Reducing Delays in the Dialysis Treatment

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Reducing Delays in the Dialysis Treatment

A Major Qualifying Project

Submitted to the faculty of

Worcester Polytechnic Institute

in partial fulfillment of the requirements for the

Degree of Bachelor of Science

in Mechanical Engineering

by

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Approved        April 30, 2015

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Abstract

The functions of the kidneys include maintenance of acid-base balance, water removal, electrolyte balance, toxin removal, blood pressure control, erythropoietin production, and the metabolism of Vitamin D. The kidneys accomplish these vital functions by filtering approximately 180 liters of blood plasma each day, but if they fail they are no longer able to perform these tasks. In the United States, the two leading causes of kidney failure are diabetes and high blood pressure. Hemodialysis is a type of dialysis treatment, which is an artificial process that is able to imitate the functions of the kidneys. The treatment process encompasses the removal of blood from the patient, pumping it through an external filtering system, and returning the cleaned blood to the body. Each treatment takes approximately three to four hours and typically a patient can receive hemodialysis treatment three to four times per week. During this process, treatment delays are common occurrences. Primary sources of delays exist within the tubing system, the water treatment system, the dialyzer, and the needle attachment process. The goal of this project is to present alternative designs and suggestions that can be used to reduce treatment delays in the hemodialysis process. We researched and recommend designs including a modified cartridge, which is based on an existing patent, an armband needle-holding fixture and incorporating a new implementation of tubing. These designs focus on reducing travel time for blood, securing the needle to the patient, increasing the efficiency of the dialyzer, and reducing water contamination. The effectiveness of the results outlined in this report are determined by comparison to relevant hemodialysis literature, thus making the treatment faster, safer, and more comfortable for the patient.
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Acknowledgements

This project could not have been completed without the help of Professor Mustapha Fofana of Worcester Polytechnic Institute. The staff of the DaVita dialysis center in Worcester was instrumental in supplying tools and imparting knowledge to help during the research process. Patty Conwell, a registered nurse at DaVita, also provided us with information and resources, which assisted in the completion of the project. We would like to give a special thank you to biomedical graduate student Kelsey Wall of Worcester Polytechnic Institute for working closely with the students to help ensure a successful conclusion of the project.
CHAPTER 1. PROJECT MOTIVATION

2. Introduction

Chronic kidney disease (CKD) is a worldwide public health issue. It is a common condition in which there is progressive loss of renal function over time. CKD is the ninth leading cause of death in the United States, with diabetes and high blood pressure being responsible for the majority of cases; they account for 38.4 and 25% of CKD diagnoses, respectively. Many people with CKD may be unaware of their illness because the symptoms of worsening kidney function are general and can easily be mistaken for other things. For this reason, routine screenings are performed on people that are considered to be at a high risk for kidney failure, such as those who already have diabetes or high blood pressure, or the elderly. Once the kidneys are unable to function and no longer remove waste and excess fluids from the body, either a kidney transplant or dialysis is necessary to sustain life.

Many applicants for kidney transplants are placed on a long waiting list due to the shortage of donated kidneys. Therefore, hemodialysis is a common option for patients with severe chronic kidney disease. Hemodialysis allows a patient’s blood to be pumped through a dialysis machine by connection through a surgically created access point, commonly located on the arm. In the machine, the blood is mixed with a dialysate mixture specific to each patient, which cleans the blood before it is pumped back into the patient. While dialysis effectively allows a person with CKD to extend the length of their life, it is also an uncomfortable and time-consuming process that can lead to that person’s loss of independence. The primary goals of this project were to identify and reduce sources of
delays that take place during dialysis treatment, to improve upon safety wherever possible, and to increase patient comfort. To accomplish these goals, the team completed three objectives. First, research was conducted to gain knowledge about dialysis delays. Second, designs were established to reduce the treatment delays. Lastly, the team analyzed the effectiveness of the components in terms of treatment delays.

The remainder of this report consists of chapters that highlight these essential components of the project. Chapter 2 provides an overview of the role of kidneys in the human body and describes what happens when they fail. Additionally, the dialysis process is explained and new options are explored. Chapter 3 presents the alternative designs and recommendations for reducing treatment delays in hemodialysis. These designs include a modified cartridge, which houses the extracorporeal circuit of the dialysis process, a needle-holding fixture, and a means to simplify the tubing system. The effectiveness of the results outlined in this report are determined by comparison to relevant hemodialysis literature and clinical studies. Chapter 4 concludes the report, discussing the project objectives, constraints, and recommendations for further improvement.
CHAPTER 2. KIDNEY DIALYSIS

2. Introduction

The definition of dialysis includes any separation of substances in solution by means of their unequal diffusion through semipermeable membranes. In a medical sense, however, dialysis refers specifically to the removal of wastes or toxins from the blood through these methods. Since the kidneys perform just such functions, medical dialysis can be used when kidneys are unable to perform for whatever reason. Naturally, to understand dialysis, one must first gain an understanding of kidney operation. This section will explore the fascinating workings of the kidneys and various courses of action to take if they should fail.

2.1 The Human Kidneys

The human kidneys are two bean-shaped organs, weighing approximately 5 ounces each. They are 11cm in length, 5cm wide, and 3cm thick. They are located in the dorsal abdominal cavity in the retroperitoneal space and are the most sophisticated filters known to man. The kidneys are kept in place by a renal capsule and are protected by layers of fat. The kidneys receive between 1000 to 1200 mL of blood every minute (Azar, 2013). Each day, they filter through a total of approximately 180 liters of blood. This filtration process is complex and specific to the human body, making it a very difficult task to completely replicate.
2.1.1 Healthy Kidneys

When kidneys are healthy and functioning properly, they perform a number of very crucial tasks for the human body. They maintain the balance of acids and bases, remove excess water and toxins, balance the level of electrolytes, control blood pressure, produce erythropoietin, and metabolize Vitamin D. Below, in Figure 1, is a diagram breaking down the parts of the nephron and the paths in which the blood travels through.

![Figure 1: Parts of the Nephron](image)

Figure 1 shows where blood enters and exits the kidney, and where urine exits. The blood goes into the kidney through the renal artery and then separates into the anterior and posterior branches, which return blood via the renal vein. The nephron of an operational kidney is what the filtrate flows through each day, which is also called glomerular filtration. Nephrons are approximately one million microscopic units and produce urine. The production of urine is crucial because it rids the body of excess fluids, electrolytes, and wastes.
The diagram in Figure 2 shows a more detailed diagram of the structure of a healthy kidney. It shows a cross-section, which highlights the major components of a kidney.

![Figure 2: The Human Kidney](image)

The kidney contains renal arteries and veins, which draw in and drain blood to and from the kidney, respectively. The figure also shows the kidney medulla, the innermost portion of the kidney that holds the nephrons.

2.1.2 Modes of Failure in the Kidneys

Renal failure, also known as kidney failure, is when there is a reduction in the normal kidney function (i.e. removing wastes from body and excess water). The two leading causes of kidney failure mentioned previously, diabetes and high blood pressure, can impact any demographic. According to the National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC), chronic kidney failure is increasing at the fastest rate in senior citizens. The incidence of recognized CKD in people aged 20–64 is less than 0.5%.
Once both kidneys begin to fail, all of the crucial functions of a kidney begin to slow down and eventually halt altogether. When the production of urine decreases, there is a buildup of fluid throughout the body that can cause various ailments such as hypertension (abnormally high blood pressure), edema (excess fluid in body cavities and tissues), and dyspnea (difficulty breathing). This decrease in urine production also leads to a dangerous increase in electrolyte levels. One electrolyte in particular, potassium, can lead to deadly changes in the rhythm of the heart. High phosphorous (another electrolyte) levels lead to bone disease and calcification of blood vessels. There is an enormous amount of possible conditions, diseases, and ailments that stem from having unhealthy kidneys. For this reason, it is imperative to be able to recognize when kidneys are headed toward failure, to properly classify kidney disease, and to make sure that a person suffering from this disease receives the proper treatment.

There are two types of renal failure: acute and chronic. As the names suggest, chronic kidney failure occurs gradually over a long period of time, whereas acute kidney failure happens very rapidly over the course of days or even hours. It is less likely that kidneys will fail quickly so CKD is more common. Chronic kidney disease usually takes years to progress, which can allow for intervention in the form of lifestyle changes and medicine. If it is caught early enough, the progress of CKD can be delayed greatly. Chronic kidney disease is broken down into five major stages, which are classified by the glomerular filtration rate, or GFR. GFR is a measure of how well kidneys are working and can be calculated by a doctor with an equation incorporating blood creatinine test results along with factors such as a patient’s age, ethnicity, gender, height, and weight. The higher the GFR, the more efficiently the kidneys are functioning.
A person with a glomerular filtration rate of 90 or more is classified as stage one CKD which is normal kidney function but may have signs indicating potential kidney disease. A GFR of 60-89 indicates stage two CKD, which is mildly reduced kidney function. A glomerular filtration rate of 30-59 is stage three CKD. A GFR falling between 15 and 29 is stage four, while a GFR of less than 15 is classified as stage five CKD, also known as end stage renal disease, or ESRD. At this final stage of CKD, the kidneys have almost lost all ability to do their job. It is at this point in the CKD progression that treatment or a kidney transplant is absolutely necessary in order to live (Renal Association, 2013).

Patients with chronic renal failure cannot be helped unless treatment is started promptly. Possible causes of chronic renal failure are diabetes, uncontrolled hypertension, polycystic kidney disease, and other genetic illnesses. In some cases of kidney failure, people don’t realize their kidneys aren’t functioning properly because of the adaptability of kidneys. This is why it is possible to live with only one functioning kidney. The surviving kidney would increase its activity to make up for the failed one. In most cases, patients will not notice any symptoms in early stages of kidney disease. It is once the kidney’s function drops to less than 10% that the body begins to retain toxic wastes and extra fluids, leading to swelling and high blood pressure. Due to the other effects that this retention of fluids causes such as difficulty breathing, anemia, and weak bones, many people also develop cardiovascular disease (DaVita, 2015).

2.1.3 Kidney Treatment Options

A person cannot live without at least one functioning kidney. Therefore, once both kidneys have begun to fail, a patient must immediately seek medical attention. The preferred solution is a kidney transplant, however it is very difficult to qualify for one, and
the surgery is risky (About Kidney Transplantation, 2015). If a person is unable to get a kidney transplant, other treatment options must be sought. Dialysis is an artificial process that keeps your body in balance when your kidneys can no longer function properly. The treatment acts to mimic the work done by kidneys in filtering blood, removing water and waste products, maintaining a safe level of chemicals in your blood, and controlling your blood pressure. While this process has been advanced greatly over time and serves to provide a proverbial lifeline for many people, dialysis cannot completely replace a healthy kidney. Medicines are required in addition to the treatment to replace the endocrine functions. Dialysis alone will not act as a fully functioning kidney; however, it is extremely helpful in reducing effects and improving the patient’s quality of life. Dialysis treatment can be administered anywhere from a few times per week to several times daily. Traditionally, a patient can expect to visit a clinic three to four times per week for three to five hours per session. The more frequently sessions are held, the shorter each session needs to be. With more improvements to dialysis machines, making them smaller and more user-friendly, it is now even possible for dialysis to be performed at home. Aside from the possible necessity of special wiring or plumbing, the only requirements for at home dialysis are to have enough space, supplies, and a water purification machine. Most people who do home dialysis have a helper or nurse who train them ahead of time at a clinic.

Dialysis is not performed exclusively for people with chronic kidney disease; it can be used whenever something needs to be filtered out of the blood. Short-term or urgent dialysis, as the name suggests, is performed under more urgent settings. The aforementioned acute kidney failure is one such instance. This type of sudden kidney failure can be caused by a number of things including but not limited to: direct physical
damage to the kidneys, cholesterol deposits, glomerulonephritis, infection, lupus, certain medications, drug and alcohol abuse, heavy metal, certain cancers, nerve damage, or blood clots located in and around the kidneys (Acute Kidney Failure, 2012). These are all instances when wastes and toxins would need to be removed from the body, and would cause kidneys to lose their filtering ability rapidly over the course of a few days or even hours. In the case of a drug overdose, dialysis can be used to filter out the drugs that are present in the blood. In some cases, dialysis can be required as a result of kidney failure due to the long-term effects that drug abuse and overdose have on a person’s organs. If treatment post overdose is not started immediately, death is the most likely result. Acute kidney injury can be fatal, but may also be reversible if treated properly and quickly. With this type of kidney injury, dialysis is continued only until blood test results indicate that adequate kidney function has been restored, as opposed to ESRF, which requires indefinite treatment. There are many different types and forms of dialysis, which will be explained at length in the subsequent sections, but each provides aid when the kidneys are unable to do their jobs (Acute Kidney Failure, 2012).

2.2 Types of Dialysis Treatments

There are two main types of dialysis: continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis. Peritoneal dialysis uses the thin lining of a patient’s abdomen called the peritoneum as the filter through which blood passes to be cleansed. Hemodialysis is more prevalent and uses an external filter instead of the peritoneum. Overall the dialysis process consists of extracting blood from the patient, filtering it to rid toxins, and returning the cleaned blood to the body (DaVita, 2015). Hemodialysis can be performed with one or two needles. All of these types of dialysis will be discussed in this section. However, in
keeping with the scope of the research project, hemodialysis will be inspected in greater detail.

2.2.1 Overview of Peritoneal Dialysis

Once a doctor has determined that a person needs dialysis treatment, it must be decided which type is most appropriate. Peritoneal dialysis may be chosen because there are no needles required during each session. At other times, peritoneal dialysis may be suggested because there is more dietary freedom with this form. This process can be done at home, at work, or on the go. The process of peritoneal dialysis and the connection to the patient is shown in Figure 3.

![Figure 3: The Peritoneal Dialysis Process](image)

The peritoneal dialysis membrane was first described by the ancient Egyptians, but not well enough to be applied to human medical services (Friedman, 2010). Then in 1923, a man named Georg Ganter of the University of Wurzburg in Germany experimented by preparing a solution and injecting it into the abdomen of a patient who was suffering from obstructive uropathy. The patient suffered from urine not being able to drain through the
ureter, which caused swelling of the kidneys. Through the injection of the solution, the patient was temporarily relieved but eventually passed away (Wilkie, 2015). This early account of peritoneal dialysis lead to more medical advances and improvements up until this point. Figure 4 shows an example of a modern peritoneal dialysis machine.

![Modern Peritoneal Dialysis Machine](image)

**Figure 4: Modern Peritoneal Dialysis Machine**

In 1975, two men named Popovich and Moncrief began to develop CAPD. They studied nine patients over a 136-week time period and realized that the kidney infection was reduced through continuous treatment (Friedman, 2010). Having a steady flow and deposit of fluids in the peritoneal cavity allowed for a removal of wastes and toxins rather than receiving intermittent treatments (Friedman, 2010). Following the development of CAPD, the compact cycler machine was acquired and another form of peritoneal dialysis was established called continuous cyclic peritoneal dialysis or CCPD. CCPD differs from CAPD in that it can be done overnight so that the patient doesn’t have to worry about taking time out of their day to go get treatment.

There are guidelines made by the *National Kidney Foundation: Dialysis Outcome Quality Initiative* for receiving CCPD or CAPD treatment. One of the main disadvantages
to using peritoneal dialysis is peritonitis, which is a bacterial or fungal infection of the abdomen lining. Peritoneal dialysis can also lead to protein loss from blood into the dialysate fluid, gastrointestinal complications, and electrolyte imbalances. Aside from increased renal function, the advantages of using peritoneal dialysis include lower costs, more efficient blood pressure, and anemia control. Compared to hemodialysis, peritoneal dialysis works better toward preserving residual renal function. The reasons for this are unknown, but some theories are that CAPD has less exposure to non-biocompatible and pro-inflammatory tissue, as well as fewer changes in volume, electrolytes, and blood pressure compared to hemodialysis (Friedman, 2010).

2.2.2 Overview of Hemodialysis

Dialysis was first termed in 1861 by a man named Thomas Graham who was working at Anderson’s University in Scotland (Friedman, 2010). He experimented with vegetables and noticed that a vegetable parchment coated with albumin operated like a semipermeable membrane and allowed crystalloids to diffuse through that coating (Friedman, 2010). Later on in 1913, three men, Abel, Rowntree, and Turner, developed the first artificial kidney. The first hemodialysis machine was then used on humans in 1943, consisting of 30-40m of cellophane tubing wrapped around a drum, which was submerged in a tank of dialysate. The advancements lead to hemodialysis being used as a long-term treatment for chronic renal failure (Friedman, 2010). Hemodialysis differs from peritoneal dialysis in that there is much more preparation for the treatment, the vascular access points are different, and the location of treatments is more specific. It incorporates the flow of the patient’s blood through an external filter that removes wastes, toxins, and extra fluids. The clean blood then travels through a dialysis machine and is returned to the patient via a
needle. Figure 5 shows how the patient’s blood is retrieved through an arterial access point and travels through tubing within the machine.

Figure 5: Schematic of the Hemodialysis Process

The dialyzer is the part of the process that performs the actual filtration of the blood. It plays a crucial role in the separation of blood and toxins by diffusion and convection and will be discussed at length in upcoming sections. Sensors are in place to detect problems during the process and immediately stop the machine so that the patient can receive medical attention from a nurse or doctor. Many case studies have been done to compare peritoneal dialysis to hemodialysis. One example is a case study done by Melissa Stanley, a nurse practitioner in the nephrology department of St. Vincent’s Hospital in Melbourne, Australia. Her research analyzed patient mortality and modality, in hemodialysis versus peritoneal dialysis. She developed a guide for new dialysis patients on what modality to choose initially. The process that she followed was a randomized controlled trial that she performed on several centers in the Netherlands. The outcomes for several of the centers are displayed in Table 1. The volunteers’ dialysis treatment was observed, along with their progress and whether they were receiving peritoneal dialysis or hemodialysis. Her results
showed that starting early treatment with peritoneal dialysis was more favorable for a patient’s improvement compared to starting with hemodialysis. Stanley also found that when the results were altered for modality changes, the peritoneal dialysis survival benefit was not as evident. Essentially, what she found was that patients who were over the age of 65 and were receiving treatment because of diabetes had a better survival rate by using peritoneal dialysis. Yet when those demographics were removed, peritoneal dialysis was not always the best option for patients (Stanley, 2009).

Table 1: Outcomes from Mellissa Stanley's Study

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study design</th>
<th>No. of subjects</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Korevaar et al. 2003</td>
<td>RCT</td>
<td>38</td>
<td>Modality, mortality • After 5 years of follow up, significant longer-term survival favoring PD • Adjusted for age, comorbidity &amp; primary kidney disease</td>
</tr>
<tr>
<td>Termorshuizen et al. 2003</td>
<td>Multicentre prospective, observational cohort of incident patients</td>
<td>1222</td>
<td>Modality, mortality • Follow up until Tx or death (or 5 years) • No statistical differences in mortality in first 2 years, then PD&gt;HD. Subgroup analysis: • Patients &lt;60 w/ DM had increased RR on HD than PD in first 2years • RR for patients &gt;60 higher on PD after 2 years (irrespective of DM status)</td>
</tr>
<tr>
<td>Liem et al. 2007</td>
<td>Dutch End Stage Renal Disease Registry</td>
<td>16,600 from 47 centres</td>
<td>Modality, mortality • Not able to adjust for comorbidity • Initial survival advantage for PD. Over time, w/ advancing age &amp; in the presence of DM (as PRD) this survival reverses</td>
</tr>
<tr>
<td>Vonesh et al. 1999</td>
<td>US registry data of incident &amp; prevalent patients</td>
<td>203,958</td>
<td>Modality, mortality • Not adjusted to comorbidity • RR (PD vs. HD) 1.28-DM&gt;50 years (sig.) 0.89-DM &lt;50 year (sig.) • Females &amp; patients &gt;50 years-significantly lower risk of death if on PD</td>
</tr>
<tr>
<td>Stack et al. 2003</td>
<td>USRDS Historical prospective cohort of incident patients</td>
<td>107,922</td>
<td>Modality, mortality • 2 years of follow up • Significantly higher mortality risk w/ patients on PD &amp; CHF (DM &amp; non-DM). • Survival advantage if non-DM &amp; non-CHF on PD at least in the first 6 mo.</td>
</tr>
<tr>
<td>Ganesh et al. 2001</td>
<td>USRDS historical prospective cohort of incident patients</td>
<td>107,922</td>
<td>Modality, mortality w/ or w/out cad • 2 years of follow up • Underreporting of comorbidities w/ registry data • Survival benefit in first 6 mo. T PD, lose this at 12 mo. • DM w/ CAD significantly higher mortality on PD • Patients w/o CAD 9% lower mortality on PD • Caution exercised in recommending PD as initial choice in those w/ proven CAD whereas either modality recommended if no CAD</td>
</tr>
</tbody>
</table>
From these studies, it can be concluded that peritoneal dialysis has an equal or improved survival rate for younger patients without diabetes (Stanley, 2009). Additionally, peritoneal dialysis has an equal or lower mortality rate for the first two years of treatment (Stanley, 2009). Finally, for patients over the age of 45 with diabetes, the best form of treatment is hemodialysis (Stanley, 2009). With a significant increase in the number of people that suffer from end stage renal disease, the demand for hemodialysis treatment has increased amongst patients. Hemodialysis totaled in nearly $17 billion in expenditures in 2006 (Friedman, 2010). This industry has expanded so much that hemodialysis has become a major part of most patients’ lives.

2.2.3 Single Needle Dialysis Treatment

Traditionally, hemodialysis is performed with two needles: one taking the blood from the patient prior to cleaning and a second needle used to return the blood afterward. This standard type of hemodialysis can be referred to as double needle dialysis. There is a less common way to perform hemodialysis called single needle dialysis (SND). With this method, a single device accesses the patient’s blood. Obviously, the needle in use cannot be extracting and returning blood simultaneously. Thus, an alternating-flow schedule is required. During the arterial phase, blood is taken from the patient over a time interval denoted $t_A$. The volume of blood extracted ($V_S$, or stroke volume) over this time must be stored within the extracorporeal system. During the venous phase, the cleaned blood is taken from the holding chamber and returned to the patient over a time interval denoted $t_V$ (Matthias, 2008).
There are two main setups for single needle dialysis, which are each shown in Figure 6. In both setups, the arterial and venous lines are connected to the cannula using a Y-shaped tube.

![Figure 6: Two Setups of Single Needle Dialysis](image)

In the first setup (Figure 6-A), the arterial line leads to the blood pump and dialyzer, denoted D. At the beginning of the arterial phase, clamp Cla is opened, clamp Clv is closed, the blood pump is started, and the dialyzed blood is pumped into the holding chamber (Co). As the volume of blood being stored in the chamber increases, the remaining air becomes
compressed. Once the pressure reaches a preset maximum, the blood pump stops and the venous phase begins. Clamp Cla closes as Clv opens. The compressed air in the chamber then forces the blood in chamber Co into the venous line and back into the patient. Once the pressure reaches a minimum, the arterial phase starts again (Matthias, 2008). The second setup (Figure 6-B) is used more often. This method uses two blood pumps, a venous one (BPv) and an arterial one (Bpa). The venous pump is paused and clamp Clv is closed as the chamber is filled during the arterial phase. During the venous phase, the arterial pump is paused and the clamp is opened. At a maximum pressure, the venous pump empties the chamber and the blood goes through the dialyzer back to the patient. Once the chamber reaches its lower limit, the arterial cycle begins again (Matthias, 2008).

The chamber pressure limits that trigger the start of the venous and arterial cycles are higher in the setup in Figure 6-A than those in Figure 6-B. A typical pressure range for the first setup could be 100–300 mmHg whereas in the second setup, the pressure range is 80–180 mmHg. In both setups for single needle dialysis, the flow rate of blood pumped during the arterial phase is denoted QA; this is the rate at which the blood is pumped into the chamber. The stroke volume, which is pumped in the arterial phase, can be found using 

\[ V_S = Q_A \cdot t_A \]

Timing and flows during SND are defined by this stroke volume VS, along with QA, QV, and the ultrafiltration rate (UFR). The average blood flow rate during SND is the blood volume pumped into the dialyzer (stroke volume VS) per cycle time (tC = tA + tV). This mean BFR can be expressed as:

\[ Q_M = \frac{V_S}{t_C} = \frac{Q_A(Q_V + UFR)}{Q_A + Q_V} \]  

(1)

Single needle dialysis has the advantage of only having one venipuncture but it otherwise has a number of disadvantages. SND is not the preferred method of
hemodialysis, but the need for it arose because there are often times when a patient’s body simply cannot handle two punctures, such as in the existence of an infection. SND is usually less efficient and requires certain modifications in order to be performed. Clearly, there is a possibility of needing an additional blood pump, a special arterial line with two pump segments, and the compliance chamber. Some dialysis machines have accommodations to allow for them to be set up for SND, but some do not, and the extra parts can be a hassle (Levy, 2009). Another major shortcoming of single needle dialysis is that it poses an increased risk of recirculation. There is expected increased recirculation of blood in the extracorporeal circuit during SN treatment, even when using the recommended administration sets, dialyzers, catheters, and fistula needles. Recirculation occurs when dialyzed blood somehow returns to the dialyzer inlet rather than returning to the systemic circulation. This poses a problem in dialysis because it reduces solute concentration gradients across the dialysis membrane by mixing dialyzed blood with blood that has not been dialyzed. It usually reduces the efficiency of dialysis by lowering the concentration of urea and other solutes that are at the dialyzer inlet (Levy, 2009).

There are two types of recirculation: cardiopulmonary and access. Cardiopulmonary recirculation occurs via an AVF or AVG. Dialyzed blood gets returned to the venous circulation and mixes with venous blood that has not been dialyzed yet. This mixed blood then becomes the arterial supply that is going to the dialyzer. Cardiopulmonary recirculation can be approximated by:

\[
\frac{Dialyser\ Clearancenextext{e} (K)}{Cardiac\ Output - Access\ Blood\ Flow}
\]

Access recirculation occurs when blood that has just been dialyzed returns directly to the dialyzer inlet. This is usually due to retrograde (opposite) blood flow within a fistula or
graft, but can also be caused by a drop in BFR below 350 mL/min. Access recirculation only occurs if access flow rate is less than the dialyzer blood pump flow rate; it can be calculated by:

\[
\frac{S - A}{S - V} \times 100
\]

where S is a measure of urea in a systemic arterial blood sample, A is a measure of urea in an arterial blood sample, and V is a measure of urea in a venous blood sample. Single needle dialysis provides a necessary alternative method for hemodialysis, but given the aforementioned dangers, it should only be used when needed (Levy, 2009).

2.3 A Detailed Look into Hemodialysis Treatment

Being that hemodialysis is the more common form of dialysis, this is what the team decided to focus the project on. It is a thorough process that requires work from trained professionals in addition to patient compliance. There are many steps from the start of treatment to the end, such as the preparation of an access point or the travel path of blood outside of the patient’s body.

2.3.1 Dialysis Access Points

Preparation is a crucial part of hemodialysis treatment and it includes accessing the veins and arteries. An access creates a way for blood to be removed from the body, circulate through the dialysis machine, and then return to the body at a rate that is higher than can be achieved through a normal vein. There are three main types of dialysis access. The first is an arteriovenous fistula (AVF), which is the preferred method. An AV fistula is a surgically made connection between an artery and a vein (NIH, 2014). These fistulas are usually created in the forearm or upper arm, as shown in Figure 7.
This type of access entails much planning because the fistula requires 2 to 3 months to mature after it is created (NIH, 2014). The advantages to using the AV fistula are that there is less of a chance to develop clots or infections.

The second type of access point for hemodialysis is an arteriovenous graft. Creating a graft for the patient is only necessary if their veins are too small to use an AV fistula. An arteriovenous graft is made by using a biocompatible plastic tube that is looped and connects an artery to a vein, as the AV fistula does. The graft is inserted into the patient through an AV graft surgery, just as the fistula is inserted into the patient (NIH, 2014). In Figure 8, you can see a schematic of the AV graft in a patient’s forearm.
If the AV graft is properly cared for there are typically no problems. Yet compared to the AV fistula, the graft is more likely to develop infection or blood clots (NIH, 2014).

The final type of access point a doctor can use for a patient is the central venous catheter. This is a temporary access point for patients that need treatment immediately and before permanent access can be surgically inserted and matured. The catheter is positioned in an internal vein located around the neck, chest, or upper leg area. This catheter that is used allows for two-way flow of blood and therefore, has two tubes with caps that are designed for the two-way blood flow. There are clamps to control the flow of the blood either from the patient to the machine or from the machine back to the patient, which are shown in Figure 9. Again, unlike the AV fistula, the catheter has a high probability of developing infection and blood clotting, which is very dangerous for the patient.

Figure 8: Arteriovenous Graft

If the AV graft is properly cared for there are typically no problems. Yet compared to the AV fistula, the graft is more likely to develop infection or blood clots (NIH, 2014).

The final type of access point a doctor can use for a patient is the central venous catheter. This is a temporary access point for patients that need treatment immediately and before permanent access can be surgically inserted and matured. The catheter is positioned in an internal vein located around the neck, chest, or upper leg area. This catheter that is used allows for two-way flow of blood and therefore, has two tubes with caps that are designed for the two-way blood flow. There are clamps to control the flow of the blood either from the patient to the machine or from the machine back to the patient, which are shown in Figure 9. Again, unlike the AV fistula, the catheter has a high probability of developing infection and blood clotting, which is very dangerous for the patient.
Once a form of access is established, a nurse can gain access to the patient’s blood through cannulation. Cannulation is a process in which a cannula, or tube, is placed inside a vein through use of a needle to provide venous access. This process can be broken down into steps that should be taken prior to, during, and after cannulation. In order to properly cannulate a dialysis access, one must identify the type of access and direction of blood flow, select the needle site, prepare the skin, administer local Anesthesia if necessary, select needle, follow cannulation technique, secure the needle, address and solve potential problems, remove the needle, and finally, discharge the patient (Brouwer, 2011). There are a number of decisions to be made throughout this procedure, most of which are medical tasks that would be commonplace to trained healthcare professionals. There are, however, many factors pertaining to cannulation that may contribute to delays in the dialysis process.

Step two in the procedure is selection of the needle site. The venous needle must always point towards the venous return, while the arterial needle can point in either direction. On a graft, if certain complications such as infections occur and make it so that only one side is usable, the needles may both be on the same side, but must point in opposite
directions, as shown in Figure 10. In these cases, the needles must be at least one inch apart, hub-to-hub.

![Figure 10: Two Needles Within an AV Graft](image)

These needle sites that are chosen for cannulation must be regularly rotated to extend the lifespan of the access and to prevent the formulation of a pseudoaneurysm, which is a solid swelling of clotted blood within the tissues. Step five in the procedure leading to cannulation is the all-important selection of the needle. Figure 11 shows the various parts of a standard surgical needle.

![Figure 11: The Parts of a Standard Needle](image)
The type of needle used during dialysis is a fistula needle, shown in Figure 12, which has rubber or plastic wings for a better grip and ease of adhesion to the patient’s body. They are also usually equipped with a color-coded clamp, which differentiates an arterial needle from a venous needle. In terms of materials, there is no variation between fistula needles and typical surgical needles, which are made of high quality stainless steel.

![Figure 12: Fistula Needle](image)

The gauge of the needles used should be ordered by the nephrologist to ensure that the proper blood flow rate (BFR) is achieved. Needles are organized by gauge, ranging from 7-34, each with different inner and outer diameters. The fistula needle, however, generally only encompasses gauges 14-18. Table 1 shows the inner and outer diameters for the needle gauges used during dialysis.
Though the diameters of the gauges are standardized, different companies claim slightly different attainable BFRs for the different gauges. However, one thing remains constant: The larger the inner diameter is and the shorter the needle length, the higher the BFR that can be attained under different pressures (FMC, 2015). An explanation for the variation in possible BFRs attainable is that the needle lengths can vary. Gauges 14-18 tend to range from 15mm to 25mm in length, but each gauge can come in multiple lengths. Figure 13 shows a graph from a German healthcare company called Bionic Medizintechnik that shows the correlations between gauge and blood flow rates at different pressures for their fistula needles, which are named “Bionic.”

<table>
<thead>
<tr>
<th>Gauge</th>
<th>Outer Diameter (mm)</th>
<th>Inner Diameter (mm)</th>
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</thead>
<tbody>
<tr>
<td>14</td>
<td>2.108</td>
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<tr>
<td>15</td>
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<tr>
<td>18</td>
<td>1.270</td>
<td>0.838</td>
</tr>
</tbody>
</table>
Figure 13: Blood Flow Rates in Bionic Brand Needles

Figure 14 shows a similar graph from another company, Fresenius Medical Care, which is the leading network of dialysis facilities across America and the world. As can be seen from comparing the two companies, there is very slight variation in flow rate for each gage, but both maintain a positive slope.

Once a doctor chooses the gauge, the length of the needles can be decided and altered by the dialysis staff members. The length of the fistula needle from tip to hub ranges from about 15mm to 25mm. The needle only needs to be long enough to reach the access.
The depth of the access beneath the skin depends upon a number of variables. Veins and arteries are located at different depths throughout different areas of the body. The depth also depends upon the size of the patient. Larger patients will have more distance to travel from the surface of the skin to the veins. In addition to consideration of dimensions, the needles chosen for dialysis should always have a “back eye” to attain the optimal flow. Figure 15 exemplifies what a back eye looks like.

![Figure 15: Back Eye on a Needle](image)

Step six in the process is the actual cannulation technique. With all of the prep work done, the nurse is now ready to insert the needle. The fistula needle must be held by its wings, with the bevel facing upward, as illustrated in Figure 16A. For an AV fistula, the needle must be held at a 20-35° angle from the skin. For a graft, it must make a 45° angle. The nurse will know when the needle is within the wall of the fistula or graft because blood flashback should be visible. Blood flashback is the appearance of blood in the hub of a catheter. At this point, the needle should be advanced no more than 1/8 of an inch. The needle bevel should then be rotated 180°, as shown in Figure 16B. This rotation is to help prevent posterior wall infiltration, which can occur if the tip of the needle accidentally
punctures the bottom wall of the fistula or graft. After rotation, the needle should be leveled out, or flattened against the skin, depicted in Figure 17. Lastly, the needle should be advanced cautiously up to the hub.

Figure 16: (A) Insert Needle, Bevel Up, (B) Rotate Needle 180°

Figure 17: Leveling out of Needle with Skin

Step seven is to secure the needle. There are many effective ways to secure a fistula needle and any legitimate technique can be followed. The important aspect is that the needle is kept from coming loose during treatment. Once such method is the butterfly tape technique. First, a piece of adhesive tape 1” x 6” is placed under the needle wings. Next, the tape is folded to cross over the needle site. A bandage is then placed over the needle and secured by a second piece of tape. If the needle shifts after it is secured, gauze pads
may be placed under the needle to correct the angle. Step eight is less of a procedural step and more damage control. There are various things that can go wrong during the cannulation process so proper problem solving is crucial. There are some tips that can and should be followed in the event of any accidents. If resistance is felt at any time during needle advancement or needle position change, the needle should be pulled back and the angle should be redirected.

In the event of infiltration of the back wall of the fistula or graft, the course of action depends on the conditions of the situation. If the patient has not yet received heparin, the needle should be pulled out and pressure should be applied to the exit site by placing two fingers along the access, covering at least a one-inch area. If, however, the patient has already received heparin at the time of infiltration, the puncture site must be carefully assessed. If the needle site remains stable with no increase in size or swelling, it is safe to keep in place for the duration of the dialysis treatment, but ice should be applied over infiltration site. If a solid swelling is observed, the needle should be removed and digital pressure should be applied. It is important to note that pressure should never be applied while the needle is inside the patient. If the needle had to be removed due to infiltration, a new needle should be used to perform cannulation and a new spot should be chosen as far away from the first as possible. The ninth step is the removal of the needles. First, the tape should be carefully and slowly removed once dialysis is complete. The needles should be withdrawn slowly, one at a time, at a 20° angle until the entire needle is out of the patient. Once out, the patient should use their index and middle fingers to apply mild digital pressure to a gauze pad over the needle exit sites, with the thumb wrapped around to the other side of the limb. This pressure should be maintained for about 10 to 15 minutes.
The final step of the cannulation process is to discharge and dress the patient. An adhesive bandage should always be placed over the cannulation sites. Before leaving the dialysis unit, the patient should be assessed by their nurse with a stethoscope over the access to make sure the rushing-roaring sound can be heard. A strong pulse or buzzing sensation should also be felt when fingers are placed over the access. These are signs that blood is flowing through the vessel and the fistula or graft is working properly. Once cannulation has taken place, the process of dialysis can begin.

2.3.2 Preparation for Hemodialysis

Hemodialysis does not solely include the filtration of blood. There are a number of steps that must be taken prior to the treatment process. To begin, a lot of work goes into preparing the dialysate. Hemodialysis patients are exposed to contaminants from the water that is mixed with the dialysate. This may not seem so crucial at first, but considering that dialysis patients are exposed to 25 times more water than a healthy person, the impurities and excess minerals can quickly add up (Friedman, 2010). Assuming a patient receives treatment 3 times per week, the total amount of water required is between 300 to 600 liters, depending on the prescription. Patients who receive dialysis during their sleep are exposed to 500 to 860 liters per week (Coulliette, 2013). This means that the water decontamination process must be done carefully. Figure 18 shows some tanks required for a dialysis water treatment system (“Up to 35 stations,” n.d).
The main source of water for hemodialysis facilities and home dialysis is usually local drinking water supplies (Coulliette, 2013). Although the cities, towns, and other suppliers of drinking water are required to follow specific standards, there are still significant amounts of contaminants in the water. Therefore, the water is treated, purified, and transported through a water distribution system prior to reaching the patient in a dialysis center. This water is then used in the preparation of dialysate concentrates and for proportioning concentrates to produce the final dialysate bath (Coulliette, 2013). Hemodialysis centers’ goal is to achieve the best care by providing high quality and safe hemodialysis water and dialysate to the patients. Dialysis water treatment, system design, and distribution material choices are all important factors when it comes to achieving that standard (Coulliette, 2013). There is no single water system design for dialysis centers because it varies based off the quality of the feed water and the local requirements. However, an example of a water treatment arrangement that is commonly used is depicted in Figure 19.
There is a Backflow Preventing Device (BFD) at the start of the system. This is where the feed water passes through. A valve is in place to prevent dialysis water from flowing back to the water supply (Ahmad, 2005). Once water enters the water treatment system, removal of chemical and microbial contaminants begins. These are done through two phases: pretreatment and water treatment. Pretreatment is the process through which contaminants are removed from feed water to protect the other components that are downstream. Pretreatment is followed the water treatment, which is the physical and/or chemical removal of the remaining contaminants in the water.

The pretreatment segment of the water purification process utilizes the following equipment: temperature blending valve, multimedia depth filter, granular activated carbon filter, softener, and additional smaller filters (Coulliette, 2013). The temperature blending valve blends heated water with cold water and assures a constant temperature. The reverse
osmosis (RO) unit works most efficiently if the feed water is at 77 degrees Fahrenheit. Filters are placed on the water line with increasingly smaller pores to remove large contaminants. The first filter is used to remove large matter such as silica and clay particles from the feed water. Activated carbon filters are either a tank or column in which granules of activated carbon are packed in a cartridge. Water flows around those granules and organic matter, chlorine, and chloramine are absorbed by the carbon. Unfortunately, activated carbon filters are not very effective filters and cannot be used alone because they release abrasive particles. Therefore, it is recommended that micro filters are inserted after the carbon tank to remove the particles. Additionally, two other challenges are present when the activated carbon filter is in use. These complications are exhaustion of the carbon and microbial growth. One can take action to prevent exhaustion of the carbon by monitoring the post-carbon water and changing the filter when needed. Microbial growth can be controlled by periodically monitoring the carbon filter and flushing with chlorine (Ahmad, 2005).

Monitoring of the activated carbon filter is very important. Chlorine and chloramine removal is one of the most important functions of the filter because chlorine and chloramines are high level oxidative chemicals. They kill bacteria in municipal water systems but destroy red blood cells if not filtered out prior to dialysis. It is necessary to remove these chemicals prior to RO because the RO unit is not capable of removing the chemicals and the chemicals have been known to destroy the RO membrane (Monitoring, 2005). Post carbon water should be monitored for chlorine and chloramine levels that exceed the acceptable range. If levels go beyond the acceptable range, the carbon filter needs to be changed.
Water softeners protect water treatment devices such as RO and deionizer (DI) by removing large concentrations of cations from the water. The water contains high concentrations of calcium and magnesium, these minerals make the water hard and in return limit the life of treatment devices. Water softeners use resin beads fixed with sodium. Water passes through the beads where there is an exchange of calcium, magnesium, iron, and manganese with sodium, producing a softer water hardness (Ahmad, 2005). Figure 20 shows a schematic of the ion exchange process.

![Figure 20: Ion exchange process in a water softener](image)

Water treatment follows the pretreatment process and consists of the following components: reverse osmosis (RO), deionization (DI), storage tank, and ultraviolet irradiator (UV) (Coulliette, 2013). Reverse osmosis is a cost effective method for water purification that removes organic and inorganic solutes by filtration through a tight
membrane. The filtered water from RO is called “permeate” or “RO water”, while the unfiltered water that contains the rejected solutes and substances is called “rejection” or “brine”. The osmolarity of the brine is stronger than the osmolarity of permeate. Therefore, the water would normally move in the direction of the filtered water to the brine because of the high osmotic pressure. However, with RO, a mechanical force is applied with a pump to the brine in order to push it across the membrane and filter the water. Shown in Figure 21 is a schematic diagram showing regular osmosis and reverse osmosis. In regular osmosis the solution moves from area of low concentration to area of high concentration. In RO, a force is applied to go against the concentration gradient.

![Figure 21: Regular Osmosis (left) & Reverse Osmosis (right)](image)

The membrane for RO is designed by selecting one of the three following materials: cellulosic, synthetic, or thin composite. RO also uses either parallel plates, hollow fibers, or spiral wounds. Water pH, disinfectants, and bacteria can destroy the RO membrane, similarly to chlorine and chloramine. Chemicals are most likely to harm synthetic membranes while composites tend to be more resistant to destruction. The membrane’s
performance must be measured to make it possible to monitor the removal of solutes. This is done by measuring the resistivity of RO water. Pure water is highly resistant to electrical current. When ions are present in the water, the electrical conductivity increases. When the production to rejection ratio is greater than 0.85, the water is acceptable. When the ratio is less than 0.80, the membrane needs to be changed. The production to rejection ratio is calculated with formula below:

\[
\text{rejection ratio: } 1 - \frac{\text{Conductivity of } RO}{\text{Conductivity of feed water}} \times 100
\]

where Deionization (DI) is an ion exchange process using cationic and anionic resins in order to remove inorganic ions. The process occurs by cationic resin exchanging dissolved cations with H\(^+\) ions, and anionic resin exchanging dissolved anions with OH\(^-\) ions. Together, H\(^+\) and OH\(^-\) ions produce pure water without cations and anions. DI is not an effective way to remove organic and additional contaminants. It is also a site for bacterial growth and can lead to downstream contamination. A continuous electric deionizer is a more efficient option. It uses an electric current ion exchange membrane and resins to remove the unwanted ions, producing high quality water that contains less bacterial growth because the water is in continuous flow. A DI is used in conjunction with an ultraviolet (UV) treatment that kills bacteria, followed by an ultra-filter that removes bacterial fragments. The efficiency of UV is dependent upon the depth of penetration and the water flow rate (Ahmad, 2005). The water treatment process is at a higher risk of bacterial infection. Parts downstream from activated carbon filter, which eliminated chlorine through its process, resin and porous elements (softeners, resinous deionizers), and filters made with activated carbon, storage tanks, and stagnant water are at an increased risk of bacterial infection (Perez-Garcia, 2000).
The dialysis water system follows a loop flow design. It is a continuous cycle throughout a dialysis facility where the purified water goes to either the RO or to a storage tank (Andrysiak and Philip, 2002). There are two categories of distribution systems. They are direct feed and indirect feed. The direct feed loop delivers water directly from the RO system to the water distribution loop. The product water that is not used for dialysis is sent back to the RO system. The direct loop was shown in Figure 19 within the common water treatment arrangement. The indirect feed loop holds water in a storage tank after RO. Purified water is delivered to a tank where water is pumped to the distribution loop that returns water back to the tank daily (Ahmad, 2005). Figure 22 shows an example of a schematic of an indirect feed loop.

Figure 22: Common Water Treatment Arrangement (Indirect Feed Loop)
There are general requirements for the system design and selecting the correct loop flow velocity. Direct feed systems require a minimum flow velocity of 1.5 feet per sec (FPS) at the end of the loop and at all systems operating and drawing water. Indirect feed systems require a minimum flow velocity of 3FPS (average of 3-6 FPS). Flow velocity is important because velocities that are too high create excess noise and heat, an increase in water, and higher costs to operate the pumps. Throughout the system design, flow rates in pipes are higher at the beginning of a system and then decrease throughout the pipes. This is because the volume of the water decreases as equipment removes components such as various contaminants. Decreasing the size of the piping throughout the loop can counteract the flow rate differences. This will help the water system remain at a high velocity, helping to maintain a constant pressure (Andrysiak and Philip, 2002).

Material choice is another important aspect of the water treatment system. There is a list of distribution materials and disinfectants that are recommended by the AAMI. Such materials are polyvinylchloride (PVC), chlorinated polyvinylchloride (CPVC), polyvinylidene fluoride (PVDF), cross-linked polyethylene (PEX), stainless steel (SS), polypropylene (PP), polyethylene (PE), acrylonitrile butadiene styrene (ABS), and polytetrafluorethylene (PTFE). Such disinfectants are sodium hypochlorite (chlorine bleach), peracetic acid, formaldehyde, hot water, and ozone (dissolved in water). Peracetic acid is compatible with all materials and is of importance because incompatibility between materials and disinfectants can cause leaching and/or corrosion of the materials. PVC and SS are the most commonly used distribution materials in hemodialysis. PVC is the most common because of its ease of availability and low cost. (Coulliette, 2013).
In a water treatment system, the question of including a storage tank in the design is proposed. If there is a tank, it should have a bowl shaped base, tight lid with a hydrophobic air filter, and receive the proper maintenance. The tank should be cleaned and disinfected weekly. If that is not possible, then it should be done on a biweekly or monthly schedule. These considerations are important because the formation of biofilm in the water distribution system is significant. From data showing outbreaks, it is demonstrated that patients require water and dialysate that is microbiologically as clean as possible. Once developed, biofilm is extremely difficult to remove. This is because it is highly resistant to disinfectants due to its bacterial structure and formation of exopolysaccharides (EPS). Therefore, it is a priority to prevent the initial growth of biofilm by selecting the appropriate materials for the distribution system and the proper disinfectants (Coulliette, 2013).

All the components in the water treatment system ensure that the water being provided to dialysis patients is of the highest quality and reaches the recommended standards. Drinking water suppliers follow the United States Environmental Protection Agency (EPA) requirements under the Standard Drinking Water Act (SDWA), which shows accepted chemical and microbial contaminant levels. A list of contaminants and their maximum allowable contamination level (MCL) regulated by the EPA can be found in the appendices. These standards are not enough alone to protect the patient. The dialysis centers are required to meet the requirements of the Centers for Medicare and Medicaid Services (CMS) conditions for coverage, which contains various other requirements in addition. The CMS usually adopts the more stringent standards set forth by the Association for Advancement of Medical Instrumentation (AAMI) (Coulliette, 2013). The AAMI recommends bacteria levels of less than 200 colony-forming unit per milliliter (CFU/ml).
with an action level at 50 CFU/ml and endotoxin levels of less than 2.0 endotoxin units per milliliter (EU/ml) with an action level at 1 EU/ml. Other countries have even stricter standards, as shown by the European recommendations. European Pharmacopoeia suggests bacteria levels at 100 CFU/ml and endotoxin levels at 0.25 CFU/ml with an action level of 25 and 0.0125 EU/ml, respectively (Andrysiak and Philip, 2002). Table 2 compares the chemical limits allowed in municipal drinking water with chemical limits allowed in dialysis water. The data is from CMS, AAMI, and EPA (Coulliette, 2013).

Table 3: Chemical Limits for Municipal versus Dialysis Water

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<th>Municipal Drinking Water</th>
<th>Dialysis Water</th>
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<tr>
<td></td>
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<td>Toxic Chemicals</td>
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</tbody>
</table>
The need for such strict standards is to help reduce the risk of microbial growth and chemical exposure that occurs when water is contaminated and not maintained properly. When water is contaminated by chemicals, bacteria, and endotoxins, there are many potential health risks for a patient. The guidelines are in place to help prevent those complications (Coulliette, 2013). Chemical contaminants will cause chemical toxicity and adverse health effects for a patient if they are exposed to certain chemicals. Chemical toxicity causes speech and motor difficulties, seizures, nausea, hypotension, and diarrhea. An example of a contaminant with adverse effects is lead, which would cause a patient abdominal pain and muscle weakness. Sulfate would cause nausea, vomiting, and metabolic acidosis. However, other chemicals are only harmful to the body at high concentrations. An example is calcium, which at excessive amounts is associated with renal disease. Microbial contamination can produce bacteremia and chronic inflammation in patients. Both health problems contribute to and complicate cardiovascular disease, the leading cause of death in dialysis patients (Coulliette, 2013).

It is important that system components are monitored on a regular basis, especially those areas at higher risk of contamination, because chemical and microbial contamination is a major threat to the safety of dialysis treatment. Chlorine is monitored before each new patient begins treatment, and after the carbon tank. The storage tanks and distribution pipes are monitored once per month for microorganisms and endotoxins. The dialysis machines are also tested monthly on a rotational basis. The need for constant monitoring of the existence of chemical, microbial, and endotoxins is to prevent outbreaks. Chemical and microbial contaminants have caused 13 and 20 outbreaks in the United States, respectively, as reported by the Center for Diseases Control (CDC). Chemical intoxication has caused
217 cases and 14 deaths, as was investigated by the CDC between 1960 and 2007. On the other hand, microbial outbreaks caused 375 cases and 2 deaths. There are many reasons why the outbreaks occurred. Chemical toxicity is a result of water treatment failures, such as incompatible dialysis solutions and distribution equipment and materials, and inadequate rinsing of dialysis systems after disinfection. Microbial outbreaks are cause mostly by improper disinfection—specifically inconsistent cleaning and disinfection of facility tap water and commercial deionizer resins, mixing an improper disinfectant solution, or not disinfecting the water system correctly when flow meter valves are open. Approximately half of the microbial outbreaks are associated with reuse of a dialyzer (Coulliette, 2013). However, with proper monitoring and reporting of the water treatment system, contaminants can be limited and kept under control.

The water treatment system is vital to ensure the safety and effectiveness of dialysis treatment. The risk of contamination is a major health concern for patients and must be taken seriously. With a proper water system design and following the water standards, in addition to frequent monitoring of the system, one can provide high quality water to dialysis patients. This treated water can then be taken in by the dialysis machine. The hemodialysis machine itself has major components that the blood must pass through to ensure the most effective and safe removal of fluid. Figure 23 shows how a typical hemodialysis machine looks.
Machine models vary depending on company, improvements, etc. However, the following significant components remain the same. First is the dialyzer, which is known as the artificial kidney of the dialysis machine. Along with the dialyzer is the blood pump, which moves the blood from the patient to the dialyzer and then back to the patient. This pump can operate at different flow rates that are adjusted depending on the patient and range between 200 to 600ml/min (Friedman, 2010). The third component of the hemodialysis machine is the dialysate pump. Its job is to move the dialysate into the dialyzer and take the ultra-filtrate out of the dialyzer. It is important to monitor and control is the flow rate of the dialysate, which is typically set from 500 to 800 ml/min, depending on the patient. The last two components are the arterial and venous pressure monitors and the alarms. The arterial pressure of the patient is taken before the blood reaches the blood
pump to ensure that there is the proper amount of suction of blood. The venous pressure is measured within the machine after the dialyzer to make sure there is the correct resistance on the venous side of the access point. Finally, the alarms are in place to make sure treatment is stopped if there are any problems throughout the process.

2.3.3 The Treatment Process

Dialysis is not an easy process and can cause major health issues if done incorrectly. Therefore, the National Kidney Foundation: Dialysis Outcomes Quality Initiative established guidelines and restrictions to initiate hemodialysis. According to Present and Future Therapies for End-Stage Renal Disease, once a doctor detects loss of kidney function in a previously healthy person, they analyze two different laboratory criteria that will be used to decide if dialysis is the proper pathway for the patient. First, the doctors determine the patient’s Kt/V value, where K is clearance or urea, t is treatment time, and V is urea volume distribution. Kt/V measures the adequacy of treatment (NKUDIC). If this value is below 2 liters/week, then the patient is to be prescribed dialysis treatment. This value became the cutoff for receiving treatment because of the CANUSA, or Canada-USA study. This study was performed on 60 incident peritoneal dialysis patients and analyzed the morbidity and mortality of these patients. What they found was that, “over a two-year period, every 0.1 U/week increase in the total Kt/V was found to correspond to a 6% decrease in the relative risk of death. The total Kt/V and creatinine clearance values that corresponded to a 78% two-year survival rate were 2.1 L/week and 70 L/1.73 m2/week, respectively.”

Secondly, the doctors measure the “normalized protein equivalent of nitrogen appearance” or nPNA. The patient’s protein excretion is measured compared to their
protein intake. A doctor will put a patient on dialysis if their nPNA value is below 0.8g/kg/day (Friedman, 2010). It is important that these tests are done quickly and efficiently so that the patient can receive treatment as fast as possible. If the patient does not receive treatment fast enough their condition can worsen and hemodialysis may longer help. If a patient is diagnosed with chronic renal failure and needs to get hemodialysis treatment, the next step for the doctor is to prescribe the patient the type of dialyzer, frequency, blood flow, dialysate flow, composition of dialysate, and the total duration the patient will have to undergo treatment for. There are three different types of dialyzers to choose from. These are the coil dialyzer, the parallel plate dialyzer, and the most commonly used hollow fiber dialyzer. The hollow fiber dialyzer is a cylindrical tube filled with thousands of hollow fibers through which the blood flows in and the dialysate flows around. The other major part of the dialyzer is the dialysis membrane, which there are also three types to choose from. The first is cellulose, the second is modified cellulose, and lastly is the most common, synthetic membrane.

All of these variables are prescribed in order to get an adequate urea clearance to help the patient. In other words, different types of dialyzers will change the clearance of urea from the blood. Also if the treatment lasts longer, then the amount of urea cleared from the blood will vary. For a new dialysis patient, the doctors are cautious and limit the duration of treatment, volume removed, and amount of urea cleared so that the patient will not acquire disequilibrium syndrome (Friedman, 2010). This often occurs when people with chronic renal failure start off with aggressive treatment.
The aforementioned dialyzer is one of the most important components of the dialysis process. Inside of this cylindrical tube is the blood compartment, the dialysate compartment (which is pre-prescribed for each patient), and thousands of hollow fibers. There are approximately 10,000-20,000 fibers in a typical dialyzer and these fibers have pores, which allow for the removal of waste from the blood (Azar, 2013). The fibers are held in place by the potting material near both headers located at the top and bottom of the dialyzer. The potting material is usually made from the polyurethane group and ensures a secure connection of the fibers in the dialyzer (Azar, 2013). The headers serve as the area between the two blood ports and the middle of the dialyzer where the fibers are located. There are three different types of dialyzers to choose from: the coil dialyzer, the parallel plate dialyzer, and the hollow fiber dialyzer. The coil dialyzer, which was an early design of the dialyzer, has since been replaced with more efficient designs, such as the parallel plate dialyzer (Types of Dialyzers, 2014). The parallel plate dialyzer allows for thinner blood and dialysate flow channels due to the parallel membranes layered in the dialyzer. Lastly, the hollow fiber dialyzer is a cylindrical tube filled with thousands of hollow fibers that the blood flows through and the dialysate flows around (Kiaii, 2013). This design is the most efficient and therefore is the most commonly used. The hollow fiber dialyzer and its main parts are shown in Figure 24.
The hollow fibers bundled inside of the dialyzer are responsible for the removal of solutes from the blood. They are porous and therefore allow molecules to pass through. There are three specific processes that occur within the dialyzer to remove these molecules. The process through which a certain molecule is filtered out of the blood by depends on the size and molecular weight of that molecule. Table 2 displays the size range and classification of some common solutes that are removed during the process of hemodialysis. Specifically, small molecules are removed through diffusion, middle molecules are removed through convection, and large molecules are removed through adsorption.

**Table 4: Classification of Solutes**

<table>
<thead>
<tr>
<th>Size Category</th>
<th>Example of Solutes</th>
<th>Molecular Weight Range (Daltons)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Small Molecules</strong></td>
<td>Urea, Creatinine, Phosphate</td>
<td>&lt;500</td>
</tr>
<tr>
<td><strong>Medium-Sized Molecules</strong></td>
<td>Vitamin B₁₂, Inulin, Vancomycin, β2-microglobulin</td>
<td>500-15,000</td>
</tr>
<tr>
<td><strong>Large molecules</strong></td>
<td>Myoglobin, Albumin, Transferrin, Retinol-Binding Protein, EPO</td>
<td>&gt;15,000</td>
</tr>
</tbody>
</table>
Diffusion is the main process that occurs inside of the dialyzer that contributes to the filtration of waste. Diffusion is the movement of particles from an area of high concentration to an area of low concentration. In the case of hemodialysis, small molecules in the blood, such as urea, flow across the concentration gradient from the blood compartment to the dialysate compartment. This is because the blood is more concentrated than the dialysate, containing the excess waste and toxins that need to be filtered out. The process of diffusion within a dialyzer is demonstrated in Figure 25. As shown, the blood flows on one side downward through the dialyzer while the dialysate flows on the opposite side upward through the dialyzer. These directions of motion represent a countercurrent flow which maximizes the concentration gradient within the dialyzer (Hemodialysis, 2014).

In addition to the process of diffusion is the process of convection within the dialyzer. Convection is the movement of middle molecules from the blood compartment to the dialysate compartment. This movement occurs because of pressure differences in the compartments of the dialyzer. The blood within the dialyzer has a negative pressure while the dialysate has a positive pressure. Middle molecules also travel through convection because of the solvent drag that results from the flow that the small solutes permeating across the membrane create (Azar, 2013). While diffusion can only remove small molecules from unclean blood, convection is responsible for filtering out middle molecules. In addition to diffusion, Figure 25 also displays the movement of solutes during the process of convection in the dialyzer.
The last process that takes place inside of a dialyzer is adsorption. Adsorption is less common than diffusion and convection because its occurrence depends on the composition of the dialyzer membrane. For example, adsorption will only occur in dialyzers with large enough pores in the membrane to allow for large solutes to pass through. This process is when large molecules, such as albumin, adhere to the dialyzer membrane. Unlike diffusion and convection, adsorption can only filter out proteins from unclean blood (Azar, 2013). The amount of large solutes that are removed from the blood depends on the affinity gradient of the membrane. Furthermore, the affinity gradient is determined based on ionic, hydrophobic, and van der Waals interactions (Rimmele & Kellum, 2010).

Figure 25: Diffusion and Convection in Dialyzer
There are many factors that affect the efficiency of solute clearance within a dialyzer. Some of these factors are blood flow rate, dialysate flow rate, surface area of the dialyzer, pore size, and length of dialysis treatment. In most cases, the blood flow rate within a dialyzer is maintained at a rate of 200-500 mL/min but can vary depending on the patient (Azar, 2013). If the blood flow rate is low, then the rate of solute clearance will be low compared to a higher blood flow rate which would result in a higher rate of solute clearance. Additionally, the size of a certain solute will also affect its reaction to varying blood flow rates. Along with the blood flow rate influencing solute clearance during dialysis is the flow rate of the dialysate. The flow rate of dialysate is maintained at a minimum of 500 mL/min. However, high-flux dialyzers, which are dialyzers that contain a high-porosity membrane for more efficient solute removal, will require a dialysate flow rate of approximately 700-800 mL/min (Azar, 2013). Correspondingly to an increase in blood flow rate, an increase of dialysate flow rate will increase the rate of solute clearance in the dialyzer. Although it can be more effective for solute clearance, opting for an increased dialysate flow rate will result in a more costly treatment because this requires more dialysate concentrate per dialysis treatment.

The surface area of a dialyzer also influences the rate of solute clearance during the treatment process. Most dialyzers range in a surface area of 0.8-1.4 m² but can be as large as 2.6m² or as small as .3m² (Azar, 2013). The larger the surface area of the dialyzer, the faster the rate of solute clearance that occurs if all other factors are kept the same. Furthermore, the length of the treatment process is the greatest determining factor of solute clearance because understandably, the longer the process is performed for, the larger the amount of waste that can be removed from the blood. All of these factors can be accounted
for mathematically in order to compare the exact changes they may have on solute
clearance. Specifically, the rate of movement of molecules per unit time can be calculated
using the formula

$$\frac{dn}{dt} = -DA \frac{dc}{dx}$$  \hspace{1cm} (5)

where $\frac{dn}{dt}$ is the rate of movement of molecules per unit time, $D$ is Fick’s diffusion
coefficient, $A$ is the area of the boundary through which the molecules move, and $\frac{dc}{dx}$ is the
distance through which the molecules move. This equation combines the factors that affect
the solute clearance so that exact numbers may be calculated.

The fibers within the dialyzers can be produced using a variety of materials. The
two main groups of membranes used for the fibers are cellulose membranes and synthetic
membranes. Furthermore, cellulose membranes can be broken down into groups of
unsubstituted cellulose or substituted cellulose. With unsubstituted cellulose membranes,
the cellulose is produced using cotton and they contain many free hydroxyl groups within
the cellulose polymer. These free hydroxyl groups are able to activate serum complement
proteins which in turn activate leukocytes and cause bioincompatibility. With substituted
cellulose membranes however, there is a chemical substitution of acetate or similar
molecules for these free hydroxyl groups (Azar, 2013). Therefore, modified cellulose
membranes are created.

Synthetic membranes can be broken into regular synthetic membranes, or more
recently, bioactive synthetic membranes. Synthetic membranes are created from non-
cellulose synthetic polymers. Compared with cellulose membranes, synthetic membranes
are not as strong. However, these types of membranes are more biocompatible. Some
Examples of the polymers used for synthetic membranes are polyacrylonitrile, polyamide, polymethylmethacrylate, polysulfone, or polycarbonate. There has been some innovation with bioactive synthetic membranes, although they have not proven to be more efficient yet. Thus far, there are polysulfone vitamin E-coated membranes and polyacrylonitrile heparin-grafted membrane. The former has proven to reduce oxidative stress markers for a dialysis patient while the latter has been able to decrease anticoagulant necessities throughout a dialysis treatment (Azar, 2013).

Synthetic membranes are most widely used due to their biocompatibility and variety. These membranes can be used to produce low-flux or high-flux dialyzers. Low-flux dialyzers are dialyzers that have small pores on the fibers, which does not allow for a fast blood flow rate. High-flux dialyzers enable a highly efficient dialysis treatment. However, there can be disadvantages to high-flux dialyzers, as well. For example, they increase the risk of hypotension for the patient. Hypotension is when a patient develops low blood pressure within their arteries during treatment. This is the opposite of hypertension, or high blood pressure. Additionally, a phenomena called backfiltration will inevitably happen with the use of high-flux dialyzers. Backfiltration is the flow of fluid from the dialysate part of the dialyzer to the blood part. It occurs because of pressure differences within the dialyzer, which are more drastic in high-flux dialyzers. When this phenomena occurs, it is dangerous for the patient once the blood is returned, especially if the patient is exposed to high-flux dialyzers frequently (Azar, 2013).
CHAPTER 3. REDUCING DELAYS IN THE DIALYSIS PROCESS

3. Introduction

Once all of the preceding background research was conducted, the project team was able to recognize two types of factors that contribute to the length of treatment time: those which are intentional components of the dialysis process, and those which are potential mishaps. The team set out to find ways to shorten treatment time in both such aspects. This goal was accomplished by first identifying the sources of delays within the system, then creating various iterations of proposed designs to address said delays, analyzing and comparing the designs to available options. The team also proposed various alternative recommendations and solutions to improve current practices. This chapter details the work done and procedures followed throughout the course of the project, and an explanation of results and observations.

3.1 Reducing Treatment Time Delays

There are various factors that contribute to the elongation of the hemodialysis treatment process. Furthermore, some factors may create safety concerns for the patient throughout the treatment. After the team investigated causes for delays and safety concerns, solutions could be formulated and analyzed.

3.1.1 Cartridge Design

Determined through our research, a separate cartridge is beneficial to the hemodialysis process when added to a dialysis machine. The cartridge is used to house the components for the blood purification system. The blood purification system involves the extracorporeal circulation of contaminated blood through a semi permeable membrane. A
disadvantage to most dialysis machines is that the blood purification system is composed of a myriad of tubes that comprise the fluid pathways. This results in an increased risk for leakage and breakage. The Fresenius 2008K² dialysis machine, modeled in Figure 26, uses a modular design that allows for flexibility in treatment applications, such as single needle and double needle dialysis.

The team also created SolidWorks® models of all of these modular components, which can be seen in Appendix G. The modular system allows for the use of disposables. However, one can see in Figure 27 that the modular system is bulky and contains empty spaces when opened up. Additionally, the modular system must be unscrewed in order to
remove a single modular, thus increasing the time required to rearrange or add additional modular prior to a treatment process.

![Figure 27: Pictures from the Modular Fresenius 2008K2 Dialysis Machine](image)

The cartridge, which is invented by Barry N. Fulkerson and Russell T. Joseph, is shown in Figure 28. This cartridge is recommended by the team to be incorporated in future dialysis machines. The cartridge is composed of sensors, pumps, and disposables.

![Figure 28: Illustration of the Current Cartridge](image)

Figure 29 can be referred to throughout this explanation. The numbers refer to the molded flow paths containing disposable tubes for the blood, dialysate, waste fluids, and substitutions fluids.
The following sensors can be incorporated in the cartridge: arterial and venous pressure monitors, air detectors, blood leak detectors, and flow meters. The sensors are not required but instead are optional. They can be inserted into the cartridge by a concave molding. Therefore, allowing for different sensors to satisfy different needs and thus improving the safety of treatment. The cartridge houses two pumps, a blood pump and a waste pump. For the current invention, the blood pump tubing is Tygon brand, formulation S-50-HL, with dimensions of 1/8” Inner Diameter by 3/16” Outer Diameter by 1/32” wall thickness. The waste pump tubing is of the same brand but the dimensions are 3/32” Inner Diameter by 5/32” Outer Diameter by 1/32” wall thickness. These dimensions and brand of tubing are not required, but were however included as a possible solution. The blood
volumetric pump draws blood into the cartridge through the blood inlet port and flow path 1. The blood volumetric pump pumps blood into the dialyzer through flow path 2. The waste volumetric pump draws waste out of the dialyzer through flow path 4 and is pumped out of the cartridge through flow path 5.

The material that was selected for the modified cartridge was of brand Tecapeek MT, which is a semi-crystalline, high performance thermoplastic. This material is used in the medical field in applications such as surgical instruments, surgical containers, pump housing, sensor housing, and sterilization containers. Tecapeek MT is FDA and ISO 10993 compatible, as well as USP Class VI biocompatible. This material can be exposed to limited contact to blood and tissue up to 24 hours. Along with being biocompatible, Tecapeek MT has the following properties, good wear resistance, chemical resistance, and excellent gamma radiation resistance. Additionally, Tecapeek MT can withstand Eto and Steam sterilization, which is important for disinfection of the cartridge. The material is well suited for the modified cartridge for it is available in both red and blue for the color-coded manifold (Tecapeek MT, 2008).

The brand of tubing that we recommend for the cartridge is Streamline from NxStage. The blood set tubing, labeled 1, 2, and 3, is where the blood enters the cartridge through the blood inlet port and goes to the dialyzer before returning back to the patient through the blood outlet port. The tubing should be of a specific length and diameter capable of supplying a blood flow of 50 mL/minute. The blood set tubing, labeled 4 and 5, removes waste from the dialyzer and brings it to the waste out port. This tubing should be capable of supplying a blood flow of 8.33 mL/minute. The molded flow paths are incorporated into a single portable composite manifold. Integrating color-coded flow paths
is greatly beneficial because they clearly represent the blood and waste paths, making connecting of tubes easier. The SolidWorks model in Figure 30 shows the modified cartridge with the tubing in place and the color-coded manifold.

![Figure 30: SolidWorks CAD of the Modified Cartridge](image)

A dialyzer is shown in the hemofilter cartridge of the aforementioned 3D model. The blood is cleansed of toxins as it passes through the dialyzer. The clean blood then follows flow path 3 and exits through the blood outlet port. An example of possible specifications of the hemofilter is shown in Table 3 (Fulkerson and Joseph, 2013).
Table 5: Possible Specifications for a Hemofilter in the Cartridge

<table>
<thead>
<tr>
<th>Component</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Membrane Surface Area (m²)</td>
<td>≤ 0.1</td>
</tr>
<tr>
<td>Prime Volume (ml)</td>
<td>≤ 10</td>
</tr>
<tr>
<td>Molecular Weight cut-off (Daltons)</td>
<td>65000</td>
</tr>
<tr>
<td>Pressure Drop3 (mmHg)</td>
<td>≤ 50 (Ob = 50 ml/min)</td>
</tr>
<tr>
<td>Max Transmembrane Pressure (mmHg)</td>
<td>≥ 500</td>
</tr>
<tr>
<td>Overall Unit Length (cm)</td>
<td>12 - 15</td>
</tr>
<tr>
<td>Filtration Rate</td>
<td>8 – 10 ml/min @100 mmHg</td>
</tr>
</tbody>
</table>

**Tubing Connections**

<table>
<thead>
<tr>
<th>Component</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>Male Luer</td>
</tr>
<tr>
<td>Filtrate</td>
<td>Slip Fit (straight)</td>
</tr>
<tr>
<td>Sterilization</td>
<td>ETO or gamma</td>
</tr>
<tr>
<td>Preferred Membrane Material</td>
<td>Polysulfone</td>
</tr>
<tr>
<td>Housing Material</td>
<td>Polycarbonate</td>
</tr>
<tr>
<td>Potting Material</td>
<td>Polyurethane</td>
</tr>
</tbody>
</table>

Figure 31 shows an enlarged, detailed view of the manifold of the present invention with color-coded pathways for the flow paths carrying blood and waste. The connection ports are molded into the module for connecting to the pumps and the hemofilter cartridge through the use of Luer connections and tubing.
The modified cartridge with Streamline tubing and the colored flow path manifold is recommended to be used in dialysis machines. The manifold system with color-coded pathways improves upon treatment by decreasing the risk of disconnection, misassembly, and leakage compared to prior dialysis machines. Assembly and cleaning segments of the treatment process would be faster with color coded flow paths, disposables, and concave moldings to quickly insert components into the cartridge.

Figure 32 shows a possible configuration of the modified cartridge in the Fresenius 2008K² machine. The cartridge simplifies the tubing pathways, minimizes the overall bulky components, and allows for ease of assembly due to the color-coded manifolds.
The cartridge replaces the modular system by incorporating all of the components of the extracorporeal circuit. Therefore, the modified cartridge is intended to decrease the delays associated with dialysis treatment and should be integrated into future dialysis machines.

3.1.2 Needle Fixture Design

Dislodgement is a very serious and potentially deadly problem in dialysis. Should any needle ever become disconnected from the patient during treatment, it will cause a time delay, however venous needle dislodgement (VND) is a lot more serious, as this is the needle that is returning the cleaned blood to the patient. There is an incidence rate of about 400 patients per year. When the venous fistula needle becomes separated from the access, there is a drop in venous blood pressure and rapid blood loss. At standard blood flow rates, it usually takes just minutes for a patient to lose 40% of their blood volume, which is the amount that causes hemorrhagic shock. Though dialysis machines have sensors and alarms to alert the staff, the drop in venous pressure is often not significant enough to trigger these means, and so other steps must be taken.

In addition to the blood pressure monitors on the machine, there are a number of other monitors and sensors that are available as add-ons, such as moisture monitoring pads and blood detection devices. Unfortunately, each of these safety measures has significant downfalls and has been found incapable of detecting small volumes, which renders them useless as early alerts. For this reason our project aimed for preventing dislodgement rather than detecting it after the fact. The team has designed a fixture to help hold fistula needles in place and prevent dislodgement. This fixture is shown in Figure 33 and takes the form of a band that can be wrapped around a patient’s arm.
The darker, outer wings are modeled with a canvas material, but could be made of any flexible, comfortable material. These wings would attach with Velcro. In the middle of the arm-band, there is a rigid triangular plastic piece, with a clamp attached to the bottom. This clamp will be the portion of the arm-band that actually holds the needle. The purpose of the triangular piece is to protect the needle and the clamp from possible outside factors. This needle-holding fixture can be snapped onto the fistula needle after cannulation, and the canvas wings can be comfortably wrapped around the arm and fastened on the other end. The clamp is designed with a flexible plastic material that can adjust to suit the range of outer diameters that it would encounter between 1.27 and 2.108
mm. The reason that the clamp is below the triangular part instead of above is because the fistula needle must be flattened against the patient’s skin during cannulation.

### 3.1.3 New Tubing

The machine the team worked with is the Fresenius 2008K2 model, which uses a brand of tubing called ReadySet. This tubing is made with several materials, with the most significant being polyvinyl chloride (PVC). This tubing contains the plasticizer diethylhexylphthalate (DEHP) to allow malleability. A risk with this type of plasticizer is that small amounts of it break off and flow into the blood stream. There are two sets of tubing involved in the hemodialysis treatment process: the arterial tubing and the venous tubing. The arterial tubing is connected directly to the patient and draws the blood from the patient into the machine to be cleaned. The venous tubing is how the cleaned blood is brought back to the patient. Both of these tubing sets are fed through the machine in a loose configuration to allow the patient to move around during treatment without dislodging the needle or other components of the machine. Additionally, these tubing sets are equipped with side branches that consist of anticoagulants, pressure monitors, and drip chambers. These side branches ensure the patients’ safety and effective cleaning process.

ReadySet tubing is currently used in the machine for many reasons. Most importantly, it is used because it is medically safe for the patient. The geometry, as well as the blood pumps, also allows for the correct blood flow rate (BFR) for the patient throughout the treatment process. Although the tubing does not directly control this fluid characteristic, the size of the tubing does differ from patient to patient altering the BFR. For example, the venous pressure will vary depending on the diameter of the bloodline tubing. Pediatric patients use a narrow tubing diameter, which in turn affects the overall
extracorporeal blood volume. The diameters for an adult patient and the diameters for a pediatric patient vary.

Considering all the variables of the bloodline tubing that can contribute to sources of delays in the dialysis treatment, we researched possible solutions to implement into the Fresenius 2008K dialysis machine. We focused on reducing the tubing length, making the tubing more lightweight, changing to a safer material, and maintaining an efficient flow rate. The first delay that is commonly encountered in the dialysis treatment process is the time it takes for the blood to travel through the machine and return to the patient. The tubing is lengthy, which causes “spaghetti loops” inside of the machine. A “spaghetti loop” is a term given to excess tubing that drape down and is loose along the path that the blood travels. An example of “spaghetti loops” in the machine is shown in Figure 34.

![Figure 34: Excess Tubing, "Spaghetti Loops"](image)

There is some tubing hanging below components and in some cases even hangs below the machine, making it a safety hazard if the machine has to be moved. This delays the process for several reasons, one being the travel time. To validate that this aspect of
the tubing could be altered, we researched other types of tubing that are being used in the dialysis field and compared it to ReadySet tubing. The length of the tubing coincides with the volume of the extracorporeal circuit, which is where the blood travels through in the machine. Therefore if the tubing is lengthy and has a large diameter the overall volume and space it takes up will cause the machine to be very bulky and heavy. This produces delays in the treatment process because the set up and clean up segments are prolonged.

The longest part of dialysis is the actual treatment time. If the tubing is less lengthy, the cleaning and mounting process will not take as long. The next source of delay that greatly impacts the time a patient has to endure treatment is the splashing of blood and formation of micro-air bubbles within the drip chamber. As the blood drips into the chamber, it can create small air bubbles, which then pass through an air bubble detector, causing the machine to sound an alarm and stop treatment. Air bubbles can be very dangerous for the patient and therefore must not be passed back into the patient’s bloodstream. According to Streamline, Medisystems, A Nxstage Company, it is very common for dialysis treatments to result in infusion of air bubbles into the patient’s bloodstream, causing inflammation, air embolism, and lung damage. The monitoring of air bubbles within the machine slows the overall dialysis treatment time. Lastly, the excess medical waste that is produced from the treatment process contributes to delays in the cleanup portion. With more waste, we found that the doctors or nurses spend more time cleaning up after the treatment process, which can extend the treatment process for the patient.

Throughout this project, we focused our research on ways to reduce the time it takes for a patient to receive dialysis treatment. Specifically we looked at how the tube can be
modified to reduce the travel time. From our research we found that a brand of tubing called *Streamline* was being tested and used for NxtStage dialysis products. NxtStage has developed a portable dialysis machine that is 15x15x18 in, weighs approximately 75 pounds, and still maintains the same flow rate of about 600mL/min. This, compared to the Fresenius 2008K with dimensions of 45in. x20in. x20in. and weight of about 154 pounds, was accomplished by using Streamline tubing (2008K User’s Guide, 2012).

After comparing the benefits of Streamline tubing to ReadySet tubing, we concluded that in order to reduce the delays of the dialysis treatment, it would be a great improvement to implement Streamline tubing to Fresenius model machines. There are several reasons why Streamline is so innovative. First, the design of this brand of tubing incorporates airless components. In other words, it eliminates the air-blood contact by replacing the typical drip chambers, which uses an air gap for pressure monitoring, with an airless arterial and venous pressure measurement, known as Pressure Oscillating Diaphragm, “POD”. As the blood travels into the POD, there is an internal flexible diaphragm that communicates pressure to the sensors within the machine. Figure 35 shows a close up view of the POD.

![Figure 35: Venous Pressure (POD)](image)
The research yielded a common area for delays in the drip chambers and tubing was the air-blood contact. By eliminating this interaction, there will be fewer delays relating to the formation of air bubbles and the patient will remain safer. Along with the airless POD, Streamline also replaces the venous chamber that ReadySet tubing uses with an airless venous “vortex” chamber. This design is advanced because it prevents any splashing of blood or stagnation of blood within the compartments. The blood enters with a horizontal, vortex-like flow and fills the chamber completely. A venous bubble trap filter that is intended to reduce clotting is also inside the chamber. The vortex chamber is shown in Figure 36, along with a close-up of the filter within.

These components are designed to improve the safety of the patient by eliminating the air to blood contact that result in delays in the dialysis treatment process. It provides safe travel of the blood throughout the machine so that the patient does not have air bubbles form within the bloodline, leading to serious health risks.

Next, Streamline has improved the tubing design inside of the machine. The tubing length was reduced, lessening the “spaghetti loops” that conventional tubing have while still be compatible with the Fresenius 2008K dialysis machine. Overall, it reduces the extracorporeal blood volume, lightens the weight of the machine, and simplifies the tubing
design. Table 4 shows the reduction of each component and the impact of this improvement.

Table 6: Streamline Versus Traditional Tubing

<table>
<thead>
<tr>
<th>Conventional Bloodline Layout</th>
<th>Streamline Layout Change</th>
<th>Clinical and Operational Impact</th>
</tr>
</thead>
</table>
| Extracorporeal Blood Volume: 143-165mL | 15-35% lower | • Less blood exposure to plastic  
• Lower saline priming volume  
• Less “spaghetti” designed for easier setup, teardown and troubleshooting |
| Set Weight: 0.64-0.70lb | 35% lower | • Designed for lower disposal costs  
• Less landfill usage  
• Fewer red bags to close and discard |
| Packaging Volume: 24 sets/case | 33-50% lower | • Lower storage space requirements  
• Reduced packaging waste |

From this table, it is clear that incorporating Streamline tubing in Fresenius model machines will reduce much of the waste and time it would take to clean and dispose of the used materials. This will result in a shorter treatment time for the patient. The reduction of “spaghetti loops” and excess tubing is important because it decreases the chance of something getting caught on the tubing and tugging on the machine and patient, which can be very dangerous. Figures 37(A) and 37(B) show a comparison of ReadySet tubing and Streamline tubing within the same machine.

Figure 37: (A) Machine with ReadySet Tubing, (B) Machine with Streamline Tubing
As can clearly be seen, the ReadySet tubing has lengthy loops and excess tubing hanging outside of the frame of the machine. On the other hand, Streamline has reduced the amount of tubing used and simplified the path in which the blood travels. Due to the laminar flow of the blood in the in the bloodline tubing, the length and angle of bend in the tubing also plays a crucial role in the blood flow rate. Simplification of the blood travel path will reduce the amount of severe angles the tubing takes to bring the blood from one component to the next. Pressure and BFR are very vital to patients’ safety and the efficiency of the dialysis treatment. As we researched more about the possible delays in the dialysis process, we found that increasing the flow can decrease the amount of time it would take for the overall treatment process.

Streamline also impacts the clinical outcomes, which helps the efficiency of the treatment process. In order to improve the safety of patients during dialysis, we researched what could cause health problems and side effects. One health risk that Streamline addresses is the unwanted side effects of heparin, the anticoagulant administered in most dialysis treatments. In some cases, patients can get heparin-induced thrombocytopenia, allergies, osteoporosis, or excessive bleeding. Streamline was designed so that the doctors would not have to give the patient as much heparin as usual. Typically, patients would receive about 0.75-1.75mL more heparin if using conventional tubing. This reduction, according to Medisystems, reduced the clotting and improved rinsebacks.

Another improvement in clinical use for Streamline is the improvement in the arterial pressure and increase in blood flow. Dialysis treatment standards usually only allow for the arterial pressure to be improved by changing the patient’s vascular access or by lowering the blood flow. Streamline tubing allows for the machines to work at a lower
arterial pressure, which improves the hemodynamics and lowers the turbulence, or movement within the bloodlines. Figures 38 and 39 show two graphs of the arterial pressure improvement and blood flow improvement based on clinical experience.

**Figure 38: Arterial Pressure Improvements with Streamline**

**Figure 39: Blood Flow Improvements with Streamline**
From these graphs, it is clear that by using Streamline the blood flow rate can be raised by 50-100mL/min without any negative effects on the patient. This will not only lead to a faster dialysis treatment, but also has a positive effect on the Kt/V, the minimum treatment urea ratio. By increasing the blood flow, the doctors can then increase the prescribed dialysis doses.

Implementation of Streamline tubing into Fresenius dialysis will greatly improve treatment in several aspects. The first is reducing the size of the extracorporeal blood volume and simplifying the tubing design within the machine. The Streamline innovation of airless components also increases the safety of the patient by reducing the chance of air bubble formation, which can cause serious health problems. Reducing the travel time of the blood will also help in decreasing the delays associated with the overall time it takes to complete treatment. Additionally, Streamline increases the blood flow and the dialysate prescription, resulting in a more effective treatment. Streamline tubing is a new tubing system designed to improve the dialysis efficiency and should be used in Fresenius dialysis machines and eventually all dialysis machines. The streamline tubing is compatible with the cartridge design.

3.2 Recommendations

This chapter discusses the suggestions that the team proposes for helping to reduce time delays in the hemodialysis treatment process. The first section presents the recommendations for needles and access points, while the second and third present recommendations for the dialyzer and water treatment system, respectively. Our recommendations are based on extensive research of the hemodialysis process and were
tested for effectiveness by comparison to the literature and previous efforts made towards reducing treatment delays.

### 3.2.1 Preventing Treatment Delays Associated with Needles and Accesses

The proper insertion, securement and removal of the fistula needle are very important, as explained in chapter two. One setback that can lead to prolonging dialysis treatment time is posterior wall infiltration. As previously mentioned, to prevent this accident, the nurse should first rotate the fistula needle $180^\circ$ during the cannulation process. Rotating the needle gives the nurse a chance to pause once the needle is within the first wall of the access, which decreases the likelihood of infiltration of the posterior wall. In the event that infiltration still occurs however, the course of action depends on the conditions of the situation.

If the patient has not yet received heparin, the needle should be pulled out and pressure should be applied to the exit site by placing two fingers along the access, covering at least a one-inch area. If, however, the patient has already received heparin at the time of infiltration, the puncture site must be carefully assessed. If the needle site remains stable with no increase in size or swelling, it is safe to keep in place for the duration of the dialysis treatment, but ice should be applied over the infiltration site. If a solid swelling is observed, the needle should be removed and digital pressure should be applied. It is important to note that pressure should never be applied while the needle is inside the patient. If the needle had to be removed due to infiltration, a new needle should be used to perform cannulation and a new spot should be chosen as far away as possible. Infiltration is one delay for which the administering nurse must be properly trained.
Dislodgement is a very serious and potentially deadly problem in dialysis. Should any needle ever become disconnected from the patient during treatment, it will cause a time delay, however venous needle dislodgement (VND) is a lot more serious, as this is the needle that is returning the cleaned blood to the patient. There is an incidence rate of about 400 patients per year. When the venous fistula needle becomes separated from the access, there is a drop in venous blood pressure and rapid blood loss. At standard blood flow rates, it usually takes just minutes for a patient to lose 40% of their blood volume, which is the amount that causes hemorrhagic shock. Though dialysis machines have sensors and alarms to alert the staff, the drop in venous pressure is often not significant enough to trigger these means, and so other steps must be taken.

To prevent needle dislodgement without the use of the needle-holding fixture design, it is important to properly care for the access site prior to cannulation. If the site is not allowed significant time to dry after it has been cleaned during prep, the bandages are more likely to slip off. To help pacify the effects of dislodgement once it occurs, the first recommendation of this project team is consistent monitoring. It is usually the case when dislodgement becomes fatal that the patient was asleep under a blanket and no one noticed the blood spillage. Nurses at dialysis centers and in the home should make consistent rounds and check on any covered or sleeping patient.

Another source of delay related to the needles and access points is the formation of a pseudoaneurysm at an access graft because it can limit the life of the graft and require the creation of a new access, which takes time to mature. A pseudoaneurysm is a solid swelling of clotted blood that forms outside the arterial wall and so is contained by the surrounding tissues. They are usually caused by repeatedly puncturing the same limited
area on an access with the fistula needle. Obviously, the best way to prevent the formation of a pseudoaneurysm would be for the nurse to avoid repeatedly cannulating the same areas of an access. Once again, this type of delay is one that a nurse or doctor would treat best. Traditional treatment includes surgically extracting the pseudoaneurysm and replacing the entire graft, perhaps one made with a different material. Access sites can also provide another source of treatment delays. Dialysis accesses can fail to mature but doing fistula hand-arm exercises can help. Ball squeezes, thumb-to-fingertip touches, hammer curls, bicep curls and clothes-pin grasps are all particularly advantageous. These exercises should be done before and after the fistula or graft surgery, and continued until the access is fully developed.

3.2.2 Suggestions to Minimize Delays Associated with the Dialyzer

As previously mentioned, the dialyzer can contribute greatly to the lengthiness of the hemodialysis process. Through previous research and tests, dialyzer characteristics have been studied since the creation of the hollow fiber dialyzer. The extensive research investigated on this aspect of the hemodialysis treatment process has enabled us to recommend the best options to ensure that each dialysis session can be optimized depending on the patient. There are many factors that contribute to the length of treatment and resulting delays of each dialysis session, such as the choice of dialyzer. This aspect of the dialysis process can be difficult as the dialyzer is essentially the “artificial kidney” of the procedure and is ultimately responsible for the removal of toxins from the blood. These performance characteristics are responsible for the amount of toxins that will be cleared out of the blood. However, it is crucial to rid the blood of wastes in addition to minimizing the length of each treatment. Therefore, we have investigated each component of the
dialyzer that may present delays to ensure that this step of the process is both efficient and time-reducing.

One delay that can be encountered in current dialyzers is a phenomenon called backtransport. This term describes two different occurrences—backdiffusion and backfiltration. Backdiffusion refers to the movement of bicarbonate from the dialysate compartment of the dialyzer to the blood compartment and is caused by the concentration gradient. This can happen in any type of dialyzer and is inevitable. However, backfiltration can be more dangerous if it occurs frequently. Backfiltration is the movement of fluid from the dialysate compartment to the blood compartment through convection. This is caused by the differences in pressure within the dialyzer during the dialysis process. At the start of treatment, the pressure of the blood inlet is always higher than that of the dialysate inlet. However, during treatment there is a pressure drop along the length of the dialyzer. The result is that the dialysate compartment has a positive pressure while the blood compartment has a negative pressure. This results in movement of the fluid in the dialysate side to the blood side in an attempt to equalize the pressure gradient. The backfiltration phenomena is not likely to occur in low-flux dialyzers. However, this occurrence is inevitable while using a high-flux dialyzer. This is because high-flux dialyzers are more inclined to have larger pressure differences between the two compartments and therefore are prone to more frequent backfiltrating. This is dangerous for the patient and if one should be exposed to high-flux dialyzers often, they can develop long-term health effects or even death (Azar, 2013). Therefore, we do not recommend the use of high-flux dialyzers even though they can rid the blood of toxins more quickly than low-flux dialyzers.
Another aspect of the dialyzer that may contribute to delays during the hemodialysis process is the chosen flow rates for each patient. These flow rates refer to the blood flow rate as well as the dialysate flow rate. The goal of reducing delays pertaining to the flow rates is to optimize the flow to be most efficient while still keeping rates safe for the patient’s heart. We determined optimal flow rates depending on certain factors, such as area of the boundary through which the molecules move. Ideal flow rates work together with the optimization of the tubing and tubing paths in order to complete each treatment in an efficient way. Once the proper flow rate is determined, the clearances of certain toxins can be calculated using various formulas. The inlet flow rates of the blood and dialysate were calculated. These flow rates were optimized but it still must be kept in mind that each patient is different and the flow rates will vary accordingly. In general, a faster dialysate flow rate will increase the rate of diffusion of urea from the blood compartment to the dialysate compartment within a dialyzer (Azar, 2009).

Lastly, a common delay encountered within dialyzers during hemodialysis is the interference of diffusing particles with the convection of other particles and vice versa. In other words, these processes are both occurring at the same time within the dialyzer, and therefore, they have effects on each other. As diffusion occurs within the dialyzer, large solutes tend to accumulate on the membrane surface because they cannot permeate through diffusion. This can prevent some of the middle molecules from being removed through convection as the large molecules are in the way. On the other hand, as convection is occurring, there is a change in local solute concentrations. This can interfere with the diffusion of small molecules since diffusion rates are dependent on the concentration of solutes as the small molecules migrate to lower concentrated areas. As these two
occurrences may contribute to delays in the clearance of solutes during the hemodialysis process, the interference is inevitable in a hollow fiber dialyzer as diffusion and convection will be taking place at the same time and in the same area. Therefore, we have no recommendation for the prevention of convection and diffusion interference in a hollow fiber dialyzer.

3.2.3 Reducing Delays within the Water System

Dialysis patients are continuously subjected to large amounts of water in order to filter their blood of toxins. An average hemodialysis patient is exposed to more water in one week of treatment than most people are exposed to in a lifetime. Therefore, it is very important to have good water quality in order to avoid complications that are associated with contamination (Coulliette, 2013). Local water must go through a water treatment system in order to remove impurities and excess minerals. Excess of magnesium, aluminum, fluoride, and other contaminants can cause problems such as anemia, bone disease, and muscle weakness (Mauro, 2015). Therefore, various water treatment system designs should be considered in order to reduce the risk of delays associated with stagnant water, contamination from bacteria and endotoxin, and biofilm formation.

When designing a water treatment system, it is important choose the right distribution system design and materials. The distribution system is at risk of bacterial colonization when there are dead ends, oversized or flat-bottom tanks, sluggish flow, and improper disinfection. It is imperative to avoid stagnant water because it is a contributing factor to bacterial growth (Oumokhtar, 2013). Dialysis centers have the option between direct feed and indirect feed. We recommend the use of the indirect feed system. One thing that is advantageous about indirect feed loops is that if the RO system fails there is time to
react. In a direct feed, failure results in no water. Direct feed loops also carry the risk of retrograde contamination of the dialysis water. In direct feed systems, there could be transient pressure fluctuation that results in the water being brought back to the feed side of RO having a higher pressure than the end of the dialysis water in the distribution loop (Kawanishi, 2011). Indirect feed systems constantly circulate the water even when machines are not in use. The direct feed system is not recommended because of the possibility of microbial growth/bio-film formation when there is low or no flow (Coulliette, 2013). Although storage tanks are not ideal with indirect feed loops and should be avoided when possible, if a storage tank is to be used, the following designs specifications should be considered. The tank should be designed so that water will enter the storage tank from above. Therefore, the water will wet the anterior surface and exit through the inferior. Also, the storage tank should be opaque as to help prevent the growth of algae (Perez-Garcia, 2000).

Additional design considerations for water systems is the placement of ultra-filters. Ultra-filters help prevent bacteria colonization by having a filter in the water line leading to the storage tank and in the water loop. Unfortunately, it also decreases the flow rate thus decreasing the velocity, as well. One should also consider an ultra-filter on each hemodialysis machine prior to the point where the dialysate enters the dialyzer. This will ensure that the water entering the machine is in fact endotoxin and bacteria free (Andrysiak, 2002).

Pipe tubing material and plumbing design considerations are to help prevent bacterial contamination, biofilm formation, and stagnant water. Suitable materials are made from PVC and stainless steel. PVC schedule 80 is usually the material of choice in
the United States because it is relatively cheap. When using PVC, it is very important to use an approved PVC cutter method in order to prevent rough edges. If there are rough edges, bacteria can adhere to material. Chamfering of edges reduces the number of burrs in the pipes and decreases the amount of stress points. This helps with the design because it decreases the likelihood of cracking of the pipes (Andrysiak, 2002). Stainless steel is more expensive than PVC but is a material to consider because it is resistant to biological corrosion (Perez-Garcia, 2000). Furthermore, a study showed that over a period of 14 years, purified water, chemical disinfectants, and water flow rates eventually breakdown PVC, causing a surface that is susceptible to bacterial growth (Coulliette, 2013). When designing the actual piping route, one must consider the angles and connection points. Instead of making a 90 degree turn, one should use two 45 degree angles. This will allow for an even flow and prevent stagnation. Connection points should also be as short as possible when connecting pipes to the hemodialysis machines. This will minimize the stagnant areas. Pipes with a smaller diameter should be used to maintain the highest flow velocity possible when entering the hemodialysis machine (Andrysiak, 2002).

Other considerations that should be made to decrease the amount of microbial contamination in the treated water is the infusion of chlorine after the activated carbon filter and before RO, in addition to submicronic filters, UV radiation, and disinfecting the treatment system with ozone. As for concentrates used in the dialysis process, it is recommended that they should have low pH and have high solute concentrations because they are less likely to become contaminated. Bicarbonate concentrations and concentrates in powdered form are not ideal because they become frequently contaminated (Perez-Garcia, 2000).
The prevention of biofilm formation is very important in the water treatment system. Biofilm is very difficult to remove once growth is underway. A study has shown that neither heat nor chemical disinfectants were able to eliminate biofilm. Therefore, it is important that the initial growth is prevented (Cappelli, 2000). In another study, two different method, for a water treatment system, method A and method B, were conducted to see which method was more efficient at preventing biofilm formation. During a 12 week period, method A, a single RO was compared to method B, a double RO with and electric DI. During the study, biofilm was observed in the tubing segment between the water piping and the dialysis module. That segment was selected because it does not receive disinfection and is more susceptible to bacterial growth than other segments. In method A, tube cultures showed positive results in 16% of samples at 22-37 degrees Celsius with amounts greater than 100 colony forming units per mL (CFU/mL). Method B was only positive in 3% of the samples. Endotoxin levels were positive in 76% of method A samples and were negative in all of method B samples. Biofilm formation was present in 91.7% of method A samples and only present in one of method B samples. In the following images, one can see examples of biofilm in tubing segments of method A and method B, taken after the 12 week period.

Figure 40: 400X Magnification for Method A Showing Formation of Biofilm
The project team concludes that method B has a significant reduction in biofilm formation, bacterial growth, and endotoxin levels. Therefore, it is more beneficial to use a water treatment system that has a double RO, electric deionization, and is continuously disinfected with UV light and treated with ozone once per week to produce highly purified water shown in method B rather than just the standard purified water in method A (Smeets et al., 2003). Through research, it is very apparent that system design and prevention of contaminants and biofilm formation are important in order to decrease the amount of delays in the dialysis treatment process. It is critical to decrease the threat of health complications associated with contaminants and biofilm, which make the treatment process more difficult and uncomfortable. We recommend an indirect feed system, proper disinfection of the system, stainless steel material, and incorporating a double RO with an electric deionizer in order to help achieve a safer and comfortable treatment for patients.
CHAPTER 4. CONCLUDING REMARKS

Overall, the dialysis machine has three main components: the dialysate delivery system, the extracorporeal blood-delivery circuit and dialyzer. Throughout these components there are various delays that through research we were able to develop alternate designs to reduce. For the extracorporeal blood-delivery circuit we focused on the tubing system, the access point for the patient, and the dialyzer. The dialysate delivery system delays were narrowed down to the water system and preventing contamination.

The sources of delays in the tubing system that we addressed were the excess tubing, large tubing volume and air to blood contact. In a Fresenius 2000K² dialysis machine there is a significant amount of excess tubing so that it develops what are called “spaghetti loops.” This increases the travel time of the blood, increasing the amount of time it takes for treatment. Also, since there is a risk of air getting into the bloodline, there is a greater risk that sensors will go off, resulting in a delay in the process. From our literature review and multiple clinical studies, we recommend implementing a new brand of tubing called Streamline tubing.

The sources of delays associated with the water treatment system are contamination of the dialysis water and the formation of biofilm where stagnant water is a major contributing factor. The design of the dialysis water treatment system is important in order to minimize areas of stagnant water. However, the design alone will not completely prevent contamination. Proper monitoring and maintenance of the system is crucial to prevent and control any bacterial or endotoxin contamination. Contamination of the water system is related to adverse health effects, making the treatment unsafe for patients and increasing treatment time. From our literature research, we recommend using stainless steel tubing,
indirect feed loop, a double RO with an electric DI, followed by proper maintenance and disinfection of the system.

In the Fresenius 2000K\textsuperscript{2} dialysis machine, a modular system is used for the extracorporeal blood circuit. The modular system is bulky, contains dead space, and has limited options for incorporating new components such as different sensors. Also, it contains a myriad of tubing, which can result in treatment delays, such as a lengthier process, when a complication associated with misassembly, leakage or breakage of tubing occurs. Through review of different patents, we recommend the integration of a modified cartridge with streamline tubing, color-coded manifolds, and disposables in future dialysis machines.
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## APPENDICES

### Appendix A. EPA’s List of Contaminants

#### Key:

- Microorganisms
- Inorganic Chemicals
- Disinfection Byproducts
- Organic Chemicals
- Disinfectants
- Radionuclides

#### EPA’s List of Contaminants with Associated Sources, MCL, and Effects

<table>
<thead>
<tr>
<th>Contaminant</th>
<th>MCL Goal (mg/L)</th>
<th>MCL or Treatment Technique (mg/L)</th>
<th>Potential Health Effects from Long-Term Exposure Above the MCL</th>
<th>Sources of Contaminant in Drinking Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Legionella</td>
<td>0</td>
<td>TT3</td>
<td>Legionnaire’s Disease, a type of pneumonia</td>
<td>Found naturally in water; multiplies in heating systems</td>
</tr>
<tr>
<td>Viruses (enteric)</td>
<td>0</td>
<td>TT3</td>
<td>Gastrointestinal illness (such as diarrhea, vomiting, and cramps)</td>
<td>Human and animal fecal waste</td>
</tr>
<tr>
<td>Bromate</td>
<td>0</td>
<td>0.01</td>
<td>Increased risk of cancer</td>
<td>Byproduct of drinking water disinfection</td>
</tr>
<tr>
<td>Chlorite</td>
<td>0.8</td>
<td>1</td>
<td>Anemia; infants and young children: nervous system effects</td>
<td>Byproduct of drinking water disinfection</td>
</tr>
<tr>
<td>Chloramines (as Cl2)</td>
<td>MRDL G=41</td>
<td>MRDL=4.0 1</td>
<td>Eye/nose irritation; stomach discomfort, anemia</td>
<td>Water additive used to control microbes</td>
</tr>
<tr>
<td>Chlorine (as Cl2)</td>
<td>MRDL G=41</td>
<td>MRDL=4.0 1</td>
<td>Eye/nose irritation; stomach discomfort</td>
<td>Water additive used to control microbes</td>
</tr>
<tr>
<td>Chlorine dioxide (as ClO2)</td>
<td>MRDL G=0.81</td>
<td>MRDL=0.8 1</td>
<td>Anemia; infants and young children: nervous system effects</td>
<td>Water additive used to control microbes</td>
</tr>
<tr>
<td>Arsenic</td>
<td>0</td>
<td>0.010 as of 01/23/06</td>
<td>Skin damage or problems with circulatory systems, and may have increased risk of getting cancer</td>
<td>Erosion of natural deposits; runoff from orchards, runoff from glass and electronics production wastes</td>
</tr>
<tr>
<td>Chromium (total)</td>
<td>0.1</td>
<td>0.1</td>
<td>Allergic dermatitis</td>
<td>Discharge from steel and pulp mills; erosion of natural deposits</td>
</tr>
<tr>
<td>Fluoride</td>
<td>4</td>
<td>4</td>
<td>Bone disease (pain and tenderness of the)</td>
<td>Water additive which promotes strong teeth; erosion of natural deposits</td>
</tr>
<tr>
<td>Substance</td>
<td>Concentration</td>
<td>Effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------------</td>
<td>---------------</td>
<td>-------------------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzene</td>
<td>zero</td>
<td>0.005 Anemia; decrease in blood platelets; increased risk of cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Discharge from factories; leaching from gas storage tanks and landfills</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlordane</td>
<td>zero</td>
<td>0.002 Liver or nervous system problems; increased risk of cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Residue of banned termiticide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vinyl chloride</td>
<td>zero</td>
<td>0.002 Increased risk of cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Leaching from PVC pipes; discharge from plastic factories</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radium 226 and Radium 228 (combined)</td>
<td>none7-5 pCi/L</td>
<td>Increased risk of cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Erosion of natural deposits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uranium</td>
<td>zero</td>
<td>30 ug/L as of 12/08/03 Increased risk of cancer, kidney toxicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Erosion of natural deposits</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Summary of Major Areas That Need Monitoring in a Water Treatment System

<table>
<thead>
<tr>
<th>Area</th>
<th>Monitoring Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Water Softener</strong></td>
<td>- Total hardness in the product water, should not exceed 1 ppm. Preferably checked at the end of the each day.</td>
</tr>
<tr>
<td></td>
<td>- Pressure drop: May need back-flushing if pressure drop changes more than 10 PSI between pre- and post- softener site.</td>
</tr>
<tr>
<td></td>
<td>- Brine tank salt level: adequate amount of salt needed in tank to allow for resin bead to regenerate by softener</td>
</tr>
<tr>
<td><strong>Carbon Tanks</strong></td>
<td>- Chlorine and chloramine levels after the last carbon tank, preferably each shift.</td>
</tr>
<tr>
<td></td>
<td>- Pressure drop change of more than 10 PSI leading to back-flush when unit is not operating.</td>
</tr>
<tr>
<td><strong>RO</strong></td>
<td>- Water pressure and flow rates through the unit to ensure optimum efficiency and life of membrane. A drop in water flow rate may mean that membrane is plugging up.</td>
</tr>
<tr>
<td></td>
<td>- Resistivity and rejection ratio. &lt;0.80 membrane must be changed.</td>
</tr>
<tr>
<td><strong>DO</strong></td>
<td>- Water pressure before and after the unit: a change of more than 10 PSI may mean that tanks may be getting plugged up.</td>
</tr>
<tr>
<td></td>
<td>- Resistivity and conductivity:</td>
</tr>
<tr>
<td><strong>Filters</strong></td>
<td>- All the filters should be regularly monitored for pressure drop across the device.</td>
</tr>
<tr>
<td><strong>Ancillary devices</strong></td>
<td>- temperature-blending valve, backflow prevention device, booster pump, and acid feed pump should also be regularly monitored and maintained.</td>
</tr>
</tbody>
</table>
Appendix C. Contaminants in Water

Contaminants in Water, Their Effects, and Concentration Limits

<table>
<thead>
<tr>
<th>Contaminant</th>
<th>Toxic health effect</th>
<th>Max concentration (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminum</td>
<td>Encephalopathy, bone disease, anemia</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Chloramines</td>
<td>Hemolysis, anemia, methemoglobinemia</td>
<td>&lt; 0.10</td>
</tr>
<tr>
<td>Chlorine</td>
<td></td>
<td>0.5</td>
</tr>
<tr>
<td>Copper</td>
<td>Hemolysis, fever, headache, hepatitis</td>
<td>&lt; 0.10</td>
</tr>
<tr>
<td>Fluoride</td>
<td>Bone disease, osteomalacia</td>
<td>&lt; 0.20</td>
</tr>
<tr>
<td>Nitrate</td>
<td>Cyanosis, methemoglobinemia, hypotension, nausea</td>
<td>&lt; 2.0</td>
</tr>
<tr>
<td>Sulfate</td>
<td>Nausea, vomiting, acidosis</td>
<td>100</td>
</tr>
<tr>
<td>Zinc</td>
<td>Anemia, nausea, vomiting, fever</td>
<td>0.1</td>
</tr>
<tr>
<td>Calcium</td>
<td>Nausea, vomiting, weakness, headache, hypertension, malaise, cardiac problems</td>
<td>&lt; 2 (0.1 mEq/L)</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Nausea, vomiting, weakness, headache, hypertension, malaise, cardiac problems</td>
<td>&lt; 4.0 (0.3 mEq/L)</td>
</tr>
<tr>
<td>Potassium</td>
<td>Muscle symptoms, bradyrrhythmia, death</td>
<td>8 (0.2 mEq/L)</td>
</tr>
<tr>
<td>Sodium</td>
<td>Hypertension, pulmonary edema, headache, thirst, confusion, seizure, coma</td>
<td>70 (3.0 mEq/L)</td>
</tr>
</tbody>
</table>
## Appendix D. Chemical Intoxication Outbreaks

### Outbreaks Caused by Chemical Intoxication 1960 - 2007

<table>
<thead>
<tr>
<th>Contamination</th>
<th>Description</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminum</td>
<td>Intoxication and seizures in 7 patients</td>
<td>exhausted deionization tanks unable to remove aluminum in incoming tap water</td>
</tr>
<tr>
<td></td>
<td>Intoxication neurologic symptoms, dementia and elevated serum levels in 64 patients, 3 deaths</td>
<td>aluminum pump was used to transfer acid concentrate to the treatment area</td>
</tr>
<tr>
<td></td>
<td>Elevated serum levels detected in 10 patients during routine screening</td>
<td>replacement pump used to pump acid concentrate contained aluminum components</td>
</tr>
<tr>
<td>Chloramine</td>
<td>Hemolytic anemia in 41 patients</td>
<td>residual disinfectant was not removed completely by the carbon tank when the facility increased the capacity of the water treatment system</td>
</tr>
<tr>
<td>Copper</td>
<td>Hemolytic syndrome in 12 patients, 32 episodes with 4 fatalities</td>
<td>six hemodialysis centers had partially exhausted deionization system resulting in low pH water causing the formation of copper ions</td>
</tr>
<tr>
<td>Fluoride</td>
<td>Intoxication in 8 patients, 1 death</td>
<td>accidental spill in hydrofluosilic acid at drinking water plant lead to excessive fluoride levels entering dialysis unit, insufficient treatment prior to dialysis</td>
</tr>
<tr>
<td></td>
<td>Intoxication in 9 patients, 3 deaths</td>
<td>exhausted deionization tanks discharged a bolus of fluoride</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>Intoxication in 5 patients, 1 death</td>
<td>disinfectant not properly rinsed from the distribution system</td>
</tr>
<tr>
<td></td>
<td>Intoxication in 12 patients</td>
<td>new filtration system was installed and not properly rinsed</td>
</tr>
<tr>
<td>Hydrogen peroxide</td>
<td>Decreased hemoglobin in 3 pediatric dialysis patients</td>
<td>H₂O₂ used to disinfect the system was not adequately rinsed from the system due to a flat bottom storage tank that could not be rinsed</td>
</tr>
<tr>
<td>Nitrate</td>
<td>Patient developed methemoglobinemia</td>
<td>home dialysis using well water that contained nitrate nitrogen (94 mg/l)</td>
</tr>
<tr>
<td>Sodium azide</td>
<td>Severe hypotension in 9 patients</td>
<td>dialysate contaminated with sodium azide used as a preservative from new ultrafilters, which were labeled “not for medical use”</td>
</tr>
<tr>
<td>Sulfate(s)</td>
<td>Nausea, vomiting, chills, some with fever in 16 patients, 2 deaths</td>
<td>source water used to prepare dialysate contained volatile organic compounds (CS₂, CH₃, etc.) and additional failures</td>
</tr>
</tbody>
</table>
## Appendix E. Microbial Contamination Outbreaks

### Outbreaks Caused by Microbial Contamination 1969 - 2008

<table>
<thead>
<tr>
<th>Contamination</th>
<th>Description</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacterial</strong></td>
<td>Gram-negative bacteria bloodstream infections in 8 patients (Burkholderia cepacia complex, Ralstonia sp., Pseudomonas aeruginosa, or Stenotrophomonas maltophilia)</td>
<td>Burkholderia cepacia complex found in reverse osmosis water, gram-negative organisms detected in a patient dialyzer and solution distribution system</td>
</tr>
<tr>
<td></td>
<td>Bacteremia episodes (~30) with the main gram-negative organisms being <em>P. aeruginosa</em>, <em>Proteus</em>, and <em>Flavobacterium</em></td>
<td>bacteria was found in tap water and dialyzer resins, while no chlorine residual was detected after deionizer columns</td>
</tr>
<tr>
<td></td>
<td>Pseudomonas cepacia recovered from 10 patients (13 cases of peritonitis)</td>
<td>insufficient disinfection of contaminated tap water that was used for cleaning dialysis machines</td>
</tr>
<tr>
<td></td>
<td>Nontuberculous mycobacterial (NTM) infection (<em>Mycobacterium chelonae</em> subspecies <em>abcessus</em>), 27 cases</td>
<td>detected in water samples</td>
</tr>
<tr>
<td></td>
<td>Pyrogenic reactions in 14 patients, 2 with bacteremia and 1 death</td>
<td>reverse osmosis water storage tank contaminated with bacteria</td>
</tr>
<tr>
<td></td>
<td><em>Intradialytic sepsis in 9 patients</em></td>
<td>gram-negative organisms detected in predialysis saline rinse, the source was either the dialysis fluid or water used for rinsing the dialyzers between uses</td>
</tr>
<tr>
<td></td>
<td><em>Bacteremia in 6 patients</em></td>
<td>likely source(s) of the gram-negative bacteria were the dialysis fluid or water used for rinsing dialyzers prior to reuse, as well as the improper preparation of the new disinfectant</td>
</tr>
<tr>
<td></td>
<td><em>Bloodstream infections of <em>Klebsiella pneumonia</em> in 6 patients</em></td>
<td>inadequate disinfection of reprocessed dialyzers, as technicians’ gloves were cross contaminating from infected patient</td>
</tr>
<tr>
<td><strong>Endotoxin</strong></td>
<td>Pyrogenic reaction in 49 patients</td>
<td>untreated tap water used to prepare the dialysate contained high levels of endotoxin</td>
</tr>
<tr>
<td></td>
<td>Pyrogenic reaction in 45 patients</td>
<td>inadequate disinfection of the fluid distribution system</td>
</tr>
<tr>
<td>Pyrogenic Reactions</td>
<td>Cause</td>
<td></td>
</tr>
<tr>
<td>--------------------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>In 13 patients</td>
<td>Bacteria was detected in tap water and water used to prepare the bicarbonate dialysate, endotoxin was detected in the faucet of the reprocessing room and the water-spraying device used for rinsing</td>
<td></td>
</tr>
<tr>
<td>In 23 patients (49 episodes)</td>
<td>Increased endotoxin levels found in the tap water used to prepare the dialysate</td>
<td></td>
</tr>
<tr>
<td>In 3 patients</td>
<td>Change in reprocessing methods potentially altered the permeability characteristics allowing endotoxins to pass through membrane</td>
<td></td>
</tr>
<tr>
<td>In 16 patients (18 episodes)</td>
<td>Endotoxin is the believed cause during reuse of dialyzers, water used to rinse dialyzers and dilute the disinfect was contaminated with high concentrations of endotoxins (&gt;6 ng/ml) and bacteria (&gt;104 CFU/ml)</td>
<td></td>
</tr>
<tr>
<td>Combined: Bacterial &amp; Endotoxin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrogenic reactions and bacteremia in 5 patients (2 with Klebsiella pneumonia, 1 with K. pneumonia and P. aeruginosa)</td>
<td>Distribution systems and machines were inadequately disinfected with sodium hypochlorite when a pump failed 2 weeks prior to the outbreak</td>
<td></td>
</tr>
<tr>
<td>Pyrogenic reactions (9 episodes) and gram-negative bacteremia (5 episodes) in 11 patients</td>
<td>Water distribution system was not routinely disinfected, machine was not disinfected according to manufacturer's instructions, poor bacterial assay resolution</td>
<td></td>
</tr>
<tr>
<td>*Pyrogenic reactions (~20) due to bacteria and/or endotoxins</td>
<td>Reverse osmosis water was believed to be the source of contamination</td>
<td></td>
</tr>
<tr>
<td>*Pyrogenic reactions in 9 and gram-negative bacteremias in 5 patients</td>
<td>Inadequate mixing of Renalin disinfectant</td>
<td></td>
</tr>
</tbody>
</table>

**Nontuberculous mycobacteria**

<table>
<thead>
<tr>
<th>Infections</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>A total of 27 cases with various infections: bacteremia in 14, soft-tissue infections in 3, and 1 with an access-graft infection, while 9 others had widely disseminated disease. Mycobacterium chelonae ssp. abscessus was identified in 26 isolates and the remaining isolate was a M. chelonae-like organism</td>
<td>The water treatment system showed widespread contamination and the processed dialyzers were contaminated with viable mycobacterium</td>
</tr>
<tr>
<td>Systemic M. chelonae abscessus infections in 5 patients, 1 patient died during antimicrobial therapy</td>
<td>A hose with a spray device was contaminated with M. abscessus and the Renalin disinfectant concentration was not high enough</td>
</tr>
</tbody>
</table>
## Appendix F. Streamline Tubing Clinical Studies

### Four Clinical Studies Evaluating Streamline Tubing

<table>
<thead>
<tr>
<th>Study Objective</th>
<th>Comprehensive Clinical &amp; Operational Analysis</th>
<th>Decreasing Dialyzer size &amp; heparin usage</th>
<th>Lowering QD</th>
<th>Maximizing Kt/V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Sample Size</td>
<td>117</td>
<td>67</td>
<td>117</td>
<td>202</td>
</tr>
<tr>
<td>Improvement in Blood Flow Rate (%)</td>
<td>18%</td>
<td>5%</td>
<td>4%</td>
<td>19%</td>
</tr>
<tr>
<td>Change in Arterial Pressure (%)</td>
<td>N/A</td>
<td>16% reduction</td>
<td>12% reduction</td>
<td>4% increase (minimal)</td>
</tr>
<tr>
<td>% of patients meeting target Kt/V with Streamline</td>
<td>98.3%</td>
<td>76%</td>
<td>100%</td>
<td>73% (target=2)</td>
</tr>
<tr>
<td>Improvement in % of patients meeting target Kt/V with Streamline</td>
<td>+27%</td>
<td>+10%</td>
<td>+4%</td>
<td>+34%</td>
</tr>
</tbody>
</table>
| Cost Savings ($ per treatment where available) | • Heparin use reduced by 28% ($0.07)  
• Biohazard waste reduction ($0.19)  
• Dialysate usage reduced ($1.39)  
• Staff overtime reduced ($1.32)  
• Heparin use reduced by 57% ($0.96)  
• Patients on large dialyzers reduced 69% ($2.52)  
• Dialysate usage decreased 7%  
• Fresh water usage reduced 27,000 liters/month  
• Focused on improving Kt/V; cost savings not reported |
Appendix G. Modular Components

Modular Components of the Fresenius 2008K^2 Dialysis Machine
Notes:

Arrows indicate access points for pressure connections. Important dimensions are detailed in the drawings of the pump.
Notes:
Clip amount by scope as. A renal module
Thickness of lines 0.1cm thick

*** most clips and lines need a distance of 0.1cm from edge of module.
Width of Syringe: 2.3cm
Height of Syringe: 11.3 cm
Appendix H. Cartridge Iterations

Design Iterations for Modified Cartridge