A PROSPECTIVE RANDOMIZED STUDY COMPARING THE INCIDENCE OF RADIAL ARTERY OCCLUSION (RAO) AND THE TIME TO HEMOSTASIS (TTH) WHEN USING A HEMOSTASIS BAND ALONE AND IN CONJUNCTION WITH A DISC COMPRISED OF POTASSIUM FERRATE (STATSEAL ADVANCED) FOLLOWING TRANSRADIAL CATHETERIZATION.

Study Sponsor:

A Physician Initiated Study

Principal Investigator:

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Investigator Signature Page

Study Title: A prospective randomized study comparing the incidence of Radial Artery Occlusion (RAO) and the Time To Hemostasis (TTH) when using a hemostasis band alone and in conjunction with a disc comprised of Potassium Ferrate (StatSeal Advanced) following transradial Percutaneous Coronary Intervention (PCI).

Study Center: _____
Name of Participating Center

We, the undersigned, have read and understand the protocol specified above and agree on its content. We agree to perform and conduct the study in conjunction with the other named participating centers, and as described in the protocol according to the Declaration of Helsinki, and all pertinent individual country laws and regulations.

_____ _____
Principal Investigator Date

_____, MD
Principal Investigator Printed

If additional investigators are participating in this study, please indicate names below:

_____ _____
Additional Investigator (Print Name & Initial) Date

_____ _____
Additional Investigator (Print Name & Initial) Date

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I. INTRODUCTION, BACKGROUND & RATIONALE

Over the past decade, transradial access (TRA) for invasive cardiac catheterization procedures has gained significant popularity in Europe, Canada, South America, Japan, and other sites outside of the United States where TRA is used in more than 60% of the cases.[1] The most compelling reason for adopting TRA is the increased patient safety that results from the potential elimination of access site bleeding and vascular complications. In addition, TRA is associated with early sheath removal, improved patient comfort, faster recovery, and lower costs in comparison with transfemoral access.[2-4] TRA provides the ability to perform a broad range of diagnostic and interventional cardiovascular procedures. In the USA, TRA catheterization procedures are gaining significant momentum with a significant growth from 2% in 2007 to approximately 15% in 2011[5], and an estimated 30- 35% in 2015. Moreover, with increased availability of training opportunities the TRA utilization rate is expected to grow to 50% or more in the next 2 – 4 years.

One important advantage of TRA is that the vascular sheath is always removed at the end of procedure regardless of the intensity of anticoagulation or antiplatelet therapy. Multiple methods for radial hemostasis have been described. Gentle manual compression with one or two fingers at the arteriotomy site is an effective method. Alternatively, a rolled piece of gauze can be placed longitudinally at the arteriotomy site and wrapped with an elastic bandage. These low tech methods have been mostly abandoned in favor of mechanical devices that apply compressive pressure to the arteriotomy site via a balloon mounted on a wrist band. These 'Hemostasis Bands' are inflated with air in a somewhat arbitrary manner and often require prolonged hemostatic pressure. The disadvantage of these methods is the complete interruption of arterial flow because of the inability to gauge the hemostatic pressure applied, regardless of the methodology developed for their use. It has been demonstrated that when occlusive pressure is maintained for a period longer than two hours radial artery occlusion (RAO) occurs more often.[6,7] In fact, RAO after TRA procedures is not uncommon and occurs in approximately 5-10% of cases, and is accurately described as a function of time and pressure.

$$\textbf{Incidence RAO} = f\,\textbf{(Time, Pressure)}$$

In order to minimize the occurrence of RAO, Pancholy introduced the "patent" non-occlusive hemostasis technique, designed to address the pressure side of the RAO equation[8]. With this technique, a Hemostasis band is placed and a pulse oximeter is attached to the ipsilateral thumb. Then, while the sheath is being removed, the balloon is fully inflated with approximately 15-18 cc of air to completely occlude the radial artery. Subsequently, the device is slowly deflated while occlusive manual pressure is applied to the ulnar artery located at the Guyon's canal, lateral to the pisiform bone. Patent hemostasis is achieved when oximetry becomes positive and a plethysmographic waveform can be visualized. This technique assures the presence of antegrade flow in the radial artery during hemostasis. Later in recovery, small amounts of air can be periodically released, until the device is completely deflated and then removed. Using this technique, late occlusion rates can be reduced to approximately less than 5%.[8]

THE CLINICAL NEED

However, despite Pancholy's technique, meticulous patent hemostasis with careful ascertainment of adequacy of the antegrade radial flow to the hand is performed in less than

50% of cases and about a third of transradial operators are unaware of the RAO rates in their own practices.[9] Even when those methods[10], which are recognized as being labor intensive, result in an appropriate pressure being applied, hemostasis bands are typically left in place for 4 hours or more in patients having undergone PCI, due to the effects of anticoagulation and the risk therein of hematoma at the access site. Because this method is labor intensive, many busy PCI programs forego this methodology in favor of alternatives, using palpable pulse methods or arbitrary inflation formulas in an attempt to achieve patent flow. In addition, the management of the band often requires actions of nursing personnel at locations outside the catheterization lab, resulting in an increased risk for complications from diminished expertise of those personnel as compared to the cath lab staff. And, even when all goes well, the impact on patient throughput and productivity when up to 4 hours of post procedure monitoring is required solely due to hemostasis band management is significant, resulting in delayed or postponed procedures, delayed discharges, additional staff expense, and other care related costs.

One method to attack these deficiencies in current program practice is to attack the time component of the hemostasis equation. In doing so, it is hypothesized that if radial artery compression time can be shortened to 40 minutes or less, the following could result: improved catheterization lab efficiency, greater patient satisfaction and lower complication rates, including RAO, may be improved. As concerns improved cath lab efficiency, a system that standardizes compression technique and shortens compression time to that which is fully under the supervision and care of cath lab holding room personnel, will also eliminate the variability of recovery staff needing to manage the hemostasis band / site, and complications typically associated with patient management being carried out in multiple settings within the hospital. To summarize, the potential advantages of a hemostasis system for PCI incorporating the benefits of the StatSeal technology used in combination with a hemostasis band as compared to a hemostasis band alone may include:

- Decreased radial artery compression times, aka Band In Place (BIP) time.
- Decreased incidence of RAO complications at discharge, or 24 hours, whichever occurs first
- Decreased incidence of other complications associated with TRA, such as hematoma, bleeding, and oozing.
- Elimination or reduction in the need for additional equipment, such as Doppler units, plethysmographs and pulse oximeters to assess hemostasis band efficacy
- Facilitate arterial site management to the more specialized catheterization lab staff/personnel that are better trained to recognize complications that occur during (BIP) band in place time.
- Decreasing the workload to the staff by virtue of shortened band in place times and improve procedural throughput.
- Facilitate greater patient comfort resulting from decrease band in place time and faster wound healing.

To do so, the effects of anticoagulation used during a PCI must be taken in to account.

II. DESCRIPTION OF THE STUDY DEVICE:

Recently, a new compound – potassium ferrate, in combination with a hydrophylic polymer which is formed in to a disc when compressed - has been used in conjunction with hemostasis bands to shorten compression times. This product (trade name StatSeal Advanced) is an FDA

approved product comprised of a topical hydrophilic polymer and potassium ferrate disc, [Photo 1] formed by compression of the compound.

Photo 1: StatSeal Advanced Disc

When in the direct contact with even a small amount of blood, the compound forms an occlusive seal through simultaneous iron-mediated agglomeration of blood solids/proteins and rapid dehydration of the blood. Seal formation is independent of the clotting cascade, facilitating sealing regardless of anticoagulation / antiplatelet status of the patient. Following cessation of pressure being applied to the site, the remnants of StatSeal form what resemble a 'scab', and remains in place for 24 hours, covered with a band-aid or Tegaderm patch.

In clinical testing using a protocol refined at the University of Miami Miller School of Medicine, the use of this compound in conjunction with commercially available hemostasis bands has demonstrated the potential to significantly shorten the time required to achieve hemostasis [11,12]. Further, these results demonstrated the ability to achieve hemostasis using StatSeal with similar, or fewer complications when compared to standard methods, and did so regardless of the patient's anticoagulation status.

INDICATION FOR USE

StatSeal Advanced is a commercially available product in the United States, and is indicated for use on patients in whom the radial artery has been used to gain vascular access for a cardiovascular procedure.

DEVICE STORAGE AND ACCOUNTABILITY

StatSeal Advanced is provided in a sterile, foil pouch to protect it from humidity / moisture. As with most medical products, it should be stored in a cool, dry, secure environment. StatSeal Advance will be provided at no charge by the manufacturer for use in the study.

Damaged devices will be returned to the manufacturer (Biolife, LLC, Sarasota,FL). All unused devices may be retained by the site for continued use, if they so choose.

III. STUDY OBJECTIVE(S)

The primary objectives of this study are to **e**valuate the performance of StatSeal Advanced used in conjunction with the TR Band (SSA) as compared to the TR Band without SSA (TRB) relative to:

1. the incidence of peri-procedural radial artery occlusion (RAO) at discharge or 24 hours, whichever occurs first, and;
2. the Time to Hemostasis (TTH)

HMS is defined as the Hemostasis Management System employed based on which group the patient is randomized to (either SSA or TRB)**.**

Radial Artery Occlusion is defined as the absence of flow to the hand based upon plethysmography – pulse oximetry (Pleth-Ox) performed using the Barbeau scale.

Time to Hemostasis (TTH) is defined as the time period required to achieve hemostasis, more specifically the time during which the subject is wearing the HMS system and the system is active, e.g. applying compressive force to the access site. For clarity, the time period that a HMS is left on the wrist while totally deflated is not considered as part of the TTH time.

IV. STUDY DESIGN AND METHODOLOGY

STUDY DESIGN

This study is a physician initiated, prospective, observational, two arm, randomized study to be performed at up to four experienced 'Radial First' centers. A minimum of 120 patients having undergone successful radial catheterization will be enrolled in the study, 60 in each arm. Enrollment with continue at each site on discretion of the investigators until each center enrolls a minimum of 30 patients, or a maximum of 180 patients are enrolled. Clinicians will perform the catheterization in accordance with local standard practice, with a minimum of 5,000 units of unfractionated heparin for anticoagulation.

STUDY METHODS;

Patient Selection CriteriaStudy subjects will be identified in the catheterization laboratory holding area and asked to sign the informed consent prior to their catheterization procedure before the administration of sedative agents.

Inclusion Criteria:

- Patient undergoing diagnostic angiography or PCI via the radial artery
- Patients with a Barbeau test prior to the procedure showing pattern A,B,or C.

Exclusion Criteria:

Candidates for this study will be excluded if any **one** of the following criteria is true.

- Use of a radial sheath larger than 6 Fr (a 7Fr-in-6 Glidesheath Slender ® is allowed).
- Use of an anticoagulant other than unfractionated heparin or bivalirudin.

- Any anticipated need for continued anticoagulation post-catheterization. Glycoprotein inhibitors are acceptable.
- Any active treatment with oral anticoagulants continued during course of procedure.
- Presence of arteriovenous dialysis fistula in the ipsilateral arm.
- Any physical deformity or trauma / injury of either wrist that would prevent proper placement or function of the hemostasis band.
- Raynaud's syndrome or known peripheral vascular disease of the forearm.
- Mental incompetence or inability to follow the instructions to complete the study.
- History or presence of Radial Artery Occlusion.
- Barbeau test showing Pattern D.
- Patients undergoing catheterization from the femoral or ulnar artery approach.
- Cardiogenic shock or any clinical instability as assessed by the physician performing the procedure.

Transradial Catheterization Procedure

Transradial Cardiac Catheterization will be performed according to local practice standards with use of a sheath diameter of up to 6 Fr. (A 7Fr-in-6 Glidesheath Slender®, with an outer diameter of 6Fr is defined as a 6F sheath and is allowed.) In accordance with current recommendations for minimizing radial artery occlusion, a minimum of 5,000 units of unfractionated heparin, or therapeutic bolus of bivalirudin, will be administered to all patients enrolled in the study.

Patients will have their activated clotting time measured at least 5 minutes following the initial dose of anticoagulant, although every patient receiving 5,000 units of heparin will be eligible for the study. Vasodilators (nitroglycerin, verapamil) will be administered in accordance with local practice.

Timing of Subject Enrollment

A subject will be consented into the study prior to the administration of sedation prior to the procedure, and randomized at the conclusion of a successful procedure (after all anticoagulation and antiplatelet medication decisions have been made), at which time placement of the assigned HMS device will occur. Eligibility for the study will be assessed at this time and the subject will have to meet all of the inclusion criteria and none of the exclusion criteria.

Randomization will be performed by means of sealed envelopes in randomization blocks of 30. Each envelope will be labeled by patient number containing device designation. Device designation in the envelopes will be random in occurrence. When a patient is officially enrolled (after successful completion of a TRA procedure), the envelope corresponding to that patient number in the Study Patient log will be pulled, opened, and the assignment revealed.

Each of 4 sites will be allotted an initial block of 30 envelopes, and sets of backup blocks of 30 envelopes. On the discretion of the site principal investigator and the lead principal investigator, enrollment may continue until each site enrolls 30 patients. The maximum enrollment at any one site shall not exceed 50% of the total study enrollment, or 90 patients.

End of Study Status / Effect of Withdrawals:

A subject will have completed the study when one of the following events is documented:

1. The patient is successfully enrolled, treated with a HMS, and completes all required follow up tests.
2. A subject withdraws consent to participate. Patients who withdraw from the study will be replaced and excluded from data analysis.

Protocol:

Control patients: Patients will have a TR band applied over the arteriotomy site and inflated with 15-18ml of air. After aspirating and clearing the contents of the sheath, the radial sheath will be removed. The TR band will be deflated until bleeding occurs, and 2 ml of air will be reintroduced to provide hemostasis. Patent hemostasis will be documented with plethysmography and oximetry as decribed below within 5 minutes after band application and removal, and within 30 min of discharge or after 24 hours. The TR band will be left inflated and in place for 2 hours following the procedure for all patients (regardless of diagnostic or PCI procedure), after which deflation attempts will commence.

Statseal Protocol: Patients will have a Statseal Advance (SSA) disc applied after withdrawing the radial sheath 2-4 cm. A Tegaderm dressing will be applied to secure the disc position. The TR band will be applied over the SSA disc with the center of the balloon (the green dot) over the center of the SSA disc. The TR band will be inflated with 8cc of air (which is typically occlusive pressure), and the sheath removed. No deflation will occur immediately. After 20 minutes of pressure, 3 cc of air will be removed from the TR band. After an additional 20 minutes (40 minutes after procedure), the TR band will be completely deflated, and the TR band left in place. After an additional 20 minutes (60 minutes after procedure) the TR band will be removed.

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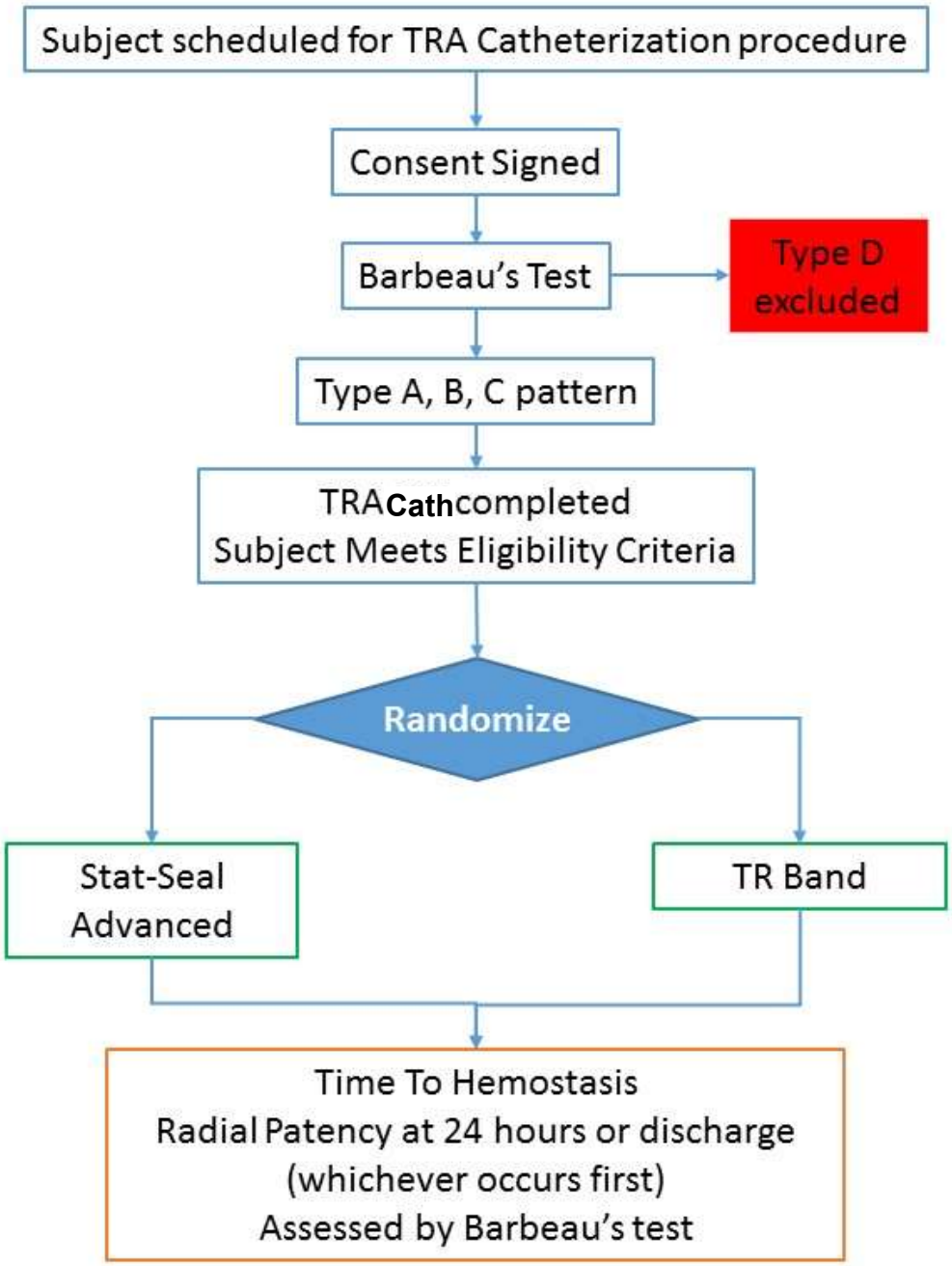
STUDY OVERVIEW GRAPHIC



V. STUDY ACTIVITIES & GUIDELINES

Inspection Prior to Use

Prior to initiating any study activities, inspect the HMS devices for any damage. Do not use any device that appears compromised or damaged.

Required Accessories for each experiment

- Hemostasis Band (TR Band, Terumo, Inc.)
- StatSeal Advanced disc (if randomized to test group)
- Pulse oximeter

ACTIVITIES AND ASSESSMENTS

Informed Consent:
Subjects must have read the contents of the written informed consent document, had all questions regarding the study adequately answered by study staff, and signed and dated the document prior to any study related activities. See Appendix 1 for a sample of the Informed Consent document.

Definitions of Baseline and Procedural Variables:

Smoking: Active smoking or >20 pack year tobacco history.

Diabetes: Hgb A1C >6.5% or active medical treatment for diabetes.

Hypercholesterolemia: LDL >130 or on treatment with antilipemic agents.

Hypertension: >140/80 or on medical treatment for hypertension.

Diagnostic procedure: Involving diagnostic catheters only.

Interventional procedure: Involving an interventional wire and therapeutic ACT typically >200, including for fractional flow reserve measurement where a stent is not placed.

Single wall puncture: Use of micropuncture wire and anterior wall puncture only.

Double wall puncture: Use of double wall puncture and sheath withdrawal technique.

Number of forward attempts: Number of forward advancements of the needle required to obtain access (not number of separate punctures of skin).

Procedure Start Time: Time when lidocaine is administered, prior to first puncture attempt.

Procedure End Time: Time when sheath is removed.

Test methodology:

All Pleth-ox testing will be done by qualified personnel with results classified according to Barbeau test pattern classifications. *[Barbeau, et al. Evaluation of ulnopalmar arterial arches with pulse oximetry and plethysmography; comparison with the Allen's test in 1010 patients. Am Heart Journal; 2004; 147:489-493]*

At the start of the TRA procedure, prior to radial artery cannulation, a baseline Pleth-ox exam will be performed for all patients and recorded on the CRF. Ulnar compression will be applied to confirm that the radial artery is patent. Patients with a type D pattern exam will be excluded from the study.

At the conclusion of a successful transradial procedure, the patient will be randomized to either SSA or TRB, each device applied per protocol & IFU.

Following placement of the HMS system, Pleth-Ox exams will be performed at the following time points with results recorded in the CRFs.

- Within 5 minutes of initial HMS placement
- In the SSA (StatSeal Advanced) group, within 5 minutes of the first partial deflation (20 minutes after initial placement).
- Within 5 minutes of full deflation of the HMS in both groups
- Within 30' of discharge or 24 hours post procedure (± 1 hour), whichever occurs first.

VI. STUDY STATISTICAL PLAN:

This is a physician initiated, prospective, randomized, two-arm study, to be conducted at up to four experienced 'Radial First' centers with the principal investigator having a (minimum) ten case experience using StatSeal Advanced.

The sample size of 120 patients is estimated to have 90% power to detect an average difference in time to removal of the TR band of 60 minutes between the SSA and TRB groups, using a relatively large standard deviation of 100 minutes and a two-sided alpha of 0.05.

Descriptive summary statistics will be presented for all study variables. Continuous variables will be displayed as means with standard deviations and medians with 75^{th} and 25^{th} percentiles. Categorical variables will be summarized as frequencies with their respective percentages with two-sided 95% exact confidence intervals of the percentages. Statistical comparisons for continuous variables will be performed using the Student's t test or Mann-Whitney U test, as appropriate. Comparisons for categorical variables will be performed using the Chi square test or Fisher exact test, as appropriate. A two-sided P value of 0.05 will be considered statistically significant.

Categorical variables will include, but are not limited to:

- Percent of patients in each arm with total TTH of 60 minutes or less.
- Percent of patients in each arm with TTH of 40 minutes or less without complication.
- The percentage of patients in each arm with bleeding, oozing or hematoma during TTH, further delineated by the EASY bleeding and hematoma classification attached.
- Percent of patients in each arm with RAO at each /all follow-up points.
- Percent of patients in each arm with radial patency as tested with Pleth-ox at each designated test time point.

<u>Primary Efficacy Outcomes:</u>
In each arm the:

- Total Time to Hemostasis (TTH), defined as the total time the HMS applies compressive force until successful hemostasis is achieved without complication.

<u>Secondary Efficacy Outcomes:</u>
In each arm the:

- Percent of patients free from radial artery occlusion at discharge or at 24 hours, whichever occurs first.
- Percent of patients with Barbeau test patterns A,B,C,D at initial application of the HMS
- Percent of SSA patients with Barbeau test patterns A,B,C,D after 20' of HMS time.
- Percent of patients with Barbeau test patterns A,B,C,D at full deflation of the HMS. (40' for SSA group; per protocol in the TRB group)
- Percent of patients with Barbeau test patterns A,B,C,D at discharge or at 24 hours, whichever occurs first.
- Percent of patients in whom successful hemostasis is achieved in one hour or less.

<u>Primary Safety Outcome:</u>
Any adverse event / complication at the vascular access site (e.g. Class III, IV, or V Hematoma,

other bleeding) at any time pre-discharge / at 24 hours other than RAO (as defined in the protocol).

Secondary Safety outcomes:
Any minor adverse event / complication (e.g. class I or II Hematoma) at the the vascular access site any time pre-discharge / at 24 hours other than RAO (as defined in the protocol).

Any complication (e.g. those typically associated with a PCI procedure) other than at the vascular access site at any time pre-discharge / at 24 hours other than RAO (as defined in the protocol).

VII. ADVERSE EVENTS:

Reports of all adverse events will be made and recorded for the duration of the study, and categorized as specific to those complications associated with radial access, such as hematoma, bleeding, RAO, and other vascular access complications, or those more typically associated with PCI, such as Major Adverse Cardiovascular Events (MACE).

Adverse events will be recorded on CRFs and adjudicated by the site Principal Investigator as to their severity and whether or not directly, indirectly, or not connected to the study HMS devices, and forwarded to the Data Center for entry in to the database.

DEFINITIONS:
Adverse Event
Any clinically relevant event that occurs during the performance of the study that puts the Subject at additional risk of injury, whether foreseen or not, and requires additional care beyond that expected as a result of the study.

Adverse Device Event
An adverse event related to the use of the device. This includes adverse events resulting from insufficient or inadequate instructions for use, deployment, or operation, or any malfunction of the device. This definition also includes any event resulting from user error or from intentional misuse of the device by the investigator.

Serious Adverse Event
A serious adverse event (SAE) is defined as an adverse event that:

- Led to death,
- Led to a serious deterioration in health that either,
    - Resulted in a life-threatening illness or injury, or
    - Resulted in a permanent impairment of a body structure or a body function, or
    - Required in-patient hospitalization, or
    - Resulted in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.

Note: This includes device deficiencies that might have led to a serious adverse event if (a) suitable action had not been taken or (b) intervention had not been made or (c) if circumstances had been less fortunate.

VIII. DATA MANAGEMENT

Data Collection Process

Data will be collected in an anonymous form using case report forms for each subject. CRFs will be transmitted to the data center for entry in to the database. Data may be collected by clinical research personnel assigned to the study, under the supervision of the investigator.

Data Confidentiality

Subject data will be collected in an anonymous form. Each site will keep a confidential, site – only log of enrolled patients connecting their identity to a coded subject identifier. Each subject will be entered on the log along with procedure date and will be assigned a patient study number comprised of the site number and sequential subject number enrolled. This coded number will be used in the CRFs. For example, John Q Doe, the 12th patient enrolled at site number 2, will be assigned study identifier 002-012. All activities will be performed in compliance with HIPPAA and Good Clinical Practice standards

Data Center

CRFs or coded anonymized data will be forwarded to the Data Center at the Long Beach VA Medical Center, checked for completeness, and entered in the Database as received. Incomplete forms will be returned to the study site for completion. Electronic submission of Data may be employed, but is not required.

See the "Study Statistical Plan" for a description of the plan.

IX. ETHICAL, REGULATORY & ADMINISTRATIVE REQUIREMENTS

The devices being studied in this clinical plan, and the tests performed under it, are approved for marketing by the US-FDA for use as described and have been in use for TRA procedures at the participating institutions. FDA approval of the study is not required. No part of the study uses any device or test that is considered investigational.

Investigational Review Board Approvals.

Data from this study may be used for publication in the scientific literature, and therefor IRB approval is required. No patient may be enrolled until IRB approval is granted, and an Informed Consent approved by the IRB is signed by the subject.

Protocol Adherence and Amendments

Investigators will be required to adhere to the protocol requirements. Deviations or violations of the protocol may result in dismissal from the study.

Informed Consent

Each subject in the study must sign the informed consent agreeing to participation.

Alternatives to Participation

As a voluntary randomized study, the patient's alternative to participation is primarily to the local standard of care, typically involving the TR band, used per local protocol (typically 1-3 hours of application). SSA devices may be used outside of the study depending on local practice and availability.

Study Activities
The Investigator is required to perform the study in accordance with the protocol and to use the HMS per the instructions for use.

Follow-Up
There is no requirement for the subjects taking part in the study to be seen or examined for any follow up relative to the study following completion of activities described herein.

CRFs
CRFs will be completed for each subject. See Appendix 1 for the CRFs.

Records and Retention
Copies of all records will be retained by the investigator at each site for 2 years.

(Model) Patient Informed Consent
See Appendix 2 for a model of the informed consent.

Communication with the Principal Investigator:
All communication regarding the study should be routed directly to the Principal Investigator. Copies of all correspondence regarding the study should be maintained in the Site Investigator study file.

Declaration of Helsinki & HIPPAA
The Principal Investigator will ensure that this study is performed in conformity with the Declaration of Helsinki, HIPPAA, and all local and national regulations.

Investigator Responsibilities

- Sign and adhere to the Investigator Agreement
- Sign and adhere to all of the required elements of the Clinical Protocol
- Resolve queries in a timely manner
- Participate in Investigator meetings, if scheduled
- Comply with the Declaration of Helsinki
- Obtain written Informed Consent from each study participant before any study specific procedures are performed
- Complete all required case report forms (CRFs) for each subject
- Comply with all applicable regulations and codes of approvals from the site IRB and other Regulatory Authorities
- Notify the Principal Investigator of personnel changes that may affect the study protocol
- Retain all records and study files as required, after which the files may be destroyed.
- Allow direct access to source data/documents, including patient records, in case of monitoring, auditing and/or inspection by the IRB and/or other regulatory authority bodies.

X. RISK BENEFIT ANALYSIS

General Risks and Presumed Benefits:
Application of a HMS in a setting absent an actual radial arteriotomy presents negligible risk to the subject. The only foreseen risk would be leaving an inflated band in place for an extended period of time. This risk is negligible provided the protocol is followed. An action of this nature would be considered a protocol violation.

Patients assigned to the SSA group may enjoy less discomfort from the shorter length of time that the HMS is in place. Patient in the TRB group should experience no difference in benefit than those having been treated with a traditional HMS prior to the study.

The potential benefit of subject participation is gratification from making a contribution to science helping to demonstrate the effectiveness of a new clinical method to achieve hemostasis following a radial artery procedure. This new method could potentially provide a safer, more efficient, and more effective HMS for clinicians to use in treating patients undergoing the radial approach for cardiovascular procedures.

Risks related to Hemostasis Bands:
Currently marketed hemostasis bands have been associated with complications such as, but not limited to, skin irritation, radial artery occlusion, hematoma, pseudoaneurysm, failure to achieve hemostasis, and general wrist discomfort.

Risks Specific to the Study Device:
There are no known risks specific to the study device.

Risk Mitigation:
Every effort will be made to mitigate risks in this Study. Those efforts include requiring investigators to be highly experienced Radialists, practicing at Radial First centers, and have used the study device in a minimum of ten cases.

Clinical monitoring will occur in real time to ensure the accurate collection and reporting of data, and ensure that the Site is in compliance with the clinical protocol requirements that mitigate risk such as patient entry criteria, use of the study device in accordance with instructions, and compliance with study test procedures and methods.

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APPENDICES:

Appendix 1: Sample Informed Consent

Appendix 2: CRF's