Randomized trial comparing VectorFlow tunneled dialysis catheter to Palindrome tunneled dialysis catheter

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Regulatory Sponsor: *Gregory Nadolski (PI)*

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Protocol Number: *TBD*

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List of Abbreviations

ESRD – End Stag Renal Disease
HD – Hemodialysis
TDC – Tunneled Dialysis Catheter
AVG – Arteriovenous graft
AVF – Arteriovenous fistula
TPA – tissue plasminogen activator
Kt/V – dialyzer clearance of urea x dialysis time/volume of distribution
URR – urea reduction ratio

Study Summary

Title	**Randomized trial comparing VectorFlow tunneled dialysis catheter to Palindrome**
Short Title	VectorFlow vs Palindrome
Protocol Number	TBD
Phase	N/A
Methodology	Randomized two-arm study examining 90 day primary patency of two FDA-approved tunneled dialysis catheters
Study Duration	15 months
Study Center(s)	Penn Medicine University City (Penn Presbyterian Medical Center), Pennsylvania Hospital
Objectives	*Primary*: 90 day primary catheter patency *Secondary:* 90 day primary assisted patency Primary, secondary, and total access site service intervals Catheter flow and lumen pressure [initial use, qMonth x3 (ie 90 days post-catheter insertion)] Kt/V, URR, and percent re-circulation [qMonth x3 (ie 90 days post-catheter insertion)] Use of TPA to restore catheter patency Cost of maintaining catheter access
Number of Subjects	100
Diagnosis and Main Inclusion Criteria	≥18yo, ESRD requiring insertion of HD catheter Exclusions: Known central venous stenosis, infected hemodialysis graft, recent bacteremia (< 7 days)
Design	Randomized trial with 1:1 allocation
Duration of participation	90 days from catheter insertion
Statistical Methodology	Primary patency at 90 days will be analyzed using survival methods with the log-rank test and Cox proportional hazards models
Principal Investigator	Gregory Nadolski, MD (IR)
Co-Investigators	Jonas Redmond, MD (IR) Raphael Cohen, MD (Nephrology)
Key Personel	Benjamin Hammelman (IR, PAH) Raymond Fabrizio (IR, PAH) Kathleen Thomas, MS, CRC (Radiology Research Coordinator, UPenn) TBD (Biostatistician, UPenn)

1 Introduction

This document is a protocol for a human research study. This study is to be conducted according to US and international standards of Good Clinical Practice (FDA Title 21 part 312 and International Conference

on Harmonization guidelines), applicable government regulations and Institutional research policies and procedures.

1.1 Background

Tunneled dialysis catheters (TDC) remain an important bridge to permanent hemodialysis access (ie arteriovenous graft or fistula) for the majority of patients in the U.S. initiating hemodialysis for end stage renal disease (ESRD). Tunneled dialysis catheters are also a critical transition to new access creation in patients with failed arteriovenous access. Finally, in the subset of dialysis patients who have exhausted their venous anatomy for surgical access options and are not candidates for peritoneal dialysis or renal transplantation, tunneled dialysis catheters serve as a virtual 'lifeline' whose patency determines remaining life expectancy(1).

During the high-flow conditions necessary for adequate hemodialysis (HD), fluid dynamics intrinsic to specific catheter configurations have implications to catheter thrombosis and dialysis adequacy(2,3). Commercially available catheter tip designs have historically comprised step-tip and split-tip configurations. In the last decade, symmetrical tip catheters have become widely-utilized alternatives to conventional step-tip and split-tip catheters, owing to ease of placement and the ability to reverse lines during dialysis without an increase in recirculation(4-6). Regardless of tip design, partial or total occlusion of the tip of the catheter is the Achilles' heel of TDC based HD access. Primary patency rates at 90 days can be less then 50%(4,5). Even with the use of thrombolytic drugs to restore patency and flow, mean primary assisted patency for TDCs has only been about 135 days in randomized trials (6).

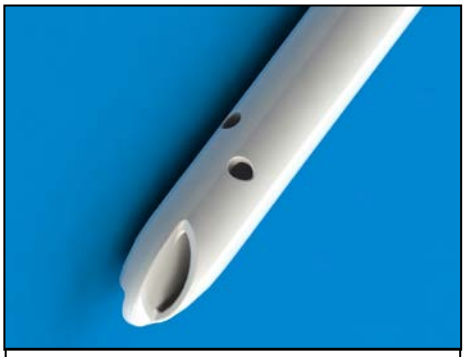

Figure 1:VectorFlow catheter tip. Helically shaped terminal lumens deflect blood flow to minimize recirculation, and to produce a transition of blood velocities and trajectories as fluid enters and leaves the device.

In late 2014, the VectorFlow (**Figure 1**), a novel symmetrical tip catheter was introduced to the U.S. market with the goal of achieving improved catheter performance by optimizing fluid dynamics through helically-shaped flow-deflecting interfaces at the catheter tip intended to reduce platelet activation while minimizing recirculation (7,8). To date, no randomized clinical trials have been performed comparing efficacy of this design to conventional symmetrical tip TDCs.

1.2 Investigational Agent

The VectorFlow is an FDA-approved TDC for patients with ESRD requiring HD. The comparison device (Palindrome TDC) in this trial likewise is FDA-approved for the same indication. Both devices are considered standard of care for catheter based HD. Both devices will be placed in accordance with their approved indication and manufacture's instructions for use.

1.3 Preclinical Data

During the FDA approval process, the flow characteristics of the novel helical tip design of the VectorFlow were examined in comparison to the conventional symmetrical tip design of the Palindrome and other catheters using both *in vitro* and *in vivo* models(8). In these studies, computational fluid dynamics were used to measure shear stress, residence time (RT), platelet lysis index (PLI), and recirculation of the study catheters. The VectorFlow catheter was associated with an 18% reduction in mean shear stress compared with the Palindrome catheter. In vitro, the VectorFlow catheter had no detectable recirculation (0%) compared to 7.3–9.5% with the Palindrome at flow rates of 400–600 ml/minute. In vivo, the VectorFlow catheter had no detectable recirculation, compared to 6.7–12% for the Palindrome. Subsequently, the absence of detectable recirculation seen with the VectorFlow has been demonstrated to be related to the helically contoured lumens which produced the greatest amount of deflection of venous flow away from the arterial lumen compared to other catheters (7). Likewise, the VectorFlow was shown to have the lowest mean shear-induced platelet activation which could greatly reduce platelet

aggregation on the catheter tip which can limit flow and result in thrombosis of the catheter or stenosis of the veins in which the catheter resides.

1.4 Clinical Data to Date

Our initial clinical experience using the VectorFlow catheter at the University of Pennsylvania has been examined and is currently under review for publication (JVIR submitted May 2015). Over a 5-month period, patients initiating hemodialysis with a tunneled dialysis catheter or undergoing exchange of a dysfunctional dialysis catheters were retrospectively analyzed. During this period, a total of 33 VectorFlow were placed and compared to another commonly used TDC placed at the University of Pennsylvania (Ash Split, n=46) TDCs. Patients in the VectorFlow group had significantly greater co-morbidities and history of thrombosis/occlusion of prior venous access sties. Despite being placed in a sicker and more complex patient population, the VectorFlow demonstrated significantly higher primary access patency. At 120 days, 89% of VectorFlow catheters remained functional compared to 45% of Ash Split catheters (P=0.046). In multivariate analysis, the risk of catheter failure was 13.3 times higher in the Ash Split group compared to the VectorFlow (P = 0.004).

2 Study Objectives

Primary Objectives:
Assess primary patency at 90 days

Secondary:

- Assess primary assisted patency at 90 days
- Assess need for thrombolytics (ie TPA) to restore catheter patency
- Assess catheter flow and lumen pressures at initial three HD sessions and then monthly for 3 months (ie up to 90 days following catheter insertion)
- Assess Kt/V (measure of HD adequacy/clearance of urea) and URR monthly for 3 months (ie up to 90 days following catheter insertion)
- Assess overall cost to maintain access patency

3 Study Design

3.1 General Design

An open label, randomized trial investigating the 90-day primary patency of the VectorFlow TDC to the Palindrome TDC. TDC insertion will be in accordance with its FDA-approved indication for HD access and per the manufacturer's instructions for use. The Palindrome catheter has been selected as the comparison device because it is also a symmetrical tip catheter design and prior studies by the manufacturer of this device suggests it has a lower occlusion rate and better flow compared to other catheter designs (please refer to Palindrome Manufacturer's Brochure).

<u>Trial Design</u>

Randomization: Patients referred to Interventional Radiology for primary placement of tunneled hemodialysis catheter will be screened for enrollment. Following recruitment of those meeting inclusion criteria, patients will be randomized 1:1 between insertion of VectorFlow TDC (Arm A) and Palindrome TDC (Arm B). Additionally, randomization will also stratify side of catheter placement such that in both arms approximately 80% of patients will have right-sided catheters and the remaining 20% left-sided catheters. This is to account for the well-established phenomenon of higher rates of catheter failure in left-side placement due to the curvature and angles induced by the left brachiocephalic vein.

By consenting to participate in this trial, patients will allow the researchers to contact their hemodialysis center, including centers outside of the University of Pennsylvania health system, to review parameters

from hemodialysis sessions as well as additional clinical information recorded at the HD center regarding function of the dialysis catheter.

Post-Insertion Follow-up: Post catheter insertion follow-up will be identical between the two arms of treatment. After insertion, patient's hemodialysis records will be reviewed for (A) Blood flow rate (Q_b), (B) Arterial and venous lumen pressures, (C) Kt/V, and (D) Urea reduction ratio (URR) These values will be recorded from the first 3 hemodialysis sessions and then again at monthly intervals following catheter insertion as performed as part of routine clinical care.

Additionally, need and use of prolonged use of thrombolytic infusion (ie t-PA) to restore or improve patency and/or need for catheter exchange for any reason will extracted from hemodialysis center records as well as the electronic medical record at the University of Pennsylvania.

3.2 Primary Study Endpoints

The primary study endpoint will be **primary patency at 90 days** following catheter insertion. Primary patency is defined as an HD catheter which provides adequate hemodialysis (flow >300mL/min) without need for additional interventions (ie TPA infusions or catheter exchange) to maintain flow or correct device failure. **Device failure** is defined as any limitation in catheter function despite technically successful catheter placement. Examples of device failure include inadequate rate of blood flow, central venous stenosis or thrombosis limiting catheter flow, catheter site infection, or catheter related blood stream infection. **Primary device service interval** is defined as the number of catheter days from TDC insertion until removal at the completion of therapy, patient death, conclusion of the study with the catheter still functioning, or device failure.

3.3 Secondary Study Endpoints

1. **Primary assisted patency** at 90 days defined as an HD catheter which provides adequate hemodialysis (flow >300mL/min) without need for catheter exchange or fibrin sheath stripping to maintain flow or correct device failure.
2. **Secondary device service interval** defined as the service interval that begins after device replacement or salvage without abandonment of the access site. Examples of interventions include device exchange over a guide wire, fibrin sheath stripping, thrombolytic infusion directly into a catheter, catheter tip repositioning, kinked catheter repositioning, and replacement/repair of a TDC component. Each device revision results in the start of a new secondary device service interval. Patients will be followed up to 12 months post-initial catheter insertion for secondary device service interval.
3. **Total access site service interval** defined as the sum of all device service intervals at a single access site. This accounts for devices replaced or manipulated due to device failure, but maintaining the original venous access site. Replacement of an inadvertently removed catheter through the existing subcutaneous tunnel results in a new device service interval, but does not end the access site service interval. Patients will be followed up to 12 months post-initial catheter insertion for total access site service interval.
4. **Catheter flow and lumen pressures at initial three HD sessions and then monthly for 3 months (ie 90 days) post insertion**
5. **URR, and Kt/V, and percent recirculation monthly for 3 months (ie 90 days) post insertion Overall cost to maintain access patency during study period**

4 Subject Selection and Withdrawal

4.1 Inclusion Criteria

1. End stage renal disease or acute renal failure requiring hemodialysis through a tunneled dialysis catheter

2. Age ≥18, Age <80
3. Capable of giving informed consent

4.2 Exclusion Criteria

1. Coagulopathy defined as international normalized ration (INR) >2 which cannot be corrected with fresh frozen plasma
2. Platelet count <50,000/microliter, which cannot be corrected with platelet transfusion
3. Active skin infections at site of TDC insertion
4. Presence of bacteremia or infected AVG/AVF within 7 days prior to enrollment
5. Neutropenia defined as absolute neutrophil count less then 1,700/microliter
6. Known central venous stenosis
7. Occlusion of bilateral external and internal jugular veins or bilateral brachiocephalic veins or stenosis of the superior vena cava (i.e. venous abnormality precluding catheter placement
8. Functioning surgical HD access (ie AVG/AVF) or AVG/AVF which is expected to be functional within 90 days of enrollment
9. Inability to provide informed consent
10. Pregnant or nursing women
11. In the event a physician does not feel that either catheter would be appropriate for a subject, the subject will not be eligible to participate

4.3 Subject Recruitment and Screening

Currently, approximately 1-3 TDCs are inserted each day by the Interventional Radiology practice at the Penn Medicine University City (Penn Presbyterian Medical Center) and Pennsylvania Hospital. These patients are referred from the Departments of Medicine and Surgery in consultation with the Division of Nephrology.

During the initial contact with the patient, potential candidates will be screened by research coordinator, PI, or co-PI for adequacy for the clinical trial. If the applicant meets inclusion criteria without any exclusion criteria, the patient will be approached by research coordinator to discuss enrollment. All patients who are identified as potential candidates for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. The potential subject will be given an opportunity to read the consent form thoroughly and ask and be provided answers to any questions that they may have regarding the study. The subject will be asked to sign the consent form only if they have indicated that they are willing to do so without reservation. The informed consent will be obtained before the subject undergoes any study procedure. The consent form must be signed by the subject or legally acceptable surrogate and the investigator or investigator-designated research professional obtaining consent. The subject will be informed that their participation is entirely voluntary and if they chose not participate their care will not be affected and that they may withdraw consent at any time.

4.4 Early Withdrawal of Subjects

4.4.1 When and How to Withdraw Subjects

- PI Decision: Subjects may be withdrawn at any time during the study if the PI believes it is in the subject's best interest. In this event, the reasons for withdrawal will be documented.
- Subject Participation: Refusal to continue treatment, follow-up, comply with the protocol or withdrawal of consent. In this event, the reasons for withdrawal will be documented.

Patients withdrawing from the study will be entitled to pursue all treatment options available for the treatment of end-stage renal disease and maintenance of hemodialysis access without prejudice from the providing physicians.

Once the subject has discontinued treatment, the primary reason for discontinuing treatment must be clearly documented in the subject's records and on the eCRF. The investigator will assess each subject for response at the time of withdrawal.

4.4.2 Data Collection and Follow-up for Withdrawn Subjects

Baseline etiology of ESRD will be recorded. Baseline data regarding treatment history of ESRD including history of prior hemodialysis access and dialysis access interventions will be collected at time of enrollment and will include number and type of prior hemodialysis access and interventions to maintain HD access.

Even though subjects may be withdrawn prematurely from the study, it is imperative to collect at least primary patency data and suspected date of TDC device failure on such subjects throughout the protocol defined follow-up period for that subject. Such data is important to the integrity of the final study analysis of the primary end-point. If a subject withdraws consent to participate in the study, attempts will be made to obtain permission to record at least primary patency data up to the protocol-described end of subject follow-up period. Methods that may be used to obtain primary patency data will include phone calls to the subject, phone calls to next-of-kin if possible, and certified letters to the subject or next-of-kin. If permission to collect or the specific primary patency data cannot be obtained after 4 phone calls and 4 letters to the subject and/or next-of-kin, the patient will be regarded as lost to follow up.

5 Study Interventions

5.1 Descriptions

TDC Insertion

TDC insertion, either VectorFlow or Palindrome, will be in accordance with its FDA-approved indication under moderate sedation or general anesthesia with local anesthesia using 1% lidocaine in per institutional protocol. In brief, using real time ultrasound guidance, access to the internal or external jugular vein will be achieved using a 21G needle and a guidewire advanced into the superior vena cava under fluoroscopic guidance. A catheter entry site will be selected on the chest wall and anesthetized. The catheter will be tunneled subcutaneously to the site of jugular vein access. A peel away sheath will be inserted into the jugular vein over a guide wire and the catheter will be inserted. The tip of the catheter will be positioned in the mid-right atrium as per the manufacturer's IFU. The skin incision overlying the venipuncture will be closed with absorbable suture and/or glue. A sterile dressing will be applied to the catheter.

Patency and Catheter Performance Measures

Following TDC insertion, the catheter may be used immediately. The goal of HD is typically to achieve a target effective blood flow of 300mL/min within the first 3 hemodialysis sessions. The dialysis records from each of the first three HD sessions will be reviewed by the study coordinator for (A) Blood flow rate (Q_B), (B) Arterial and venous lumen pressures, (C) Kt/V, and (D) Urea reduction ratio (URR). Additionally, need and use of thrombolytic infusion (ie t-PA) (other than single dose injection) to restore or improve patency and/or need for catheter exchange for any reason will extracted from hemodialysis center records as well as the electronic medical record at the University of Pennsylvania. Subsequently, these measures will be recorded monthly up to 90 days following catheter insertion. All times and indication for catheter removals and exchanges will be recorded up to 12 months following initial catheter placement.

5.2 Treatment Regimen

Following TDC insertion, the catheter may be used immediately. The goal of HD is typically to achieve a target effective blood flow of 300 mL/min within the first 3 hemodialysis sessions. The dialysis records from each of the first three HD sessions will be reviewed by the study coordinator for (A) Blood flow rate (Q_B),, (B) Arterial and venous lumen pressures, (C) Kt/V, and (D) Urea reduction ratio (URR).

Additionally, need and use of thrombolytics (ie tPA) to restore or improve patency and/or need for catheter exchange for any reason will extracted from hemodialysis center records as well as the electronic medical record at the University of Pennsylvania. Subsequently, these measures will be recorded monthly up to 90 days following catheter insertion. All times and indication for catheter removals and exchanges will be recorded up to 12 months following initial catheter placement.

5.3 Method for Assigning Subjects to Treatment Groups

The study is a 1:1 randomized open label two arm clinical trial comparing two FDA-approved TDCs. Additionally, randomization will take into account likely side of catheter placement such that in both arms approximately 80% of patients will have right-sided catheters and the remaining 20% left-sided catheters.

Monthly, the coordinators will provide documentation of the number of patients screened at each site (PUMC and PAH) who chose not to enroll in the study. Otherwise, when a screened patient is recruited to the study, the coordinator will register the patient into the study database (RedCAP) and generate a study identification number which will be recorded on the eCRF.

5.4 Preparation and Administration of Study Interventions

Both VectorFlow and Palindrome are FDA-approved TDCs and will be inserted using standard clinical practice as outlined in manufacturer's instructions for use. Thus, no special preparation or administration of this intervention is necessary.

Women who are able to become pregnant will be tested for pregnancy by urine pregnancy test. The results of this test must be negative to join the study. At the time of enrollment, documentation of pregnancy status will be recorded on eCRF as one of the following: (a) reproductive age UPT negative, (b) unable to become by nature means and approximate date of menopause, or (c) unable to become pregnant by surgical means and date of surgery.

5.5 Subject Compliance Monitoring

N/A

5.6 Prior and Concomitant Therapy

Patients may undergo placement of surgical dialysis access during the study period. Patients who subsequently use the surgical access for HD and have their TDC removed less than 90 days after enrollment can be replaced one for one with additional subjects.

5.7 Blinding of Study Intervention

This protocol does not utilize blinding. Subjects and investigators will know the treatment being administered.

6 Study Procedures

6.1 Visit 1: Date of Enrollment and TDC insertion

Initial consult for TDC insertion. Patient will be evaluated for enrollment in the clinical trial at the time of IR consult/procedure visit after consenting to undergo TDC insertion to treat ESRD. After enrollment, the patient will be randomized to treatment Arm A (VectorFlow) or treatment Arm B (Palindrome). Following randomization, the assigned TDC will be inserted as described above. At time of enrollment, use of anti-

platelet, anti-coagulants, and/or immunosuppressants will be recorded as these may impact catheter patency or infection rates.

6.2 Visit 2: Initial HD sessions

Following TDC insertion, the catheter may be used immediately. The goal of HD is typically to achieve a target effective blood flow of 400mL/min within the first 3 hemodialysis sessions. The dialysis records from each of the first three HD sessions will be reviewed by the study coordinator for (A) Blood flow rate (Q_B), (B) Arterial and venous lumen pressures, (C) Kt/V, and (D)Urea reduction ratio (URR. Additionally, need and use of thrombolytic infusion (ie tPA) (other than single dose administration) to restore or improve patency and/or need for catheter exchange for any reason will extracted from hemodialysis center records as well as the electronic medical record at the University of Pennsylvania. Subsequently, these measures will be recorded monthly up to 90 days following catheter insertion.

6.3 Visit 2: Follow Up of HD Records

Subsequently, all measures recorded during the first three HD sessions will be recorded monthly up to 90 days following catheter insertion. To allow for differences in HD regimens (ie Monday, Wednesday, Friday treatment versus Tuesday, Thursday, Saturday treatment regimens), the closest HD session within a range of +/- 5 days of the desired follow up date may be used if the exact follow-up date following TDC insertion does not fall on a day HD was administered. All times and indication for catheter removals and exchanges will be recorded up to 12 months following initial catheter placement.

7 Statistical Plan

7.1 Study Objectives, Sample Size Determination and Power Calculation

Objectives
This trial is designed to be the initial randomized trial evaluating the primary patency of the VectorFlow TDC compared to a commonly used TDC. The knowledge gained from this investigation will serve as the basis for future randomized clinical trials comparing VectorFlow to additional TDC designs.

Primary Objective: To evaluate the primary patency at 90 days of the VectorFlow TDC compared to the Palindrome TDC.

Additionally, the trial is designed to assess additional measures of catheter patency as well as catheter performance at hemodialysis throughout the study period as detailed in the following secondary objectives:

- Assess primary assisted patency at 90 days
- Assess need for thrombolytic infusion (ie TPA) to restore catheter patency
- Assess catheter flow and lumen pressures at initial three HD sessions and monthly for 3 months (ie up to 90 days following catheter insertion)
- Assess Kt/V (measure of HD adequacy/clearance of urea) and URR monthly for 3 months (ie up to 90 days following catheter insertion)
- Assess overall cost to maintain access patency

Sample Size Determination and Power Calculation

Sample size estimation is based on our Primary Objective, the primary patency at 90 days of the VectorFlow TDC compared to the Palindrome TDC. In a prior retrospective analysis, the Palindrome has been shown to have a 70% 90-day patency (9); since this patency proportion is associated with only right internal jugular placement we expect the Palindrome TDC primary patency to be 60% in this trial attributed to the lower patency proportion among left-sided catheter insertions. In our experience at the University of Pennsylvania with the VectorFlow catheter, primary patency at 90 days was between 90-

95% including right and left-sided catheter insertions (see Clinical Data to Date Section 1.4). Using the log-rank test for survival proportions (assuming 60% of Palindrome and 90% of VectorFlow catheters will remain patent at 90 days), with a two-sided Type I error of 5% and a power of 80%, we will need to enroll 70 subjects (35 subjects in each arm of the study) (StatMate 2.0, GraphPad Software, San Diego, CA). We anticipate 10-15% of subjects in this study will be lost to follow-up during the first 90 days following catheter insertion. Therefore, we will need to enroll 80 subjects (40 in each arm of the study). If 12 patients are enrolled per month, then we expect 12-15 months will be needed to complete enrollment and follow-up.
Amendment: Loss of subjects to follow-up or early termination of catheter usage due resuming peritoneal dialysis or placement of immediately puncturable AV grafts was higher then the initially anticipated 10-15%. Thus, to obtain enough analyzable subjects in each arm, we are requesting to increase enrollment to 100 subjects (50 in each arm of the study).

7.2 Statistical Methods

Primary Objective: Primary patency at 90 days will be analyzed using survival methods with the log-rank test and Cox proportional hazards models adjusting for side of catheter insertion (ie left versus right). Patients whose catheter remains patent will be censored at the end of study, removal for functioning surgical HD access or death. Device failure has been defined above under section 3.2.

Secondary Objectives: Primary assisted patency at 90 days will be analyzed using survival methods with the log-rank test and Cox proportional hazards models. When comparing dichotomous variables in the 2 treatment groups, a 2-sided $\chi 2$ test will be used. Fisher's exact test will be used for contingency tables with fewer than 10 subjects in each category. When comparing continuous variables, a 2-sided t test will be used, provided that the distributions are sufficiently close to the normal distribution. Otherwise, a 2-sided Mann-Whitney test will be used.

7.3 Subject Population(s) for Analysis and Duration of Study

Analysis of both primary and secondary end points will be performed on an intention to treat basis. Approximately 80 patients will be enrolled in this trial. Each patient will be followed for 90 days following catheter insertion. We expect 12-15 months will be needed to complete enrollment and complete follow-up of all patients.

8 Safety and Adverse Events

8.1 Definitions

Unanticipated Problems Involving Risk to Subjects or Others
Any incident, experience, or outcome that meets <u>all</u> of the following criteria:

- <u>Unexpected in nature, severity, or frequency</u> (i.e. not described in study-related documents such as the IRB-approved protocol or consent form, the investigators brochure, etc.)
- <u>Related or possibly related to participation in the research</u> (i.e. possibly related means there is a reasonable possibility that the incident experience, or outcome may have been caused by the procedures involved in the research)
- <u>Suggests that the research places subjects or others at greater risk of harm</u> (including physical, psychological, economic, or social harm).

Adverse Event

An ***adverse event*** (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries should be regarded as adverse events. Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:

- results in study withdrawal
- is associated with a serious adverse event
- is associated with clinical signs or symptoms
- leads to additional treatment or to further diagnostic tests
- is considered by the investigator to be of clinical significance

Serious Adverse Event
Adverse events are classified as serious or non-serious. A ***serious adverse event*** is any AE that is:

- fatal
- life-threatening
- requires or prolongs hospital stay
- results in persistent or significant disability or incapacity
- a congenital anomaly or birth defect
- an important medical event

Important medical events are those that may not be immediately life threatening, but are clearly of major clinical significance. They may jeopardize the subject, and may require intervention to prevent one of the other serious outcomes noted above. For example, drug overdose or abuse, a seizure that did not result in in-patient hospitalization, or intensive treatment of bronchospasm in an emergency department would typically be considered serious.

All adverse events that do not meet any of the criteria for serious should be regarded as ***non-serious adverse events***.

Adverse Event Reporting Period
The study period during which adverse events must be reported is normally defined as the period from the initiation of any study procedures to the end of the study treatment follow-up. For this study, the study treatment follow-up is defined as 30 days following completion of the last survey.

Preexisting Condition
A preexisting condition is one that is present at the start of the study. A preexisting condition should be recorded as an adverse event if the frequency, intensity, or the character of the condition worsens during the study period.

General Physical Examination Findings
At screening, any clinically significant abnormality should be recorded as a preexisting condition. At the end of the study, any new clinically significant findings/abnormalities that meet the definition of an adverse event must also be recorded and documented as an adverse event.

Post-study Adverse Event
All unresolved adverse events should be followed by the investigator until the events are resolved, the subject is lost to follow-up, or the adverse event is otherwise explained. At the last scheduled visit, the investigator should instruct each subject to report any subsequent event(s) that the subject, or the subject's personal physician, believes might reasonably be related to participation in this study. The investigator should notify the study sponsor of any death or adverse event occurring at any time after a subject has discontinued or terminated study participation that may reasonably be related to this study. The sponsor should also be notified if the investigator should become aware of the development of cancer or of a congenital anomaly in a subsequently conceived offspring of a subject that has participated in this study.

Abnormal Laboratory Values

A clinical laboratory abnormality should be documented as an adverse event if any one of the following conditions is met:

- The laboratory abnormality is not otherwise refuted by a repeat test to confirm the abnormality
- The abnormality suggests a disease and/or organ toxicity
- The abnormality is of a degree that requires active management; e.g. change of dose, discontinuation of the drug, more frequent follow-up assessments, further diagnostic investigation, etc.

Hospitalization, Prolonged Hospitalization or Surgery
Any adverse event that results in hospitalization or prolonged hospitalization should be documented and reported as a serious adverse event unless specifically instructed otherwise in this protocol. Any condition responsible for surgery should be documented as an adverse event if the condition meets the criteria for and adverse event.

Neither the condition, hospitalization, prolonged hospitalization, nor surgery are reported as an adverse event in the following circumstances:

- Hospitalization or prolonged hospitalization for diagnostic or elective surgical procedures for a preexisting condition. Surgery should ***not*** be reported as an outcome of an adverse event if the purpose of the surgery was elective or diagnostic and the outcome was uneventful.
- Hospitalization or prolonged hospitalization required to allow efficacy measurement for the study.
- Hospitalization or prolonged hospitalization for therapy of the target disease of the study, unless it is a worsening or increase in frequency of hospital admissions as judged by the clinical investigator.

8.2 Recording of Adverse Events

At each contact with the subject, the study team and investigator must seek information on adverse events by specific questioning and, as appropriate, by examination. Information on all adverse events should be recorded immediately in the source document, and also in the appropriate adverse event module of the case report form (eCRF). All clearly related signs, symptoms, and abnormal diagnostic procedures results should recorded in the source document, though should be grouped under one diagnosis.

All adverse events occurring during the study period must be recorded. The clinical course of each event should be followed until resolution, stabilization, or until it has been determined that the study treatment or participation is not the cause. Serious adverse events that are still ongoing at the end of the study period must be followed up to determine the final outcome. Any serious adverse event that occurs after the study period and is considered to be possibly related to the study treatment or study participation should be recorded and reported immediately.

8.3 Reporting of Serious Adverse Events and Unanticipated Problems

Investigators and the protocol sponsor must conform to the adverse event reporting timelines, formats and requirements of the various entities to which they are responsible, but at a minimum those events that must be reported are those that are:

- related to study participation,
- unexpected, and
- serious or involve risks to subjects or others
  (see definitions, section 8.1).

If the report is supplied as a narrative, the minimum necessary information to be provided at the time of the initial report includes:

- Study identifier
- Study Center
- Subject number
- A description of the event
- Date of onset
- Current status
- Whether study treatment was discontinued
- The reason why the event is classified as serious
- Investigator assessment of the association between the event and study treatment

8.3.1 Investigator reporting: notifying the medical monitor

N/A

8.3.2 Investigator reporting: notifying the Penn IRB

This section describes the requirements for safety reporting by investigators who are Penn faculty, affiliated with a Penn research site, or otherwise responsible for safety reporting to the Penn IRB. The University of Pennsylvania IRB (Penn IRB) requires expedited reporting of those events related to study participation that are unforeseen and indicate that participants or others are at increased risk of harm. The Penn IRB will not acknowledge safety reports or bulk adverse event submissions that do not meet the criteria outlined below. The Penn IRB requires researchers to submit reports of the following problems within 10 working days from the time the investigator becomes aware of the event:

- Any adverse event (regardless of whether the event is serious or non-serious, on-site or off-site) that occurs any time during or after the research study, which in the opinion of the principal investigator is:

  Unexpected (An event is "unexpected" when its specificity and severity are not accurately reflected in the protocol-related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document and other relevant sources of information, such as product labeling and package inserts.)

  AND

  Related to the research procedures (An event is "related to the research procedures" if in the opinion of the principal investigator or sponsor, the event was more likely than not to be caused by the research procedures.)

Reporting Process
Unanticipated problems posing risks to subjects or others as noted above will be reported to the Penn IRB using the form: "Unanticipated Problems Posing Risks to Subjects or Others Including Reportable Adverse Events" or as a written report of the event (including a description of the event with information regarding its fulfillment of the above criteria, follow-up/resolution and need for revision to consent form and/or other study documentation).

Copies of each report and documentation of IRB notification and receipt will be kept in the Clinical Investigator's study file.

Other Reportable events:
For clinical drug trials, the following events are also reportable to the Penn IRB:

- Any adverse experience that, even without detailed analysis, represents a serious unexpected adverse event that is rare in the absence of drug exposure (such as agranulocytosis, hepatic necrosis, Stevens-Johnson syndrome).
- Any adverse event that would cause the sponsor to modify the investigators brochure, protocol or informed consent form, or would prompt other action by the IRB to assure protection of human subjects.
- Information that indicates a change to the risks or potential benefits of the research, in terms of severity or frequency. For example:

  - An interim analysis indicates that participants have a lower rate of response to treatment than initially expected.
  - Safety monitoring indicates that a particular side effect is more severe, or more frequent than initially expected.
  - A paper is published from another study that shows that an arm of your research study is of no therapeutic value.
- Change in FDA safety labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
- Breach of confidentiality
- Change to the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research participant.
- Incarceration of a participant when the research was not previously approved under Subpart C and the investigator believes it is in the best interest of the subject to remain on the study.
- Complaint of a participant when the complaint indicates unexpected risks or the complaint cannot be resolved by the research team.
- Protocol violation (meaning an accidental or unintentional deviation from the IRB approved protocol) that in the opinion of the investigator placed one or more participants at increased risk, or affects the rights or welfare of subjects.

8.3.3 Sponsor Reporting: Arrow-Teleflex

Investigators must report serious adverse events (SAE) attributed to TDC insertion to Arrow-Teleflex within the timelines described below. The completed case report should be faxed immediately upon completion to Arrow-Teleflex.

- Relevant follow-up information such as resolution and duration of the SAE attributed to TDC insertion should be submitted to Arrow-Teleflex as soon as it becomes available.
- Serious AE reports that are related to TDC and AEs of Special Interest (regardless of causality) will be transmitted to Arrow-Teleflex within fifteen (15) calendar days from the date investigators are made aware of the AE.
- Serious AE reports that are unrelated to the TDC will be transmitted to Arrow-Teleflex within thirty (30) calendar days from the date investigators are made aware of the AE.
- AEs of Special interest are defined as AEs involving central venous occlusion/stenosis occurring any time during the study period after TDC has been inserted or catheter related blood stream infection occurring less then 7 days after catheter insertion. These events are of special interest because they are rare events that can be fatal or result in loss of hemodialysis access.
- All Non-serious Adverse Events originating from the study will be forwarded in a quarterly report to Arrow-Teleflex.

8.3.4 Sponsor reporting: Notifying FDA

Medical Device Reporting (MDR): In accordance with FDA regulation (21 CFR 803), the sponsor will report to the FDA when they learn that any of their devices may have caused or contributed to a death or serious injury. Manufacturers must also report to the FDA when they become aware that their device has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

8.4 Unblinding Procedures

N/A

8.5 Stopping Rules

The study will be terminated after completed follow up of the last patient enrolled (ie 90 days after this patient has TDC inserted).

8.6 Medical Monitoring

It is the responsibility of the Principal Investigator to oversee the safety of the study. This safety monitoring will include careful assessment and appropriate reporting of adverse events as noted above, as well as the construction and implementation of a site data and safety-monitoring plan (see section 9 Auditing, Monitoring and Inspecting).

8.6.1 Auditing and Inspection

This protocol will be audited and inspected in accordance with DSMP submitted separately.

9 Data Handling and Record Keeping

9.1 Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

9.2 Source Documents

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents. Examples of these original documents, and data records include: hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial.

9.3 Case Report Forms

The study case report form (eCRF) is the primary data collection instrument for the study. eCRFs will be created in the RedCap system to capture the data that the investigator wishes to collect for the purposes of research and for safety monitoring. Data will be entered into this system in a timely manner. Forms used in the source document should reflect the information needed for the completion of the eCRFs in RedCap.

9.4 Records Retention

It is the investigator's responsibility to retain study essential documents for at least 2 years after the last follow up visit with the last enrolled patient.

10 Study Monitoring, Auditing, and Inspecting

10.1 Study Monitoring Plan

The study PI is responsible for ensuring the ongoing quality and integrity of the research study. In addition, this study will be monitored or audited in accordance with Institutional Data and Safety Monitoring Plan. The investigator will allocate adequate time for such monitoring activities. The Investigator will also ensure that the monitor or other compliance or quality assurance reviewer is given access to all the above noted study-related documents and study related facilities (e.g. pharmacy, diagnostic laboratory, etc.), and has adequate space to conduct the monitoring visit.

10.2 Auditing and Inspecting

The investigator will permit study-related monitoring, audits, and inspections by the EC/IRB, the sponsor, government regulatory bodies, and University compliance and quality assurance groups of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.).

Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable University compliance and quality assurance offices.

Certain studies, as identified by the ORA, will be monitored on an on-going basis by the DOCM. Each study will have an individualized monitoring plan developed by the DSMC and the study team. This plan must be approved by the DOCM Director. Once the ORA determines that a study needs prospective monitoring, the DSMC will work with the PI and study team to develop a monitoring plan that will cover

- All of the Regulatory documentation
- Informed Consents
- Eligibility criteria
- Treatment administration and accountability
- Adverse/Serious Adverse Events and toxicities
- Response assessment
- Subject follow-up
- Data completeness
- Source documentation to Case Report Form (CRF)
- Manufacturing (where applicable)

At the conclusion of the monitoring visit, the monitor will spend time with the PI and/or study team to discuss the findings and to provide guidance on resolving deficiencies. A formal letter will be sent to the PI within about five business days. The PI does not have to respond the monitoring letter unless specifically requested to do so by the monitor. Studies that are high risk protocols are audited approximately six months from their first subject accrual and approximately every six month thereafter for the duration of the study. However, this schedule may be changed at the discretion of the DSMC. High enrolling or quick enrolling studies will be audited more frequently as necessary. Investigators are notified in advance of the selection of their protocol for review and cases are randomly selected. Three subjects or 10% of the total accrual, whichever is higher, are audited. A formal report is provided to the PI within about five business days of the audit. The Committee may alter the frequency of re-monitoring based on the audit findings and degree of deficiencies. If an audit is unacceptable due to major deficiencies, representatives from the DOCM acting on behalf of the DSMC meet with the PI to discuss the findings of the audit and necessary corrective actions. If the deficiencies involve subject safety or serious regulatory violations, DSMC Chair, and DOCM Director will meet to discuss necessary actions concerning study status.

10.3 Study Exceptions and Deviations

In order to harmonize with the IRB, the DSMC has changed its designations from Deviations and Violations to Exceptions and Deviations

Exception

A one time, intentional action or process that departs from the IRB and CTSRMC approved study protocol, intended for one occurrence. If the action disrupts the study progress, such that the study design or outcome (endpoints) may be compromised, or the action compromises the safety and welfare of study subjects, advance documented IRB and DSMC approval is required.

For in-house studies with a Medical Monitor or Safety Monitoring Committee (not DSMB), approval must be obtained from the Medical Monitor or Safety Monitoring Committee prior to submitting your exception request to the DSMC.

Deviation

A one time, unintentional action or process that departs from the IRB and DSMC approved study protocol, involving one incident and identified retrospectively, after the event occurred. If the impact on the protocol disrupts the study design, may affect the outcome (endpoints) or compromises the safety and welfare of the subjects, the deviation must be reported to the DSMC within 5 business days and the IRB within 10 business days.

11 Ethical Considerations

This study is to be conducted accordance with applicable US government regulations and international standards of Good Clinical Practice, and applicable institutional research policies and procedures.

This protocol and any amendments will be submitted to a properly constituted independent Ethics Committee (EC) or Institutional Review Board (IRB), in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the EC/IRB concerning the conduct of the study will be made in writing to the investigator and a copy of this decision will be provided to the sponsor before commencement of this study. The investigator should provide a list of EC/IRB members and their affiliate to the sponsor.

All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. See Attachment B for a copy of the Subject Informed Consent Form. This consent form will be submitted with the protocol for review and approval by the EC/IRB for the study. The formal consent of a subject, using the EC/IRB-approved consent form, must be obtained before that subject undergoes any study procedure. The consent form must be signed by the subject or legally acceptable surrogate, and the investigator-designated research professional obtaining the consent.

12 Study Finances

12.1 Funding Source

Arrow-Teleflex

12.2 Conflict of Interest

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) must have the conflict reviewed by a properly constituted Conflict of Interest Committee with a Committee-sanctioned conflict management plan that has been reviewed and approved by the study sponsor prior to participation in this study. All University of Pennsylvania investigators will follow the applicable University conflict of interest policies.

12.3 Subject Stipends or Payments

None

13 Publication Plan

The Principal Investigator and Institution shall be free to publish and present the results and data from the Study, subject to Company having the opportunity to review and provide comments to such publication pursuant to the terms of the Clinical Trial Agreement. Any such publication or presentation shall acknowledge, as appropriate, the contribution of Company, its employees, agents and representatives.

Company may utilize all data and results for regulatory compliance filings only, subject to the use limitations set forth in the Clinical Trial Agreement concerning protection of Confidential Information and process for Publication..

14 References

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4. Kakkos SK, Haddad GK, Haddad RK, Scully MM. Effectiveness of a new tunneled catheter in preventing catheter malfunction: a comparative study. JVIR. 2008 Jul;19(7):1018–26.

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6. Van Der Meersch H, De Bacquer D, Vandecasteele SJ, Van den Bergh B, Vermeiren P, De Letter J, et al. Hemodialysis catheter design and catheter performance: a randomized controlled trial. Am J Kidney Dis. 2014 Dec;64(6):902–8.

7. Clark TWI, Isu G, Gallo D, Verdonck P, Morbiducci U. Comparison of symmetric hemodialysis catheters using computational fluid dynamics. J Vasc Interv Radiol. 2015 Feb;26(2):252–2.

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15 Attachments

eCRF
Monitoring Plan
ICF

Randomized trial comparing VectorFlow tunneled dialysis catheter to Palindrome tunneled dialysis catheter

NCT02685995

Informed Consent date August 10, 2018

University of Pennsylvania Research Subject Informed Consent and Health Insurance Portability and Accountability Act (HIPAA) Authorization Form

Protocol Title:	**Randomized trial comparing VectorFlow tunneled dialysis catheter to Palindrome tunneled dialysis catheter**
Investigators:	Gregory Nadolski, MD Department of Radiology, Vascular and Interventional Radiology Hospital of the University of Pennsylvania 1 Silverstein, 3400 Spruce Street, Philadelphia, PA 19104 Daytime Phone Number: 267.251.9926 Jonas Redmond, MD Department of Radiology, Vascular and Interventional Radiology Penn University Medical Center 4 Wright Saunders, 51N. 39th Street, Philadelphia, PA 19104 Daytime Phone Number: 215.662.9122
Sponsor:	Teleflex Medical Incorporated 4350 Lockhill Selma Road Shavano Park, Texas 78249 USA
24-Hour Emergency Contact	Interventional Radiology Fellow On Call 215.662.2222 (ask to be connected to Interventional Radiology Fellow on Call)

Why am I being asked to volunteer?

You are being invited to participate in a research study, because you have been diagnosed with kidney disease requiring hemodialysis through a tunneled dialysis catheter.

Hemodialysis is a process that replaces the function of the kidneys by filtering toxins and waste materials from the blood. During hemodialysis, blood must be removed, filtered by a machine called a dialyzer, and then returned to the body. A tunneled dialysis catheter is one method of providing access to the blood stream for hemodialysis. The tunneled dialysis catheter is a piece of synthetic tubing that is inserted under the skin of the chest and into a vein in the neck. This procedure is frequently performed by Interventional Radiologists.

Your participation is voluntary which means you can choose whether or not you want to be part of the study. If you choose to participate, you will be randomly assigned (like flipping a coin) to receive one of two FDA approved tunneled dialysis catheters. You have an equal chance of receiving either catheter.

Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of participating in the study, and what you will be asked to do if you choose to participate. The research team is going to talk to you about the study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, other doctors, or whoever helps you make medical decisions. You may find some of the medical language difficult to understand. Please ask the research team and/or the study doctor any questions you have regarding this form or the research study. If you decide to participate, you will be asked to sign this consent form.

What is the purpose of this research study?

Tunneled dialysis catheters are constructed with different designs meant to improve blood flow to make dialysis more efficient and minimize occlusion, or blockage, of the catheter. Occlusion requires the catheter to be changed and can increase chances that the blood vessel it sits in will become narrow or that an infection of the blood stream will occur. For these reasons, catheters which occlude less often are more desirable.

The purpose of this study is to examine which of two FDA approved tunneled dialysis catheters has the lowest rate of occlusion 90 days after insertion.

Prior laboratory experiments comparing the two catheters being studied suggest one catheter may have better performance during hemodialysis and have lower risk of becoming occluded. The present study would provide more conclusive evidence of these preliminary findings.

How many people will be in this research study?

A total of 100 patients will be recruited between two sites (Penn Medicine University City and Pennsylvania Hospital).

What am I being asked to do?

You are being asked to allow the study team to contact you and your hemodialysis center after insertion of the catheter to obtain information about the function of the catheter after the first three dialysis sessions and then monthly for about 3 months. After this point, you are being asked to allow the study team to contact the dialysis center and review your medical records to determine when and why the initial catheter was replaced or removed for a period of up to12 months following the insertion of the initial catheter.

No additional tests, therapies or interventions beyond those performed for routine clinical care will be performed if you participate.

Information regarding medications and other health conditions also will be obtained from your medical records during these reviews.

Women who are able to become pregnant will be tested for pregnancy by urine pregnancy test. The results of this test must be negative to join the study.

What are the possible risks?

The direct risks of participating in the study are minimal. Both catheters in the study and their insertion have the same risks as all currently used dialysis catheters including infection, minor bleeding, occlusion of the catheter, and narrowing of the blood vessel in which the catheter is inserted. One of the two catheters is more commonly placed at the University of Pennsylvania. The insertion method and complications of the two catheters are identical. However, participation may mean you receive the catheter that is less commonly placed.

Your participation in this study would permit the investigators to collect personal health information and data about you. Personal health information and data from your dialysis center regarding function of the catheter will be recorded in a password protected electronic database, which is only accessible by members of the study team. This information may be shared between study members at all participating sites. The results of the data will be reported in aggregate and anonymously. This means your information will not be reported by itself or with any personal identifiers, such as name or date of birth. However, risk of loss of confidentiality is still possible. Finally, as with all investigations, the research may involve risks that are currently unforeseeable.

What are the possible benefits?

There may be no direct benefit to you. Future patients may benefit from the better understanding of the rate of occlusion of the two types of dialysis catheter.

What other choices do I have if I do not participate?

You do not have to participate in this study. If you choose not to participate in this study, you could choose to receive a currently approved catheter as part of routine clinical care, to participate in another research study, or to receive no care at all.

Will I have to pay for anything if I participate?

You will incur no additional charges for participating in the study.

Will I be paid for being in this study?

No, there will be no financial compensation for participation in this study.

What happens if I am injured from being in this study?

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if

appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in this consent form.

How long will I be in this research study if I participate? Can I leave the study before it ends?

Patients who participate in this study will be followed for 3 months (90 days) after the initial insertion of the dialysis catheter. Additionally, your clinical records may be reviewed to determine when and why the initial catheter was replaced or removed for up to 12 months following catheter insertion. Your participation in this study is completely voluntary and you may withdraw at any time without affecting your present or future care. You may be withdrawn from the study if your physician finds it necessary or in your best interest.

What information about me may be collected, used, or shared with others?

Your name, age, medical record numbers, telephone number and dates and results from examinations, tests, procedures, and imaging related to the treatment of kidney failure and management of your dialysis catheter.

Why is my information being collected?

Your information will be used by the investigators to perform the research, to oversee the research, and to contact you if necessary. Your personal information will not be used in reporting the outcomes of this study. This information is collected to ensure the data from the investigation is recorded correctly. This information may be shared between study team members at different sites.

Who may use and share information about me?

The investigators for the study and the study team may use or share your information for this research study. Your information will be shared with the sponsor of study, Teleflex Medical Incorporated, a division of Arrow International. Additionally, information may be shared with regulatory oversight organizations such as the Institutional Review Board at the University of Pennsylvania and the FDA. All information shared between study team members will be through a password protected electronic database system to protect privacy and confidentiality. However, there is still potential risk to confidentiality and privacy.

How long may the investigators use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire. Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study, unless you have given written authorization, the University of Pennsylvania's Institutional Review Board grants permission, or as permitted by law.

Can I change my mind about giving permission for use of my information?

Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to participate in this research study.

Who can see or use my information? How will my personal information be protected?

Every attempt will be made by the investigators to keep all information collected in the study strictly confidential, except as may be required by a court order or by law. If necessary, authorized representatives at the University of Pennsylvania's Institutional Review Board (IRB), a committee charged with protecting the rights and welfare of research subjects, or the FDA (Food and Drug Administration) may be provided access to our research records. If any publication or presentation results from this research, study participants' data will be reported only in aggregate form without any individually identifiable information. Additionally, a description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

What if new information becomes available about this study?

You will be provided with a copy of this document for your records. If new information about this study is discovered, you will be informed.

Electronic Medical Records and Research Results

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record. If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient), and

are participating in a research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

If you have never received care within either of these systems and are participating in a research study that uses services at University of Pennsylvania, an EMR will be created for you for the purpose of maintaining any results of procedures performed as part of this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Results of research procedures performed as part of your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR, these results are accessible to appropriate University of Pennsylvania workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by University of Pennsylvania to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

Who can I call with questions, complaints, or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

Disclosure of Money received outside of the study:

This research study is supported by money from Teleflex Medical. In addition, the person leading this research study receives compensation from Teleflex Medical for work that is not a part of this study and unrelated to hemodialysis, renal disease, and dialysis catheters. These activities may include consulting, advisory boards, giving speeches or writing reports. If you would like more information, please ask the researchers or the study coordinator.

Conclusion:

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, you have been given the opportunity to ask questions, your questions have been answered to your

satisfaction, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study. Upon signing below, you will receive a copy of this consent form.

Name of Subject (Please Print)	Signature of Subject	Date
Name of Person Obtaining Consent (Please Print)	Signature of Person Obtaining Consent	Date

IRB APPROVAL FROM: 08/10/2018 TO: 08/09/2019