radiological requirements.

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LIST OF ABBREVIATIONS

ABS	Acrylonitrile Butadiene Styrene
ASTM	American Society for Testing and Materials
CDC	Centers for Disease Control and Prevention
CPDP	Cyclic Potentiodynamic Polarization
ETO	Ethylene Oxide
EU/mL	Endotoxin Unit per milliliter
FDA	United States Food and Drug Administration
FMEA	Failure Modes and Effects Analysis
ISO	International Standards Organization
IV	Intravenous
IVAD	Implanted Vascular Access Device
PBMC	Peripheral Blood Mononuclear Cell
PPE	Personal Protective Equipment
SIR	Society of Interventional Radiology

INTRODUCTION

Numerous diseases and disorders require repeated venous access for diagnostic testing and drug administration.[1–3] Implanted vascular access devices (IVADs) has been the one device to revolutionize the world of long-term venous access. They were first used in 1982 and have significantly increased the quality of life of numerous individuals.[4,5] IVADs are widely used for patients with poor peripheral venous access and patients who need long-term vascular access, such as but not limited to patients receiving chemotherapy, antibiotics, total parenteral nutrition, or frequent blood samples.[4] While the ease of these procedures has increased greatly, there is still a large portion of patients that have "needle-phobia" and "procedure-phobia". Both phobias lead to lower overall patient compliance.[3] "Needle-phobia" and "procedure-phobia" is especially prevalent in children.[3] Where patients can be as young as 4 months old for IVADs to be implanted.[6] The majority of all children, 20-50% of adolescents, and 20-30% of adults indicated a large fear of needles.[3] IVADs are used frequently in cancer patients for the delivery of intravenous chemotherapy, in which 1.7 million people are diagnosed with cancer each year within the United States, and 17 million people globally. [7,8] The global estimate is projected to increase to 26 million by 2040, creating a larger need for chemotherapy in the near future.[8] Nearly half of cancer patients receive chemotherapy during their course of treatment and the majority of all patients have fear of needles (up to 87%).[3] Chemotherapy can be used in conjunction with radiation, surgical removal of tumors, etc.[9]

Traditional intravenous infusion consists of repeated skin puncture, which can be damaging to veins and surrounding tissue over time. A catheter can be used for these applications as well, however, IVADs provide several advantages, including improved body image and minimizing maintenance while not in use, improved mobility, and lower infection rates.[5]

Figure 1: Catheter vs IVAD[10]

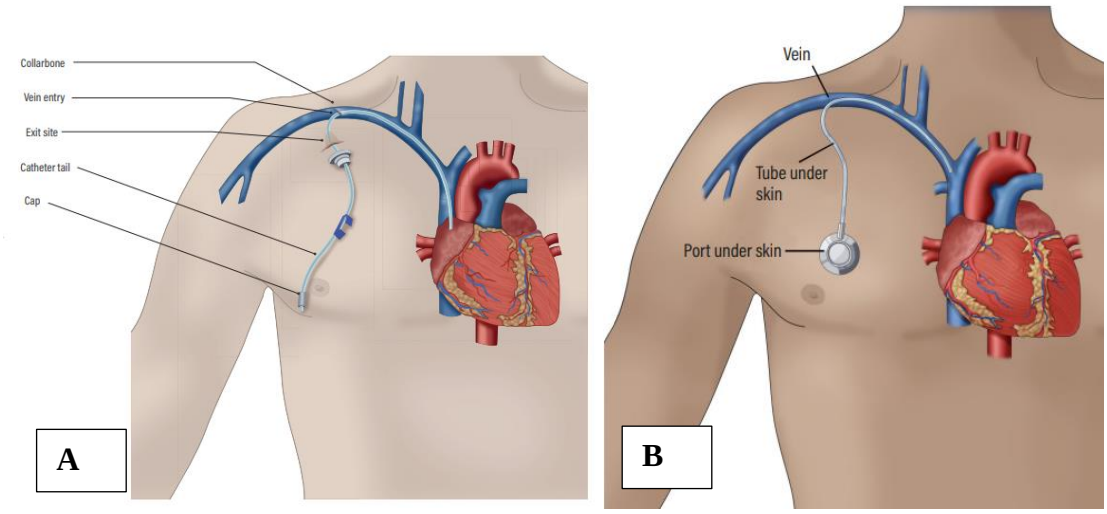
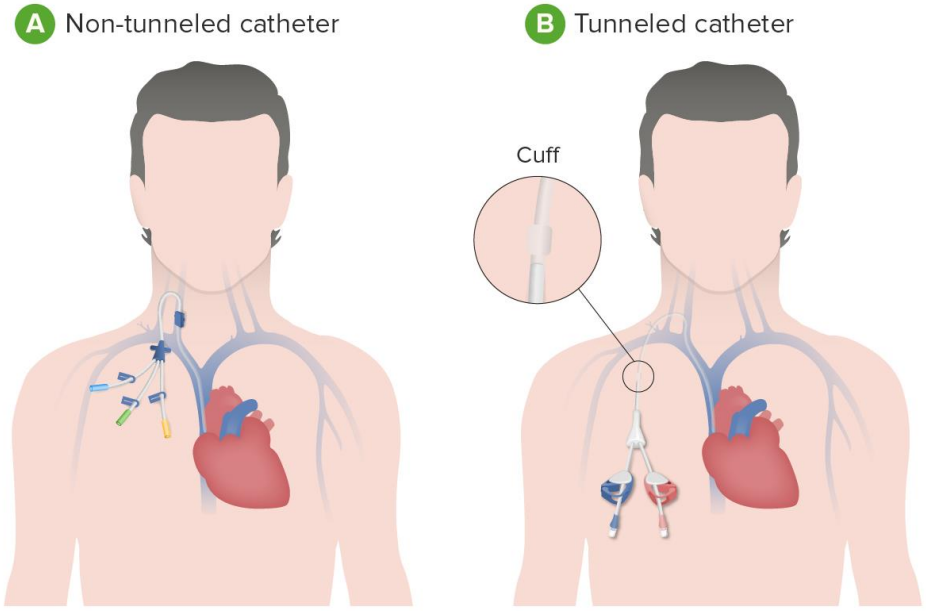


Figure 1-A: Catheter implanted with connection to subclavian vein. Entry site is the point that the catheter is inserted into the skin. **Figure 1-B:** An IVAD placed subcutaneously with catheter extending into the subclavian vein like the catheter. Port is accessed with a huber needle.

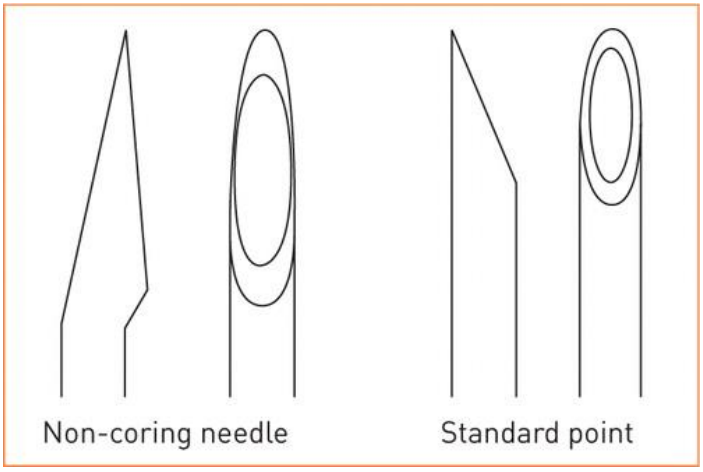
The catheters can be either tunneled (implanted subcutaneously) or non-tunneled (not subcutaneously implanted with entry site). Non-tunneled catheters have higher rates of infections when compared to both IVADs and tunneled catheters.[4] Non-tunneled catheters have a decreased distance between the skin and the bloodstream when compared to IVADs and tunneled catheters. This decreased distance makes it more likely for pathogens to enter the bloodstream. Additionally, non-tunneled catheter tip placement in the vena cava often results in insufficient blood flow rate.[11]

Figure 2: Tunneled vs Non-tunneled[12]



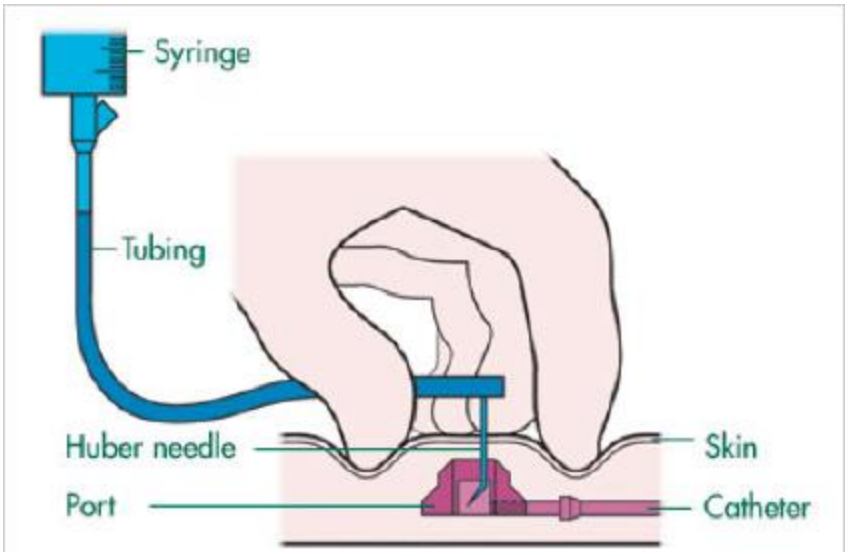
Implantation under the skin is a distinct characteristic of IVADs. Benefits of a concealed venous access device include permanent insertion, improved body image of the patient, and reduced physical limitations.[13] IVADs include a reservoir connected to a large vein through a catheter and are accessed by Huber needles. Huber needles are non-coring needles specially designed to access implanted vascular devices. Non-coring needles have a 45º angle at the end of the needle which prevents "coring," or the removal of silicon from the implant.

Figure 3: Non-coring vs Standard Needle[14]



Huber needles can vary in shape, length, diameter, mechanism of protection against the blood and bevel design. Upon insertion of an IVAD, the correct size and length of a Huber needle must be assessed based on the location of the port septum and the patient's body type.

Figure 4: Huber Needle Accessing IVAD[15]



Huber needle is inserted at a 90° angle into the septum to access the reservoir to deliver medication or take blood samples.

The smallest size needle appropriate for the patient must be used. If the needle length is too long, then the needle or port may be damaged upon insertion. If the needle length is too short, the needle may not pierce the septum. Sterile gauze squares should be placed under the wings of the port to support the access needle at a 90º angle if the access needle is not already in perfect position. Using sterile gauze squares to fix imperfect needle sizing has been a common practice for years. Gauze is an inexpensive material and serves as a cushion between the skin and the wings of the port. However, this practice should be reevaluated for the patient's comfort and safety. Using gauze to support a 90º angle may not ensure permanent stability for the duration of the needle's use. Additionally, patient injury such as a piercing of the septum may occur if the gauze is not properly applied.

In addition, to the delivery of treatments, IVADs allow for blood samples to be taken easily. When the Huber needle pierces the septa, it creates negative pressure and allows for an influx of blood. However, it was not until 2017 that an IVAD was made specifically for apheresis.[4] Apheresis is the removal of blood plasma from the body and its separation into plasma and cells and reintroducing the cells back into the body. This can be used for patients being treated for autoimmune diseases, in which antibodies are removed from the blood.

While IVADs have significantly increased the quality of life of patients, there has been little change to the overall design since its conception. All IVADs have a septa, reservoir, and catheter. However, sizing issues with Huber needles can lead to a number of complications (seen in Tables 1-3), including damage to the IVAD requiring surgery to replace the damaged IVAD. The device described in this document seeks to eliminate the need of non-coring needles all together and use a needle-less port system, the IrisPort

System, to deliver the same quality of long-term venous access, with reducing the number of complications caused by improper Huber needle sizing.

Table 1: Complications Related to IVAD Insertion[16]

Complication	Symptoms	Etiology
Air embolism	Cardiac arrest, chest pain, hypotension, breathing difficulties, tachypnea	Intrathoracic pressure becomes less than atmospheric pressure at the open needle or catheter
Cardiac Tamponade	Anxiety, chest discomfort, cyanosis, face and neck distention, hypotension, tachycardia, tachypnea	Cardiac compression of fluid accumulation within pericardial sac due to perforation
Carotid artery puncture	Hypotension, internal or external bleeding, hematoma, stroke	Carotid artery punctured during percutaneous insertion into internal jugular vein
Catheter migration	Pain, palpitations, occlusion	Catheter tip no longer located in superior vena cava
Chylothorax, Hemothorax, Hydrothorax, Pneumothorax	Pain, cyanosis, dyspnea, tachypnea	Caused by air, blood, lymph, or fluid infusion into pleural cavity due to injury during insertion
Bleeding/hematoma	Persistent bleeding, discoloration	Catheter insertion is traumatic or if inducer sheath is left in place

Table 2: Types of IVAD Related Infections[16]

Type	Location	Symptoms	Treatment
Blood stream	Systemic	Fever, hypotension, purulent drainage	IV antibiotics and remove device
Local	Insertion site or exit site	Edema, erythema, induration, local tenderness	Oral or IV antibiotics
Port Pocket	Subcutaneous pocket	Edema, erythema, induration, purulent drainage	IV antibiotics, pack pocket with antibacterial gauze, possible removal of device
Tunnel	Subcutaneous tunnel	Edema, erythema, induration, purulent drainage	Catheter removal, IV antibiotics, pack tunnel with antibiotic gauze

Table 3: Types of Occlusions[16]

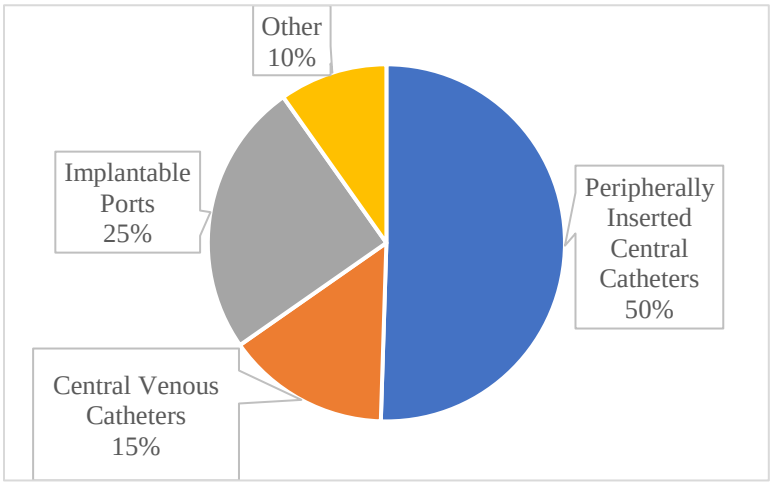
Occlusion	Etiology	Outcome	Treatment
Drug precipitates	Drug crystallization in catheter or tip from infusion of incompatible solutions or lack of flushing	Partial or total occlusion	Infuse solution to alter pH, possible removal of device
Fibrin deposits	Sheath: fibrin adheres to external catheter, can extend full length of catheter	Partial or total occlusion	Change position, fibrinolytic therapy, flush, IVAD removal
	Tail: fibrin located at the catheter tip acting as one-way valve	Partial occlusion	Change position, fibrinolytic therapy, flush
Thrombus	Deep vein: clot formation at distal tip, subclavian, axillary, or brachiocephalic vein	Total occlusion	Anticoagulation or fibrinolytic therapy, possible IVAD removal
	Intraluminal: Fibrin or clot within catheter	Partial or total occlusion	Anticoagulation or fibrinolytic therapy, possible IVAD removal
	Mural: Fibrin forms from a vessel wall injury and binds to the fibrin covering on the catheter surface	Partial or total occlusion	Anticoagulation or fibrinolytic therapy, possible IVAD removal

LITERATURE REVIEW

Market Research

The Huber needle is the primary use for venous access for chemotherapy, dialysis, among other treatments. The venous access market is defined by the use of catheters, ports, and catheter securement devices.[17] The venous access market will be our primary focus. Revenue is valued at 6.5 billion dollars with a 1.2% growth. Most of the revenue comes from the purchasing of venous access devices. Growth projections were made due to increasing demographics requiring venous access, health care reform and product innovation.[17] Medicare increased physician visits but made cuts to reimbursing hospital acquired infections. This has led to hospitals purchasing more expensive, antimicrobial devices.[17] There is a profit margin of 10.3%, coming from the reduction of inefficient manufacturing plants, improving supply chains post COVID-19 pandemic, and low market saturation of competitors. An important thing to note is the higher skilled labor required to manufacture implantable devices, which somewhat limits profits. Alongside manufacturing, many companies have in house sales teams to improve sales growth.[17]

Figure 5: Venous Access Market Breakdown



As the population continues to age, there is an expanding market for venous access.[17] In addition to the aging demographic within the world, there is the ever-growing presence of cancer. Chemotherapy is one of the leading treatments and is used in most cancers. There is a large market totaling nearly 200 billion dollars for initial, continuing, and final treatments for patients across all cancer types.[18] This cost includes the cost of the drugs and all the equipment. The IrisPort seeks to reduce the cost of chemotherapy by reducing the required equipment to purchase for infusion procedures.

Table 4:Proportion of patients who receive chemotherapy in the U.S.[9]

Cancer Type	**Stage 1**	**Stage 2**	**Stage 3**	**Stage 4**
Bladder	50%	55%	61%	60%
Breast	17%*		62%	66%
Colon	9%*		66%	65%
Rectal	34%	79%*		78%
Uterus	26%	70%	75%	73%

*Chemotherapy rates were combined within 2 stages

Table 5: Cost of Chemotherapy per Year[18]

Cancer Type	Initial	Continuing	Last
Bladder	1.5 billion	2.7 billion	1.6 billion
Breast	8.1 billion	10.6 billion	5.6 billion
Colorectal	8.6 billion	5.8 billion	6.3 billion
Uterus	1.5 billion	1.1 billion	1 billion

Dialysis makes up another part of the venous access and is worth 2.5 billion dollars. Profit margins are smaller due to lower insurance reimbursement rates. This is due to Medicare continually decreasing reimbursement rates over the past 5 years and the increasing wages for manufacturing. Dialysis is done primarily in dialysis centers and hospitals.[19] Hospitals have the largest revenue and profit, 968.6 billion and 68.8 billion dollars respectively. Hospitals have both inpatient and outpatient settings. Outpatient is cheaper to maintain and is more cost-efficient.[20] All three of the previously mentioned markets are largely impacted by the reimbursement rates of insurance companies. Medicare and other private insurance companies already have existing reimbursement pathways to which this device would be eligible for. Medicare will typically reimburse between $1,341.23-$2,770.97, with varying fees depending on site of procedure.[21] Revenue can be limited by insurance companies, other companies, and other sources of funding.

As mentioned previously, a large portion of patients report having a fear of needles. Where most of all children and patients receiving chemotherapy are included in that

proportion as seen in Table 6. This fear leads to 20% of people to avoid any and all procedures.[3] In addition to age, women are more likely to have a fear of needles when compared to men.[3] By eliminating a needle using a mechanical septum, the IrisPort hopes to target patients with a fear of needles and increase patient compliance.

Table 6: Prevalence of "Needle-Phobia" in Cancer Patients[3]

Category	First author	Year of publication	Prevalence	95% confidence interval		Description of injection fear or phobia
Conditions/Disease:						
Cancer:						
	Kettwich	2007	84.0%	69.6%	98.4%	Needle phobia of syringe. Children undergoing chemotherapy
	Kettwich	2007	68.0%	49.7%	86.3%	Needle phobia of butterfly needle. Children undergoing chemotherapy
	Kettwich	2007	64.0%	45.2%	82.8%	Needle phobia of syringe. Adults undergoing chemotherapy
	Kettwich	2007	52.0%	32.4%	71.6%	Needle phobia of butterfly needle. Adults undergoing chemotherapy
	Cox	2007	41.0%	30.1%	51.9%	Would avoid future injections. Women with breast cancer with injection anxiety
	Cox	2007	37.5%	30.9%	44.1%	Injection anxiety in women with breast cancer
	Harris	2009	16.9%	10.8%	24.7%	Patients with blood–injection–injury fear undergoing chemotherapy
	Carey	2005	15.7%	10.7%	20.8%	Fear of injections in patients undergoing intravenous chemotherapy

When comparing the different markets, a few different companies were involved in all 3 markets. Baxter, BD, and Fresnius makes up the majority of dialysis and a larger portion of the venous access market. The venous access market is more evenly spread out with over 150 companies. Baxter is seeing a large revenue growth due to small business acquisitions.[17] These companies typically buy up smaller companies leading to a monopoly.[19] Hospital systems are continuing to get larger as they band together. As time goes on the global market continues to grow, there has been an overall decrease in American exports and an increase in imports. The majority is coming out of Ireland and Mexico, and cost less overall. Our company has to be aware of key players undercutting prices or attempting to buy out the company.[17,19] The final thing that forces competition

is the existence of group purchasing organizations. They can hinder growth as they have a better ability to negotiate the prices of materials and medical devices.

User Needs

The design of the IVAD sought to eliminate needle punctures through the arm and allow for a higher quality of living. From a higher risk of infection to the possibility of a re-stick, external catheters and IV administration through the arm can cause great discomfort to the patient.[22] With the IVAD, these risks are reduced. An IVAD provides constant access to the bloodstream without the possibility of missing the vein through needle access. The device can remain in the body for up to 5 years, and the time of treatment is reduced. Although the IVAD has changed the way long-term patients receive treatment, there are still user needs that remain.

The main cause of discomfort in patients receiving IV treatment is the needle. Regardless of needle size, patients still feel some level of pain. In pediatric patients, a phobia of needles may develop as they progress through their treatment path, leading them to become less compliant.[3] A needleless device could improve patient comfort and compliance. In addition, infection rates caused by puncturing the skin with a needle could decrease. Through antimicrobial materials and the absence of a needle, infection would be less likely to develop. The size of the device may overall decrease with the reduction of the septum size. Without a needle to puncture, the septa do not serve much purpose and can possibly be eliminated.

Keeping in mind the nurses and physicians who will access the device, the port must be easily accessible without a needle. An adapter similar to the tip of a standard 10 mL Luer lock syringe will be connected to the device. This adapter will be designed as the male

component with a swivel-skirt mechanism. The swivel-skirt mechanism allows for connection without twisting the intravenous tubing. This simple, yet stable, connection will allow for administration of fluids or withdrawal of blood. With easier access, the time of treatment may be reduced, which would benefit both the patient and the administrator.

Figure 6: Luer Lock Universal Adapter Predicate Device-Unengaged[23]

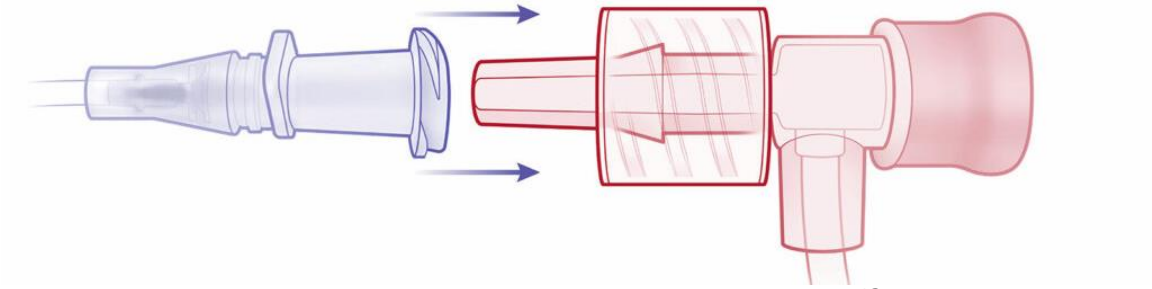
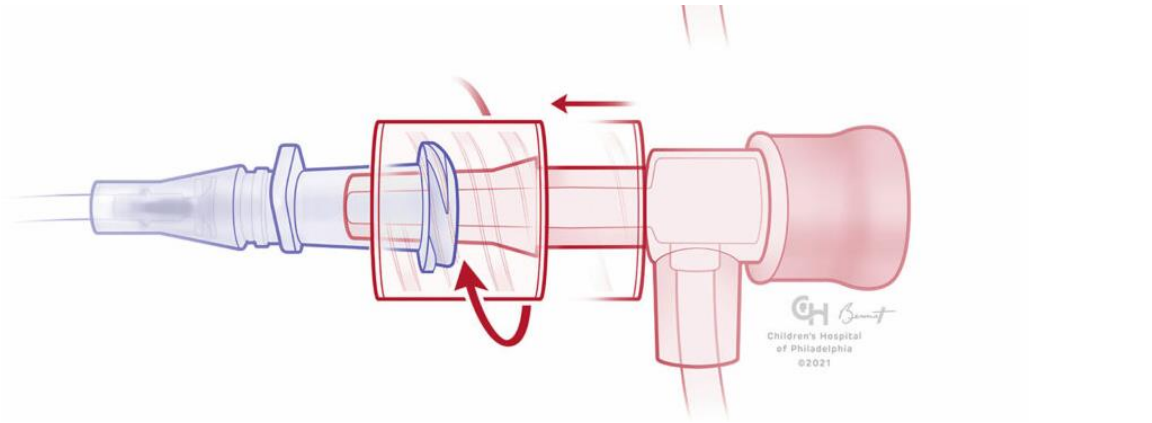


Figure 7:Luer Lock Universal Adapter Predicate Device- Engaged[23]



Device Features

With the user needs considered, the IVAD features become clear. The most radical feature is a new way to access the bloodstream without the use of a needle. There is no way to access the internal body without an opening in the skin. Therefore, the IVAD must rest in the skin rather than under it. To allow for a continuous opening in the skin, it will be imperative to keep the site clean and keep the area covered with an antimicrobial

covering. To prevent blood from leaking through the opening in the skin, a secure yet stable opening system covering the reservoir is required. The opening must be collapsible to avoid unnecessary increase in size of the device. The most prominent design is the iris mechanism. The iris mechanism would consist of 5 leaflets that are fixed in between 2 circular discs. When turned clockwise, the leaflets retract between the 2 circular discs to create a circular opening to the reservoir. This feature will allow for fluids to move between the syringe and port reservoir by either injecting fluids into the reservoir or withdrawing blood with the syringe. A connecting device (or a syringe adaptor) will need to be attached to the iris mechanism. A male-end adaptor design for a standard syringe female-end will allow the design to be universal.

In addition to the new opening feature of the device, the rest of the IVAD will resemble its predecessors. A cylinder-shaped port reservoir with an opening for catheter tubing will lie underneath the iris mechanism to serve as a gateway to the bloodstream. The reservoir will need to manipulate turbulence of the bloodstream to create a vortex before exiting the body through the syringe. The catheter will connect to the port reservoir and insert into the intended vein.

The IVAD size needs to be minimized without making venous access with the syringe difficult. Keeping an opening in the skin can cause discomfort but decreasing the size of the IVAD may reduce the potential pain.

Materials

Materials are considered biocompatible if they do not produce an immune response and are not cytotoxic. Biocompatibility can be shown through *in vivo* and *in vitro* testing.[24–26] These tests include cellular response and blood assays to quantify if a material causes an immune response. As previously mentioned, IVADs consist of a septum, reservoir, and catheter. While the shape of the reservoir may change depending on the manufacturer, the materials rarely change. Typically, reservoirs and covers are made of either titanium or polyurethane depending on patient's needs and allergies.[4] These materials have high mechanical strength, are resistant to degradation are less expensive than other alloys.[24–26] Raw materials would cost approximately $18-22/kilogram and $6/kilogram for titanium and polyurethan, respectively.[27] Polyurethane has been shown to have low monocyte reactivity, high thermal and oxidative stability, and does not produce toxic leachable materials.[5,26] Titanium is also considered to be biocompatible as it has low electrical conductivity allowing for an inert oxide layer to form spontaneously. It is this oxide layer that resists corrosion over time, making it one of the preferred materials.[25]

Most septa are made with silicone and other self-healing polymers that allow for access to the reservoir itself. Catheters are made with primarily silicone and polyurethane.[5,24] Silicone is a synthetic polymer that has been used widely since 1940 due to its extensive mechanical properties and high biocompatibility. Silicone has been proven to have high thermal and chemical stability under a wide range of temperatures and conditions. Due to its hydrophobic nature, silicone is considered to have high hemocompatibility.[24] All of these characteristics have been confirmed with *in vitro* and *in vivo* testing. Both silicone and polyurethane offer different benefits. Silicone catheters have lower infection rates

when compared with polyurethane catheters. However, silicone catheters have high rates of mechanical failure in which they disconnect from the port. Both materials resist surface degradation and allow for good blood flow.[5] However, the majority of current IVADs on the market use a polyurethane catheter (about 2:1).[4] All the materials mentioned are the most commonly used by current manufacturers.[4]

Infection Rates and Prevention

Infection is one of the several complications that can occur when implanting devices. IVADs have been shown to best deliver long term venous access while limiting infection rates. However, infection is a leading cause for replacing implanted ports. These infections can be acquired by repeated, consecutive needle punctures and can be local or systemic. Localized infections are confirmed by culturing exudate samples. Infected portions of the port may be removed and replaced, or complete removal of the device may be necessary. Systemic infections are seen if the infection has reached the blood stream. The device should be removed, and patient be treated with antibiotics. In both instances of infection, a replacement port should not be placed until the infections have cleared.[4]

Infections detailed above can be mostly prevented with proper catheter maintenance and hygiene. The Centers for Disease Control (CDC) created standardized guidelines for proper catheter maintenance. Clinicians should wash their hands prior to palpating, accessing, or dressing and IVAD. The skin at the site of the IVAD should be disinfected with either chlorhexidine solution or 70% alcohol using a sterile swab. Cleansing of the site should continue for 30 seconds with friction to kill as many harmful organisms as possible. All IVADs should be flushed with 20 mL of normal saline before and after each

access.[28] The IVAD dressings should be replaced at least once a week, whenever the dressings become dislodged, or if infection is suspected. In addition to proper hand hygiene, IVADs should undergo catheter flushing. This is since biofilms tend to form on the catheters. The biofilms can cause occlusions that can lead to a number of issues, including infection (seen in Tables 1-3). IVADs can be flushed with either saline or heparin. This should be done regularly to prevent occlusions and infection. Flushing is essential especially when IVAD is not in use. [4]

Sterilization Methods and Packaging

Infections can be largely prevented by sterilizing all medical devices and instruments. There are several methods in which things can be sterilized. The majority of medical devices and implants are sterilized in two ways, ethylene oxide (ETO) and radiation.[29,30] ETO terminally sterilizes materials after they have been manufactured and packaged, allowing for large quantities to be sterilized at one time. ETO is done by preconditioning the load (materials) to get to a predefined temperature and humidity and air is removed to create a vacuum. Steam may be added to maintain the desired humidity. The ETO is then injected into the load, with nitrogen gas following to create top pressure and force the ETO into the materials. After the proper amount of exposure time, the gases are removed, and nitrogen is used to wash the materials. The final steps include ventilation and aeration to ensure that no ETO remains. ETO is the preferred choice for medical devices because it can sterilize most materials, including temperature and moisture sensitive devices.[29,30]

The second most used form of sterilization is radiation, commonly gamma radiation. Gamma radiation has short processing time, can penetrate multiple layers, and penetrate

different types of packaging. Similar to ETO, gamma radiation sterilization is not affected by humidity, temperature, and does not significantly heat the materials. The radiation is emitted from an atom or molecule as the energy level drops. This method uses the self-disintegration of cobalt-60. [29]

The IrisPort will be packaged in standard plastic and paper containers that will be sealed. Our product will likely use heat sealed sterilization pouches that cost between $0.38-0.51/ pouch.[31] Packaging must be strong enough to resist punctures and tears.[30] Following packaging, the device will undergo either ETO or gamma radiation to be sterilized prior to use. This packaging and sterilization will work to prophylactically prevent infections.

Table 7:Comparison of Sterilization Techniques[29,30]

	Ethylene Oxide (ETO)	**Radiation**
Sterilant source	ETO gas	Gamma radiation
Uses	Single use devices, surgical instruments, heat/moisture sensitive devices	Some single use devices, heat sensitive, radiation resistant plastics
Cost	>$45000	$150,000-$45000
Pros	Penetrate packaging, easy to use, compatible with most medical materials	Penetrate multilayer packaging, sort processing time, not affected by humidity levels
Cons	Toxic, aeration time to get rid of residue, flammable, can contribute to CO_2 emissions	Expensive, can cause cracking in plastics

RESEARCH PROPOSAL

Needs Statement and Value Proposition

The improved design for the issue at hand was based on an initial needs statement: “A way to better administer long term fluid treatment using venous access devices to eliminate patient discomfort and administration complications resulting from accessing the device via a needle.” This statement was formulated based on the observation that complications with intravenous access resulting from piercing or perforating the septum by needles. By improving methods of long-term fluid treatment, a patient’s quality of life can improve, nurses and physicians have less trouble administering treatment, and engineers may have a new starting point for further improvement of the method of treatment.

Potential Solutions

There are a few ways the needs statement can be solved. The first way is with a collapsible needle. Before the needs statement was solidified, the focus was the sizing of the needle. Many patients with an IVAD must use gauze underneath the wings of the port to hold the needle in place during treatment. With a collapsible needle, the sizing of the needle could be more compatible with the patient’s skin thickness. Each patient has a different body type. While current non-coring needles come in a variety of sizes, it is difficult for the needles to accommodate each skin thickness. With an adjustable needle, patients would not be susceptible to multiple sticks, and hospitals would not have to purchase different sized needles in bulk. However, while this solution would allow for a comfortable fit of the port, the discomfort from needle insertion remains.

The next focus was to eliminate the needle entirely from the IVAD access process. The first method was to use magnets to access the reservoir. A magnet would lie between the skin and push out of the way at the presence of a syringe. The magnet would securely prevent backflow of blood out of the body and eliminates the needle. However, the magnet would have to be strong enough to remain in place overtime, and it would be difficult to comfortably access the reservoir. Additionally, magnets may interfere with other devices such as pacemakers.

The second method was to use a venus box that twists to open.[32] A base connects to 4 curved doors that, upon twisting the base, securely close or open the box. With this design, the accessing process would flow smoothly by eliminating the needle and would not require magnetic materials. However, the venus box does not ensure total closure, and it would be possible for blood to leak.

Figure 8: Venus Box with Petals Open and Closed[32]

Figure 9: Venus Box Partially Closed[32]

With the venus box still in mind, the final method was to use an iris mechanism that also twists to open. There are 5 leaflets fixed in between 2 circular cases that retract when the cases rotate in opposite directions. This method eliminates the needle, does not require magnetic materials, and ensures a tighter closing. The mechanism of opening will be discussed in the next section.

Implant Design

The design possibilities in the previous sections would theoretically solve the needs statement, but the most stable design is the iris mechanism. The iris mechanism would be the most comfortable method to access. With an adaptor for the syringe, the iris mechanism would open with ease and close securely to prevent the leakage of blood. The iris mechanism inner and outer case size would correspond with the Luer lock adaptor dimensions. The dimensions for the prototype and proposed scaled down model can be

found in Tables 8-10. For prototyping purposes, the device was scaled up 7.5 times larger. The stages of the iris opening can be seen in the images below.

Table 8: Scaled Up Prototype IrisPort Dimensions

Part	Inner Diameter	Outer Diameter	Height	Length
Outer case	37.04 mm	74.37 mm	6.29 mm	-
Inner case	37.04 mm	70.13 mm	2.18 mm	-
Leaflet	-	-	2.45 mm	23.27 mm
Internal Reservoir	90 mm	-	37.5 mm	-

Table 9: Scaled Down IrisPort Prototype Dimensions

Part	Inner Diameter	Outer Diameter	Height	Length
Outer case	2.1 mm	4.22 mm	0.36 mm	-
Inner case	2.1 mm	3.98 mm	0.12 mm	-
Leaflet	-	-	0.14 mm	1.32 mm
Internal Reservoir	12 mm	-	5 mm	-

Table 10: Reservoir Casing Dimensions

Protype Type Size	Equatorial axis (a)	Polar axis (c)
Large	54.5 mm	23.8 mm
Scaled Down	7.26 mm	3.17 mm

Figure 10: Spheroid Axes and Dimensions Diagram[33]

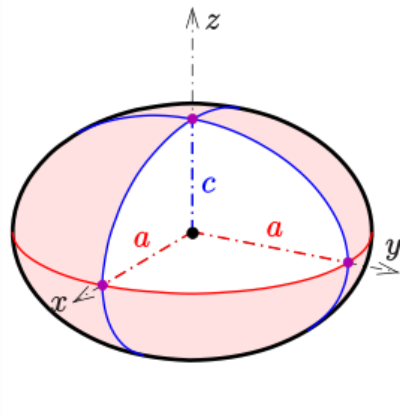


Figure 11: Closed Iris on Z and -Z Axes of Scaled Up Prototype

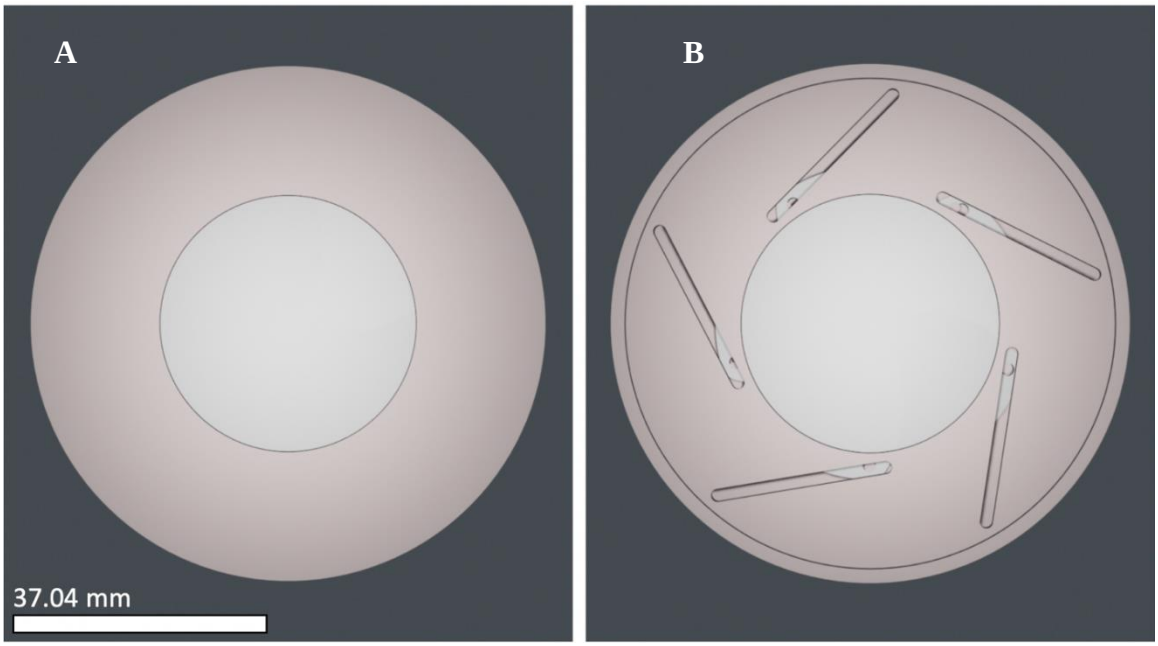


Figure 11-A: Closed iris on the Z axis. **Figure 11-B:** On the right is the closed iris on the -Z axis.

Figure 12: Partially Open Iris on Z and -Z Axes of Scaled Up Prototype

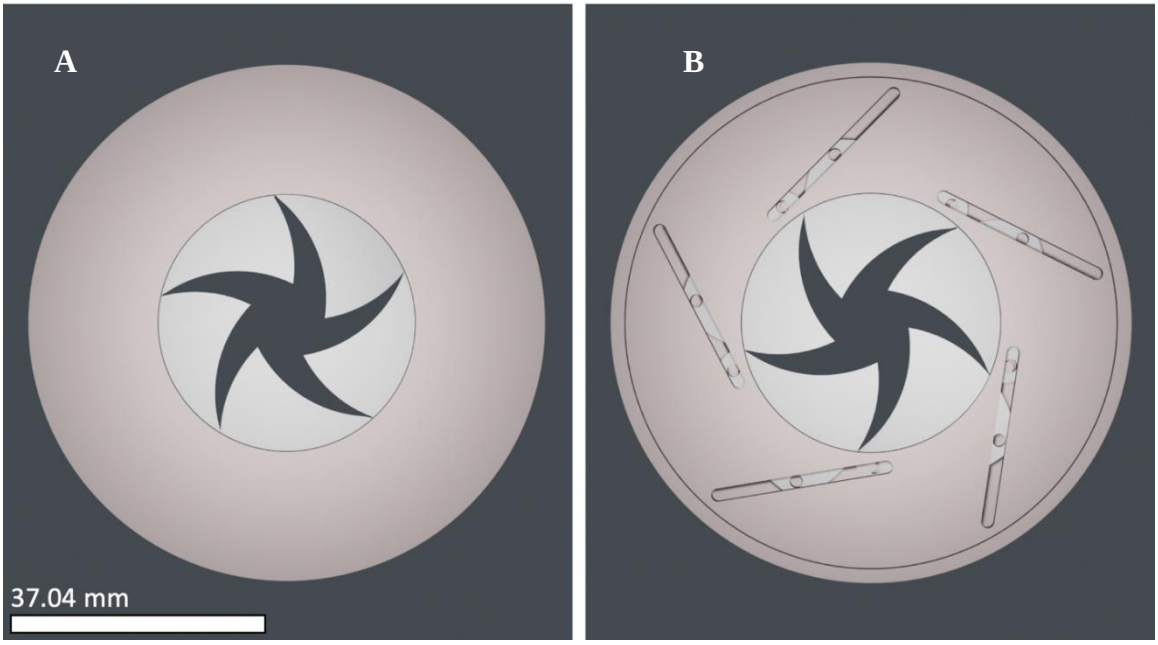


Figure 12-A: Partially open iris on the Z axis. **Figure 12-B:** Partially open iris on the -Z axis.

Figure 13: Completely Open Iris on Z and -Z Axes of Scaled Up Prototype

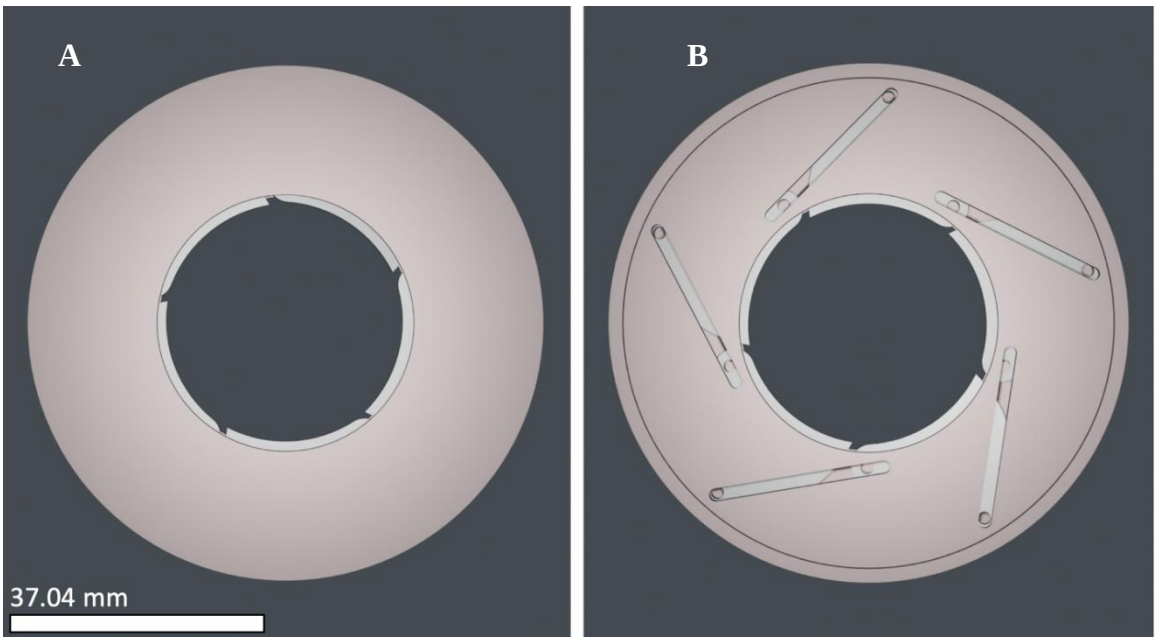
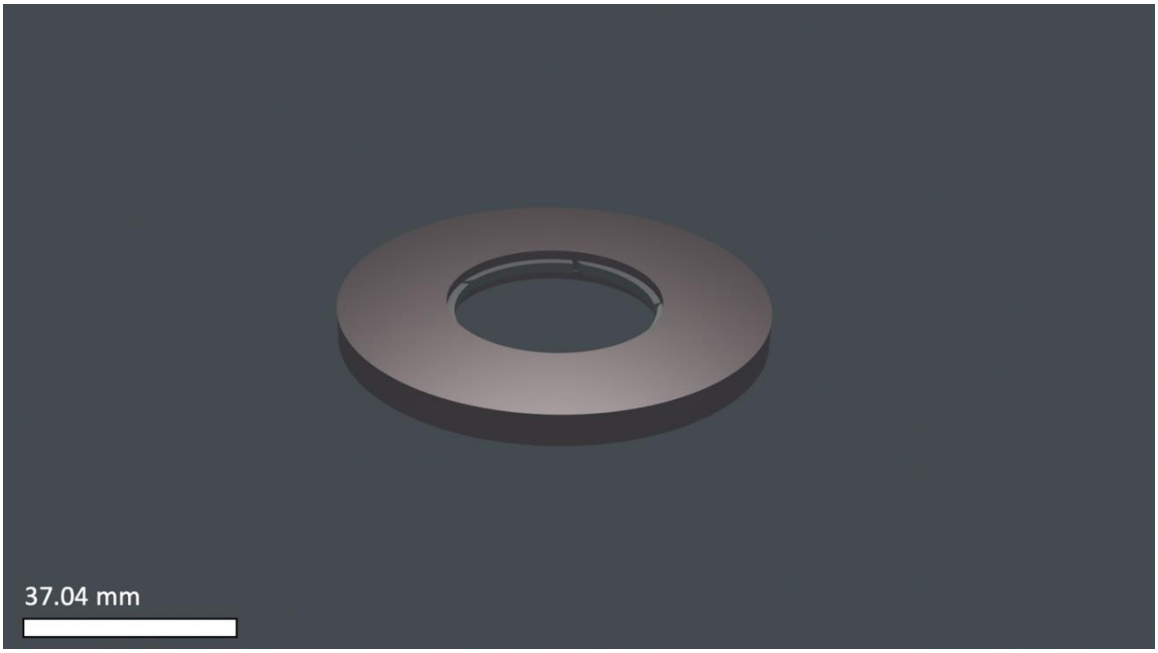


Figure 13-A: Completely open iris on the Z axis. **Figure 13-B:** Completely open iris on the -Z axis.

Figure 14: Port and Iris Side View of Scaled Up Prototype



The photo above is the side view of the iris mechanism completely open.

Additionally, the port reservoir is modeled after existing port reservoirs that have been optimized for fluid flow. The round design of the reservoir will promote a vortex that ensures fluid flow reaches all areas of the reservoir. The catheter opening lies tangentially within the wall of the reservoir to further allow a consistent flow of blood or fluids. The opening of the reservoir will match the outer diameter of the inner case of the iris mechanism at 2.2 mm.

Figure 15: Reservoir Z and -Z View of Scaled Up Prototype

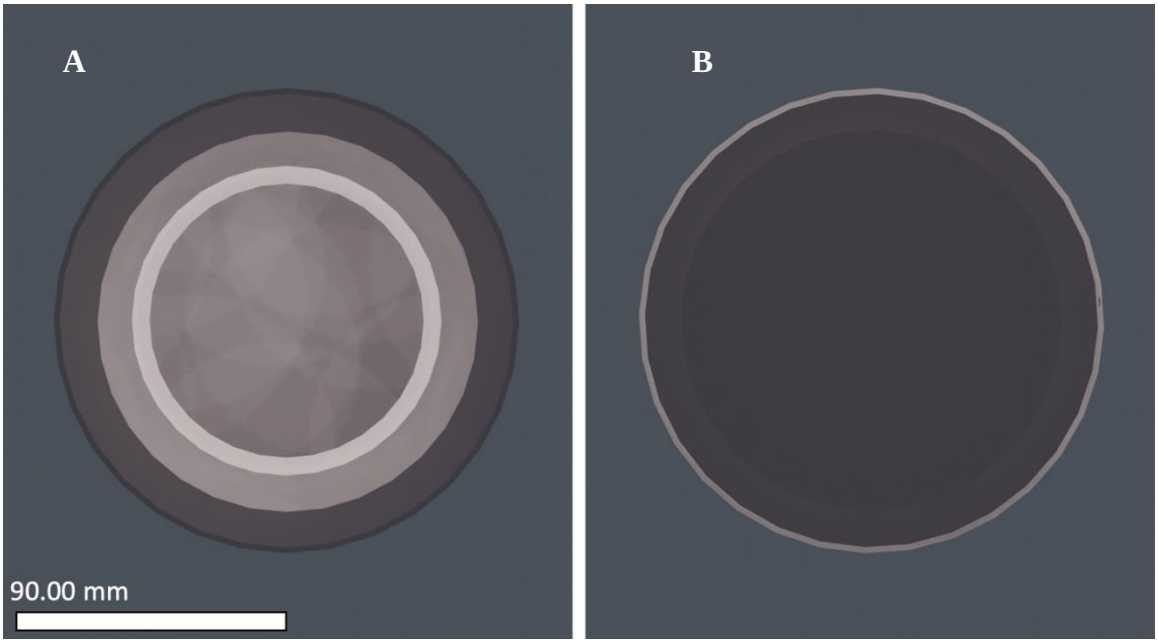


Figure 15-A: Port reservoir on the Z axis. **Figure 15-B:** Port reservoir on the -Z axis.

Figure 16: Reservoir Side Views of Scaled Up Prototype

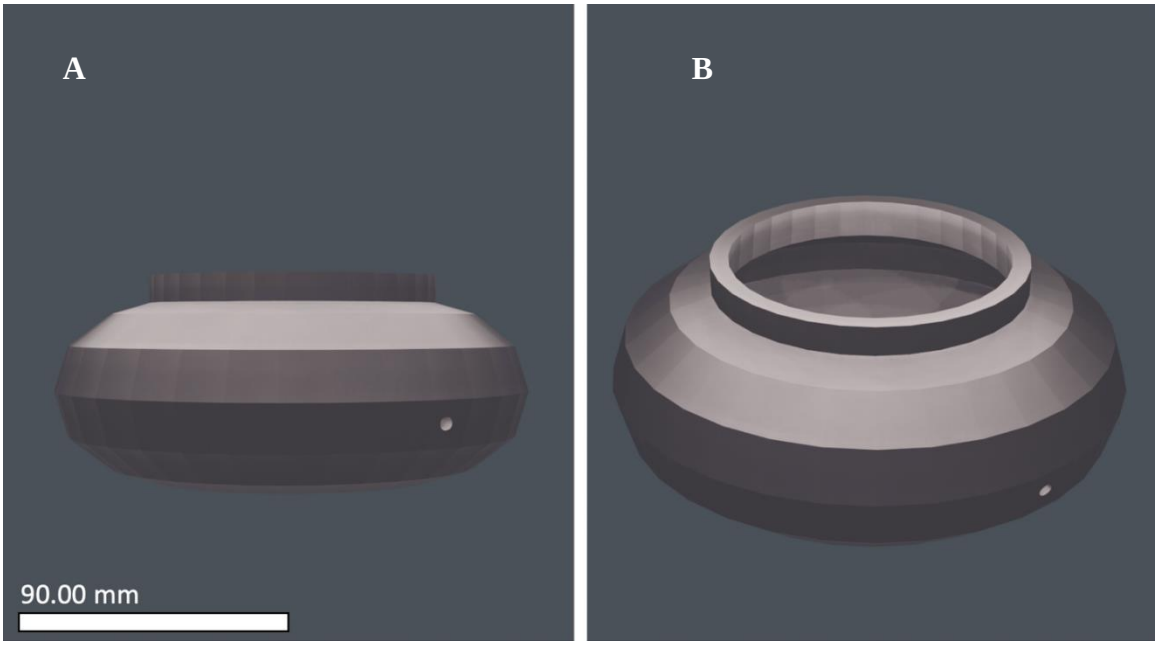


Figure 16-A: Side view of the reservoir. **Figure 16-B:** Elevated side view of the reservoir.

Figure 17: Leaflet Design of Scaled Up Prototype

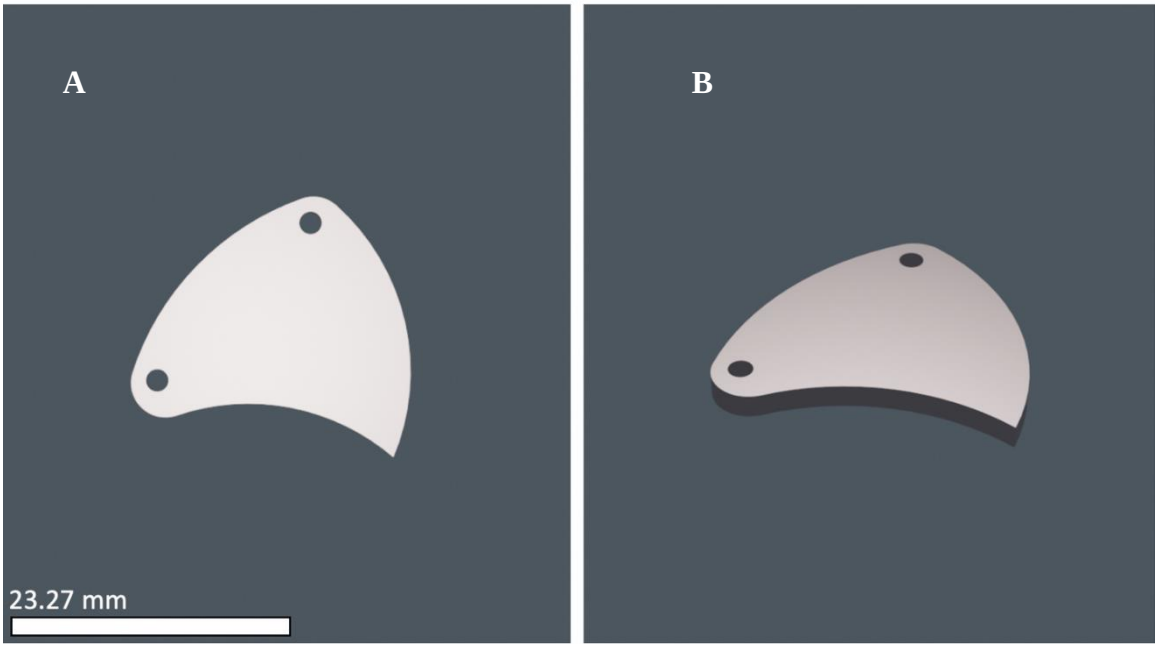


Figure 17-A: Leaflet on the Z axis. **Figure 17-B:** Elevated side view of the leaflet.

Proposed Surgical Protocol

The following protocol is adapted from existing surgical procedures that have been approved by the FDA.[34] Prior to the procedure, health care providers must have a comprehensive medical history including previous procedures and allergies. Patients also should go through routine blood work to confirm that their platelet count is <50,000 and prothrombin values >18. Cancer patients should discontinue all chemotherapy at least 2 weeks prior to the procedure.

Step 1: Sterilize the chest and neck region with chlorhexidine and drape the patient so that the face is covered. All individuals involved in the procedure must have proper personal protective equipment (PPE) including surgical gowns, gloves, masks, and eye protection. The patient should be given prophylactic antibiotics. Per the Society of Interventional Radiology (SIR) Standards of Practice Committee 1 gram of intravenous cefazolin or an equivalent antibiotic.

Step 2: Using an ultrasound, puncture the internal jugular vein to gain access to the right atrium. An angled access point will eliminate entry scar. The needle sheath is advanced into the vena cava and the port catheter is inserted.

Step 3: Administer subcutaneous local anesthesia and make an incision for the port pocket. Incisions should be at least 3 cm from the catheter entry. A distance of 5 cm is often preferred as it decreases the chance of bacterial migration from the port pocket into the blood stream. The port should be between 5 and 20 mm beneath the skin. Ideal placement of the port would be over an anterior rib to provide support for future palpation and access.

Step 4: Following the creation of the port pocket and tunnel, the catheter is pulled through the IVAD and through the tunnel. The catheter tip should be approximately 2 vertebral bodies below the carina. To prevent movement of the port, suture the port to the fascia with a resorbable 4-0 polyglactin suture.

Step 5: Prior to closure, the port function must be verified. This can be done by aspiration and injection using a noncoring needle, following with a 100 u/cc heparin. Once function has been verified, the incision may be closed using 2 to 3 interrupted deep sutures and a running subcuticular resorbable suture (ideally 4-0 polyglactin).

Step 6: Patients must be observed for at least one hour after the procedure to allow for the anesthesia to wear off and ensure there is no pain or bleeding at the surgical site.

Validation

To proceed with the proposed IVAD device, there will be several tests that need to be performed. The first test will be mechanical testing. The strength of the device features will need to be considered because the device will undergo minor stress during accessing. The IVAD device prototype was 3D printed using ABS plastic filament from a Stratasys printer. The prototype was scaled up to visualize the iris mechanism. The iris mechanism open and closed with ease. However, the pegs that hold the leaflets onto the top circular case broke when too much force was applied. This signals that the pegs, regardless of material, may need to be adjusted to prevent stress. No other features of the prototype indicated failure upon mechanical stress.

The next step will be to test the flow within the port reservoir. The round design of the reservoir is to ensure all surfaces of the interior are reachable by the fluid. The flow of fluid resulting from the tangent opening in the reservoir will reduce buildup of materials and potentially reduce infection. The catheter opening is set at a tangent angle to promote a circular flow of fluids. However, there have been no tests to confirm if the current design will accomplish these goals. Testing must be conducted before the prototype may proceed, including functional tests to ensure high patient compliance. The device should be able to withstand the pulling and movement of the cannulas and medical tubing.

FUTURE WORKS

The next prototype will be made from titanium and polyurethane. Each device will cost between $225-275 and $50 to 3D print for titanium and polyurethane respectively. They will be 3D printed as it is much more cost effective than injection molding for smaller quantities. Future tests include mechanical stress testing, biocompatibility assays, and corrosion testing. Our device would need to undergo mechanical fatigue tests to confirm that the device can handle the repeated forces placed on it for port access.[35] Fatigue testing is carried out cyclically (repeatedly loaded) until failure. Previous studies have shown that grade 2 titanium can withstand up to 109 MPa in stress and up to 350 MPa in loading. Our device should be able to withstand similar amounts of stress and forces. In addition to fatigue testing, the IrisPort should undergo torsion testing, both axial and functional testing. Torsion testing is done by applying a rotational motion, either with or without compression forces.[36] Pure grade 2 titanium has a breaking angle of 253° and shear stress of around 260 MPa in shear stress. [37] Functional testing must also be conducted to verity that the IrisPort can handle repeated twisting of the syringe adapter piece. [36] Finally, there are luer lock tests that can be done to ensure the lock does not leak (connection integrity testing) and there is an ease of connection. The leaking tests would consist of 27.5 N of top loaded axial force and simultaneous 0.12 N*m of torque for metals and 20 N and 0.08 N*m for plastics, respectively. These tests are described in the international standard ISO 594 ½. [38,39] As the iris mechanical septum is novel, it must be tested separately and attached to the port to ensure limited mechanical failure.[40]

Biocompatibility assays will include a hemocompatibility test following the ISO standard 10993-4.[41] Hemocompatibility testing is required because the IrisPort system will consistently come in contact with blood. To be considered hemocompatible, the device must not cause any significant reactions including: thrombosis, hemolysis, platelet, leukocyte and complement activation or any other blood-related adverse event.[40,41] Hemocompatibility tests include coagulation (clotting caused by thrombin confirmed with ELISA), hemolysis (quantified by increased plasma hemoglobin levels caused by damage), and a simulated circulatory system via a Chandler Loop or parallel-plate chambers.[41,42] Chandler Loops are an *ex vivo* testing that allows blood to flow through tubing, much like in blood vessels, from a pump that pushes the blood through tubing. A Chandler Loop can be linked to the catheter of the IrisPort to confirm that blood can flow smoothly and without clotting. In addition to monitoring flow, Chandler loops can monitor anti-inflammatory properties of the device.[42] In addition to hemocompatibility testing it is essential to go through pyrogenicity testing to determine if the device is non-pyrogenic or meet pyrogen limit specifications.[40] The limits set forth by the FDA are 0. .5 EU/mL or 20 EU/device for products that directly or indirectly contact the cardiovascular system and lymphatic system.[43]

The last *in vivo* testing includes corrosion testing. Our device will focus on cyclic polarization testing. Cyclic polarization tests for the pitting and crevice corrosion resistance.[44,45] The CPDP measurements should follow the ASTM standards (F2129, G5, G59, G61) and will likely be done in an external lab due to the difficult nature of interpreting the results.[44,45]

Once sufficient initial testing has been done, we would look to do an animal study, in which our product specific port maintenance routine can be established. Many implanted port systems are evaluated using pigs.[46] Swine are commonly used for diagnosis, treatment, and prevention of diseases in humans.[46] Due to their similar cardiovascular systems, researchers can induce a number of human diseases- atherosclerosis, myocardial infarction, etc. [46] They also have similar wound-healing pathways, which will allow us to see how viable the IrisPort is when implanted flush with the skin. Intracutaneous testing can be done to ensure that the device does not cause excess skin irritation.[40] Additionally, isolation of PBMC, monocytes, granulocytes, cytokine quantification can be done via ELISA testing to confirm biocompatibility. The initial maintenance would follow current protocols and then be adapted to ensure the mechanical septum remains clean and occlusion free. A more detailed pig study will be established following all *in* vitro and *ex* vivo testing. All of the previously mentioned testing must ensure that it meets the requirements of the ISO 10993-1:2009 recommended endpoints for cytotoxicity, sterilization, implantation, and hemocompatibility.[40]

Biomedical devices are developed to help the patient. Sales, while vital to the success of the device, are secondary. The IrisPort began with the user need to ease discomfort during the venous access process. As is apparent, the initial idea of the design to the first prototype can radically change. Upon successful testing, the IrisPort is expected to succeed in the medical and market fields.

Appendix A: Literature Review

BIOMEDICAL ENGINEERING
UNIVERSITY OF MISSISSIPPI

The Needlers
BME 461 – Fall 2021
Literature Review

BACKGROUND

- **Summary:**

Implanted vascular access devices (IVADs) are widely used for patients with poor peripheral venous access and patients who need long-term vascular access, such as but not limited to patients receiving chemotherapy, antibiotics, total parenteral nutrition, or frequent blood samples. Traditional intravenous infusion consists of repeated skin puncture, which can be damaging to veins and surrounding tissue over time. A catheter can be used for these applications as well, however, IVADs provide several advantages, including improved body image and minimizing maintenance while not in use, improved mobility, and lower infection rates. IVADs include a reservoir connected to a large vein through a catheter and are accessed by Huber needles.

- **Search Terms:**

Implanted vascular access device
Types of implanted vascular devices

- **References:**

[1] O. Blanco-Guzman, Implanted vascular access device options: a focused review on safety and outcomes

[2] D. Wynne, Your Clinical Guide to implant ports and non-coring needles.

[3] J. Fougo, Huber Needle: Different Types, Uses, Prevention of Accidents

CURRENT TREATMENT OPTIONS

- **Summary:**

Huber needles are non-coring needles specially designed to access implanted vascular devices. Non-coring needles have a 45° angle at the end of the needle which prevents "coring," or the removal of silicon from the implant. Huber needles can vary in shape, length, diameter, mechanism of protection against the blood and bevel design. [1] Upon insertion of an IVAD, the correct size and length of a Huber needle must be assessed based on the location of the port septum and the patient's body type. The smallest size needle appropriate for the patient must be used. If the needle length is too long, then the needle/port may be damaged upon insertion. If the needle length is too short, the needle may not pierce the septum. [2] Sterile gauze squares should be placed under the wings of the port to support the access needle at a 90° angle if the access needle is not already in perfect position. [3] Using sterile gauze squares to fix imperfect needle sizing has been a common practice for years. Gauze is a cheap material and serves as a cushion between the skin and the wings of the port. However, this practice should be reevaluated for the patient's comfort and safety. Using gauze to support a 90° angle may not ensure permanent stability for the duration of the needle's use. Additionally, patient injury such as a piercing of the septum may occur if the gauze is not properly applied.

- **Search Terms:**
  Huber needle, too long
  Non-coring needles
  Huber needle insertion

- **References:**
[1] J. Fougo, Huber Needle: Different Types, Uses, Prevention of Accidents

[2] Bard Access Systems: EZ Huber* Safety Infusion Set Informational Wall Chart

[3] H. Carroll, Guideline: Totally implantable central venous access ports

IDENTIFY USER NEEDS

- **Summary:**

The greatest risk that a patient faces with the Huber needle is piercing or perforation of the septum, but the occurrence is highly unlikely. Physical factors such as body physique/build and mechanical factors such as different needle sizes can complicate needle insertion. Therefore, the likelihood of perforation increases. [1] Because the parameters of the needle are very case-specific, weight variations can have a large effect on required needle parameters. Thicker tissue covering the access sight, common in heavier weight patients requires a longer needle, while thinner tissue a shorter needle. Weight fluctuations in patients can lead to improper fitting of needles [2]. Patients who did not have weight fluctuations were more likely to have the Huber needle successfully inserted on the first attempt. [3] While Huber needles can vary in shape, length, diameter, mechanism of protection against the blood and bevel design, most of these factors depend on what the access port is being used for, except length heavily depends on the patient, therefore having a length adjustable Huber needle would be beneficial to patient care by allowing the needle to by adjusted to any possible weight fluctuations.

- **Search Terms:**
  Huber needle complications
  Implanted Vascular Access Device complications

- **References:**
[1] D. Dillon, Journal of Pediatric Surgery, Complications associated with an implantable vascular access device

[2] J. Fougo, Huber Needle: Different Types, Uses, Prevention of Accidents

[3] G. Civetta, The Journal of Vascular Access, Needle Insertion Difficulty Algorithm (NIDA): A novel pilot study to predict Huber needle insertion difficulty in totally implanted devices

MARKET RESEARCH

- **Summary:**

The Huber needle is the primary use for venous access for chemotherapy, dialysis, among other treatments. The venous access market is defined by the use of catheters, ports, and catheter securement devices. The venous access market will be the primary focus. Revenue is valued at 6.5 billion dollars with a 1.2% growth. There is a profit margin of 10.3%. There is a high profit margin and revenue growth. As the population continues to age, there is an expanding market for venous access. Dialysis makes up a part of the venous access and is worth 2.5 billion dollars. Profit margins are smaller due to low reimbursement rates. Dialysis is done primarily in dialysis centers and hospitals. Leading us to the last market, the hospital market. Hospitals have the largest revenue and profit, 968.6 billion and 68.8 billion dollars respectively. Hospitals have both inpatient and outpatient settings. Outpatient is cheaper to maintain and is more cost-efficient. All three of the previously mentioned markets are largely impacted by the reimbursement rates of insurance companies. Revenue can be limited by insurance companies, other companies, and other sources of funding. [1-3]

- **Search Terms:**

  Port access
  dialysis market
  hospital (all on IBIS world)
  healthcare

- **References:**

[1] Holcomb, G. federal funding. 1–38 (2020).

[2] Curran, J. Medicaid reimbursements. 1–41 (2021).

[3] May, J. C. Hospitals in the US On the mend : Industry revenue is expected to slowly grow once the pandemic passes. 1–40 (2021).

COMPETITIVE LANDSCAPE

- **Summary:**

When comparing the different markets, a few different companies were involved in all 3 markets. Baxter makes up the majority of dialysis and a larger portion of the venous access market. The venous access market is more evenly spread out with over 150 companies. Baxter is seeing a large revenue growth due to small business acquisitions. Our company must be aware of this. Dialysis is dominated by Baxter and Fresenius. These companies typically buy up smaller companies leading to a monopoly. Hospital systems are continuing to get larger as they band together. They are not very competitive; insurance companies determine how reimbursement will go. As time goes on the global market continues to grow, there has been an overall decrease in American exports and an increase in imports. They are coming out of Ireland and Mexico, and have cost less overall. Our company has

to be aware of key players undercutting prices or attempting to buy out the company. The final thing that forces completion is the existence of group purchasing organizations. They have the ability to negotiate and hinder growth.

- **Search Terms:**
  Port access

  dialysis market

  hospital (all on IBIS world)

  healthcare

- **References:**

[1] Holcomb, G. federal funding. 1–38 (2020).

[2] Curran, J. Medicaid reimbursements. 1–41 (2021).

[3] May, J. C. Hospitals in the US On the mend : Industry revenue is expected to slowly grow once the pandemic passes. 1–40 (2021).

Appendix B: Prior Art Search

BIOMEDICAL ENGINEERING
UNIVERSITY OF MISSISSIPPI

Access Medical
BME 461 – Fall 2020
Prior Art Search

I would like a minimum of two (2) prior art references to be from international sources – i.e., outside the US Patent Office and from international journals or sources.

Prior Art Reference #1 (*Patent Number:* 5,620,419 *and Title: Port Stabilizer Ring*)[1]

- **Search Terms:**
  Venous access, implanted port support, vascular access

- **Summary:**
  Abstract: Non-invasive, perforate, locator for accessing port. Stabilizer is pressed on the skin to locate the septum, but can be removed by sliding past the needle
  Background: IVAD require a port and access to use. Requires palpitation to insert needle due to depth of the implant. Great for visualization of the septum
  Summary: Invention also provides stability while injecting the needle and fluids. Can be slid off at any time. Stabilizer is rigid enough to form a bulge around the implant
  Claims: Noninvasive ring defines where the implant is and is adhesive to the skin. The ring is made of an inert material. Use of the ring will stabilize the port while locating the septum.

- **Source:**

1. Powers, I. K. B. *et al*. Patent No.: US 8.475,417 B2. vol. 2 (2013).

Prior Art Reference #2 (*Patent Number:* 6,960,185 *and Title:* Subcutaneous Access Port)

- **Search Terms:**
  Venous, port, access, implantable

- **Summary:**
  Abstract: Implantable access device, includes a port for guiding a filament (needle) into the device. The space between the walls of the port are five times greater than the height of the wall to provide a large filament strike area.
  Background: Repeated direct cannulation of a vessel with a needle can be damaging and increase complications such as vessel thrombosis in patients. A subcutaneous implanted port, as opposed to a transcutaneous implanted port, is located beneath the skin where non-coring needles can access the device via a percutaneous puncture.
  Summary: A large strike area from increased distance of the walls allows for multiple skin/tissue puncture sites, while the relatively short height of the port minimizes tension on the insertion wound of the patient.
  Claims: An implantable device with a port for receiving/guiding a filament. An uncovered strike plate for receiving the filament with a first and second end. Distance between walls is at least five times greater than height of walls and distance between first and second ends of the plate is at least five times greater than the height of the walls.

- **Source:**

2. Adaniya, G. & Fenton, P. SUBCUTANEOUS ACCESS PORT. 1–10 (2005).

Prior Art Reference #3 (*Patent Number: CN103328021A and Title: Protective device for protecting a port needle or Huber needle*)

- **Search Terms:**
  Huber needle support

- **Summary:**
  Abstract: A frame-like spacer for a port/Huber needle that protects the port needle puncture/incision site and protects against shifting.
  Background: When a port needle must stay in place for a prolonged period of time, an aseptic plaster was used to secure the needle in position to prevent movement. However, each case varies, and the needle can still move.
  Summary: The purpose of the device is to protect the port needle against movement more reliably than current methods.
  Claims: A spacer that surrounds the port needle. Spacer is fixed to skin with an adhesive layer. Spacer can be composed of glycerogel material.

- **Source:**

3. AG, P. M. Protective device for protecting a port needle or Huber needle. (2011).

Prior Art Reference #4 (*Patent Number: JP4573830B2 and Title: Device for securing a catheter to a patient's body*)

- **Search Terms:**
  Huber needle support
- **Summary:**
  Background/ Summary: Catheters are used to administer medicine to a patient, and require a diameter of catheter tubing smaller than that of the respective vein or artery. In central venous catheters, the catheter is connected to a support at the skin level. The support must be secured to the skin, and is susceptible to infection. Huber needles can also be used to access central venous catheters, but are not secured well at the skin and can also be susceptible to infection. The invention intends to reduce the risk of infection for said catheters, by protecting the skin puncture area. The device consists of a case that encloses the Huber needle imbedded into the patients catheter, and covers the exposed access sight. It consists of two chambers, housing a "pedestal," which passes liquid though to the catheter or needle.
  Claims: There are 21 claims. A case that can be closed with a lid. A pedestal that fixes the case to the skin Two connected chambers in the case separated by a partition. The pedestal has a small tank for connecting to the catheter and an outer tube. The first chamber has a thin membrane for attaching to the skin. There are two other raised portions on the inner surface of the lid.

- **Source:**

4. Device for securing a catheter to a patient's body. (2004).

Prior Art Reference #5 (*Patent Number: US 8,808.254 B2 and Title: Luer Receiver And Method For Fluid transfer*)

- **Search Terms:**
  Luer lock access, luer lock ports

- **Summary:**
  Abstract: Luer lock receiving septum with better resealing and penetration of the septum with low forces, using a central slit in the septum. Negative pressure is eliminated that occurs from withdrawal of Luer cannula
  Background / summary: Looking to link luer access devices with luer lock connectors. Allowing for a needle free access point. Meets the 9 characteristics of fluid access/ delivery (including: backward compatibility, no flow limitation, absence of negative pressure, low force of insertion, tip will remain in place, low profile, central flow path, fluid deployed into dead space, and similar cost to existing things). Invention has a central slit with low penetrations resistance and tight sealing lower septum. Shape will return upon removal of catheter.
  Claims: There are 18 claims. The male luer would have a distal tip and the luer receiving valve will have an inlet and outlet, a septum, a sealed slit partially through the septum. Male luer will go through the septum, septum will provide a sealing force to slit.

- **Source:**

5. Lynn, L. LUER RECEIVER AND METHOD FOR FLUID TRANSFER. 1–59 (2014).

**Prior Art Reference #6 (*Patent Number: US 2017/0043152 A and Title: Low Profile Venous Access Port Assembly)*

- **Search Terms:**
  Venous Access Port

- **Summary:**
  Abstract: The device can be described in four main parts: A housing base, a discharge stem, septum, and interior revisor.
  Background/ Summary: Venous access ports are implanted subcutaneously, attached to catheters and provide access to provide a method of infusion and withdrawal of fluids from patients, and can be accessed with a needle. This port differs from other venous access ports by having a shorter cap, housing base, and septum to reduce visibility of the port from the exterior of the body. Vertical ribs between the cap and the housing base are crushed during the last stages of assembly of the port, which precisely center the housing base in the cap, providing a centering system.
  Claims: There are 21 claims. Rounded, annular ridges on the discharge port that connect the catheter, recesses on the discharge port to help connect the catheter. Housing base and cap snap fit together.

- **Source:**

6. Bizup, R. LOW PROFILE VENOUS ACCESS PORT ASSEMBLY. 1–6 (2017).

Appendix C: Design and Development Plan

BIOMEDICAL ENGINEERING UNIVERSITY OF MISSISSIPPI Document Type: Form	QD006F01, Version A **Design and Development Plan**	
Medical Access Needless Port	DHF # QD006F01	D&D Plan Revision: C

Description of the Product

Executive Summary	Upon looking into unmet needs in the medical field, our company has seen that many patients have a large discomfort when receiving long term fluid treatments via intravenous access. Our company has spent the past few months looking into the problem as a whole, the market, budgeting, etc. We are aiming to create a needless port system that eliminates the discomfort caused by incorrect needle lengths. The needless port will allow patients to receive their treatment without the fear of needles and all the possible complications that can arise from improper port access. Many patients report discomfort and ports can become damaged if the port is not accessed correctly, or if the needle punctures the silicone portion of a port. Currently, there is a large profit margin (10.2%) within the venous accent market (6.5 billion of revenue), and with dialysis (2.5 billion of revenue). Neither market is completely dominated by one company, however the key players to keep in mind are BD and Baxter. They hold the largest portion of the market and tend to buy up other smaller companies. However, neither company has a large presence in the needleless port market. We will focus on a port system that uses luer locks to deliver drug and draw blood. This port can be used for chemotherapy, chemoradiation, and dialysis. We can market this product for individuals with needle phobia and those who dislike repeated injections. Our product will strive to be flush with the skin and come in varying sizes to best fit patients of varying weight and sizes. Based off of competitor pricing, cost of port is around $625/port with an 80% profit. We expect to finalize our CAD diagrams within the next 2 months and begin prototyping shortly after that. We will create a larger scale model and begin mechanical testing. Depending on our findings we will adjust where we need to and work to downsize the port size. Our team comprises of 3 Ole Miss senior BMEs, each with background of human physiology and growing knowledge of venous access devices. By the end of April, we aim to have a finalized prototype of our port system.
Description of the Problem to be Solved	Complications with intravenous access result from piercing or perforation of the septum by needles. Patients also commonly experience pain associated with needle insertion used to access the device, and experience "needle phobia."
Needs Statement	A way to better administer long term fluid treatment using venous access devices to eliminate patient discomfort and administration complications resulting from accessing the device via a needle.
Literature Review	Implanted vascular access devices (IVADs) are widely used for patients with poor peripheral venous access and patients who need long-term vascular access, such as but not limited to patients receiving chemotherapy, antibiotics, total parenteral nutrition, or frequent blood samples. Traditional intravenous infusion consists of repeated skin puncture, which can be damaging to veins and surrounding tissue over time. A catheter can be used for these applications as well, however, IVADs provide several advantages, including improved body image and minimizing maintenance while not in use, improved mobility, and lower infection rates. IVADs include a reservoir connected to a large vein through a catheter and are accessed by Huber needles. Huber needles are non-coring needles specially designed to access implanted

	vascular devices. Non-coring needles have a 45° angle at the end of the needle which prevents "coring," or the removal of silicon from the implant. Huber needles can vary in shape, length, diameter, mechanism of protection against the blood and bevel design. Upon insertion of an IVAD, the correct size and length of a Huber needle must be assessed based on the location of the port septum and the patient's body type. The smallest size needle appropriate for the patient must be used. If the needle length is too long, then the needle/port may be damaged upon insertion. If the needle length is too short, the needle may not pierce the septum. Sterile gauze squares should be placed under the wings of the port to support the access needle at a 90° angle if the access needle is not already in perfect position. Using sterile gauze squares to fix imperfect needle sizing has been a common practice for years. Gauze is a cheap material and serves as a cushion between the skin and the wings of the port. However, this practice should be reevaluated for the patient's comfort and safety. Using gauze to support a 90° angle may not ensure permanent stability for the duration of the needle's use. Additionally, patient injury such as a piercing of the septum may occur if the gauze is not properly applied. *See attached*
Prior Art Search, Assessment, & Patentability	Existing patents exhibit a general template design for IVADs. Most IVADs consist of a port that is puncturable with a specialized needle called a "Huber" needle and a catheter that attaches to the port and inserts into the desired vein. There are several patents filed to improve components of IVADs. Such patents include a device for securing a catheter to a patient's body and a protective device for protecting a port/Huber needle. In each patent, the main goal is to improve patient comfort and decrease chance of infection. Our company's goal is to optimize the overall design and cater to patients' comfort and health. We have evaluated each component of the current IVAD patents and come to the conclusion that the needle component of the IVAD can be eliminated. We plan to use the Luer lock system for our design along with a catheter and reservoir.
Competition & Differentiation	When comparing the different markets, a few different companies were involved in all 3 markets. Baxter makes up the majority of dialysis and a larger portion of the venous access market. The venous access market is more evenly spread out with over 150 companies. Baxter is seeing a large revenue growth due to small business acquisitions. Our company must be aware of this. Dialysis is dominated by Baxter and Fresenius. These companies typically buy up smaller companies leading to a monopoly. Hospital systems are continuing to get larger as they band together. They are not very competitive; insurance companies determine how reimbursement will go. The final thing that forces completion is the existence of group purchasing organizations. They have the ability to negotiate and hinder growth.
Value Proposition & Differentiation	A better venous access solution would limit patient complications and discomfort, while reducing the number of required accessory devices and overall cost of treatment.
Anticipated Regulatory Pathway	FDA- Class II device

Reimbursement Strategy	Insurance companies Medicare: CPT codes: 36560 (<5 years old insertion of subcut. port), 36561 (>5 years old insertion of subcut. port), 36590 (removal of device)
Estimated Manufacturing Cost	$700 for 80% profit margin for manufacturing based off of competitor prices of $3500, including cost of raw materials and labor
Potential Market & Global Impact	The Huber needle is the primary use for venous access for chemotherapy, dialysis, among other treatments. The venous access market is defined by the use of catheters, ports, and catheter securement devices. The venous access market will be the primary focus. Revenue is valued at 6.5 billion dollars with a 1.2% growth. There is a profit margin of 10.3%. There is a high profit margin and revenue growth. As the population continues to age, there is an expanding market for venous access. Dialysis makes up a part of the venous access and is worth 2.5 billion dollars. Profit margins are smaller due to low reimbursement rates. Dialysis is done primarily in dialysis centers and hospitals. Leading us to the last market, the hospital market. Hospitals have the largest revenue and profit, 968.6 billion and 68.8 billion dollars respectively. Hospitals have both inpatient and outpatient settings. Outpatient is cheaper to maintain and is more cost-efficient. All three of the previously mentioned markets are largely impacted by the reimbursement rates of insurance companies. Revenue can be limited by insurance companies, other companies, and other sources of funding. As time goes on the global market continues to grow, there has been an overall decrease in American exports and an increase in imports. They are coming out of Ireland and Mexico, and have cost less overall. Our company has to be aware of key players undercutting prices or attempting to buy out the company.
Intended Use / Indications for Use	The IRISPORT implanted port is indicated for patient therapies requiring repeated access to their vascular system. The port system can be used for infusion of medication, I.V. fluids, parenteral nutrition solutions, blood products, and for withdrawal of blood samples. When used with POWERPORTSYSTEMNAME the IRISPORT is indicated for power injection of contrast media. For power injection contrast media, the maximum recommended infusion rate is 5 mL/s with maximum pressure of 300 psi.
Patient Population	Chemo, dialysis, long term treatment patients
Materials	silicone suture holders, ChronoFlex C polyurethane plastic, radiopaque silicone
Features	Needless access, nonmetal, antibacterial biomaterials
Components	Catheter, reservoir, luer lock, luer lock connectors

User Needs

Transfer User Need # and Design Input to QD0006F02, Design Summary Matrix.

If a user need will not be fulfilled provide a rationale for not fulfilling need.

User Needs #	Description (User request)	Design Input or Rationale for Not Fulfilling Need
U1	Limit Use of needles	Luer lock for access
U2	Access the port easily	Luer lock to port for access
U3	Low infection rates	Antimicrobial materials, limit needle puncturing
U4	Able to be imaged	Nonmetal materials for MRI
U5	Can be used for contrast agents	Power injectable port
U6	Make port size smaller	Reduce septa size by alternate method of port access other than needles.
U7	Shorter treatment times	Increase flow rate with pump, plastic to withstand pressure
U8	Proper depth of device/aim to get device flush with skin	Vary sizes for patients to allow for the 1-3 mm depth
U9	Biocompatible	Using proven biocompatible materials

Part Number

Part Number	Description
IB001	Base behind the lid with peg attachments for PTL001, PTL002, PTL003, PTL004, PTL005
IL001	Iris opening base with opening for pegs for petals to slide open/close
RSV001	Port reservoir for fluid transfer
PTL001	Petal slide over one another to open/close the mechanical septa attach to IB001 and IL001 (1/5)
PTL002	Petal slide over one another to open/close the mechanical septa attach to IB001 and IL001 (2/5)
PTL003	Petal slide over one another to open/close the mechanical septa attach to IB001 and IL001 (3/5)
PTL004	Petal slide over one another to open/close the mechanical septa attach to IB001 and IL001 (4/5)
PTL005	Petal slide over one another to open/close the mechanical septa attach to IB001 and IL001 (5/5)

PG001	Pegs attached to PTL001, PTL002, PTL003, PTL004, PTL005
PG002	Pegs attached to IB001

[1] Document UDI if UDI needs to be included on the CAD and/or etched on the physical part.

Timeline

Attach a project timeline that defines at a minimum the project tasks, the name of the responsible team member, milestones, and the start date, and the due dates. The project timeline should be updated throughout the project and a copy of the current timeline should be reviewed during design review meetings. It is acceptable to use Excel, Project, or other project management tools.

Start Date	Due Date	Project Task	Milestones	Team Member
10/5/2021	10/21/2021	Researched User needs	Identified source of complications in current intravenous devices	Elizabeth
10/5/2021	10/21/2021	Researched Competitors and market information	Identified competitors, market size, and possible profit margins	Mallory
10/12/2021	10/25/2021	Looked at prior art	Identified similar products, broadened design ideas	Elizabeth, Mallory, Katie Rose
11/11/2021	NA	Researched design concerns	Identified methods of reducing infection rates Identified need for Power injectable ports	Elizabeth, Mallory, Katie Rose
11/16/2021	In Progress	Virtual Design	Hand drawn and converting to CAD/Blender	Katie Rose
2/8/2022	In Progress	Learn how to 3D Print	Go through info session/training	Elizabeth, Mallory, Katie Rose
2/8/2022	2/15/2022	Drawings/Specifications	revisions from review	Elizabeth, Mallory, Katie Rose
2/8/2022	2/15/2022	Tolerance Stack-Up	revisions from review	Elizabeth, Mallory, Katie Rose
2/8/2022	3/1/2022	Packaging Review	how twisting parts work together/with skin	Elizabeth, Mallory, Katie Rose
2/8/2022	3/10/2022	QD009F01 Failure Modes Effects Analysis	First draft	Elizabeth, Mallory, Katie Rose

2/8/2022	3/10/2022	QD009F02 Risk Mgmt Plan & Report	First draft	Elizabeth
2/8/2022	3/22/2022	QD006F04 Design Review 2	Get feedback from advisor and edit documents	Elizabeth, Mallory, Katie Rose
29-Mar	5-Apr	QD006F01 Design Development Plan	revisions from review	team
29-Mar	5-Apr	QD006F02 Design Summary Matrix	revisions from review	team
29-Mar	5-Apr	Validation Activities	fitting user needs and user friendly	team
29-Mar	5-May	QD009F01 Failure Modes Effects Analysis - Final	revisions from review	team
29-Mar	5-May	QD009F02 Risk Mgmt Plan & Report - Final	revisions from review	team
29-Mar	5-May	Regulatory Submission	finalized documents	team

Project Team

Function Required	**Name**
Product Development	Elizabeth Hale
Quality Assurance	Katherine Rose O'Quinn
Regulatory Affairs	Mallory Moffett
Independent Reviewer	Troy Drewry
Additional Functions As Needed	
Manufacturing	Katherine Rose O'Quinn
Sterilization	Mallory Moffett
Packaging	Mallory Moffett

Access Medical	DHF # QD006F01	D&D Plan Revision: C

Approvals			
Title	Name	Signature	Date
Product Development	Elizabeth Hale		4/7/2022
Quality Assurance	Katie Rose O'Quinn		4/7/22
Regulatory Affairs	Mallory Moffett		4/7/22
Independent Reviewer	Troy Drewry	Troy D. Drewry	4/7/22

Description of Design and Development Plan revisions.

Revision	Effective Date	Author	Description of Change
A	12/3/21	team	Initial Draft
B	1/27/22	team	Design Review #1
C	4/7/22	team	Design Review #2

Revision History (Form)

Version	**CR number**	**Approval Date**
A		12/3/21
B		1/27/22
C		4/7/22

Appendix D: Design Summary Matrix

BIOMEDICAL ENGINEERING UNIVERSITY OF MISSISSIPPI
Document Type: Form

QD006F02, Version A

Design Summary Matrix

Access Medical	DHF #2	Matrix Revision: C

User Need #[1]	Design Input[2]	Design Output[3]	Essential Req[4] (Yes/No)	Verification Activity[5]	Validation Activity[6]
U1	Luer lock for access	Polyurethane male and female luers (sterilized packaging)	Yes	Mechanical testing: compression tests Pull out test: ensures it can be connected properly without damaging skin	Animal testing, clinical study
U2	Luer lock to port for access	Polyurethane male and female luers (sterilized packaging)	Yes	Mechanical testing: compression tests Usability: liquid volumes can flow through	Animal testing, clinical study
U3	Antimicrobial materials, limit needle puncturing	ChronoFlex ® C polyurethane plastic (sterilized packaging)	Yes	Mechanical testing: compression tests	Animal testing, clinical study
U4	Nonmetal materials for MRI	ChronoFlex® C polyurethane plastic, radiopaque silicone (sterilized packaging)	No	Mechanical testing: compression tests Image testing looking at the radiopaque material	Animal testing, clinical study
U5	Power injectable port	ChronoFlex® C polyurethane plastic, radiopaque silicone (sterilized packaging)	No	Can properly pump liquid volumes through the device	Animal testing, clinical study

Access Medical	DHF # 2	Matrix Revision: C

U6	Reduce septa size by alternate method of port access other than needles.	ChronoFlex® C polyurethane plastic, radiopaque silicone (sterilized packaging)	No	Mechanical testing: compression tests Usability: maintain similar volumes and minimal shearing	Animal testing, clinical study
U7	Increase flow rate with pump, plastic to withstand pressure	ChronoFlex® C polyurethane plastic, radiopaque silicone (sterilized packaging)	No	Mechanical testing: compression tests	Animal testing, clinical study
U8	Vary sizes for patients to allow for the 1-3 mm depth	ChronoFlex® C polyurethane plastic, radiopaque silicone (sterilized packaging)	Yes	Mechanical testing: compression tests	Animal testing, clinical study
U9	Prevent shearing of blood cells	Vortex and have smooth edges	Yes	Test with simulated blood to see if they shear after flowing through device	Animal testing/clinical trials following simulated blood trial

[1]Need # from QD006F01, Design and Development Plan

[2]Design Inputs are to be reviewed by team to ensure they are complete, not ambiguous, and do not conflict.

[3]Design outputs should include catalog numbers, drawings/specifications, material specifications, sterilization, packaging, labeling, features/components of the device, etc.

[4]Essential design requirements include those that if they are not met the product could cause harm to a patient or the device could malfunction. The essential design requirements are the features of the design that are deemed critical for function of the component. For these features, validation of the final parts should be performed or alternatively, 100% inspection of the essential design output requirement features may be performed.

[5] Verification activities could include mechanical testing, animal testing, review of drawings/specifications, tolerance stack-ups, labeling reviews, packaging, etc. List applicable document numbers and document names.

[6] Validation activities could include animal testing, clinical studies, saw bone labs, cadaver studies, visual inspection of product, etc. List applicable document numbers and document names.

Access Medical	DHF # 2	Matrix Revision: C

Add Rows as needed

Approvals			
Title	Name	Signature	Date
Product Development	Elizabeth Hale		4/7/2022
Quality Assurance	Katie Rose O'Quinn		4/7/22
Regulatory Affairs	Mallory Moffett		4/7/22
Independent Reviewer	Troy Drewry	Troy D. Drewry	4/7/22

Description of matrix revisions.

Revision	Effective Date	Author	Description of Change
A	12/3/21	team	Initial Draft
B	1/27/22	team	Design Review #1
C	4/7/22	team	Design Review #2

Revision History (Form)

Version	CR number	Approval Date
A		12/3/21
B		1/27/22
C		4/7/22

Appendix E: Risk Management Plan

BIOMEDICAL ENGINEERING UNIVERSITY OF MISSISSIPPI Document Type Form	QD009F02, Version A **Risk Management Plan and Report**

Project Name:

1. Purpose of Revision

☒ Risk Management Plan (initial) ☐ Risk Management Report

☐ Modification to Risk Management Plan ☐ Modification to Risk Management Report

2. Plan and Report Approvals

Revision	Team Member Function	Team Member Name (printed)	Team Member Approval Signature	Date
A	Product Development	Elizabeth Hale		4/7/2022
	Quality Assurance	Katie Rose O'Quinn		4/7/22
	Regulatory Affairs	Mallory Moffett		4/7/22
	Executive Management	Troy Drewry	Troy D. Drewry	4/7/22
	Other			

3. Risk Management Details

Risk Management Plan: This Risk Management Plan outlines Risk Management activities for the lifecycle of the products listed in Table 1-3 from the initial product development through post market surveillance. Post market surveillance will be performed as needed, but at a minimum an annual review is required for each product, as outlined in QD006, Design and Development.

Table 1: Part Number

Part Number	Description
IB001	Base behind the lid with peg attachments for PTL001, PTL002, PTL003, PTL004, PTL005
IL001	Iris opening base with opening for pegs for petals to slide open/close
RSV001	Port reservoir for fluid transfer
PTL001	Petal slide over one another to open/close the mechanical septa attach to IB001 and IL001 (1/5)

PTL002	Petal slide over one another to open/close the mechanical septa attach to IB001 and IL001 (2/5)
PTL003	Petal slide over one another to open/close the mechanical septa attach to IB001 and IL001 (3/5)
PTL004	Petal slide over one another to open/close the mechanical septa attach to IB001 and IL001 (4/5)
PTL005	Petal slide over one another to open/close the mechanical septa attach to IB001 and IL001 (5/5)
PG001	Pegs attached to PTL001, PTL002, PTL003, PTL004, PTL005
PG002	Pegs attached to IB001

Add rows as needed or attach list.

Table 2: Indications for Use

Indications for Use	The IrisPort implanted port is indicated for patient therapies requiring repeated access to their vascular system. The port system can be used for infusion of medication, I.V. fluids, parenteral nutrition solutions, blood products, and for withdrawal of blood samples. When used with contrast media the IrisPort is indicated for power injection of contrast media. For power injection contrast media, the maximum recommended infusion rate is 5 mL/s with maximum pressure of 300 psi.
Foreseeable Misuse (In what way(s) might the medical device be deliberately misused?)	Insertion of nonmedical objects into port; at home operation; reusing connector piece.

Table 3: Description of the Product

Risk Item	Description
Materials and / components	Titanium/polyurethane/silicone
Energy delivered to and/or extracted	N/A
Substances delivered to and / or extracted from the patient	Delivered: Chemotherapy, antibiotics, IV fluids, medication, contrasting agents for imaging (MRI) Extracted: Blood/blood components (apheresis)
Duration of Use	At least 6 months, up to 6 years
What is the lifetime of the device?	Up to 6 years
Biological materials processed by the device for subsequent re-use	N/A
Supplied sterile or intended to be sterilized by users	Supplied sterile to user

Risk Item	Description
Intended to be routinely cleaned and disinfected by the user	Yes, routine cleaning will be done by flushing fluids. The outside of the device should also be cleaned regularly with non harsh cleaning solutions. Change dressing at least every 7 days, or more frequently if needed. Site scrub to clean surrounding area. Biopatch around the port site. Aquaguard shield.
Intended to modify the patient environment?	No
Measurements?	Measuring the correct incision diameter and depth for the port during implantation by the surgeon.
Is the device interpretative?	No
Intended for use in conjunction with medicines or other medical technologies?	Yes, it will be used to deliver drugs, connect to iv kits, contrast, etc.
Unwanted outputs of energy or substances?	Yes, possible leaking of circulatory fluids.
Is the device susceptible to environmental factors?	Yes, it is susceptible to pathogens, water exposure could possible effect device performance, material wear.
Essential consumables or accessories associated with the device?	Yes, there will be an adaptor to connect device to tubing, injection
Routine maintenance and/or calibration?	Yes, the port will need to flushed regularly to prevent occlusions
Software?	No
Restricted "shelf life"?	No
Is the device subject to mechanical forces?	Yes

Risk Item	Description
Is the device intended for single use?	The device is not intended to be reimplanted, however it is intended to be repeatedly used for transfer of fluids to the circulatory system. All other associated devices are intended to be single use.
Is safe disposal of the medical device necessary?	It will be considered biowaste and must be disposed properly.
Is installation or special training required?	Yes, there will be a surgical protocol to follow for implantation into the patient. There will also be a manual of how to access the device.
How will information for safe use be provided?	In a user manual
Can the user interface design features contribute to user error?	Yes, they could break the opening mechanism or cause skin irritation.
Is the medical device used in an environment where distractions can cause use error?	Yes, hospitals and doctor offices can be hectic. Emergency circumstances can also lead to error of use.
Will new manufacturing processes be established or introduced?	No
Is device critically dependent on human factors such as user interface?	Yes, the user must use the opening mechanism and adaptor to access the port
Does device have connecting parts or accessories?	Yes, a specific connector will be required to unlock the device.
Does device have control interface?	No
Does device display information?	No

Risk Item	Description
Is device controlled by menu?	No
Will the medical device be used by persons with special needs?	Possibly
Can the user interface be used to initiate user actions?	No
Does the medical device use an alarm system?	No
Does the medical device hold data critical to patient care?	No
Is device intended to be mobile or portable?	No it will be implanted
Does the user of the medical device depend on essential performance?	Yes, the user should not touch the device while in use.

Add Rows as needed

3.1. For each risk area, mitigation activities actions are defined that are typically examined as part of risk management. For each action, the appropriate evidence consists of several different items. The evidence documents (physical copies or references) are placed in the Design History File and/or Risk Management File.

3.2. The following documents, at a minimum, should be included in the Risk Management File for each product:

3.2.1. Complaint Review

3.2.2. Clinical / Literature Review

3.2.3. Risk Analysis

3.2.4. Trending related to product complaints, CAPAs, Non-Conforming Reports (NCR)

4. Risk Management Report

4.1. At the completion of the project, this document becomes the cover sheet for the Risk Management Report. Documents are compiled and approved to verity that risk mitigation evidence is complete or a rationale has been written to justify whey the activity was not necessary. Any key assumptions should be included in the objective evidence or rationale. Mark the items included in the report. For items not included a rationale to justify why the activity is not necessary must be attached.

☐ Complaint Review

☐ Clinical / Literature Review

☐ Risk Analysis

☐ Trending related to product specific complaints, CAPAs and/or NCRs

For items not included provide a rationale to justify why activity was not necessary:

Comments: ☐ n/a

5. Risk Acceptance Criteria

5.1. Risk acceptance is defined in QD006, Design and Development and QD009F01, FMEA and document in the risk analysis.

6. Risk / Benefit Summary

6.1. Document an assessment of overall residual risk, if applicable.

6.2. Address the following questions:

6.2.1. Is the risk level acceptable? ☑ Yes ☐ No

6.2.2. Do the benefits outweigh the potential risk? ☑ Yes ☐ No

If risk level is not acceptable, document how the benefits outweigh the potential risk.

Comments: ☐n/a

7. Post Market Surveillance

7.1. Post market surveillance will consist of periodic review and update, as needed, of applicable risk management documents, but at a minimum an annual review is required for each product, as outlined in QD006, Design and Development.

7.2. Specific post market surveillance activities will typically include complaint and adverse event analyses and review/update of appropriate risk analysis documents (i.e., FMEA).

8. Dates

8.1. Anticipated Launch Date: TBD

8.2. Next Risk Management Review (Month/Year): TBD

Revision History (Form)

Version	CR number	Approval Date
A		4/7/22

Appendix F: Failure Modes and Effects Analysis (FMEA)

Failure Modes and Effects Analysis (FMEA)

Process or Product Name:	Access Medical Iris Port					Prepared by: Elizabeth Hale								
						FMEA Date (Orig):		(Rev:)	A		CR			

Risk #	Feature / Function	Potential Failure Mode	Effects of Failure	SEV	Potential Causes	OCC	Current Controls	Risk Index	Recommended Actions (if needed)	Responsible Person(s)	Actions Taken	SEV	OCC	Risk Index
#	What is the feature/function under investigation?	In what ways does the key input go wrong?	What is the impact on the key output variables (customer requirements) or internal requirements?	How severe is the effect to customer?	What causes the key feature/function to go wrong?	How often does cause or failure mode occur?	What are the existing controls that prevent either the cause or the failure mode?	Severity x Occurrence	What are the actions for reducing the RPN. Should have actions only on high RPN's or easy fixes.	Who is responsible for the recommended action?	What actions have been taken and date completed?			
1	Iris Mechanism	does not close properly	leaking blood/bodily fluids	4	misalignment of iris leaves	2	polyurethane or silicone flexible lip material that closes within the leaf directly adjacent. device quality checklist after implantation for surgeon	8	Device quality check after manufacturing	Quality assurance	designed an advanced flexible lip closing mechanism 2/28/2022	4	2	8
2	Iris Mechanism	not opening properly	inability to apply treatment; infection	3	blood buildup within mechanism closing mechanisms	2	flushing/ proper care of port. Proper sealing of exposed moving pieces. Antibacterial coatings on exposed surfaces	6	routine cleaning, dressing replacement	Nurse, user		3	2	6
3	adaptor	not fitting	inability to apply treatment	2	manufacturer error; improper assembly of port	1	port preassembled; device quality checklist after implantation for surgeon	2		surgeon		2	1	2
4	Iris Mechanism	negative pressure in port	leaking blood/bodily fluids	4	PTL seal material inefficient; locking mechanism inefficient	2	durable, flexible material lining iris mechanism; lock to maintain tight closed seal	8	removal of device	surgeon		4	2	8
5	Iris Mechanism	improper sealing ability	leaking blood/bodily fluids	4	PTL seal material inefficient; locking mechanism inefficient	2	durable, flexible material lining iris mechanism; lock to maintain tight closed seal	8	removal and replacement of device	surgeon		4	2	8
6	Port Material	Rejection of implant material	Requires removal, adverse immune reaction	4	The port material	2	biocompatible materials; use of existing successful implant material	8	removal of device	surgeon		4	2	8
7	Adaptor	Intrathoracic pressure becomes less than atmospheric pressure at catheter	Air embolism	4	Inefficient seal; not flushing before/after use	2	Luer-lock IV equipment used, extension tubing clamped at all times with IVAD not in use	8	routine protocol for air embolism; removal of device	nurse/ surgeon		4	2	8

Risk #	Feature / Function	Potential Failure Mode	Effects of Failure	SEV	Potential Causes	OCC	Current Controls	Risk Index	Recommended Actions (if needed)	Responsible Person(s)	Actions Taken	SEV	OCC	Risk Index	
#	What is the feature/function under investigation?	In what ways does the key input go wrong?	What is the impact on the key output variables (customer requirements) or internal requirements?	How severe is the effect to customer?	What causes the key feature/function to go wrong?	How often does cause or failure mode occur?	What are the existing controls that prevent either the cause or the failure mode?	Severity x Occurrence	What are the actions for reducing the RPN. Should have actions only on high RPN's or easy fixes.	Who is responsible for the recommended action?	What actions have been taken and date completed?				
8	Iris Mechanism	leaves becoming unattached from bottom of iris mechanism	leaking blood/bodily fluids	4	loosening of PTLs of PG1	2	add a head to the bottom pegs to permanently hold the leaves in place	8	surgery to tighten screws in PG3; possible removal of device	surgeon	added cap design feature to PG1	4	2	8	
9	Port Material	port moves under skin	infection from increased wound exposure; patient discomfort	2	unsecure stitching; tear in port material that stitch is secured to; user misuse	3	stitchable material on port below surface allowing for port to be secured in place.	6	replace stitching or port casing	suregon		2	3	6	
10	Port Material	scar formation	port discomfort; appearance	2	incision site from continuously open wound forms advanced scaring	2	stitching port in place	4				2	2	4	

Scales

Severity (SEV)		
Ranking	Definition	Effect
5	Catastrophic	Device failure or defect may cause death or permanent injury with or without warning of failure
4	Severe	Device failure or defect will cause severe injury which would necessitate revision surgery
3	Moderate	Failure renders device useless or will result in a minor injury of a non-permanent nature
2	Minor	Failure will result in no loss of product performance but may create some annoyance to user
1	None	No effect
Occurrence (OCC)		
Ranking	Definition	Frequency
5	Extremely High	Failure almost inevitable
4	High	Repeated failure
3	Likely	Occasional failure
2	Rare	Failure unlikely
1	Remote	Remote chance of failure

Revision

Version	CR Number	Approval Date
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REFERENCES

1. Wells, S. Venous access in oncology and haematology patients: Part two. *Nurs. Stand.* **23**, 35–42 (2008).

2. Armenteros-Yeguas, V. *et al.* Prevalence of difficult venous access and associated risk factors in highly complex hospitalised patients. *J. Clin. Nurs.* **26**, 4267–4275 (2017).

3. McLenon, J. & Rogers, M. A. M. The fear of needles: A systematic review and meta-analysis. *J. Adv. Nurs.* **75**, 30–42 (2019).

4. Blanco-Guzman, M. O. Implanted vascular access device options: a focused review on safety and outcomes. *Transfusion* vol. 58 558–568 (2018).

5. Wildgruber, M. *et al.* Polyurethane versus silicone catheters for central venous port devices implanted at the forearm. *Eur. J. Cancer* **59**, 113–124 (2016).

6. Peynircioglu, B., Canyigit, M., Ergun, O., Pamuk, G. & Cil, B. Radiologically Placed Venous Ports in Children. *J. Vasc. Interv. Radiol.* **18**, P1389-1394 (2007).

7. Preventing Infections in Cancer Patients. *Centers for Disease Control and Prevention* https://www.cdc.gov/cancer/preventinfections/providers.htm#:~:text=Each year%2C about 650%2C000 cancer,chemotherapy schedules%2C and even death. (2021).

8. Wilson, B. E. *et al.* Estimates of global chemotherapy demands and corresponding physician workforce requirements for 2018 and 2040: a population-based study.

Lancet Oncol. **20**, 769–780 (2019).

9. American Cancer Society. Cancer Treatment and Survivorship Facts and Figures 2019-2021. *Am. Cancer Soc.* 1–48 (2019).

10. Clare, C. S. Role of the nurse in acute stroke care. *Nurs. Stand.* **35**, 68–75 (2020).

11. Mendu, M. L. *et al.* Non-Tunneled versus tunneled dialysis catheters for acute kidney injury requiring renal replacement therapy: A prospective cohort study. *BMC Nephrol.* **18**, 1–7 (2017).

12. Dialysis: Types and overview: Concise medical knowledge. *Lecturio* https://www.lecturio.com/concepts/overview-and-types-of-dialysis/ (2022).

13. Anderson, R., Doyle, G. R. & McCutcheon, J. A. Clinical Procedures for Safer Patient Care. *Thompson Rivers University* https://pressbooks.bccampus.ca/clinicalproceduresforsaferpatientcaretrubscn/chapter/8-3-types-of-venous-access/ (2018).

14. Wynne, D. Your clinical guide to implanted ports and non-coring needles. *Br. J. Nurs.* **30**, 1–7 (2021).

15. Implanted Venous Access Devices (Port-A-Cath®). *Premier Oncology Hematology Associates* https://www.premieronc-hem.com/device/.

16. Camp-sorrell, D. Troubleshooting complications of vascular access devices. **4**, 19–25 (2011).

17. Curran, J. Venous Access Device Manufacturing. *IBISWorld* 1–41 (2021).

18. NIH. Financial Burden of Cancer Care. *National Cancer Institute*

https://progressreport.cancer.gov/after/economic_burden (2021).

19. Holcomb, G. Dialysis Equipment Manufacturing. *IBISWorld* 1–38 (2020).

20. May, J. C. Hospitals in the US. *IBISWorld* 1–40 (2021).

21. Medical, C. Central Venous Lines , PICCs , Ports and Pumps. (2012).

22. Sundaram, J., Agarwal, P., Ramasundaram, M. & Barathi, S. Implantable Venous Access Devices in Pediatric Malignancies - Institutional Experience in a Developing Nation. *J. Indian Assoc. Pediatr. Surg.* **25**, 286–290 (2020).

23. Sessler, D. NEWSLETTER. *J. Anesth. Patient Saf. Found.* **36**, 89–129 (2021).

24. Zare, M., Ghomi, E. R., Venkatraman, P. D. & Ramakrishna, S. Silicone-based biomaterials for biomedical applications: Antimicrobial strategies and 3D printing technologies. *J. Appl. Polym. Sci.* 1–18 (2021) doi:10.1002/app.50969.

25. Sidambe, A. T. Biocompatibility of advanced manufactured titanium implants-A review. *Materials (Basel).* **7**, 8168–8188 (2014).

26. Marois, Y. & Guidoin, R. *Biocompatibility of Polyurethanes*. (Landes Bioscience, 2013).

27. alibaba.com. *alibaba* (2022).

28. CENTRAL VENOUS ACCESS DEVICES (CVADs): CARE AND MAINTENANCE OF IMPLANTED VENOUS ACCESS DEVICES (IVADs). *BC Cancer Agency* (2016).

29. Administration, U. S. F. & D. FDA Executive Summary Reduction of Ethylene

Oxide Sterilization Emissions for Medical Devices and Potential for Utilizing Other Sterilization Modalities. 1–21 (2019).

30. Rutala, W. A. & Weber, D. J. Guideline for Disinfection and Sterilization in Healthcare Facilities, 2008. *Bennett Brachman's Hosp. Infect. Sixth Ed.* (2013) doi:10.1017/9781107153165.009.

31. Cardinal Health TYVEK Sterilization Pouches - Sterilization Pouch, Heat-Seal, 10" x 15" - 91015. *Grayline Medical* https://www.graylinemedical.com/products/cardinal-health-tyvek-sterilization-pouches-sterilization-pouch-heat-seal-10-x-15-91015?variant=31850105405497&gclid=Cj0KCQjw06OTBhC_ARIsAAU1yOWnBQoXqlLhxiaanriHyF9_Z3LOBOMjWTUR20GlxNNUiG9bU5QxYtcaAkjeEALw_wcB.

32. Venus Box. *MakerBot Thingiverse* https://www.thingiverse.com/thing:1559232 (2016).

33. Spheroid. *Wikipedia* https://en.wikipedia.org/wiki/Spheroid (2022).

34. Walser, E. M. Venous access ports: Indications, implantation technique, follow-up, and complications. *CardioVascular and Interventional Radiology* vol. 35 751–764 (2012).

35. Fidder, H., Botes, A., Woudberg, S. & McGrath, P. J. Characterization of microstructure and fatigue life of CP titanium grade 2 specimens subject to various bending processes. *WIT Trans. Eng. Sci.* **78**, 25–33 (2013).

36. What is Torsion Testing? *INSTRON* https://www.instron.com/en-us/our-company/library/test-types/torsion-test.

37. Al-ahmad, A., Al-zahrani, A. & Al-shehri, M. Torsional property of Nano Structured Titanium for use in Biomedical Application. (2017).

38. Fastening torque - Capability Statements. *Mecmesin* https://archive.mecmesin.com/fastening-torque-capability-statements.

39. An Examination of Needle and Syringe force testing. *Mecmesin* https://archive.mecmesin.com/an-examination-of-needle-and-syringe-force-testing.

40. U.S. Food & Drug Administration. Use of International Standard ISO 10993-1, "Biological evaluation of medical devices-Part 1: evaluation and testing within a risk management process" guidance for industry and Food and Drug Administration staff. *U.S. Dep. Heal. Hum. Serv. Food Drug Adm.* 1–68 (2020).

41. Nalezinková, M. In vitro hemocompatibility testing of medical devices. *Thromb. Res.* **195**, 146–150 (2020).

42. Slee, J. B., Alferiev, I. S., Levy, R. J. & Stachelek, S. J. The use of the Ex Vivo Chandler Loop Apparatus to assess the biocompatibility of modified polymeric blood conduits. *J. Vis. Exp.* 1–8 (2014) doi:10.3791/51871.

43. FDA. 0027-Guidance for Industry Pyrogen and Endotoxins Testing: Questions and Answers. *Required* **1**, 1–10 (2012).

44. CYCLIC POLARIZATION TESTS. *METALogic* (2017).

45. Esmailzadeh, S., Aliofkhazraei, M. & Sarlak, H. Interpretation of Cyclic

Potentiodynamic Polarization Test Results for Study of Corrosion Behavior of Metals: A Review. *Prot. Met. Phys. Chem. Surfaces* **54**, 976–989 (2018).

46. Swindle, M. M., Smith, A. C. & Helke, K. Recommendations for medical device implantation in swine. *Isr. J. Vet. Med.* **68**, 3–11 (2013).