UCLA Health System
Radiology

Research Study Proposal v4

ClinicalTrials.gov# : **NCT02796300**

Study Title: **Study to Compare Palindrome vs. BioFlo DuraMax Dialysis Catheters**

Protocol Number: UCLA Bioflo 2016

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Last Update : **08/03/2016**

BioFlo Study Protocol

1. Objectives
    a. Specific Aims:
        i. To investigate the clinical efficacy and complications of Bioflo Duramax dialysis catheter by comparing and monitoring a catheter thrombosis rate and catheter exchange rate of Bioflo Duramax catheter vs. Palindrome catheter

    b. Objectives
        i. To monitor catheter thrombosis rate and catheter exchange rate of Bioflo catheters vs. Palindrome catheters in 1 month.
        ii. To compare a mid-term (3 months) catheter thrombosis rate and catheter exchange rate of Bioflo catheters vs. Palindrome catheters
        iii. If necessary, to compare a long-term (6 months) catheter thrombosis rate and catheter exchange rate of Bioflo catheters vs. Palindrome catheters
        iv. To perform a cost-analysis and economic burden of using Bioflo catheters compared to Palindrome catheters due to catheter thrombosis and exchange.

            * Catheter thrombosis is defined as the therapeutic use of tPA to restore catheter patency.

2. Study Procedures
    a. Study Design
        i. This is a single-centered, prospective, randomized controlled trial.
        ii. Total N = 60
        iii. Patients will be randomized based on randomized software to either the **BioFlo Group** or **Palindrome Group**.
        iv. The following information will be obtained at the time of catheter insertion:
            1. Demographic information
            2. Clinical information (e.g. medical history)
            3. Procedure information (e.g. insertion site and length)
        v. The catheter placement procedure will be performed as a standard of care and routine procedure performed in the interventional radiology (angio) suite and the following is a brief description of the procedure:
            1. The right neck will be prepped and draped in the usual sterile fashion. 1% lidocaine will be administered for local anesthesia. The right internal jugular vein access will be achieved under ultrasound guidance with a micropuncture kit. An .035 Amplatz wire will be then advanced into the right atrium. Next, attention will be turned to the right upper chest, where an appropriate site will be selected for the tunnel and lidocaine will be also administered subcutaneously from the upper chest to the neck. The catheter will

be then tunneled subcutaneously in a retrograde fashion from a skin incision in the chest through the tract. The right neck tract will be serially dilated and a peel-away sheath will be placed. The catheter will be then advanced to the right atrium as the peel away sheath will be removed. The incision in the neck and tunnel site will be closed with dermabond. The catheter will be secured to the skin with 2-0 silk. Sterile dressings will be applied.

vi. Each patient will be followed for 3 months (primary endpoint) and/or 6 months if needed, for the following parameters:
    1. Updated clinical information (e.g. interval medical history)
    2. Hemodialysis information (e.g. flow rate)
    3. Frequency of tPA thrombolysis
    4. Frequency of catheter exchange
    5. Complications
        a. If 3 months follow up data is not statistically significant, additional 3 months follow up will be performed.

b. Subject Population
    i. Number of subjects = 60 (30 BioFlo vs. 30 Palindrome)
    ii. Inclusion Criteria
        1. Males and females 18 - 65 years of age;
        2. First de novo dialysis catheter placement or second catheter exchange, no more than 3 replacements on a same site
        3. Requiring at least 3 months dialysis catheter usage
        4. No clinical or radiographic evidence of SVC narrowing
        5. Patent right internal or external jugular vein
        6. Willing to provide the dialysis center information for F/U
        7. No known diagnosis of hypercoagulapathy
    iii. Exclusion Criteria
        1. Short term catheter usage plan (< 1 months)
        2. No right jugular venous access
        3. Catheter use for bone marrow transplant or plasmaphresis

3. Scientific Background and Rationale
    a. Vascular access has always been a significant issue for patients receiving long-term hemodialysis. National clinical practice guidelines state that arteriovenous fistulae (AVF) are the preferred method of vascular access for chronic hemodialysis.[1] However, in the United States in 2012, 19% of hemodialysis patients still received treatment using an indwelling catheter and 77% of dialysis patients in their first 30

days of end-stage renal disease received treatment using a catheter.[2] Catheters are advantageous because they are low cost, universally applicable, have easy insertion, can insert into multiple sites, and do not require maturation time or venipuncture.[3] Thus, catheters are still widely used for chronic dialysis treatment and there is a pressing need to explore methods to improve catheter use.

b. Numerous catheter designs have been studied to increase efficacy and minimize complications of catheter hemodialysis. Major complications of catheters include catheter thrombosis, central venous stenosis, infection, and dialysis inadequacy. Catheter thrombosis must be avoided if possible because using too many catheters may exhaust all of the catheter insertion sites on the body, as well as increase the risk of infection.
c. The Palindrome catheter, developed in 2005, has a symmetrical "Z" shape outlet to reduce the risk of poor blood flow and increase dialysis adequacy.[4] It is widely used for hemodialysis purposes in United States hospitals today. According to the AngioDynamics Inc. manual, BioFlo DuraMax is the first dialysis catheter created with Endexo technology and is made of more catheter thrombosis-resistant material.[5] Benchtop testing using bovine blood showed that the BioFlo DuraMax catheter has 84% less thrombus accumulation compared to non-coated Palindrome dialysis catheters.[5] Although this result is not indicative of clinical outcomes, it is still a promising development for hemodialysis treatment. In clinical setting, this finding translates as less in-catheter thrombosis and therefore, less thrombolytic tPA usage for decloting the catheter and less frequent catheter exchange.
d. In this study, we will perform a single center, prospective, randomized controlled short-term study comparing the mainstream Palindrome catheter to the new BioFlo DuraMax catheter with a focus on catheter thrombosis rate and catheter exchange rate. Currently in the literature, no studies exist which compare BioFlo catheters to other hemodialysis catheters on the market. This study is unique because it is the first investigation to provide clinical data examining the clinical advantages of the BioFlo DuraMax dialysis catheter compared to another major hemodialysis catheter.

4. Monitoring and Safety Mechanisms
    a. The data security will be followed by OHRPP Data Security in Research guidance and procedures. Clinical data will be entered into a database; each patient will be assigned a unique identifier. The key to the code that links to individual patients will be maintained on a separate secure computer behind the UCLA firewall with encryption; controlled access privileges based on user ID and password will be used on the hardware storing the key as well as the clinical database under the authority of the investigators. All electronic data will be fully encrypted and password-protected and they will only be stored in the secure network server provided by our IT department. Any hardcopy data will be locked in a locked file cabinet or locked room with a limited access by only authorized personnel. At the completion of the study, all data files will be completely stripped of personal identifiers and key to the code will be destroyed.
    b. Patient safety monitoring will be performed routinely by the patient's primary care physician, nephrologist, interventional radiologist and the dialysis center staff as these end staged renal disease patients are very closely monitored by several multi-disciplinary team. Any adverse events or unforeseen complications may arise after the procedure and during the follow up period. These will be promptly

assessed and any required intervention will be performed to minimize any compromise of patient care and safety.

5. Statistical Analysis and Method of Data Analysis
    a. Sample Size Calculation:
        i. This is for a study comparing two independent study group (Group A Palindrome vs. Group B BioFlo) with the primary endpoint of decreased number/percentage of tPA usage during the hemo-dialysis due to catheter thrombosis.

Continuous Endpoint, Two Independent Sample Study

Sample Size	
Group 1	26
Group 2	26
Total	**52**

Study Parameters	
Mean, group 1	30
Mean, group 2	2420% dec
Alpha	0.05
Beta	0.05
Power	0.95

        ii. With current usage of tPA (approximately 30 +/- 6 tPA use in 3 months) with the Group A, we anticipate at least 20% reduction in tPA use.
        iii. With the type I/II error rate of Alpha = 0.05, Beta = 0.05 and Power of 0.95 (95%) in 1:1 enrollment ratio, the required sample number is 26 for each group.

$$k = \frac{n_2}{n_1} = 1$$

$$n_1 = \frac{(\sigma_1^2 + \sigma_2^2/K)(z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2}$$

$$n_1 = \frac{(6^2 + 6^2/1)(1.96 + 1.64)^2}{6^2}$$

$$n_1 = 26$$

$$n_2 = K * n_1 = 26$$

        iv.
    b. The main objective of this project is to compare/measure the catheter thrombosis rate which is one of the main complications of the dialysis catheter. The catheter thrombosis is determined by usage of tPA prior to the dialysis as no flow or significantly decreased flow is noted by the dialysis center staff. Often, a tPA infusion would improve the flow and therefore, the patient can receive a complete dialysis session. However, if the catheter thrombosis is severe, a tPA infusion may not improve the flow and therefore, the catheter exchange or reposition has to be performed.

i. The main data collection for measurement of efficacy/complication is to monitor the number of tPA being infused at each dialysis session per each catheter.

c. This project has a single primary endpoint at 3 months with comparing a catheter thrombosis rate at 3 months. Our description of having 1 month and 6 months follow up may have caused some confusion of having multiple primary endpoints. The 1 month follow up is for purely to confirm that the patient is not lost to follow up.