TriHealth Research Protocol Outline

Date	June 6, 2017
Title	Maintaining Patency in BioFlo Implanted Port Catheters with Saline Only Flushes
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Purpose of Study: In this institution, the majority of cancer patients have implanted port catheters. Maintenance of implanted port catheters is critical for the delivery of safe and effective care for cancer patients who need dedicated venous access for purposes of blood draws, blood product infusions, intravenous medications, intravenous fluids, and/or antineoplastic therapy. One of the most common complications of implanted port catheters is occlusion. The primary cause of catheter occlusion is the formation of a thrombus within or surrounding the catheter (McGee & Gould, 2003). The formation of a thrombus starts as a fibrin sleeve or sheath consisting of platelets and fibrin. Routine flushing of implanted port catheters is conducted as a measure to prevent the formation of a fibrin sleeve.

According to the TriHealth Nursing Policy and Procedure Intravenous Site Guidelines, an implanted port catheter should be flushed with 20 ml of normal saline after IV medication, blood, or blood draws. Heparinized saline in the amount of 5 mL (concentration 100 units/mL) should be used as a final flush when no IV fluids are running and before de-accessing. However, routine use of heparinized saline flushes has been known to result in heparin induced thrombocytopenia (HIT), an immune reaction to heparin that can have serious consequences (Cooney, 2006). Additionally, heparin does not have fibrinolytic activity; therefore, it will not lyse existing clots (Heparin Lock Flush Solution). It is recommended that the use of heparin be avoided or minimized whenever possible (Cooney, 2006).

While evidence in the literature is scant, there is no clear consensus on the need and efficacy of heparinized saline as the solution for maintaining patency in implanted port catheters (Camp-Sorrell, 2010). Therefore, a nursing research study to determine the safest and most effective flushing solution(s) for maintaining patency in implanted port catheters began in the TriHealth Infusion Centers in January of 2013. This is an ongoing non-inferiority study using a randomized controlled trial methodology to compare the efficacy to a 20 mL normal saline flush with a 20 mL normal saline flush followed by a 5 mL heparinized saline (100 units/mL), the standard of care at TriHealth. As of October 30, 2015, 135 of 396 target population have been enrolled in the study.

A few months ago, the BioFlo Port with Endexo Technology (referred to hereafter as the BioFlo Port) was introduced in some of the TriHealth facilities inserting implanted port catheters and providing care to patients with implanted port catheters. The catheter in the BioFlo Port contains a "permanent and non-eluting polymer that is 'blended' into the polyurethane from which the catheter is made" (Navilyst Medical, Inc., 2014, pg. 3). Navilyst Medical, Inc., the manufacturer

of the BioFlo Port claims that this port has 96% less thrombus accumulation on the surface of the catheter as compared to the non-coated conventional port catheters. However, the data supporting this claim is from in-vitro studies. Materials from Navilyst Medical, Inc., state that this technology provides a saline-only flushing option but does not specifically state that use of heparinized saline in the flushing protocol is not needed. Additionally, no studies on human patients have been conducted evaluating the rate of occlusions among patients with a BioFlo Port catheter. The implanted port-catheters in use by patients in the study currently in progress within the TriHealth Infusion Centers are made of a different material, thus the efficacy of flushing solutions in those catheters cannot be extrapolated to BioFlo Port. The desired outcome of the studying flushing solutions for implanted port- catheters is to change practice, (i.e., policy and procedure related to care of all implanted port-catheters) if appropriate. Therefore, another randomized control trial using the same methodology among patients with the BioFlo Port is needed.

The purpose of this study is to determine the rate of occlusion in BioFlo implanted port-catheters flushed with 20 mL of normal saline only vs those flushed with the standard practice of 20 mL of normal saline followed by 5 mL of heparinized saline (100 units per mL). The researchers also hope to conclude that the complication rate in patients whose ports are flushed with saline only is no greater than those of patients whose ports are flushed with the combination of saline and heparinized saline. These complications might include partial or complete obstruction, infection of the central line, and/or the onset of heparin induced thrombocytopenia.

Research Question(s):

1. Does a saline only flush maintain the patency of BioFlo Port at a rate comparable to a heparinized saline solution?

2. Is there any difference in the type and rate of complications among BioFlo Ports flushed with saline only versus heparinized saline?

Null Hypothesis:

We are proposing a non-inferiority trial. Thus, the null hypothesis is: BioFlo Ports flushed with saline only will experience an occlusion rate of more than 10% over the occlusion rate experienced in implanted port catheters flushed with a heparinized saline solution.

The alternative hypothesis is: BioFlo Ports flushed with saline only will experience an occlusion rate less than 10% over the occlusion rate experienced in implanted port catheters flushed with heparinized saline solution.

Background Information/Literature Review:

Currently at TriHealth, Inc. all implanted port catheters are flushed according to the TriHealth Nursing Policy and Procedure Intravenous Site Guidelines (See Appendix A). An implanted port catheter is flushed with 20 mL of normal saline after IV medication, blood, or blood draws. Heparinized saline in the amount of 5 mL (concentration 100 units/mL) is used as a final flush

when no IV fluids are running and before de-accessing. This is intended to maintain patency of the catheter until the next use.

Frequency of flushing depends on the use of the implanted port catheter (ie. frequency of visits in the out-patient/in-patient units for blood draws or intravenous treatments). At TriHealth, implanted port catheters that are not in use are flushed a minimum of every three months with the same solutions and volumes as noted above (i.e., 20 mL normal saline plus 5 mL heparin (100 units/mL)). The policy also recommends turbulent flushing (see Appendix A). The turbulent flushing technique is accomplished by a push-pause rhythm every one mL for the entire flush volume. Turbulent flushing helps remove built-up residue, medication, and fibrin from the walls of the catheter. Additionally, TriHealth has adopted the use of a neutral displacement needle-free connector with a clear housing (the MicroCLAVE® Clear, ICU Medical, Inc., San Clemente, CA, USA) that features a split septum with a straight internal fluid path design and minimal dead space to help minimize blood reflux into the tip of the catheter upon connection and disconnection of the luerloc, thus reducing the risk of occlusions due to blood reflux. This connector meets recommendations of the Infusion Nursing Society, Center for Disease Control, Federal Drug Administration and Society for Healthcare Epidemiology in America regarding the prevention of intravascular catheter-related bloodstream infections and enables clinicians to view the fluid pathway to verify effective flushing and clamp the IV line without requiring a specific clamping sequence.

Heparin induced thrombocytopenia (HIT), an immune reaction to heparin, remains a serious consequence of heparin use in some patients. Patients experiencing HIT can develop deep venous thrombosis, pulmonary emboli, stroke, or myocardial infarction. Patients developing HIT thrombotic syndrome may require limb amputation and are at an increased risk for death. The actual incidence of HIT is 1-5% of patients exposed to heparin (Cooney, 2006). Many clinicians think that HIT is under-recognized and under diagnosed. The first response to the diagnosis of HIT is the discontinuation of all forms of heparin, including heparin flushes. The use of heparin should be avoided or minimized whenever possible. If saline only flushes were found to be as effective as heparinized saline flushes all types of implanted port-catheters, it would significantly decrease the patient's exposure to heparin, and therefore the potential to develop HIT. However, the evidence for recommending saline only vs saline plus heparin flushing of implanted port-catheters remains inconsistent (Camp-Sorrell, 2010; Kannan, 2008, Lee & Johnson, 2005).

The reasons for placing a BioFlo Port in a patient and the indications for use of the catheter (Navilyst Medical, Inc., 2014) are the same as for placing any type of implanted port-catheter in a patient and maintaining the patency of the port remains a primary concern. The BioFlo Port, when used with a power injectable needle, can also be used for the power injection of contrast media. As noted above, the manufacturer of the BioFlo Port claims that the Endexo Technology provides a catheter material more resistant to thrombus accumulation. However, as also noted by the manufacturer, the reduction in thrombus accumulation is based on platelet count in the catheter and supported by acute in-vitro testing only.

The BioFlo Port also contains PASV Valve Technology that is "designed to resist backflow, thus maintaining long-term patency and provide a saline-only flushing option" (Navilyst Medical, Inc., 2014, pg. 2). Unfortunately, an evidence-based citation for the last statement is not

provided. The BioFlo Port with PASV Valve Technology also claims to provide fewer complications when compared with nonvalved ports, namely a 47% (p=0.02) reduction in inadequate blood draw, a 51% (p<0.03) reduction in nursing time for troubleshooting port problems, and a 35% (p=0.20) reduction in tPA usage (Carlo, Lamont, McCarty, Livingston, & Kuhn, 2004). In the study by Carlo et al., the valved ports were flushed with 10 mL of normal saline while the nonvalved ports were flushed with 10 mL of heparinized saline (number of units of heparin per mL of saline not specified). These results are promising but it only included 73 patients (37 in valved port group and 36 in the non-valved port group) who were followed for 180 days. Additionally, it is only one study; subsequent studies replicating this methodology have not been located. The purpose of the MicroCLAVE® Clear connector which is used with all implanted port catheters at TriHealth is to also help minimize blood reflux into the tip of the catheter upon connection and disconnection of the luerloc, thus reducing the risk of occlusions due to blood reflux. Therefore, in this study and the one already in progress, the type of flushing solution is the main focus as the materials and mechanics of the implanted port in each study are the same.

In conclusion, Level 1 evidence for the use heparin flushes versus saline flushes for the maintenance of implanted port catheters is lacking in the current literature. No study has been conducted exclusively among patients with implanted port catheters of the same type. For nursing to establish an evidence-based practice guideline for flushing of implanted port catheters, more research is needed to generate the knowledge necessary to make recommendations that will change and standardize practice.

Research Plan

Study Design: Non-inferiority trial in which participants will be randomly assigned to one of two groups: the control group or the intervention group.

S**etting for the Study:** The TCI Infusion Centers, specifically: the TCI Good Samaritan (GS) Infusion Center at GSH; the TCI GS Infusion Center Butler County; the Ambulatory Treatment Center at Bethesda North Hospital; the TCI GS Infusion Center, Cheviot; TCI Infusion Center, Kenwood; TCI Infusion Center, Arrow Springs; and the TCI GS Infusion Center, Anderson.

Participants: Patients receiving care in the identified settings who have an implanted port catheter will be recruited to participate in this study.

Inclusion Criteria:

- over the age of 18 years
- able to read and understand English
- has a BioFlo implanted port in place less than one (1) year
- evidence of a patent BioFlo port catheter prior to enrollment in the study
- is receiving active treatment i.e., receiving a therapeutic drug through the BioFlo implanted port

- current treatment protocol projected to continue for a minimum of three (3) months
- anticipates receiving care at the identified centers for 12 months following enrollment in the study
- receives routine care of the implanted port catheter at any of the identified TriHealth Cancer Institute Infusion Centers

Exclusion Criteria:

- has documented Heparin platelet antibody (could not be randomized to either group) or other allergy to Heparin
- receiving therapeutic dose of an anticoagulant, i.e., warfarin, heparin, enoxaparin, etc.
- Does not meet one or more of the inclusion criteria

Recruitment

Prospective study participants will be identified the day prior to their appointment in the treatment center by a member of the research team. Their chart will be reviewed for inclusion criteria and flagged as a potential study participant.

When the potential study participant arrives in the treatment center, a member of the research team will escort the patient into a treatment room and explain the study by reading a prepared script (see Appendix B). If the patient expresses interest, the Informed Consent Statement and HIPAA Authorization form will be reviewed and signed. After obtaining informed consent, a participant will be randomly assigned to the heparinized saline flush (control group) or saline only flush study group (intervention group). A color coded sticker will be placed on the patient's treatment folder indicating participation in the study and group assignment. The random assignment process will be achieved using sequentially-numbered opaque sealed envelopes (SNOSE) containing the group assignment. An yellow colored data collection face sheet (see Appendix C) will indicate control group; a blue colored data collection face sheet will indicate the intervention group.

During FY 2012, 391 patients with implanted port catheters were treated in the OPCC. Seventy of these patients experienced an occlusion of their port that required the administration of alteplase (CathFlo) (Kelly Dornheggen, personal communication, October 12, 2012). Thus, 70 of 391 experienced an occlusion resulting in an occlusion rate of 18%. Some of these 70 patients experienced an occlusion more than once during that time. Additionally, during that time, a few patients had their implanted port catheters removed due to infection or malfunction. The exact number of patients who experienced multiple occlusions or had their implanted ports removed/replaced during FY2012 is unknown.

During the planning of the current study evaluating implanted port catheters, we engaged the consultation of a biostatistician through the Center for Clinical and Translational Science and Training (CCTST) to conduct a power analysis to

establish the number of participants needed in each group to determine the non-inferiority of the alternative therapy (saline only flush). Consultation was provided by Mekibib Altaye, PhD, Associate Professor Cincinnati Children's Hospital Medical Center, University of Cincinnati.

Based on the literature and our own experience we estimated an approximate occlusion rate of 20% with the standard treatment (saline + heparinized saline flush as described above). The power analysis conducted by Dr. Altaye determined that, using a two group normal approximation test of proportions with a one-sided .05 significance level, a sample size of 198 participants per group will have 80% power to reject the null hypothesis that the proposed method is not inferior (i.e. the difference in proportions between the proposed method and the standard method is greater than 0.10). Thus, we will continue to recruit participants in that study until 198 have been enrolled in each group for a total of 396 study participants.

Dr. Altaye was consulted again when the introduction of the BioFlo Port at TriHealth was discovered. It is Dr. Altaye's recommendation that this second randomized controlled trial using the same methodology and power analysis calculations be conducted. Thus, we will recruit 198 participants per group for a total of 396 participants in this study.

Data Collection:

Independent Variables: Method for flushing implanted port catheters:

- 20 mL of saline followed by 5 mL of Heparinized saline in a concentration of 100 units/mL

OR

- 20 mL of saline only

Dependent Variables:

Primary Outcomes

- Occurrence of first complete (can neither withdraw blood nor flush the catheter) occlusion
- Occurrence of first partial (able to flush but unable to withdraw blood) occlusion
- Frequency with which alteplase (CathFlo) has to be utilized to resolve an occlusion

Secondary Outcomes

- Number of subsequent occurrences of complete or partial occlusions after the first occurrence.
- Amount of time in days that a port remains patent (flushes easily and able to obtain a blood return).
    - Amount of time between entrance in study and first incidence of partial or complete occlusion

    - Amount of time between incidences of partial or complete occlusion.
- Occurrence of other complications:
    - Central Line-Associated Blood Stream Infection (CLABSI) – a laboratory-confirmed (recognized pathogen cultured from one or more blood cultures; organism cultured from blood is not related to an infection at another site) blood stream infection that is considered central line associated (CDC, 2012).
    - Develops complication related to Heparin
        - HIT (Heparin induced thrombocytopenia as measured by a positive HIT antibody test)
        - Other heparin allergy

Moderating variables: other things that could also affect patency of the port

- Number of times port flushed per month or frequency of flushing.
- Use of prophylactic doses of anticoagulant drugs (e.g., enoxaparin, heparin, warfarin)
- Development of a hypercoaguable state, as diagnosed by primary hematologist/oncologist
- Mechanical difficulties related to port placement e.g. "Pinch-off syndrome"
- Length of time port has been in place prior to entrance in study

Extraneous variables:

- Type of cancer
- Age of participant

Data collection tool

The data collection tool (see Implanted Port Catheter Flushing Data Collection Form – Face Sheet: Appendix C and Record of Flushes: Appendix D) were developed by the principal and sub-investigators specifically for the purpose of this study. The tool was reviewed by the OPCC nurses for completeness and clarity. In addition to basic demographic information (age, gender), the nurse will record the patient's type of cancer, and the diagnosis or history of any hypercoaguable state or use of anticoagulant medication as documented in the patient chart. The nurse will also document the type of implanted port catheter (single/double), the port location (right/left, subclavian vein (described in the operative note or chest x-ray), and the date the port was inserted so that length of time the port has been in place can be calculated. Data will be recorded on the Face Sheet when the patient is enrolled in the study and as pertinent information/events become known, i.e., as complications occur.

With each visit to the identified treatment center, the nurse will document the date and characteristics related to the patency of the port catheter on

the Record of Flushes data collection tool. In the event the blood withdrawal is sluggish or absent, the patient will receive a dose of alteplase (CathFlo) according to the TriHealth Nursing Policy: VAD: Care & Maintenance (Appendix A) and as ordered by the physician. Dosage and results of that intervention will also be recorded on the Record of Flushes data collection tool. In the event that any study participant (regardless of group assignment) requires alteplase (CathFlo) on three (3) consecutive visits to the treatment center, the patient's participation in the study will be terminated and they will be excluded from further data collection. The patient will be returned to a standard maintenance protocol for flushing of the port as prescribed by the afore-mentioned TriHealth Nursing policy (see Appendix A) or as prescribed by attending physician.

Participants in the control group will have yellow colored data collection Face Sheets while participants in the intervention group will have blue colored data collection Face Sheets. The Record of Flushes sheet will be white for patients in both groups. A blue or yellow sticker will be placed on the cover of the patient folder housed in treatment center noting the patient's involvement in the study. The data collection Face Sheet and the current Record of Flushes sheet will be kept in the individual patient folder as long as they remain a participant in the study. As the Record of Flushes data sheet becomes full, they will be collected by study staff and placed in locked drawer in a TriHealth office.

Experimental Aspect of the Study:

Patients who agree to participate in this study will be randomized to either the control group or intervention group as explained above.

Participants in the control group will have their implanted port catheters flushed according to the established TriHealth Nursing Policy: Venous Access Devices (VAD): Care and Maintenance (see Appendix A). Following the use of the port catheter with no continuous fluids running, or before de-accessing a port catheter (removing the port needle), the port will be flushed with 20 ml of normal saline and 5 ml of heparinized saline in the concentration of 100 units of heparin per ml.

Participants in the intervention group will have their ports flushed with normal saline only. That is, following the use of the port catheter with no continuous fluids running, or before de-accessing a port catheter (removing the port needle), the port will be flushed with 20 ml of normal saline. Turbulent flushing technique (the solution is injected using a push/pause technique every 1 mL) will be used in both groups and all accessed port catheters will have a neutral displacement connector. The MicroCLAVE® Clear displacement connector (ICU Medical, Inc., San Clemente, CA, USA) is the current product in use. Participants in both groups will be seen in a TriHealth Cancer Institute Infusion Center at a frequency consistent with their individual treatment plan and as outlined in the TriHealth

Nursing Policy: Venous Access Devices (VAD): Care and Maintenance (see Appendix A). Participants will remain in the study for 12 months or until they experience one of the potential risks noted below. Participants will be considered as having completed the study if they participate for 12 months.

Potential risks for study participants in either arm of the study include partial occlusion (can instill flush solution but not withdraw blood) and complete occlusion (can neither instill flush solution nor withdraw blood). Study participants could require removal of the port if an occlusion cannot be resolved, and possibly require re-insertion of a new implanted port. In the event of any occlusion, alteplase (CathFlo) in the policy established dose and frequency (see Appendix A) will be instilled to resolve the occlusion. Study participants whose implanted ports are found occluded on three (3) consecutive visits to the treatment center will be excluded from further data collection, i.e., their participation in the study will be terminated. The standard flushing as prescribed by the TriHealth Nursing Policy (see Appendix A) or as prescribed by the attending physician will be used. Study participants whose occlusion cannot be resolved with alteplase and require removal of the port will also be terminated and excluded from further data collection. Patients who develop port infections necessitating port removal will be terminated and excluded from further data collection. Study participants who develop HIT (heparin induced thrombocytopenia) or other heparin allergy will be terminated and excluded from further data collection. Likewise, patients who have thrombotic or embolic phenomenon requiring therapeutic anticoagulation will be terminated and excluded from further data collection.

The study will be closed if there is evidence that study participants in the intervention arm experience implanted port occlusion at a disproportionate rate. The amount of alteplase (CathFlo) used in each group will be assessed each month for monitoring purposes.

The undertaking of this research does require the participation of other personnel, facilities or departments other than those used in data collection. In the event the study participant is admitted to the hospital or requires some intervention using their implanted port catheter (e.g., CT scan with contrast), the study participant will have an information card describing his/her participation in the study and the group to which he/she has been randomized, so that the assigned flush solution is used, and integrity of the study can be maintained. The study participant will receive the card with instructions at the time of his/her enrollment in the study (see Appendix E Wallet Study Card).

Statistical Analysis: Descriptive statistics will be used to describe the participants. Differences between groups on the dependent variables will be calculated using t-test, Chi-Square or Fisher's exact test as appropriate for the level of data under analysis (also see discussion regarding interim analysis). Regression analysis will be used to determine the effect of the moderating variables on the occurrence of occlusion in the implanted ports. Participants in the

control group and intervention group will be further stratified based on frequency of port flushing. Differences in the rate of occlusion between stratified groups will also be calculated.

Ethical Considerations: The purpose of this study is to determine the safest and most effective flushing solution(s) for maintaining patency in implanted port catheters. In so doing, study participants could be placed at potential risk for catheter occlusion. All catheter occlusion will be treated according to TriHealth policy, i.e., the instillation of alteplase (CathFlo) (see Appendix A). Potential study participants will be made aware of the risk when enrolled in the study (See Appendix B) script for recruiting patients into the study and the Informed Consent Statement).

Informed Consent: Patients who meet inclusion criteria will be approached by a member of the research team who will explain the study, implications of their participation and review the Informed Consent Statement and HIPAA Authorization Forms (see the attached). One signed copy of the Informed Consent Form and HIPAA forms will be given to the study participant and another placed in their folder in the TriHealth Infusion Center to be scanned into their EPIC electronic health record (EHR). The original signed Informed Consent Statement and HIPAA will be stored in a locked drawer in a TriHealth office until the study is completed and closed with the IRB. The RN seeking consent and PI will document the informed consent process in the participant's EHR. Additionally, the blue or yellow sticker on the patient folder in the treatment center and presence of data collection forms in the patient folder will indicate that the patient is a participant in the study.

Privacy Information: Once enrolled in the study, each participant will be assigned a study code and referred to by that code on all study related documentation. A study enrollment log will be created to record each participant's name and medical record number, which will be correlated with the study code so that information may be retrieved to check or verify missing data. To maintain confidentiality, the study enrollment log will be kept in a password protected file in the Nursing Research Folder on the Udrive of the secure TriHealth server. All completed data collection forms will stored in a locked cabinet in a TriHealth office. Upon completion of the study, the data collection sheets will be entered into a statistical database. After all data have been entered, the data collection tools and spreadsheets will be stored in a locked drawer in locked TriHealth office until the study is complete and closed with the IRB. The data file will be stored on the U drive in the "Implanted BioFlo Port Catheter" subdirectory of the Nursing Research folder until the study is complete and closed with the IRB. Only the PI and Sub-investigators and Nursing Lead Study Coordinator will have access to the Nursing Research Implanted BioFlo Port Catheters folder on the U drive. Following closure of the study with the TriHealth IRB, all study materials will be collected, boxed and placed in TriHealth designated storage for 10 years.

Once IRB approval for the study is granted, all nurses in the treatment center who deliver care to patients with implanted ports will receive training from Sue Partusch, MSN, RN-BC, AOCNS (original PI), Sharon Sanker, RN, OCN, Sarah Pelgen, BSN, RN,

OCN and/or Nursing Lead Study Coordinator regarding study procedures. The nurses designated on the personnel roster who will be obtaining Informed Consent will also receive training specific to that process.

Cost/Budget:

There is no increase in cost related to the maintenance of implanted port anticipated among study participants. Patient will be billed for care received based on the current TriHealth standards of care.

Estimated Period of Time to Complete Study	
When will study begin?	Once IRB approval received – approximately February, 2016
Protocol Development Completed	Complete 12-1-2015
Admin Review Time	2 weeks
IRB Approval	6 weeks for FULL Board
Data collection	Approximately 3 years
Data analysis	6 months from completion of all data collection and entry
Presentation development (if applicable)	6 months
Manuscript Development (if applicable)	6 to 9 months
Journal submission process (if applicable)	12 to 18 months
Study closure	Five years

References

Camp-Sorrell, D. (2010) State of the science of oncology vascular access devices. *Seminars in Oncology Nursing*. 26(2), pp.80-87.

Carlo, J. T., Lamont, J. P., McCarty, T. M., Livingston, S., & Kuhn, J. A. (2004). A prospective randomized trial demonstrating valved implantable ports have fewer complications and lower overall cost than nonvalved implanted ports. *The American Journal of Surgery, 188*(6), 722-727.

Cooney, M.F. (2006). Heparin-Induced Thrombocytopenia*, Critical Care Nurse. 26,* pp. 30-36.

Kannan, A. (2008). Heparinized saline or normal saline? *Journal of Perioperative Practice, 18(10),* pp. 440-441.

Lee, O, & Johnston, L. (2005). A systematic review for effective management of central venous catheters and catheter sites in acute care paediatric patients. *Worldviews on Evidence-Based Nursing, 2(1),* pp. 4-13.

Navilyst Medical, Inc. (2014). BioFlo ports with Endexo Technology by AngioDynamics. Manufacturer's product brochure, Marlborough, MA: Author.