Physician-Sponsored IDE for the Talent Endoluminal Stent Graft System for the Treatment of Thoracic Lesions

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1. Report of Prior Investigations

1.1 Introduction

A vascular aneurysm is a permanent, localized dilatation of a blood vessel at least 1 1/2 to 2 times the normal vessel diameter. The aorta is the most frequent site for aneurysms, with approximately 10% of aortic aneurysms located above the renal arteries in the thoracic segment. (Coselli and LeMaire, 1995.) Thoracic aortic aneurysms (TAAs) are less common than abdominal aortic aneurysms, however, detection of TAAs is increasing, perhaps due to an aging population, increased diagnostic capability or an increase in prevalence. (Mitchell, Miller and Dake, 1997.) Ascending and transverse arch aneurysms each comprise 25% of TAAs; the remaining 50% occur in the descending thoracic aorta. The most common cause of TAA is medial degenerative disease of the aortic wall, responsible for most ascending aortic aneurysms and most fusiform aneurysms involving the descending aorta. Arteriosclerosis, commonly found superimposed on aneurysmal disease of other etiologies, frequently results in saccular aneurysms. Additional causes of TAA are dissection, aortitis, trauma, and infection. (Coselli and LeMaire, 1995.) In cases of aortic dissection, which typically involves the descending thoracic aorta, the origin of the dissection is in the proximal descending aorta in about 25% of the cases. Traumatic TAA is typically caused by blunt chest trauma that produces partial aortic disruption. (Coselli, Buket and Crawford, 1996.)

Untreated thoracic aneurysms can be life-threatening. As many as 78% of untreated patients with TAA die within 5 years after diagnosis, most often from

rupture of the aneurysm. (Pressler and McNamara, 1980.) Conventional surgical treatment, either tube graft replacement or patch aortoplasty, is a high-risk surgical procedure. Repair of the descending thoracic aorta is performed with a thoracotomy and cross-clamping of the aorta, with or without a shunt by-pass to maintain distal perfusion. Cardiopulmonary bypass is used to control rising blood pressure. (Najafi, 1994.) Mortality associated with surgical repair of the thoracic aorta ranges from 12% to more than 50%, depending on the urgency of the procedure, coexisting debilitating diseases or conditions, and the patient's general health. (Moreno-Cabral, Miller, Mitchell, et al, 1984.)

As an alternative to conventional surgery, a less invasive endovascular procedure has been developed that may be used to treat certain aneurysms. A collapsed stent-graft, a metal stent coupled with a fabric graft, is introduced into the vasculature, advanced to the site of the aneurysm, and deployed to span the aneurysm. The device creates a new aortic lumen, excluding the aneurysm sac from blood flow while maintaining flow within the stent-graft, this less invasive technique is designed to prevent or decrease the need for open surgery, to reduce the need for blood transfusions, to decrease the use of anesthetics and other drugs, and to speed recovery time. A reduction in intensive care and total hospital stay should result, leading to an increased quality of life following the procedure and a reduction in cost.

Experience in the endovascular treatment of thoracic aneurysms is limited. Miller, et al, have published results from a series of 108 patients with descending.

TAA treated with a (homemade) endoluminal stent-graft. (Mitchell, Miller and Dake, 1997; Dake, Miller, Semba al, 1994; Skeens and Dake, 1997.) Atherosclerotic,

anastomotic, and post-traumatic true or false aneurysms and aortic dissections were treated. Complete aneurysm thrombosis and technical success was achieved in 103 of the 108 patients. There were 10 deaths (9.25%) patients experienced perioperative strokes, and there were 4 cases of paraplegia. During an average follow-up of21.8 months (range 1 to 57 months), there were 2 documented cases of stent-graft failure and 5 late deaths (more than 30 days post operative). (Skeens and Dake, 1997.)

More recently, Nienaber et al prospectively evaluated the safety and efficacy of elective transluminal endovascular stent-graft implantation in twelve (12) consecutive patients with descending (Type B) aortic dissection and compared the results with conventional surgical repair in twelve (12) matched surgical control patients (Nienaber, 1999). Stent-graft treatment resulted in no morbidity or mortality, whereas surgery for Type B dissection was associated with four deaths (33%, $p = 0.09$) and five serious adverse events (42%, $p = 0.04$) within twelve (12) months. Stent-graft implantation was successful in all patients, with no endoleaks. There were no deaths or instances of paraplegia, stroke, embolization, side branch occlusion, or infection in the stent-graft group; nine patients had postimplantation syndrome, with transient elevation of C-reactive protein levels and body temperature as well as mild leukocytosis. All patients who received stent grafts recovered, as did seven (7) patients who underwent surgery for Type B dissection (58%, $p = 0.04$). The authors conclude that these preliminary results suggest that elective, non-surgical implantation of a stent-graft is safe and effective in selected patients who have thoracic aortic dissection and for whom surgery is indicated. Compared to standard surgical repair, this study supports the clinical utility of the stent-graft for the treatment of thoracic aortic dissection. The first-generation Medtronic/Talent stent-graft has been investigated in a US DE Phase I pilot study involving 20 high-risk surgical candidates. The clinical study

described in this protocol is a study involving the second-generation Medtronic/Talent system. Compared to the first-generation stent-graft, the Medtronic/Talent endoluminal spring stent-graft system also features an enhanced delivery system, which is designed to facilitate insertion and negotiation through tortuous and calcified vasculature. The first and second-generation devices are identical in every way except for the differences in graft material thickness and the presence of the system's new delivery system. The delivery system features a flexible tapered tip as well. as a flexible stainless-steel coil at the delivery-system catheter's tip, both of which facilitate negotiation through tortuous vessels and reduce the potential for device kinking.

Since 1998, Harbor UCLA has treated 31 thoracic aortic lesions with the Medtronic Aneurx device, all of which have been part of commercial manufacturer DEs. A published review of 26 of these patients who were siY1ificant risks for surgical repair and who were implanted with the Aneurx thoracic stent-graft showed that 25 were treated successfully with no surgical conversions. Moreover, there was an overall decreased incidence of morbidity and mortality. (White, et al, 2001.)

An additional 14 subjects were treated with the Medtronic/Talent thoracic device and 1 Gore device between June 1998 and January 2002, either on a compassionate or emergency basis. In our experience, the Talent device has been particularly useful for patients with descending aortic aneurysms and dissections with the only limitation being adequate access for the 22 to 27 French delivery catheters.

1.2 Device Description

This study will utilize the most advanced generation Medtronic/Talent system including the enhanced delivery system. The information needed for the use of this device is available in Medtronic's DE G980116. (Please refer to the letter from Medtronic Inc. dated December 19, 2001 (Attachment A) granting the investigator permission to reference the IDE number.) The use of this device in this study will be for the same aneurysm morphology as described in the reference.

2. Investigational Plan

2.1 Purpose

2.1.1 Name and Intended Use of the Device

The Medtronic/Talent Stent-Graft System is a flexible, implantable vascular stent graft endoluminal device preloaded in a delivery system that is used to exclude

thoracic aortic lesions (thoracic aneurysms, thoracic dissections, penetrating ulcers, traumatic transections and both traumatic and degenerative pseudoaneurysms).

The devices and intended use are described in IDE # G980116.

2.1.2 Objectives of the Investigation

Both high risk and low risk patients with thoracic aortic lesions will be enrolled and treated. This includes patients with true thoracic aortic aneurysms (i.e., all layers of the vessel are affected; generally, of atherosclerotic origins, thoracic dissections, penetrating ulcers, traumatic transections and traumatic and degenerative pseudoaneurysms).

The primary objective of this investigational plan is to determine the safety of the Medtronic/Talent device when used to exclude thoracic lesions: true descending thoracic aortic aneurysms, dissections, penetrating ulcers, traumatic transections and traumatic and degenerative pseudoaneurysms from blood flow in high risk and low risk patients who are candidates for endoluminal repair.

2.1.3 Duration of the Investigation

Accrual of study subjects will occur over approximately 3 years with all 50 subjects to be followed according to the Lifeline Registry of Endovascular Repair protocol for the life of the patient (Please see Attach C for the protocol).

2.2 Protocol

This study-will be conducted with high risk and low risk patients who are considered suitable candidates for endoluminal repair of descending thoracic aortic lesions

including those with true aneurysms, aortic dissections, penetrating aortic ulcers, traumatic transections and pseudoaneurysms (both traumatic and degenerative). Adult male and female patients who fulfill the inclusion/exclusion criteria listed below, are eligible for enrollment.

2.2.1 Inclusion Criteria

Subjects who participate in this study as study patients must fulfill the following criteria:

- Subject is ≥18 years of age.

- Subject is not pregnant or lactating. Females of child-bearing potential must practice a reliable method of contraception.

- Subject is diagnosed with one of the following conditions of the descending thoracic aorta. All conditions must be verified by diagnostic imaging [ultrasonography, computed tomography (CT), magnetic resonance (MRI) or angiography].

  - a true (i.e., atherosclerotic) supraceliac aneurysm (fusif0Km or saccular type) with or without a CO-existing aortic dissection or penetrating aortic ulcer,

    - aortic dissection of DeBakey Type I or (Stanford A, proximal) in the absence of an aneurysm; or

  - penetrating aortic ulcer in the absence of an aneurysm; or

  - traumatic transection; or

  - pseudoaneurysm — traumatic or degenerative (i.e., one that does not involve all layers of the vessel and is not atherosclerotic in origin.

- Subject's anatomy is suitable for placement of the Medtronic/Talent Stent-Graff, with a distinct proximal aneurysm neck of 10 mm or more in length and a distal aneurysm neck of at least 10 mm.

- Subject has a TAA that is dilated to $\geq$ 5 cm in diameter, $\geq$1.5 times the diameter of the adjacent native/non-aneurysmal aorta or is symptomatic.

- Subject has a proximal and distal aortic neck diameter $\geq$18 mm and $\leq$ 42 mm.
- Subject has an arterial access site, either peripherally or via infrarenal abdominal aorta that is adequate for introduction of the stent-graft delivery system..

- Subject is competent to give informed consent.
- Subject will be available for the periodic follow-up (surveillance) after the procedure.

2.2.2 Exclusion Criteria

Subjects who would participate as study subjects and who fulfill any of the following criteria may not participate in this study:

- Subject has TAA with less than 10 mm proximal fixation length.
- Subject has an aneurysm that would require exclusion by the stent graft of the segment of the aorta that gives rise to dominant spinal cord/intercostal arteries.
- Subject has a lesion that prevents delivery or expansion of the device.
- Subject has systemic infection or is suspected of having systemic infection.
- Subject has a known mycotic aneurysm.

- Subject is not available or is not willing to come back for periodic follow-up (surveillance) after the procedure.

2.2.3 Withdrawal and Lost-to-Follow-up

Patients may be withdrawn from the study for a number of reasons. The following is a summary of the possible reasons for withdrawal.

Subjects may voluntarily withdraw from the study. The reason for withdrawal must be documented on the Termination CRF (Attachment E).

After the implant procedure, some subjects may not return for follow-up visits. A minimum of three (3) attempts to contact such patients must be made. All attempts are to be documented on the Termination CRF.

Subsequent to enrollment, if new information demonstrates that a patient does not meet the inclusion/exclusion requirements, the patient must be withdrawn from the study. The reasons for withdrawal must be documented on the Termination CRF. If such information is not discovered until after the implant procedure, the patient will still be followed for safety reasons but will not be included in the final analysis.

In some cases, an implant procedure will be initiated (i.e., an attempt to pass or deploy the device) but is aborted prior to device deployment. Such patients maintain their enrollment status (since this is an intent-to-treat study) but need not

be followed. On the other hand, if a patient is initially screened and enrolled, but no procedure is ever initiated, the patient is cancelled and his/her enrollment position is made available to another patient.

Patients who are enrolled in the study group and are converted to surgery due to peri- or post-implantation complications will be followed for a minimum of 12 months after enrollment. Conversion to surgery is documented on the Procedure CRF.

2.2.4 Study Design

This study is a prospective evaluation of patients receiving the investigational device to determine the proportion in whom successful implantation is achieved, as indicated by aneurysm exclusion and graft patency at implant, time of discharge, and 1-, 6-, and 12-months following implantation, and to determine the proportion of patients who experience adverse events during and after the implantation procedure, including comorbidities and overall mortality rates. The percentage of patients in whom technical and clinical success is achieved, and the percentage who experience serious adverse effects will be determined. Additional endpoints that will be evaluated are length of stay in intensive care following the procedure, total length of hospital stay and recovery time.

Patient data and follow-up information and images will be stored with the Lifeline Registry for Aneurysm Repair with periodic reports to the FDA up to the 5-yearfollow-up supplemented with reports from the Registry database.

2.2.5 Study Procedures

2.2.5.1 Subject Screening and Evaluation

Prospective subjects will be evaluated for enrollment in the study at the time they are considered to be candidates for repair of thoracic aortic lesions. Initial screening will include all diagnostic imaging tests performed as part of the patient's routine medical care. Spiral CT scan with possible angiogram is the minimum diagnostic imaging required to determine suitability for Medtronic/Ta1ent stent-gaff implantation. Prospective subjects who meet the inclusion/exclusion criteria specified in Sections 2.2.1 and 2.2.2 will be invited to participate in the study and give written informed consent. The patient will be given two consents: one for the implantation of the device and the other one for enrollment in the Endovascular Lifeline Prosthesis Registry.

2.2.5.2 Pre-Procedure Evaluation

Subjects who have elected to undergo implantation of the Medtronic/Ta1ent stent gaff will undergo pre-procedure evaluation. Proper sizing and selection of the device will be based on the measurements recorded on the TAA Vessel Measurement CRF. As noted previously, information that is required for subjects in the study group include spiral CT scan results, angiogram results, dimensions of the aneurysm and aorta, the type, morphology, and clinicopathology of the aneurysm, and pre-existing risk

factors (Appendix E, Case Report Forms), as well as results of hematology, serum chemistry, and urinalysis laboratory testing, and current medications.

The following must be performed prior to implantation:

- physical examination, including femoral pulses, brachial and ankle blood pressure, and assessment of neurological functions; (Note that if any neurological deficit is observed, it must be documented and characterized on the Pre-operative Medical History CRF.)

- medical history, including concomitant medications, and demographic information.

- clinical laboratory tests:

    - hematology [CBC, platelet count, hematocrit, hemoglobin]
    - coagulation studies [prothrombin time, partial thromboplastin time, or activated partial thromboplastin time]
    - serum chemistry [sodium, potassium, chloride, bicarbonate, calcium, phosphorus, creatinine, glucose, total bilirubin, albumin, total protein, alkaline phosphatase, aspartate aminotransferase, serum glutamic pyruvic transaminase, lactic dehydrogenase, total cholesterol, triglycerides, blood urea nitrogen, uric acid].

- urinalysis

- spiral CT (recommend a minimum of3mm slices, to adequately assess vessel dimensions)
    - angiography (with graduated marker catheter to measure/assess lengths and access vessel dimensions).

The results of all imaging studies will be verified according to mechanisms described in the Lifeline Registry for Endovascular Aneurysm Repair protocol.

2.2.5.3 Sizing and Selection of a Medtronic/Talent Endoluminal Stent-Graft

Prior to the Medtronic/Talent stent-graft implant procedure, an angiogram, and a spiral CT scan, when appropriate, must be available to correctly measure and assess the aneurysm and vasculature.

2.2.5.3.1 Proper-sizing of stent-graft

For proper sizing of the Medtronic/Talent Endoluminal Stent-Graft, the information listed below must be measured and recorded on the TAA Worksheet CRF:

- diameter of the proximal aortic neck.
- diameter of the aneurysm.
- diameter of the distal aortic neck; landing zone.
- length of the posterior proximal aortic neck, from the proximal end of the aneurysm to the left subclavian artery, along the outer curve of the aorta.

- length of the anterior proximal neck, from the proximal end of the aneurysm to the left subclavian artery, along the inner curve of the aorta.
- aneurysm length: area of the aorta to be excluded by graft.
- length of the distal aortic neck, from the distal end of the aneurysm to the celiac trunk.
    - desired length of graft coverage.
    - access artery diameters
- sketch/tracing of aneurysm, penetrating ulcer, dissection

The condition of the arteries that will be used to access the descending aorta must also be assessed and documented to determine if access to the aneurysm can be achieved with the Medtronic/Talent Stent-Graft System. Vessel diameter, tortuosity, stenosis, plaque, etc., will affect the ease of insertion.

2.2.5.3.2 Proper selection of stent-graft design

Selection of the open web or the bare spring design at the proximal and/or distal aortic end of the stent-gaff is dependent on the length of the proximal and distal aortic aneurysm necks and proximity to the subclavian artery and celiac axis respectively. In general, the bare spring design is intended for use in cases of short proximal and/or distal aortic aneurysm necks (e.g., less than 25 mm in length). The bare spring version is designed to

allow placement of the bare spring across the left subclavian artery and the celiac axis that may be involved in the aneurysm. The open web design generally intended for use in cases of proximal and/or distal aortic aneurysm necks that are greater than or equal to 25 mm in length.

2.2.5.4 Treatment

2.2.5.4.1 Implantation Requirements

Equipment needed to perform a Medtronic/Talent endoluminal stent graft implantation includes:

- C-arm that can be angled freely, with the following:

-high resolution fluoroscopy,

-high quality angiography,

-digital subtraction angiography.

- puncture needles, Seldinger or single needles (18G or 19G)
- Angled Glidewire (180 cm 0.035" with torque device), or equivalent
- Bentson wire (180 cm 0.035"), or equivalent
- Amplatz Super Stiff wire (260 cm 0.035") or equivalent
- Pigtail catheter (100 cm 5F multi-purpose),

- Selection of Cobra 5F, Berenstein 5F, Tegtmeyer 5F or modified DAV (Cook)
- 5F Simmons 1, 5F Chuang 2.5
- Snare (nitinol goose neck, 10 —15 snare diameter)
- Non-ionic contrast (approximately 300 mg/mL)
- Angioplasty catheters (8 mm — 20 mm, depending on cases)
- Inflation device with pressure gauge
- Angio introducer sheaths 5F, 6F, 7F, 8F, etc.
- High pressure angiographic injector and extension tubing
- High pressure flush system
- Stopcocks (selection of2-way and 3-way)
- Sterile placement markers to mark skin, endovascular instruments, or monitor - screens to plan precise graft placement
- Surgical suite standby in case conventional surgical repair is necessary.

2.2.5.4.2 Anticoagulation/Antiplatelet Therapy

Patients should be heparinized during the implant procedure.

(Recommended activated clotting time is 200 - 300 seconds). An initial heparin bolus (or drip) of at least 5,000 units, followed by 1,000 units per hour bolus or drip is recommended.

2.2.5.4.3 Implantation Procedure

The following is a brief summary of the procedure. Refer to the Instructions for Use in Appendix D for further detail.

During implantation of the Medtronic/Talent Endoluminal Stent-Graft, the pre-implant angiogram and CT scan are used together with (on-the-table) intravascular ultrasound (IVUS), digital subtraction angiography (DSA), road mapping, and angiography for proper implant positioning.

The Medtronic/Talent Stent-Graft endoprosthesis is inserted by delivery catheter and introducer sheath via a surgical cutdown (e.g., external iliac artery, femoral artery, common iliac artery conduit, etc.) approach. The insertion method depends on each patient's anatomy and is determined by the Clinical Investigator. The introducer sheath and delivery catheter containing the stent-graft is inserted over a guidewire and advanced into the aorta and above the aneurysm. The introducer catheter should be rotated so that the connecting bar of the compressed stent-graft is in the best position to match with bends in the target vessel.

With the delivery catheter in the correct position, the push rod is held stationary in one hand while the outer sheath is slowly withdrawn with the other hand. After

verifying that the stent-graft is in the correct position, the introducer sheath is then withdrawn further until the stent-graft is completely deployed. The balloon maybe inflated along the full length of the implanted device to model the springs against the vessel wall and to unravel possible winkles in the graft fabric.

After deployment of the stent-graft, angiography is performed to verify implant position and to check for the presence of endoleaks. Final arteriography is then performed to determine presence of leaks. If no leaks are detected, the introducer sheath and delivery catheter system are withdrawn from the patient. The entry site is closed by surgical means.

If endoleaks are detected during the implantation procedure, the stent-graft should be re-ballooned to ensure that the device has been properly modelled against the vessel wall. Endoleaks present after remodeling should be covered with an extension cuff; all other leaks that remain after remodeling may be treated with a cuff or may be monitored postoperatively, as determined by the Clinical Investigator. If patent collateral vessels are suspected of causing leaks, the vessels may be embolized at the Clinical Investigator's discretion. Endoleaks that are successfully treated during the endovascular operative procedure are not considered a complication or adverse event. Section 2.2.6, Adverse Events, has more information on treating endoleaks.

A Procedure form (Appendix E, Case Report Forms) will be completed after implantation has been accomplished. Fluoroscopy time and the amount of contrast material used will be recorded.

2.2.5.5 Pre-discharge

Prior to hospital discharge, a pre-discharge examination will be completed for all study group patients. This will include a physical examination and laboratory testing (including hematology, serum chemistries, and urinalysis). The spiral CT may be done at any appropriate interval within four weeks after the date of implantation. Any new (or worsened) neurological deficits observed post-procedure require a neurological consult.

2.2.5.6 Post-Discharge Follow-up

After hospital discharge, patients will be seen I, 6, and 12 months 30 days) and annually for life after the implant procedure with annual reports to be submitted to the FDA based on a 5-year data. Patients may also be seen for additional follow-up visits, if clinically appropriate. Post-

Operative Assessment form (Appendix E) will be completed for each visit.

At each post-discharge examination, patient status, vasculature and aneurysm status, and device efficacy will be assessed. Any new (or worsened) neurological deficits observed post-procedure require a neurological consult. If additional follow-up visits occur, information obtained at that visit will be recorded on the Post-Operative Assessment form.

2.2.5.7 Final Assessment

Subjects who have completed 12 months of follow-up will continue annual follow-up examinations for life with annual reports submitted to the Food and Drug Administration for 5 years. These follow-up visits will include a physical examination, a CT, and a plain film x-ray as defined in the Chart of Study Procedures (Appendix F). Subjects who received a Medtronic/Talent stent-graft implant and who choose to discontinue participation in the study prior to study completion will be contacted to perform a final assessment prior to study closure. The final assessment will be recorded on Post-Operative Assessment and Termination CRFs.

A Termination Case Report Form will be completed for every subject regardless of the reason for study termination. A chart may be found in Appendix F indicating the times at which procedures and tests will be performed.

2.2.6 Adverse Events

Any adverse experiences reported by a subject in the study or noted by the Clinical Investigator/Sponsor, will be reported on the Post-Operative Assessment CRF (Appendix E). Each experience must be categorized by the Clinical Investigator/Sponsor by its degree of severity (mild - the event did not require treatment, moderate - the event was treated locally or by minimally invasive treatment, or severe - the event was fatal or resulted in permanent injury or disability), its relationship to study device and implantation procedure (not related,

associated with, caused by), and whether or not the adverse experience was unanticipated. An unanticipated adverse effect as defined by the FDA is any serious adverse effect on the health and safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem or death was not previously identified in nature, severity or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety or welfare of subjects (Section 812.3). Refer to Appendix D, Instructions for Use, and the Study Subject Informed Consent (Appendix H) for a listing of known events.

Adverse events are to be scored as follows:

=None; the event was not observed

=Mild; the event was observed, but no treatment was required or the event resolved without treatment

=Moderate; the event was treated locally or by minimally invasive means

=Severe/Serious as defined below

- life-threatening (or fatal).
- results in permanent impairment of a body function or permanent damage to a body structure; or
- necessitates medical or surgical intervention to preclude permanent impairment of body function or permanent damage to a body structure.

The Clinical Investigator/Sponsor will report all unanticipated, device deterioration events to the FDA.

Historical data have demonstrated that several types of complications are known to occur with this procedure. These complications are described in the following sections

2.2.6.1 Endoleaks

Immediately after placement of the Medtronic/Talent Endoluminal Stent-Graft, or upon later evaluation, endoleaks may be detected. Endoleaks are considered any extravasation of contrast outside of the flow channel established by the stent-graft. For purposes of this study, endoleaks that are detected and corrected during the implantation procedure are not considered a complication of the Talent device or procedure. However, uncorrected endoleaks that develop during implantation or endoleaks that develop after implantation are considered complications and must be reported on the Procedure or Post-Operative Assessment CRF. The type and possible cause of the endoleak should be noted on the CRF.

Treatment of endoleaks is at the discretion of the Clinical Investigator/Sponsor. In general, it is recommended that endoleaks be corrected during the initial procedure unless the Clinical Investigator believes that there is a likelihood that the endoleak

may spontaneously seal after a few days. The decision to intervene at later intervals will be based on the severity of the endoleak, the possible cause of the endoleak, the status of the aneurysm, and the subject's general health. Known or suspected endoleaks must be monitored carefully postoperatively with appropriate diagnostic imaging.

Attempts to correct postoperative endoleaks may be done by any of the following procedures:

- using an endovascular balloon to remodel the stent-graft near the endoleak.
- implanting an extension cuff over the endoleak; or
- surgical intervention.

Any procedure performed to correct postoperative endoleaks will be recorded on the Post-Operative Assessment CRF.

2.2.6.2. Conversion to Surgery

In some subjects there may be difficulty inserting the Medtronic/Talent System during the procedure. If it is not possible to complete implantation of the device, or if peri- or post-operative complications arise that place the subject at risk, the Clinical Investigator/Sponsor may elect to convert the patient to open surgery. Alternatively, the Clinical Investigator/Sponsor may elect not to repair the TAA, and to manage the patient with observation only. In such cases, the reason for conversion must be recorded on the Procedure CRF.

Also, as noted previously, subjects who convert to surgery or who are managed by observation will be followed in an identical manner as the other subjects. A Post-Operative Assessment CRF will be completed at 1, 6, and 12 months after the attempted implantation.

2.2.6.3 Death

Autopsies will be requested for subjects who expire following implantation of a Medtronic/Talent stent-graft. If the patient or the family consents to a post- mortem exam, the device will be explanted whenever possible for examination and histological analysis. The Clinical Investigator/Sponsor will request that the explanted device be sent to the designated facility for examination and histological analysis. The Clinical Investigator/Sponsor will determine whether or not the device (or procedure) caused or contributed to the subject's death.

2.2.6.4 Other Adverse Events

The health risks associated with use of the Medtronic/Talent Endovascular System may be less than for conventional surgical treatment. However5 as .with any medical procedure, there are some risks. There is the potential for discomfort or complications resulting from the procedure and the implanted Stent-Graft. It is hypothesized that the rate of serious adverse events in stent-graft patients will be less as compared to an expected serious adverse event rate for surgical patients.

Following is a non-exhaustive list of potential serious complications that may occur during or following implantation of a Medtronic/Ta1ent Endoluminal Stent-Graft:

- distal or proximal embolization that may lead to stroke, amputation, kidney failure, multiple organ failure, or death.

- renal insufficiency or failure, that may necessitate dialysis.

    - immediate leaking into the aneurysm, possibly leading to rupture of the aneurysm and death;

- later leaking into the aneurysm, possibly leading to rupture of the aneurysm and death.

- vessel rupture, possibly leading to shock, conversion to surgery, or death.

- migration of the device, possibly leading to rupture of the aneurysm, open surgery, or death.

- blood loss, possibly leading to shock or death.

    - gaff twisting or kinking, possibly leading to shock or death.

- infection, possibly leading to septicemia or death.

- occlusion of blood flow to the spinal cord, possibly leading to temporary or permanent paraparesis or paraplegia;

- conversion to open surgery with all the risks associated with an open surgical repair;

- myocardial infarction, arrythmia and/or congestive heart failure possibly leading to shock or death.

- respiratory failure possibly leading to death.

Similarly, there are a number of minor risks and discomforts that could result from the implant procedure or adjunctive tests/analyses. The following is a summary of those potential discomforts.

- Heart and lung testing may involve some discomfort.
- Blood collection may cause bruising and/or discomfort.
- The CT and angiography procedures may cause discomfort during scanning but should not cause pain.
- The radiopaque dyes used during CT and angiography procedures can cause nausea, vomiting, or other reactions.
- Some pain and bruising at the site may result in the groin where the device is insertero

2.2.7 Scientific Soundness and Analysis of Data

All patients will be treated using the same inclusion/exclusion criteria and are treated under the same protocol. Standard data forms will be used to collect information about all procedures and evaluations performed, to provide comprehensive documentation of the study. Each patient will be carefully monitored following treatment at specified intervals for evaluation of adverse effects and clinical effectiveness of the device.

2.3 Risk Analysis

2.3.1 Risks to the patient

Treatment with the Medtronic/Ta1ent Endoluminal Stent-Graft is an invasive procedure that poses significant risks to the patient. Patients participating in this trial as study patients will be exposed to such risks. These risks include the potential for discomf01t or complications resulting from the procedure and the implanted stent-graft as described in Section 2.2.6.4.

2.3.2 Manner in which risks will be minimized

These risks to the subject are minimized by the design of the stent-gaff, using materials with a history of vessel repair and a strong kink-resistant self-expanding, conforming spring that aids in establishing a good seal with the vessel wall. Correct sizing of the stent-graft and quick placement with little manipulation reduces the risk of adverse events such as embolization, endoleak, thrombosis, device migration, or rupture. Adequate modeling of the stent onto the vessel wall decreases the chance of leakage or migration of the device. Hemostasis valves incorporated into the delivery system help minimize blood loss. Risk of infection is minimized by quick placement with little manipulation and the use of prophylactic antibiotics. The risk of conversion to open surgery is minimized by the design of the delivery and placement system, availability of extension pieces, and the ability to move the stent-graft after placement, prior to ballooning.

2.3.3 Justification of the study

Experience with other stent-grafts and with the Medtronic/Talent Endoluminal Stent-Graft in thoracic aortic aneurysms has shown-this to be an effective method for treatment of aortic aneurysm in patients who meet the anatomic criteria.

Patients who undergo stent-graft implantation and are found to have inadequate repair of the TAA may be treated by conventional surgical repair. Implantation of the Talent Stent-Graft requires a much less extensive surgical procedure than conventional surgical TAA repair, thus the patients who are enrolled as study subjects are likely to have adequate TAA repair with less risk than that associated with the standard technique. Patients who receive the Talent Stent-Graft will be followed for life to ensure adequate TAA repair. Alterative treatment will be available to any patient in the study group who is found to have inadequate TAA repair.

2.3.4 Patient population

The patients who will be enrolled in this study will have documented descending thoracic aneurysms, dissecting aneurysms, penetrating ulcers, traumatic transections and pseudoaneurysms (traumatic or degenerative). People at risk for TAA are predominantly elderly (over 65), either male or female, of all ethnic backgrounds. The study will include high risk and low risk males and females between 18 and 90 years of age, of any race who have been diagnosed with supraceliac lesions of the descending thoracic aorta including true aneurysms, dissecting aneurysms, penetrating ulcers, traumatic transections or traumatic or degenerative pseudoaneurysms, who are considered to be good candidates for endoluminal repair of the aneurysm, and whose vascular anatomy fulfills the requirements for Medtronic/Talent Endoluminal Stent-Graft implantation.

2.4 Device Description

The Medtronic/Talent Endoluminal Stent-Graft System is composed of a flexible, implantable vascular stent-graft endoluminal device preloaded in a delivery system.

An illustration of the system may be found in Appendix D, Instructions for Use.

2.4.1 Medtronic/Talent Endoluminal Stent-Graft

The Medtronic/Talent endoluminal stent-graft system is a second-generation device designed to permit the treatment of a potentially larger number of patients by means of a reduction in the diameter of the device's introducer delivery system by on average two French sizes. This reduction is achieved by using a monofilament graft material that is thinner yet is just as strong and in some cases stronger than the first-generation graft material. The reduction in French size potentially allows for the treatment of patients with smaller diameter and more tortuous and calcified access arteries without sacrificing device strength and durability.

Like the first-generation system, the Medtronic/Ta1ent system is composed of a stent-graft end prosthetic device and a placement system. The stent graft is provided preloaded within a delivery catheter and introducer sheath. The endoprosthesis is inserted via the delivery catheter and introducer sheath through the femoral or iliac artery by surgical cutdown.

The implanted endoprosthetic portion of the stent-graft device is composed of a vascular graft sewn to a self-expanding nickel-titanium (nitinol) wire stent frame. This is the same stent-frame material that was used in the first-generation system. Similarly, the vascular graft component is a thin woven polyester which is commercially available for surgical repair of blood vessels. The first-generation system uses a polyester manufactured by Meadox and by Bard. The material used in the Talent system is a thinner (monofilament) polyester material. Polyester fabrics have been used routinely in vascular surgery for 50 years. Metallic stents are commonly used to treat peripheral vascular disease. The Medtronic/Talent Endoluminal Stent-Graft device used to repair TAAs is available in a straight configuration consisting of one or more pieces.

The Stent-Graft for thoracic implantation is a straight tubular design. Depending on the patient's aortic and aneurysm anatomy, the stent-graft may be supplied as a single section or a modular multi-section system. Additional sections, referred to as extensions, may be added as needed (e.g., if a leak resulting from incomplete exclusion of the aneurysm (endoleak) is discovered either during the implantation procedure or post procedure). Each section is introduced separately into the vasculature and mated in vivo to sections already in situ. All sections are composed of a metal stent coupled to a fabric vascular graft. The metal stent frame is made of small diameter nitinol monofilament wire with a titanium oxide coating formed into a-series of ring-like zig-zag springs connected by connecting bars. The stent is sewn with suture to the lumen of a proprietary low-permeability polyester material. This material is thinner than the Meadox and Bard graft materials used in the first-generation system, but is it is chemically-equivalent in its composition.

The Talent stent-graft system will be custom built for each patient (i.e., patient-specific).

Anatomical measurements from each patient are used to manufacture a stent-

graft. The stent-graft can vary in diameter, length, end design, and axial cross-section (cylindrical tube versus tapered tube), as required for each patient's anatomy.

Depending on physician preference and specific anatomical requirements, the proximal and distal ends of the Talent stent-graft are available with or without coverage with the polyester fabric. In the uncovered version (referred to as the bare spring design) there is an additional 1.5 cm length (nominal) spring that is uncovered and is joined to the most proximal or distal spring of the stent-graft. The bare spring design is intended to allow placement of the most proximal or distal portion of the device across involved arteries (e.g., the left subclavian artery) that originate from the aorta. The covered version is referred to as the open web design and may be used when the device is not intended for placement adjacent to a patent vessel.

Anatomical measurements from each patient are used to manufacture a Talent Stent-Graft. The stent-graft can vary in diameter, length, proximal and distal design (open web versus bare spring), and axial cross-section (cylindrical tube versus tapered tube), as required for each patient's anatomy. The diameter of the stent-graft may range from 20 to 46 mm, in 2 mm increments. The range for stent-graft length is 70 to 200 mm per section, in 10 mm increments. Due to the required 2-6 mm diameter oversizing, the diameter of the Stent-Graft will be approximately 2-6 mm larger than the diameter of the native aorta. Oversizing is required to provide for the necessary outward radial force to hold the stent-graft in place against the aortic wall.

The nitinol spring stent is collapsed for pre-loading over a polyurethane balloon delivery catheter and placed into the tip of a Teflon delivery sheath. The spring stent self-expands upon exiting the sheath to conform to the shape and size of the aorta. Platinum iridium marker bands are sewn onto the most proximal and distal portions of the stent-graft to aid in the visualization and accurate placement of the device under fluoroscopy. When multiple sections of the main device or extensions are used, the marker bands are used to aliB1 the pieces and ensure adequate overlap of the mating sections.

For those cases in which an additional length of stent-graft is needed to extend an implanted device, shorter Talent stent-graft sections (extension cuffs); either open web or bare spring desiY1s, are available. The open web version is used to seal leaks that are not closely adjacent to a patent artery, and the bare spring version is used to seal leaks when a patent artery will be crossed. Extension cuffs can be manufactured in a straight or a tapering configuration.

The diameter of an extension cuff can range from 20 nun to 46 mm, in 2 mm increments. The range for cuff lengths is 70 to 200 mm per section, in 10 mm increments. Depending on the diameter of the target vessel, the extension cuffs are oversized by the same 2-6 mm as the main aortic sections.

2.4.2 Medtronic/Talent Placement System

The systems intended for use in this study will have the improved Talent delivery system. Like all Talent systems, the delivery system is composed of a catheter and an introducer sheath. A pushrod with a distal plunger is included with the delivery catheter to allow deployment of the stent-gaff from the introducer. The delivery catheter is equipped with a central balloon, which is used after stent-graft deployment to model the stent-graft against the vessel wall and to remove any wrinklesin the graft material. The Talent system also features several improvements over previous delivery systems: a flexible tapered tip, a coil within the introducer to permit smoother navigation through vasculature, a stainless steel bullet to reduce sheath kinking, a radiopaque sheath marker to improve visualization of the sheath, and a reinforced pushrod with ergonomic luer handle for improved handling and control.

2.4.3 Stent-Graft System

The complete Medtronic/Talent Endoluminal stent-graft system is composed of the vascular spring stent-graft and the placement system. During manufacture, the stent-graft device is collapsed over the delivery catheter and preloaded into the delivery introducer sheath. The spring stent self-expands upon deployment

from the sheath and conforms to the shape and size of the blood vessel. The stent may be balloon-modeled against the aortic vessel wall.

2.5 Monitoring Procedures

2.5.1 Procedure for Monitoring

A designated study monitor will periodically inspect relevant study records to ensure that the study is being conducted in accordance with FDA regulations, the signed Investigator Agreement, and the approved investigational plan.

2.5.2 Name and Address of Monitor

The monitor for the study will be Mary Ann Abeline LoBue, RN, CCRN, MA, Department of Vascular Surgery, Box 11, Harbor UCLA Medical Center, 1000 W. Carson Street, Torrance, CA 90502.

2.6 Bibliography

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clinical results with the Aneurx device. Journal of Vascular Surgery, 33 (5): 927-934.

3. Manufacturing Information

Please refer to the letter from Medtronic, Inc. dated December 19, 2001 (Attachment A) granting the investigator permission to reference Medtronic's IDE # G980116 for information on manufacturing, processing, packing, storage, and installation of the Medtronic/Talent Endoluminal Stent-Graft.

4. Investigator Information

Please refer to Attachment G for a sample Investigator agreement and the Investigators' curriculum vitae. The investigators are not involved in an investigation or other research that was terminated. The investigators are committed to conduct the investigation in accordance with the agreement, the investigational plan, Part 812, and other applicable FDA regulations, and the conditions of approval imposed by the reviewing IRB and FDA. They are also committed to supervise the testing of the device involving human subjects and in ensuring that the requirements for obtaining the informed consent are met.

All the participating investigators have signed the agreement and no investigator will be added until the agreement is signed.

4.1 Name and address of investigators:

Rodney A. White, MD

Professor of Surgery

Chief, Vascular Surgery

Harbor-UCLA Medical Center Box 11

1000 West Carson Street

Torrance, CA 90509

Carlos E. Donayre,MD

Associate Professor of Surgery

Harbor-UCLA Medical Center Box 11

1000 West Carson Street

Torrance, CA 90509

Irwin Walot,MD

Chief, Vascular/Interventional Radiology

Harbor-UCLA Medical Center Box 27

!000 West Carson Street

Torrance, CA 9050

5. IRB Information

Harbor-UCLA Medical Center Research and Education Institute has 2 IRBs:

1. John F. Wolf Human Subjects Committee (1)

Jeffrey Phillips, MD, IRB Chair

Harbor-UCLA Research and Education Institute

1124 West Carson Street

Torrance, CA 90502

2. Human Subjects Committee (2)

Jeffrey Phillips, MD, Chair

Harbor-UCLA Research and Education Institute

1124 West Carson Street

Torrance, CA 90502

1 (one) committee will review and approve the investigation.

6. Sales Information

The devices will be sold at $ 1661.66 according to the agreement with Medtronic/World to cover the cost of production of the devices.

The sale of devices does not constitute commercialization because it only covers the cost of device production.

7. Labeling

Please refer to the December 19, 2001, letter from Medtronic, Inc. (Attachment A) granting the investigator permission to reference Medtronic's DE # G980116 for all labeling information. Labeling shall contain the statement "CAUTION — Investigational Device. Limited by Federal (or United States) Law to Investigational Use."

8. Informed Consent Materials

Please refer to Attachment G for a sample of the informed consents.