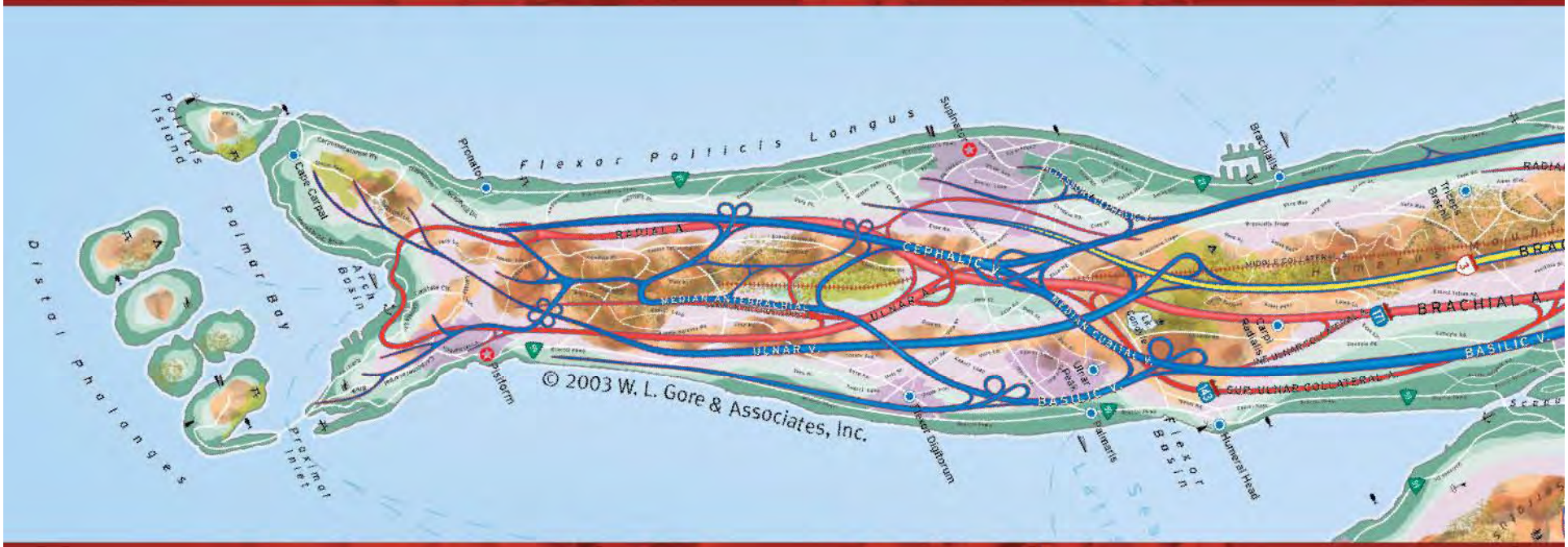
DIALYSIS CENTER TRAINING



GORE® VIABAHN® Endoprosthesis Versus Percutaneous Transluminal Angioplasty to Revise Arteriovenous Grafts at the Venous Anastomosis in Hemodialysis Patients

AVR 06-01 Study

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REVISE STUDY

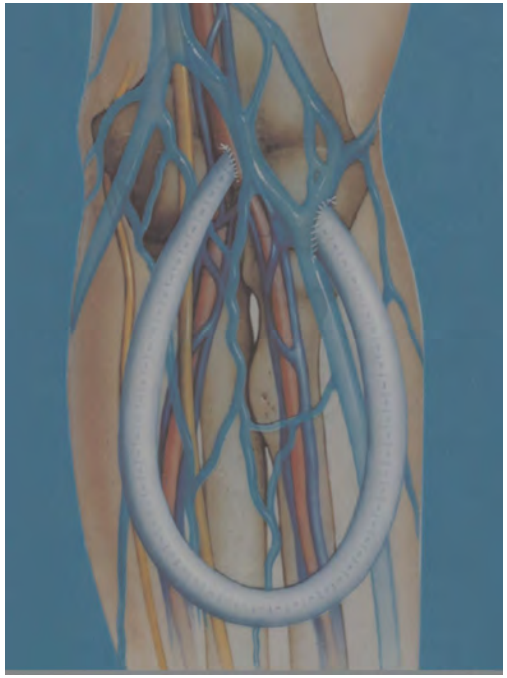
(VascularR AccEss ReVision with VIabahn® EndoproSthesis vs PercutanEous Transluminal Angioplasty Study)

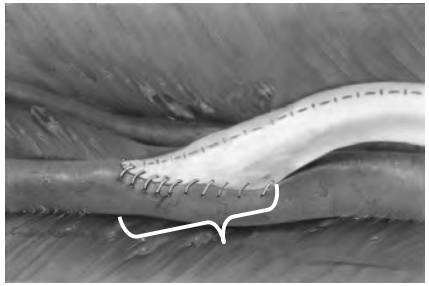
SPONSOR

W. L. Gore & Associates, Inc.

PURPOSE

To establish efficacy and safety of the GORE® VIABAHN® Endoprosthesis with PROPATEN Bioactive Surface when used to revise arteriovenous (AV) prosthetic grafts at the venous anastomosis in the maintenance or re-establishment of vascular access for hemodialysis.





Device placement or PTA

HYPOTHESIS

GORE® VIABAHN® Endoprosthesis with PROPATEN Bioactive Surface will extend the period of target lesion primary patency as compared to PTA.

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STUDY OVERVIEW

- Failed upper or lower arm dialysis prosthetic graft patients are screened, sign an informed consent and treated by the study physician (study site hospital/clinic)
  - Study subjects are randomized to either the GORE® VIABAHN® Endoprosthesis or PTA at the venous anastomosis *(junction of graft and outflow vein)*
- Following treatment, patient is discharged and resumes regular dialysis at your center per your standard of care
- Study endpoints and patient outcomes are collected from the run sheets, patient charts at your dialysis center
- The study staff will call on your dialysis center point person at regular intervals to collect study data and patient outcomes
- Your center will need to maintain the patient's chart, including original documentation of dialysis treatments (or source documents) as data collection for the study

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STUDY FLOW AND LOGISTICS

Hospital or
Outpatient Vascular Access Center

Clinical Study Site

- Study Investigator (treating physician)
- Clinical Research Coordinator

ROLE

Overall Study Management

- Patient Screening / Enrollment
- Perform study-related procedures
- Collects, retains and reports all study data collected from dialysis centers

* PREFERENTIAL OPTION
Subject returns to Clinical Study Site for all additional interventions

Dialysis Centers

- Vascular Access Coordinator (or designee)

ROLE

- Provide study data to Clinical Study Site
- Identify and document adverse events (AE)
- Document and report all graft-related repeat interventions, etc.
- Report long-term patient outcomes

New Event

SECONDARY OPTION
If event requires emergent care and Clinical Site cannot perform procedure then intervention can be performed at non-study facility

Outside Vascular Access Facility

EXPECTATIONS

- Provide procedure-related information to Dialysis Center and Clinical Coordinator

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STUDY ENDPOINTS

- **Study Treatment Groups:**
  - Conventional PTA **(Control Group)**
  - GORE® VIABAHN® Endoprosthesis with PROPATEN Bioactive Surface **(Test Device)**

- **Study endpoints** (Safety and Efficacy data) are collected from your dialysis center as part of this study

- **The study was developed as a '*real world*' design:**
  - Time to repeat intervention
  - *"How long does the dialysis circuit remain open from the time of initial treatment..."*

- **Study patients are followed at your center through <u>two</u> years**
  - Since all study endpoint data is collected from your center, it is vitally important to maintain and report accurate clinical data to the research staff

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ELIGIBLE STUDY PATIENTS

Potential study subjects require the following:

- Have a failed upper or lower forearm prosthetic graft used for hemodialysis and may be referred to the study physician;
  - Must sign a study informed consent form
  - Must meet **all** clinical Inclusion / Exclusion criteria
  - Must meet **all** angiographic Inclusion / Exclusion criteria for study consideration
- At the time of study treatment, subjects are randomized to either treatment group (intra-operatively)

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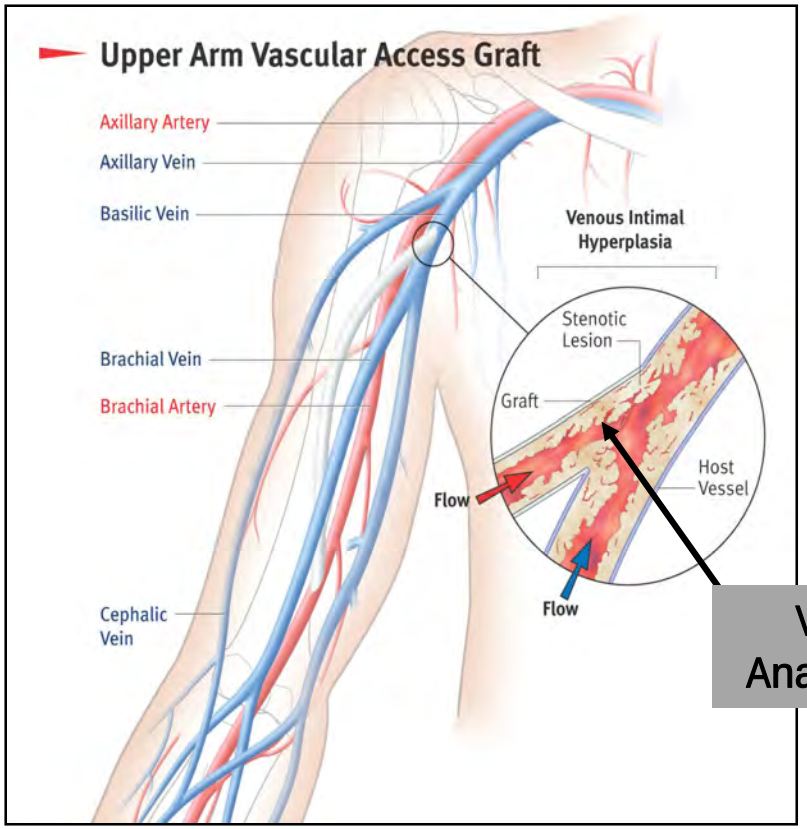
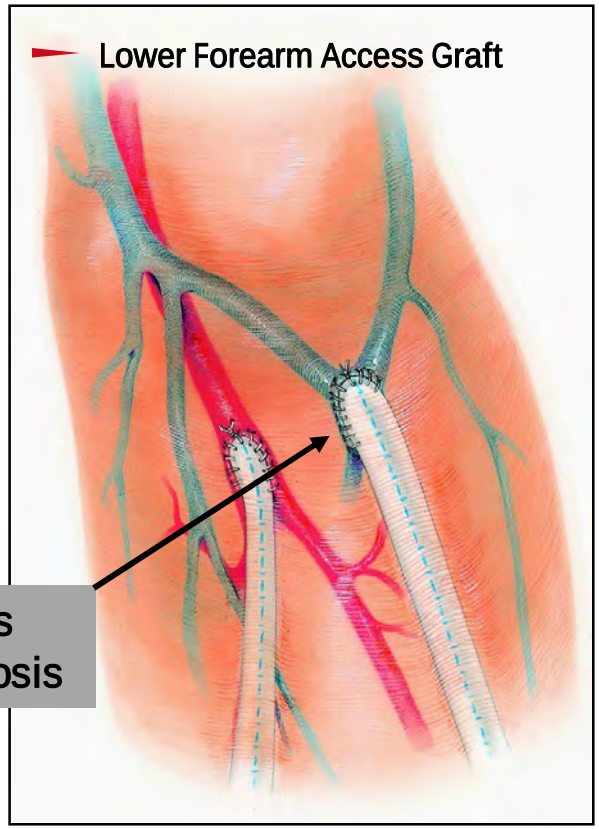
ELIGIBILE STUDY PATIENTS
UPPER AND LOWER FOREAREM GRAFTS



Venous Anastomosis



<u>Prosthetic Grafts only</u>. Native Fistulas & bovine excluded from study consideration.

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VENOUS OUTFLOW STENOSIS

Stenosis
at the venous
anastomosis

Do not place
needles near
anastomosis

Appropriate
Cannulation
Sites

Courtesy of Ingemar Davidson, M.D.

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CLINICAL INCLUSION CRITERIA

INCLUSION

1. Hemodialysis patient with a dysfunctional or thrombosed forearm or upper arm prosthetic vascular access graft
2. The patient is ≥ 18 years of age
3. The patient has a reasonable expectation of remaining
   on hemodialysis for 24 months
4. The patient or his / her legal guardian understands the study and is willing and able to comply with follow-up requirements
5. The patient or his / her legal guardian is willing to provide informed consent

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CLINICAL EXCLUSION CRITERIA

EXCLUSION

1. The age of the hemodialysis access graft is ≤ 30 days old from the date of the study procedure.
2. The patient has undergone an intervention (surgical or percutaneous) of the vascular access circuit ≤ 30 days from the date of the study procedure.
3. The patient has a native arteriovenous fistula currently used for hemodialysis.
4. The patient has an existing stent or stent graft anywhere within the current vascular access circuit.
5. The patient has an existing hemodialysis graft that has not been used successfully for hemodialysis.
6. The patient's hemodialysis graft is located in the thigh.
7. The patient has a compound or hybrid vascular access (i.e. graft-fistula hybrid).
8. The patient has steal syndrome related to the current vascular access sufficient to warrant a surgical intervention to treat hand ischemia.
9. The patient has a known or suspected systemic infection.
10. The patient has a known or suspected infection of the hemodialysis graft.
11. The patient is currently taking maintenance immunosuppressant medication such as: rapamycin, mycophenolate or mycophenolic acid, prednisone > 10 mg daily dose, cyclosporine, tacrolimus, or cyclophosphamide.
12. The patient has known bleeding disorder (e.g., hemophilia or von Willebrand's disease).
13. The patient has a defined hypercoagulable disorder.
14. The patient has known sensitivity to heparin.
15. The patient is scheduled for a live donor kidney transplant.
16. The patient is enrolled in another investigational study.
17. The patient has comorbid conditions that may limit their ability to comply with the follow-up requirements.
18. Life expectancy is ≤ 24 months.
19. The patient has an untreatable allergy to radiographic contrast material.
20. The patient is pregnant.
21. In the opinion of the operating physician, the patient's hemodialysis graft is unsuitable for endovascular treatment.

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ANGIOGRAPHIC INCLUSION AND EXCLUSION CRITERIA

INCLUSION

1. The target lesion starts ≤ 30 mm from the venous anastomosis.
2. The target lesion has > 50% stenosis as measured per protocol.
3. The patient has no secondary stenosis or a maximum of one secondary stenosis if the following criteria are satisfied:
   a. The secondary stenosis must be located in the graft or a peripheral vein.
   b. The secondary stenosis must be ≤ 50 mm in length.
   c. The secondary stenosis must be located ≥ 30 mm away from the edge of the target lesion.
   d. The secondary lesion causes > 50% stenosis.
   e. The secondary lesion is treated before randomization, using a conventional angioplasty balloon.
   f. Treatment of the secondary lesion with conventional angioplasty is successful with < 30% residual stenosis and no complications.

EXCLUSION

1. The secondary lesion is an occlusion.
2. The patient has central venous stenosis requiring treatment.
3. The physician is unable to fully inflate a conventional PTA balloon at the target lesion. (i.e., focal waist remains in balloon upon inflation).
4. There is an angioplasty induced rupture that is unresponsive to balloon tamponade.
5. Diameter of prosthetic graft adjacent to target lesion is < 4.8 mm.
6. The target lesion is entirely within the prosthetic graft.
7. The target lesion is in such a location that the GORE® VIABAHN® device, once deployed, would be within the zone of cannulation in the prosthetic graft.

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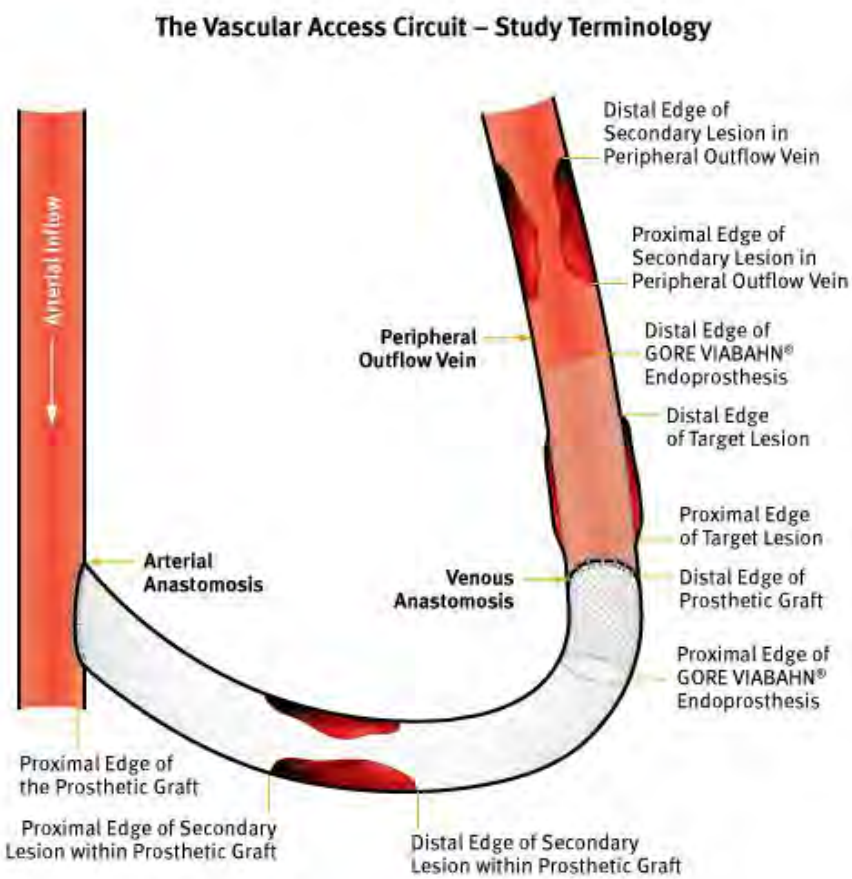
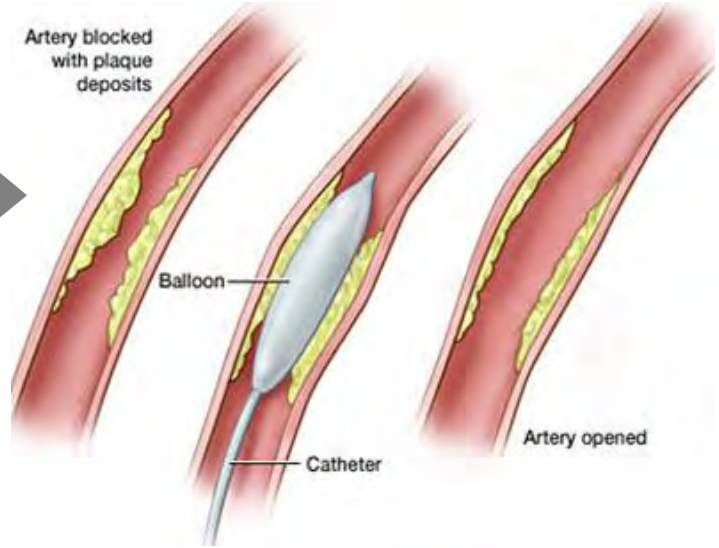
STUDY TREATMENT

GORE® VIABAHN® Endoprosthesis or PTA at the Venous Anastomosis





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FOLLOW-UP REQUIREMENTS

- Enrolled study patients will be followed at your dialysis center
- No need to return to study site unless repeat intervention to the vascular access is required;
  - Need for repeat intervention based on institutional surveillance protocols
  - Contact the research staff immediately to schedule the repeat intervention at the study site
- Research coordinators will call on your dialysis center at specified time intervals to collect source documentation and information on any repeat intervention and adverse events (AEs) at:
  - 1, 3, 6, 12, 18, and 24-months

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DATA COLLECTED FROM THE DIALYSIS CENTER

The Study Staff will contact you at regular follow-up intervals to collect the following:

- Date of last hemodialysis session
- If applicable, information regarding repeat intervention(s) including graft abandonment
- If applicable, adverse event (AE) per study profile
- Collection of withdrawal, cause of death, or lost to follow-up information (if applicable)
- No collection of concomitant medications

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CANNULATION DO'S AND DON'TS

DO:

- Be conscientious of access location during dialysis session treatments (**avoid** the venous anastomosis area)
- Rotate access needles per standard of care, etc.
- Check and report any graft related issues
- Report any graft dysfunctions or inability to cannulate the graft to the research staff immediately

DON'T:

- Do not cannulate the graft area of the GORE® VIABAHN® Endoprosthesis placement or the area of PTA at the venous anastomosis
- Do not under report device issues, study related Adverse Event (AEs), repeat interventions, etc.
- Do not hesitate to contact the research staff with any questions

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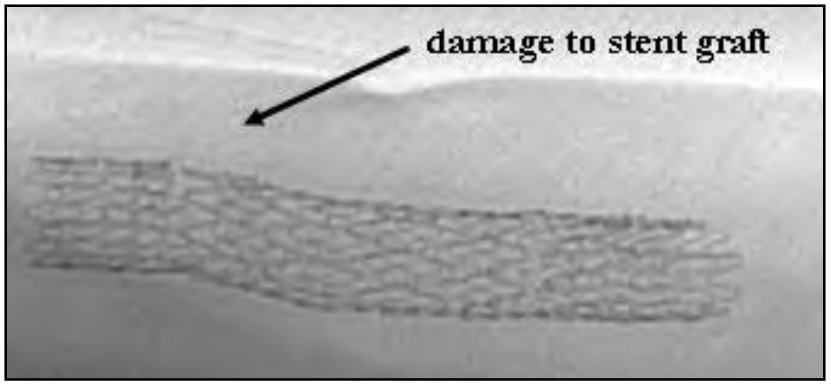
CANNULATION (Continued)

'Do not cannulate or puncture the GORE® VIABAHN® Endoprosthesis. Cannulating or puncturing the endoprosthesis may result in damage to the ePTFE lining and / or the external nitinol support, resulting in compromised performance or failure of the endoprosthesis.'

GORE® VIABAHN® Endoprosthesis Instructions for Use (IFU)

No stent-graft currently has indication, approval, or testing to support cannulation



Courtesy of TM Vesely, MD

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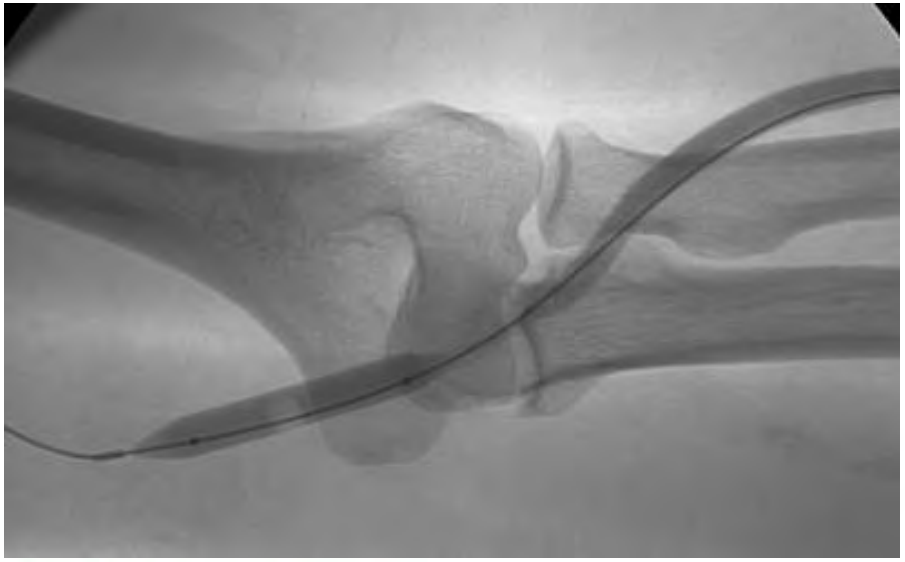
REPEAT INTERVENTIONS

- Make every attempt to schedule a repeat intervention with the subject's study physician (study research site)
- Repeat interventions may be performed anywhere in the hemodialysis circuit per the Investigator or institution's standard of care
  - Source documentation will be collected and reported to the research staff
  - Study devices allowed as part of a repeat intervention



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REPEAT INTERVENTIONS – SCHEDULING

- **First Choice**:
  Schedule the repeat intervention at the clinical site with the Study Investigator or physician.
  - Make every attempt to bring subject back to Investigator
  - Contact the research staff and physician immediately
- **Second Choice**:
  If emergent, schedule the repeat intervention at the study site with a non-study vascular access physician.
- **Third Choice**:
  If emergent and scheduling the procedure at the clinical site is not possible, to protect the safety of the Subject, the repeat intervention may be conducted at a non-study vascular access facility.

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ADVERSE EVENT (AE) REPORTING

- An adverse event (AE) includes any undesirable clinical occurrence whether or not the AE is considered to be procedure or device-related. Adverse events include, but are not limited to:
  - Procedure-related events (e.g. puncture site complications), disease-related events (e.g. myocardial infarction), device-related events (e.g. deployment failure or device migration) and target lesion-related events (e.g. dissection, spasm).
  - Adverse events with unknown relationship(s) to the procedure, disease, device and/or target lesion should also be reported.
  - Events that fall outside pre-specified AE categories should be reported as "Other, Access Related" or "Other, Non-access Related"
- The following information will be provided to study staff for each AE:
  - Onset date
  - AE name and description
  - Primary relationship
  - Maximum severity (Major / Minor)
  - Treatment and outcome
- Original records will be maintained as source documentation and provided to the study site

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ADVERSE EVENT (AE) REPORTING

- Bleeding: Major
- Bleeding: Minor
- Device Deployment Failure
- Device Fracture
- Device Malposition
- Device Migration
- Dissection
- Drug Reaction
- Embolism, Arterial
- Embolism, Pulmonary: Symptomatic
- Heparin Induced Thrombocytopenia (HIT)
- Infection: Access-related
- Infection: Systemic
- Intraprocedural Access Thrombosis
- Myocardial Infarction (MI)
- Perforation or Rupture
- Pseudoaneurysm
- Spasm: Intraprocedural
- Other: Access-related
- Other: Non access-related

Stenosis and Thrombosis are efficacy outcomes NOT AEs
Death is not an AE, the cause of death is the AE

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ADVERSE EVENT (AE) DEFINITIONS

AE source documentation collected during entire study participation:

- Provide to study staff
- Copies of relevant source documents may be required
- Protocol specified AEs will be collected by the research staff
- You will not be responsible for entering data

Code	Adverse Event Name	Adverse Event Description
1	**Bleeding: Major**	Procedural blood loss (hematoma or other) resulting in a requirement for transfusion and / or increased level of care.
2	**Bleeding: Minor**	Procedural blood loss (hematoma or other) without a need for transfusion and / or increased level of care.
3	**Device Deployment Failure**	Malfunction or breakage of the VIABAHN delivery system.
4	**Device Fracture**	Fracture of any component of the VIABAHN device with or without clinical sequelae.
5	**Device Malposition**	Deployment of the device in a position other than that which was intended requiring the insertion of an additional device.
6	**Device Migration**	Movement of the device within the vascular access circuit > 10 mm from the original position relative to anatomic landmarks; or, any movement of the device requiring additional therapy.
7	**Dissection**	Separation of a wall of a vessel visible on venography limiting blood flow.
8	**Drug Reaction**	Documented adverse reaction directly related to a drug administered during the procedure such as radiocontrast, medications for conscious sedation / analgesia, and antibiotics.
9	**Embolism, Arterial**	Thromboembolus that lodges in the arterial vasculature confirmed by appropriate diagnostic assessment.
10	**Embolism, Pulmonary: Symptomatic**	Thromboembolus that lodges in the pulmonary circulation confirmed by appropriate diagnostic assessment.
11	**Heparin Induced Thrombocytopenia (HIT)**	Unexpected decrease in platelet count, generally at least 30%, with or without confirmatory assays such as serologically-detectable heparin, platelet Factor 4 antibodies, or positive serotonin release assay. Event noted in medical chart.
12	**Infection: Access-related**	Microbial infection directly related to the prosthetic graft or VIABAHN device with or without systemic infection.
13	**Infection: Systemic**	Intravascular blood stream infection confirmed by blood cultures thought to have a source unrelated to the vascular access.
14	**Intraprocedural Access Thrombosis**	Intraprocedural thrombosis requiring treatment occurring within a previously patent access.
15	**Myocardial Infarction (MI)**	A condition caused by partial or complete occlusion of one or more of the coronary arteries. Event noted in medical chart.
16	**Perforation or Rupture**	Extravasation in the prosthetic graft, VIABAHN device, or vascular wall requiring therapy.
17	**Pseudoaneurysm**	A new contained rupture, usually at the puncture site, occurring anytime following the study procedure.
18	**Spasm: Intraprocedural**	Spasm requiring treatment beyond nitroglycerin.
88	**Other: Access-related**	Complications not specifically listed which are determined to be related to the prosthetic graft, VIABAHN device, or any study-related treatment location within the vascular access circuit.
99	**Other: Non-Access-related**	Complications not specifically listed which are determined to be unrelated to the vascular access, or have an unknown relationship to the vascular access.

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DATA COLLECTION REQUIREMENTS FOR THE STUDY

- Maintain study patient data and source documentation:
  - Run sheets, Adverse Events, access issues, clinical indications for repeat interventions, cause of death or discontinuation, etc.
  - Maintained for each subject for the entire study
- Provide copies of original source documentation to the study staff
- Monitoring or chart review by an independent CRO
  - At the dialysis center, if indicated
  - May include additional training to the Vascular Access Coordinator or designee
  - Will require access to study patient data (paper chart, electronic records)
- Availability and timely response to the study staff is expected

DATA COLLECTION REQUIREMENTS (Con't)

- Study patients will be followed for two years post treatment;
  - Any subjects lost to follow-up will require attempts to contact and documentation
- Only study specific data will need to be collected and reported, including;
  - Study follow-up data including: date of last hemodialysis session, study related AEs, repeat interventions and cause of death or subject discontinuation, etc.
- Contact the research staff with any questions
  - Refer to the study contact sheet

CRITICAL TO STUDY SUCCESS

- Establish good working relationship and on-going communication with the research study staff
- Identify a key contact personnel at your dialysis center (ex: Vascular Access Coordinator or designee) to provide source documentation, data requests to research study staff
- Training documentation required of the Vascular Access Coordinator or point person at your center
- Immediate communication with study staff for repeat interventions or issues accessing the patients' graft
- Provide adequate data on adverse events, etc.
- Timely response to questions and data requests
- Record retention is required

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STUDY CONTACTS

Contact your study staff with questions

- Refer to your site contact sheet

Sponsor Contacts:

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